

# CONCEPT OF PRODRUG AND ITS CLINICAL APPLICATIONS

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**ABSTRACT-** In the realm of drug disclosure and advancement, prodrugs become an amazing strategy for improving biopharmaceutical, physicochemical or pharmacokinetic properties of pharmacologically dynamic agents. The reason for this survey is to give a few sorts of prodrugs which are bio-reversible derivatives of drug particles that experience an enzymatic as well as synthetic change in vivo to discharge the dynamic parent drug, which would then be able to apply the ideal pharmacological impact. The objective of prodrug configuration is to beat the unwanted drug properties, for example, low objective selectivity, low dissolvability in water or lipid layers, synthetic flimsiness, aggravation or torment after neighborhood organization, pre-foundational lethality and digestion. Right now, centered around to portray the fundamental utilitarian gatherings that are amiable to prodrug structure and feature the significant uses of the prodrug technique. Moreover, the concepts of prodrug and the groupings of prodrugs will be offered right now.

**KEYWORDS-** Prodrug, Agent, Concepts, Derivatives of drug, Antiviral.

## **INTRODUCTION**

Albert has first presented the articulation "prodrug" in 1958. All things considered, "predrug" is such an off base term. Be that as it may, the first form was utilized too broadly to be in any way changed. This idea has been utilized before Albert's distribution. Acetanilide which was presented (under the name of Antifebrin) into the clinical practice by Cahn and Hepp in 1867 as an antipyretic agent was the principal compound considered as a prodrug. In 1887, von Mering presented phenacetin (acetophenetidin) as pain relieving drug. In 1897, Felix Hoffman structured anti-inflammatory medicine (acetylsalicylic corrosive), which was brought into medication by Dreser, in 1899. Be that as it may, the prodrug idea was utilized without precedent for the center of the twentieth century by the Parke-Davis organization during examines. Prodrug is a novel drug conveyance framework to improve drug conveyance and consequently drug viability and security. Prodrug approach is a methodology towards showing signs of improvement bioavailability thus quicker activity.

Prodrugs are mixes which experience compound (bio) change inside the body preceding displaying their pharmacological activities. The concoction change of drugs to conquer pharmaceutical issues has likewise been named "drug latention". The term was first utilized by Harper. Harper characterized drug latention as the synthetic adjustment of an organically dynamic compound to frame another compound which upon in vivo enzymatic assault will free the parent compound. The substance adjustment of the compound is with the end goal that the change in physico-concoction properties will influence the retention, appropriation and enzymatic digestion". The most significant and essential imperative of prodrug way to deal with be valuable in taking care of drug conveyance issues is the reconversion of the prodrug to parent drug in-vivo. This prodrug-drug transformation may happen before assimilation (i.e., in the gastro intestinal tract), during, a great many ingestions or at the particular site of drug activity in the body, all ward upon the particular objective for which the prodrug is planned. Preferably, the prodrug ought to be changed over to the drug when the objective is accomplished. The prodrug in essence is a dormant species and accordingly, when its activity is finished, unblemished prodrug speaks to inaccessible drug.

It is evaluated that 10% of the drugs affirmed worldwide can be named prodrugs. Prodrugs, which have no or poor organic action, are artificially changed forms of a pharmacologically dynamic agent, which must experience change in vivo to discharge the dynamic drug. They are planned so as to improve the physicochemical, biopharmaceutical and additionally pharmacokinetic properties of pharmacologically intense mixes. This article portrays the fundamental practical gatherings that are agreeable to prodrug plan, and features the significant utilizations of the prodrug technique, including the capacity to improve oral retention and watery solvency, increment lipophilicity, upgrade dynamic vehicle, just as accomplish site-particular

conveyance. Unique accentuation is given to the job of the prodrug idea in the structure of new anticancer treatments, including counter acting agent coordinated catalyst prodrug treatment (ADEPT) and quality coordinated compound prodrug treatment.

### **CONCEPT OF PRODRUG**

The idea of prodrug was first presented in restorative science by Albert in 1951: "A prodrug is an atom which doesn't have any inborn natural movement however which is proficient during the various periods of its digestion to produce an organically dynamic drug". As per this definition and to that acknowledged by IUPAC, a prodrug is any intensify that experiences biotransformation before showing its pharmacological impacts. Prodrugs would thus be able to be seen as drugs that contain specific nontoxic defensive gatherings utilized in a transient way to adjust or to dispense with bothersome properties in the parent atom. For the most part, the metabolic change important to change over the prodrug into the drug is catalyzed by explicit compounds, basically hydrolases, and in a perfect world this ought to specifically happen at the objective tissue to forestall bothersome symptoms.

