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## ABSTRACT

P.berghei-infected mouse red cells and protease-treated red cells can accumulate much more chloroquine than normal red - cells. Blood plasma from P.berghei-infected mice, although containing significant proteolytic activity, cannot activate the chloroquine accumulation in normal mouse red cells. Red cells containing late stages of parasites can accumulate much more chloroquine than those containing early stages. The apparent distribution of chloroquine in P.berghei-infected cells may depend on the method by which the cells are fractionated. Upon saponin lysis and N<sub>2</sub>-decompression, most of the drug is found to be associated with the intact parasites. These two methods of cell fractionation indicate that host-cell membrane and host cytosol are not the major sites for chloroquine binding. Fractionation of P.berghei-infected cells by freeze-thaw lysis and hypotonic lysis also result in most of the drug associated with the pellet fractions. The former method seems to be more - appropriate than the latter since there is no artificial enhancement of electrostatic effect in binding. All the methods used in - fractionating the infected cells indicate that most of the chloroquine is associated with the pellet fractions and therefore suggest the possible existence of chloroquine binding sites in these fractions.

The distribution of chloroquine in protease-treated cells is different from those of P.berghei-infected cells. Freeze-thaw lysis and saponin lysis show that most of the drug is in the lysate fraction. Upon hypotonic lysis, most of the drug is associated with the membrane pellet; this confirm the importance of electrostatic

binding of chloroquine to membrane fragments when cells are -  
fractionated with hypotonic buffer. Moreover, it indicates that  
protease-treated cells may lack binding sites for chloroquine.

The efflux of chloroquine can be enhanced in P.berghei-  
infected cells by inhibitors of glycolysis or by 2,4-dinitrophenol,  
but not by cyanide. Glycolysis inhibitors cannot enhance the efflux  
of chloroquine in protease-treated or normal cells. Fractionation  
by freeze-thaw lysis of the chloroquine-containing infected cells  
after incubation with iodoacetamide or 2,4-dinitrophenol indicates  
that chloroquine associated in the pellet fraction is more sensitive  
to ATP-depletion and uncoupling than that in the lysate fraction.  
It is concluded therefore that energy is required for both uptake  
and retention of chloroquine in P.berghei-infected cells but not  
in protease-treated cells. The membranous organelles or some -  
particulate fractions of the parasites may play a critical role  
in energy-coupled chloroquine uptake and retention.