

Novel Approaches to Enhance, Bioavailability of Solid Dosage Forms

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Abstract

Solid dosage forms, which were being used since ancient days, have been made modifications in terms of their drug delivery systems. As there are many adverse effects caused by solid dosage forms, recent advanced techniques were developed to minimize the adverse effects. These techniques are encapsulating the drug with matrix, and polymer micelles. These two techniques have a good significant use in the recent era. They optimize the bioavailability, pharmacokinetic and Pharmacodynamic properties of the drug. Further advance in their drug delivery system is by applying nanotechnology in their drug delivery system. Applications of Nanotechnology in drug delivery would further minimize the adverse reaction.

Keywords: Solid dosage forms; Nanotechnology; Pharmacokinetic; Pharmacodynamic; Sustained release tablets; Polymer micelles

Introduction

Solid dosage forms were been considered to be easiest forms of drug delivery systems. Among all the solid dosage forms, tablets, and capsules are commonly employed. They can be produced in a non-sterile environment. The main goal of pharmaceutical formulation is to achieve better therapeutic activity by using smallest quantity of drug administered by the most suitable route. Usually, solid oral drug products are produced, to give an immediate result upon administration. Oral route of drug administration has wide acceptable and of the drugs administered orally in solid dosage forms represents the preferred class of products. The reasons are tablets and capsules represent unit dosage forms in which one usual dose of drug has been accurately placed. Commonly, Tablet is preferable than capsules, because, tablets have an advantages of being tamper resistant. And any adulterant of the tablet after its manufacture is almost certain to be observed. As there are many advantages of tablets and capsules, there are few disadvantages as well, which may delay the absorption and also decrease the efficacy of the drug. Some of the disadvantages are, they delay the onset of action, are not suitable in emergency and for unconscious patients. The drug content of the tablet must be bioavailability. Accurate bioavailability can be obtained from the drug levels of the drug after its administration. Tablets must be elegant in appearance and must have characteristic shape, color, and other markings necessary to identify the product. Tablets must retain all these functional attributes, which include drug stability and efficacy [1].

An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is typically seen using immediate-release dosage forms.

In order to overcome and to enhance better rate of absorption, various techniques have been introduced. They are sustained drug delivery system thorough matrix, micelle. the novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration [2].

Concept of Sustained Release Tablets

The first sustained-release tablets were made by Howard Press in Hoboken, New Jersey in the early 1950s. The first tablets released under his process patent were called "Nitroglyn" and made under license by Key Corp. in Florida. These days most time-release drugs are formulated so that the active ingredient is embedded in a matrix of insoluble substance(s) like acrylics, even chitin such that the dissolving drug must find its way out through the holes in the matrix. Some drugs are enclosed in polymer-based tablets with a laser-drilled hole on one side and a porous membrane on the other side [1].

In some sustained release formulations, the drug dissolves into the matrix, and the matrix physically swells to form a gel, allowing the drug to exit through the gel's outer surface. Sustained release tablets and capsules are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect. Typically, sustained release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period.

The sustained plasma drug levels provide by sustained release products often times eliminates the need for night dosing, which benefits not only the patients but the care given as well. The basic rationale of a sustained drug delivery system is to optimize the Biopharmaceutical, Pharmacokinetic and Pharmacodynamic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administered by the most suitable route. The sustained release systems for oral use are mostly solid and based on dissolution, diffusion or a combination of both mechanisms in the control of release of drugs.

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In this type of dosage forms, a sufficient amount of drug is initially made available to the body to cause a desired pharmacological response. The remaining fraction is released periodically and is required to maintain the maximum initial pharmacological activity for some desirable period of time in excess of time expected from usual single dose.

Therapeutic Advantages Of The Sustained Release Forms

- Frequency of administration is reduced.
- Patient compliance can be improved.
- Blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced because a more even blood level is maintained.
- Total amount of drug administered can be reduced, thus maximizing availability with minimum dose.
- Better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drugs can be reduced by formulation in sustain action form.
- The safety margin of high potency drugs can be increased and incidences of both local and systemic adverse side effects can be reduced in sensitive patients.

Disadvantages of Sustained Release Dosage Forms

- Administration of Sustained release dosage forms dose not permits the prompt termination of therapy.
- Physicians have less flexibility in adjusting dosage regimens. This is fixed by the dosage form regimen.
- SR forms are designed for normal population i.e. on the basis of average drug biological half lives. Consequently, diseases states that alter drug disposition, significant patient variation are not accommodated.

