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Review Article

Matrix tablet: a review

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ABSTRACT

In order to achieve the therapeutic purpose, the choice of the most suitable delivery route is of indisputable importance. Therefore, certain factors must be taken into consideration when delivering a active substance, namely its own properties, the disease to be diagnosed and the desired beneficial time. The active substances can be directly to the target tissue or organ or can be delivered by systemic routes.

Introduction

The transfer of active substances in human body may be consummate by several anatomic routes. In order to achieve the therapeutic purpose, the choice of the most suitable delivery route is of indisputable importance. Therefore, certain factors must be taken into consideration when delivering a active substance, namely its own properties, the disease to be diagnosed and the desired beneficial time. The active substances can be directly to the target tissue or organ or can be delivered by systemic routes. Systemic active substance transferring routes are presented systematically in Table 1. Pharmaceutical treatments started plenty of decades, or even centuries ago either with the oral administration of solid pills or with injectables active chemical active substances. When either of these methods is applied, active substance dose maintenance in the body is accomplished by repeated deliveries. Despite the effectiveness of these treatments, dose peaks at administration times alternated with sub-beneficial active substance levels are inevitable. Therefore, the impossibility of controlling the active substance level over a long period of time constituted an important drawback. During the past two decades, new advancements and strategies have been developed to monitor certain parameters considered essential for improving the treatment performance such as the rate, period of time and targeting of transfer. This was the beginning of the so called active substance transfer systems. [1]

The main purpose of using a DDS is, as implied, not only to transfer a biologically active compound in a controlled manner (time period and releasing rate) but also to persist the active substance level in the body within beneficial window. Besides, one can direct the active compound towards a specific organ or tissue. The first two features were addressed by using active substance carriers, usually polymers (either biopolymers or synthetic polymers) which properties could be manipulated in order to enhance DDS efficiency. Although both natural and synthetic polymers are being used in the preparation of DDS, there are some profits that can be pointed to synthetic macromolecules. When the polymers are man-made, it becomes possible to monitor some manner of polymer structure that allows generating tailor-made materials suitable to the desired biological advancement. Also, three-dimensional structure as well as chemical composition can be monitored in order to adjust materials properties and orientation of specifics functional groups that can collaborate with the active compound in spite of, consideration must be paid to molecular weight of fiber polymers which are not biodegradable. Since biodegradation does not always takes place, synthetic polymers must be diminished through renal elimination. [2] Therefore, they should present a uniform molecular weight distribution that fits under the entrance of renal elimination. As further defined in this paper, sustained/living radical polymerization is a very predictable and applied technology in order to produce well defined

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macromolecular structures with definite range molecular weights dissemination. DDS present certain profits. These include important factors from minimize of active substance side-effects to enhanced patient compliance. In spite of, DDS disadvantages are also well-known, e.g., DDS final cost amid others. Targeted active compound transfer around the interest of the scientific community and therefore has authenticated excellent advancements over the last decade. The active compounds targeting accomplice the agreement of different areas associated to active compounds design, active compounds carriers, biological systems, genetic advancements and definitive design of new molecules. In order to maximise the capability of the current methods for active substance deliver, certain steps need to be consummate. The main goal is currently associated to transfer applicable active compounds at a desiderate target without any sign of degradation during the whole process. The advancement of a sustained delivery system that can dose orally, being less cost and less painful for the patients and at the same time exceedingly sufficient considering a specific disease represents a final target for the research community. DDS must possess some features. The system should be accepted by the specific target tissues. In fact, the transferring of the active substance in a specific area of the body is excessively important, in terms of lowering possible side effects of the active compounds, when enter non-targeted organs and tissues. [3]

Modified drug delivery system: The term modified-discharge of active substance product is used to describe products that change the timing and the rate of discharge of the active substance compound. The modified drug delivery is defined as the drug to discharge the active substance for a longer period of a time. The modified drug delivery diminishes the side effects and adverse effects. The therapeutic efficacy of drug is enhanced. The modified drug release system involves the sustained and controlled and prolonged release systems. They may release the drug in a controlled or sustained manner for a prolong period. [4]

