

# Journal of Scientific & Industrial Research

A — General



## IN THIS ISSUE

### A: GENERAL

Measuring with the electron

Chemotherapeutic search for amoebicides

Indigenous drugs used in the treatment of diabetes

### B: PHYSICAL SCIENCES

Radioactivity of sea-floor sediments

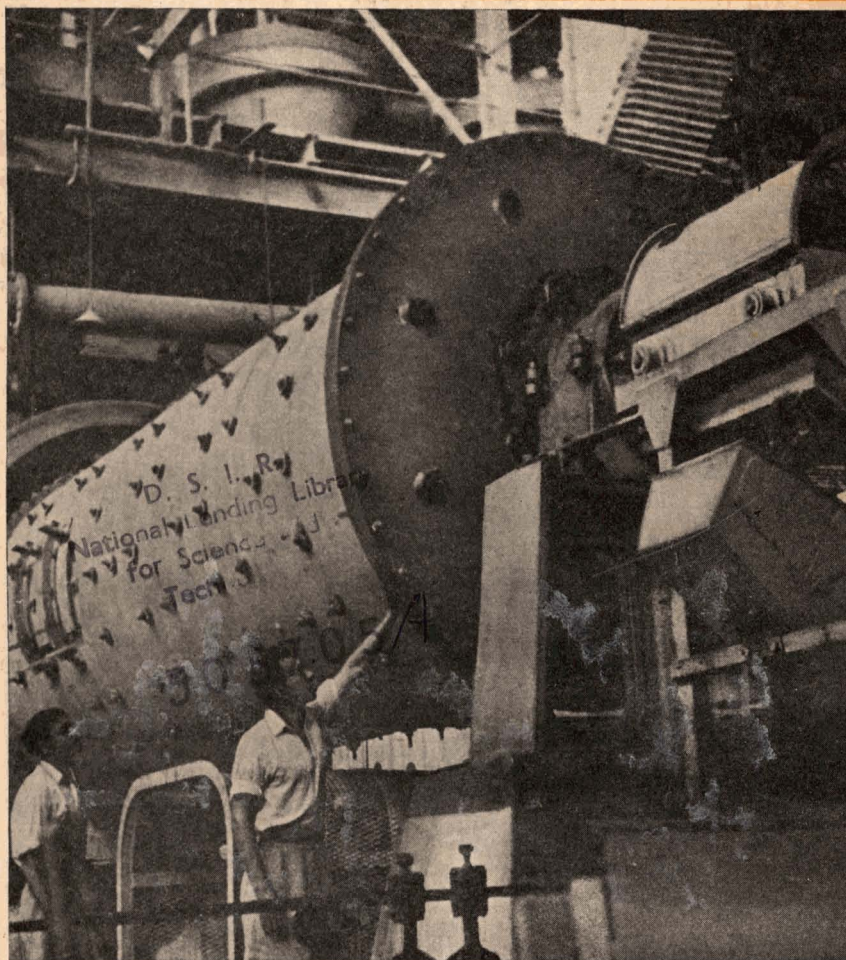
Contour generator for X-ray crystal structure analysis

Combustion of pulverized coal

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Isolation of L-arginine hydrochloride

Effect of processing on the trypsin inhibitor in jack fruit seed



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J. sci. industr. Res., Vol. 16A, No. 10, Pp. 429-476

OCTOBER 1957

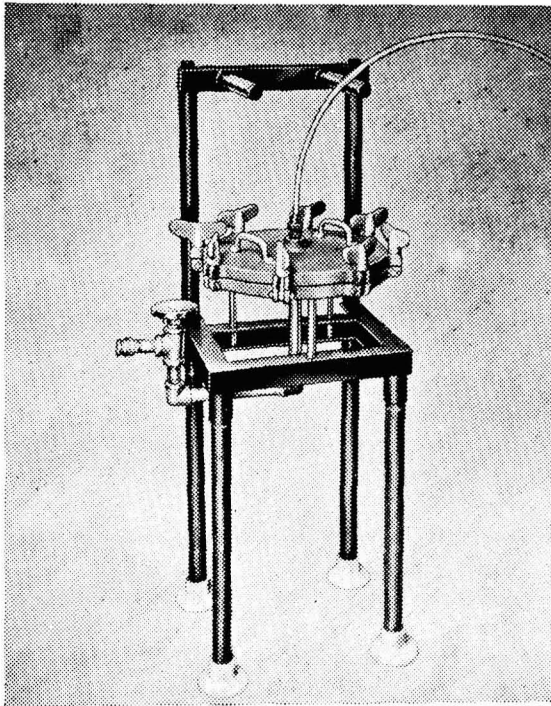
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A view of one of the tube mills for crushing ores in the gold  
mines in the Mysore Kolar Goldfields. The mills employ  
large special quality steel balls, 'pebbles', which roll inside  
the tube and crush the ore material.

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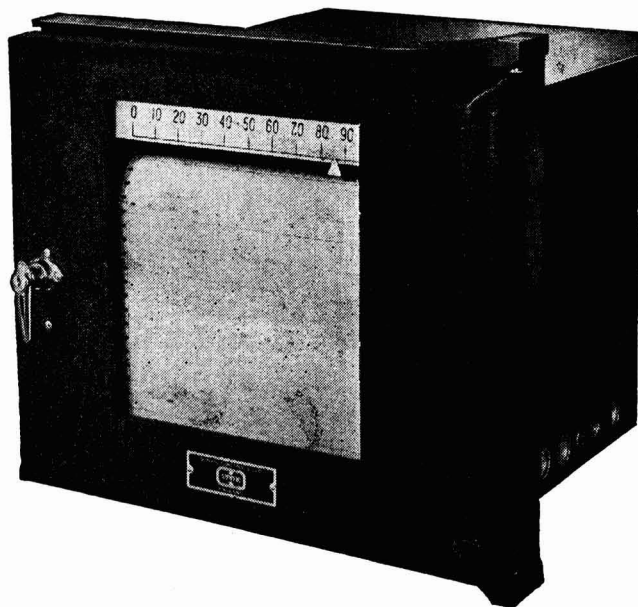
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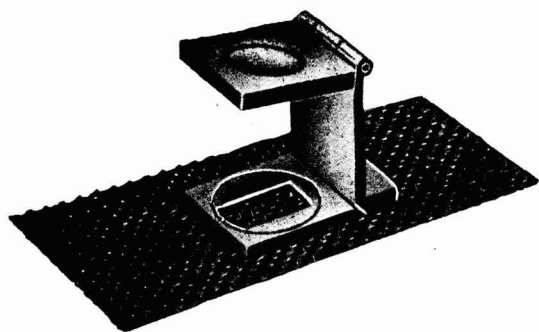
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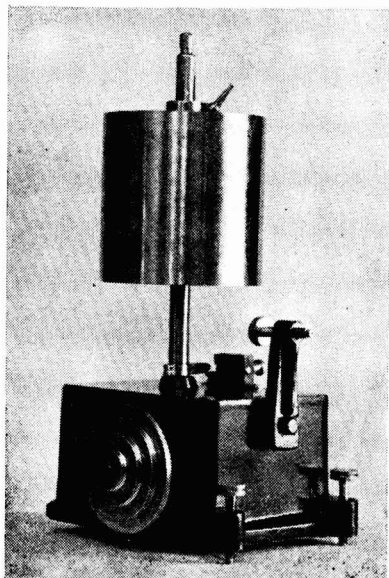
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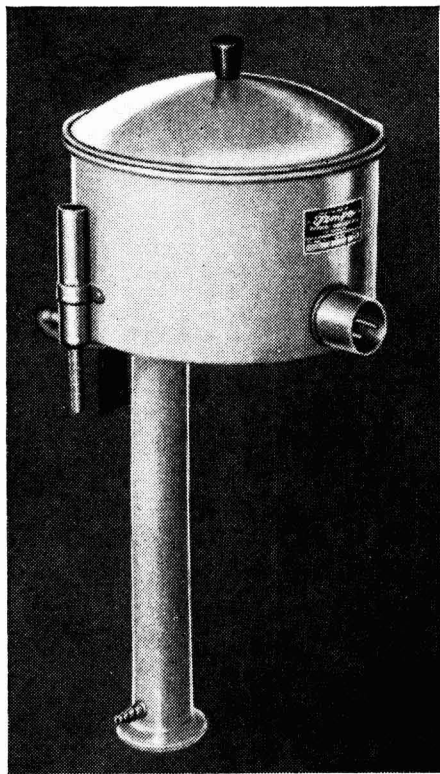
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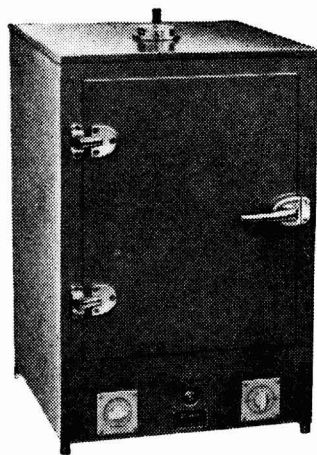
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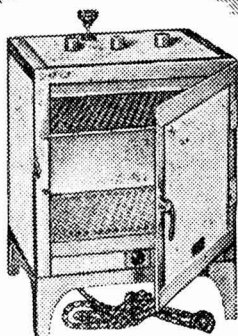


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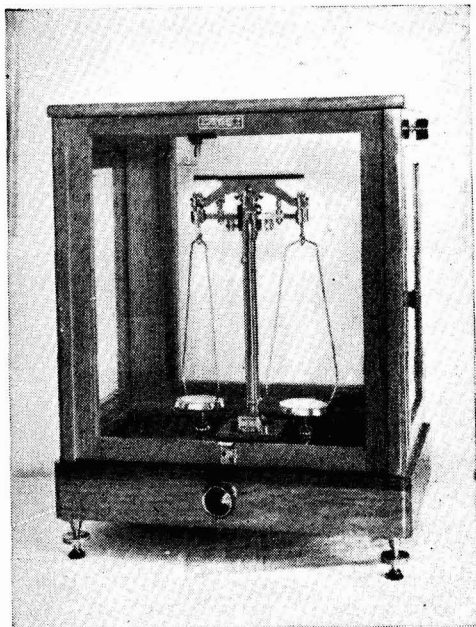
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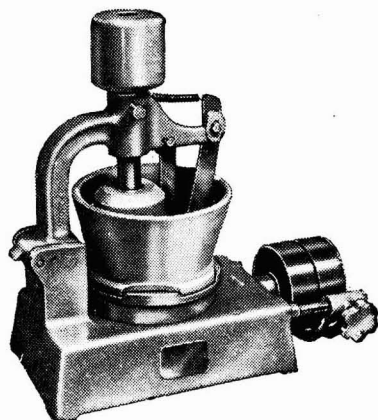
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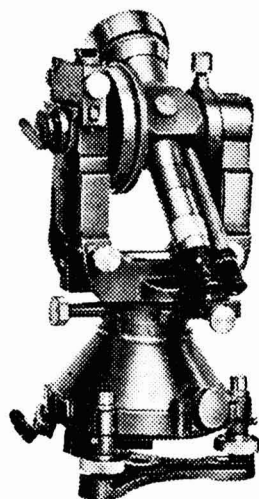
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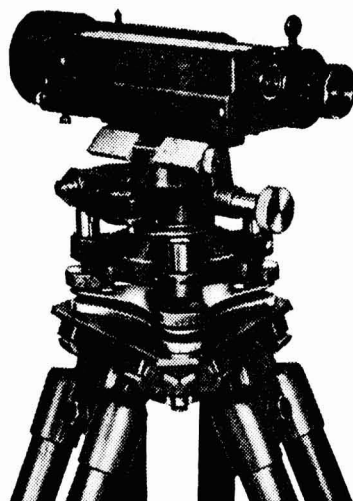
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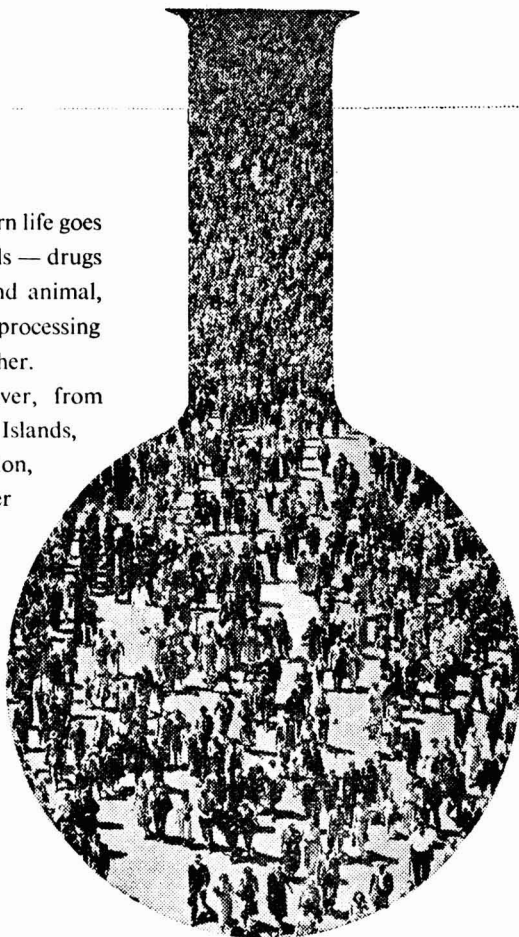


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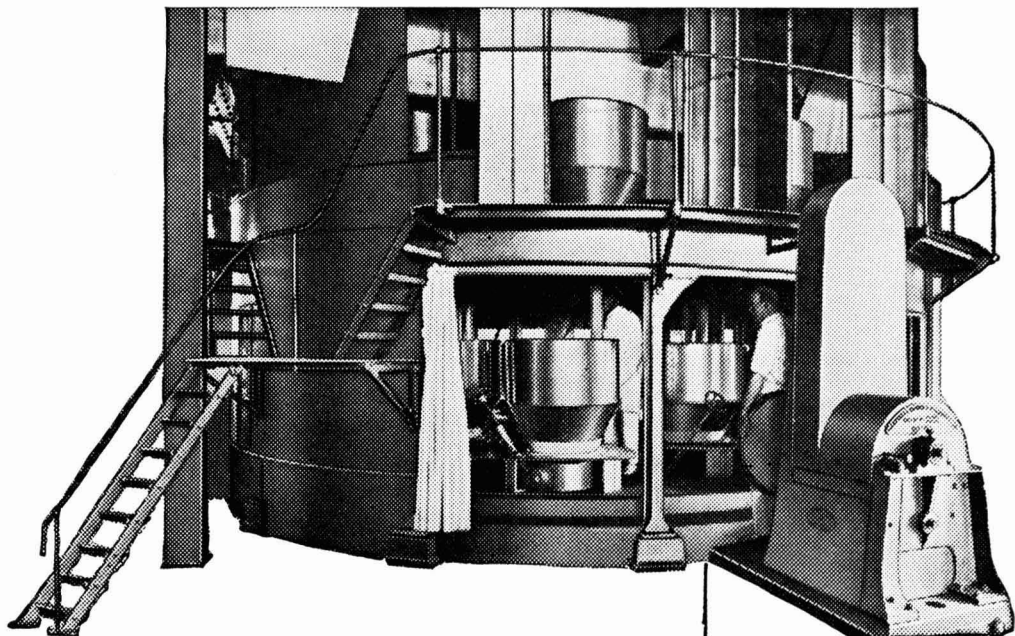
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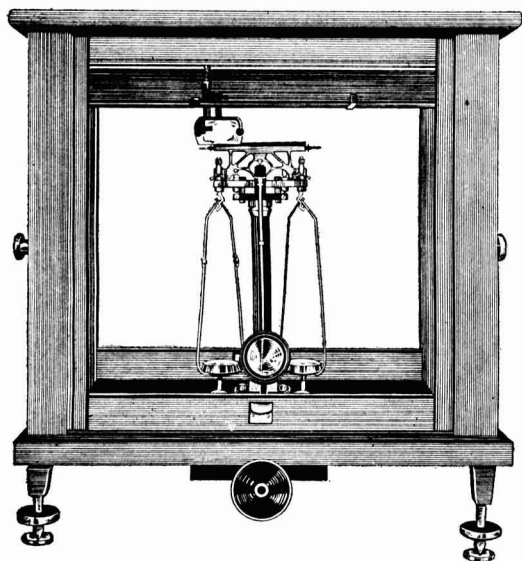
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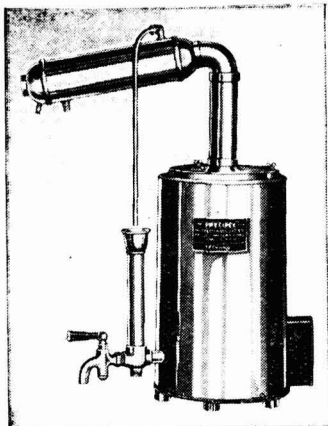
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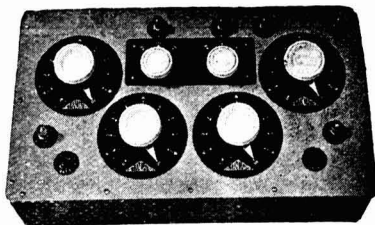
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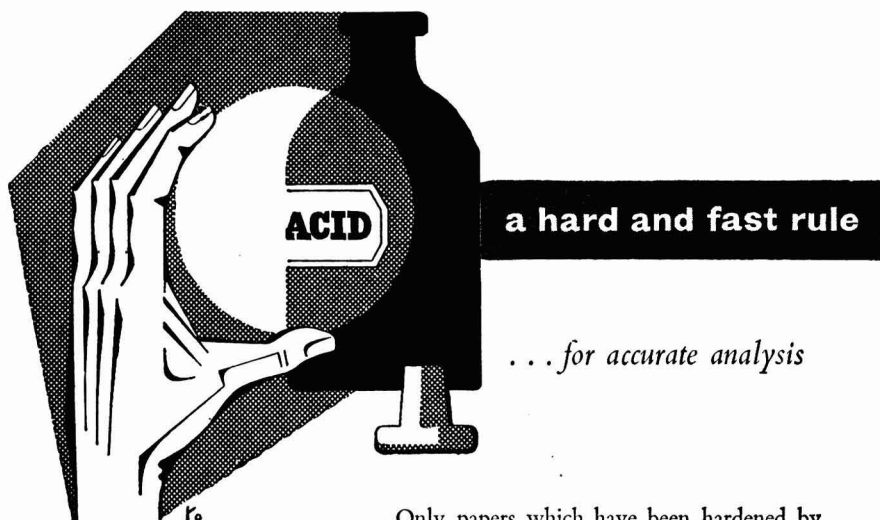
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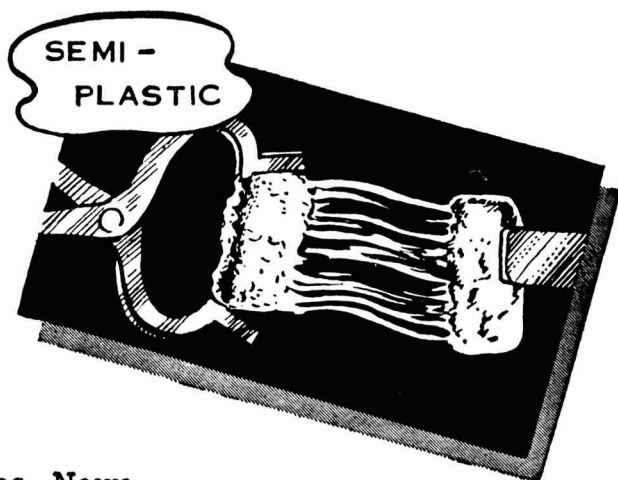
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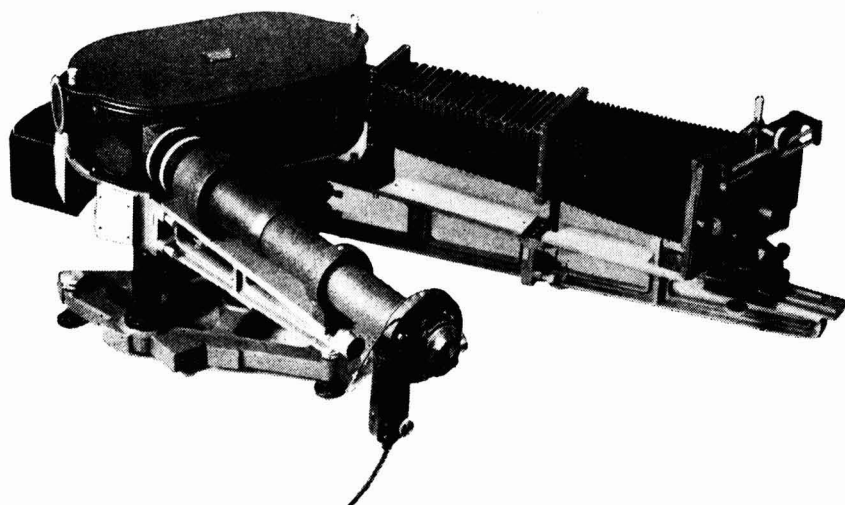


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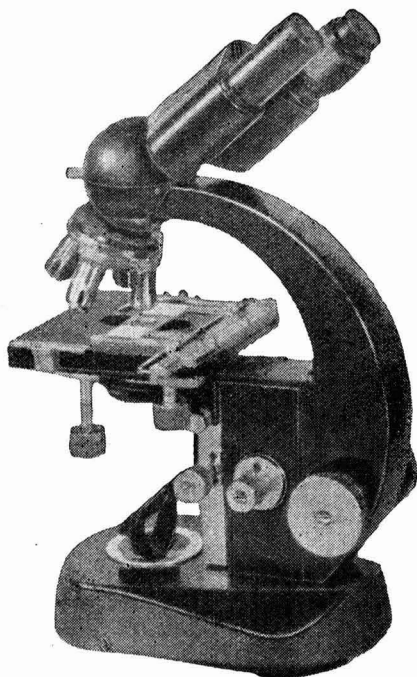


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## Measuring with the Electron\*

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THERE are a number of properties of the electron like the charge, mass, etc., which can be used as yardsticks for measuring purposes. Generally these properties are not the most practical for measuring purposes. The property of interaction with matter and with fields of force, similar to the interactions of light, makes the electron an excellent medium for conveying information in a measuring process.

In optical systems, be it with light or with electrons, the limit of observation is set by the wavelength of the radiation. Applying the usual relation of Abbe

$$d = \frac{\lambda}{n \sin \alpha}$$

it is seen that the smallest resolved distance,  $d$ , is proportional to the wavelength,  $\lambda$ , divided by the numerical aperture of the system. While light optical systems can operate with very large numerical apertures, order of magnitude of one, electron microscopes are restricted to numerical apertures of about 0.001 which gives a resolution of 5Å. Efforts were directed in the last 10-15 years towards increasing the numerical aperture by reducing the lens aberrations, but with no great success, as the spherical aberration is the main limiting factor. It can be shown easily that resolution is a function of the fourth root of the aberration constant. This calls for considerable reduction of the lens aberration to achieve a significant change in resolving power.

For attaining the desired reduction of lens aberration Gabor proposed a two-step process of microscopy, called microscopy by reconstructed wavefronts. A diffraction pattern of an object, in principle, contains significant information about the shape of the object,

but the extraction of all this information is difficult. Gabor has shown that, in principle, it is possible to do such a reconstruction. Because the diffraction pattern is a product of the interference between the diffracted wave and the coherent background, by recording a diffraction pattern on a photographic plate and illuminating it from a suitably placed coherent source of light, a lens can reconstruct the image of the object which produced the pattern in the first place. Efforts were made in England by Haine and collaborators about five years ago to reproduce the same process with electrons, but were abandoned due to the difficulties involved in the process. The field emission microscope does not attempt to form an image by optical means, but does so by projecting a very enlarged pattern reproducing some property of the object. The principle is briefly illustrated as follows. If to a spherical surface a sufficiently high electric field can be applied to produce cold emission of electrons, electrons will be emitted from a point very close to the centre of curvature of that surface. By etching the tip of a tungsten wire, the tip becomes a paraboloid of rotation and the emission from it satisfies the necessary conditions closely. By applying a potential to a ring-shaped electrode at a certain distance from the wire tip, a pattern similar to the one shown in Fig. 1 is obtained on the fluorescent screen. This pattern contains information about the disposition of atoms on the wire tip and can, therefore, be of great help in studying surface layers. A modification of this type of microscope, operating with ions instead of electrons, succeeded in pushing the limits of resolution down to atomic dimensions. There is enough evidence now available that specially located

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\*Lecture delivered by Dr. L. Marton, National Bureau of Standards, Washington, at the Forty-fourth Session of the Indian Science Congress, Calcutta, on 17 January 1957.

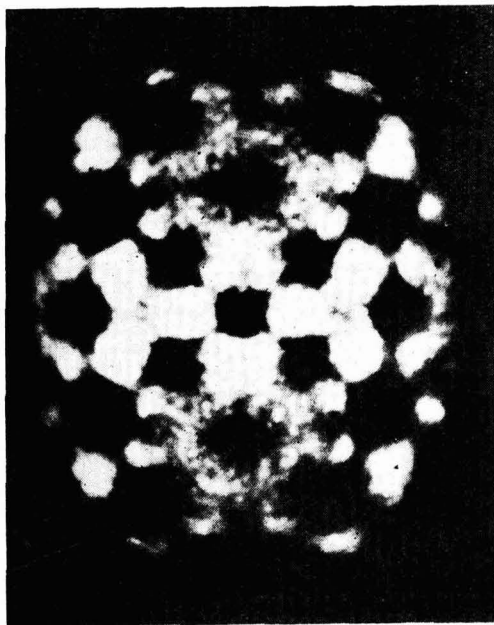


FIG. 1 — EMISSION PATTERN FROM A TUNGSTEN POINT (courtesy: E. W. Muller)

single atoms on a surface can be seen by means of such an instrument.

Another way of measuring atomic dimensions is by using electron diffraction techniques. Electron diffraction, due to the very short wavelength, gives the same type of information about lattice structures as X-ray diffraction does. It is, however, distinguished by its penetration being much shorter than that of X-rays, and hence the information is mostly restricted to surface layers. This may appear at first sight as a disadvantage; however, it can be turned to an advantage. Electron diffraction, thus, may be useful for the study of surface layers and their constitution, their crystalline structure, etc., where the X-ray diffraction can give practically no information. Furthermore, if sufficiently thin layers or sufficiently fine powders are used in transmission, electron diffraction can give the same type and volume of information as X-ray diffraction does, and may even provide more information about internal potentials than X-ray diffraction can. In modern electron microscopes means are provided for a combination of electron diffraction observation with electron microscope image forma-

tion. Selected areas of a specimen can be examined under electron diffraction condition and thus the crystalline structure of very small crystals can be investigated.

The measuring range can be extended by taking advantage of the property of electrons of interacting with fields of force and a geometrical optics of the electron similar to that of light in which the refractive medium is replaced by an electric or magnetic field can be developed. Consequently, not only are we able to use this property for image formation in the ordinary sense but it can also be employed for a study of the variations of an index of refraction in a manner similar to that of the 'schlieren' optics of light. If a parallel beam of light is sent through a lens and a suitable stop is placed at the focal point of this lens, in the absence of any change in refractive medium, all light will be intercepted by that stop. If, however, in a plane close to the lens there is a change in refractive medium, the rays will be deflected in such a manner that a dark field image of that refractive medium will appear in a conjugate plane of the lens. Such an experiment can easily be translated into electron optics by replacing a beam of light by a beam of electrons, a glass lens by an electron lens

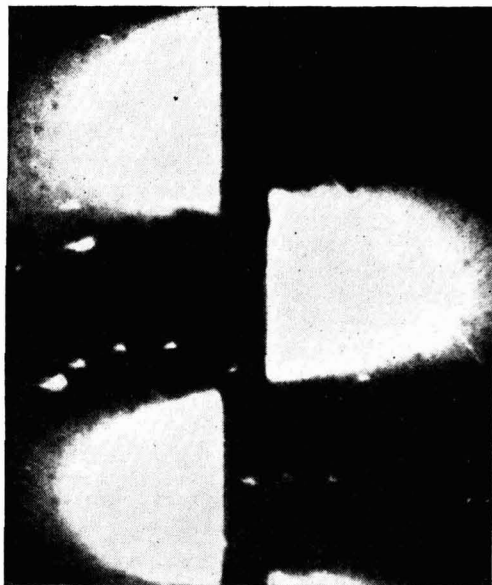


FIG. 2 — SCHLIERIEN PATTERN OF FIELD ABOUT A MAGNETIZED WIRE



and the refractive medium by an electric or magnetic field. Fig. 2 shows the kind of results obtained by using a sample of a magnetized steel wire normally used for sound recording purposes. The wire is represented by the dark horizontal stripe across the middle of the image and the alternating fields are shown as the light areas above and below the wire. Fig. 3 shows a somewhat different visualization of the same fields by means of the well-known technique of iron filings.

Such a 'schlieren' image gives interesting information about the location and extent of small fields. If, however, a quantitative measure of the field strength is required, the 'schlieren' method is not very suitable. The main difficulty lies in the fact that the

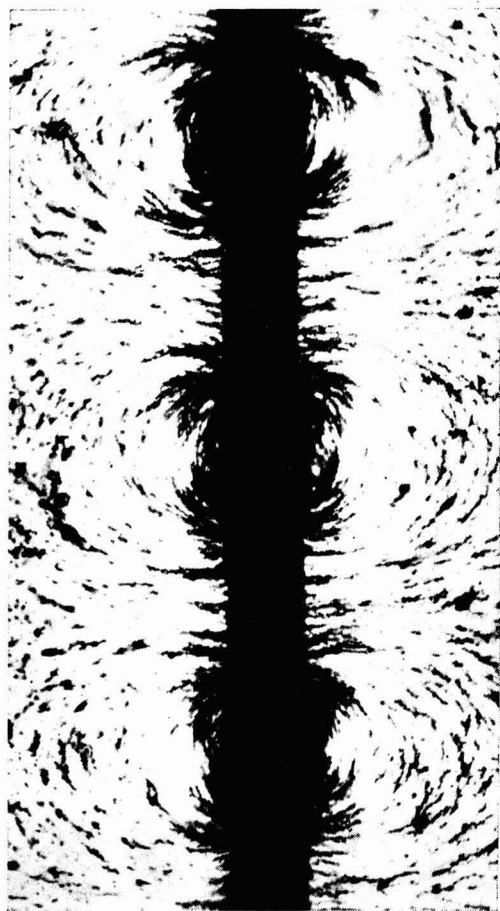


FIG. 3 — SAME MAGNETIC FIELD AS IN FIG. 2, SHOWN BY THE 'IRON FILINGS' TECHNIQUE

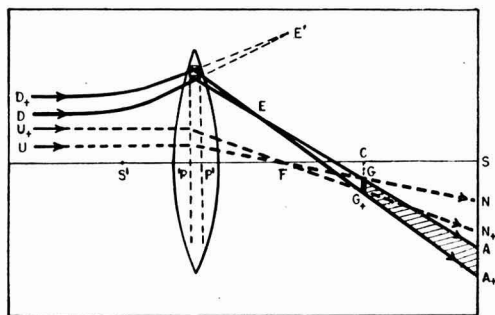


FIG. 4 — ELECTRON - OPTICAL DIAGRAM — SHADOW METHOD

intensity at each point is a function of the angle of deflection of the electron at different points of the field. If the field from intensity measurements on such a pattern had to be deduced all the difficulties inherent in light optics will be encountered, for intensity measurements are generally unreliable. Hence, it was found advantageous to modify the method. These modifications are illustrated in Fig. 4. In the modified version instead of placing a stop in the focal plane of the lens, a small obstacle is placed at a short distance behind the focal plane. In the absence of a change of refractive medium the focal point, acting as a virtual source of electrons, produces a magnified shadow of that obstacle in the image plane. The strictly parallel beam may be replaced by an approximately parallel one due to the source being at a great distance. In that case the magnified shadow is produced by the reduced image of the source acting as a virtual source. In the presence of a field in a plane conjugate to the image plane, the deflection of the rays will produce a displacement of the virtual source. If that field is a homogeneous one the displacement will be both lateral and axial. In both cases the shadow of the obstacle will be displaced and in the latter case the displacement will also be accompanied by a change of magnification. If, instead of a single obstacle, a periodic array of obstacles are placed, such as a wire mesh, the resulting shadow will give an indication of the beam deflection over the whole field. Fig. 5 shows the same recording wire with its magnetic field represented by the distorted shadows of the wire mesh. A schematic representation of this process is shown in Fig. 6. The top part shows the formation

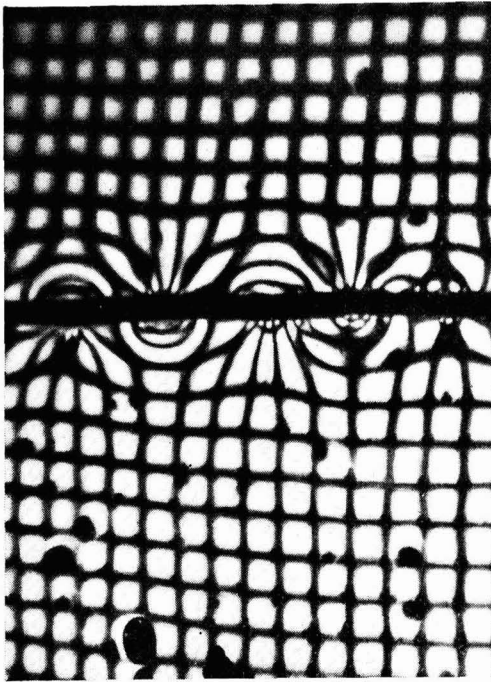


FIG. 5 — ELECTRON-OPTICAL SHADOW IMAGE OF SAME WIRE USED IN FIG. 2

of the shadow in the absence of any field, while the bottom part of the figure shows how the virtual source is 'washed out' in the presence of an inhomogeneous field with a resulting distorted shadow.

The importance of this method lies in its application to the mapping of electrostatic or magnetic fields which are inaccessible to exploration by other means. Such an inaccessibility may be due to either of the following causes. (1) The physical dimensions of the field to be explored are small compared with the size of the usual probes of conventional field mapping. (2) The dimensions may be commensurate with the size of conventional probes, but the probe interacts with the field in such a manner that the field distribution to be measured is perturbed or altered.

A relevant example of the first kind of application is the mapping of the fringe fields of a single ferromagnetic domain. Fig. 7 shows the surface of a cobalt crystal, where the domain boundaries were made visible by means of a ferromagnetic colloid. While

the domains themselves are reasonably large the domain walls are only a few hundred angstrom units thick. The field due to the domain is confined to a small space and it is difficult to make a conventional probe small enough for its quantitative exploration. In using the electron optical field mapping method, the crystal, shown schematically in Fig. 8, was mounted such that an electron beam could be shot at right angles to one of its edges. A series of several shadowgraphs has been taken at different orientations of the crystal. A typical shadowgraph of this kind is shown in Fig. 9. Several shadowgraphs at different orientations are taken because the fields emerging from the domain boundaries have only one plane of symmetry and possess no other property of symmetry. To describe such a field at least three measuring parameters are required, whereas a single shadowgraph contains only two — a lateral displacement of the shadow and the change of magnification. To obtain a third measuring parameter, variation of orientation of the field may be attempted.

In principle, the information contained in a single shadowgraph is the angle of deflection of the electron beam passing through a given field as a function of position in the field.