In drug innovative work, the prodrug idea has discovered various helpful applications since it permits a few, in some cases conflicting, organic as well as physicochemical destinations to be fulfilled. A few models are, including cell pervasion, solvency, concoction or enzymatic solidness, bioavailability, lethality, or blood mind obstruction infiltration. One need to shoulder as a top priority that huge numbers of these targets interlaced. A powerful reasonable prodrug ought to conquer the essential oddity: it must be sufficiently lipophilic to cross a layer or metabolic barrier and all the while it ought to be sufficiently hydrophilic to satisfy dissolvability, bioavailability and transport criteria. Numerous restoratively dynamic agents have low bioavailability after oral organization because of poor assimilation or vulnerability to first pass digestion, which prompts drug inactivation as well as the creation of dangerous metabolites. A potential way to deal with improve the oral retention is a detailing arrangement, which improves oral bioavailability using appropriate excipients that expansion intestinal layer porousness. Such pervasion enhancers can be surfactants, unsaturated fats, glycerides, steroidal cleansers and amino corrosive derivatives among others. Be that as it may, these excipients now and again cause genuine harm to the intestinal epithelium.

### **CLINICAL APPLICATIONS**

The application of current revelation advances, for example, high-throughput screening and combinatorial science can create novel lead structures with high pharmacological strength, yet the physicochemical and biopharmaceutical parts of the underlying leads have as often as possible been disregarded. This can prompt drug applicants with poor drug-like properties that face critical issues later in drug improvement. The advancement of prodrugs — artificially

changed variants of the pharmacologically dynamic agent that must experience change in vivo to discharge the dynamic drug — is currently settled as a procedure to improve the physicochemical, biopharmaceutical or pharmacokinetic properties of pharmacologically powerful mixes and in this way increment the developability and handiness of a potential drug. For instance, prodrugs give prospects to beat different boundaries to drug detailing and conveyance, for example, poor watery solvency, concoction shakiness, deficient oral assimilation, fast pre-foundational digestion, insufficient mind infiltration, harmfulness and nearby bothering. Prodrugs can likewise improve drug focusing on, and the advancement of a prodrug of a current drug with improved properties may speak to a real existence cycle the executive opportunity.

- Prodrugs, metabolites of drugs, directed drugs are generally utilized in the pharmaceutical field. Prodrug is utilized to imply pharmacologically inert synthetic moieties which are utilized to change the physiochemical properties of drugs incidentally so as to improve their adequacy and decrease their lethality.
- Prodrugs are bio reversible derivatives of drug particles which experience compound change or enzymatic transformation in vivo to discharge the dynamic parent drug which shows wanted pharmacologic impact. In both drug revelation and improvement, prodrugs have become a built up instrument for upgrading biopharmaceutical, physiochemical, or pharmacokinetic properties of helpful agents. The utilization of a prodrug is generally urged to advance retention, appropriation, digestion, and discharge (ADME) forms.
- Pharmaceutical researchers are often confronting genuine definition issues, for example, poor solvency, poor organoleptic properties and concoction precariousness. Because of postponed pharmaceutical answer for dissolvability or steadiness issue, researchers liked to exploit a prodrug system.
- Prodrugs are generally intended to upgrade oral bioavailability because of poor assimilation from the gastrointestinal tract. The prodrug technique has been utilized to improve the selectivity of drugs. Prodrug Design improves bioavailability, fluid dissolvability, tastefulness and furthermore gives security against quick digestion.

### **Mechanism of Transformation of Prodrug**

The systems engaged with change of prodrug to drug can be substance or enzymatic

- **Chemical Reversal** - Prodrug change by non-enzymatic systems shows less entomb subject changeability as contrasted and enzymatic inversion. Not very many substance triggers exist for prodrug transformation and most basic is hydrolysis emerging from contrasts in pH in the body.

- **Enzymatic reversal** - The rundown of compounds that are utilized in prodrug application. These drug processing proteins might be available in the particular piece of certain organ or might be ubiquitous wide entomb tolerant inconstancy might be normal except if the catalyst present is in abundance (for example esterases). In spite of this downside enzymatic inversion assumes a more noteworthy job than substance inversion process.