Extended-release drug products: The extended release dosage forms defined as the drug to release the extended period of the time. They may reduce the side effects and adverse effects. The dosing frequency is less when compared to the immediate release delivery.
Examples of extended-release dosage forms include controlled-release, sustained-release, and long-acting drug products. [5]

Delayed-discharge active substance products: The delayed drug delivery is defined as the the delayed system will discharge the active compound in a dosage form that releases a distinct portion of active substance after delivery of the active substance. Enteric-coated dosage forms are the most common delayed-release products.

Targeted-release drug products: The targeted drug delivery products are defined as the they will discharge the active substance at or a dosage form that releases drug at or near the designed physiologic site of action. Targeted-discharge dosage forms may have either immediate or extended-discharge characteristics. The word monitor release product was the term controlled-release drug product was contracted used to illustrate different types of oral extended-discharge dosage forms, including along with sustained-discharge , sustained-action, prolonged-action, long-action, slow-release, and programmed active substance discharge. [6]

Conventional Drug Delivery System: The conventional drug delivery is to deliver the drugs to the systemic circulation. The conventional drug delivery having the so many drawbacks the dosing frequency is less, they having the so many disadvantages like occurring of the side effects and adverse effects. The conventional dosage forms they will immediately discharge the dosing frequency is more. By passing of these problems the sustained release dosage farms are designed. The dosages forms will deliver the drug up to the longer period reduce the side effects and adverse effects. To enhance the therapeutic efficacy of a drug. The sustained drug delivery is does not depending up on the time they release the drug up to sustained manner. The dosing frequency is less. The patent compliance will improve. Pharmaceutical products designed for oral transfer are mainly conventional active substance delivery systems, which are designed for immediate release of drug for rapid/immediate absorption, administration of the conventional dosage form by extra vascular route does not continue the drug level in blood for an extended period of time.[7] The conventional dosage forms like solution, suspension, capsule, tablets and suppository etc. have some limitations such as

1) For sustained release preparation the drugs should have the shorter half life. The shorter half life of the products will eliminate quickly.
2) A typical peak valley plasma concentration time profile is assemble which made steady state condition is different.
3) The changes in the active substances they may lead to precipitation they undergo for the side effects and adverse effects. [8]

Oral Controlled Drug Delivery Systems: Oral controlled release drug delivery system is defined as the deliveries of drugs in a pre determine rate and pre determine time without any side and adverse effects. The oral drug delivery is a system that provides continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the transfer of a active substance to a specific region within the GI tract for either a local or systemic action.

Classification of Oral Controlled Release System

A) Diffusion Controlled Systems
I. Reservoir Devices
II. Matrix Devices
B) Dissolution controlled system
I. Matrix Dissolution Controlled System

II. Encapsulation Dissolution Controlled system
C) Diffusion and Dissolution Controlled System.[9]

A) Diffusion Controlled Systems

I. Reservoir Devices A core of active substance (the reservoir) enclosed by a polymeric membrane characterizes them. The nature of the membrane determines the rate of active substance discharge. The characteristics of reservoir diffusion systems are

1. Zero order active substance discharge is possible.
2. The active substance discharge rate is dependent on the type of polymer.
3. High molecular weight compounds are difficult to transfer through the device. Coating and microencapsulation technique can be applied to formulate sub devices. [10]

II. Matrix Devices: The matrix devices defined as the it is having the active substance dissolved homogeneously in a matrix. The characteristics of the matrix diffusion system are

1. Zero order discharge cannot be produced.
2. Easy to manufacture than reservoir devices.
3. High molecule weight of substances are transferred through the devices.[11]

B) Dissolution controlled systems:

I. Matrix Dissolution Controlled System Aqueous dispersions, congealing, spherical agglomeration etc. can be used.
II. Encapsulation Dissolution Control Particles, seeds or granules can be coated by technique such as microencapsulation.

