

Contents

Preface XIII

List of Contributors XV

1 Extraction of Natural Products from Plants – An Introduction 1

Hans-Jörg Bart

1.1 Introduction 1

1.2 Cultivation 6

1.3 Extraction 8

1.3.1 Solvents 8

1.4 Extraction Techniques 15

1.5 Purification 17

1.5.1 Chromatography 17

1.5.1.1 Adsorption Chromatography 17

1.5.1.2 Partition Chromatography 18

1.5.1.3 Ion Exchange Chromatography 18

1.5.1.4 Gel Chromatography 19

1.5.1.5 (Bio-) Affinity Chromatography 19

1.5.2 Continuous Techniques 19

1.5.2.1 True Moving Bed (TMB) Chromatography 20

1.5.2.2 Simulated Moving Bed (SMB) Chromatography 20

1.5.2.3 Annular Chromatography 22

1.5.2.4 Carrousel Adsorbers 22

References 24

2 Solubility of Complex Natural and Pharmaceutical Substances 27

Feelly Ruether and Gabriele Sadowski

2.1 Introduction 27

2.2 Solubility Calculations 27

2.2.1 Solubility of a Pure Solute in Solvents and Solvent Mixtures 27

2.2.2 pH-Dependence of Solubility 29

2.2.3 Solubility of Racemic Compounds 29

2.3 Thermodynamic Modeling 30

2.3.1	PC-SAFT Equation of State	30
2.3.1.1	Hard-Chain Contribution A^{hc}	30
2.3.1.2	Dispersion Contribution A^{disp}	31
2.3.1.3	Association Contribution A^{assoc}	31
2.3.2	Estimation of PC-SAFT Parameters	33
2.4	Examples	35
2.4.1	Solubility of Estriol, Estrone, and Sitosterol in Different Solvents	35
2.4.2	Solubility of Beta-carotene in Supercritical Carbon Dioxide	37
2.4.3	Solubility of Paracetamol in Pure Solvents and Solvent Mixtures	40
2.4.4	Solubility of DL-Methionine as Function of pH	44
2.4.5	Solubility of Mandelic Acid Enantiomers and Racemic Mandelic Acid in Water	45
2.5	Summary	49
	Symbols	49
	Latin Symbols	49
	Greek Symbols and Special Characters	50
	Superscripts	50
	Subscripts	50
	Appendix	51
	Hard-chain Reference Contribution	51
	Dispersion Contribution	52
	Association Contribution	53
	References	53
3	Alternative Solvents in Plant Extraction	55
	<i>Volkmar Jordan and Ulrich Müller</i>	
3.1	Introduction	55
3.2	Ionic Liquids in the Extraction of Natural Compounds from Plant and Fungi	56
3.2.1	Characteristics of Ionic Liquids	57
3.2.1.1	Physicochemical Properties	57
3.2.1.2	Environmental and Safety Aspects	60
3.2.2	Application of Ionic Liquids in Plant Extraction	61
3.2.2.1	Application of ILs in Extraction	61
3.2.2.2	Removal of Target Substance from Extract and Separation of Solvent from Spent Biomass	61
3.2.2.3	Example 1: Extraction of Artemisinin	62
3.2.2.4	Example 2: Extraction of Lignin	64
3.3	Surfactants and Aqueous Two-Phase Systems in Plant Extraction	65
3.3.1	Characteristics of Surfactant–Water Mixtures	67
3.3.2	Behavior of Nonionic Surfactants in Aqueous Solution	71
3.3.3	Micellar Extraction and Cloud Point Extraction	73
3.3.4	Reversed Micellar Extraction	74
3.3.5	Equilibrium Partition of Target Substances in Aqueous Surfactant Solutions	75

