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Editorial Note on Pro Drug Design

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EDITORIAL

Drug design and development aim to achieve a good correlation between structure and activity. They target increased selectivity and specificity associated with drug action. However, unacceptable physicochemical properties limit drug use. Instead of searching for new drugs, it has always been a better approach to correct the limitations linked with existing drugs. The prodrug concept has opened an innovative area for researchers and serves as a "magic bullet" in the drug development process. This concept has set a lifeline for the drugs whose use is restricted due to unwanted side effects. Thus, prodrug design comprises an area of research devoted to optimizing drug delivery.

The prodrug concept has been used to improve undesirable properties of drugs since the late nineteenth century. Prodrugs are inactive, bioreversible derivatives of active drug molecules that must undergo transformation in vivo to release the active parent drug, which can then elicit its desired pharmacological effect in the body. In most cases, these are simple chemical derivatives that are only one or two chemical or enzymatic steps away from the active parent drug. Numerous prodrugs designed to overcome barriers to drug utilization have reached the market. Although the development of a prodrug can be very challenging, the prodrug approach represents a feasible way to improve the erratic properties of investigational drugs or drugs already on the market. This chapter introduces the rationale behind use of the prodrug approach from past to present, and also considers the possible problems that can arise in future from inadequate activation of prodrugs.

The most important factor in deciding the faith of a prodrug is its promoiety. As conjugation with promoiety is important, equally important is its cleavage. Depending upon these criteria, prodrugs are classified into several types and subtypes. A few prodrugs are also the result of serendipitous discovery. From a chemical point of view, prodrugs are classified into carrier-linked, mutual, bioprecursors, or polymeric. Some subtypes are also designated as double prodrugs, macromolecular, or site-specific. In a few cases a spacer may be introduced to modify the prodrug into a tripartate. Depending upon the conversion it may also be described as intra- or extracellular. This section deals with the detailed account of types of prodrugs, supported by examples. The structure of various pharmacologically active agents can be modified by using functional groups. The prodrug strategy can be successfully applied to a wide range of drug molecules with the help of these functional group studies. Thus, modification of functional groups helps to improve the physicochemical, biopharmaceutical, or pharmacokinetic properties of a drug molecule. The variety of different types of prodrugs and a comprehensive discussion of individual agents is outside the scope of this chapter. However, the major types of prodrugs grouped according to functional groups and, in the case of bioprecursor drugs, grouped according to type of metabolic activation. The various obstructions associated with drugs can be overcome by applying the concept of prodrugs. This helps in improvement of unwanted physicochemical properties of existing drugs and increases their therapeutic effectiveness. The various properties that can be improved include aesthetic and drug formulation properties. This chapter deals with the detailed outlook of such properties and a remedy to overcome it. Each and every physicochemical property is an argument of drug action. Brief explanatory data supported by examples help to understand the concept of prodrugs and serve their utility in medicinal chemistry in order to obtain good drug candidates.

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