C) Diffusion and Dissolution Controlled System:

The diffusion and dissolution controlled system is defined as the bio erodible matrix the active substance is homogeneously dissolved in a matrix and they discharged either by bilging monitor mechanism or by hydrolysis and enzymatic attack. [12]

Types of Extended-Release Products: The extended drug release is defined as the drug should be released in a predetermine rate and predetermine time with extended period of a time. The extended release substances shows the many advantages they are the reducing the side effects and adverse effects and release the drug in a longer period of time. The drug will reach the bio-availability in a pre determine time. The extended release substances include general advancements for release the drug into a site of action. General advancements to preparation an extended-discharge active substance product include the use of a matrix structure in which the active substance is suspended or dissolved, the use of a rate controlling membrane through which the drug diffuses, or a combination of both. For preparation of the extended release products the wide variety of the polymers are used such as the natural and synthetic polymers are used The natural polymers are such as the xanthin, tragacanth, guargum. The synthetic polymers such as the ethyl cellulose, HPMC, sodium alginate were used for development of the extended release products. The extended release products are discharged by the mechanism such as the dissolution, diffusion and permeation studies. [13]

Factors effecting the Design and Performance of extended Release Products: The type of delivery system and route of administration of the drug presented in sustained drug delivery system may depend upon two properties. They are

I. Physicochemical Properties of drugs
II. Biological Factors. [14]

Physicochemical Properties of Drugs

Dose size: For designing of the dosage form the dose size is maximum required. For orally administered systems, there is an upper limit to the bulk size of the dose to be administered. In general a single dose of 0.5 to 1gm is considered maximum.[15]

Ionization, PKa & Aqueous Solubility: The designing of the extended release dosage form the ionization and Pka and aqueous solubility is important. The pH Partition hypothesis simply states that the uninterrupted form of a active substance species will be alternative immersed through many body tissues. Therefore it is important to note the relationship between the PKa of the compound and its assimilative environment. For many substances, the site of maximum penetration will also be the area in which the active substance is least soluble. For traditional dosage forms the active substance can generally totally dissolve in the stomach and then be penetrated in the alkaline pH of the intestine.[16] For sustained discharge formulations much of the active substance will come in to the small intestine in solid form. This means that the solubility of the active substance is likely to change several orders of magnitude during its discharge. Compounds with very low solubility are genetically controlled, since their discharge over the time course of a dosage form in the GIT will be limited by dissolution of the active substance. The lower limit for the solubility of a active substance to be formulated in a extended discharge system has been reported to be 0.1mg/ml. Thus for slightly soluble active substances, diffusional systems will be poor choice, since the concentration in solution will be low. For example Tetracycline has maximum solubility in the stomach and least solubility in the intestine where it is maximally absorbed. Other examples of drugs whose incorporation into sustained release systems are limited because of their poor aqueous solubility and slow dissolution rate are digoxin, warfarrin, griseofulvin and salicylamide. Very soluble drugs are also good candidates for the sustained release dosage forms.[17]

Molecular size and diffusivity: The active substance is directly ability of drug to disperse through membrane is called diffusivity & diffusion coeffic**i**ent is function of molecular size (or molecular weight). Commonly, values of diffusion coefficient for intermediate molecular weight active substances, through elastic polymer range from 10-8 to 10-9 cm2 / sec. with values on the order of 10-8 being most common for active substances with molecular weight greater than 500, the diffusion coefficient in many polymers regularly are so small that they are difficult to quantify i.e. less than 16-

12 cm2 /sec. Thus high molecular weight active substances and / or polymeric active substances should be expected to display very slow discharge kinetics in sustained discharge device applying diffusion through polymer membrane. [18][19]

Partition coefficient: The designing of the extended release dosage forms the partition co efficient is very important parameter. The partition co efficient is more for the approximately predominantly lipid soluble and easily absorbed through the membranes resulting more bioavailability. The low partition co-efficient is not suitable for the designing of the dosage farms. These leads to the poor bio availability. [20]

