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Measurement of log D and pK(a); Abbreviations; Symbols; 2.1 Introduction; 2.2 Relationship between Ionization and Lipophilicity; 2.3 Measuring log D; 2.3.1 Shake-flask Method; 2.3.2 pH-metric Method; 2.3.3 Direct Chromatographic Methods; 2.3.3.1 Chromatographic Hydrophobicity Index (CHI); 2.3.3.2 Microemulsion Electrokinetic Chromatography (MEEKC) 2.3.3.3 Chromatography in the Presence of Octanol 2.3.3.4 Reversed-Phase Chromatography; 2.3.3.5 Liquid-Liquid Partition Chromatography; 2.4 Measuring pK(a); 2.4.1 Review of Methods; 2.4.2 The Effect of Co-solvents on pK(a); 2.4.3 pH-Metric Titration; 2.4.4 Hybrid pH-Metric/UV Method; 2.4.5 Other Methods; 2.4.6 pH Gradient Titration; 2.5 Some Thoughts about High-throughput Analytical Chemistry; Acknowledgments; References; 3 High-throughput Measurement of Permeability Profiles; Abbreviations; Symbols; 3.1 Introduction 3.2 Key Historical Developments in Artificial-Membrane Permeability Measurement 3.3 The Ideal in vitro Artificial Membrane Permeability Model; 3.3.1 Lipid Compositions in Biological Membranes; 3.3.2 Permeability-pH Considerations; 3.3.3 Role of Serum Proteins; 3.3.4 Effects of Cosolvents, Bile Acids, and other Surfactants; 3.3.5 Components of the Ideal; 3.4 New Directions in PAMPA; 3.4.1 Concentrated and Charged Phospholipid Membranes; 3.4.2 Gradient-pH Permeability Equation; 3.4.3 Permeability Measurements: High-phospholipid in Surfactant-free Solutions 3.4.4 Membrane Retention Measurements: High-phospholipid in Surfactant-free Solutions 3.4.5 Egg Lecithin and the Degree of Negative Charge; 3.4.6 Summary: Increasing Phospholipid Content in the Absence of Sink Conditions; 3.4.7 Effects of Surfactant on High-phospholipid Membrane Permeability and Retention; 3.4.8 Quality and Usefulness of the UV Spectra; 3.4.9 Iso-pH and Gradient-pH Mapping in 2% DOPC-Dodecane; 3.4.10 Iso-pH Mapping in 20% Soy Lecithin-Dodecane, with Surfactant 3.4.11 Predictions of in vivo Human Jejunal Permeabilities using the Improved 20% Soy Lecithin with Surfactant in vitro PAMPA Technique

Sommario/riassunto

The peroral application (swallowing) of a medicine means that the body must first resorb the active substance before it can begin to take effect. The efficacy of drug uptake depends on the one hand on the chemical characteristics of the active substance, above all on its solubility and membrane permeability. On the other hand, it is determined by the organism's ability to absorb pharmaceuticals by way of specific transport proteins or to excrete them. Since many pharmacologically active substances are poorly suited for oral intake, a decisive criterion for the efficacy of a medicine is its so-