CHAPTER 12

Prodrugs in the Treatment of Viral Diseases

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12.1 Introduction

Progression of a molecule with interesting pharmacological properties into clinical development is frequently hampered by undesirable characteristics such as poor pharmacokinetic properties, metabolic or chemical instability or poor pharmaceutical properties. To overcome these limitations, the use of prodrug strategies has become an increasingly important tool in the development of drugs to treat human disease.[1–3] In the realm of drugs used to treat viral diseases, the implementation of prodrug approaches has long been used to improve the drug characteristics of therapeutically interesting molecules that include small molecules, nucleosides and nucleotides.

A prodrug is defined as a compound that undergoes biotransformation or chemical transformation *in vivo* prior to eliciting its pharmacological effect. The administered prodrug is typically pharmacologically inactive and is transformed into the active agent after it is delivered to the biological system. A prodrug approach can be executed either by attaching a promoiety to the active drug or by relying on chemical degradation or biotransformation of a molecular unit integral to the structure of the molecule. A promoiety is generally a temporary structural unit that is ultimately released after its

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