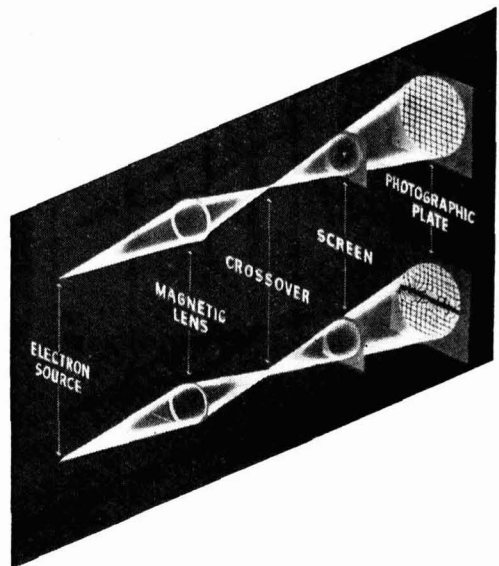


FIG. 6 — SCHEMATIC REPRESENTATION OF THE ELECTRON-OPTICAL SHADOW METHOD

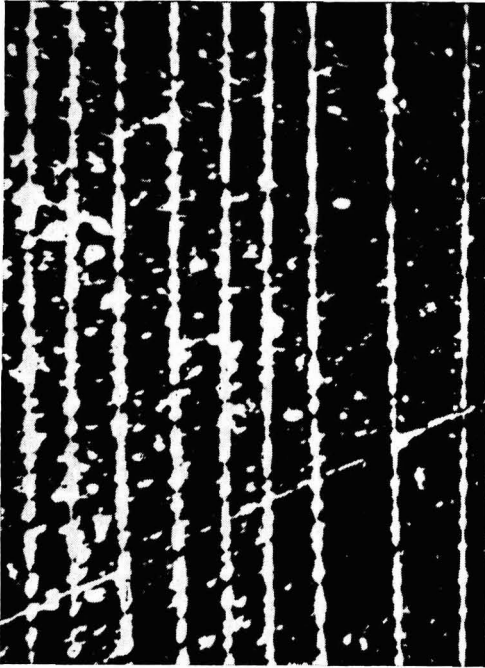


FIG. 7 — SURFACE OF A COBALT CRYSTAL SHOWING DOMAIN BOUNDARIES BY MEANS OF A FERROMAGNETIC COLLOID (courtesy: Bell Telephone Laboratories)

This deflection is proportional to the line integral of the field along the trajectory:

$$a = K \int H dx$$

From this line integral the field through which the electron passes is to be deduced. A number of points arise in this connection. (i) Does a shadowgraph give an accurate representation of line integral through the object field? (ii) Can  $K$  be determined *precisely* from the instrumental constants? (iii) Is it possible to synthesize the field from the curves of  $\int H dx$ ? Some of these questions cannot be answered straight. Optical aberrations of the system may sometimes distort the representation and difficulties can be encountered in deducing the line integral. The instrumental constants may not be easy to determine with sufficient accuracy, but if these two problems are solved with reasonable accuracy then one of the following two ways suggests itself for proceeding further. In one way, the analytical form of the field can be assumed to be known *a priori*, in which case

there exist three subgroups: (a) assuming that the field is a simple continuous function involving two parameters; (b) that the field can be expressed as a series; and (c) that a field plane can be divided into regions and the field assumes a step function constant in each region. The other possibility is that the unknown field can be obtained by a direct mathematical operation on an experimental function such as, for instance, the inversion of a linear integral operator in function space.

An example of how some of the principles outlined can be carried out is the mapping of fringe fields of the cobalt crystal (shown in Fig. 9). A further assumption has to be made that all mathematical operations are first order operations and all higher order terms are negligible. The space off the crystal edge, or more precisely, a plane at right angles to the crystal edge, is divided into a number of squares as shown in Fig. 10. If

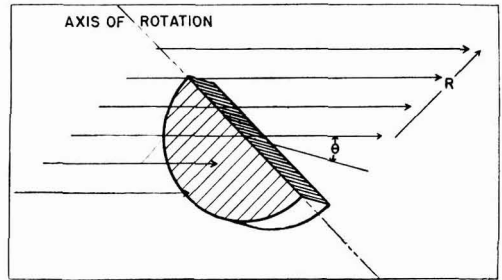


FIG. 8 — SCHEMATIC DIAGRAM OF CRYSTAL POSITION IN ELECTRON-OPTICAL FIELD MAPPING METHOD

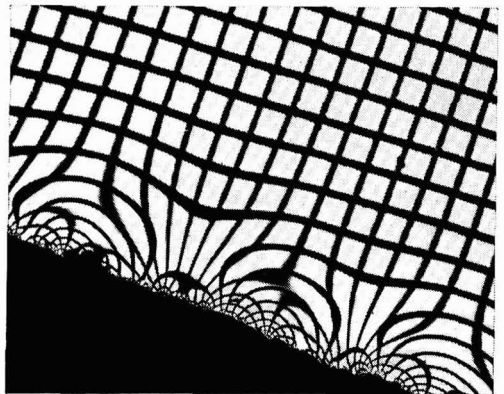


FIG. 9 — SHADOW PATTERN OF THE MAGNETIC FIELD AT THE EDGE OF A COBALT CRYSTAL

it is assumed that the field can be represented by a step function, a start can be made by assuming that the field is constant within each square and that the field is zero outside the area shown in Fig. 10. In this case the outermost square will be the one through which an electron can go with the least deflection. From the measured amount of deflection and other instrumental constants that square can be assigned a given field value. Next, a ray which passes through two squares including the one to which a field value has already been assigned is considered. The deflection thus has to be proportional to the combined effects of the two squares and, therefore, the field of the second square can be

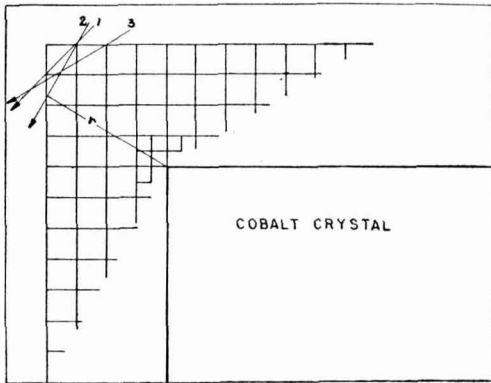


FIG. 10 — METHOD OF CALCULATING THE MAGNETIC FIELD STRENGTH AROUND A COBALT CRYSTAL

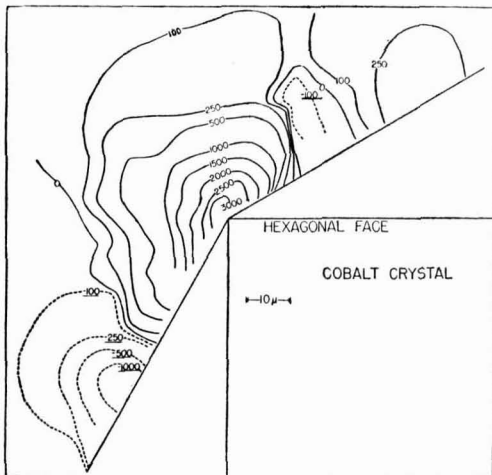


FIG. 11 — CALCULATED FRINGE FIELD PATTERN OF A COBALT CRYSTAL

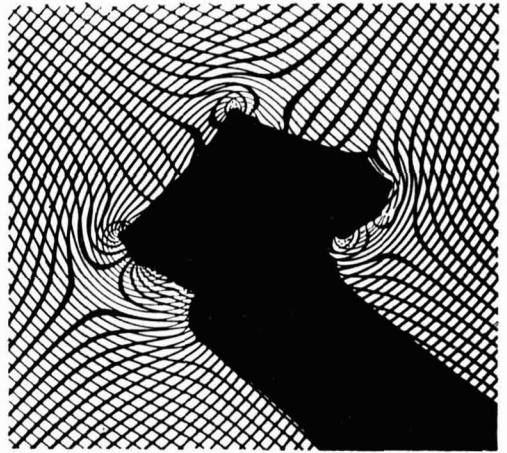


FIG. 12 — ELECTRIC FIELD ABOUT A CHARGED BARIUM TITANATE CRYSTAL AS SHOWN BY THE ELECTRON-OPTICAL SHADOW METHOD

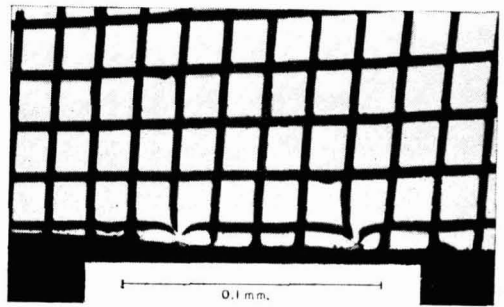


FIG. 13 — ELECTRON-OPTICAL SHADOWGRAPH OF FERROELECTRIC DOMAINS ON THE EDGE OF A BARIUM TITANATE CRYSTAL

calculated. In this manner, progressing from square to square, the field can be calculated by successive approximation. The result of such a procedure is shown in Fig. 11.

The accuracy of the method may not exceed  $\pm 50$  per cent and in the absence of any other method giving even this approximation, the method is a useful tool.

Fig. 12 shows the field distribution around a barium titanate crystal, in which the fields of ferroelectric domains are explored; it is noticed that the field is not due to domain fields, but due to charges accumulating on the surface of the crystal. Elimination of these charges finally made the domain fields manifest which are much weaker as seen in Fig. 13.

Another interesting application is the change with temperature of the fringe fields of the cobalt crystal (Fig. 14). The disappearance of the field which is visible around 400°C. is not due to a change at the Curie point but to a change in the magnetic anisotropy of the crystal.

An example of the application of this field mapping method to fields where conventional probes interact with the field is the investi-

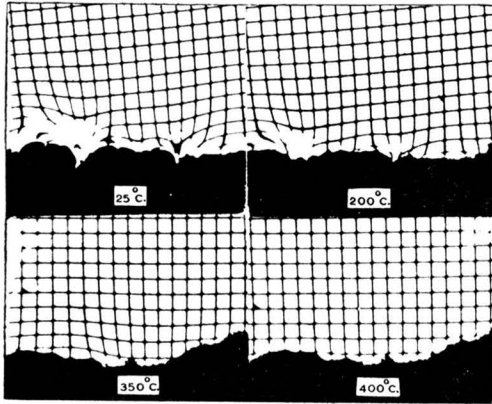


FIG. 14 — EFFECT OF TEMPERATURE ON THE FRINGE FIELDS OF A COBALT CRYSTAL

gation of space-charge distribution. For a demonstration of the procedure in such measurements the space charge distribution in a d.c. cut-off magnetron has been investigated. An electron beam is shot through the magnetron parallel to its axis and two wire meshes are placed, one in front of the magnetron and the other behind the back focal plane of the lens. Shadowgraphs (Fig. 15A, B) in the absence of space charge and in the presence of space charge are taken. From the relative displacement of the shadows the space charge density can be deduced. Preliminary values obtained are shown in Fig. 16. There is a marked disagreement with the theoretically expected distribution.

The usefulness of this method is not restricted to macroscopic fields, but can be applicable down to atomic fields even. Deflection of the electron by these powerful, but very small, fields is commonly called scattering, and scattering phenomena in combination with the 'schlieren' optics can be a powerful tool for producing special kinds of images. Fig. 17 shows a dark field image of a cadmium atomic beam. On one side of this image can be seen the dark shadow of the slit jaws through which an atomic beam issues, and outside the slit region the propagation of a well-collimated beam can be seen.

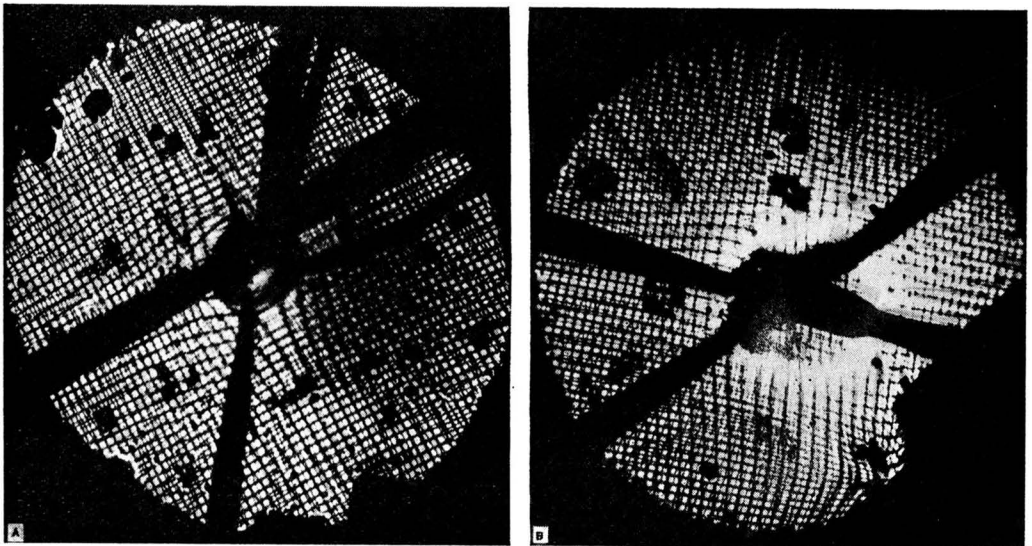


FIG. 15 — SHADOWGRAPHS OF THE D.C. CUT-OFF MAGNETRON (A) IN THE ABSENCE OF SPACE CHARGE AND (B) IN THE PRESENCE OF SPACE CHARGE



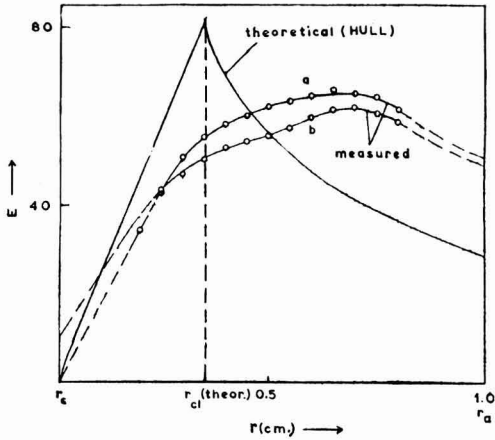


FIG. 16 — RADIAL FIELD DISTRIBUTION IN MAGNETRON EXPERIMENT (A) AND (B) AND THE THEORETICAL FIELD CURVE

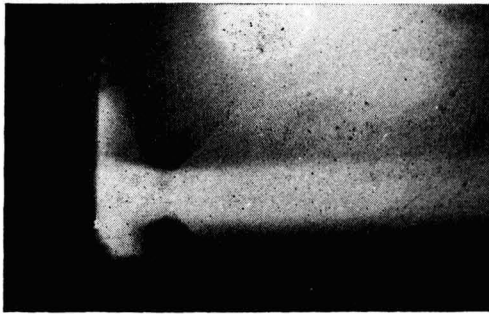


FIG. 17 — DARK FIELD IMAGE OF A CADMIUM ATOMIC BEAM

Studies of this kind afford powerful means for the observation of accommodation coefficients, and, at present, work is under way to transform this method into a direct determination of the velocity distribution of the individual atoms.

A field gradient corresponds to the variation of the light optical index of refraction, and consequently leads to the possibility of an electron interferometer for measuring variation of the electromagnetic index of refraction. A few years ago the present author suggested that there may exist means to imitate the wide beam interferometer of light optics, such as the Michelson type. Such an interferometer requires the use of an efficient beam splitter. True reflection is non-existent in electron optics and for that

reason semi-transparent mirrors cannot be made. Electron diffraction, however, offers a suitable means for splitting an electron beam into several coherent components and an electron interferometer may be built up using this principle.

Several lamellar crystals are needed as indicated in Fig. 18. Let an incident parallel beam of electrons passing through a thin crystal in the manner indicated be considered. Part of the beam is transmitted and part of it is diffracted. At a certain distance a second crystal is placed. Part

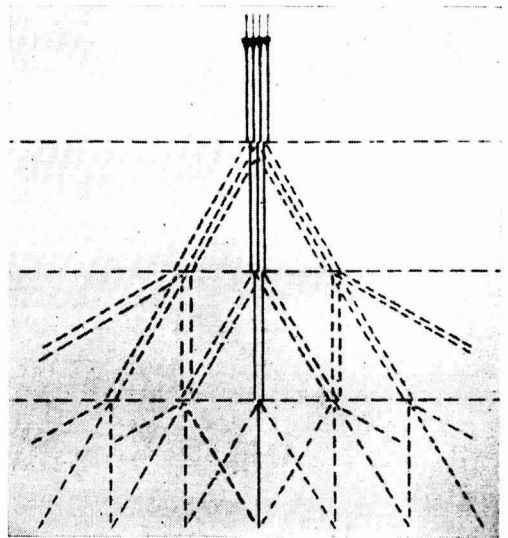


FIG. 18 — SCHEMATIC REPRESENTATION OF ELECTRON RAYS PASSING THROUGH THREE CRYSTALS OF AN ELECTRON INTERFEROMETER

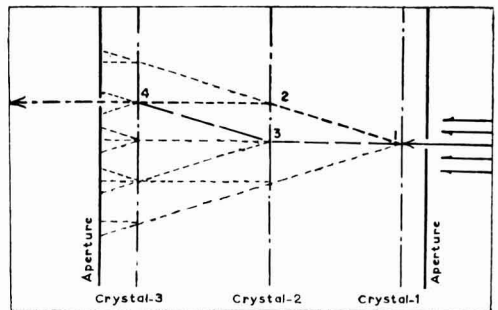


FIG. 19 — ELECTRON RAYS AS LIMITED BY APERTURES OF AN ELECTRON INTERFEROMETER



of the original beam is again transmitted and part of it is diffracted. The same applies to the beams diffracted on the first crystal. The same phenomenon is repeated again on a third crystal placed at an equal distance. By placing convenient limiting apertures two diffracted beams can be selected out of the multitude of beams and have a total path as indicated in Fig. 19. The resulting trajectories correspond roughly to the equivalent of the Mach-Zehnder type interferometer. A field gradient across the two paths will produce a path difference

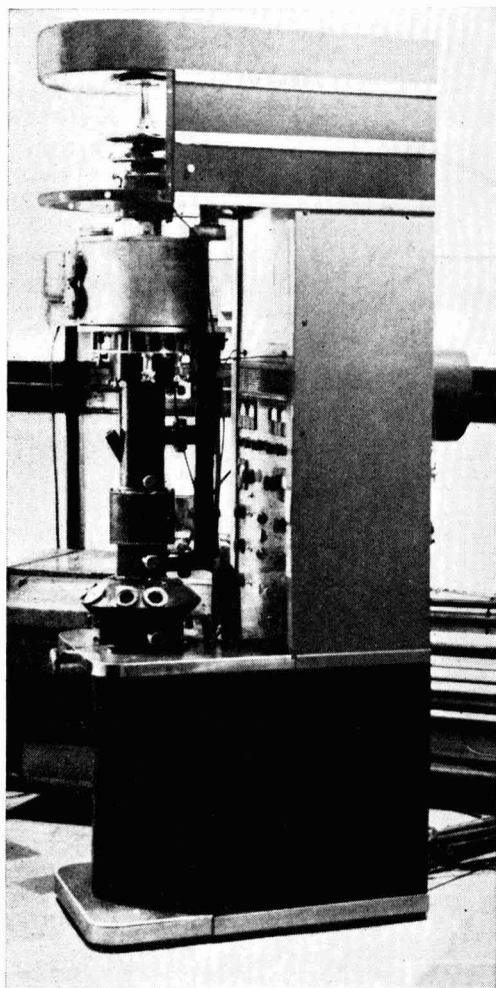


FIG. 20 — ELECTRON INTERFEROMETER REPLACING THE OBJECT CHAMBER OF A CONVENTIONAL ELECTRON MICROSCOPE

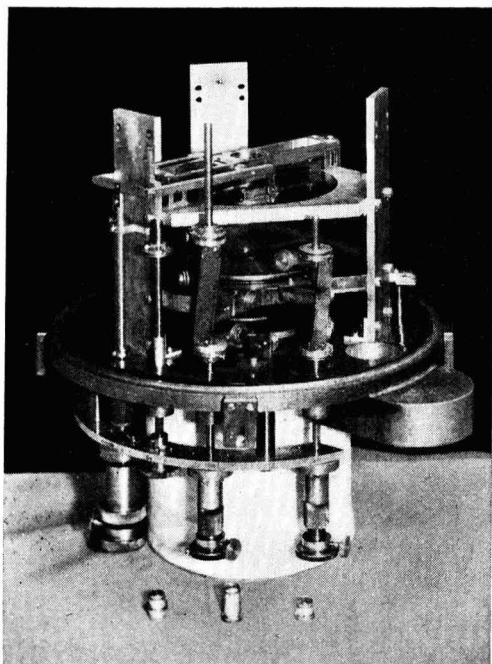


FIG. 21 — INTERNAL CONSTRUCTION OF THE INTERFEROMETER

which can be observed by means of the shifting of the fringes.

Fig. 20 shows the external appearance of the interferometer which replaces the object chamber of a conventional electron microscope. The inside appearance of the interferometer is shown in Fig. 21. It has been shown that the behaviour of the instrument, and the variation of fringe spacing and fringe alignment, could be predicted on the basis of a relatively simple wave optical theory. The same theory shows that fringes were obtained with path differences exceeding those derived from earlier observations. In fact, observed fringes can be calculated to correspond to 6000 wavelengths path difference as compared to the earlier observed 200 wavelengths path difference. This first instrument, however, gave fringes rather low in intensity, and modifications in the optical design have been attempted. A modification is shown in Fig. 22. One of the beam splitting crystals is eliminated, retaining only two instead of three, and reducing by one-third the attenuation of the beam due to the crystals.

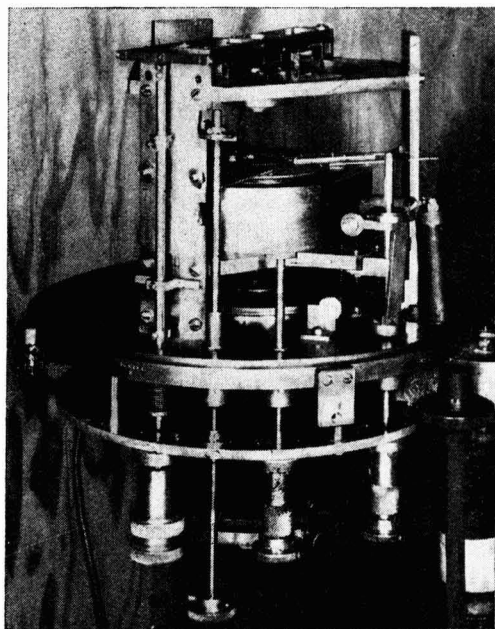


FIG. 22 — LATER MODIFICATION OF INTERFEROMETER SHOWING REPLACEMENT OF ONE OF THE CRYSTALS BY A MAGNETIC LENS

A different type of interferometer using the optical analogue of a Fresnel bi-prism was recently built in Germany. It showed very well formed fringes; however, the use of the instrument is limited to a maximum of about a few hundred wavelengths path difference.

The possible applications of an electron interferometer are interesting. One type of investigation which could be carried out by means of an interferometer is directly related to the field mapping method outlined earlier. Optical path differences in the two legs of the electron interferometer may be produced by a difference in the electromagnetic index of refraction. Thus, an electron interferometer might constitute an extremely sensitive instrument for measuring very weak field gradients. Another possible use is for length measurements, although the extreme sensitivity of the instrument restricts it to very specialized cases, such as high precision measurements of thermal expansion. Other interesting applications are due to the fact that an interferometer is probably the best or most precise instrument to measure a wavelength. By determining with precision

the wavelength as a function of energy of the electron, we can have a new method for a re-determination of Planck's constant. Several other interesting possibilities exist in which an interferometer may be used to contribute to our knowledge of solid state physics. The development of an electron interferometer may open up new avenues in different fields of physics which are at present partially or completely unexplored.

A very interesting line of research is the investigation of electron scattering phenomena in solids. This line of research has gained a new importance in the last few years due to the availability of improved means of investigation. It has been found that the energy distribution of electrons scattered from solids is not as simple as had always been assumed. The scattered electrons can be divided roughly into two groups: those which have been scattered without losing any significant part of the energy (elastically scattered) and those which have lost some part of their energy (inelastically scattered). These latter do not lose their energy in any



FIG. 23 — ELECTRON INTENSITY VS. ENERGY LOSS FOR ALUMINIUM

random manner. It has been found that there exist definite quantum values and that the energy is lost in processes which are characteristic of the solids with which the electron is interacting. Some examples are shown in Figs. 23, 24 and 25. Fig. 23 shows the energy losses suffered by electrons passing through a thin film of aluminium. The largest peak due to the elastically scattered electrons which have not lost any energy can be noted in Fig. 23. To the left of this peak several peaks of different heights showing the electrons that have lost 7, 15, 21, 28 and so on electron volts of their primary energy can be seen. The height of these different peaks is varying considerably. Fig. 24 shows the behaviour of electrons scattered through magnesium. The primary energy is shown on the left and the energy losses consist of very narrow lines. These lines follow each other at equal distances. In other words, the energy losses are multiples of a primary energy loss. Fig. 25 shows the energy losses in a thin film of carbon. Here, only a very small peak followed by a broad band around

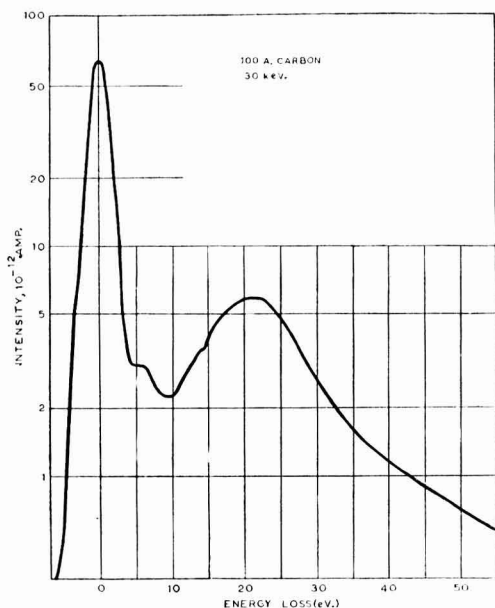


FIG. 25 — ELECTRON INTENSITY VS. ENERGY LOSS FOR CARBON

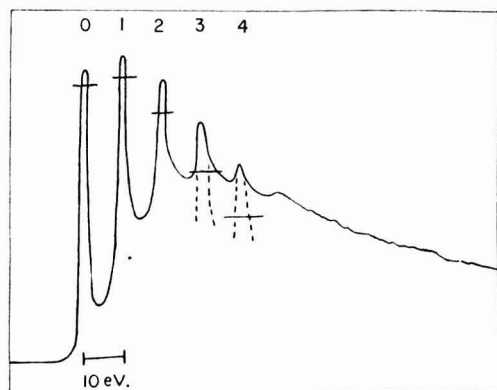


FIG. 24 — ELECTRON INTENSITY VS. ENERGY LOSS FOR MAGNESIUM (courtesy: H. Watanabe)

22 or 23 eV. is seen. The spectra are thus characteristic of different materials, and these are different types of spectra, either very fine lines, wider lines spread at random, or broad bands. The study of the behaviour of the electron helps to draw conclusions about the energy bands in the solid and thus adds information about the structure of solids as well as some of the processes of energy degradation of the electron in passing through different materials. This type of investigation helps also in understanding better, the image formation in an electron microscope and in understanding how the resolution of an electron microscope is limited by the energy losses of electrons in the specimen itself.

# Chemotherapeutic Search for Amoebicides

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THE search for amoebicides has been going on since the time emetine was first discovered as a potent amoebicide. In more recent times a large number of amoebicidal agents have been prepared and intensive studies on their chemical constitution and biological activity relationships have been made with a view to finding more effective drugs. The biological aspects of the problem have been exhaustively reviewed by different authors<sup>1-5</sup>. The present paper reviews the chemotherapy of amoebiasis mainly from the chemical point of view, and indicates the lines along which research has progressed on the synthesis of known amoebicides and the newer compounds based on the structure of known and proven drugs.

**Biological aspects** — Since one of the key approaches to chemotherapy is through a study of the nutritional requirements, growth factors, growth stimulants and the general metabolism of the parasite, numerous attempts have been made to study the metabolic pattern of *Entamoeba histolytica*. The results, so far, have been rather discouraging.

The nutritional requirements and growth factors for *Entamoeba histolytica* have not yet been established because till now, a pure culture of this organism has not been obtained. For the same reason it is difficult to evaluate the claims made for various growth factors and growth stimulants for *E. histolytica*. Ordinarily, substances which stimulate growth of bacteria indirectly stimulate amoebic growth also. Blood, serum, egg, liver, liver extract, peptone, rice powder and a variety of complex materials have been used for the cultivation of *E. histolytica* but it is not easy to establish the component or components contained in these media which act as growth factors.

Since bacteria are practically essential for the cultivation of amoebae, it is of importance to know whether actively metabolizing bacteria are necessary for the growth of the amoebae or some factor found in the bacterial cell is stimulatory when ingested by the

amoebae. Experimental results indicate that the material supplied by actively multiplying bacteria is also possibly furnished by killed bacterial cells but not in high enough concentrations to maintain the growth of amoebae<sup>6-8</sup>. The other possibility, however, is that the bacterial metabolism maintains a low oxidation-reduction potential<sup>9,10</sup> which is optimal for the growth of *E. histolytica*.

Another approach to the study of the role of bacterial associates has been to incorporate enzymes into the media as substitutes for bacteria. The enzymatic make-up of the amoebae themselves is also bound to throw some light on the metabolic pathways of the various foodstuffs available in the media. The number of enzyme systems involved is, however, formidable.

Practically nothing is known of the metabolism of the amoebae, and metabolic studies of significant importance cannot be undertaken unless a pure culture of the organism is obtained. Studies by Nakamura *et al.*<sup>11,12</sup> using manometric techniques have shown that small amounts of acid are produced with glucose as the substrate. The nature of the acids and whether or not, other carbohydrates such as rice starch can be utilized as an energy source still remain to be elucidated. It is thus clear that the chemotherapy of amoebiasis based on a study of the nutritional requirements and the metabolic patterns of *Entamoeba histolytica*, sometimes described as a 'more rational' approach, is not a short cut to the solution of the problem of amoebiasis. It also involves the study of as large a number of variables as in the case of syntheses based on an empirical approach.

An ideal amoebicide<sup>2</sup> is one that (a) can be administered orally, (b) is effective against the trophozoites and cysts in the lumen of the intestine, (c) is accumulated in effective concentration in the tissues of the large bowel, and (d) is distributed to the liver and other tissues and there, retaining its effective form, reaches therapeutically effective levels against trophozoites. No single available amoebicide is known to meet all these requirements.

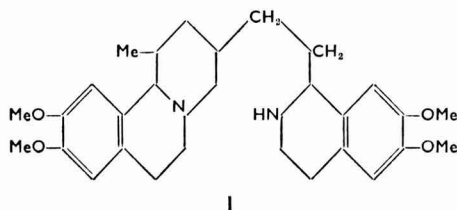
The agents that have been prepared in the course of the search for the ideal compound can be divided into five classes based on their chemical origin.

#### Plant products and synthetic substitutes

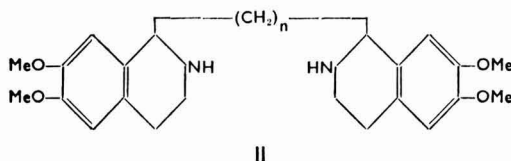
The important members of this group are the active principles isolated from *ipecacuanha*, *kurchi* alkaloids, and *ko-sam* or *ya-tan-tzu*. There is, however, a reference to the use of dihydrolycorine<sup>13</sup> from *Lycoris radiata* as a substitute for emetine.

**Emetine and its analogues** — Emetine is the most important member of this group and the most useful also due to its prompt pharmacodynamic action in stopping diarrhoea. It has been shown<sup>14</sup> that emetine is present in several viscera other than in the large intestines of experimental animals in large quantities. This explains the effectiveness of emetine in hepatic amoebiasis and its lack of specificity in intestinal amoebiasis.

Emetine was formulated as (I) by Brindley and Pyman<sup>15</sup> in 1927.

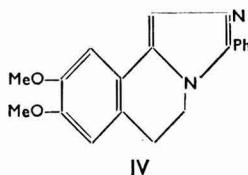
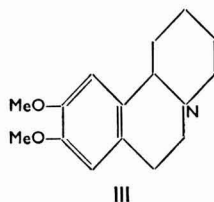


Based on this formula, Child and Pyman<sup>16</sup> synthesized a series of compounds (II) having similar constitutional features in that they contained two 6, 7-dimethoxytetrahydro-isoquinoline nuclei united through the 1-1' positions by chains of methylene groups<sup>17</sup>.

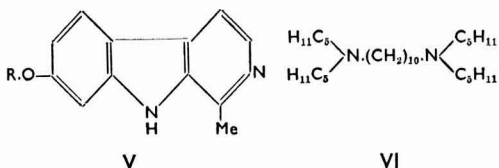


None of these compounds prevented the growth of *Entamoeba histolytica* in cultures at a dilution of 1 in 5000, whereas emetine was effective at a dilution of 1 in 500,000. Further series of compounds prepared by Child and Pyman<sup>18</sup> were also tested with a view to find whether the reduced benzpyridocoline

ring (which is a feature of Brindley and Pyman's formula for emetine) or other systems in which the tertiary N atom of emetine is common to two rings conferred amoebicidal properties or not. This group of compounds which included 10, 11-dimethoxy-1, 2, 3, 4, 6, 7-hexahydrobenz-pyridocoline (III), proved to be only feebly active compared with emetine, for the most highly amoebicidal member of the series — 9, 10-dimethoxy 3-phenyl-5, 6-dihydrobenz-glyoxalocoline (IV) — only prevented the growth of *Entamoeba histolytica* in cultures at a dilution of 1 in 25,000.

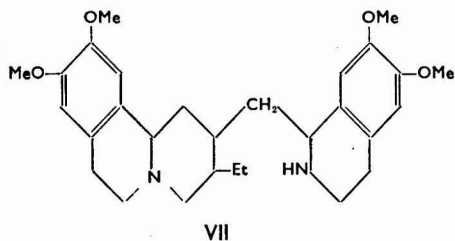


Pyman and collaborators<sup>19</sup> also tested a series of harmine and harmaline derivatives for amoebicidal activity *in vitro* and found that the activity increased on ascending the homologous series of alkylharmols up to a point and then started to fall. The peak for the amoebicidal activity was reached at O-*n*-nonylharmol (V; R = C<sub>9</sub>H<sub>19</sub>), but this substance suffered from the disadvantage that it was very sparingly soluble in water. Consequently, a further series of compounds were prepared by replacing R by a dialkyl-aminoalkyl radical and maximum activity, far superior to that of O-nonylharmol, was found in the O-dibutylaminoundecyl derivative [V; R = (C<sub>4</sub>H<sub>9</sub>)<sub>2</sub>N.C<sub>11</sub>H<sub>22</sub>].