3.3.6	Examples for the Use of Surfactants in Plant Extraction	77
3.3.6.1	Plant Extraction Using Micellar and Cloud Point Extraction	77
3.3.6.2	Plant Extraction Using Reverse Micelles	80
3.4	Summary	83
	References	84
4	High Pressure Processing	87
	<i>Rudolf Eggers and Stephan Pilz</i>	
4.1	Introduction	87
4.2	Supercritical Fluids	90
4.2.1	General	91
4.2.2	Physical Properties	93
4.2.3	Solvent Power and Solubility	94
4.3	Physical Properties–Mass Transfer Characteristics	95
4.4	Process Units	99
4.4.1	Pre-Treatment	99
4.4.1.1	Mechanical Pre-treatment	100
4.4.1.2	Thermal and Hydrothermal Treatment	103
4.4.1.3	Innovative Methods	104
4.4.2	Extraction	104
4.4.3	Separation	106
4.4.4	Post-Treatment	107
4.4.4.1	Degassing	107
4.4.4.2	Further Separation	107
4.4.4.3	Stabilization	107
4.4.4.4	Formulation	108
4.5	Process Design and Operation	108
4.5.1	Process Concept	108
4.5.2	Pressurization and Depressurization	109
4.5.3	CO ₂ Recycle Loop	110
4.5.4	Scale-Up	111
4.5.5	Costs	113
4.6	Applications	113
	Acknowledgments	120
	References	120
5	Process Engineering and Mini-Plant Technology	123
	<i>Jochen Strube, Werner Bäcker and Michael Schulte</i>	
5.1	Introduction	123
5.2	Chromatographic Screening	132
5.3	Preparative Task	134
5.3.1	Crude Mixture Pre-Treatment	137
5.3.2	Final Purification of the End Product	139
5.3.2.1	Batch Chromatography	140
5.3.2.2	Annular Chromatography	140

5.3.2.3	Steady-State Recycling Chromatography	141
5.3.2.4	Simulated Moving Bed (SMB) Chromatography	142
5.4	Liquid–Liquid Extraction	143
5.4.1	Introduction	143
5.4.2	Choice of Extracting Agent	144
5.4.2.1	Selection Criteria	145
5.4.3	Data of Chemical and Physical Properties	146
5.4.4	Specification of Separation Sequence	147
5.4.5	Operation Concepts in Extraction	148
5.4.6	Determination of Equipment Efforts	151
5.5	Mini-Plant Technology for Extraction Process Development	155
5.6	Cost Estimation	159
5.7	Total Process Development	160
5.7.1	Mini-Plant Technology	160
5.7.2	Examples of Typical Processes	164
5.7.2.1	Quassia Extracts	164
5.7.2.2	Spruce Bark Extracts	165
5.7.2.3	Pepper Extracts	167
5.7.2.4	Vanilla Extracts	167
5.7.2.5	Taxol Extracts	168
5.7.3	Process Modeling and Scale-Up	171
5.8	Future Developments	175
	Acknowledgments	175
	References	176

6 Extraction Technology 181

Andreas Pfennig, Dirk Delinski, Wilhelm Johannissbauer and Horst Josten

6.1	Introduction	181
6.2	Extraction Process Basics	181
6.2.1	Introduction	181
6.2.2	Extraction Techniques	183
6.2.2.1	Solid–Liquid Extraction	183
6.2.2.2	Process Alternatives	185
6.2.2.3	Continuous or Discontinuous Extraction	186
6.2.3	Further Considerations	186
6.3	Experimental Procedures	187
6.3.1	Extraction Curves	187
6.3.2	Determination of Equilibrium and Kinetics	187
6.3.3	Standard Laboratory Experiment	190
6.3.4	Example Extraction of Pepper	191
6.3.4.1	Calibration with Pure Component	191
6.3.4.2	Pre-treatment of Solid Raw Material	191
6.3.4.3	Extraction Kinetics	192
6.4	Theoretical Modeling and Scale-Up	193

6.4.1	Macro-Model	194
6.4.1.1	Ideal Stirred Tank	194
6.4.1.2	Ideal Plug-Flow Extractor	195
6.4.1.3	Other Macro-Models	195
6.4.2	Micro-Models	196
6.4.2.1	Other Micro-Models	197
6.4.3	Fitting to Experimental Data and Model-Based Experimental Design	199
6.4.4	Scale-Up Design	199
6.5	Industrial Extraction Equipment	200
6.5.1	Pre-processing of Plant Material	200
6.5.2	Selection of Extraction Solvents	201
6.5.3	Solid-Liquid Extraction Processes	202
6.5.3.1	Batch Processes	202
6.5.3.2	Continuous Processes	204
6.5.4	Extractor Design	205
6.5.4.1	Batch Equipment	206
6.5.4.2	Continuous Extractors	208
6.5.5	Future Developments	212
6.5.6	Extract Treatment	215
6.5.7	Depleted Plant Treatment	216
	Symbols	217
	Latin Symbols	217
	Greek Symbols and Special Characters	218
	Subscripts	218
	References	218

