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A Short Note on Prodrug

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Description

A prodrug is a pharmacologically inert molecule that becomes active when it interacts or is metabolised in mammalian systems.

Prodrug can be defined as a physiologically inactive derivative of a parent drug molecule that is activated within the body by a chemical or enzymatic transition that results in the release of the active drug. The purpose of using a prodrug is to improve the parent drug's absorption, distribution, metabolism, excretion, and undesired toxicity.

Applications

There are three primary uses of prodrug include: Pharmaceutical, Pharmacokinetics, and Pharmacodynamics

Pharmaceutical

- Inadequate chemical stability: A drug may be rapidly absorbed and expressed as inter active before it reaches its target region.
- Inadequate solubility: It has been discovered that several injectable medicines are insoluble in water. A litre of brackish water may be required to regulate the effective dose. The medications, on the other hand, may be safe, effective, and active. The medication can be linked with a water-soluble fragment. After injection, this part might be metabolically cleft in the body.
- Odour: An effective medication may have an unpleasant flavour. It may induce stomach discomfort as well as pain. In this case, the molecule's structure can be changed to avoid these complications. The prodrug, on the other hand, should be converted to the active medicament at the location.

Pharmacokinetics

- Weak oral absorption and pre-systemic metabolism: It is critical that a medicine be absorbed orally and reaches the target location in adequate quantity. Some medications, however, may not have these qualities. In these cases, water-soluble or lipid-soluble medications can be developed. Once the medicine has been absorbed, the water or lipid-soluble part can be eliminated by an enzymatic mechanism or when the pharmaceuticals reach the location of the sickness.
- Short duration of action: It is sometimes preferable to have a little supply of medicine on hand for an extended period of time. The medication can be chemically altered such that it is metabolically turned into the potent medicine gradually.

Pharmacodynamics

A drug's active constituents can be harmful. It may have a high healing index if it can be administered in a safe or less toxic form that creates the dynamic drug at the site of injury.

Types of Prodrug

Carrier-linked prodrugs

These are those in which the promoiety is covalently attached to the active drug but is readily broken by enzymes (such as an ester or labile amide) or non-enzymatically to release the parent drug. The removed group should ideally be pharmacologically inactive, nontoxic, and non-immunogenic, while the promoteiety should be labile for effective *in vivo* activation. Carrier-linked prodrugs are further classified as (a) bipartite, consisting of one carrier (promoiety) connected directly to the drug, and (b) tripartite, consisting of a spacer or connecting a group between the drug and a promoiety. Due to the fundamental nature of the drug-promoiet, bipartite prodrugs may be unstable in some instances linkage. This can be solved by designing a tripartite prodrug and (c) mutual prodrugs, which are consisting of two drugs linked together.

Bio precursors

These are chemical entities that are converted into new compounds that may or may not be active or are further metabolised to active metabolites (such as amine to aldehyde to carboxylic acid). There is no carrier in this sort of prodrug, but the chemical should be easily metabolised in order to induce the required functional groups.

Prodrugs are further classified into two types based on how the body transforms the prodrug into the final active drug form:

Type I prodrugs are bioactivated inside the cells (intra-cellular).

- Sub type A: Therapeutic Target Tissues/Cells: Acyclovir 5-Flurouracil L-Dopa
- Sub type: B Metabolic Tissues (Liver, GI mucosal cell, lung, etc.,): Cabamazepine, Captopril, Suldinac

Type II prodrugs are bio-activated outside cells (extra-cellular).

- Sub type A: GI Fluids: Loperamide, Sulfasalazine
- Sub type B: Systemic circulation and other extracellular fluid compartments: Acetylsalicylate Bacampicillin, Fosphenytoin
- Sub type C: Therapeutic Target ADEPs, GDEPs, VDEPs