### **Approaches for Improved Drug Efficacy**

There are fundamentally 3 ways to deal with the issue of drug adequacy.

**Formulation approach:** This is the speediest, simplest and least expressive methodology of the three since it includes no amalgamation and just insignificant investigational new drug revising, it ought to in this manner be viewed as first. Yet, this methodology is of no incentive for expanding layer transport and it can't generally be utilized to change drug solidness.

**The analog approach:** Analogs are commonly characterized as sub-atomic adjustment comprising of a skeletal biotransformation of a substituent gathering. These irreversible derivatives are incorporated with the goal of adjusting or improving characteristic movement. Since they often collaborate diversely with the receptor, the analogs every now and again have distinctive range of exercises and reactions than the parent drug. Hence the simple methodology isn't typically used to improve ingestion.

**The Prodrug Approach:** This methodology lies somewhere close to plan and simple methodologies as for both time and cost of improvement. The essential utility of this methodology is to improve biopharmaceutical property. Adjustment of the physical and additionally compound properties of a drug so as to conquer the hindrance constraining the convenience of drug through bioreversible substance change has been called as the prodrug approach.

### **Prolonged duration of drug action**

Albeit different pharmaceutical definitions are much of the time used to drag out the span of drug activity, a couple of models that utilization prodrugs exist. Exceptionally lipophilic prodrugs of a few steroids (for instance, testosterone nandrolone) and neuroleptics (for instance, fluphenazine, flupenthixol, haloperidol) are gradually discharged in the flow from the site of intramuscular infusion and result in a drawn out term of activity. Once discharged from the infusion site, prodrugs are normally quickly bio-converted, with no lessening of their restorative activity much of the time. For instance, the beginning of activity of fluphenazine is by and large between 24–72 hours after infusion of its lipophilic decanoate ester prodrug, which proceeds for 1 two months with a normal term of 3 a month. On account of the bronchodilator and  $\beta_2$  - agonist terbutaline, supported drug activity is given its bisdimethyl carbamate prodrug, bambuterol.

Assurance of a phenolic moiety, which is defenseless for fast and broad pre-foundational digestion, additionally dodges first-pass intestinal and hepatic digestion. After oral organization, bambuterol is gradually bioconverted to terbutaline, prevalently outside the lungs by means of a course of hydrolysis and oxidation responses. Because of delayed activity, a once-day by day bambuterol treatment furnishes help of asthma manifestations with a lower frequency of symptoms than terbutaline, which is taken three times each day.

### **Enzymes for Bioconversion of Prodrugs**

- The instrument of proton move between two oxygens in Menger's unbending carboxylic amides has prompted the structure of prodrugs that veil the unpleasant taste of dopamine, atenolol, amoxicillin and cephalexin, The job of the linker in these prodrugs is to obstruct the free amine bunch in the parental drug and to upgrade the arrival of a drug in a very much characterized way.
- The striking productivity of protein catalysis has enlivened numerous natural scientists to investigate catalyst instruments by examining certain intra atomic procedures, for example, chemical models which continue quicker than their intermolecular partners. This examination realizes the significant inquiry of whether chemical models will supplant regular proteins in the change of prodrugs to their parental drugs.
- Proteins are obligatory for the bury change of numerous prodrugs to their parental drugs. Among the most significant proteins in the bioconversion of prodrugs are amides (eg. trypsin, chymotrypsin, elastase, carboxypeptidase, and aminopeptidase) and ester-based prodrugs (ex. paraoxonase, carboxylesterase, acetylcholinesterase and cholinesterase). The majority of these compounds are hydrolytic chemicals, nonetheless, non-hydrolytic proteins, including all cytochrome P450 catalysts, are additionally fit for catalyzing the bioconversion of ester and amide-based prodrugs.

## **CONCLUSION**

Prodrug approach has been used to overcome undesirable drug properties and to optimize the clinical drug applications. Prodrug approaches enhanced solubility, site specificity, prolonged release and toxicity limited bioavailability. Nowadays, the modern computational design uses a design of linkers with bitter tasting drugs to release the parental drugs in a well-defined manner. Thus the rate of release of the parental bitter tasting drugs will be controlled. Site specific targeting with prodrugs can be improved by the use of gene delivery with the help of enzymes and transporters. Thus produg design is widely used in the development of selective drug delivery systems.

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