7 Extraction of Lignocellulose and Algae for the Production of

Bulk and Fine Chemicals 221

Thomas Hahn, Svenja Kelly, Kai Muffler, Nils Tippkötter and Roland Ulber

7.1	Introduction	221
7.2	Products from Lignocellulose	222
7.2.1	Cellulose Fraction	222
7.2.2	Hemicellulose Fraction	224
7.2.3	Extraction of Fermentation Inhibitors	225
7.2.4	Lignin Fraction	226
7.2.5	Continuous Extraction of Lignocellulose	227
7.3	Polysaccharides and Sporopollenin from Marine Algae	227
7.3.1	Agar	227
7.3.2	Carrageenan	230
7.3.3	Alginic Acid	232
7.3.4	Fucoidan	235
7.3.5	Sporopollenin/Algaenan	238
	References	242

8	Natural Products—Market Development and Potentials	247
	<i>Sybille Buchwald-Werner and Friedrich Bischoff</i>	
8.1	Introduction	247
8.2	Natural Product Market Overview	247
8.2.1	Market for Extracts	248
8.3	Natural Products in Food and Functional Food	249
8.3.1	Functional Food Concept Based on Natural Products	249
8.3.2	Natural Product Development	250
8.3.3	Food Applications of Natural Products	252
8.3.4	Success Story Plant Sterols for Heart Health	256
8.3.5	Baobab—The New Superfruit	257
8.4	Natural Products for Pharmaceutical Applications	259
8.4.1	Existing Products and Innovation	259
8.4.2	Terpenes: Paclitaxel (Taxol)—The Posterchild	262
8.4.3	Alkaloids: A Group of Potent APIs	263
8.4.3.1	Camptothecin-derived APIs	263
8.4.3.2	Omacetaxine (Homoharringtonine)	264
8.4.3.3	Opiate Alkaloids	264
8.5	Summary	266
	References	267
9	Regulations and Requirements	269
	<i>Guido Ritter and Alwine Kraatz</i>	
9.1	Introduction	269
9.2	Definition of Plant Extracts as Medicines or Foods— A Borderline Issue	270
9.2.1	Medicines	270
9.2.2	Foods	271
9.3	Application of Plant Extracts in Flavorings, Functional Foods, Novel Foods and Food Supplements	272
9.3.1	Flavorings	272
9.3.2	Functional Foods	273
9.3.3	Regulation on Nutrition and Health Claims Made on Foods	273
9.3.3.1	Nutrition Claim	275
9.3.3.2	Health Claim	275
9.3.3.3	Reduction of Disease Risk Claim	276
9.3.4	Regulation Concerning Novel Foods and Novel Food Ingredients	276
9.3.5	Regulation Concerning Food Supplements	277
9.3.6	The Health Benefits of Food Products Containing Plant Extracts	278
9.3.6.1	Mode of Function Plant Extracts as Antioxidants	278
9.3.7	Examples of Applications of Plant Extracts in Functional Foods and Dietary Supplements	278
9.3.7.1	Black and Green Tea	279
9.3.7.2	Ginkgo Biloba	280
9.3.7.3	Soy Protein	280

9.4	Requirements Concerning Quality and Safety Issues	281
9.4.1	Technical Data	283
9.4.1.1	Identity and Nature of the Source Material	283
9.4.1.2	Manufacturing Process	284
9.4.1.3	Chemical Composition	284
9.4.1.4	Specifications	284
9.4.1.5	Stability of the Botanical or Botanical Preparation used as Ingredient in Food Supplement	284
9.4.1.6	Proposed Uses and Use Levels	284
9.4.1.7	Information on Existing Assessments	285
9.4.2	Additionally Data on Exposure and Toxicological Exposure: Extent and Time	285
9.4.3	Toxicological Data	285
9.5	Conclusions	286
	References	286
	Index	291