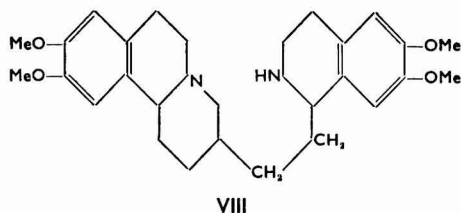
This led them to suspect that the harmol residue might not be an important contributor to the amoebicidal properties of the molecule. A number of compounds were thus prepared in which the heterocyclic nucleus was omitted and the basic side chain was terminated by another basic group. A series of tetra-alkyldiaminoparaffins<sup>20,21</sup> of the general formula  $R'R''N(CH_2)_n.N.R'''R''''$ , where  $n$  is an integer from 7 to 13 and  $R'$ ,  $R''$ ,  $R'''$  and  $R''''$  are the same or different alkyl groups or  $R'$ ,  $R''$  and (or)  $R'''$ ,  $R''''$  represent the pentamethylene chain, were then prepared, maximum activity being found in *ak*-tetra-*n*-amyldiaminodecane (T.A.D.D., VI). The *in vitro* tests showed that a concentration of 1 in 3,000,000 was lethal to *Entamoeba histolytica*. Clinical tests on this compound were, however, disappointing.

Goodson and colleagues<sup>22,23</sup> examined a series of compounds including some of the type  $[3, 4, 1-(OMe)_2.C_6H_3NH]_2 > (CH_2)_n$  and also the primary diamine  $NH_2(CH_2)_{10}NH_2$ . The biological tests by Goodwin *et al.*<sup>24</sup> in the rat as well as *in vitro* with a single bacterial species indicated pronounced amoebicidal activity in many of these compounds, but these were inferior to those of Pyman and co-workers.



In 1948, Robinson<sup>25</sup> suggested the formula (VII) for emetine based mainly on biogenetic grounds. This formula received support from the degradative work on emetine by Battersby and Openshaw<sup>26,27</sup> and Pailer *et al.*<sup>28</sup> and was finally confirmed by the synthesis of ( $\pm$ ) rubremetinium bromide<sup>29</sup> and later of emetine<sup>30</sup>.

Previously, Sugawara and co-workers<sup>31,32</sup>, basing their syntheses on the Pyman's formula had succeeded in preparing *rac*-*c*-nor-emetine (Pyman; VIII) as well as *rac*-emetine (Pyman).



Pailer and co-workers<sup>33</sup> synthesized benzo (g) pyrrocoline and 11bH-benzo-(a)-quinoline but no report of any considerable amoebicidal activity seems to have been recorded.

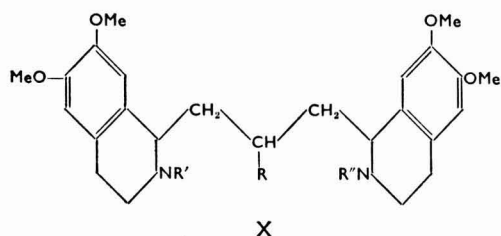
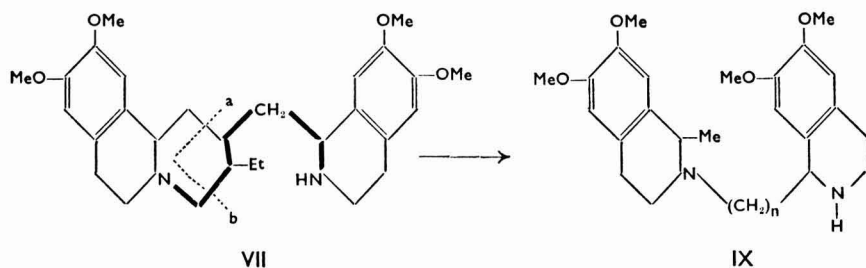
Encouraged by the results of Pyman and co-workers on diaminodecane, Hall *et al.*<sup>34</sup> synthesized a number of long-chain diamines containing two primary amino groups of general formula  $NH_2.CHR.(CH_2)_n.CHR.NH_2$  ( $R$  = alkyl groups, etc.). Some of these compounds showed considerable activity *in vitro* against *Entamoeba histolytica* and in the case of 7,13-diamino-5,15-diethylnonadecane dihydrochloride it was as high as 1 in 500,000. Recently Mahboob and Dhar<sup>35</sup> prepared (cf. also Pyman *et al.*<sup>20,21</sup>) some symmetric and unsymmetric polymethylene diamines carrying a secondary and a tertiary or two tertiary nitrogen atoms with an intervening bridge of 3 and 9 carbon atoms. Kaushiva<sup>36</sup> reported high activity *in vitro* in nonane diamines.

To determine the part of emetine molecule responsible for biological activity Osbond<sup>37</sup> prepared a few  $\alpha$ -(1, 2, 3, 4-tetrahydro-6, 7-dimethoxy-1-methyl-*isoquinolino*)- $\omega$ -(1, 2, 3, 4-tetrahydro-6, 7-dimethoxy-1-*isoquinolyl*)-alkanes (IX) which may be regarded as being derived from the emetine molecule by rupture of the bond at (a), linking the two tetrahydro-*isoquinolyl* nuclei by a carbon chain, as shown by heavy bonds.

Osbond *et al.*<sup>38</sup> also prepared certain *bis*-tetrahydro-1-*isoquinolyl*alkanes (X;  $R$  = alkyl;  $R' = R'' = H$  or Me), the chief aim being the synthesis of the compound (X;  $R = Et$ ;  $R' = Me$  and  $R'' = H$ ), derived from the emetine formula by bond fission at (b). These compounds possessed two basic groups, one secondary and the other tertiary, separated by five carbon atoms as in emetine. Although active, these compounds did not compare favourably with emetine *in vitro*.

A slightly different approach was that of Popli *et al.*<sup>39</sup> who made use of naturally occurring alkaloids as intermediates for the synthesis of emetine-like compounds. Thus





by starting with cinchona alkaloids (XI; R=H or OMe) and by reducing the secondary alcoholic bridge to  $-\text{CH}_2-$ , the vinyl group to ethyl, and the quinoline ring to 1, 2, 3, 4-tetrahydroquinoline, they prepared compounds of the type (XII) and (XIII). These compounds have two basic nitrogen atoms, both tertiary in (XII) and one tertiary and the other secondary in (XIII) and separated in both cases by a bridge of 5 carbon atoms (shown in heavy lines) just as in emetine. By starting with a naturally occurring substance like quinine, the 6-methoxy group was also retained in a position which is known in many therapeutically active compounds to enhance biological activity.

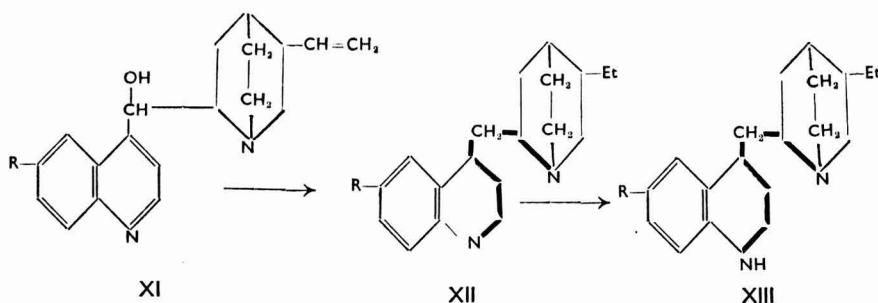
**Conessine and its analogues** — The alkaloid conessine has attracted attention, though not to the same extent as emetine. It is the most abundant and important of the *kurchi* alkaloids isolated from the seeds or the bark of *Holarrhena antidysenterica* and other

species, where it is associated with related bases frequently differing only in the degree of N-methylation<sup>40,41</sup>. Conessine is less toxic to the heart but causes psychic disturbances requiring concurrent administration of sedatives<sup>42</sup>.

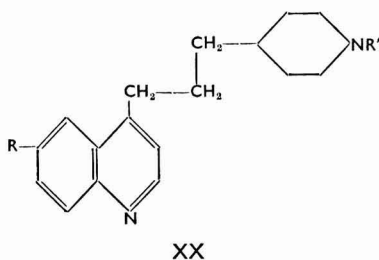
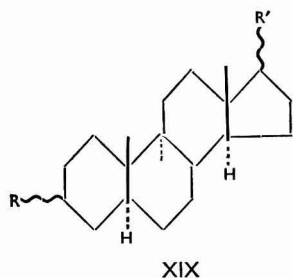
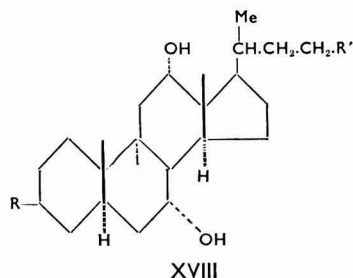
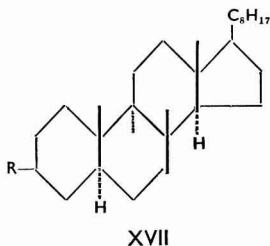
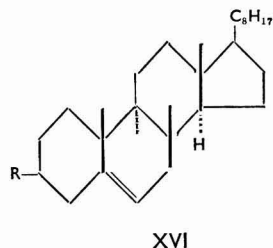
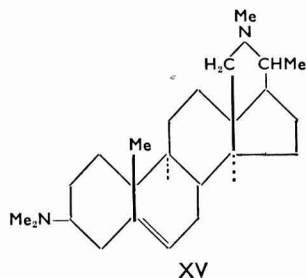
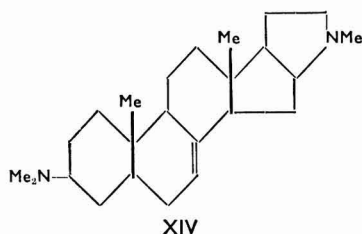
Bertho<sup>43</sup> had proposed the structure (XIV) for conessine, but the latest evidence favours the structure (XV) assigned by Haworth and co-workers<sup>41,44,45</sup>.

To develop new amoebicidal agents, a number of 3-amino-steroidal bases<sup>46,47</sup> were prepared by the reduction of 3-oximino compounds with sodium and alcohols or by the action of bases on 3-toluene-*p*-sulphonates. The compounds, none of which was sufficiently active in low doses, included 3- $\beta$ -dimethylaminocholest-5-ene (XVI; R = N.Me<sub>2</sub>), 3- $\beta$ -dimethylaminocholestane (XVII, R = N.Me<sub>2</sub>), 3-2'-diethylaminoethylaminocholest-5-ene (XVI; R = NH.CH<sub>2</sub>.CH<sub>2</sub>.NEt<sub>2</sub>), 23-amino-3- $\alpha$ -7- $\alpha$ -12- $\alpha$ -trihydroxynorcholane (XVIII; R = OH; R' = NH<sub>2</sub>) and 3- $\xi$ -17- $\xi$ -bisdimethylamino androstane (XIX; R = R' = NMe<sub>2</sub>).

Based on considerations similar to those applied in the case of emetine, Popli *et al.* prepared compounds<sup>39</sup> of the type (XX; R=H or OMe; R'=alkyl groups) by suitable modifications of the cinchona alkaloid molecules (also Popli *et al.*, unpublished data). These compounds simulate conessine in as







far as they contain two tertiary nitrogen atoms separated by a chain of nine carbon atoms just as in conessine.

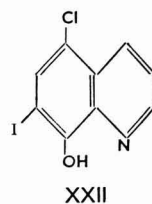
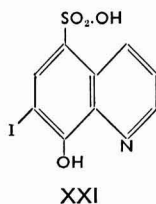
**Active products from other plants**—The drug *ko-sam* or *ya-tan-tzu*, which is the seed of *Brucea javanica* Linn. Merr., has been used in China as a remedy for diarrhoea<sup>48,49</sup>. The alcoholic extracts of this plant show amoebicidal activity somewhat less than that of emetine and have a very low toxicity<sup>49</sup>. Conflicting views have been expressed about the chemical identity of the active principle. Chen-yu-Sung<sup>49</sup> ascribes it to a glycoside 'brucellin' whereas Shao-Kwang Liu *et al.*<sup>50</sup> report the activity to be due to an alkaloid 'yatanine' which they claim to have isolated from the seeds of *ya-tan-tzu*.

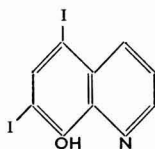
#### 8-Hydroxyquinoline derivatives

The halogenated hydroxyquinolines, like chiniofon<sup>51</sup> (XXI), vioform<sup>52</sup> (XXII) and

diiodoquin<sup>53</sup> (XXIII), have found considerable use as amoebicides. In spite of recent adverse opinion as to its effectiveness, diiodoquin is still used in high dosages and with other agents.

Studies on the metabolism of chiniofon, in which radioactive iodine was utilized, have shown that some absorption of this halogenated hydroxyquinoline may occur. According to Albright *et al.*<sup>54</sup>, the uptake was small and averaged 12.9 per cent of the dose given. Blood levels of clinical importance

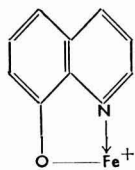




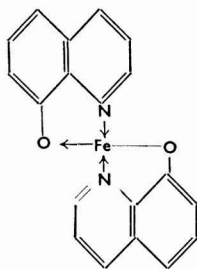
XXIII

could not be attained in spite of prompt absorption due to low percentage absorbed, rapid urinary excretion, and breakdown into free iodine and organic rings. Distribution studies of radio-iodine after intravenous injection in rabbits by Mann *et al.*<sup>55</sup> have indicated that of all the tissues the liver contains the least amount of radio-iodine.

The mechanism of the activity of 8-hydroxyquinoline derivatives is still not clear. According to Albert<sup>56,57</sup> they act as antibacterial agents by virtue of chelation with traces of polyvalent metals like iron or cobalt to give feebly dissociated complexes in which the metal forms part of a heterocyclic ring system. This metal complex is the toxic agent<sup>58</sup>, and of the two known complexes the evidence favours (XXIV) rather than (XXV). The action of 8-hydroxyquinoline appears to take place inside the cell, and the work of Albert *et al.* shows that it is necessary that these substances should have an optimal liposolubility<sup>59-61</sup> to be able to penetrate the cells better and thereby to manifest their activity.



XXIV

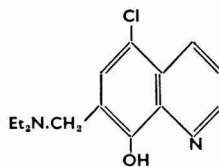


XXV

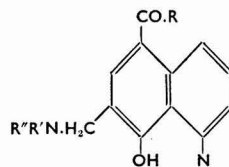
A series of 8-phenoxyquinoline, its *p*-amino, *p*-acetamino and *p*-hydroxy derivatives as well as a series of 8-alkoxyquinolines were found to possess definite antibacterial activity<sup>62</sup>. Thus it appears that the explanation proposed by Albert *et al.* for the antibacterial activity of 8-hydroxyquinolines is inadequate.

Further, according to the chelation which is essential for the antibacterial action of oxine derivatives is not the source of their efficacy as amoebicides<sup>57</sup>. The common feature for chiniofon and diiodoquin is that they split off iodine with surprising readiness when boiled with water and more slowly when the solutions are kept at room temperature. Since the corresponding chlorine analogues do not have amoebicidal activity<sup>63</sup> (cf., however, Thompson *et al.*<sup>64</sup>), it seemed likely that these types of drugs owe their activity to the weakness of the C-I bond in 7-position of the oxine nucleus, and to the steady evolution of inorganic iodine.

Burckhalter and Edgerton<sup>65</sup>, with the object of improving the solubility of vioform, prepared 5-chloro-7-diethylaminomethyl-8-quinolinol (XXVI) and found it to be more active *in vitro* and in experimental animals with considerable promise in the treatment of intestinal amoebiasis. The oral activity in the hamster against hepatic amoebiasis was only slight. Burckhalter and Edgerton<sup>66,67</sup> and Thompson *et al.*<sup>64</sup> prepared a large number of other Mannich bases derived from 8-hydroxyquinoline and showed conclusively that iodine is not essential for the amoebicidal activity of oxine compounds.

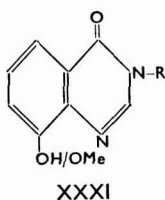
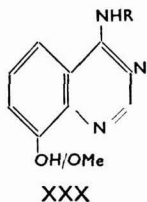
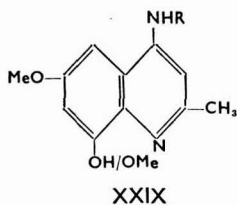
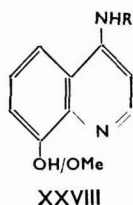


XXVI



XXVII

A large number of 8-hydroxyquinolines<sup>68</sup> of the type (XXVII) (where R = aryl, alkyl, arylkenyl, heterocyclyl, and R' and R'' are alkyl groups or together with N form a heterocyclic ring to give a 7-tert. amino-methyl derivative) have been characterized by high amoebicidal activity, suggesting that chelation may be important in the amoebicidal activity of these compounds. To verify this assumption and with a view to prepare compounds which incorporate in themselves certain characteristics of 8-hydroxyquinolines as well as of chloroquin, a large number of 4-substituted amino-8-hydroxy and 8-methoxyquinolines (XXVIII) and 6,8-dimethoxy and 6-methoxy-8-hydroxyquinolines<sup>69</sup> (XXIX), their corresponding quinazo-



lines (XXX) and 3-substituted 8-hydroxy and 8-methoxy-4-quinazolones<sup>70</sup> (XXXI, R=alkyl, aryl or diethylaminoalkyl group) were synthesized. *In vitro* studies on the 8-methoxyquinoline and quinaldine derivatives by Kaushiva<sup>71</sup> showed activity equal to that of emetine in some of the quinaldine derivatives.

#### Arsenicals

Among the arsenicals that have been used are acetarsone (stovarsol; XXXII), carbarsone (XXXIII), bismuth glycolylarsanilate (Wia or Milibis, XXXIV) and the trivalent arsenicals, notably the thioarsenites 914 and 1037 (XXXV and XXXVI respectively)<sup>72</sup>.

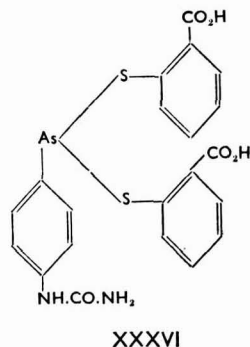
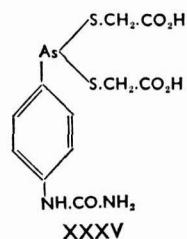
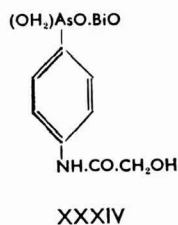
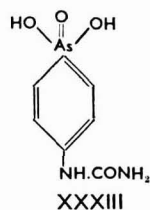
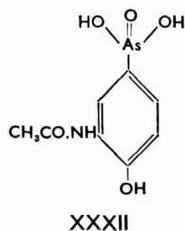
Acetarsone was introduced in 1923 primarily for use in syphilis<sup>73</sup>. The reported frequent cutaneous and other reactions<sup>74</sup> to therapeutic doses of acetarsone have led to its abandonment as an amoebicide in the United States. Thus among the members of this class, carbarsone, introduced by Leake and associates<sup>75</sup> in 1932, is widely used and considered as a safe drug in the absence of contraindications to arsenical therapy. Carbarsone, alone or in combination with other drugs, is satisfactory. Experience during World War II supported the contention of Hakansson<sup>76</sup> that doses larger than those originally recommended can be used even under field conditions. Distribution studies<sup>72</sup> have shown that high concentrations of arsenic occur in hepatic tissue and in the intestine following administration of this agent and its trivalent analogues.

'Milibis' is among the locally active agents. It was originally studied in amoebae-

infected kittens by Hauer<sup>77</sup>. The studies of Dennis *et al.*<sup>78</sup> show that it is less active orally than carbarsone against the natural non-pathogenic amoeba of Syrian hamsters. Lack of absorption renders this drug effective in the lumen of the colon but ineffective in controlling deep-seated lesions.

More recently, Anderson *et al.*<sup>72</sup> have found certain thioarsenites to exert topical effects on the gastric mucosa similar to, but less harmful than, those produced by arsine oxides. Substitution of -SH groups for oxygen detoxifies arsenicals for host's tissue cells. Substitution of methyl or phenyl groups for hydrogen in the dithio portion of the molecule, accompanied by the addition of carboxyl groups to the thiol radical for solubilizing the compound, results in agents effective orally or rectally in amoebiasis, in generally tolerated amounts.

The two arsenites (No. 914 and No. 1037) exhibited a range of activity comparable to



that of carbarsone oxide and significantly greater than that of carbarsone, U.S.P. Appreciable tissue levels, especially in the blood, persisted in rats for at least 9 days after the last dose in short-term chronic toxicity tests. These findings, as well as the low levels of arsenic detected in the brain, favoured consideration of trivalent thioarsenites for trial in human amoebiasis.

### Antibiotics

The use of penicillin<sup>79</sup>, aureomycin<sup>80-82</sup>, bacitracin<sup>80</sup>, terramycin<sup>83</sup> and fumagillin<sup>84</sup> in the chemotherapy of amoebiasis has been investigated either alone or in combination with other drugs. All these antibiotics, except fumagillin, act in amoebiasis by reason of their effect on the bacterial symbionts in the bowel necessary to the survival of the amoebic infection<sup>1,85</sup>.

The chemistry of aureomycin and terramycin was studied by Woodward and co-workers<sup>86</sup> and has been reviewed by Johnson<sup>87</sup>. Terramycin has been formulated as (XXXVII; R=H; R'=OH) and aureomycin as (XXXVII; R=Cl; R'=H) and the portion of the molecule common to both structures (XXXVII; R=R'=H) has been designated as 'tetracycline'.

Albert reported that aureomycin and terramycin combine strongly with ions of heavy metals particularly with ferric ion<sup>88</sup>. Weidenheimer<sup>88</sup> prepared aureomycin-metal complexes having therapeutic properties superior to those of free base and its salts. The presence of Co diminished the activity of aureomycin<sup>89</sup>. It is thus possible that the antibacterial activity of the tetracyclines is attributable to the same factors as were proposed by Albert for oxine derivatives<sup>56,57</sup>.

Fumagillin is, perhaps, the only antibiotic known having a direct amoebicidal action. It has, however, little antibacterial or no antifungal action<sup>85</sup>. Studies *in vivo* have shown it to be remarkably devoid of toxicity and capable of exerting an effective amoebi-

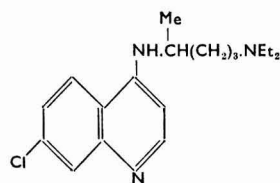
cidal action in experimentally infected animals. The reports of clinical trials, so far, are encouraging<sup>85,90</sup>.

The chemistry of fumagillin has not yet been completely elucidated. Schenck and co-workers<sup>91,92</sup> and Tarbell *et al.*<sup>93</sup> have shown that it has an empirical formula  $C_{26}H_{34}O_7$  and is a mono ester of decatetraenedioic acid and an alcohol,  $C_{16}H_{26}O_4$  (cf. Landquist<sup>94</sup>).

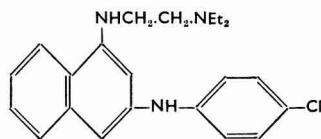
### Miscellaneous compounds

These include the various quinoline, quinoxaline, pyridine, pyrimidine and thiazolidine derivatives. Among the quinolines, chloroquin (XXXVIII) is of interest chemically as well as therapeutically. It successfully combats hepatic amoebiasis but no consistent effect on intestinal amoebiasis has been noted<sup>95</sup>. Further, chloroquin was found effective<sup>96</sup> in liver abscess which are resistant to emetine.

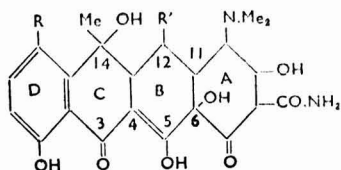
A large number of other quinoline compounds have been prepared<sup>97</sup> from 2-anilino-4-chloroquinoline (XL) and 4-chloroquinoline (XLI) respectively by building up various types of basic side chains in place of the reactive chlorine atom in the 4-position of quinoline nuclei. In the quinaldyl series the three compounds (XLII; R =  $C_8H_{17}$ ,  $C_9H_{19}$ ,  $C_{10}H_{21}$ )



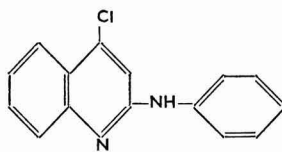
XXXVIII



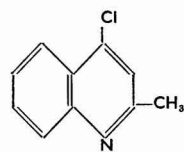
XXXIX



XXXVII



XL



XLI

and  $-\text{CH}_2\text{CH}_2\text{CHMeCH}_2\text{CMe}_3$  respectively) had activity up to a dilution of 1 in a million.

Landquist and Stacey<sup>98</sup> and Jones *et al.*<sup>99</sup> studied quinoxaline 1, 4-dioxide (XLIII) and its derivatives. Quinoxaline 1, 4-dioxide exerts a therapeutic effect against amoebiasis in rats, cats, dogs and monkeys. Related compounds, mainly 2-alkyl- and 2, 3-dialkyl derivatives, were also found effective against laboratory infections. Compound (XLIII) showed only weak therapeutic action and also gave rise to serious toxic effects. 6-Chloro-2, 3-dimethylquinoxaline 1, 4-dioxide had no therapeutic effect in human infections and was also toxic.

Jones and co-workers<sup>100</sup> also prepared some pyrimidine derivatives. In the course of their screening 1-azanthraquinone (XLIV) was found to have moderate activity both *in vitro* and *in vivo*; and on the basis of this observation numerous nitrogenous anthraquinone derivatives and similar polycyclic compounds were examined. Of these, 6-aminoanthrapyrimidine (XLV) was found to be slightly active *in vitro* and strikingly active over a wide range of doses *in vivo* when administered to rats infected with *Entamoeba histo-*

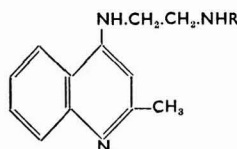
*lytica*. However, an undesirable photodynamic effect occurred even at low doses. The compound also showed a therapeutic effect against experimental amoebic dysentery in cats but had no action on the infection in monkeys and men. A large number of variously substituted 6-amino anthrapyrimidines were also tried but no appreciable improvement on the parent compound was made.

Other pyrimidine compounds with promise were reported by Jacob and Liakhoff<sup>101</sup> who synthesized compounds of the type (XLVI) where A indicates a bivalent aliphatic radical with 2-6 carbon atoms.

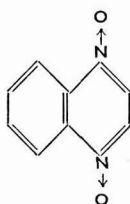
Certain halohydroxy-phenethyl pyridines of the type  $\text{R-A-C}_6\text{H}_4(\text{OH})\text{X}_2$  (where R is a substituted pyridine, quinoline or a piperidine nucleus;  $\text{A}=\text{C}_2\text{H}_4$  or  $\text{C}_3\text{H}_5$  and  $\text{X}=\text{halogen}$ ) were found to be useful amoebicides<sup>102</sup>. Some pyridine and pyridoquinolines with some activity have been described<sup>103,104</sup>.

Following their observation<sup>105</sup> of significant amoebicidal activity of 2-(3, 4-dichlorophenyl)-4-thiazolidone-1-dioxide (XLVII) Surrey and co-workers investigated several series of compounds derived from the thiazolidone structure (XLVII). Since benzylacetamide, obtainable by the removal of  $-\text{SO}_2-$  group showed appreciable amoebicidal activity, extensive study<sup>106</sup> of compounds having general formula (XLVIII;  $n = 1$ , R = alkyl, alkoxy, chloro, dichloro;  $\text{R}' = \text{CH}_2\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{CHOHCH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ ; and  $\text{R}'' = \text{CHCl}_2$ ,  $\text{CHBr}_2$ ) have been reported. Some of these compounds especially N-(2, 4-dichlorobenzyl)-N-(2-hydroxyethyl)-dichloroacetamide (Win 5047) were highly potent amoebicides. (Win 5047) was very effective both *in vitro* and *in vivo*. In intestinal amoebiasis in hamsters its amoebicidal activity is greater than that of chlorotetracycline or oxytetracycline. In addition, the compound is well tolerated in several species of laboratory animals. Preliminary clinical investigations in human amoebiasis are also encouraging.

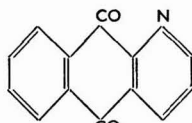
Studies on some derivatives<sup>107</sup> of the general formula (XLVIII) showed that in



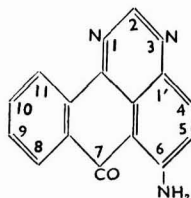
XLII



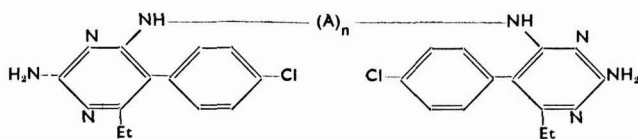
XLIII



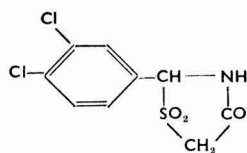
XLIV



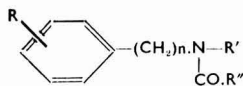
XLV



XLVI



XLVII



XLVIII

general the most active compounds were those in which R is 4-butoxy, 2, 4-dichloro and 3, 4-dichloro; R' is isopropyl and R'' is  $\text{CHCl}_2$ . Replacing the isopropyl group by *n*-propyl or by higher alkyl groups results in a sharp drop in activity. The order of amoebicidal activity with variation in R'' is similar to that found in several other series,  $\text{CHCl}_2 > \text{CCl}_3 > \text{CH}_2\text{Cl}$ . The compounds substituted in the phenyl ring (e.g. R = dichloro or 4-butoxy) were considerably more active than the unsubstituted derivatives where R = H. A free hydroxyl group at R' is not essential for high activity<sup>108</sup>. The least active derivatives were those which contained a solubilizing group such as a free carboxylic acid or a diethylamino group.

### Conclusion

Chronic amoebiasis is a major health hazard in wide areas of the tropics and in certain regions as many as 14 per cent of the dysentery cases have been diagnosed as of amoebic character. The complications of chronic amoebiasis are also such that chronic invalidism may result if the infection cannot be completely eradicated. The need for the discovery of a really effective drug can never be overstated.

The large amount of chemical and biological data available is still insufficient for the formulation of any definite theory of chemical constitution and amoebicidal action. This is so mainly because modifications in chemical structure that bring about parallel changes in the overall chemotherapeutic effect of various drugs may do so by influencing different and separate pharmacological characteristics. Also, the effect of a drug itself is dependent upon a number of variables such as solubility, absorption from the

host alimentary canal, rate and mode of excretion, permeability considerations with respect to cells, etc.<sup>109</sup>. In spite of these inherent difficulties, the search for an ideal amoebicide, taking advantage of the already known leads, has provided some useful drugs. A thorough sifting of the data obtained in the course of this worldwide search has also made it possible to formulate certain 'working hypotheses'. These appear worth while pursuing in the expectation that a still better chemotherapeutic agent may be discovered.

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# REVIEWS

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TECHNICAL ASPECTS OF SOUND, PART II, by E. G. Richardson (Elsevier Publishing Co., Amsterdam, Netherlands, London; *Distributors*: Cleaver-Hume Press Ltd., London), 1957. Pp. xii + 412. Price 70s.

The second volume of this admirable work, expected in 1954, has been published now, nearly four years after the appearance of Vol. I which has become an indispensable reference work to research workers in the field of acoustical technology. The present volume is devoted entirely to ultrasonic range and underwater acoustics, and, like its preceding volume, it is a compilation of contributed articles from experts in their respective fields of specialization.

Except for Chapter I, contributed by the Editor, on the general subject of "propagation of sound in the atmosphere and the sea", the other ten chapters have been grouped under three main divisions, each devoted respectively to: (I) Ultrasonic transducers and applications, (II) Underwater acoustics, and (III) Aircraft noise with a chapter on underwater propulsion noise.

Division I comprises of Chapters 2 and 3, both contributed jointly by B. E. Noltingk and N. B. Terry. Design considerations of piezoelectric and magnetostrictive types of ultrasonic transducers have been given along with the basic principles and materials involved as well as descriptions of some of the equipment which utilize these transducers for specific purposes. Applications of ultrasonics in diverse fields such as inspection and communicating systems, mechanical applications, effects in liquids, chemical and biological effects have been described at some length and principles underlying each application have been clearly brought out. Many useful practical hints are also given.

Four contributions from German workers on underwater acoustics form Division II. Prof. Erwin Meyer of Göttingen University and the foremost German worker on acoustics, discusses, in Chapter 4, techniques of underwater measurements describing various types of apparatus used and comparing these techniques with those used in air measurements. In the next chapter Prof. Meyer has

dealt with the very important aspect of air bubbles in water giving a brief theoretical account of pulsation of air bubbles and properties of single as well as swarms of such bubbles and cavitation phenomenon. Next chapter, contributed by Tamm, describes broad-band absorbers for water-borne sound. Various types of absorbing structures such as porous framework in liquids, fine mesh screens, absorbing wedges, rib structures made of highly compressible substances, etc., are dealt with at some length. Oberst describes resonant sound absorbers in the last chapter of this division. Experimental results are compared with theoretical calculations and practical applications of such absorbers are then discussed.

Aircraft noise forms the subject matter of the first three chapters (8, 9 and 10) of Division III comprising of contributions from American workers, Regier, Hubbard and Laster of Langley Aeronautical Laboratory, U.S.A. Chapter 8 gives a brief description of the nature and sources of aircraft noise from various kinds of propulsive units, and develops the theory for calculating noise intensity and its characteristics. Propeller noise is related to aerodynamic forces — both steady and unsteady. Jet noises are discussed in the next chapter under various categories — continuous jets, intermittent or pulse jets, ramjets and rockets. These have recently been of great concern to the acoustical engineer. Other noises such as aerodynamic noise, reciprocating engine noise, etc., are dealt with in Chapter 10 which also gives a comparative study of noise levels from various aircraft propulsive systems.

In the final chapter of the book, Richardson deals with noises due to underwater propulsion and then brings out the main features which distinguish them from the propulsion noise in the air. These are low natural frequencies, the mode of excitation of such vibrations and formation of cavities.

The volume is well illustrated and the printing and general get-up are excellent. Exhaustive lists of references at the end of each chapter form an important feature as in the case of the first volume.

The two volumes fulfil a very vital need of a handbook to cover nearly all the technical aspects of the subject and provide the research and development worker in this field, a survey, at a fairly advanced level, of the various important aspects of sound and its technology.

N. B. BHATT

# THE MANUFACTURE OF IRON AND STEEL:

VOL. I — IRON PRODUCTION by G. Reginald Bashforth (Chapman & Hall Ltd., London; *Distributors in India*: Asia Publishing House, Bombay), Second Revised Edition, 1957. Pp. xi + 306. Price 45s. Bashforth's *Manufacture of Iron and Steel* has always been a popular book with students of metallurgy and steelmen and the second edition, brought out nearly 10 years after the first, fills a distinct gap in recent metallurgical literature. The author has brought the book up to date and has added nearly 80 pages of new matter. Several sections such as geographical distribution of iron ores, drying of ores, blast-furnace hearth, use of carbon blocks, scaffolding, blast furnace instruments, blast furnace calculations and alloy cast irons, have been expanded, and new sections, viz. recent research and developments, thermodynamics of the blast furnace, changes in design of the blast furnace, high top-pressure operations, low-shaft blast furnace and modern electric furnace, have been incorporated. The number of illustrations has been increased and lists of references at the end of each chapter amplified. It is a painstaking piece of work, written in lucid style, by an authority on the subject, and will be useful both as a standard text-book and a work of reference to those engaged in steel-making.

