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Review Article

A Review on Extended Release Drug Delivery System

Gaurav Sharma [1], Vijay Sharma [2], Sunil Kumawat [3]

[1] Research Scholar, Goenka College of Pharmacy, Lachhmangarh, Sikar.

[2] Professor, Goenka College of Pharmacy, Lachhmangarh, Sikar.

[3] Associate Professor, Goenka College of Pharmacy, Lachhmangarh, Sikar.

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Corresponding author: Gaurav Sharma
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Abstract:

Extended-release tablets have revolutionized the field of pharmaceuticals by providing a convenient and effective means of drug delivery. This comprehensive review article aims to provide an in-depth analysis of extended-release tablets, discussing their drugs suitable of the manufacturing of ER tablets, benefits as well as their limitations. The extended-release drug delivery method is affected by a variety of physiochemical and biological factors. Various types of evaluation parameters are mentioned here which can be employed for the evaluation of ER tablets.

Key words: Extended-release tablets, physiochemical, biological factors.

Introduction

Oral administration is the most traditional and practical way to provide therapeutic agents since it is easy to administer and results in a better degree of patient compliance due to the cheap cost of treatment. Oral drug delivery systems make up around half of all drug delivery systems on the market, and oral medication administration has long been the most common method of drug delivery. It does not cause sterility issues and has a low chance of causing harm at the administration site. [1]

Several oral delivery systems had been developed during the last three decades to operate as drug reservoirs through which the active ingredient may be delivered over a specific length of time at a planned and regulated pace. The oral controlled release formulation was created for drugs that are readily absorbed via the gastrointestinal tract (GIT) as well as having a short half-life, allowing them to be removed from the bloodstream swiftly. [2]

To address various unmet clinical requirements, extended release formulation is a significant program for new medication research and development. There are several reasons why these dosage forms are appealing, including increased bioavailability of the drug product, reduced frequency of administration to extend the duration of effective blood levels, reduced fluctuation of peak trough level and side effects, and possibly improved drug specific distribution. [3]

Suitable Drug for Extended Release Drug Delivery System: [4]

- Drugs having a short half-life, particularly one with a half-life of 2 to 4 hours, are attractive candidates for

formulation into ER dosage forms, such as captopril and salbutamol sulfate.

- The medication dosage should be less than 0.5g, since the oral route is acceptable for pharmaceuticals with doses as high as 1.0g, such as metronidazole.
- The drug's therapeutic spectrum must be broad. A medication for ERDDS should have a broad enough therapeutic range so fluctuations in release do not result in concentrations over the minimal lethal limits.

Benefits of Extended-Release Drug Delivery System: [5]

- The therapeutic concentrations are sustained for longer periods of time by the extended release formulations.
- Extended release formulations prevent excessive blood concentrations.
- Longer-acting formulations have the potential to increase patient compliance.
- Slowing medication absorption helps to reduce toxicity.
- Increase medication stability by shielding it from hydrolysis and other gastrointestinal degradative processes.
- Reduce both local as well as systemic side effects.
- Treatment effectiveness has improved.
- Reduce medication buildup by using persistent dosing.
- Drug use should be kept to a minimum.
- Some medications' bioavailability may be improved.

Limitations of Extended-Release Drug Delivery System:

- Preparation is expensive.
- Food and the pace of transit through the stomach are two variables that influence release rates.
- Because extended release formulations have a larger drug load, any loss of integrity impacts the dosage form's release properties.
- The greater size of prolonged release products may make ingestion or transit through the intestines more challenging.
- There is little room for dose modification.

Factors Affecting the Extended-Release Drug Delivery System [6,7,8,9]

A. Physiochemical Properties of the drug:

a) Partition Co-efficient

Because the biological membrane through which the medication must travel is lipophilic in nature, the partition coefficient of the drug has a significant impact on its bioavailability. Drugs with lower partition co-efficient values than the optimal activity are unfavorable for oral ER drug delivery systems because they have very little lipid solubility and are localized in the first aqueous phase with which they come into contact, such as barbituric acid.

Drugs with higher partition co-efficient values than the optimal activity are undesirable for oral ER drug delivery systems because more lipid soluble drugs will not partition out of the lipid membrane once they enter it. The ideal n-octanol/water partition coefficient for maximal flow is about 1000.

b) Protein Binding

Drug protein binding affects drug distribution equilibrium. Plasma proteins serve as a buffer in drug disposal, particularly distribution; the medications' elimination half-life will be protracted, and they may not be suitable for formulation into extented release dosage forms. Only the drug's free, nonprotein-bound component can permeate into tissue from blood vessels. Through the dissociation of the drug protein complex, the equilibrium

between free and bound drug works as a buffer mechanism, maintaining a relatively constant concentration of the drug over a lengthy period of time.

