

A Note on Retrometabolic Drug Design for Developing Drugs

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EDITORIAL NOTE

Retrometabolic drug design, in the area of developing drugs, is a method for building safer medications by using either known metabolism to an inactive moiety or tailored drug delivery approaches. Nicholas Bodor developed the word "retrometabolic drug design." The process is similar to retrosynthetic analysis, which involves planning the synthesis of a target molecule backwards. The metabolic response information of medicines is utilized in retrometabolic drug design to create parent drugs whose metabolism and distribution may be manipulated to target and eliminate the drug, increasing efficacy while reducing undesired side effects substances that have a higher therapeutic index.

The terminology "retrometabolic drug design" refers to two different approaches to medication synthesis. One strategy is to create Soft Drugs (SDs), which are novel, active therapeutic agents that are often isosteric or isoelectronic analogues of a lead substance and have a chemical structure that allows predictable metabolism into inactive metabolites once they have achieved their therapeutic impact (s). The design of Chemical Delivery Systems (CDSs) is the other technique. CDSs are biologically inert compounds that are used to improve drug delivery to a specific organ or site and require many conversion stages before the active gas is released.

SDs are active initially administered and are designed to be rapidly metabolized into inactive species, whereas CDSs are inert when administered and require sequential enzymatic processes to provide differential distribution and finally release the active medication. In an ideal circumstance, a CDS would have the drug present just at the site and nowhere else in the body since

enzymatic processes degrade the drug at those locations. Whereas CDSs, which are designed to target drugs to a certain organ or site, SDs are designed to allow for a differential distribution, which can be thought of as reverse targeting.

Nicholas Bodor, one of the first and most famous advocates for the early integration of metabolism, pharmacokinetic, and general physicochemical factors in the drug design process, presented these retrometabolic design methodologies. These drug design approaches highlight the relevance of design-controlled metabolism and directly focus on increasing the activity/toxicity ratio (therapeutic index) rather than increasing activity alone in order to provide maximum benefit while reducing or eliminating unwanted side effects.

The theory of designed-in metabolism was unique at the time of its introduction, and it went against popular thinking at the time, which concentrated on decreasing or completely eliminating drug metabolism. Bodor's work on these design principles began in the late 1970s and early 1980s, but he became well-known in the mid-1990s.

Bodor's soft corticosteroid, loteprednol etabonate, was approved by the Food and Drug Administration (FDA) in 1998 as the active ingredient in two ophthalmic preparations. It really is currently the only corticosteroid approved by the FDA for use in all inflammatory and allergy-related ophthalmic disorders. Its long-term safety contributes to the soft medication concept, and loteprednol etabonate was approved as a part of a combination product in Zylet. A new generation of soft corticosteroids, such as Etiprednol and Diclloacetate, is being developed for a variety of other uses, including nasal spray for rhinitis and asthma inhalation products.

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