S. K. NANAVATI

# MODERN CHEMISTRY FOR THE ENGINEER AND SCIENTIST.

Edited by G. Ross Robertson (McGraw-Hill Book Co. Inc., New York, Toronto, London), 1957. Pp. ix + 442. In these days of specialization when the reading range of scientists is becoming increasingly narrow, it is highly refreshing to meet a book of this type where the acknowledged leaders of many fields of study are brought together to hold out a panorama of recent developments with kaleidoscopic variety. Granting all the defects of poly-authorship, the result has been highly satis-

fying: and every chemist can do no better than to enlarge his range of vision and knowledge than to give liberally his time to read this book. It is difficult to conceive of another single source wherefrom a chemist can at the same time come to know that the laevo isomer of epinephrine raises the blood pressure fifteen times as much as the dextro and twice as much as the racemic form; the *d*-band valencies in metals are involved in the activation of hydrogen in hydrogenation catalysis; the statistical calculation of entropy and heat content of the geometrical isomers of dimethyl cyclohexanes has helped to correct some of the existing erroneous assignments of the *cis* and *trans* structures; the life-time of methyl free radical ( $\text{CH}_3 + \text{CH}_3 \rightarrow \text{C}_2\text{H}_6$ ) is of the order of  $10^{-3}$  to  $10^{-2}$  sec., and in some fast reactions the pre-exponential factors may be as high as  $10^{17}$ , a figure few orders higher than the total number of collisions; the formation of 'bird-cage' hydrocarbon by a complex succession of rearrangements involves carbon participation,  $\pi$ -electron delocalization, hydrogen participation and proton expulsion; a perfluoro compound, say perfluorotributylamine, can be heated to 500°C. without evidence of decomposition and when added to hydrocarbons and other organic liquids reduces the surface tension, fire hazard, toxicity and rate of evaporation because of the crowding of the relatively non-volatile fluorochemical surfactant molecules into the surface; the rare earth elements are actually not at all rare in the earth's crust but are even much more abundant than the common elements, mercury, bismuth, etc.

The nineteen chapters of the book deal with the fundamentals of chemistry and its bearing to life in abundant richness. They have been written by specialists in the subjects: (1) Chemical Thermodynamics by Kenneth S. Pitzer; (2) Twenty Years of Progress in Contact Catalysis by Paul H. Emmett; (3) Photochemistry, Its Interest and Its Value by W. Albert Noyes, Jr.; (4) Chemical Kinetics and Fast Reactions by Norman Davidson; (5) Isotopic Tracers in Chemistry by Clifford S. Garner; (6) Column Chromatography and Some Applications in Stereochemistry by Laszlo Zechmeister; (7) Organic Reaction Mechanisms by Saul Winstein; (8) Fundamental Aspects of Rubber Elasticity by Herman F. Mark; (9) Carbon-fluorine Compounds, A New Field

of Chemistry by Nelson W. Taylor; (10) Silicoes by Eugene G. Rochow; (11) The Petrochemical Industry by Theodore W. Evans; (12) Some Chemical Relations in the Earth by George C. Kennedy; (13) Creep of Metals as a Reaction-rate Phenomenon by John E. Dorn; (14) Crystal Chemistry and Pyrochemistry of Clay Materials by Joseph A. Pask; (15) New Developments in Food Technology by Donald K. Tressler; (16) The Biochemistry of Insecticides by Robert L. Metcalf; (17) Some Relations between Chemical Constitution and Physiological Action by Gordon A. Alles; (18) Chemical Synthesis in Living Organisms by Theodore A. Geissman; and (19) The Configuration of Polypeptide Chains in Proteins by Linus Pauling.

A successful attempt such as this made to present a wealth of scientific details with all its implications and potentialities in such a lucid manner by masters is sure to find a worthy response.

S. R. PALIT

ENGINEERING ANALYSIS — A SURVEY OF NUMERICAL PROCEDURES by S. H. Crandall (McGraw-Hill Book Co., New York), 1956. Pp. x + 417. Price \$ 9.50

In this publication, a much needed text on the above subject is met for the benefit of engineers and physicists working on the solution of engineering problems of great complexity. Several methods have been developed for the reduction of complex mathematical problems to a numerical procedure. The text is a collection of lectures given at the Imperial College of Science and Technology, London, and in the Massachusetts Institute of Technology, U.S.A.

The treatment of the subject by the author is unique and detailed to give the reader an insight into the methods employed and a physical picture of the merits and demerits of the various methods employed. The problems dealt with are concerned with equilibrium, Eigen value and propagation encountered in a variety of cases in the field of Applied Physics and Engineering. Another feature of the text is the large number of practical problems worked out as illustrations and the comprehensive treatment of the subject including non-linear systems in a manner to help the solution of complex engineering problems by employing the numerical methods on a desk calculator.

The book will be an important and useful addition to any library.

N. SRINIVASAN

PHARMACOGNOSY OF AYURVEDIC DRUGS (KERALA) by K. Narayana Aiyar, A. N. Namboodiri and M. Kolammal (The Central Research Institute, University of Travancore, Trivandrum), Series I, No. 3, 1957. Pp. iv + 109. 37 plates

The third number of this interesting and useful series contains a study of 11 more ayurvedic drugs and covers 20 plant species belonging to 10 different genera. As in previous issues, each ayurvedic drug is authenticated with quotations from various Sanskrit works. This is followed by a descriptive narration of the botanical characteristics of the plant or plants to which the drug is attributed. Each description includes the botanical name of the plant with its synonyms, vernacular names, distribution of the plant in India, its habitat, general external features, morphological characteristics of the leaves, flowers and fruits and an anatomical study of the parts considered official. The botanical descriptions are supported with neatly executed colour plates and line drawings depicting the external and internal characteristics of the plant parts examined. Histological details are confined mainly to the root and stem barks.

The work as stated in part one of this series, is intended to correlate scientifically a particular ayurvedic drug with its proper botanical source. In Kerala where the ayurvedic drugs are extensively used, a clarification such as the one attempted here is essential, since many vernacular names have come to be applied to more than one species. While appreciating the highly useful nature of the work done, particularly the detailed description of the plant parts considered official, supported with neatly executed drawings, it is rather unfortunate that a large number of mistakes have been made in the nomenclature of the plants dealt with. The names need checking up, as regards their correct usage, correct spelling and proper citation of the authority, as per rules of international nomenclature. In some cases even certain avoidable mistakes have not been remedied. For example, the illustrations of the common Nim tree are titled *Melia azadirachta*, while the descriptions are

covered under the title *Azadirachta indica*. Even in giving the former name, the specific epithet starts with a capital in one plate and lower case in another. A similar spelling mistake occurs regarding the name *Melia azedarach*. The specific epithet *azedarach* is spelt *azadarach* in the two plates. A mistake fairly common throughout the work is the citation of author's name without a fullstop whenever it is abbreviated: such names as Linn., Benth., Willd., Spreng., etc., appear frequently without a stop. Lastly, one is left guessing whether *Ficus* belongs to Urticaceae or Moraceae. Under *F. glomerata*, name Urticaceae is given within brackets indicating Moraceae as preferable, but all other species are given under Urticaceae.

OLIVE OIL PROCESSING IN RURAL MILLS prepared by G. Frezzotti, M. Manni & A. Aten (Food & Agriculture Organization, United Nations, Rome), 1956. Pp. viii + 103. Price \$1.00 or 5s.

In this handy publication of about 100 pages published by the Food and Agriculture Organization of the United Nations, the methods of olive oil processing from the cultivation of the fruit up to the refining and storage of the oil have been dealt with concisely and in simple language. The book is well illustrated and attractive. Very useful information has been supplied which is of particular interest for those countries in which olives are produced and processed.

The subject matter has been appropriately divided into several sections. The earlier sections deal with the methods of cultivation of the olive tree and of harvesting, collecting, transportation and storage of olives. Also the composition of the fruit, oil and the cake as well as the world statistics on production of olive fruit and its oil have been given. The sections which follow, deal with the processing methods and machinery both of the old and modern types. The latter sections describe the methods of clarification and storage of the oil and precautions to be taken when shutting down the plant at the end of the season.

Lastly, the latest trends in olive oil processing have been given, the chief of them

being centrifugal treatment of olive paste in place of the pressing techniques and the continuous pressing in place of the old discontinuous process.

OM PRAKASH

## PUBLICATIONS RECEIVED

SWITCHGEAR PRINCIPLES by P. H. G. Crane (Cleaver-Hume Press Ltd., London), 1957. Pp. vii + 238. Price 25s.

JOURNAL OF THE MADRAS UNIVERSITY — CENTENARY NUMBER (Vol. 27B, January 1957), with a Supplement. Edited by Prof. T. S. Sadasivan (Madras University, Madras), 1957. Pp. vi + 286; Suppl. iii + 128. Price Rs. 4.00

UNSTABLE CHEMICAL SPECIES: FREE RADICALS, IONS AND EXCITED MOLECULES — *Annals of the New York Academy of Sciences* (The New York Academy of Sciences, New York), 1957. Pp. 447-670

VITAMIN A by T. Moore (Cleaver-Hume Press Ltd., London for Elsevier Publishing Co., London), 1957. Pp. xx + 645. Price 76s.

STRENGTH OF MATERIALS by G. H. Ryder (Cleaver-Hume Press Ltd., London, for Elsevier Publishing Co., London), Second Edition, 1957. Pp. x + 337. Price 22s. 6d.

PRINCIPLES OF ENGINEERING INSPECTION by G. K. King & C. T. Butler (Cleaver-Hume Press Ltd., London), 1957. Pp. viii + 264. Price 25s.

A HANDBOOK OF SOFTWOODS (Her Majesty's Stationery Office, London), 1957. Pp. vii + 73. Price 8s. 6d. net

LA DIFFUSION DANS LES METAUX by J. D. Fast, H. G. Van Bueren & J. Philibert [Bibliothèque Technique Philips, Netherlands; *Distributors in India*: Philips Electrical Co. (India) Private Ltd., Bombay], 1957. Pp. 134. Price 37s. 6d.

INDUSTRY AND TECHNICAL PROGRESS — FACTORS GOVERNING THE SPEED OF APPLICATION OF SCIENCE by C. F. Carter & B. R. Williams (Oxford University Press, London; *Distributors*: Oxford University Press, Bombay), 1957. Pp. viii + 244. Price 25s. net

AN ATLAS OF THE COMMONER PAPER MAKING FIBRES — AN INTRODUCTION TO PAPER MICROSCOPY by F. D. Armitage (The Guildhall Publishing Co. Ltd., London), 1957. Pp. 172. Price £ 3.3s.

GOLDEN JUBILEE COMMEMORATION VOLUME — PROGRESS OF THE MINERAL INDUSTRY OF INDIA, 1906-55 (The Mining, Geological & Metallurgical Institute of India, Calcutta), 1957. Pp. 567

A PRACTICAL GUIDE TO PLANT SOCIOLOGY by F. R. Bharucha & W. C. De Leeuw (Orient Longmans, New Delhi), 1957. Pp. viii + 46

THE PHYSIOLOGY OF FISHES: VOL. I — METABOLISM. Edited by Margaret E. Brown (Academic Press Inc., New York; *Distributors*: Asia Publishing House, Bombay), 1957. Pp. xiii + 447. Price \$12.00

# NOTES & NEWS

## Element 102

A NEW ELEMENT 102 HAS BEEN produced by bombarding curium 96 with carbon ions accelerated in a cyclotron at the Nobel Institute, Stockholm. The element named *Nobelium* is a new link in elaborating the structure of the atom.

## New radio channels

A NEW METHOD OF RADIO COMMUNICATION over long distances similar to the audible radio waves produced by lightening, has been developed by Dr. R. A. Helliwell and Dr. E. Gehrel of the Stanford University. The artificial signals known as 'whistlers' made of radio energy in the very low frequency range travel from one hemisphere to another along the earth's magnetic lines of force, reaching at least 8000 miles into space during their journey. An antenna hooked to an amplifier suffices to tune in these semi-musical sounds. The descending pitch of whistlers is caused by slower transit of low frequency waves as they follow the magneto-ionic duct, making them gradually lag behind the faster moving higher pitched waves [*Sci. Newslett., Wash.*, 71 (1957), 355].

## A new ferroelectric material

RESEARCH WORK CARRIED OUT at the Bell Telephone Laboratories with a view to add to the number of substances like barium titanate, known to possess desirable ferroelectric properties, has led to the discovery of triglycine sulphate possessing promising characteristics—even superior to those of the available materials—for use in switching and memory devices.

A rapid switching time, a low switching voltage and perfect retention of the amount and correct direction of the polarization till further switching are essential features of a memory and switching device. The suitability of triglycine sulphate for use in a memory or switching device arises from its desirable properties detailed below: (1) chemical stability, i.e. it does not decompose when exposed to moisture or the atmo-

sphere; (2) adequate mechanical strength to permit handling in thin sheets; (3) ease of growing large, single crystals and cutting large-area slices from them; (4) lower coercive field, permitting a lower switching voltage; (5) insusceptibility to fatigue by repeated switching; and (6) retention of polarization indefinitely without deterioration. The polarization of this compound results in a lower output pulse when switched; however, the size of the pulse can be increased by increasing the area of the switching electrode. Heating beyond its curie point (c. 47°C.) causes the material to lose its ferroelectric properties but they are restored completely when it is cooled. Also, the curie point can be raised up to 60°C. by replacing some of the hydrogen atoms with deuterium which can be easily accomplished while the crystal is being grown.

Electrodes can be applied to a slice cut from a single crystal by evaporating thin strips of metal on each side of the slice, the strips on one side being perpendicular to those on the other. Thirty or more strips per inch can be applied, resulting in a memory or switching device capable of storing 900 or more 'bits' of information on a square inch of the crystal. A number of such slices can be assembled in a relatively small volume, resulting in a very compact assembly.

The thickness of the slice can be from 5 to 10 mils, depending on the available pulsing voltage and the desired output. Switching can be accomplished with about 20 V., a value easily obtained with transistorized circuitry. The actual power required for switching is very small, thus minimizing internal heating. Switching times of the order of 1-2  $\mu$ sec. are easily obtained with this new material [*News from Bell Telephone Laboratories*].

## Radioactive fallout risk

IN PINPOINTING THE HAZARDS OF fallout, Willard F. Libby, Atomic Energy Commissioner, U.S.A., said that the  $\text{Sr}^{90}$  present in the stratosphere will fall out at a rate equal to the decay of the material

already deposited. Thus no additional increase in  $\text{Sr}^{90}$  from weapons fired in the past is likely. The  $\text{Sr}^{90}$  tolerance set for general public is 100 mc./g. of body calcium or 100 sunshine units. Currently adult body contains 0.1 or 0.2 sunshine unit while children have c. 0.5 unit. If testing continues at the rate of the past five years, according to Libby, 4-15 sunshine units of  $\text{Sr}^{90}$  will accumulate in human bones during the next 50 years. Work relating the calcium effect to  $\text{Sr}^{90}$  uptake by humans shows the increase in  $\text{Sr}^{90}$  in food due to low calcium soils can hardly be more than fivefold for a fiftyfold deficiency. Where normal soil carries c. 20 g. of available calcium in the top 2.5 in., a region with only 0.4 g. would produce a human body burden five times greater than that built up from foods grown in the normal soil.  $\text{Sr}^{90}$  content in humans also depends on the amount of fallout in a given area. For average soil areas, a body burden between 1.7 and 3.9 sunshine units is produced. Among people living in the same locality, only one person in 300 will have more than twice the average  $\text{Sr}^{90}$  burden [*Chem. Engng. News*, 35(19) (1957), 38].

## A new uranium mineral

A NEW URANIUM MINERAL, NAMED Boltwoodite, after Bertram Boltwood, the radiochemist of Yale University, has been discovered at Pick's Mine, at the western edge of the San Rafael Swell, Emery County, Utah. Its composition approximates to  $\text{K}_2(\text{UO}_2)_2(\text{SiO}_3)_2(\text{OH})_2 \cdot 5\text{H}_2\text{O}$ , and it is related to the magnesium uranyl hydroxysilicate named sklodowskite (after Madam Curie). It is a yellow, fibrous ore, derived from black uranium minerals by aerial oxidation with gypsum, brochantite and becquerelite. It is the only known uranium ore containing an alkali metal [*Atomics*, 8 (1957), 237].

## Elastic moduli of diamond

AN ULTRASONIC TECHNIQUE FOR accurately measuring the elastic moduli of diamond and a variety of other small specimens has been developed at the Bell Telephone Laboratories.

The technique consists in determining the velocity of ultrasonic waves through the specimen from which, knowing the density, the



elastic moduli can be calculated. For diamond both longitudinal and shear waves were used.

Two type I single crystals which, before cutting, were natural dodecahedrons of a pale yellow colour and quite transparent, were used. Flat and parallel surfaces were ground on opposite sides of the diamond and the thickness measured accurately. The specimen was fastened to one end of a fused silica 'buffer' rod by means of a thin film of a viscous liquid. To the opposite end of the buffer was attached a suitable quartz transducer. Ultrasonic waves at frequencies up to 200 Mc/s. generated by the transducer were continuously transmitted along the buffer rod and were principally reflected at the buffer-specimen interface and were also partially transmitted into the specimen and reflected back and forth between its parallel surfaces, resulting in a series of multiple reflections. At certain critical frequencies these echoes were precisely in phase and combined to give rise to a characteristic pattern on an oscilloscope to which the transducer was connected. The velocity was calculated from these frequencies and the specimen thickness; knowing the density, the adiabatic elastic constants were computed. The elastic moduli, expressed in  $10^{12}$  dyne/sq. cm., were found to be  $10.76 \pm 0.6$  per cent for  $C_{11}$ ;  $1.25 \pm 5.4$  per cent for  $C_{12}$  and  $5.76 \pm 0.3$  per cent for  $C_{44}$ . The value for  $C_{11}$  agreed reasonably well with previous measurements; the value for  $C_{12}$ , however, was much smaller and that for  $C_{44}$  larger than that reported by other workers.

With suitable auxiliary equipment, the method can be applied to specimens under widely varying conditions of temperature and pressure [*News from Bell Telephone Laboratories*].

### New type of flare

A RARE TYPE OF CHROMOSPHERIC flare has been reported from the Division of Physics, C.S.I.R.O., Australia. An ejection, c. 10,000-30,000 km. in size, occurred several minutes before flare maximum and moved outward with an unusual velocity of 300 km./sec. across the line of sight. As it moved, it brightened up appreciably reaching maximum intensity  $3\frac{1}{2}$  min. after expulsion, its height then being 25,000 km. above the sun's surface at 0007

U.T. The ejection was quite unlike the dark surge prominences often emitted from flares; except for its motion, it possessed all the properties of a small flare, like brightness of ejection, rise to a maximum and concentrated appearance, etc. [*Aust. J. Phys.*, **10** (1957), 319].

### Origin of 'dawn chorus'

A STUDY CONDUCTED AT THE Dominion Physical Laboratory, New Zealand, of the audio-frequency phenomenon known as 'dawn chorus', closely akin to whistlers, has yielded much information on the characteristics and probable nature of the phenomenon. The data have been collected at two stations, Wellington and Dunedin (geomagnetic latitudes  $45^\circ\text{S}$ . and  $50^\circ\text{S}$ . respectively), during the period July 1955-Oct. 1956. A loop aerial was used for the reception of the signals which, after passing through an amplifier of about 80 db. gain and of band-pass between 1 and 7 kc/s., were recorded on magnetic tape on a schedule of 4 min. recording every 3 hr. on two days per week commencing at 0235, 0535 ... 2335 U.T.

The study of whistlers at various latitudes has been giving useful information on the electron density and the earth's magnetic field at heights well above the level of maximum ionization of the presently highest known ( $F_2$ ) ionospheric layer. Unlike whistlers where the pitch of the whistling tone steadily falls, dawn chorus consists of many rising tones (typical frequency range, 2-4 kc/s.) and is likened to the sound of a distant rookery. The phenomenon was called 'dawn chorus' from the observation that with its marked diurnal variation over a wide range, its intensity reaches a peak generally at about dawn. Its occurrence has also a marked correlation with the magnetic activity.

A comparative study of the data collected at Wellington and Dunedin with that obtained from three other stations in North America led to the following conclusions: There is a significant association between neighbouring and magnetically conjugate stations, and a weak association between distant non-conjugate stations except for instances of worldwide occurrence of dawn chorus; some degree of simultaneity at neighbouring stations, as in the case of whistlers, is observed with

dawn chorus too, with an occasional 'burst' of activity; coincident bursts have been identified at two stations 600 km. apart; there is considerable evidence to assume that the same bursts are heard at conjugate stations (as far apart as Wellington in New Zealand and Unalaska in Aleutian Islands).

A study of diurnal variation curves for the stations, College (Alaska), Cambridge (England), and for Wellington and Dunedin showed that only in middle latitudes is the dawn chorus a predominantly dawn phenomenon.

Because of the magnetic linkage, simultaneous reception of dawn chorus would be expected if dawn chorus signals also are propagated along the lines of force, as in the case of whistlers. Hence, the above results suggest that both the propagation path and the magneti-ionic mode of propagation are the same for both dawn chorus and whistlers. It is thus probable that dawn chorus consists of electromagnetic radiation which is propagated in the extraordinary mode along the lines of force of the earth's magnetic field. The rising tone must have originated at the source itself as it cannot be caused by the dispersive properties of the medium.

Based on the above observations a hypothesis has been put forward that the dawn chorus signals are generated in the vicinity of the geomagnetic equatorial plane. A polar diagram drawn between the local geomagnetic time (angular co-ordinate) and the height above the equator of the magnetic line of force passing through the observing station (radial co-ordinate) showed it to be characteristic of the locus of a positively charged incoming particle travelling in the equatorial plane and being deflected by the earth's magnetic field. This evidence warrants the assumption that the charged particle may be of solar origin. It is suggested that a cloud of such particles excites ions already present in the outer ionosphere. These ions would then re-emit the excess energy acquired as electromagnetic radiation at a natural resonance frequency which increases as the incoming cloud penetrates to lower heights [*Aust. J. Phys.*, **10** (1957), 286].

### South Pole temperatures

THE RESULTS OF THE FIRST SOUNDINGS of temperatures at the

Amundsen-Scott South Pole station established for the International Geophysical Year observations have been announced. The lowest temperature observed thus far at the South Pole is  $-89^{\circ}\text{F}$ . (on 2 April 1957) which is lower than the lowest ever recorded for North America, viz.  $-81^{\circ}\text{F}$ . observed at Snag, Yukon Territory, Canada, in February 1947 and is only  $1^{\circ}$  above the world's record of  $-90^{\circ}\text{F}$ . noted in north-eastern Siberia. The temperatures are expected to drop further down to  $-120^{\circ}\text{F}$ . as the South Pole midwinter approaches.

The study of temperatures and the circulation of air in the Antarctic will yield knowledge of the polar icecap and its effect on the world's weather and world climate. Comparison of the relatively clean air of the Antarctic with the atmosphere of coal and oil-consuming regions is expected to give data on the 'greenhouse' effect supposed to be caused by the release of large amounts of carbon dioxide [*Science*, **125** (1957), 925].

### Stellarator at Princeton

THE U.S. ATOMIC ENERGY Commission has approved plans for the design and construction of a large experimental device for research on controlled thermonuclear reactions at the Forrestal Research Centre at Princeton University. The machine, named the Model C Stellarator (coined for *stellar* and *generator*) will be exclusively a research tool meant for experimental work which cannot be performed as effectively with smaller models.

The stellarator consists of a hollow tube containing ionized gas. Around the tube are external coils which produce a magnetic field to confine the gas. The research programme aims at heating the gas to temperatures of millions of degrees and at the same time to confine the heated gas within the tube long enough to allow fusion reaction to take place. Experiments with the stellarator are expected to begin by 1961 [*Science*, **125** (1957), 981].

### Recent advances in spectroscopy

A CONFERENCE ON SPECTROSCOPY held in the Department of Chemistry, University of W. Australia, during 20-21 February 1957 devoted itself to some recent develop-

ments in spectroscopy. The major theoretical advance in recent years has been the introduction of the free electron approximation in quantum mechanics and its subsequent development. New techniques of special importance are the magnetic methods based on nuclear and electron spin resonance which can provide useful chemical information. Other notable advances in technique are echelle spectroscopy, the high intensity Raman source, the development of multiple-pass spectroscopy and a method of analysis based on atomic absorption spectra. Also of importance are the developments of direct-reading vacuum ultraviolet spectroscopy and of electron-impact spectroscopy. Important new observations include the measurement of rotational Raman spectra, the discovery of intermolecular combination bands, and the discovery of spurious bands in solution spectra near the edge of intense solvent absorption bands.

The infrared absorption due to free and hydrogen-bonded (intramolecular) hydroxyl groups in a series of cyclohexane-1, 2-diols, each of which carries one or two other substituents of different sizes in the axial (a) and/or equatorial (e) position, was described.

A new electrodeless source for obtaining the necessary intensity for Raman spectra consists essentially of an annular jacket containing a rare gas and an alkali metal or mercury. For excitation a high frequency diathermy source (2-450 Mc/s.) provides extremely intense illumination. By using caesium as the alkali metal, a Raman source of wavelength 8521 Å is possible. Very few molecules absorb appreciably in this region.

The intensities of the  $\text{C}=\text{O}$  stretching frequency in acetone and other ketones, of the  $\text{C}\equiv\text{N}$  stretching frequency in a series of aliphatic and aromatic nitriles, and of the  $\text{S}-\text{H}$  stretching frequency in several mercaptans were measured in a series of solvents with a wide range of dielectric constants. All the spectra showed changes of intensity with change of solvent, the change being particularly large for the  $\text{C}\equiv\text{N}$  and the  $\text{S}-\text{H}$  bands. The general trend observed was that intensities increase with the dielectric constant of the solvent, but there are marked individual exceptions to this rule. The results could not be ex-

plained on the basis of the current theories.

The theory of solvent effects presumes that in general, the nearest-neighbour environment of a particular solute molecule is unsymmetrical. The perturbation due to the environment can be expressed in terms of three components, which are respectively independent, and even and odd functions of the co-ordinates. The application of first-order perturbation theory makes it possible to set up a formal expression for the transition moment in solution. A significant result is that not only transitions which are allowed in the free molecule will be altered in intensity, but also that transitions which are totally forbidden in the free molecule will acquire a first-order transition moment in solution owing to the operation of the unsymmetrical part of the perturbation. This general theory can be applied to the intense ultraviolet band shown by halogens in aromatic hydrocarbon solutions. Although this band has been attributed to complexes, the present theory suggests that it is more likely to be associated with a known totally forbidden transition in the free molecule.

Changes in the ultraviolet spectrum of *s*-trinitrobenzene with the composition of seven binary solvent mixtures all containing aniline and covering the complete composition range were described. Aniline was chosen because of its notable effect in enhancing the absorption in the 4000 Å region. On plotting the results in accordance with Scott's rearrangement of the Ketelaar equation, which predicts a straight line for 1:1 solute-solvent complex formation, and from which the equilibrium constant can be determined, it was noted that points of discontinuity appeared in the vicinity of 0.5 aniline mole fraction in all the seven systems showing that, although linear plots could be drawn in several cases on both sides of the point, they are incompatible with the postulate of complex formation. In the two systems hexanol-aniline and ethylene glycol-aniline, the effect of temperature on the *s*-trinitrobenzene spectrum was studied. The heat of formation was calculated on the highly improbable assumption that one of the plots on either side of the point represented solvation. In both systems the *H* values were low and their sign changed on



either side of the point of discontinuity. It is suggested that the point of discontinuity indicates a molecular rearrangement arising in the course of a physical perturbation.

The causes of certain anomalies in the spectrum of iodine were mentioned. These anomalies are lack of reproducibility of the molar extinction coefficients,  $\xi$ , high values of the coefficients in the region 4000-2200Å, and a sharp rise in the spectral curve from approximately  $\xi=100$  to  $\xi=600$  in the region 2100-2000Å. Furthermore, a shift of the order of 500 kaysers, generally towards longer wavelengths, has been observed in the peak of the curve in the visible region. The anomalies are very probably due to the formation of an adsorbed iodide layer on the end-windows of the cell. Experiments on cells made up with internal windows, which allow greater concentrations of the adsorbed layer, have shown the expected increase in the molar extinction coefficients.

In the final session of the Conference the analytical advantages of absorption spectroscopy and the technique of measuring atomic absorption spectra were described. Analyses by emission spectra lack sensitivity since even at very high temperatures only a small proportion of atoms is excited to emission, while almost all the atoms are potential absorbers. Measurements of absorption spectra, which are free from complications such as inter-element effects, self-absorption and self-reversal, therefore, have many advantages. Rather than use a continuous source, it is more feasible to measure the absorption coefficient at the centre of the line using a sharp-line source such as a hollow-cathode discharge tube. Modulation of the incident radiation is necessary to avoid recording radiation emitted by the vaporized sample. By using copper as standard, it has been possible to determine approximately the oscillator strengths of a number of elements. While the method has proved successful for the analysis of many elements, some, such as aluminium, are not atomized in a flame. Samples have been vaporized both from solutions sprayed into a flame, and from alloys by a sputtering discharge through a rare gas. In the latter case inter-element effects are present, but the

method is likely to prove useful both for analysis and for the study of sputtering behaviour. Several optical variants of the apparatus used were described.

A grazing-incidence high-vacuum spectrometer constructed specifically for the study of the soft X-ray band emission spectra of metals in the range 50-1000Å was described. The spectrometer utilizes two interchangeable ruled aluminium gratings with 570 and 1150 grooves/mm. The diffracted, focused radiation is detected by an Allen-type, open, beryllium-copper photomultiplier and attached analyser slit, which are mechanically driven around the Rowland circle. The output pulses from the multiplier are amplified and counted on a counting rate meter; a continuous record of detected intensity is given by a recording potentiometer as the analyser slit traverses the spectrum. In such an instrument the resolution achieved depends not only on the optical resolution of the combination of grating and slits, but also on the statistical deviation and response-time of the counting rate meter and the speed of traverse of the spectrum. A certain minimum speed is fixed by considerations involving long and short-term contamination of the specimen surface and consequent modification of the observed band shape. A study has been made of the variation of contamination of specimens with time by observing the fall in intensity at a particular wavelength as the contamination proceeds. The 'roll-over' on the high-energy side of the peak of the lithium-potassium spectrum has been indisputably observed. The 'emission edges' observed for the *M*-spectrum of copper also were not observed with the present instrument.

The luminescence of the alkali halides irradiated in the vacuum ultraviolet was described. The variation in fluorescence efficiency with respect to exciting wavelengths for some KCl:Ti and KI:Ti phosphors was studied in the wavelength region 900-2300Å. At long wavelengths, this was found to be correlated closely with the transmission spectrum of the pure crystal. This was considered evidence that only direct excitation of the  $Tl^+$  centres occurred and that no excitation-induced fluorescence took place. A fluorescence growth under steady excita-

tion and a phosphorescence decay in the dark were observed at wavelengths less than those corresponding to the series limit for the respective crystals. This was interpreted in terms of a series of trapping and excited energy levels in  $Tl^{2+}$ . A series of experiments on photoconductivity gave negative, though not necessarily conclusive, results at wavelengths less than that generally accepted for the series limit [*Nature, Lond.*, **179** (1957), 1340].

## Mass spectrometry

THE USE OF MASS SPECTROMETRY as an analytical technique for microanalysis has been growing in importance. The amount of sample required is extremely small, e.g. *c.* 1 ml. of gas at N.T.P.

In the mass spectrometer the molecules of the sample gas are ionized by electron impact and the resulting charged fragments are accelerated in an electric field. A constantly changing magnetic field constrains the particles to move in curved paths and impinge on a collector in order of their mass. Reproducibility of results is ensured by the fact that for the given instrument over short periods of time the relative abundances of the fragments is constant and provides a unique and characteristic 'cracking pattern' for each compound. When the mass spectrometer is used for the qualitative analysis of completely unknown mixtures, no specific tests are required and provided that a sufficiently wide mass range has been scanned, all the information is contained within the spectrum, whatever the nature of the mixture. The interpretation of the spectrum is based upon a knowledge of isotope abundance ratios, the probability of peaks due to doubly charged ions or to metastable species, the cracking patterns characteristic of many of the simpler compounds and of the more common functional groupings. By a study of the reference catalogue of the mass spectra of organic compounds, it is possible to detect the similarity in the spectra within certain classes of compounds and it provides a basis for the detection of light paraffins in the presence of heavier hydrocarbons, for the differentiation of straight chain and highly branched hydrocarbons, for the detection of oxygenated compounds such as ethers, alcohols and esters in

hydrocarbon mixtures and for the identification of aromatic types. A knowledge of isotope abundance ratio is made use of in the qualitative analysis of halogen compounds, e.g. if a compound contains a single chlorine atom then any mass peak due to an ion containing the chlorine atom will be duplicated two mass numbers higher but one-third the size. The inclusion of a second chlorine atom in the ion leads to the formation of two subsidiary peaks two and four mass numbers higher respectively.

Mass spectrometry is useful in the analysis of multicomponent mixtures of gases and low boiling liquids found in the process streams of oil refineries. Recent modifications of the mass spectrometer have enabled it to be used in the analysis of the hydrocarbons containing 40 C atoms and having molecular weights in the region of 600.

The isotope dilution method may be used in conjunction with the mass spectrometer to determine the percentage of oxygen in an organic compound. This is achieved by combusting the sample in  $O^{18}$  and measuring the concentration of this isotope in the  $CO_2$  produced. The method is also applicable to sulphur determination using  $S^{34}O_2$  as the tracer substance. Many volatile compounds have been examined by first submitting them to pyrolysis and then passing the volatile pyrolysis product into a mass spectrometer.

Mass spectrometry may be used for plant monitoring and control of process streams, for elucidation of reaction mechanisms or kinetics, for detection of minute quantities of a chemical in the bulk of other substances, i.e. in leak detection in vacuum systems, and for tracer studies on biological systems [*Chem. Prod.*, **20** (1957), 252].

### The colour of ruby

AN EXPLANATION FOR THE OBSERVED distinct red colour of the ruby, which is consistent with all the available experimental evidence, has been given by Dr. L. E. Orgel of the Department of Theoretical Chemistry, University of Cambridge.

The optical properties of ruby are considered anomalous. While rubies which consist of a small quantity of  $Cr_2O_3$  dissolved in  $Al_2O_3$  matrix are expected to be green in colour from the

observed colour of the prepared solutions of such compositions, actually the rubies are unmistakably red. The red solutions of  $Cr_2O_3$  become green on heating but revert to their original colour on cooling. This colour reversal on cooling rules out the probability of the change in colour being connected with the antiferromagnetic exchange coupling which is possible in  $Cr_2O_3$ . Evidence from magnetic and other studies excluded any suggestion to explain the observed facts on the presence of an oxidation state of chromium other than three.

Correspondence between the spectra of extensively studied hydrated ions (for which fairly complete assignments have been made and successfully interpreted by means of the crystal-field theory) and the transition-metal ions dissolved in glasses and other oxide materials is very close, provided the metal ion is octahedrally coordinated in the host lattice.

Orgel put forward the hypothesis that though the Cr ions are octahedrally co-ordinated (the corundum structure definitely supports this view), they are subjected to an anomalously large crystal field, in terms of a slight compression of the Cr ion.