c) Solubility in Aqueous Medium

Because the medication must be in solution state before absorption, drugs with low aqueous solubility often have poor oral bioavailability owing to the restricted GI transit time of un-dissolved drug and the limited solubility at the absorption site. As a result, certain sorts of drugs are undesired. Extreme water solubility drugs are unfavorable for ER because they are difficult to manage drug release from the dose form. Physiological pH dependent solubility, i.e. change in solubility at various GI pH (e.g., aspirin, which is less soluble in the stomach but more soluble in the intestine), is undesirable since it results in fluctuation in dissolving rate. A medication with strong water solubility and pH independence is desired for an oral novel drug delivery system.

d) Drug pKa & Ionization at Physiological pH

As we know, only unionized drugs are absorbed, and penetration of ionized drugs is minimal since their absorption rate is 3 to 4 times that of unionized drugs. For optimal positive absorption, the pKa range for acidic drugs where ionization is pH sensitive is around 3.0 - 7.5 while the pKa range for basic drugs where ionization is pH sensitive is around 7.0-11.0. The drug must be unionized at the location to the amount of 0.1 - 5.0%. Drugs that are mostly in ionized form are poor choices for the oral ER drug delivery method.

e) Mechanisms and Absorption Sites

Drugs absorbed by carrier-mediated transport and those absorbed via a window, for example, numerous B vitamins, are poor candidates for oral ER drug delivery systems. Drugs that are absorbed by passive diffusion, pore transport, or over the whole length of the GIT are good candidates for oral ER drug delivery systems.

f) Dose Amount

If a product has a dosage size more than 0.5g, it is a poor fit for an oral ER drug delivery system since the bulk of the medicine rises, as does the volume of the product.

B. Biological Properties of Drug:

a) Absorption

The rate of drug absorption (ka) from the dosage form should be greater than the rate of drug release (kr) through the dosage form for oral ER systems for drug delivery, i.e. kr <<< ka. Slowly absorbed drugs or drugs with a variable absorption rate are weak candidates for oral ER drug delivery systems. Poor water solubility, a small partition coefficient, acid hydrolysis, as well as metabolism or absorption site are all potential causes of limited absorption.

b) Distribution

Drugs having a large apparent volume of distribution, that influences the drug's rate of elimination, are poor candidates for the oral ER drug delivery method.

c) Metabolism

A medication that has been substantially metabolized is unsuitable for the ER drug delivery system. A medication capable of stimulating metabolism, blocking metabolism, or being metabolized at the site of absorption of first-pass action, such as nitroglycerine, is a poor option for ER administration since it may be difficult to maintain a steady blood level.

d) Drug Half-Life

A medication with a biological half-life of 2 to 8 hours is ideal for the oral ER drug delivery method. Because if the biological half-life is less than 2 hours, the system will need an excessively high rate and big dosage to sustain the study condition, and if the biological half-life is more than 8 hours,

formulation of such medication into an oral ER drug delivery system is unnecessary.

e) Safety margin

As we all know, the higher the value of the therapeutic index, the safer the medicine. Drugs having a low therapeutic index are often poor candidates for the development of an oral ER drug delivery system.

Evaluation Parameters of Extended-Release Tablets: [10,11,12,13]

A. In Vitro Dissolution Testing: This is a critical evaluation parameter for extended-release tablets. Dissolution testing measures how the tablet releases the drug over time. The dissolution profile should match the desired release characteristics and be consistent across batches.

B. Content Uniformity: Ensuring that the active pharmaceutical ingredient (API) is uniformly distributed throughout the tablet is essential. Variations in API content can result in inconsistent drug release.

C. Weight Variation: Tablets should have a uniform weight to ensure that patients receive the correct dosage. Weight variations can lead to dosing errors.

D. Hardness: The hardness of the tablet affects its mechanical strength. Tablets should be hard enough to withstand handling and packaging without breaking.

E. Friability: Friability testing assesses the tablet's resistance to abrasion and breakage during handling and transportation. Excessive friability can lead to tablet damage.

F. Thickness and Diameter: Measuring the tablet's thickness and diameter ensures uniformity and consistency in size, which is important for manufacturing and patient dosing.

G. Drug Release Kinetics: Kinetic modeling of drug release profiles can provide insights into the mechanisms governing drug release, such as zero-order, first-order, or Higuchi release kinetics.

H. Stability Studies: Evaluating the stability of extended-release tablets over time is crucial to ensure that the tablet maintains its release characteristics throughout its shelf life.

Conclusion

We concluded from the preceding discussion that extended release formulations are very beneficial in boosting the efficacy of medications with short half-lives while simultaneously improving patient compliance by reducing dose frequency. Extended-release tablets are an essential component of modern drug delivery, offering numerous advantages over immediate-release formulations. Different factors are there which affect the ER drug delivery system. Evaluating different parameters are essential for the successful development and manufacturing of extended-release tablets.

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