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Perspective

An Overview on the Significance of Prodrug and its Applications

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ABOUT THE STUDY

The word "prodrug" refers to a bioreversible molecule that, *in vivo*, releases an active substance in the biological environment by chemical or enzymatic activation. This sort of innovative method can increase a prototype's biopharmaceutical, pharmacokinetic, and, indirectly, pharmacodynamic qualities. Dendrimers, on the other hand, are a new family of well-defined branching macromolecules with three basic components: A multifunctional core that facilitates the attachment of branches, repetitive branches from the central core, and peripheral functions. Dendrimer synthesis, which can be done in a convergent, divergent, or orthogonal manner, is done step by step, and the coupling of a new branch results in a different generation.

Dendrimers, as drug carriers, can facilitate regulated and/or targeted drug delivery. The bioactive molecule can be attached to the dendrimer by directed conjugation to the surface; interaction *via* a spacer group; and branches with drug/bioactive compound, resulting in an exponential increase of the active component in each subsequent generation. Many dendrimer prodrugs have been created, with various biological uses in consideration, including anticancer, anti-inflammatory, and antibacterial properties. Poly (amidoamine) (PAMAM), poly (propylene imine) (DAB or PPI), and poly (etherhydroxylamine) (PEHAM) dendrimers have been coupled with bioactive compounds.

Prodrugs are increasingly being used as alternatives for active compounds that have encountered difficulties during the development process. Since 2008, more than 10% of new chemical entities authorised by the US FDA have been prodrugs; more impressively, between 2014 and 2017, 17% of new chemical entities approved by the Food and Drug Administration (FDA) were prodrugs. Despite being utilised for almost a century, the technique was invented by Adrien Albert in 1958 and is described as an inactive molecule undergoing some biological alteration to produce the active metabolite. In essence, a prodrug method allows a complicated molecule to overcome a biological barrier, such as low bioavailability, low absorption, instability, poor specificity, formulation challenges, or other undesirable effects or toxicity concerns.

The masking of previously trouble functional groups is a fundamental aspect of the prodrug approach. Phosphate is one such example: Phosphonates frequently present opportunities for novel interactions with a target, but they are characterised by a strong negative charge and, as a result, low bioavailability. The phosphonate group is frequently isosteric to a phosphate by substituting one of the phosphate's ester oxygens with a carbon atom. Because enzymes traditionally associated with cleaving an oxygen-phosphorus link may not be as efficient at cleaving a carbon–phosphorus bond, this alteration may result in increased metabolic stability. However, because phosphonates are charged at physiological pH, diffusion through biological membranes remains challenging. To overcome this, a number of phosphonate-protecting groups are developed. Each technique, however, must strike a ratio between allowing sufficient moiety absorption and cleavage while avoiding the production of toxic byproducts.

CONCLUSION

Phosphonate prodrugs are classed based on the substituents they include, which are most typically esters and amides, as well as the substitution pattern they carry. Phosphate prodrugs can be mono- or di-substituted, and if di-substituted, can be symmetrical or asymmetric. When asymmetrically di-substituted, a new chiral centre is created into the molecule at the phosphorus atom, perhaps resulting in delayed cleavage of the protective groups around the phosphonate. The rationale for employing the prodrug, as well as the method by which the protecting group (s) will be cleaved, must be evaluated in order to establish the ideal pattern of substitution.

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