The red colour of ruby is due to an absorption band with a maximum at  $c. 19,000 \text{ cm}^{-1}$ . This gives a 20 per cent increase of the crystal field parameter  $\Delta$ , in ruby, relative to that in other oxide materials which in the electrostatic theory ( $\Delta \propto R^{-5}$ ) corresponds to a reduction of the metal-anion distance by 4 per cent, i.e. Cr-O distance is reduced by about 0.08 Å.

Orgel's interpretation is strongly supported by the work of Thilo and co-workers. The latter have shown that at room temperatures  $Al_2O_3-Cr_2O_3$  solutions containing up to 8 atom-per cent  $Cr_2O_3$  are red in colour, but that solutions containing a greater amount become progressively more green. Also there is little change in the lattice parameter of  $Al_2O_3$  until 8 atom-per cent of  $Cr_2O_3$  has been added and then the lattice parameters increase linearly until those for pure  $Cr_2O_3$  are reached. The temperature at which the colour transition occurs is also observed to decrease with the concentration of the chromium ions presumably because the lattice relaxation takes place more easily when a larger amount of chromium ions is

present. The same mechanism as in ruby is possibly at work in the cases where certain  $Cr^{3+}-Al^{3+}$  spinels are also red when the chromium ion concentration is sufficiently low, but green otherwise [*Nature, Lond.*, **179** (1957), 1348].

### Gamma irradiation and origin of life

THE PRODUCTION OF SIMPLE organic compounds including amino acids by irradiating ammonium carbonate by gamma radiation from a cobalt-60 source reported by General Mills Research Laboratories, Minnesota, is probably the first instance in which amino acids have been directly obtained from completely oxidized forms of carbon in the absence of free hydrogen. Gamma radiation from terrestrial sources is considered a more probable agent than lightning and sunlight for the generation of most of the 'organic milieu', the non-living mixture of carbon compounds which is generally considered to be a prerequisite for the origin of life.

Ionizing radiation can cause the destruction of organic compounds as well as affect their formation. Therefore, the organic substances would not concentrate on even a sterile earth unless some great shield were available to protect them once they are formed. The seas could be this shield. Inorganic and simple organic compounds on or close to radioactive sources, especially gamma emitters above or below the sea, could be transformed into amino acids. These amino acids, with the help of rain and ocean currents, could migrate to dark, non-radioactive areas where they could be accumulated and oriented by adsorption on clays or quartz (as sand).

There appears to be little doubt that enough radioactivity to accomplish such reactions existed after the earth had cooled sufficiently to permit condensation of the water vapour to form the oceans. An upper limit on the irradiation time may be obtained if it is assumed that the terrestrial radioactivity was the same as it is today. Considering the three major series ( $U^{238}$ ,  $4.5 \times 10^9$  yr;  $Th^{232}$ ,  $13.9 \times 10^9$  yr; and  $U^{235}$ ,  $0.7 \times 10^9$  yr), allowances for decay would not result in significantly greater magnitudes. High-activity ores existing today could deliver the necessary radiation doses in

tens of years [*Science*, **125** (1957), 881].

### Viable count of bacteria

IN A NEW TECHNIQUE FOR COUNTING living bacterial cells developed at the Institute of Nuclear Physics, Calcutta, bacteria were grown in the nutrient broth, to 100 ml. of which 1 g. of 2, 3, 5-triphenyltetrazolium hydrochloride was added. Bacteria were inoculated on nutrient agar slants and after incubation for 18 hr. they were washed with 5 ml. sterile nutrient broth. The number of bacteria per ml. in this slant-washed suspension was counted. The nutrient broth with the tetrazolium salt was inoculated with 1 ml. of that suspension and incubated at 37°C. After incubation for 1 hr. the number of bacteria in the broth was counted with the conventional haemocytometer, using 4 per cent formalin as diluting fluid. Formalin kills the bacteria and at the same time fixes them. Moreover, formalin does not impair the effect of tetrazolium salt in staining the bacteria. The killed and fixed bacteria were counted with the ordinary light microscope having objective with 0.65 N.A. and 12x eyepiece. The living bacteria were observed to have a reddish tinge whereas the dead cells were completely transparent. The fact that the stained cells were alive was proved by their ability, before treatment with formalin, to produce a colony when inoculated, whereas the unstained bacteria did not develop any colonies [*Nature, Lond.*, **179** (1957), 1360].

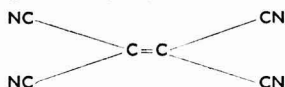
### Steric effects in alkylbiphenyls

RECENT ULTRAVIOLET SPECTROSCOPIC studies on the effects of substitution in the biphenyl chromophore have shown that the changes in the ultraviolet absorption spectra which accompany substitution in the *ortho* positions of the biphenyl system were closely paralleled by correspondingly large changes in the relative retention volumes of the compounds. A number of alkyl-substituted biphenyls were prepared and were checked for their purity by the use of gas-liquid chromatographic apparatus in the National Institute of Medical Research, London. It was observed that for all compounds unsubstituted in 2 or 6 (*ortho*) positions, values for the

retention volume increments (*i*) for each additional carbon atom ( $\text{CH}_2$ -separation factor) varied from 1.46 to 1.69, whereas if substitution occurred in these positions values for *i* did not exceed 1.26 even in the presence of additional substitution elsewhere. For normal straight chain aliphatic hydrocarbons, the value of *i* under the same conditions was 1.54 and the substitution of alkyl groups in the *meta* and *para* positions of biphenyl gave values of *i* which might be regarded as normal. The values for *para* substitution (1.56-1.65) were greater than those for *meta* substitution (1.46-1.55), since the overall conjugation and hence degree of interaction with the stationary phase is slightly increased in the *para*-substituted biphenyls by hyperconjugation. The greatly reduced values of *i* in *ortho*-substituted alkylbiphenyls are presumably due to a correspondingly reduced degree of interaction with the stationary phase and it is attributable to the reduction in overall biphenyl type conjugation in these sterically hindered compounds where the minimum possible angle between the benzene plane rings is quite large. A comparison of the chromatographic behaviour in the vapour phase of various partially reduced polycyclic aromatic hydrocarbons shows that decreased conjugation produces large decrease in retention volume. The increase in the size of the individual substituents group induces greater steric effect, e.g. *isopropyl* group in *ortho* position has a greater steric effect than a *n-propyl* group and the retention volume is considerably smaller [*Nature, Lond.*, **179** (1957), 490].

### First percyano-olefin

FUNDAMENTAL STUDIES ON CYANOCARBONS and their derivatives have led to the preparation of tetracyanoethylene, the first example of a percyano-olefin:



The compound is exceptionally reactive and readily undergoes a series of addition and substitution reactions. Tetracyanoethylene is used as an intermediate for preparing other cyanocarbons, e.g. metal salts of pentacyanopropylene; very strong acids—hexa-

cycanoisobutylene; heterocyclic compounds including pyrroles, thiophenes, pyrazoles, isoxazoles, naphthyridines and pyridines; and highly coloured compounds of high extinction coefficient. Tetracyanoethylene is synthesized by refluxing dibromomalononitrile-potassium bromide complex with copper powder in benzene (yield 65 per cent) [*Chem. Engng. News*, **35** (20) (1957), 28].

### Gastro-intestinal physiology

A NEW RADIO BROADCASTING CAPSULE which can be swallowed like a medicinal pill has been developed at the Rockefeller Institute, New York. As it passes through the intestine, this small FM broadcasting transmitter signals the activity of the digestive tract to an outsider receiver. The device is plastic, c. 1.125 in. long and 0.4 in. in diameter. The various electronic components of the capsule—transistor, oscillator, a ferrite cup inductance core and other circuit elements are combined in the centre of the pill. Housed in one end is a minute, replaceable storage battery which powers the oscillator. The other end of the capsule is sealed by a flexible rubber membrane. The membrane transmits the body's pressure variations to a diaphragm which supports the armature of the ferrite cup inductance core. This core contains a coil whose inductance varies with the pressure exerted on the diaphragm. The signal generated by the radio pill at a frequency of c. 1 megacycle, varies in frequency as the inductance is varied by changing pressure on the diaphragm. The radio pill is radiopaque, so its course through the gastro-intestinal tract may be traced by fluoroscopy or other means. Since it has magnetic properties, it may be possible to manipulate it by magnetic forces outside the body [*Science*, **125** (1957), 877].

### New drug for diabetes

A NEW ORAL DRUG, PHENETHYLFORMAMIDINYLIMINOUREA-HCl (DBI), for the control of diabetes has been developed by U.S. Vitamin. DBI is not a sulpha compound, its chemical composition being  $\text{C}_8\text{H}_{12}(\text{CH}_2)_2(\text{HN}=\text{C}=\text{NH})_2\text{NH}_2\text{HCl}$ . It is non-toxic to humans and its side effects are not critical. Clinical trials have shown that DBI is effective in 86 per

cent cases (104 patients 10-80 years). Blood sugar level in adults must drop to 25 per cent for the drug to be effective and in youths to 50 per cent. It was effective even in the cases where insulin had failed. DBI causes no drug resistance and it shows synergistic effects when administered together with insulin. In severe diabetics, the insulin dosage can be reduced to 25-50 per cent when 150 mg. of DBI is given orally per day. In less severe cases, DBI has replaced insulin entirely [*Chem. Engng. News*, **35**(23) (1957), 30].

### False negative pregnancy test

**PREGNANCY DIAGNOSIS TEST** based on the gametokinetic action of chorionic gonadotrophin present in the urine of a pregnant woman often gives false negative results. An investigation of the probable cause has been carried out at the Indian Institute of Biochemistry and Experimental Medicine, Calcutta. The false negative test was attributed to the presence of quinine and ergot compounds administered to the pregnant woman. A mixture of the hormone HCG (human chorionic gonadotrophin) and compounds such as quinine dihydrochloride, ergotoxine ethanesulphonate, atropine sulphate, emetine hydrochloride and *m*-xylohydroquinone was injected to *Bufo melanostictus*. The biological potency of HCG was inhibited. However, when the drug-hormone mixture was injected in the ventricle of the toad or dialysed against running water before use, no inhibition was observed. Thus, the inhibitory effect is not due to the destruction of the hormone but due to the paralysing effect on the lymph heart system of the toad. It is, therefore, suggested that in a case of suspected pregnancy, a negative result with toad test should be re-investigated by dialysis or by direct injection of pregnancy urine into the ventricle of the toad, to avoid any false reaction [*Ann. Biochem. exp. Med.*, **17** (1957), 63].

### Isolation of diosgenin from *Dioscorea*

A SIMPLIFIED PROCESS FOR THE isolation of diosgenin (an important intermediate in the production of cortisone) in a highly purified form from *Dioscorea* tubers

involves direct acid hydrolysis of the pulverized tubers followed by preferential extraction of the sapogenin with hydrocarbon solvents such as petroleum benzin or heptane.

A finely pulverized, uniform sample of the tuber is prepared by passing 4 kg. of fresh *Dioscorea barbasco* amarillo through a micro-pulverizer equipped with a 0.013 in. (slot width) herringbone screen; this is followed by thorough hand mixing. The pulverized tuber is placed in a three-necked 2-litre round-bottomed flask equipped with Trubore stirrer. The mixture is made 2N by the addition of concentrated hydrochloric acid (31 ml.) and 2N HCl (750 ml.). This provides a slurry that can be conveniently stirred. The mixture is stirred at reflux temperature for 2 hr. and the flask cooled under a stream of water. The hydrolysate is filtered on Buchner funnel and the precipitate, after being washed free of acid with about 500 ml. of cold tap water, is allowed to dry at room temperature overnight. The dry, brown residue, weighing about 30 g. and consisting of crude diosgenin, soil particles and undigested tuber cellulose, is placed together with the filter paper in a 43 × 123 mm. thimble and extracted overnight in a Soxhlet apparatus with petroleum benzin (300 ml.) at 30°-60°C. As the extraction proceeds, the diosgenin begins to crystallize in the boiling flask and at completion most of the sapogenin crystallizes out. Maximum recovery is attained by reducing the volume of the solvent to about 50 ml. by evaporation in a hooded stream bath and by chilling the flasks in a refrigerator for several hours. White crystalline diosgenin is recovered on a tared sintered-glass funnel and washed with two small portions of cold solvent. Pigments and oily materials pass into the filtrate. From one sample 2.35 g. (4.80 per cent yield on a dry weight basis) of crystalline diosgenin, melting at 201°-203°C., were obtained. Diosgenin thus obtained is 95-100 per cent pure [*Industr. Engng. Chem.*, **49** (1957), 186].

### Pyroceram

THE CORNING GLASS WORKS, U.S.A., has reported the development of a versatile new substance, Pyroceram, which is harder than steel and lighter than aluminium.

The first practical use of pyroceram will be in radomes, the nose cones that protect the directional instruments in guided missiles.

Pyroceram starts out as glass and is melted and fashioned in the same way, but each batch of raw material includes chemical ingredients that contain a nucleating agent, which, under heat treatment, forms crystals. Glass is non-crystalline, whereas pyroceram is crystalline.

The new material can be cast like metal in a foundry, thus allowing the fabrication of large and complex shapes. The substance is extremely hard and fine grained. It can be made transparent or opaque and, by controlling the chemical composition and growth of the pyroceram crystals, materials of widely different properties can be produced [*Science*, **125** (1957), 1191].

### Polyester wax

**POLYESTER WAX**, A MIXTURE OF 400 polyethylene glycol distearate (99 g.) and cetyl alcohol (1 g.), has been found to be a better ribboning embedding medium for histology than paraffin wax. On account of its low m.p. (37°C.), the polyester wax reduces hardening and shrinkage of tissues as well as other heat-induced artefacts. Its low melting point permits its use without expensive infiltration ovens [*Nature, Lond.*, **179** (1957), 1345].

### Tetrahedron

WE WELCOME THE APPEARANCE OF *Tetrahedron*, a new international journal of organic chemistry, founded by Sir Robert Robinson and published by Pergamon Press, London. The journal is intended to cover all aspects of organic chemistry. Papers on applied chemistry which have a pure organic chemical content will also be acceptable. Original contributions will be printed in one of the three languages, English, French or German. Besides, the journal will contain the English, French or German rendering of the outstanding research work published in other languages, along with latest developments. The first part of Vol. I of this quarterly journal has already appeared this year. Subscription rates for institutes, libraries, firms, etc., will be £ 6 and for individuals £ 3 10s.



## Canadian Journal of Chemical Engineering

THE *Canadian Journal of Chemical Engineering*, a bimonthly, being published by the Chemical Institute of Canada since June 1957, is a continuation of the *Canadian Journal of Technology* (which is in its 35th volume now), formerly being published by the National Research Council, Ottawa. The new journal will be entirely devoted to chemical engineering and to closely allied subjects, e.g. applied chemistry.

The first number of the journal contains a number of technological and research contributions of interest to chemical engineers, important among which are: factors affecting heat transfer in a fluidized bed; studies in flocculants; counter diffusion of ions in water; effect of sonic energy on mass transfer in solid-gas filtration in the Sherritt Gordon process; and flooding phenomena in packed gas absorption columns.

## Announcements

■ The Corday-Morgan Commonwealth Fellowship of the value of £ 700 per annum will be awarded for post-doctorate (or equivalent) study in any branch of chemistry for one year in any part of the Commonwealth, other than that in which the candidate has received his education. The scholarship is open only to the citizens of the British Commonwealth countries. The application in the prescribed form should reach the Secretary, Corday-Morgan Memorial Fund Executive, c/o The Chemical Society, London, not later than 1 March 1958.

■ *International Iron and Steel Meeting* — An International Iron and Steel Meeting reviewing 'New Developments in Iron and Steel-making' will be organized on the occasion of a special meeting of the Iron and Steel Institute of London to be held in Belgium and Luxembourg from 18 to 28 June 1958. The technical sessions will be devoted to the following subjects: The Bottom-blown Converter; Top-blown Oxygen Processes; Steel-making in the Open-hearth Furnace; Large Arc Furnaces; Low-shaft Furnaces; New Direct Processes; Blast-furnace Burden Preparation; New Techniques in Blast-furnace Operation; Theory of Continuous Casting and Deve-

lopment of Experimental Machines; and Industrial Applications of Continuous Casting.

■ An International Congress of Mathematicians will be held during 14-21 August 1958 at Edinburgh. There will be eight sections devoted to: logic and foundations; algebra and theory of numbers; analysis; topology; geometry; probability and statistics; applied mathematics, mathematical physics and numerical analysis; and history and education. Further information about the Congress can be obtained from the Secretary, Mathematical Institute, Edinburgh.

■ *Proceedings of the Conference on 'Electron Transport in Metals'* — The complete proceedings of the International conference on 'Electron Transport in Metals and Solids' attended by about 60 eminent scientists from U.S.A., U.S.S.R., Canada, U.K., India and Japan and held in the National Research Council Laboratories, Ottawa, during 10-14 September 1956, have been published as a supplementary number of the *Canadian Journal of Physics* [12A (1956)]. This welcome volume published soon after the conference adds to the value of the conference. In it are contained the full text and the discussions of the 23 papers submitted to the conference [*Nature, Lond.*, **179** (1957), 811].

■ *Symposium on 'Industrial Failure of Engineering Metals & Alloys'* — The National Metallurgical Laboratory, Jamshedpur, has recently (1957) published full text with discussions of the 29 papers submitted at the Symposium on 'Industrial Failure of Engineering Metals & Alloys', organized by the laboratory at Jamshedpur, during 5-7 February 1953. Distinguished foreign scientists from U.S.A., U.K., Japan and Australia participated in the symposium.

Most of the papers submitted focus attention on the causes and prevention of service failure of metals arising from sharp stresses resulting from improper design, fatigue, residual stress, brittleness, flow and fracture of metals, corrosion problems in the foundry, locomotive, aeronautical and marine engineering fields and imperfect lubrication. Two papers deal with the new materials of construction for heat engines in

high temperature service, and the photoelastic method of stress analysis.

■ *Award of Doctorate degrees* — Sri Vishnu Mittre and Sri S. C. D. Sah have been awarded Ph.D. degree by the Lucknow University for their theses, 'Studies on the Fossil Flora of Nipania (Rajmahal Series), Bihar' and 'Contributions to Jurassic Palaeobotany' respectively.

Sri K. Subba Rao has been awarded the D.Sc. degree in Physics, by Andhra University, on his thesis entitled 'Ultrasonic Studies in Solid and Liquid Media by New Methods'.

## INSTRUMENTS AND APPLIANCES

### ELECTRONIC SURVEYING

A versatile electronic system for accurate surveying has been developed by the South African Council for Scientific and Industrial Research. The accuracy obtainable with this device known as the Tellurometer is such that the distance between London and Reading could be measured with an error not likely to exceed 7 in.

The tellurometer system operates in the 10 cm. wavelength region and measures the travel time of radio waves over the length to be measured with an accuracy of a fraction of a millimicrosecond. Measurements can be made by day or night and visibility is immaterial, although optical line of sight is required.

A single line is measured by a master station operating in conjunction with a remote station. A built-in duplex radio telephone circuit is included in the system and is used in the measurement procedure. If a number of remote stations are employed, a corresponding number of lines can be measured from the master station in the course of a single setting-up. The instruments in use at master and remote stations are similar but are not interchangeable [*Overseas Engr.*, **30** (1957), 369].

### GAMMA GAUGE

A gamma gauge for measuring the thickness of a hot steel strip as it emerges from the mill has been developed by the Baldwin Instrument Company, U.K. A permanent record is made simultaneously by a teleprinter. The gauge enables the accuracy of the section

to be checked as the trial strip is going through and adjustments to the rolls can be made more quickly. The instrument is set to measure thickness between the limits of 0.03 and 0.25 in. The tolerance limit is usually between 0.002 and 0.010 in.

The radioactive source is strontium<sup>90</sup> contained in a water-cooled jacket. The amount of radiation absorbed by the strip and, therefore, the amount reaching the detector varies with the thickness of the metal. The sensitive element in the detector head is a thallium-activated sodium iodide crystal which glows when radiation falls on it. Light from the crystal is picked up by two photomultipliers: one measures the amount of light given off by the crystal to determine the thickness of the strip; the other is connected to a relay which reacts to the sharp increase of radiation when there is no strip in the measuring head, and introduces a metal disc of standard thickness into the radiation beam. The gauge measures this disc and adjusts itself, if necessary, to give the correct reading and eliminate any 'drift'. The leading edge of the next strip produces a sharp drop in the radiation measured, and the relay withdraws the disc.

The output from the measuring photomultiplier is fed into an integrating circuit which averages the current over a time cycle of one second. The output from the integrator is then fed into the amplifier in the electronic unit, and thence the signal passes through a discriminator, which classifies it according to its strength. The strength depends on the average thickness of the strip passing through the measuring head during that second, and the signal can be interpreted to denote the nature of thickness whether it is correct or out of tolerance, positive or negative [*Times Rev. Industr.*, (May 1957), 34].

#### SLAG WOOL FILTERS

Harvard Air Cleaning Laboratories, U.S.A., have developed slag wool filters to clean high temperature gas streams. Although single-pass performance of these filters is low, efficiencies as high as 99 per cent have been obtained with multiple slag layers. These filters are made up of fine refractory slag fibres, packed for separating sub-micron aerosols. Slag wool filter

systems have been maintained at 100 ft./min./sq. ft. with gases up to 1000°F. These filters may also be used to remove both particulate matter and acid gases [*Chem. Engng. News*, **35** (1957), 98].

#### ELECTRONIC AIR FILTERS

The Electronic Division of the Harris Engineering Co., London, have introduced the Trion electronic air filters which can collect dust particles up to 0.01  $\mu$  size. The suspended particles are given a positive charge as they pass through a high voltage ionizing screen. These particles are then attracted and adhere to the collecting plates which form the negative elements of an electrostatic set up between a series of parallel plates. The collecting plates are cleaned periodically by washing with water [*Chem. Age*, **77** (1957), 678].

#### AUTOMATIC ULTRASONIC TESTING

Messrs Kelvin & Hughes (Industrial) Ltd., London, have introduced an automatic and versatile ultrasonic testing device, called Autosonics system, which overcomes limitations of manual inspection and facilitates high speed testing in large-scale continuous production.

The equipment comprises a travelling probe located on a carriage which is driven transversely and longitudinally over the material to be inspected, a control console with cathode ray display, alarms, and recording equipment to be used when desired.

The probe, which is in contact with the material through a liquid, transmits energy pulses into the material, amplifies the reflected pulses and transmits the sequence of events as a trace on a cathode ray screen. Any flow indication will operate alarms or can be recorded on instruments such as a strip chart recorder. The circuit incorporates automatic gain control and a system-fault alarm section of the fail-to-safe type. An important feature of autosonics is that a predetermined scan or search plan is accurately followed by the probe.

The equipment can be used for fixed-site testing of components, forgings, billets, etc., or as part of a production line for the continuous inspection of strip for laminar

defects, etc. It can also be used for sequence testing of small parts, the components being applied successively to a stationary probe. Another variation employing a probe mounted on a wheeled carriage which can be pushed manually over large surfaces is available. Automatic recording of defects can be applied.

Specimens up to 25 ft. long and 6 in. wide can be inspected. The speed of inspection for targets equivalent to  $\frac{3}{4}$  in. flat bottom holes is up to 100 ft./min. and for gross defects up to 400 ft./min. [*Overseas Engr.*, **30** (1957), 339].

#### SILICON JUNCTION RECTIFIERS

The British Thomson-Houston Co. Ltd. has developed a series of low-power silicon junction rectifiers. These rectifiers, small in size, can be used up to a maximum junction temperature of 200°C. and ambient temperatures up to 175°C. At these high temperatures inverse voltages up to 300 V. are attainable. Alternatively, if the maximum junction temperature is limited to 120°C., allowing operation in ambients up to 100°C., inverse voltages up to 400 V. are obtainable. The silicon rectifiers can also be used as a voltage reference (Zener diode) in the range of 4.8 V. and junction temperature up to 250°C. [*Beam J.*, **64** (1957), 29].

#### ULTRAVIOLET COLOUR MICROSCOPY

An instrument termed UCTM (ultraviolet colour-translating television microscope) has been developed at the Rockefeller Institute, New York, to study cell constituents without staining them chemically. The instrument uses ultraviolet light, which is converted to the visible range by means of colour television. The new instrument is useful for tracing utilization and metabolism of specific materials within the cell, without disturbing the cell in its motion and development. The UCTM provides higher magnification than visible light. The chemical composition of cells can also be studied since the density of the different parts of the image on the TV screen depends on their chemical composition and concentration [*Sci. Newslett., Wash.*, **71** (1957), 360].

## AUTOMATIC ANALYSIS OF STEELS

Hilger & Watts Ltd., London, have introduced a new instrument, the fluorite vacuum polychromator, which is capable of automatically and speedily analysing the carbon, phosphorus and sulphur content of steels. The instrument consists of a 3-prism spectrograph and makes use of the resonance lines of the elements in the far ultraviolet or the Schumann region. The spectrograph is enclosed in an 18 in. diameter drum-like container and is mounted on a cabinet which houses the necessary measurement and control equipment. The quartz window E.M.I. photomultipliers are employed as detectors, one for each of the elements and one for the internal standard. The sample is mounted in a spark-chamber through which an inert gas is circulated. If the carbon content is less than 0.05 per cent, a single sparking will suffice for all the three elements but when it exceeds the above value it is advisable to determine the carbon content separately with different source conditions. The time taken for complete analysis is not more than 3 min. [*Overseas Engr.*, **30** (1957), 369].

## WATER PURIFIER

The Elgastat major, newly introduced by Elga Products Ltd., London, is claimed to provide purified water at tap speed far exceeding pharmacopoeia requirements. Conductivity water provided is said to equal three distillations in quartz and at lower cost than that of distilled water; no supervision or maintenance, such as defurring, are required and a cartridge exchange service avoids regeneration *in situ*.

Model B 104 (without conductivity meter) provides washing water for slides and for any work where single distilled water is required. Model B 104/CON (with conductivity meter) is designed for the research laboratory. Facilities include the monitoring of effluent purity which is claimed to be well above 4,000,000 ohms/cm. (conductivity water). The effluent may be piped to any number of benches.

The Elgastat method of de-ionization involves the passage of the crude water through an intimate mixture of strongly acidic cation and strongly basic anion-exchange resins. Hydrogen ions produced

during the cation-exchange process are almost immediately removed from the scene of reaction by adsorption or neutralization on the anion-exchange resin. Since hydroxyl ions produced on the anion resin immediately react with hydrogen ions from the cation resin, even very unfavourable exchange equilibria may be driven to completion [*Chem. Age*, **77** (1957), 1114].

## DETERMINATION OF SULPHUR CONTENT

Pye & Co. Ltd., Cambridge, Mass., has developed an instrument for the determination of sulphur. Based on the American Society for Testing Materials' 'Proposed method of test for sulphur in petroleum products by the rapid high temperature combustion method', a quartz boat is pushed into a special combustion tube mounted in a furnace which produces a temperature gradient along the tube.

Sulphur dioxide is given off and is carried along by a stream of nitrogen to an absorber. As the sulphur dioxide passes through the absorber a metal indicator electrode signals to a pH meter/millivoltmeter. This is connected to Pye automatic titration equipment which starts a flow of reagent from a burette which is continued until the sulphur dioxide is neutralized [*Chem. Age*, **77** (1957), 1116].

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## Erratum

Article entitled "Brass Plating from the Pyrophosphate Bath", **16A** (1957), 326, Table 1: Against conc. of Cu in soln., 0.0125, 0.0250 and 0.0375, the figures under cathode potential at c.d. 19.2, 28.8 and 38.4 should be under c.d. 9.6, 19.2 and 28.8 respectively; for 'cathode potential (—V)' read 'cathode potential (—V), H<sub>2</sub> scale'.

# Progress Reports

## INDIAN CENTRAL COCONUT COMMITTEE

THE ANNUAL REPORT OF THE INDIAN CENTRAL Coconut Committee for the year 1955-56 records the activities of the Committee in many directions in enhancing the coconut production both by improvement in the breed of the trees and prevention of the pests.

A fund of information useful in improving coconut cultivation has been gathered at the two Central and the various Regional Research Institutes on such aspects like botanical characteristics of different kinds of coconut saplings, their breeding and hybridization, agronomical aspects of cultivation, manurial and cultural treatment of the trees, symptomatology and control of a number of coconut palm root and leaf diseases like palm weevil, rhinoceros beetle, cockchafer, 'band' disease, etc.

The Committee's efforts in the expansion of research facilities have resulted in bringing into existence two more Regional Research Stations, one for Andhra State, at Ambajipeta in the East Godavari district, and another for Bombay State, at Bhatye in Ratnagiri district.

Important research activities of the Central and Regional Research Institutions are summarized below.

**Breeding** — Spraying of a hormone mixture, 2-4-D mixed with cow's urine or coconut water, was found to be the best for the control of undue shedding of buttons. Judicious thinning appeared to improve development of nuts where 20 or 25 buttons were retained in the bunch.

Root sap studies indicated a variation from 4.0 to 8.5 in the pH of the root sap. The pH of a majority of healthy roots was acidic and for diseased roots either neutral or alkaline. Exudation of root sap from diseased trees was less than that from healthy trees.

**Agronomy and soil chemistry** — Observations on the yield of trees in two plots, one of which was regularly cultivated and the other not given any cultivation or manuring for the past 37 years, showed that the yield per tree in the cultivated plot was 39 nuts compared to 20 in the uncultivated and unmanured plot, pointing out the obvious benefit of regular cultivation and manuring.

'Piling mounds' and 'digging' treatments gave an average increase in yield of 6 nuts per tree over other treatments.

Manuring of *Crotalaria striata* with phosphoric acid (60 lb. per acre) increased the yield of green stuff by 11.2 per cent over the unmanured controls.

Examination of leaf samples exhibiting a seasonal foliar yellowing indicated a critical value of 5 for K<sub>2</sub>O: MgO ratio for either manifesting the yellowing or not, the yellowing showing up only when the ratio was above 5. Applications of magnesium sulphate both to the soil and as spray to the foliage showed some beneficial effect in trees showing the seasonal foliar yellowing. Seedlings grown in containers with the soil water maintained at pH 4 developed the yellowing but the leaf tips withered 2 months after the commencement of this treatment.

**Plant pathology** — Sap inoculation trials by injecting extracts from diseased coconut leaves into

healthy seedlings and older trees gave positive results in the case of trees below 40 and above 3 years of age.

A mixture of sawdust and coconut oil cake was found to be a suitable breeding medium for the pest known as rhinoceros beetle, under laboratory conditions. In beetle control field experiments, where to the axils of the palms was applied a mixture of insecticide (B.H.C.) and sand or clay, the incidence of fresh attack remained below 3 per cent, while in the control block the same was 15 per cent.

Investigations on the effect of spray deposits on coconut leaves of 0.2 per cent DDT or B.H.C. on the Eulophid parasite *Trichospilus pupivora* showed that the B.H.C. spray deposit remained toxic up to 10 days while that of DDT persisted for 2 months. A bacterium closely resembling *Bacillus prodigiosus* was isolated from diseased larvae.

From symptomatological studies of the pest palm weevil, to which the young palms are particularly susceptible, the following observations were made: In infested palms the dying of the leaves commences from the outer whorl and the central shoots show the effect of infestation only at a later stage. In naturally infested trees treatment with Aldrin, Dieldrin, Endrin, Basudin and Folidol was not so effective as pyrethrins-piperonyl butoxide combination (Pyrocone E). In heavily infested areas, filling the leaf axils with 5 per cent B.H.C. and 5 per cent Chlordane dust gave a good measure of prophylactic effect, no infestation being observed for nearly a year, whereas freshly cut stems were found to attract the beetle for oviposition. The above mixture of B.H.C. (wetttable) and Chlordane dust was effective in checking the pest cockchafer also. Best control was obtained when Chlordane was applied to the soil at 28 lb. per acre.

In pot culture experiments with coconut seedlings grown in quartz sand the possibility of reproducing the 'band' disease under artificial conditions of growth was studied with culture solutions of known chemical compositions. Analysis of the uppermost one foot layer of soils for pH, nitrogen, phosphate, potassium and manganese contents showed that the quantities of these nutrients present in the soil were slightly greater for diseased palms than for the healthy ones. Microbiological analysis gave higher microbiological activities in soils from under the healthy palms than in those from under diseased palms. This suggests that the soils round about the diseased palms were somewhat deficient in the supply of major plant nutrients of the palm. The rate of nitrification in soils from under the diseased palms was actually found to be lower. Chemical analysis of the leaves of 'band' affected and healthy palms showed a concentration of the two micro-nutrients, copper and manganese, in the tender and mature leaves.

## THE BRITISH IRON & STEEL RESEARCH ASSOCIATION, 1956

DURING THE PERIOD UNDER REVIEW THE ASSOCIATION devoted its attention mainly to the research and development programmes closely linked with

the immediate and future needs of the industry. The mechanization of forges, problems of waste gas cleaning, utilization of slags and attempts to improve methods for preparing ores for the blast furnace received special attention. A method for the continuous production of formable plastic-coated steel strip has been developed.

A brief account of the research work carried out in the various laboratories of the Association is recorded below.

**Iron making** — Laboratory investigations have shown that pores of air-cooled slag contain elemental sulphur and that it should be possible to control porosity to produce either dense or light-weight slag. A study of the fundamental factors controlling sintering has shown that the main role of the air is to transfer heat rather than to provide a source of oxygen for combustion. Experiments using the coarse, medium and fine fractions of normal rod-milled coke have shown that, although the flame front travels through the bed faster with the decreasing coke size, the highest bed temperatures are obtained with medium-sized fuel. Laboratory studies on sulphur removal have shown that by improving ignition stronger sinter was made at the top of the bed and as much sulphur was removed from the top of the bed as from the bottom. A survey of ignition practice has revealed that the amount of oxygen in the atmosphere over the bed during ignition influences the strength of the sinter at the top of the bed, with coke oven gas, the best sinter is obtained when 60 per cent of excess air is supplied, whereas with fuel of a lower calorific value, 40 per cent of excess air gives the best sinter. Another way of increasing the strength of the sinter at the top of the bed is by improving the distribution of materials down the bed. Recent sinter plant assessment trials have shown that a large proportion of the air passing through the fan enters through leaks in the fan system, and that the actual airflow through the grate is usually only about half the total passing through the fan. For each set of plant operating conditions there is a value of the leakage for which the airflow through the grate is maximum. The maximum flow through the grate could be obtained if the leakage measured were halved. Reducing the leakage by more than half would save considerable power but would draw less air through the bed. The behaviour of fine partially reduced ores carried in hot gases was studied with particular reference to the question of build-up and blockages in ducts, cyclones, etc. Accretions and blockages do not usually occur at temperatures below 850°C. if conveying velocities are high enough to prevent any particles from settling.

**Steel making** — The open-hearth furnace method of steel making continued to be adopted. By varying the steam pressure, it was possible to reduce the rate of oxidation in the furnace. A model furnace with a calorimeter hearth that can operate at 1550°C. has been built to obtain precise information on the relative values of radiation and convection in heat transfer in the open-hearth furnace. Radiation measurements on open-hearth furnace have been made practicable by the BISRA twin-image radiation pyrometer. Perforated-tape equipment has been built for recording and analysing temperatures and flow rates during trials. New cermet for immersion thermocouple sheaths have

been investigated and molybdenum-alumina has given good results.

