i) the conformation and steric structure of a solute molecule affects its hydrophobic character;
ii) the principle of additivity of hydrophobic increments of substituents seems to be valid for nonpolar solutes and only for a very limited number of polar and amphiphilic solutes;
iii) the relative hydrophobicity of many biological (and synthetical) solutes and of their ionizable fragments depends upon the chemical composition of an aqueous medium, and this dependence is likely to regulate transport and functions of these solutes in biological systems.

8 Conclusions

The above examples imply that the modern concepts of the hydrophobic properties of both biological and synthetical solutes are far from adequate. As is usually the case, an advancement of the concepts seems to depend upon the development of new experimental techniques. We believe that the most important question at present is the one of the influence of the chemical composition of an aqueous medium on the hydrophobic character of a solute. This question is, on the one hand, essential for the progress of the concepts of hydrophobic properties of solutes and of fundamentals of water structure and solution theory and, on the other hand, it seems important for better understanding the factors regulating biological processes and biological potency of chemical agents.

The aforementioned examples of deviations from the principle of additivity of hydrophobic increments of constituents compel us to take a "retrograding" position. It is generally accepted [1,2] that one of the main achievements provided by the Hansch approach [3] is the possibility to calculate the relative hydrophobicity of solutes which takes a lot of burden from the experimenter. On the strength of the aforementioned experimental data and theoretical concepts, however, the authors of the present review are forced to stress the necessity to return to experimental measurements of the relative hydrophobicity of solutes. It seems to us that this is essential in order to turn the QSAR studies of drugs and biological molecules from the correlation analysis field into that of the study of the mechanism of biological action of chemical compounds. We believe that the possibility to quantify the relative hydrophobicity of solutes of different chemical nature provided by the method of partitioning in the aqueous ficoll-dextran biphasic system serves as the basis for this perspective.

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