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SUSTAINED RELEASE DOSAGE FORMS: A REVIEW

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Introduction:

The word 'Sustained Release' is known to have existed in the medical and pharmaceutical literature for many decades. Sustained release technology has been constantly used to retard the release of therapeutic agent such that its appearance in the circulation is delayed and/or prolonged and its plasma profile is sustained in duration. The onset of its pharmacological action is often delayed and duration of therapeutic action is sustained. The objective of sustained release of drug, in a general way is to modify the normal behavior of drug molecule in a physiological environment. It leads to the following:

1. Sustaining the drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with minimization of desirable side effects.
2. Localization of the drug action by spatial placement of a controlled release system usually rate controlled adjacent to or in the diseased tissue of organ.
3. Targeting the drug action by use of carriers of various chemical derivatives to deliver the drug to particular target cell type.

The ultimate criterion for a sustain release tablet is to achieve a blood level and the drug comparable to that of liquid product administered every 4 h. To this end, prolonged release dosage forms have been designed to release the drug, so as to provide a drug level within the therapeutic range for 8 to 12 h, with a single dose rather than a dose every 4 h. Prolonged drug forms are no without disadvantages. Since gastrointestinal tract is not all uniform, certain individuals may release too much drug too soon and experience toxic or exaggerated response to the drug, where as other may liberate the drug more slowly and not receive the proper benefit or response anticipated. This is especially true for older people whose gastrointestinal tract is less active than that of the younger. Also liberation is slow; there is danger of accumulation of the drug after several days resulting in high blood levels and a delayed exaggerated response.

Objectives:

The objective of designing a sustained release system is to deliver drug at a rate necessary to achieve and maintain a constant drug level. This rate should be analogous to that achieved by continuous IV infusion where drug is provided at a constant rate equal to its rate of elimination. This implies that the rate of delivery must be independent of the amount of drug remaining in the dosage form and constant over time that is release from the dosage form should follow zero order kinetics. It is shown by the following equation. Zero order kinetics shown by following equation:

$$kr0 = \text{Rate In} = \text{Rate out} = ke \cdot Cd \cdot Vd$$

Where, kr0 - Zero order rate constant for drug release.
ke - First order rate constant for overall drug elimination.
Cd - Desirable drug level in the body.
Vd - Volume space in which drug is distributed/volume of distribution.

To achieve a therapeutic level promptly and sustaining the level for a given period of time, the dosage form generally consists of two parts, an initial priming or loading dose, Di, that release drug immediately and a maintenance or sustaining dose, Dm. The total dose, W, thus required for the system is,

$$W = Di + Dm$$

For a system where the maintenance dose release drug by a zero order process for a specified period of time, the total dose is,

$$W = Di + Kr0\ Td$$

Where, Kr0- Zero order rates constant.
Td - Total time desired for sustained release form and dose.

The drug in blood level or tissue level versus time profile is the ideal goal of a sustained release which is achieved by use of a maintenance dose that release its drug by zero order release kinetics. To maintain drug blood level within the therapeutic range over the entire time course of therapy, most sustained release drug delivery system and like conventional dosage forms, administered as multiple rather than single dose. For those sustained release systems utilizing the release kinetics other than zero order the multiple dosing is more complex.

Results:

This type of drug delivery system combines diffusion & dissolution of both drugs as well as matrix material. Drug can not only diffuses out of dosage form; as described in previous matrix system, but matrix itself also under goes dissolution process. The complexity of the system arises from the fact that as the polymer dissolves the diffusional path length for the drug may change. This usually results in a moving boundary diffusion system. Zero-order release is possible only if surface erosion occurs and surface area does not change with time. Swelling-controlled matrixes exhibit a combination of diffusion & dissolution mechanisms. Here the drug is dispersed in a polymer, but instead of an insoluble or non-erodible polymer, swelling of the polymer occurs. This allows for the entrance of the water, which causes dissolution of the drug & diffusion out of the swollen matrix. In these types of systems the release rate is highly dependent on the polymer swelling-rate & drug solubility. This system usually minimizes the burst effects, as rapid polymer swelling occurs before drug release. Mainly used excipients for these types of drug delivery systems are HPMC, Xanthan gum, etc.

Osmotic controlled oral drug delivery systems utilize the principle of osmotic pressure for controlled delivery of active agents. Drug delivery from these systems is independent of the physiological factors of the gastrointestinal tract and these systems can be utilized for systemic as well as targeted delivery

of drugs. The release of drug(s) from osmotic systems is governed by various formulation factors such as solubility and osmotic pressure of the core component(s), size of the delivery orifice and nature of the rate controlling membrane. Drug release from this system is independent of pH and other physiological parameter to a large extent and it is possible to modulate the release characteristics

Conclusion:

Concept of sustained release is being explored tremendously due to its lucrative advantages over conventional therapy. To fulfill these medical needs, the pharmaceutical technologists have devoted considerable effort to develop a novel type of dosage form for oral administration, prolonged release matrix tablets which can release drug in controlled fashion. The field of sustained drug delivery is one of the most interesting and challenging endeavors faced by the pharmaceutical scientist. The ways in which medicinal chemicals or the newer biologicals are administered have gained increasing attention in the past three decades. Normally, a drug is administered in high dose at a given time and then dose has to be repeated several hours or days later. As a consequence, increasing attention has been focused on methods of giving these drugs continuously for sustained period in a controlled fashion. The primary method of accomplishing this controlled release has been through incorporating these agents within polymers.