**Metallurgy** — From work on the development of a ferrite steel with high scaling resistance, suitable for high-temperature operation, it has been found that a 7 per cent Cr, 2 per cent Mo,  $\frac{1}{2}$  per cent Ti steel can be made, whose resistance to creep at 650°C. compares favourably with the existing Cr-Mo and Cr-Mo-V steels of lower Cr content. The steels containing fine dispersion of vanadium carbide have the better creep properties. X-ray fluorescent analysis of the extraction replicas has shown that the vanadium/carbon ratios of the carbide change with tempering. A study of the high-temperature parts of equilibrium diagrams for alloys of iron and manganese with the transition elements (Ti, V, Cr, Mn, etc.) has indicated that solid and liquid solutions are monatomic.

Chemical analyses of the mild steel residual series of spectrographic standards for Cu, Co, Cr, Ni, Mo, Sn, W and V have been completed.

**Chemistry** — Thermodynamics of iron oxide-bearing slags of the systems  $\text{FeO-Fe}_2\text{O}_3\text{-SiO}_2$ ;  $\text{FeO-Fe}_2\text{O}_3\text{-P}_2\text{O}_5$  and  $\text{FeO-Fe}_2\text{O}_3\text{-SiO}_2\text{-P}_2\text{O}_5$  have been studied. The melts were equilibrated with  $\text{CO}_2/\text{CO}$  mixtures at 1500°C. over a wide composition range. The results indicate that, throughout the systems, increasing  $\text{SiO}_2$  or  $\text{P}_2\text{O}_5$  decreases the ferric/ferrous iron ratio appreciably,  $\text{P}_2\text{O}_5$  being more effective than  $\text{SiO}_2$ . The solubility of silica in molten iron oxide increases linearly with temperature for a given  $\text{CO}_2/\text{CO}$  gas ratio, and for a given temperature, the solubility of silica increases as the oxygen potential of the system decreases. These results together with the available data make it possible to construct curves relating the ferric/ferrous iron ratio to  $\text{SiO}_2$  and  $\text{P}_2\text{O}_5$  concentration for  $\text{CO}_2/\text{CO}$  ratios from 75.0 down to *c.* 0.1, where slags are in equilibrium with liquid iron. The pre-refining of hot metal by top-blown oxygen has shown that under favourable conditions, the iron containing 3.4-3.6 per cent C, 1.3-1.5 per cent P, and 1.2 per cent Si was dephosphorized to 0.3-0.4 per cent P, whilst the carbon was lowered to 2.5 per cent. Iron-silicon alloys containing up to 3 per cent Si have been equilibrated with ammonia-hydrogen or nitrogen-hydrogen mixtures at various temperatures. Silicon lowers the solubility of nitrogen in  $\alpha$ - and  $\gamma$ -iron. Silica bricks, on account of their low thermal expansion and high viscosity, have been found to be far less liable to crack and drop off than those of basic refractories.

**Physics** — A study of the interaction between the process of creep and fatigue shows that for metals which exhibit a recovery from work-hardening, fatigue stresses are deleterious because they accelerate the rate of softening. Investigations on the mode of heat transfer through liquid metals and of the effect of such transfer on temperature distribution have shown that horizontal transfer from a hot to a cold face across a liquid occurs predominantly by the convective movement of a fairly thin film of liquid, surrounding a central region which remains at an almost constant temperature. A new type of automatic control system for the continuous casting process, using water as a working fluid, has been tested. Liquid flow in the mould is regulated by pneumatic pressure controlled from the liquid level in the mould.

# Comparative Efficacy & Economics of Pyrethrins & Mixtures of Pyrethrins & Piperonyl Butoxide as Space Sprays against Flies & Mosquitoes

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(Manuscript received 28 December 1956)

The toxicity of pyrethrin-piperonyl butoxide mixtures in relation to pyrethrins when used as space sprays against the house-fly, *Musca nebulo* Linn., and the mosquito, *Culex fatigans* Wied., have been investigated. The relative costs based on efficacy have also been worked out.

For comparable rates of knockdown the pyrethrins are more economical than the mixtures of pyrethrins with piperonyl butoxide against both flies and mosquitoes. In effecting comparable levels of high knockdown and high mortality, however, the mixtures are more economical than the pyrethrins against both flies and mosquitoes.

THE importance of synergists for use in fly and mosquito sprays containing pyrethrins is now well recognized<sup>1</sup>. Wachs<sup>2</sup> and Dove<sup>3</sup> using flies as test insects and Pal *et al.*<sup>4</sup> and Fales and Bodenstein<sup>5</sup> working with mosquitoes demonstrated the synergistic activity in relation to both knockdown and mortality of piperonyl butoxide when used in combination with pyrethrins. These investigators did not specifically study the rate of knockdown of the mixtures in relation to pyrethrins alone. The object of the present investigation was to ascertain how far mixtures of pyrethrins with piperonyl butoxide retain the two desirable properties of rapid knockdown and mortality possessed by pyrethrins and to estimate the economics of the mixtures in relation to pyrethrins.

## Experimental procedure

**Pyrethrins** — 0.1 per cent (w/v) pyrethrin solution in superior grade kerosene oil served as the stock solution.

**Piperonyl butoxide** — A sample of technical grade piperonyl butoxide received from Messrs Cooper McDougall & Robertson Ltd., Berkhamsted, Herts., England, was used.

**Test insects:** *Musca nebulo* Linn.— The method of rearing the insect in the laboratory was the same as described by Basden<sup>6</sup> for *Musca domestica* L. Adult flies, 4-5 days old, were used in the assay.

*Culex fatigans* Wied.— The method for rearing was the same as described by Newman *et al.*<sup>7</sup>. Adult females, 40-60 hr. old, were used in the assay.

**Biological assay** — This was carried out using the modified Peet-Grady chamber described by Parkin and Green<sup>8</sup>. The experimental details were essentially the same as described by Dixit *et al.*<sup>9</sup>. The assessment was carried out at  $82.5^\circ \pm 2.5^\circ\text{F}$ . and  $50 \pm 5$  per cent R.H. Approximately 100 insects were introduced in the chamber and exposed for 10 min. to the mist formed by the atomization of the spray insecticide at an air pressure of 50 cm. Hg. After atomization the count of insects knocked down at intervals of 2, 4, 6, 8 and 10 min. was made. At the end of 10 min. all insects including those knocked down were collected and per cent mortality determined 24 hr. after exposure. There were two replicates in each assay.

## Results

The results of tests on the toxicity of pyrethrins and piperonyl butoxide-pyrethrin mixtures against flies and mosquitoes are summarized in Table 1.

## Discussion

Pyrethrins when used as space sprays against flies and mosquitoes show rapid knockdown and high killing power. Piperonyl butoxide synergizes the killing power but slows down the rate of knockdown. Taking gross knockdown after 10 min. as the factor for comparison, the same dosage of pyrethrin-piperonyl butoxide mixtures is



TABLE 1—TOXICITY OF PYRETHRINS AND MIXTURES OF PYRETHRINS AND PIPERONYL BUTOXIDE

CONCENTRATION OF THE SPRAY		DOSAGE ml.	RATE OF KNOCKDOWN AFTER					MORTALITY IN 24 HR.* %
Pyrethrins (w/v) %	Piperonyl butoxide (w/v) %		2 min. %	4 min. %	6 min. %	8 min. %	10 min. %	
Test insect: <i>Musca nebulosa</i> Linn.								
0.025	—	0.500	12	42	71	84	93	16
0.050	—	0.400	38	68	92	95	98	37
0.100	—	0.250	26	51	87	95	98	56
0.100	—	0.500	70	88	100	—	—	85
0.100	—	0.600	74	90	100	—	—	92
0.025	0.2	1.500	66	91	100	—	—	100
0.025	0.4	0.500	8	32	55	72	87	93
0.025	0.4	1.500	76	89	99	100	—	100
0.050	0.4	0.250	10	40	62	82	94	94
0.050	0.4	0.300	19	45	64	80	90	91
0.050	0.4	0.400	31	58	90	97	100	100
0.060	0.6	0.125	4	23	48	65	73	74
0.060	0.6	0.250	21	73	84	92	97	97
0.060	0.6	0.300	36	74	90	96	98	98
0.060	0.6	0.500	79	93	99	100	—	100
Test insect: <i>Culex fatigans</i> Wied.								
0.05	—	0.250	15	24	65	79	90	35
0.05	—	0.500	41	64	97	100	—	52
0.10	—	0.125	8	48	74	100	—	51
0.10	—	0.250	13	48	76	100	—	94
0.05	0.4	0.125	3	13	33	55	75	83
0.05	0.4	0.250	4	19	47	69	87	96
0.05	0.4	0.500	16	44	82	100	—	100
0.06	0.6	0.125	3	29	65	87	92	95
0.06	0.6	0.250	21	62	90	97	99	98

\*No mortality in unsprayed insects.

more efficacious than pyrethrins alone against both flies and mosquitoes (Table 1). It is, however, to be remembered that in space sprays and in aerosols the rate of knockdown is vitally important. The comparative efficacy of pyrethrins and mixtures of pyrethrins and piperonyl butoxide as space sprays has, therefore, been compared separately for (1) rate of knockdown and (2) per cent kill of flies and mosquitoes.

The economics of pyrethrins and mixtures of pyrethrins and piperonyl butoxide as space sprays against flies and mosquitoes has not been studied earlier. This has been attempted in the present study. The specific data on equivalent doses for both comparable rates of knockdown and per cent mortality derived from Table 1 are presented in Tables 2 and 3 respectively.

The cost of basic materials, viz. pyrethrins\* (1.0 per cent), piperonyl butoxide† (technical grade) and kerosene oil (superior grade), used in the experiments is Rs. 34.00, Rs. 34.19

and Rs. 1.19 respectively. Based on rate of knockdown, gross knockdown after 10 min. and per cent kill of flies and mosquitoes the cost of different mixtures of pyrethrins with piperonyl butoxide and pyrethrins alone have been estimated and the data are presented in Tables 2 and 3.

The results in Table 2 show that for comparable rates of knockdown the pyrethrins would be more economical than the mixtures of pyrethrins with piperonyl butoxide against both flies and mosquitoes. For example, against flies a dosage of 0.5 ml. of spray mixture containing 0.06 per cent pyrethrins and 0.6 per cent piperonyl butoxide produces the same rate of knockdown of flies as is produced by 0.5 ml. of 0.1 per cent pyrethrins. Against mosquitoes a dosage of 0.5 ml. of spray mixture containing 0.05 per cent pyrethrins and 0.4 per cent piperonyl butoxide produces the same rate of knockdown as produced by 0.25 ml. of 0.1 per cent pyrethrins. Thus 2 gal. of the mixture would be required to produce the same effect as produced by 1 gal. of pyrethrins. From the results in Table 3 it is clear that for effecting comparable levels of high knockdown and high mortality the mixtures would be more economical than the pyrethrins

\*Rate quoted by Messrs Bombay Chemicals Ltd., Bombay.

†Rate quoted by Messrs Cooper McDougall & Robertson Ltd., Berkhamsted, Herts., England, at 38s. per lb. f.o.r. U.K. To this has been added 35 per cent as customs duty and freight.

TABLE 2—EQUIVALENT DOSES FOR COMPARABLE RATES OF KNOCKDOWN

CONCENTRATION OF THE SPRAY		DOSAGE ml.	RATE OF KNOCKDOWN AFTER					COST OF EQUIVALENT DOSES FOR COMPARABLE RATES OF KNOCKDOWN Rs./gal.
Pyrethrins (w/v) %	Piperonyl butoxide (w/v) %		2 min. %	4 min. %	6 min. %	8 min. %	10 min. %	
<i>M. nebulosa</i>								
0.100	—	0.50	70	88	100	—	—	4.47
0.060	0.6	0.50	79	93	99	100	—	4.75
0.025	0.4	1.50	76	89	99	100	—	10.12
0.100	—	0.25	26	51	87	95	98	4.47
0.050	0.4	0.40	31	58	90	97	100	6.70
<i>C. fatigans</i>								
0.100	—	0.25	13	48	76	100	—	4.47
0.050	0.4	0.50	16	44	82	100	—	8.37

TABLE 3—EQUIVALENT DOSES FOR COMPARABLE PER CENT MORTALITY

CONCENTRATION OF THE SPRAY		DOSAGE ml.	KNOCK- DOWN IN 10 MIN. %	MORTA- LITY IN 24 HR. %	COST OF EQUIVALENT DOSES FOR COMPARABLE % MORTALITY Rs./gal.
Pyrethrins (w/v) %	Piperonyl butoxide (w/v) %				
<i>M. nebulosa</i>					
0.100	—	0.600	100	92	4.47
0.050	0.4	0.250	94	94	1.75
0.060	0.6	0.250	97	97	1.97
0.050	0.4	0.300	90	91	2.08
0.060	0.6	0.300	98	98	2.37
0.025	0.4	0.500	87	93	2.77
<i>C. fatigans</i>					
0.100	—	0.250	100	94	4.47
0.060	0.6	0.125	92	95	2.37
0.050	0.4	0.250	87	96	4.19

against both flies and mosquitoes. Against flies a dosage of 0.25 ml. of the mixture containing 0.05 per cent pyrethrins and 0.4 per cent piperonyl butoxide effects the same order of high knockdown and high mortality of flies as produced by 0.6 ml. of 0.1 per cent pyrethrins. Thus 5/12 gal. of the mixture would be required to produce the same effect as produced by 1 gal. of pyrethrins. Against mosquitoes a dosage of 0.125 ml. of the mixture containing 0.06 per cent pyrethrins and 0.6 per cent piperonyl butoxide effects the same order of high knockdown and high mortality as produced by 0.25 ml. of 0.1 per cent pyrethrins. Thus 1/2 gallon of the mixture will be required to produce the same effect as produced by 1 gallon of pyrethrins.

Thus it will be obvious that if the rate of knockdown of insects in the course of first

10 min. after the insecticide has been atomized is to be taken into consideration the mixture of pyrethrins and piperonyl butoxide will be less efficacious against both flies and mosquitoes in the same dosage thereby adding to the cost of the spray mixture. If, however, the gross knockdown after 10 min. and the per cent kill of insects effected in 24 hr. (Table 3) are the factors to be considered, the mixtures will be more economical than the pyrethrins against both flies and mosquitoes.

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# Viscosity Studies on Industrial Nitrocellulose

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**The viscosity characteristics of the industrial nitrocellulose type C.F. 2·8-3·5 cs. produced by the Cordite Factory, Aruvankadu, have been determined. The product compares favourably with imported varieties of nitrocellulose in viscosity and degree of polymerization.**

At present the bulk of nitrocellulose produced in the country for industrial use is consumed in the leather cloth industry. It is, however, finding increasing use in cement and lacquer industries. The variety of industrial nitrocellulose designated C.F. 2·8-3·5 cs. (ester soluble) manufactured at the Cordite Factory, Aruvankadu, has successfully replaced the imported material used in leather cloth industry.

Data on technical viscosities of solutions of industrial nitrocellulose, on which the flow properties depend, are of importance to the consumers. Predictability of viscosity at any concentration and temperature or of a concentration required with any group of solvents to get a workable consistency of the solution is an essential requisite for the manufacturer in making nitrocellulose solutions for various purposes. The technical viscosity of such solutions having appreciably high concentrations, however, does not follow the laws of free molecular movement. Therefore, for complete assessment of the viscosity characteristics of a nitrocellulose sample it is necessary to obtain data on its viscosities in dilute solutions also; the viscosity in dilute solution is a linear function of the number of molecules in solution.

In the present investigation the viscosities of representative samples of the C.F. 2·8-3·5 cs. variety of nitrocellulose, produced at the Cordite Factory, in different solvents were determined and the results are given in this paper. The limiting viscosities of nitrocellulose in pure acetone were also determined to assess the degree of polymerization.

## Experimental procedure

The nitrocellulose sample used had characteristics conforming to the following specification limits: nitrogen content,  $12.0 \pm 0.2$  per cent; ash (max.) content, 0.3 per cent; organic matter (max.) insoluble in acetone, 0.5 per cent; viscosity in 1 per cent solution (w/w), 2·8-3·5 cs.; stability at  $132^{\circ}\text{C}$ . (max.), 1.5 mg.  $\text{N}_2/\text{g}$ . nitrocellulose; heat test value at  $170^{\circ}\text{F}$ . (min.), 10 min.

The following solvents were used:

1. Butyl acetate (*tech.*) conforming to I.S. 230 (1950) or A.S.T.M. D303-40 (1952); sp. gr.  $\frac{20}{20}^{\circ}$ , 0.874; ester content, 90 per cent; boiling range,  $120^{\circ}$ - $30^{\circ}\text{C}$ .

2. Ethanol conforming to I.S. 323 (1952) or B.S.S. 507 (1950); sp. gr.  $\frac{20}{20}^{\circ}$ , 0.811;  $\text{C}_2\text{H}_5\text{OH}$  content, 96 per cent (vol.).

3. Acetone (*tech.*) conforming to I.S. 170 (1950) or B.S.S. 509 (1950); sp. gr.  $\frac{20}{20}^{\circ}$ , 0.791; boiling range,  $56.0^{\circ}$ - $56.3^{\circ}\text{C}$ .

4. Ethyl acetate (*tech.*) conforming to I.S. 229 (1950) or B.S.S. 553 (1950); sp. gr.  $\frac{20}{20}^{\circ}$ , 0.888; ester content, 88 per cent; boiling range,  $72^{\circ}$ - $80^{\circ}\text{C}$ .

5. Toluene (*tech.*) conforming to I.S. 537 (1955) or B.S.S. 805 (1953); sp. gr.  $\frac{20}{20}^{\circ}$ , 0.865; boiling range,  $107^{\circ}$ - $25^{\circ}\text{C}$ .

The solutions were made in 250 ml. glass stoppered cylinders using requisite quantities of dry nitrocellulose and the solvents to give 200 g. of solution. The cylinders were shaken on a rotary shaker for 6-8 hr. and then left undisturbed for 24 hr. before determining viscosities. The determinations were completed within 48 hr. of making the solutions.

The viscometers used were standardized Ostwald and Falling Sphere types conforming to B.S.S. 188 (1937). In addition, the Falling Sphere Viscometer with  $\frac{5}{16}$  in. diam. steel balls was used. Standardizations were carried out using distilled water, sucrose solutions, glycerine-water mixtures and pure

castor oil. The bath temperatures were controlled to within  $\pm 0.1^\circ\text{C}$ .

Technical viscosities were determined in the temperature range  $10^\circ\text{--}40^\circ\text{C}$ . ( $2.5^\circ\text{C}$ . intervals) for solutions of 1, 3, 5, 10, 12.2, 15 and 20 per cent concentrations. For each concentration, solutions were made in the following solvent mixtures:

(i) Butyl acetate-ethanol (3:1, w/w); (ii) acetone-water (19:1, v/v); and (iii) ethyl acetate-ethanol-toluene (4:5:11, w/w).

Viscosities in dilute solutions were determined at  $20^\circ\text{C}$ . in acetone solutions containing 0.2, 0.4 and 0.6 g. nitrocellulose per litre of the unfractionated material.

### Results and discussion

The results obtained are given in Table 1 and graphically represented in Figs. 1 and 2. It is clear from Fig. 1 that temperature variation of the log of viscosity follows a linear relationship in practically all the solvents. Viscosities in an ester-rich solvent like butyl acetate-ethanol mixture or acetone-water (19:1) mixture are lower than the viscosities in a thin solvent containing ethyl acetate

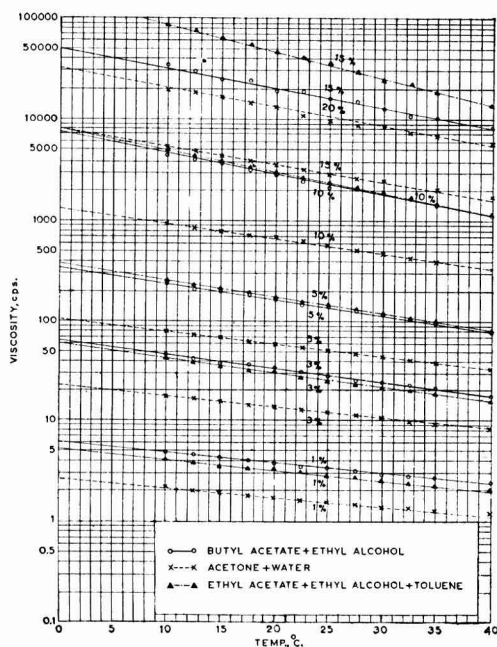


FIG. 1 — VISCOSITY VS. TEMPERATURE

TABLE 1 — VISCOSITY OF INDUSTRIAL NITROCELLULOSE

TEMP. °C.	VISCOSITY (cps.) AT CONCENTRATION (%)						
	1	3	5	10	12.2	15	20
Solvent: Butyl acetate-ethanol (3:1)							
10.0	4.90	46.9	237.3	4381	10160	34490	—
12.5	4.58	42.7	216.1	3978	9422	29875	—
15.0	4.28	39.6	197.5	3640	8272	25725	—
17.5	4.04	37.0	181.1	3303	7201	23750	—
20.0	3.76	33.5	165.6	2886	6474	19790	—
22.5	3.54	31.3	150.9	2496	6032	18565	—
25.0	3.36	28.8	137.0	2288	5324	16495	—
27.5	3.16	26.7	125.9	2106	4712	15075	—
30.0	2.97	24.3	114.9	1859	4335	13100	—
32.5	2.82	23.0	106.0	1645	3770	11610	—
35.0	2.67	20.8	94.7	1456	3392	10400	—
40.0	2.41	18.9	79.6	1138	2639	8293	—
Solvent: Acetone-water (19:1)							
10.0	2.09	17.5	78.85	949	2005	5230	19000
12.5	1.99	16.6	73.15	868	1820	4770	17670
15.0	1.90	15.6	67.90	796	1715	4360	16330
17.5	1.80	14.4	63.55	736	1565	3950	14600
20.0	1.74	13.5	59.10	680	1420	3620	13200
22.5	1.67	12.7	55.45	626	1325	3290	10420
25.0	1.60	12.1	51.95	583	1225	2850	9780
27.5	1.52	11.3	48.00	514	1090	2590	8920
30.0	1.47	10.6	44.25	469	1015	2390	8240
32.5	1.40	9.9	41.10	447	917	2170	7250
35.0	1.35	9.3	38.45	400	858	2030	6910
40.0	1.26	8.4	33.95	345	732	1730	5590
Solvent: Ethyl acetate-ethanol-toluene (4:5:11)							
10.0	4.02	43.39	254.1	4900	17530	87460	—
12.5	3.81	39.00	223.2	4147	15450	78030	—
15.0	3.53	36.60	205.4	3770	13190	64070	—
17.5	3.40	32.90	183.0	3393	11500	55800	—
20.0	3.17	31.30	166.3	3016	9988	47230	—
22.5	3.01	27.60	150.6	2639	9046	40610	—
25.0	2.81	25.71	137.9	2405	7729	36380	—
27.5	2.69	23.60	124.4	2224	7163	29410	—
30.0	2.49	22.03	114.8	1885	5842	24690	—
32.5	2.39	20.20	103.5	1696	5467	19980	—
35.0	2.23	19.00	93.3	1508	4712	18280	—
40.0	2.02	16.30	80.1	1180	3370	13670	—

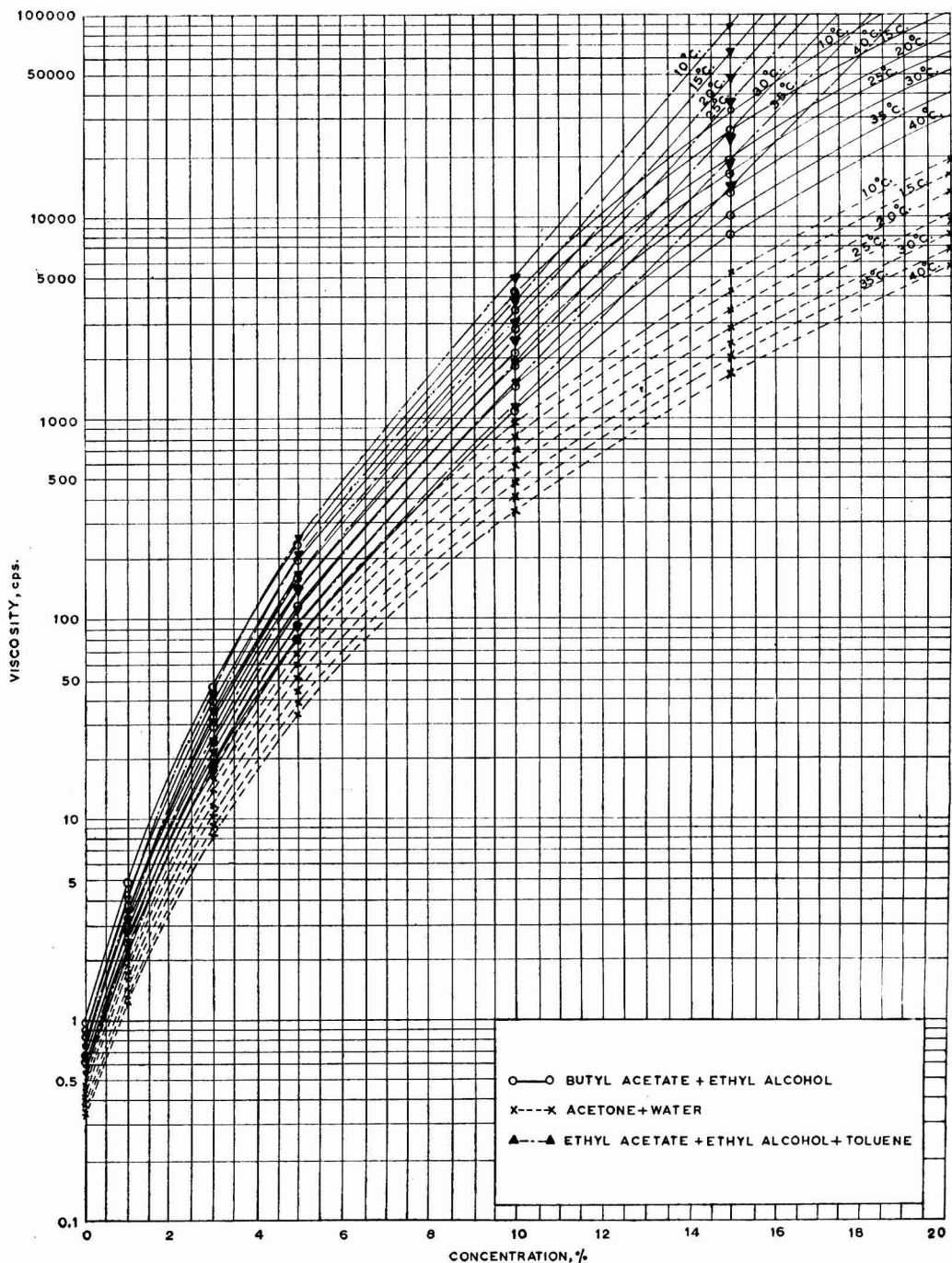


FIG. 2 — VISCOSITY VS. CONCENTRATION

TABLE 2—VISCOSITY IN DILUTE SOLUTIONS

(Solvent, acetone; temp., 20°C.)

CONCENTRATION g./litre C	VISCOSITY OF SOLUTION cps. $\eta_s$	VISCOSITY OF PURE SOLVENT cps. $\eta_0$	RELATIVE VISCOSITY $\eta_r = \frac{\eta_s}{\eta_0}$	SPECIFIC VISCOSITY $\eta_{sp} = \eta_r - 1$	VISCOSITY CONCENTRATION RATIO $\frac{\eta_{sp}}{C}$
0.60	0.3612	0.3250	1.1115	0.1115	0.1858
0.40	0.3492	0.3250	1.0740	0.0740	0.1850
0.20	0.3370	0.3250	1.0370	0.0370	0.1850

(20 per cent), ethanol (25 per cent) diluted with a non-solvent, toluene (55 per cent). This effect is more marked at higher concentrations. Fig. 2 shows the relationships between viscosity and concentration in the above-mentioned solvents. The graphs in this figure closely follow the pattern that is generally obtained for similar data in respect of foreign products<sup>2</sup>.

The results for viscosities in dilute solutions (Table 2) indicate that in pure acetone the viscosity concentration is limiting and constant at concentrations below 0.6 g./litre. Corresponding to the concentrations given in Table 2 the limiting value for the viscosity concentration ratio was attained thus obviating the need for extrapolation to infinite dilution. This limiting value (0.185) can be taken as the intrinsic viscosity of the nitrocellulose sample. Using Staudinger's equation as modified by Mark

$$[\eta] = K_m \cdot P^a$$

(where  $[\eta]$  is the intrinsic viscosity,  $K_m$ , a constant with an accepted value of  $1.1 \times 10^{-3}$  for nitrocellulose of 12 per cent nitrogen content,  $P$ , degree of polymerization, and  $a$ , the index with value 1.06), the average degree of polymerization of nitrocellulose comes to 163.3. The value agrees well with that for imported nitrocellulose of the type under examination.

#### Acknowledgement

Our thanks are due to Messrs P. K. Vaidyanathan and B. Venkateswar Rao for viscosity measurements and to Dr. V. Subramaniam, Superintendent, Cordite Factory, for his kind interest in the work.

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2. *Handbook of Nitrocellulose* (Hercules Powder Co., Wilmington), 1944.

## Letters to the Editor

### TESTING OF DOUBLE SQUIRREL CAGE INDUCTION MOTORS

THE MACHINE CONSTANTS OF NORMAL INDUCTION motors with single cage rotors are determined sufficiently accurately by the no-load and locked rotor tests and measurement of the stator winding resistance. The performance characteristics of the motor can then be predetermined, making use of the equivalent circuit. In the case of the double squirrel cage induction motors such tests

give only the no-load and starting performance of the motor because the effective resistance  $R_{2s}$  and reactance  $X_{2s}$  of the rotor of these motors are functions of the slip  $s$  for rotors with separate end rings as given by the following equations:

$$R_{2s} = \frac{r_2 r_3 (r_2 + r_3) + s^2 (x_2^2 r_3 + x_3^2 r_2)}{(r_2 + r_3)^2 + s^2 (x_2 + x_3)^2}$$

$$X_{2s} = \frac{x_2 r_3^2 + x_3 r_2^2 + s^2 x_2 x_3 (x_2 + x_3)}{(r_2 + r_3)^2 + s^2 (x_2 + x_3)^2}$$

where suffix 2 refers to the inner cage and 3 to the outer cage.

From the machine design data  $r_2$ ,  $r_3$ ,  $x_2$  and  $x_3$  can be calculated and the performance characteristics of the machine predetermined. It is suggested that  $R_{2s}$  and  $X_{2s}$  can be determined fairly accurately, for different values of slip, by conducting the locked rotor test at various frequencies (say for a 50 cycle motor from 50 cycles down to 5 c/s.). From the locked rotor test conducted at a frequency  $sf$ , the short circuit reactance and resistance at this frequency are determined. The difference between the stator winding resistance and this resistance gives  $R_{2s}$ . If the stator leakage reactance at frequency  $f$  is known, the leakage reactance at frequency  $sf$  can be calculated and by subtracting this from the short circuit reactance the value of  $sX_{2s}$  is obtained from which  $X_{2s}$  can be calculated. Fig. 1 shows the plots of  $R_{2s}$  and  $X_{2s}$  against slip  $s$ . Making use of these graphs the characteristics of the motor can be determined on the lines of the single cage rotor (Figs. 2 and 3).

The leakage reactance of the stator may be taken as half the total short circuit reactance at line frequency as is usually done in the case of single cage rotors. If the approximate equivalent circuit where the magnetizing branch is put before the stator resistance and leakage reactance, thereby assuming the magnetizing current to remain constant, is accepted, then there would be no necessity to separate the stator and rotor leakage reactances and the computations would be greatly simplified.

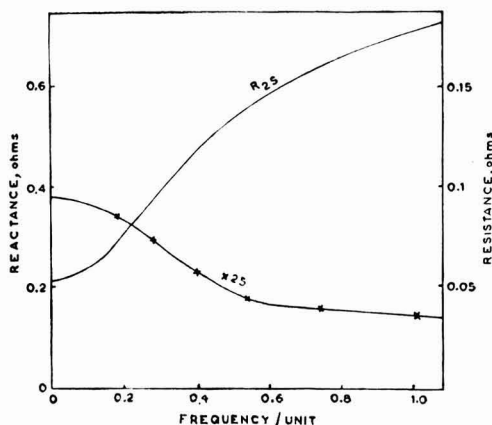


FIG. 1 — PLOTS OF  $R_{2s}$  AND  $X_{2s}$  VS. SLIP

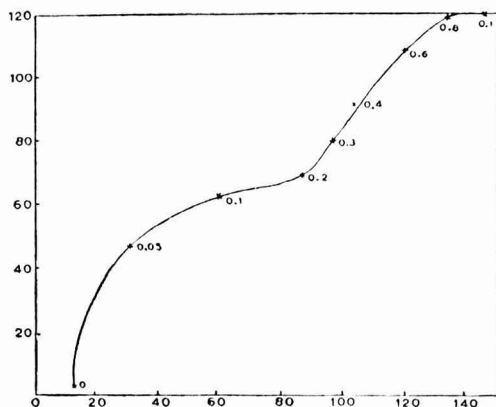


FIG. 2 — POLAR DIAGRAM OF THE MOTOR CURRENT

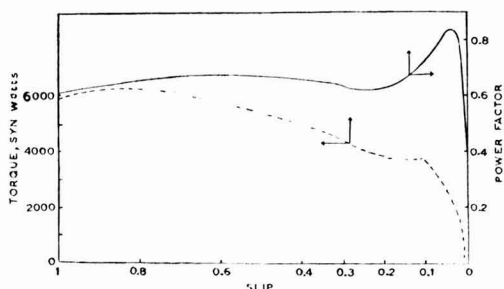


FIG. 3 — PERFORMANCE CHARACTERISTICS OF THE MOTOR

Difficulty is experienced in conducting the tests at frequencies below 5 c/s. due to the low values of the reactances and inaccuracies in the instruments. A hot wire or thermocouple instrument can be used for such low frequencies. But in most cases it is not necessary to use such special instruments as the main requisite is the speed torque characteristic from standstill to about 0.1 slip. If necessary, the  $R_{2s}$  and  $X_{2s}$  curves can be extrapolated for values of slip below 0.1.

This method was adopted in the case of a 110 V., 3 $\phi$ , 50 c/s., 36 amp., 1500 r.p.m., 5 kVA. double cage machine with common end rings. The agreement between the characteristics, predetermined by this method and as obtained by actual loading at reduced voltage and subsequent correction, was fairly satisfactory in view of the approximations made.