Drug Stability: The active substances some are unsuitable in stomach, can be placed in a slowly soluble form and their discharge delayed until they reach the small intestine. Inspite of such a strategy would be destructive for active substances that either are precarious in the small intestine (or) undergo considerable gut wall metabolism, as pointed out in the minimise bioavailability of some anti cholinergic active compounds from controlled discharge production. In general the active substances, which are not stable in GIT environment, are poor candidates for oral sustained discharge forms.[21]

Protein Binding: The protein binding is also necessary for the designing of the sustained drug delivery. In this many active substances are bind to the plasma proteins with it is well known that many drugs bind to plasma proteins with a complementary effecting on the duration of active substance action. Considering blood proteins are mainly re circulated and not eliminated active substance protein binding can serve as depot for active substance formulating a longer discharge profile, especially if a high degree of drug binding occurs. [22]

Biological Factors

Biological Half-Life: The biological factors are mainly effecting on the sustained release preparation. The half life of the drug is low they suitable for the sustained release preparation the compounds should have the 2-3 hrs. The does not show any side effects and adverse effects. If drug should have the longer half life they do not suitable for the sustained release preparation. The compounds are having less half life they are suitable for the sustained release dosage forms these are excellent candidates for the sustained release dosage forms. So the active substances, which have long -half life and short half- life, are poor candidates for sustained release dosage forms. Some examples of drug with half-lives of less than 2 hours are ampicillin, cephalexin, cloxacillin, furosemide, levodopa, penicillin G and propylthiouracil. [23]

2. Absorption: The absorption is main important candidates for the designing of the dosage farms. The absorption of the active substance is most effectively suitable for the sustained release compound. The mostly selected active substances are the penetrated through the specialised transport system. The drug absorption through the gastrointestinal tract are poor candidates for the designing of the sustained release compounds. [24]

Metabolism: The drugs which are incorporating into the sustained form the metabolism is important parameter. The mostly drugs under metabolism in liver with respective enzyme. The drugs which are metabolised before absorption either in the lumen or the tissue of the intestine can show minimising bioavailability from slower-transformation dosage form. Hence criteria for the drug to be applied for development sustained-Release dosage form is, [25]

Drug should have low half-life.
Drug should be freely soluble in water.
Drug should have greater therapeutic window.
Drug should be penetrating throughout the GIT.

Distribution: After the metabolism the undergo for distribution .The drugs which are distributed through the entire GIT. The drugs which are having high apparent distribution volume they effect elimination. The drugs are poor candidate for oral SR drug delivery system e.g. Chloroquine.[26]

Monolithic Matrix System In pharmaceutical CRDDS

The monolithic matrix system is defined as the discharge the drug in a monitor manner technology. The preparation of the tablets by the direct compression method and dry granulation and wet granulation process. For preparation of the tablets many types of the polymers are using they are the natural type and synthetic polymers are used. The natural polymers are xanthin pectin, cellulose derivatives. The synthetic polymers are HPMC, Sodium alginate, ethyl cellulose. [27]

1. Chemical nature of the support.
2. The physical state of the active substance.
3. The matrix and changes in volume as the function of the time.
4. The routes of transformation.
5. The discharge kinetics model .The classification of the matrix-based systems is based on the following criteria.

Matrix structure
Release kinetics Controlled release properties
Chemical nature and the properties of the applied release retardant(s). [28]

Mechanism of Drug Release from Matrix Tablets: In erodible matrices, polymer erosion from the surface of the matrix determines the drug release; whilst in hydrophilic matrices, formation of the gel layer and its dynamics as a function of time determines the drug release. Gel layer thickness, which regulate the diffusion path length of the drug, resemble to the distance between the diffusion and erosion fronts. As the swelling process proceeds, the gel layer gradually becomes thicker, resulting in progressively slower active substance -release rates. [29]

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