Today, most time-release drugs are formulated so that the active ingredient is embedded in a matrix of insoluble substances like some acrylics, even chitin such that the dissolving drug must find its way out through the holes in the matrix. Some drugs are enclosed in polymer-based tablets with a laser-drilled hole on one side and a porous membrane on the other side. Stomach acids push through the porous membrane, thus pushing the drug out through the laser-drilled hole. In time, the entire drug dose releases into the system while the polymer container remains intact, to be later excreted through normal digestion [3].

Possibility of dose dumping due to food, physiological or formulation variables or chewing or grinding of oral formulations by the patient and thus, increased risk of toxicity

Polymer Micelles

Polymer micelles are one of the novel approaches to increase the bioavailability of a drug. They also optimize pharmacokinetics and pharmacodynamics properties of a drug which in turn lead in optimize the bioavailability of a drug. Polymer micelles are usually amphiphilic in nature. Micelles are generated when the hydrophobic portions are driven to an interior structure while hydrophilic portions are turned outward facing toward the water. Polymer micelles are nanoscopic core shell structure formed by amphiphilic block copolymers.

special stability of Polymer micelles, the controlled release properties of pH-sensitive Polymer micelles, the prolongation of residence time with mucoadhesive Polymer micelles, and the P-gp inhibitors commonly used in Polymer micelles, respectively. Theoretically, the formation of micelles is driven by decrease of free energy. The removal of hydrophobic fragments from the aqueous environment and the reestablishing of hydrogen bond network in water decrease free energy of the system and finally form the micelles Polymeric micelles (PM) system, is one of the efficient drug carriers, which has received a significant importance in the field of drug discovery and drug delivery systems [4].

As the micelles structure is complicated and its understanding as a novel drug delivery systems is important to enhance its usage Micelles are surfactant molecules, which aggregate in aqueous or oily liquids; the micelles occupy the dispersed phase of a colloidal system. Micelles contain hydrophilic and hydrophobic part which lead to its Amphiphilic nature. Each micelle containing a hydrophilic and hydrophobic domain, make up a polymeric micelle.

Polymeric micelles are biodegradable, thus they help in minimizing adverse effects caused by uses age of conventional drug delivery system [5]. Biodegradable polymeric micelles have emerged as one of the promising approaches which involves in reducing adverse effects caused by conventional drug. They could also optimize the bioavailability of the drug in the body. Micelle's are collide particles with a size of around 5nm to 100 nm which are currently have a significant usage across the world. When the concentration of surfactant reaches a maximum level, it forms a certain stage called as Critical Micelles Concentration. Critical Micelles Concentration is property of aggregation of surfactants, and is ability to aggregate and carry drugs. Usually amphiphilic monomers, do not aggregate until CMC is reached. Nano polymers have been used significantly, for nano medicine applications. Usually nano polymers are used in treating cancer. Nano polymers are also used in diagnosing and treating various neurological disorders especially, brain tumor. When micelles enter into body, it gets diluted. As the process of dilution continues, then the concentration below its Critical Micelle Concentration would lead to loss of structural integrity. The hydrophobic cores of micelles are desired for encapsulating hydrophobic drugs. These Hydrophobic drugs in turn help in treating many Central nervous System Disorders. Formation of van der Waals bonds between the hydrophobic polymer core and drug help stabilize the micelle. The hydrophilic part of the micelles also helps to stabilize the formation of hydrogen bonds. These Hydrogen bonds are formed with the surrounding aqueous solution. Some of the drugs have been encapsulated with the polymer. But usages of them were not upto the desired level. Nanoparticle polymers are synthesized by considering various parameters like, there are several popular methods: emulsification solvent evaporation, solvent displacement, and salting out [6].

It is been almost about two decades, since, Micelles were discovered. But the use of micelles in Nano scale as a medicine was emerged few years ago. Polymer micelles have become one of the main players in nanoparticle research. Formation of Micelles is one of the efficient methods for delivering poorly water-soluble drugs, and its usefulness is in particular applicable to chemotherapeutic agents. Cancer has unique characteristics that can be exploited for drug delivery. Polymeric micelles are used widely in treatment of cancer, because they enhance the permeability and retention effect and they also distribute the drug selectively to tumor cells and opposed to normal tissues.

There are a number of formulation strategies that could be used to improve the bioavailability of poorly soluble drugs either by increasing the Polymeric micelles or by matrix encoating. These two approaches can overcome some limitations of the oral delivery acting as carriers able to enhance drug absorption, by providing (1) protection of the loaded drug from the harsh environment of the GI tract (2), release of the drug in a controlled manner at target sites, (3) prolongation of the residence time in the gut by mucoadhesion, and (4) inhibition of efflux pumps to improve the drug accumulation. The primary applications for rate controlling polymers is for decreasing dissolution rate and extend the release of water soluble drug. Successful drug design with polymers depends largely on understanding the physical, chemical and physiological factors to promote bioavailability [7].

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