T. V. SREENIVASAN

Indian Institute of Technology  
Kharagpur  
25 March 1957

## INDIGENOUS INDIAN DRUGS USED IN THE TREATMENT OF DIABETES

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**D**IABETES as a distinct disease was recognized in India at least 2000 years ago. Hindu physicians of the pre-Christian era were the first to describe the most important symptom complexes of this disorder, e.g. thirst, sweet urine and weight loss. *Susruta*, a well-known medical classic, written around A.D. 100-500, gives a clear description of *Madhu-meha* or *Ikshu-meha*, i.e. diabetes. All the symptoms of diabetes, viz. thirst, foul breath, voracious appetite and langour, have been recorded in this book. Furthermore, the diabetic conditions were clearly recorded in *Charaka Samhita*, an earlier medical compendium of the ancient Hindus and also in the works of 'Agnivesa' and 'Atreya' as far back as 400 B.C. Curiously enough, in a contemporary early authentic Egyptian treatise *Ebers Papyrus*, mention of a disease called 'Polyurea' has been made. This disease bears a close resemblance to diabetes and was known to the ancient Greeks, for Aretaeus of Cappadocia, an ancient Greek writer, gave a fairly clear description of it in his writings nearabout the year A.D. 200. The early European writers, however, did not notice the presence of sugar in the urine of diabetics. In fact, the real cause of sweetness of diabetic urine came to be recognized in modern medicine only around 1776.

Although the disease and its symptoms were clearly recorded by the early Hindu

and Unani physicians, the corresponding reliable records on the lines of treatment followed by them are lacking. Since the time of *Charaka* and *Susruta* to about A.D. 1000, many herbal remedies, individually or in combination in different formulations such as leaf powder, pastes, decoctions and infusions, pills, etc., have been recommended in various medical treatises during the peak period of Hindu medical progress. After that, Hindu medicine started to decline and many drug items not necessarily of tried value have crept into the core of early Indian materia medica mostly from folklore and hearsay evidences. It is, therefore, an almost impossible task for a modern physician to find out the most authenticated lines of treatment which had given really promising results in the hands of early Hindu physicians in the treatment of diabetes.

No medicine capable of giving radical cure of diabetes has yet been discovered. Insulin has undoubtedly given great relief to millions of sufferers but it cannot be said to be an ideal drug for various reasons. Frequent injections have to be given which is quite unpleasant particularly for chronic diabetics who have to take injections for years. Apart from this, the action of soluble insulin tends to be too dramatic — it is usually too quick and too short. A smoother blood sugar curve is very much desirable to minimize the risk of serious hypoglycaemia. In a

chronic disease like diabetes, oral treatment is naturally the most desirable course as this can be continued without physical pain or discomfort to the patients for years together, sometimes every day throughout his life. Several attempts have been made to combine insulin with other substances to make it effective when administered orally but so far no encouraging results have been recorded.

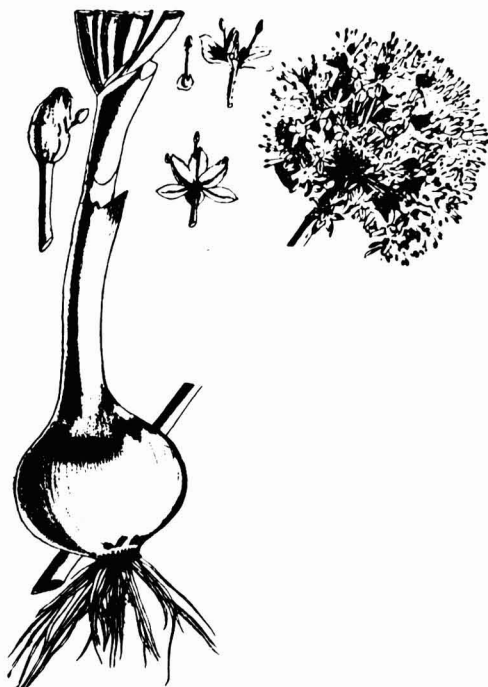
After nearly 23 years of intensive research with a view to finding out an effective oral remedy for diabetes, German workers reported towards the latter part of 1955 that certain synthetic sulphanilylbutylurea compounds administered orally might give encouraging results particularly in chronic elderly diabetics. This finding is under confirmation by workers in various countries. If proved conclusively, this method of treatment may revolutionize the whole concept of the treatment of diabetes.

In ancient Hindu medicine, the treatment of diabetes (*Madhu-meha*) had always been attempted with different drugs and combinations by the oral route and many wonderful claims of cure are on record. A proper evaluation of these claims on modern scientific lines has not been systematically attempted before. It was, therefore, felt that it would be worth while to look into the merits or demerits of these drugs, mainly on experimentally produced diabetes-like condition in laboratory-bred rabbits and also on human diabetics.

Quite a number of herbal remedies and mineral combinations have been considered useful in diabetes. Some of these have been investigated by both Indian and foreign workers by modern scientific methods under strictly controlled conditions in the laboratory as well as on human patients. The important indigenous drugs have been discussed in this article with regard to their present status of knowledge regarding pharmacognosy, chemistry, pharmacology and therapeutic uses.

#### *Allium cepa* Linn. (Liliaceae)

**Indian names**—Assam—*Pivas*; Bengali—*Palandu*, *Piyaz*; Bombay—*Kanda*; Gujarati—*Dungari*; Hindi—*Piyaz*; Kanarese—*Nirulli*; Malayalam—*Bawang*; Marathi—*Kanda*; Punjab—*Piyaz*; Sanskrit—*Palandu*; Tamil—*Vengayam*; Telugu—*Nirulli*.



*Allium cepa* Linn.

**Distribution**—It is cultivated throughout India.

**Description of the plant**—A bulbous herb; bulb thick, globular, tunics membranous. Leaves in 2 rows, shorter than the scape. Scape tall, hollow, inflated and leafy near the base; umbel globular, many-flowered; pedicels 4-5 times as long as the flowers; perianth white, segments ovate-oblong, acutish; filaments longer than the perianth, connate with each other and the perianth at its base, dilated, the outer toothless, the inner with a triangular, obtuse tooth on either side at the base.

**Chemistry**—Fresh onions contain water, 86.8; carbohydrate, 11.6; protein, 1.2; fat, 0.1<sup>1</sup>; sugar, 6.9; citric acid, 0.2-0.5<sup>2</sup>; calcium, 0.18; phosphorus, 0.05 per cent; iron, 7 mg./100 g.<sup>1</sup>; aluminium, 4.3 mg./100 g.<sup>3</sup>; copper, 2.9 mg./100 g.<sup>4</sup>; zinc, 13.1 mg./100 g.<sup>5</sup>; manganese, 63.3 parts per million<sup>6</sup>; iodine, 81.2 µg./100 g.<sup>7,8</sup>; vitamin A, 25 I.U./100 g.; vitamin C, 11 mg./100 g.<sup>9</sup>; nicotinic acid, 0.77 mg./100 g.<sup>10</sup>; thiamin, 64 mg./100 g.; riboflavin, 79 mg./100 g.<sup>11</sup> and pantothenic acid, 1.42 mg./100 g.<sup>12</sup>. It also contains essential oil (0.005 per cent) having sp. gr.<sup>97</sup>,



1.041 and  $(\alpha)_D^{20} = -5^\circ$ . The chief constituent of the essential oil is allyl propyl disulphide<sup>13</sup> ( $C_6H_{12}S_2$ ). It contains a dihydroxy maleic acid oxidase<sup>14</sup>.

**Pharmacology** — The extracts of the juice of onion were found to possess a marked hypoglycaemic activity when administered parenterally to fasting rabbits<sup>15,16</sup>. The blood sugar reducing effect of the extract was observed by Kreitmair<sup>17</sup>.

Oral administration of extracts of onion to rabbits and pancreatectomized dogs causes a lowering of blood sugar. The active principle is volatile with steam and soluble in ether. In addition to the hypoglycaemic substance a substance which raises blood sugar is also present. The lowest blood sugar values are obtained after 1-5 hr.; with prolonged control experiments, an after-effect has been observed in numerous instances. The various active fractions lose their activity when kept for 1-10 days in the ice box despite addition of antiseptics. By fractionation in high vacuum and subsequent recrystallization, a white crystalline substance having m.p.  $174^\circ$  was obtained<sup>18</sup>.

The lipid portion of the juice was extracted with ether. It was found to have no hypoglycaemic effect. The non-dialysable residue from dialysis of lipid-free juice, when injected into rabbits, show a strong hypoglycaemic action; the dialysate also had some action<sup>16</sup>.

Extract of the bulb, when injected subcutaneously into rabbits, showed an action similar to that of insulin; extracts stabilized in solid carbon dioxide give better results than those treated with boiling alcohol. The presence of sugar in the extract may be responsible for the failure to establish glucæmic equilibrium<sup>15</sup>.

Collip<sup>19</sup> obtained active extracts from green tops of sprouting onion plants and from roots and bulbs. Detailed study of these extracts in diabetes has not been reported.

#### *Allium sativum* Linn. (Liliaceae)

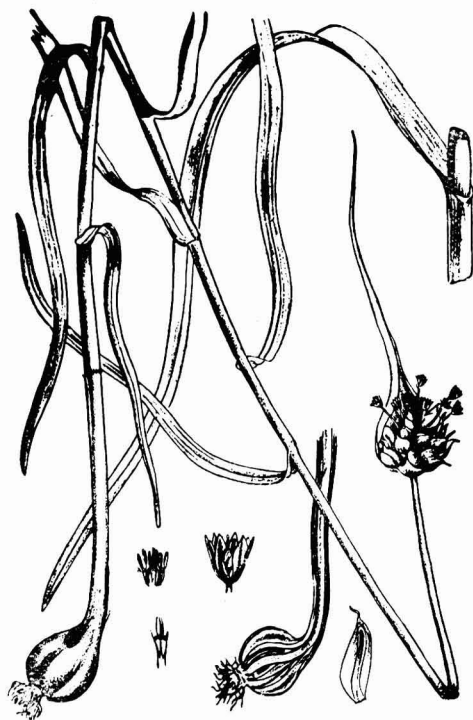
**Indian names** — Assam — *Nahuru*; Bengali — *Rasun*; Gujarati — *Lasun*; Marathi — *Lasun*; Tamil — *Vallaippundu*; Telugu — *Veluli tellagada*; Urdu — *Lehsun*.

**Distribution** — The plant is widely cultivated in India.

**Description of the plant** — A hardy perennial herb. Bulbs with several parts or

cloves, all enclosed in a silky white or pink general envelope or tunic. Leaves several from base of crown, flat, 2.5 cm. or less wide, long pointed. Scape to 60 cm. high, terete, exceeding leaves; umbels small and dense, with long scarious bracts. Flowers, often-displaced by bulbils, usually sterile, pinkish, about 4 mm. long, exceeded by the slender pedicels, with equal lance-acute segments; anthers and style exserted; ovary oblong-ovoid and emarginate at apex.

**Pharmacognosy**<sup>20</sup>: (a) *Macroscopic* — Garlic occurs as a sub-globular, compound bulb, greyish white, 4-6 cm. in diam. and made up of 8-20 cloves, the whole surrounded by 3-5 whitish, papery, membranous scales from the leaf bases of the previous year's bulb and terminating in a thick, papery outgrowth. The cloves attached to a flattened, circular, woody axis with numerous thin, wiry roots on the underside and short, sub-cylindrical outgrowths on the upper surface. Each clove is ovoid, appearing from 3 to 4 sided, surrounded by two papery scale leaves, the outer one whitish and loose, the inner one pink and adherent, but easily separable from



*Allium sativum* Linn.

the solid portion of the clove; the papery scale leaves enclose two whitish, fleshy scales, the inner one thinner and smaller than the outer. Two yellowish green, conduplicate foliage leaves, present in the centre. Odour, when bruised, strongly alliaceous; taste persistently pungent, alliaceous.

(b) *Microscopic* — Cloves show a number of concentric bulblets; each bulblet is 5-10 mm. in diameter consisting of an outer scale, an epidermis, a ground tissue and a layer of lower epidermal cells. Dry scales consist of 2-3 layers of cells rectangular in appearance but with broadly angular slant end walls. These cells contain plenty of rhomboid crystals of calcium oxalate. The upper epidermal cells next to the dry scale layer consist of rectangular to cubical cells of one layer next to which there are several layers of large parenchymatous cells among which there are interspaced many vascular bundles each of which consists of xylem and phloem arranged alternately. Lower epidermis consists of cubical cells which are much smaller than the upper epidermal cells. The same series of arrangements of tissues is met with in different bulblets which are arranged in concentric adjustment. Two to three such bulblets are arranged concentrically.

*Chemistry* — Garlic contains water, 62.8; protein, 6.3; fat, 0.1; carbohydrate, 29.0<sup>21</sup> (sucrose, 3.9); reducing sugar, 0.14; dextrine, 7.69; and starch, 8.22 per cent<sup>22</sup>. It also contains calcium, 0.03; phosphorus, 0.31 per cent; iron, 1.3 mg./100 g.<sup>21</sup>; zinc, 1 mg./100 g. in fresh and 3.17 mg./100 g. in dry state<sup>5,23</sup>. 30.5 per cent of phosphorus is present as phytin and 65 per cent as hexose-monophosphate<sup>24</sup>. It also contains vitamin B<sub>1</sub>, 187 µg./100 g.<sup>25</sup> (free aneurin and aneurin disulphide), riboflavin; 32 µg./100 g.; niacin, 0.395 mg./100 g.; and ascorbic acid, 5 mg./100 g.<sup>11</sup>. It contains an enzyme which is a typical peroxidase<sup>26</sup>.

Garlic contains 0.06-0.1 per cent essential oil having sp. gr.<sup>14,50</sup>, 1.0525. The essential oil contains allyl propyl disulphide (6.0 per cent) and diallyl disulphide (6.0 per cent) and two more sulphur-containing compounds<sup>27</sup>. Dutta *et al.*<sup>28</sup> reported the presence of two active substances, allisatin I and allisatin II, and a third crystalline substance. Stoll and Seebeck<sup>29,30</sup> isolated a crystalline odourless principle, alliin, C<sub>6</sub>H<sub>11</sub>O<sub>3</sub>NS,  $\frac{1}{2}$ H<sub>2</sub>O, m.p. 163°-65°; ( $\alpha$ )<sub>D</sub><sup>20°</sup> = 62.8°. Cavallito *et al.*<sup>21</sup> obtained from the cloves of garlic 0.15

per cent allicin, sp. gr.<sup>20°</sup>, 1.112 and ( $n$ )<sub>D</sub><sup>20°</sup>, 1.561. It has probably the formula C<sub>6</sub>H<sub>10</sub>OS<sub>2</sub>.

*Pharmacology* — Laland and Havrivid<sup>32</sup> extracted from garlic an ether-soluble, steam-volatile alkaloidal substance which, when mixed with the disulphides found in garlic juice and injected into dogs and rabbits, gave a hypoglycaemic reaction. This substance was not considered analogous to insulin.

#### *Coccinia indica* Wight & Arn. (Cucurbitaceae)

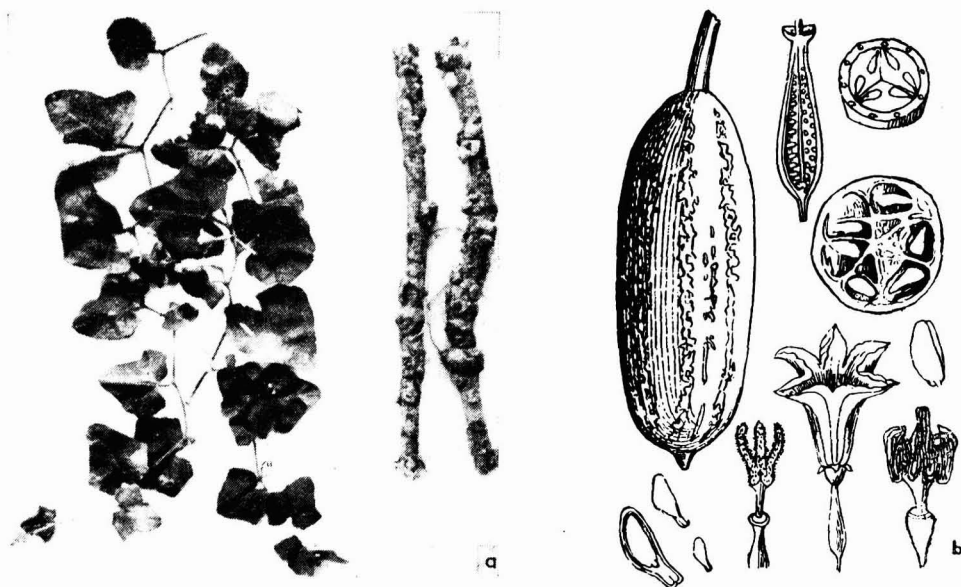
*Synonyms* — *Cephalandra indica* Naud, *Coccinia cordifolia* Cogn., *Momordica monadelphica* Roxb.

*Indian names* — Bengali — *Telakucha*; Bombay — *Tendli*; Gujarati — *Galedu*; Hindi — *Kunderi*; Kanarese — *Tondekai*; Malayalam — *Kova*; Marathi — *Bimbi*, *Tendli*; Punjab — *Kanduri*; Sanskrit — *Bimba*; Tamil — *Kovai-kai*; Telugu — *Dondakaya*; Urdu — *Kundaru*.

*Distribution* — The plant grows wild throughout India.

*Description of the plant* — Perennial, scandent or prostrate, much branched herb. Root thick tuberous. Stems grooved, slender, glabrous. Tendrils slender, striate, simple. Leaves 5-10 cm. long and broad, bright green above, paler beneath, studded and sometimes rough with papillae, palmately 5-nerved from a cordate base, often with circular glands between the nerves, obtusely 5-angled or sometimes deeply 5-lobed, the lobes broad, obtuse or acute, apiculate, more or less sinuate-toothed; petioles 2.3-2 cm. long. Male flowers: solitary, pedicels, 2.3-8 cm. long, subfiliform; calyx tube glabrous, broadly campanulate, 4.5 mm. long; teeth 2.5 mm. long, linear; corolla 2.5 cm. long, veined, pubescent inside, glabrous outside; segments 4.5-7.5 mm. long, triangular, acute; staminal column glabrous; capitulum of anthers subglobose. Female flowers: peduncles, 1.3-2.5 cm. long; staminodes 3, subulate, 3 mm. long; ovary fusiform, glabrous, slightly ribbed. Fruit fusiform-ellipsoid, slightly beaked, 2.5-5 × 1.3-2.5 cm., marked when immature with white streaks, bright scarlet when fully ripe. Seeds somewhat obovoid, rounded at the apex, slightly papillose, much compressed yellowish grey.

*Chemistry* — The tender fruits contain moisture, 93.1; protein, 1.2; fat, 0.1; fibre, 1.6; carbohydrates, 3.5; calcium, 0.04; phosphorus, 0.03; total mineral matter, 0.5 per



*Coccinia indica* Wight & Arn.

cent; iron, 1.4 mg./100 g.; carotene evaluated as vitamin A, 260 unit per 100 g. and vitamin C, 28 mg./100 g.<sup>33</sup> The plant also contains a small quantity of an alkaloid, a hormone and an amylolytic enzyme<sup>34-36</sup>.

**Pharmacology** — The enzyme isolated from *Coccinia* had amylolytic properties. Subcutaneous injection of the hormone in rabbits showed no marked effect on blood sugar. The alkaloid also did not show any pharmacological action on the heart, respiration, blood pressure and isolated uterus. Neither the alkaloid nor the enzyme had any sugar-reducing properties when administered to rabbits<sup>36</sup>. The expressed fresh juice when injected subcutaneously to rabbits showed no effect on the blood sugar level. The fresh juice itself produced no reduction in the sugar content of blood or urine, when administered orally to patients suffering from glycosuria<sup>35,36</sup>.

The antidiabetic properties of the roots have been studied<sup>37</sup>. The water-soluble fraction of the alcoholic extract of the roots has been used in the treatment of experimentally produced alloxan diabetes of rabbits for 58-71 days. In the majority of animals the blood sugar came down to normal or near normal. Glycosuria disappeared and signi-

ficant improvement in general diabetic status was noticed including an increase in weight of the diseased animals. The improvement persisted for 21-34 days following stoppage of treatment during which the animals were kept under observation. Studies are under progress to see if the encouraging results can be duplicated in human diabetics.

**Therapeutic uses** — The drug is used as a household remedy for diabetes in Bengal and Bihar.

#### *Eucalyptus globulus* Labill. (Myrtaceae)

**Indian names** — Hindi — *Neeli-gond*; Tamil — *Karpura maram*.

**Distribution** — The plant was introduced in India in 1843. It grows well in the Nilgiris, at altitudes of 5000-8300 ft., in Annamalai and Palni hills in the south and in Simla hills in the north at altitudes of about 4000-8000 ft. It is also grown in Kumaon, Darjeeling and Shillong.

**Description of the plant** — A handsome gigantic tree. Bark smooth, peeling off in long strips which often remain hanging on the stem or branches. Leaves 20-25 cm. long, falcate, curved, rather thick; those of seedlings sessile, opposite, horizontal, broadly

*Eucalyptus globulus* Labill.

ovate, very glaucous, with a bluish hue. Flowers large, axillary, 1-3 together, nearly sessile; operculum thick, warty, low, abruptly pointed; anthers opening by slits. Fruit 1.8-2.5 cm. diam., warty, angular, valves exserted.

**Chemistry** — The leaves yield 0.8-1.5 per cent of a volatile oil<sup>38</sup> of sp. gr., 0.90-0.9155; ( $\alpha$ )<sub>D</sub> = 5.27-9.68; refractive index, 1.46-1.466; saponification value, 8.9-37.5; cineole content, 54-62 per cent<sup>39</sup>. The oil consists of 2.5 per cent of lower boiling alcohols, aldehydes, ketones and acids; pinenes, 24.0; pino-carveol, 0.4; cuminaldehyde, 0.5; sesquiterpene alcohols, 5.0; aroma-dendrene, 1.0; and phenol, 0.3 per cent<sup>38</sup>. Semmler and Mayer<sup>40</sup> obtained a crystalline camphor, endesmol (C<sub>15</sub>H<sub>26</sub>O), from the oil of *Eucalyptus globulus*.

**Pharmacology** — The use of infusions of the leaves of *Eucalyptus globulus* in the treatment of diabetes mellitus was first advocated by Faulds<sup>41</sup>. Perez<sup>42</sup> obtained good results from infusions or decoctions of the leaves of other species of *Eucalyptus*. Trabut<sup>43</sup> confirmed these findings, but considered that benefit was due rather to the presence of tannins than to any specific antidiabetic principle. John<sup>44</sup> found the infusion ineffective.

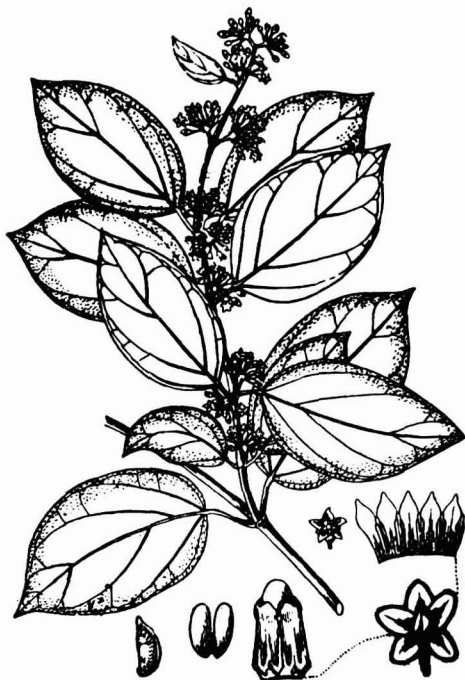
#### ***Gymnema sylvestre* R. Br. (Asclepiadaceae)**

**Indian names** — Bengali — *Medashinge*, *Meshasingi*; Bombay — *Kavali*; Gujarati — *Dhuleti*, *Mardashinge*; Hindi — *Medhashingi*, *Merasingi*; Marathi — *Kavali*; Sanskrit — *Ajashringi*, *Meshashringi*; Tamil — *Adigam*;

Telugu — *Podapatri*; Urdu — *Kakrasingi*, *Mendhasingi*.

**Distribution** — The plant grows abundantly in Madhya Pradesh and Southern India, especially in Konkan, North Kanaras, North Circars, South Maratha countries, Carnatic, Western Ghats and Banda. It also occurs in Ceylon and tropical Africa.

**Description of the plant** — A large woody much-branched climber running over the tops of high trees. Young stems and branches pubescent, often densely so, terete. Leaves 3.2-5 × 1.3-2.2 cm., ovate, elliptic, or ovate-lanceolate, acute or shortly acuminate, more or less pubescent on both sides, sometimes densely so beneath, especially on the nerves, base rounded or cordate, sometimes cuneate; petioles 6-13 mm. long, pubescent. Flowers in pedunculate or nearly sessile cymes; peduncles densely pubescent, shorter than the petioles and arising from between them, sometimes producing successive umbels or whorls of flowers; pedicels 3-13 mm. long, pubescent; bracts minute, ovate-oblong, hairy ciliate; calyx pubescent, divided to the base or nearly so, segments 2 mm. long, oblong, obtuse, ciliolate; corolla yellow, 4-5 mm. across, campanulate, 1.5 mm.

*Gymnema sylvestre* R. Br.

long, about equalling the lobes; lobes thick, ovate-deltoid, spreading, recurved, glabrous; corona of 5 processes inserted on the corolla tube, alternate with its lobes, free at the short deltoid subacute tip which protrudes above the sinus, the lower adnate portion decurrent, channeled and with strongly ciliate margins; style-apex thick, subhemispherical, much exerted beyond the anthers, pearly white. Follicles  $6.3-7.5 \times 0.8$  cm., terete, rigid, lanceolate, attenuated into a beak, glabrous, one follicle often suppressed. Seeds 1.3 cm. long, narrowly ovoid-oblong flat, with a thin broad marginal wing, brown, glabrous.

**Chemistry** — The first systematic examination of the leaves was made by Hooper<sup>45</sup>, who isolated two resins, one insoluble in alcohol and the other alcohol soluble; 6 per cent of an organic acid possessing anti-saccharine property, supposed to be a glucoside, designated as gymnemic acid,  $C_{32}H_{55}O_{12}$ ; a bitter principle; tartaric acid; and calcium oxalate. Power and Tutin<sup>46</sup> isolated gymnemic acid, quercitol and hentriacontane ( $C_{31}H_{64}$ ) from the leaves. They, however, observed that gymnemic acid is not a glucoside nor did it possess any anti-saccharine property. Chopra *et al.*<sup>47</sup> re-investigated the drug, isolated gymnemic acid and prepared a sodium salt. They also isolated some enzymes and tested their sugar hydrolysing action. Later Mhaskar and Caius<sup>48,49</sup> examined the leaves and reported that the air-dried leaves on ignition yield 11.5 per cent of ash consisting of alkali, 46.8;  $P_2O_5$ , 6.7;  $Fe_2O_3$ , 5.4; and Mn, 1.3 per cent. The leaves also contain hentriacontane 0.05 per cent, pentatriacontane, chlorophyll A and B, phytin, resins, tartaric acid, inositol, anthraquinone derivatives and a dark resinous complex substance; gymnemic acid. According to Posternak and Schopfer<sup>50</sup>, the leaves contain cyclitol (1-quercitol), which is identical with viburnitol obtained from *Viburnum tinus*. Noronha and Pinto<sup>51</sup> stated that the leaves contain fats, essential oils, tannins, anthraquinone derivatives, saponins and acid resins. They, however, could not find any component having a direct action on blood sugar. It is presumed that the material stimulates insulin secretion.

**Pharmacology** — According to Mhaskar and Caius<sup>48</sup>, the leaves cause hypoglycaemia in experimental animals which sets in soon after the administration either by mouth or by

injection. This hypoglycaemia has been explained on the assumption that the drug acts indirectly through stimulation of insulin secretion of the pancreas as it has no direct action on the carbohydrate metabolism. They further observed that the leaves stimulate the heart and circulatory system, increase urine secretion and activate the uterus. The leaf extracts have no bactericidal action.

The leaves contain a substance which has a hydrolytic action on cane sugar. There is also an oxidase-like substance which produces glucolysis in a solution containing glucose. When administered subcutaneously to rabbits, the extracts of the leaves or gymnemic acid and its sodium salt have no effect on the blood sugar<sup>45</sup>.

**Therapeutic uses** — The plant has been described in Indian materia medica as an antiperiodic, diuretic and stomachic. *Susruta* describes it as a remedy for glycosuria and other urinary disorders. More than a century ago, Edgeworth noticed that when the leaves of this plant are chewed the taste of sugar and other saccharine substances is abolished. Hooper also confirmed this and discovered that the taste of bitter substances such as quinine is completely removed by chewing the leaves. Dyer reported that after eating one or two leaves it is impossible to taste sugar although other tastes are not obscured<sup>52</sup>.

For the treatment of glycosuria, Mhaskar and Caius<sup>48</sup> recommended 2-4 g. of dry leaf per day in divided doses.

#### *Lochnera rosea* Reichb. (Apocynaceae)

**Synonym** — *Vinca rosea* Linn.

**Indian names** — Bengali — *Nayantara*; Marathi — *Sadaphul*; Punjab — *Rattan jot*; Telugu — *Billaganneru*; Oriya — *Ainskati*.

**Distribution** — The species is probably a native of West Indies and America. It is commonly grown in Indian gardens.

**Description of the plant** — A beautiful herbaceous or somewhat suffruticose plant, 0.3-0.6 m. high with opposite deep green, polished, oval, obovate or oblong leaves and pure white or deep rose-coloured, sessile flowers, usually paired in the axils; base of petiole 2-glandular; corolla 2.5-5 cm. diam.; follicles 2.3 cm. long.

**Chemistry** — The plant contains an amorphous alkaloid<sup>53-55</sup>. Cowley and Bennett<sup>56,57</sup>



*Lochnera rosea* Reichb.

isolated from various specimens of dried leaves 0.53-0.85 per cent of an alkaloidal residue. By fractional crystallization they were able to separate three compounds from this residue.

Preliminary chemical study of leaves of Philippine variety of this plant was carried out by Adaba *et al.*<sup>58</sup>. According to them, the leaves are rich in extractives which include oleoresin, volatile oil containing aldehydes, sesquiterpenes and sulphur compounds, glucoside, various saturated and unsaturated fatty acids, a new alcohol lochnerol,  $C_{21}H_{35}O_2(OH) \cdot 0.5 H_2O$ , m.p.  $244^\circ-46^\circ$ , soluble in petroleum ether and forming an acetate, m.p.  $252^\circ$ , another new alcohol lochnerallol,  $C_{26}H_{39}O(OH)_2$ , m.p.  $285^\circ$ , insoluble in petroleum ether but extracted by ether and forming a diacetate, m.p.  $277^\circ$ , a mixture of several phenolic and non-phenolic alkaloids, one or more quaternary ammonia bases, tannins and other substances. Ash of the leaves contains lithium.

The diploids have a higher riboflavin content than the tetraploids. It has also a higher mucin content in the diploids<sup>59</sup>.

According to Pillay (private communication) some of the alkaloids isolated are of the *Rauwolfia* type. Water extract of *Vinca* contains only a fourth of the total alkaloids present in the plant.

**Pharmacology** — According to Lee and Drew<sup>60</sup> there is no definite evidence that an infusion of leaves of *V. rosea* fed orally to normal rabbits produces a fall of blood sugar

level. On the other hand, Jones<sup>61</sup> reported that patients taking infusion showed definite decrease in glycosuria with a rise in blood sugar suggesting an increase in tubular re-absorption of glucose.

**Therapeutic uses** — The plant is used as a remedy for diabetes particularly in Natal and in other parts of South Africa and in Queensland<sup>62</sup>. Though its utility in diabetes could not be confirmed, several workers found that the leaf extract acts as a good purgative in chronic constipation. The amorphous alkaloid acts as a heart poison<sup>62-65</sup>.

According to Pillay (private communication), pills prepared from watery extract give remarkable improvement in all the secondary symptoms associated with diabetes without significant reduction in the urine glucose. The result of his survey showed that *Vinca rosea* contains a powerful antidiabetic factor in admixture with other factors possibly harmful to some people.

Experiments carried out at the Central Drug Research Institute showed that when whole extract was administered orally, it did not produce any change in the blood sugar level of both normal and alloxan-diabetic rabbits.

#### ***Pterocarpus marsupium* Roxb. (Leguminosae)**

**Indian names** — Bengali — *Piyashal*; Gujerati — *Bia*; Hindi — *Bija*, *Hira-dokhi*; Malayalam — *Vennap paska*; Marathi — *Asana*; Oriya — *Piyasalo*; Sanskrit — *Asana*, *Bandhuka-pushpa*; Tamil — *Asanam*, *Kandamiruga mirattum*; Telugu — *Gandamrugamneethurn*, *Peddagi*; Urdu — *Damulakhvain*.

**Distribution** — The tree is found in South India, the Western Peninsula and Ceylon.

**Description of the plant** — A large deciduous tree with a stout crooked stem and widely spreading branches. Bark thick, yellowish grey, the outer layer corky. Leaves 15-23 cm. long, rachis glabrous, prolonged 2-2.5 cm. beyond the insertion of the upper lateral leaflet; leaflets 5-7, coriaceous, 6.3-10 × 3.8-5 cm., oblong, obtuse, rounded, truncate, or more or less retuse at the apex, glabrous on both surfaces, shining above, base subacute, main nerves numerous, close, prominent. Flowers yellow in short lateral and terminal racemes, branches thinly clothed with brown pubescence; pedicels shorter than the calyx; calyx 6 mm. long, brown-downy, teeth very short, broadly triangular, the upper the



*Pterocarpus marsupium* Roxb.

largest; corolla twice the length of the calyx, pale yellow; stamens monadelphous or the sheath of the stamens sometimes finally split down the keel as well as the top; ovary shortly stalked, ovules, 2. Pods 2.5-5 cm. diam., nearly circular, stalk of the pod scarcely exceeding the calyx, beak of the pod at the basal corner, single seeded; seed small.

**Pharmacognosy**<sup>66</sup>—Kino is the dried exudation from the trunk obtained by incising the bark. It occurs in small (about 3-5 mm.), angular, glistening, brittle fragments appearing almost black in colour, but the edges, when viewed by transmitted light, are ruby-red and transparent; fragments breaking with a glassy fracture and yielding a brownish red powder; on being chewed, it adheres to the teeth and colours the saliva red; odourless; taste very astringent.

**Chemistry**—The bark contains  $H_2O$ , 9.9; tannin, 4.2; non-tannin extractive, 12.9; and ash, 9.6 per cent<sup>67</sup>. Wood-shavings on extraction with petroleum ether (b.p. 40°-60°) yield 0.52 per cent of an oil having the following constants: sp. gr.<sup>25°</sup>, 0.9082; ( $n$ )<sup>25°</sup>, 1.4648; acid value, 18.68; acetyl value, 40.5; iodine value (Wijs), 105.8; Hehner value, 94.4; saponification value, 189.9; unsaponi-

fiable matter, 7.5 per cent<sup>68</sup>. The unsaponifiable matter contains two phytosterols, (i) pterocarpol A (0.011 per cent),  $C_{27}H_{46}O$ , ( $\alpha$ )<sub>D</sub><sup>20°</sup> = -27.7°, and (ii) pterocarpol B (0.005 per cent),  $C_{27}H_{46}O$ , m.p. 161°. The oil consists of linolenic acid, 3.4; linoleic acid, 35.9; and oleic acid, 41.6 per cent; palmitic and stearic acids are also present. It also contains 0.25 per cent essential oil and a yellow colouring matter. Sawhney and Seshadri<sup>69</sup> studied in detail *P. marsupium* and found that the heart wood yields a small quantity of a neutral compound, m.p. 160°. From the alkali-soluble portion they isolated liquiritigenin, isoliquiritigenin and pterostilbene; the sap wood contains pterostilbene along with minor quantities of isoliquiritigenin. The bark contains 1-epicatechin and pterostilbene. Pterostilbene is present in all woods and barks and justifies the claim that it is the most characteristic component of the genus *Pterocarpus*. (More recently Puri and Seshadri<sup>70</sup> isolated from liquorice root chalkone as its glucoside, isoliquiritigenin along with the isomeric flavone glucoside liquitrin.) Liquiritigenin crystallizes in colourless rectangular plates, m.p. 207°-8°; isoliquiritigenin crystallizes in yellow prisms, m.p. 202°-3°. Pterostilbene crystallizes in colourless needles, m.p. 85°-86°; acetate, colourless needles, m.p. 126°-27°.

