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Prodrugs as Emerging Tool for Increasing Safety Profile of Existing Drugs

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The process of drug discovery is never ending, time consuming and expensive one. With the openings of high throughput screening and computer aided techniques; even though various drugs are identifying but the final outcome is very less. When a new chemical entity has some barrier/limitation to utility, it may not be developed as a therapeutic agent. This fact is attributed to the undesirable physico-chemical properties of the existing drug molecule. The steady improvement in the physicochemical, biopharmaceutical and/or pharmacokinetic properties of pharmacologically active compounds is due implementation of a prodrug strategy. Thus prodrug designing leads to raising the therapeutic effectiveness of medicinal compound through derivatization. Even though numerous prodrugs have been designed and developed but safety of promoiety is always the great concern. The acceptance of prodrug is dependent on proper selection of promoiety. A wide variety of promoieties have been used to overcome liabilities associated with drugs. The selection of promoiety depends on the purpose of the prodrug, type of functional groups available on the parent drug, chemical and enzymatic conversion mechanisms of prodrug to parent drug, safety of the promoiety, and ease of manufacturing. Various promoities are found to be safe, effective and cleaved after biotransformation. The promoities used to convert into prodrugs are selected based on several criteria. Various promoieties like phytophenols, amino acids, glycerides or polymers can serves as safer. Most of the time these counter parts are also associated with desired pharmacological effects which is beneficial and adds up to the effectiveness. This leads to all over increasing the therapeutic profile of the of drug molecule. The synthesis of prodrug is a straight forward one and in almost cases reaction leads to completion. In the past, the prodrug approach was viewed as a last resort after all other ways were exploited, whereas, now-a-days the prodrug approach is being considered in the very early stages of the drug discovery and development process. While the traditional prodrug approach was focused on altering various physiochemical parameters, the modern computational approach considers using a design of targeted prodrugs to certain enzymes or transporters or being interconverted to their parent drugs without a metabolic activation process. With the possibility of designing prodrugs with different linkers, the rate of release of the parent drug will be controlled and the drug's moiety, responsible for a bitter sensation, will be blocked.

Thus, prodrug design comprises an area of research devoted to optimize drug delivery, where the pharmacologically inactive species required transformation within the body in order to release the parent active drug. As a result, prodrug approach gives an opportunity in medicinal chemistry to improve the clinical and therapeutic effectiveness of a drug by utilizing the safer promoiety.