EPITHEORESE KLINIKES FARMAKOLOGIAS
KAI FARMAKOKINETIKES, INTERNATIONAL
EDITION 3: 67-68 (1989)

Editorial

The trial and error approach in the development of new drugs, which had prevailed in the past, is now yielding to sophisticated procedures based on advanced physical chemical technics rapidly available to the scientific community.

We felt, therefore, that this issue of the "Epitheorese Klinikes Farmakologias kai Farmakokinetikes, International Edition" be primarily devoted to presenting to its readers some of these technics, of particular importance to rational drug design.

X-ray diffraction methodology combined with the technics of Gene Cloning and site-directed mutagenesis have led to wide applications of engineered enzymes in industry. N. Oikonomakos et al, taking as an example glycogen phosphorylase b, introduce the basic concepts of X-ray diffraction by protein crystals and describe how this method has furthered our knowledge on the structure of the enzyme and how this knowledge has deepened our insight on the function of phosphorylase b and on its control.

In the following paper A. Makriyannis and T. Mavromoustakos probe drug-membrane (isolated membrane or model membrane) interaction using solid state NMR, small angle X-ray diffraction and differential scanning calorimetry. In the focus of interest are two classes of drugs, anaesthetic steroids and cannabinoids, which seem to exert their effects by interacting with cell membranes. The authors demonstrate how the results, amassed by application of the above mentioned technics in probing drug-membrane interaction, lead to a deeper understanding of drug action at the molecular level, as a prelude for a rational design of new and more potent drugs.

The last part of this issue deals with the important problem of metabolic transformation of non-active to highly potent compounds. C. Ioannides centers his article on a class of environmental carcinogens, the polycylcic aromatic hydrocarbons, involved in several human cancers. These substances are metabolically transformed to dihydrol-epoxides, the ultimate carcinogens. Their formation involves oxidations by cytochrome P-450-I-dependent mixed function oxidase.

The polycyclic aromatic hydrocarbons induce the cytochrome P-450-I- family, thus stimulating their own metabolic activation. This induction could be a major determining factor of the carcinogenic potential of this class of carcinogens and such a mechanism could have a direct bearing to human cancers, induced by these carcinogens.

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