The gum contains an optically active phlobatannin which is probably a hydroxy flavone derivative<sup>71</sup>. Kino consists of a non-glycosidal tannin kino-tannic acid, a colourless principle kinonin,  $C_{28}H_{24}O_{12}$ , and a phlobaphene kino red,  $C_{28}H_{22}O_{11}$ . On losing two molecules of water kinonin forms a dianhydride,  $C_{28}H_{20}O_{10}$ ; it also contains pyrocatechin, pyrocatechinic acid<sup>72,73</sup> and an enzyme which converts kino-tannic acid into kino red.

Bose *et al.*<sup>74</sup> reported the presence of 0.017 per cent alkaloid, 0.9 per cent resin and a sterol body in the heart wood of the drug.

**Pharmacology**—Ozha *et al.*<sup>75</sup> found that an extract of the wood given orally is effective in lowering blood sugars in rabbits as well as diabetic patients. The maximum reduction in blood sugar occurs during the second hour after the administration of the drug. Urine sugar level also falls along with the blood sugar level. In *in vitro* test, no alteration in concentration of glucose was observed. It produced no toxic symptoms.

**Therapeutic uses** — The wood has a reputation of possessing antidiabetic properties. Some medical practitioners maintain that the sugar content of urine is reduced by drinking water in vessels made from the wood<sup>76</sup>. Sepala and Bose<sup>77</sup> treated several cases of diabetes with *P. marsupium* and reported that in 7 per cent of the cases it was effective in lowering the blood and urine sugars. There was no untoward effect or reaction except in two cases which developed albuminuria. The drug probably increases the kidney threshold for sugar. They observed that *Eugenia jambolana* (*Syzygium cuminii* Skeels) possesses more antidiabetic property than this drug, the former being effective in 42 per cent of the cases.

Preliminary results of experiments with alcoholic and aqueous extracts from authentic material at the Central Drug Research Institute have shown that neither the alcoholic nor the aqueous extract when administered orally or intramuscularly has any effect on blood sugar of normal and alloxan diabetic rabbits. When administered intravenously no change in blood sugar was observed, though muscular relaxation was noticed and the animal became flaccid.

***Rivea cuneata* Wight (Convolvulaceae)**

**Synonym** — *Argyreia cuneata* Ker.

**Indian name** — Kanarese — *Kallana gida*.

**Distribution** — It is found in Southern India, particularly in Mysore.

**Description of the plant** — A shrubby plant, branches often virgate, sometimes somewhat twining. Leaves short-petioled, elliptic or obovate, 5-10 cm., villous beneath, glabrate above, obtuse, mucronate or emarginate. Flowers bright purple; peduncles numerous, short, 3-8 cm., often 3-flowered; bracts deciduous; sepals 5 mm., ovate, subobtuse; corolla bright purple, 5-1 cm., infundibuliform, hairy without; ovary 4-celled. Fruit 2-7 cm., ovoid, shining yellow-brown, nearly dry.

**Chemistry** — The leaves yield a glucoside soluble in water and alcohol, but insoluble in other organic solvents. On acid hydrolysis, it yields glucose and a water-insoluble aglucone. The latter gives colour reactions characteristic of steroids<sup>78</sup>.

**Pharmacology** — The effect of the glucoside on experimental alloxan-diabetes in albino rats was very encouraging. The glucoside was given orally to rats in daily doses of 5 mg.



*Rivea cuneata* Wight

dissolved in water; after 8 days they received subcutaneous injection of 200 mg./kg. of alloxan. At the end of 25 days, all the rats in the treated group had normal blood sugar and no sugar in urine. Mortality was 20 per cent as compared to 60 per cent in the control group. The treated rats had relapses after 30-40 days. A second course of treatment was beneficial in 10 per cent of these rats. Post-mortem examination of pancreas in normal rats receiving the glucoside orally for 30 days and killed 30 days after treatment showed evidence of hyperplasia and hypertrophy of the 'islets of the langerhans'. Other organs appeared normal. Toxicity test

on mice showed that it is non-toxic even in large doses (1.0 g./kg. body weight).

**Therapeutic uses** — Oral administration of milk extract of the leaves of the plant for 3-5 days brought about a significant remission of the characteristic symptoms of diabetes. The glucoside when administered orally has little effect on fasting blood sugar level in man, rabbit and rats and when given subcutaneously it had no effect on blood sugar level in rabbits<sup>78</sup>.

***Scoparia dulcis* Linn. (Scrophulariaceae)**

**Indian names** — Mundari — *Chinibuta*, *Chinisakam*, *Gurara*.

**Distribution** — It is a native of America, but is widely grown in different parts of India.

**Description of the plant** — An erect much-branched foetid herb. Leaves 3-nately whorled, glandular, rhomboid or elliptic, 1.3-3.8 cm., serrate with tapering bases. Flowers 3-6 in each whorl on slender 8-13 mm. long pedicels; corolla delicate white, 5 mm. diam. Capsule subglobose 2.5 mm., valves ultimately 2-fid.

**Chemistry** — Very little work has been done on the chemistry of the active principle of this plant. Nath<sup>79</sup> prepared an aqueous and alcohol-aqueous extract from the fresh green plant. The extract was purified and the residue obtained by evaporation was used as the active principle, named by him as 'amellin'.

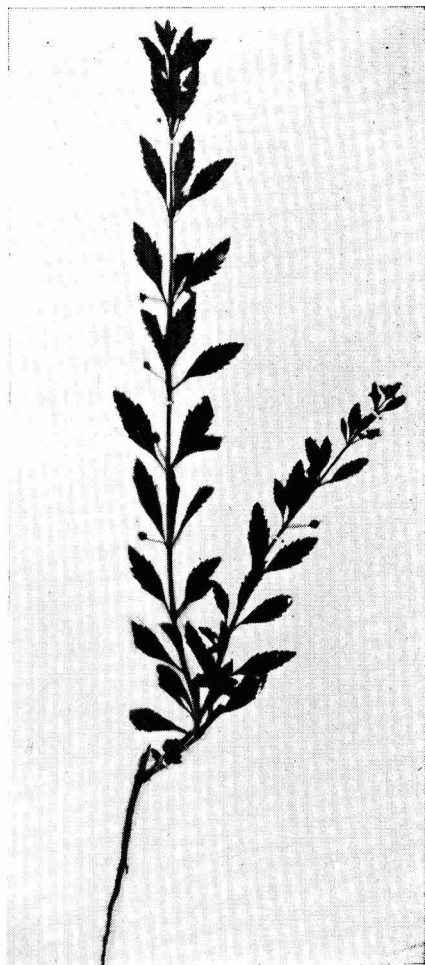
**Pharmacology** — The addition of amellin to high carbohydrate diets in doses of 5 mg./100 g. was found to check the depletion of glycogen storage and the high percentage of lactic acid in the liver and muscle was significantly reduced in albino rats<sup>80</sup>.

Determinations of hyperglycaemia and alkali reserve in cases of diabetes have shown that though there is no definite relationship between the degree of hyperglucaemia and the depletion of alkali reserve, there was gradual and steady rise of alkali reserve in all cases through the use of amellin<sup>81</sup>.

When amellin was injected daily at 10-12 mg./kg. per day into hyperglycaemic rabbits caused by the repeated daily injection of sodium acetoacetate, it reduced the blood sugar to normal. Insulin, although it relieved the fasting hyperglycaemia initially, had little effect on hyperglycaemia in the later stages. Increasing the insulin doses in

such cases caused death. Administration of amellin for 40 days returned the glucose tolerance to normal in the sodium acetoacetate treated animals. Prolonged treatment considerably decreased blood glutathione<sup>82</sup>.

Continued injection of sodium acetoacetate in normal rabbits brought about a progressive increase in the urea and inorganic phosphate of blood as in progressive development of human diabetes. The effect of simultaneous injection of amellin or insulin on animals treated with sodium acetoacetate was studied. Simultaneous injection of amellin into the animals treated with acetoacetate for about three months brought the



*Scopia dulcis* Linn.

value of blood urea and blood inorganic phosphate to the normal limits within 40 days. Insulin used under the same condition was found to be less effective than amellin. The elimination of excessive amounts of urea and inorganic phosphate in the urine caused by acetoacetate was prevented considerably by amellin<sup>83</sup>.

The action of amellin in effecting proper utilization of blood phosphate was also studied. All the cases showed reduction of phosphate from abnormally high values to the range of 1.6-1.75 mg./100 mg. of whole blood over a period of several months. Less severe cases showed a more rapid reduction to normal value than the more severe cases. The superiority of amellin over insulin was demonstrated in that amellin did not cause reduction of blood phosphate below 1.5 mg. level<sup>84</sup>.

Accumulation of intermediary fat metabolism products such as  $\beta$ -hydroxybutyric acid, acetoacetic acid and other acetone bodies is responsible for the onset of hyperglycaemia and possibly other diabetic symptoms associated with decreased sugar tolerance in experimental animals (rabbits). However, the simultaneous oral administration of amellin checks glycogenolysis either by direct activation of the process or by removing or neutralizing the inhibitors of the enzymic reactions<sup>85</sup>.

Oral administration of amellin to mice at high dose level of 1000 mg./kg. was non-toxic. A subcutaneous acute toxicity dose of over 700 mg. was fatal. Cumulative effect of 200 mg./kg. per dog was non-toxic<sup>86</sup>.

Diabetic patients treated with amellin showed after 6 months of urinary elimination of urea, uric acid and creatinine and the initially high values of blood urea and blood creatinine were reduced to normal values. A linear relationship between the blood urea and blood creatinine existed. The view that a high protein diet cannot be beneficial to the patient unless the metabolic disturbances are corrected has been confirmed. Amellin prevents tissue wastage and causes better utilization of protein<sup>87</sup>. Although all patients had diets of high caloric value and carbohydrate content, there was a marked reduction of glycosuria and hyperglycaemia within one month of daily treatment with 15-20 mg. amellin. Unlike insulin, amellin does not cause the blood sugar

level to go below normal and reduction of both blood and urine sugar occurs gradually. In certain patients relief was obtained in conditions associated with diabetes such as acetonuria, albuminuria and acidosis. Amellin treatment caused a reduction of fat from adipose tissue and promoted proper wound healing<sup>88</sup>.

A daily dose of 15-20 mg. of amellin along with simultaneous administration of calcium salts was shown to give relief from diabetes mellitus by oral administration. Experiments *in vitro* indicated that amellin can oxidize glucose in the presence of human plasma and physiological saline. In the presence of diabetic plasma, the extent of oxidation was smaller than with normal plasma<sup>89</sup>.

The high cholesterol content of blood associated with diabetes mellitus responded to amellin treatment in a manner similar to the reduction of blood sugar and phosphate. In a study of patients having initial blood cholesterol values in the range 160-280 mg./100 ml. of blood, a reduction to normal values in the neighbourhood of 130 mg. took place over a period of 2-10 months depending upon the severity of the disease. Administration of 100-200 g. of glucose to diabetic patients caused a rise in both blood sugar and cholesterol while in normal subjects only a temporary rise in blood sugar occurred<sup>90</sup>.

The iron content of the blood of patients was observed over a period ranging from several months to one year. These patients showed anaemia associated with diabetes of long duration and were treated with amellin. During the first two months of treatment there was definite improvement in anaemia characterized by a decrease to normal value of the non-haemoglobin cellular iron, rise in reticulocyte count and fall of blood colour index. In general, a reduction of hyperglycaemia occurred only after the initial adjustment of anaemia<sup>91</sup>.

Budde and Sriner<sup>92</sup> reported that the drug does not possess true insulin-like effect. The changes noted were all within normal variations of blood sugar. In view of the results reported by Nath<sup>79,81,89</sup> the failure to find definite hypoglycaemic effects may be due to the facts that: (a) amellin was obtained by the foreign investigators from some other variety of *Scoparia dulcis*; (b) amellin might be present in the fresh plant and not in the dried material used by other workers; and

(c) the improvement of the patients observed by Nath was due to improved diets, rest and other ancillary factors not directly connected with drug therapy.

Whittaker<sup>93</sup>, in a critical survey of the work of Nath and his associates, found no evidence for supposing that amellin had an important therapeutic action.

***Securigera securidaca* Linn. (Leguminosae)**

*Synonym* — *S. coronilla* DC.

*Distribution* — The herb is found in Western Asia, Syria, Palestine, Dalmatia, North Africa, Germany, France and Southern Europe. It is now cultivated in many areas of Bengal and Bihar.

*Description of the plant* — It is a glabrous diffuse herb, usually scandent or trailing. Leaves alternate, simple, entire. Flowers in terminal or axillary, simple or paniced racemes; calyx short deciduous, lateral, lobes subequal, vexillum suborbiculate, also oblique oblong; carina incurved, subrostrate; stamens detachable, free, filaments especially alternate, superior, slightly dilated; anthers uniform, ovary sessile, many ovulate, style incurved, glabrous, stigma capitate. Fruit linear legume, falcate (scythe-like), acuminate. Seeds exalbuminous, bitegmic, small, compressed, parallelogrammic, about

3.5-5 × 2.3 × 1.1-5 mm. with the hilum in a marginal depression nearabout the middle of one of the long arms; testa thin, membranous, yellowish to dull reddish; tegmen thick, hyaline, tough, celluloid and more or less elastic when soaked; embryo comparatively large, with a pair of slipper-shaped yellowish more or less leafy flat cotyledons, a stout radicle and a minute plumule pressed between the cotyledons.

The seeds when crushed develop a peculiar nauseating odour. The kernel of the seed possesses an intensely and persistently bitter taste.

*Chemistry* — Ghose and Ghose<sup>94</sup> first isolated from the seeds a non-glucosidal bitter principle. Ghosh and Dutta<sup>95</sup> later found that the seeds contain a bitter crystalline glycoside, securigerin, two bitter substances, securin and coronillin, a bland olive-green fixed oil, a sterol (m.p. 115°-16°) and a bitter resin.

*Pharmacology* — The non-glucosidal bitter principle was examined by De<sup>96</sup> and found to produce pressor effect on circulation by its direct action on the cardiac musculature and plain muscle of the blood vessels and also by its action on the sympathetic nerve endings. Higher doses produced a fall in blood pressure.

*Therapeutic uses* — The chloroform-soluble extracts of the seeds have been reported to give encouraging results in cases of diabetes<sup>95</sup>.

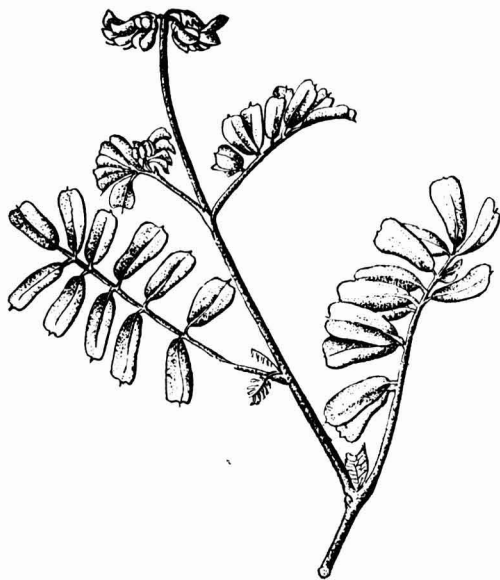
***Syzygium cumini* Skeels (Myrtaceae)**

*Synonyms* — *Syzygium jambolana* Lam.; *Eugenia jambolana* Lam. — Jambul; Jambol; Rose Apple.

*Indian names* — Assam — *Jumu*; Bengali — *Jam*, *Kalajam*; Bombay — *Jamphul*, *Jambu*; Gujerati — *Jambu*; Hindi — *Jaman*, *Jamun*; Marathi — *Jaman*, *Jambul*; Sanskrit — *Jambu*, *Jambula*; Tamil — *Arugadam*, *Sambal*; Telugu — *Jambu*; Urdu — *Jaman*.

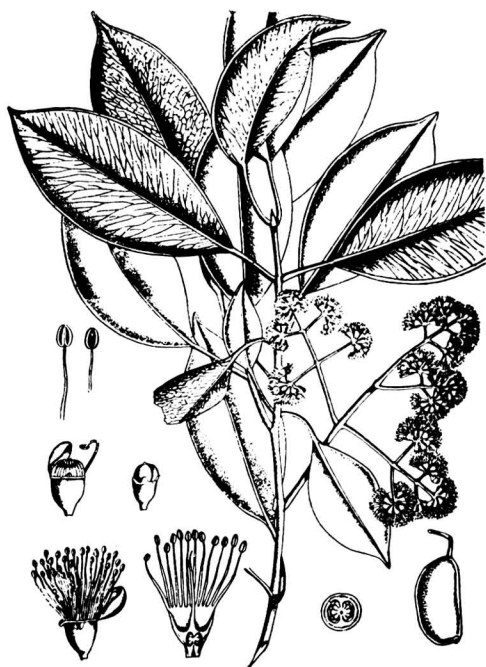
*Distribution* — The plant is a native of most parts of India, except the driest regions, and extends through Malaya to Australia. It is often planted.

*Description of the plant* — It is a large evergreen glabrous tree. Bark smooth, light grey with broad patches of darker colour. Leaves 7.5-15 × 3.8-6.3 cm., elliptic, elliptic-lanceolate, ovate or oblong, obtuse or acuminate, glabrous, shining, coriaceous, petiole



*Securigera securidaca* Linn.



*Syzygium cuminii* Skeels

10-25 mm. Flowers whitish, sessile, scented, in compound trichotomous cymes; calyx tube, turbinate, 3-6 mm. long. Petals calyptrate, stamens many, as long as the calyx tube. Drupe juicy, pink when ripening, black when ripe, 1.2-3.7 cm. long, ovoid, oblong, or globose, usually single seeded.

**Chemistry** — Gerrard<sup>97</sup> reported the presence of an alkaloid jambosine in the seeds and bark. Power and Callan<sup>98</sup> found ellagic acid in the seeds. The bark and fruits contain tannic acid, gallic acid and resin<sup>99</sup>. Rangaswamy *et al.*<sup>100</sup> obtained from the green leaves 0.016-0.018 per cent of an essential oil having the following characteristics: sp. gr.<sup>20°</sup>, 0.8943-0.8986; refractive index at 20°, 1.4934-1.4990; ( $\alpha$ )<sub>D</sub><sup>20</sup> = 13.12°-20°54'; acid value, 1.05-1.43; ester value, 25.3-35.4; ester value after acetylation, 66.9-93.1; solubility in 90 per cent alcohol, 1 in 5 volumes; phenols and aldehydes absent. The oil contains limonene and dipentene (20-30 per cent), sesquiterpene of the cadeninic type about 40 per cent, with small quantities of an azulenic sesquiterpene.

The constituents of the seeds are, a glycoside, antimellin, a resin and gallic acid<sup>101</sup>.

**Pharmacology** — The jambul bark extract is considered to affect the glycogenolysis and glycogen storage in animals, the toxicity depending upon the amount of stored glycogen. The lowering of blood sugar in well-fed experimental animals may not be analogous to that in diabetes in which high blood sugar is associated with low glycogen stores, but may correspond to experiments in which the animals are glycogen-starved and a temporary hyperglucæmia is produced by intravenous injections of glucose<sup>102</sup>.

**Therapeutic uses** — Extracts of the seeds were found by Kramer<sup>103</sup> and Stephenson<sup>104</sup> to reduce glycosuria in diabetic patients and Mercier and Bonnafous<sup>105</sup> demonstrated their hypoglycaemic action. In contrast, Kaufmann<sup>106-108</sup> obtained only hyperglycaemic extracts from the seeds while Mercier and Bonnafous (*loc. cit.*) were unable to obtain active extracts from the bark. The beneficial effects found by Kramer<sup>103</sup> and Stephenson<sup>104</sup> cannot be attributed to any definite active principle or principles. The seeds are astringent to the bowels. A sterile aqueous extract of the seeds caused marked and prolonged decrease in blood sugar upon hypodermic injection into dogs. Oral administration had no such effect<sup>109</sup>. Vaish and Kehar<sup>110</sup> recorded a lowering of blood sugar in alloxan diabetes in rabbits. Recently, Gujral *et al.*<sup>111</sup> reported that oral administration of jamun seeds (0.8 g. orally in 3 divided doses) had no effect in alloxan diabetic animals. Experiments at the Central Drug Research Institute, Lucknow, revealed that the dried alcoholic extract of jamun seeds administered orally to diabetic patients reduced blood sugar and glycosuria. Jambul fruits have been used in India and in the East Indies in the treatment of diabetes mellitus; the fresh seeds are stated to be much superior to the dried ones<sup>62</sup>. Sepalia and Bose<sup>77</sup> compared the antidiabetic property of *S. cuminii* with that of *Pterocarpus marsupium* Roxb. and found that it is more effective than the latter.

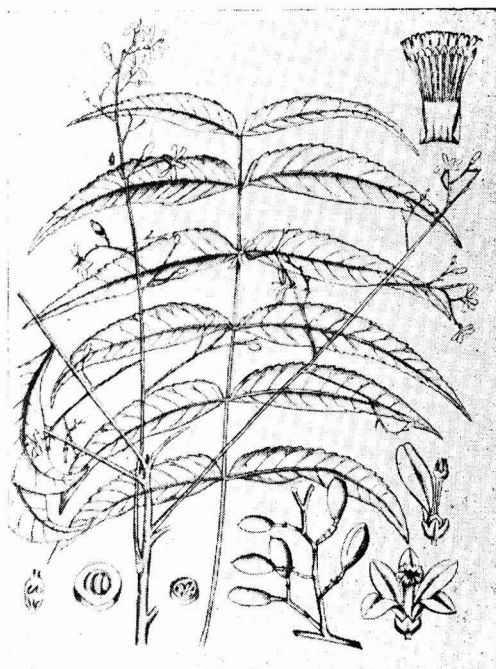
#### Other substances of vegetable origin

Several other plants of indigenous origin such as *Ficus bengalensis* Linn. (*Indian names* — Bengali — *Bot*; Hindi — *Bor*; Sanskrit — *Vata*), *F. glomerata* Roxb. (*Indian names* — Bengali — *Jagya domur*; Hindi —

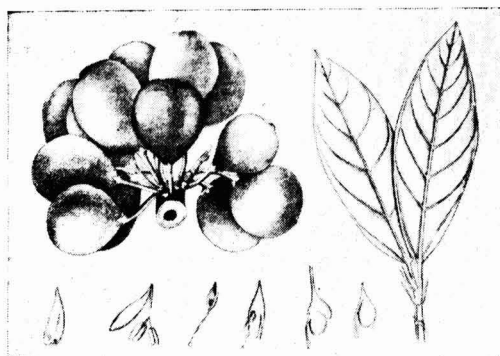




*Ficus bengalensis* Linn.



*Melia azadirachta* Linn.



*Ficus glomerata* Roxb.



*Ficus religiosa* Linn.



*Kandelia rheedii* Wight & Arn.

*Gular*; Sanskrit — *Udumbara*) and *F. religiosa* Linn. (Indian names — Bengali — *Asvatha*; Hindi — *Pipal*; Sanskrit — *Asvatha*) of the family *Urticaceae* in root powders, and *Melia azadirachta* Linn. (Indian names — Bengali and Hindi — *Nim*; Sanskrit — *Nimba*) of the family *Meliaceae* in extracts of the leaves have been found ineffective in alloxan diabetic rabbits by Gujral *et al.*<sup>111</sup>. Experiments carried out at the Central Drug Research Institute showed that neither aqueous nor alcoholic extracts of *Kandelia rheedii* Wight & Arn. (Indian names — Bengali — *Guria*; Tamil — *Kandal*; Oriya — *Rasunia*) of the family *Rhizophoraceae* produced any effect on blood sugar of normal or alloxan diabetic rabbits. Alcoholic extracts of *Adiantum caudatum* Linn. (Indian names — Sanskrit — *Mayurashikha*; Punjab — *Adhsarita-ka-jari*) of the family *Polypodiaceae* were also tried, but no effect on the blood sugar level of either normal or diabetics was observed. Neither it had any effect on glycosuria.

Various workers outside India devoted their attention towards finding a suitable substance analogous to insulin in their action upon the blood sugar from vegetable kingdom. Glaser and Wittner<sup>112</sup> found that mushrooms contain a substance which produces a lowering in the blood sugar level of rabbits. Collip<sup>113</sup> extracted from the roots and sprouted grains of barley substances which were claimed to lower fasting blood sugar level of normal rabbits. This was later confirmed by Donnard and Labbe<sup>114</sup>. Best and Scott<sup>115</sup> prepared extracts from rice which on subcutaneous injection into rabbits produced hypoglycaemia, but these results could not be confirmed by Braun and Rees<sup>116</sup>. Collip<sup>113</sup> found that extracts of green leaves and stems of beans were active. Eisler and Porthin<sup>117</sup> and Mercier and Bonnafous<sup>118</sup> obtained from the dried beans (*Phaseolus* species) active concentrates which caused a lowering of the blood sugar level of fasting rabbits. Kaufman<sup>106-108</sup> isolated from the testa of the pea (*Pisum sativum*) a potent hyperglycaemic extract. He also obtained from the whole pea an extract which when fed to rabbits was effective in lowering the blood sugar level and in reducing alimentary hyperglycaemia. Thalimer and Perry<sup>119</sup> found that raw potato juice when administered parenterally to rabbits produces hypoglycaemia.

#### Mineral preparations in the treatment of diabetes

*Abhra Bhasma*, or ash of mica, was tried in a number of patients suffering from diabetes without producing any apparent effect on the urine or blood sugar<sup>120</sup>. *Silajit* (mineral pitch), an exudation from rock surfaces, is an important drug in the ancient Hindu materia medica and is extensively used by Hindu physicians in a variety of diseases. Chopra *et al.*<sup>121</sup> tried the drug in a series of cases of diabetes mellitus and found that in doses ranging from 5 to 10 grains, 3 times a day, for a period of 8-12 days, it had no effect on blood sugar or sugar in the urine. There was neither a decrease in the total quantity of urine passed nor any amelioration of such symptoms as thirst, exhaustion, etc. The assimilation of carbohydrates was not improved. Ajgaonkar<sup>122-124</sup> treated several diabetic patients with 'Nawajas' which is composed of *Banga Bhasma* (calcined tin), 22 mg.; *Jist Bhasma* (calcined zinc), 22 mg.; *Abhra Bhasma* (ash of mica), 5 mg.; *Louha Bhasma* (calcined iron), 22 mg. with traces of copper and cobalt and obtained improvement in clinical diabetes. According to him, mineral therapy is effective in diabetes starting at a late stage (elderly diabetics) of life. In order to control diabetes in such cases, treatment by oral route has to be continued for a long period. In all such cases mineral therapy either alone or in addition to insulin and diet control was found to be effective.

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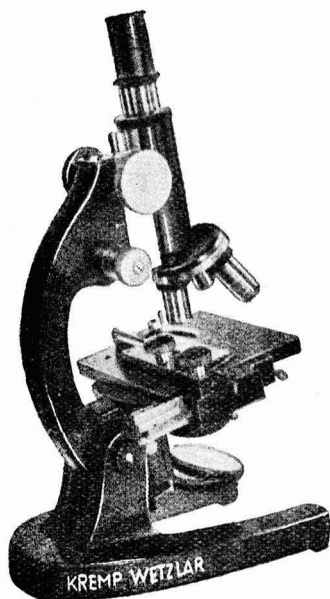
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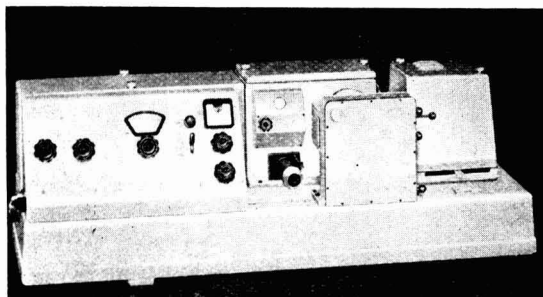
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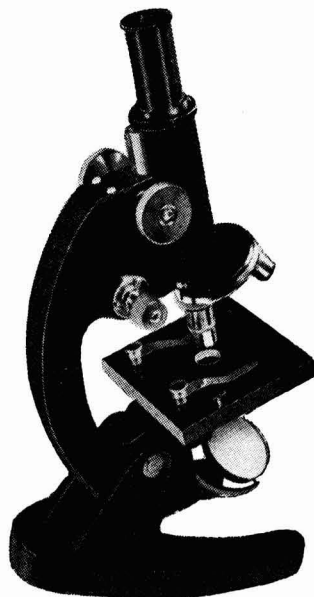
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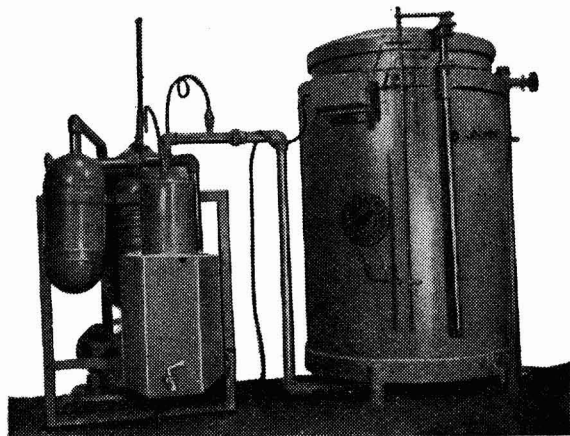
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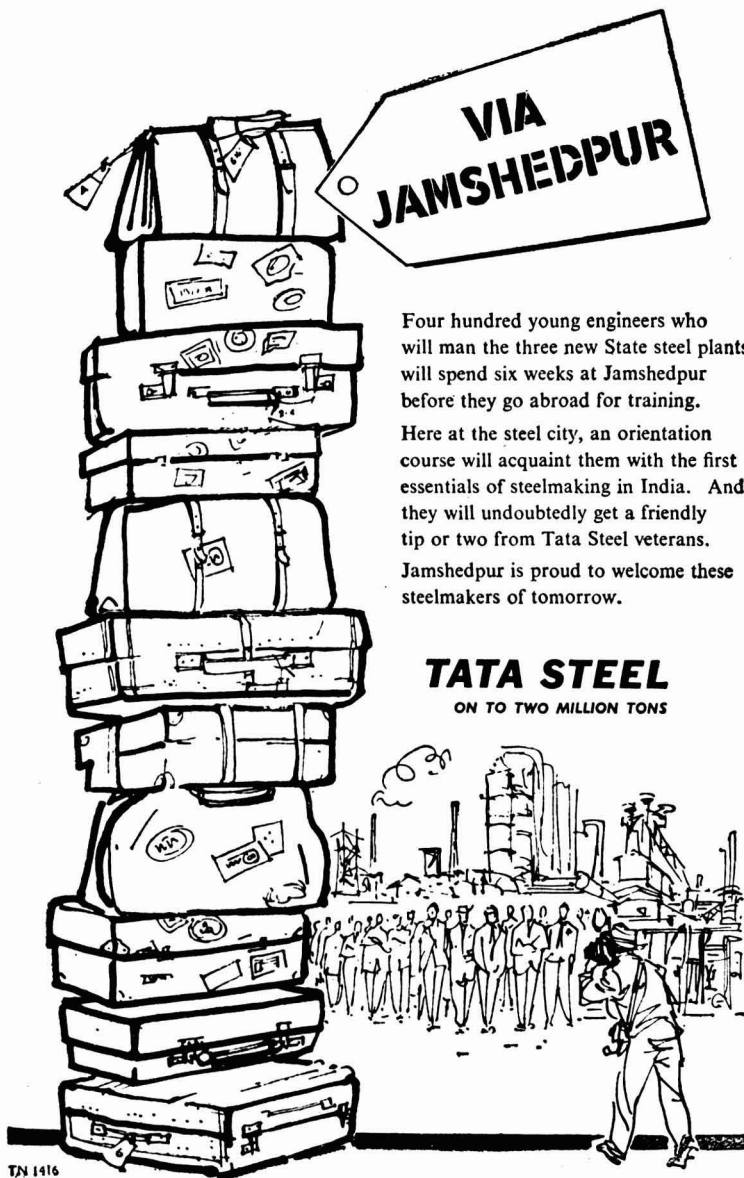
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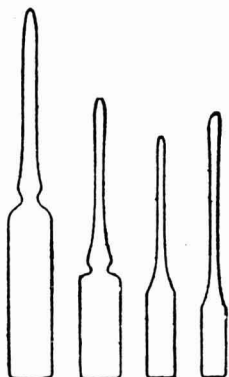
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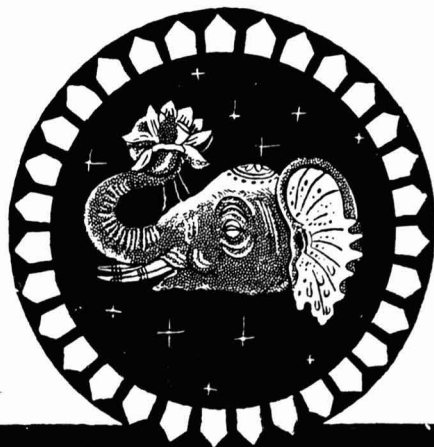


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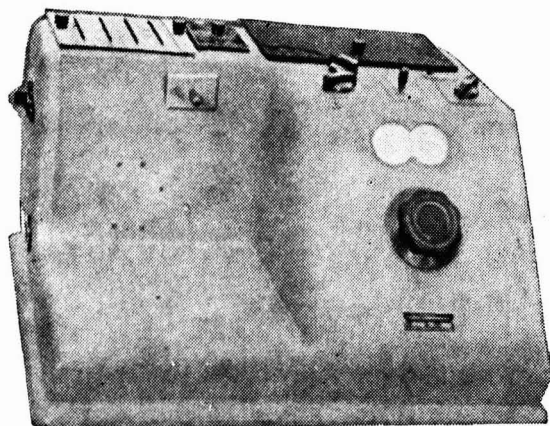
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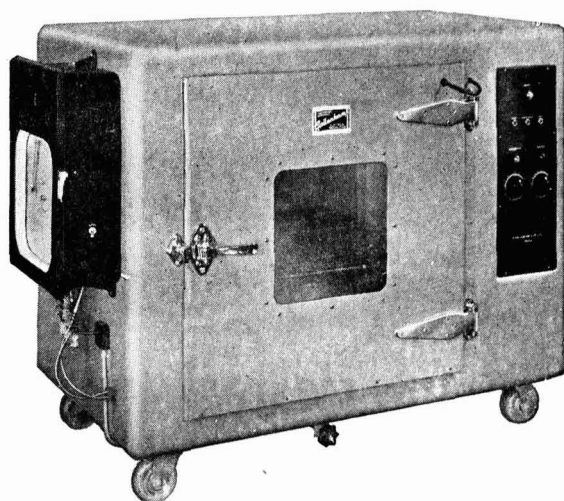
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