Cell as Receptor System

Until relatively recently, the cell membrane has been conceptualized as a fixed structure surrounding the liquid cytoplasm. A growing literature now maintains that the cell membrane is also a liquid but that its degree of viscosity exceeds that of the cytoplasm. It would follow from this reasoning that the total cell may thus be considered to be a solution, subject to the physical-chemical laws that govern such states[1]. If one views the total cell as a solution, then the cytoplasm can be conceptualized in terms of a coacervate[2].

The proposal of the total cell as a solution has a number of immediate applications to cell-drug interactions. First, the model we advocate is consonant with Ferguson's thesis for those drugs whose action is a function of the chemical potential of the drug in solution, the cell in this instance being the solution. The extremely fine tuned specificity implicit in our model of the cell is verified by the facts pertaining to geometric and optical isomers. Thus, geometric isomers are known to have different solubility values. Even optical isomers, in the optically active media of the total solution of the cell, have different physical-chemical properties, one of which is different solubility values.

An important clinical and theoretical application involving drug activity is immediately evident. The conventional view of drug-receptor interaction presupposes a fixed, highly stereospecific similarity between the drug and the receptor surfaces of the cell. However, if the cell is to be considered a solution, as we maintain, then one may speak of different degrees of drug-solvent solubility. Thus, drugs with subtle differences in activity would be expected to have correspondingly subtle differences in their cell solution solubility values. If one considers the fact that each of the thousands of drugs now available has a different saturation point, it becomes clear that the apparently amorphous solvent system is in reality a continuum consisting of an equilibrium of an infinite number of points contributing to solvent specificity.

The classic "lock and key" concept carried to its logical conclusion implies that a universe of a thousand drugs infers a corresponding universe of a thousand receptor sites. By contrast, totality of the cell solution as a single receptor system means that it can assume a configuration specific to the slightly varying configuration of each innumerable, individual drug.

Other facts also support our proposed model. Present concepts of the cell do not satisfactorily explain paradoxical and biphasic drug dose response. Solution theory as applied to the cell does. Thus, in solution theory, it is recognized that as a point of saturation in the solution is reached and exceeded, aggregation of the drug molecules occurs. Depending on the structure of the aggregate, the drug response can level off, reverse itself, or be paradoxical, *i.e.*, contrary to expectation.

In our view, these facts and others argue for the proposition that the cell as a solution acts as a single receptor system.

Bernard Ecanow
Bernard H. Gold
College of Pharmacy
University of Illinois
Chicago, Ill.
and
Department of Anesthesiology
Rush Medical Center
Chicago, Ill.

Received March 8, 1974.

[1] B. Ecanow and H. L. Klawans, in "Physical Chemical Models of Membranes in Models of Human Neurological Disease," 1st ed., H. L. Klawans, Ed., Excerpta Medica, Amsterdam, The Netherlands, 1974.
[2] B. Ecanow and B. Gold, *N. Engl. J. Med.*, in press.