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A Comprehensive Review on formulate and evaluate sustained release matrix tablets of rabeprazole sodium using hydrophilic polymer hydroxypropyl methylcellulose (HPMC) alone, of two different viscosity grades of Hydroxypropyl methylcellulose (HPMC K4M & HPMC K15M.).

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ABSTRACT

A sustained release product may be considered one in which a drug is initially made available to the body in an amount sufficient to cause the desired pharmacological response as rapidly as is consistent with the properties of the drug determining its intrinsic availability for absorption; and one which provides for maintenance of activity at the initial level for a desirable number of hours in excess of the activity resulting from the usual single dose of drug. Sustained release and controlled release will represent separate delivery processes; sustained release constitutes any dosage from that provides medication over an extended period of time. Controlled release however, denotes that, system is able to provide same actual therapeutic control, whether this is temporal nature, spatial nature, or both. In other words, the system attempts to control drug concentration in target tissue. This correctly suggests that there are sustained-release systems that cannot be considered as controlled release.

With most of orally administered drugs targeting is not primary concern, and it is usually intended for drugs to permeate to the general circulation and perfuse to other body tissues (the obvious exception being medication intended for local gastrointestinal tissue treatment), for this reason, most systems employed are of the sustained-release variety. It is assumed that increasing concentration at the absorption site will increase the rate of absorption and, therefore, increase circulating blood levels, which in turn promotes greater concentrations of the drug at the site of action. If toxicity is not an issue, therapeutic levels can thus be extended. Theoretically and desirably a sustained release delivery device, should release the drug by a zero-order process which would result in a blood-level time profile similar to that after intravenous constant rate infusion.

KEYWORDS: SUSTAINED RELEASE MATRIX TABLET , HPMC (HPMCK4M & HPMCK15M)

INTRODUCTION

Sustained drug delivery is to alter the pharmacokinetics and pharmacodynamics of pharmacological active moieties by using novel drug delivery system or by modifying the molecular structure and physiological parameters inherent in the selected route of administration. It is desirable that the duration of drug action becomes more a design property of a sustained dosage form and less or not at all a property of the drug molecules inherent kinetic properties. Thus optional design of sustained release system necessitates a thorough understanding of the pharmacokinetics and Pharmacodynamics of the drugs.22 The aim of sustained drug delivery is to optimize the biopharmaceutic, 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 disease condition in the shortest possible time by using smallest quantity of drug, administered by the most suitable route .

There are certain considerations for the formation of sustained release formulations: If the active compound has a long half-life (over six hours), it is sustained on its own. If the pharmacological activity of the active compound is not related to its blood levels, time releasing than has no purpose. If the absorption of the active component involves an active transport, the development of a time-release product may be problematic. Finally, if the active compound has a short half-life, it would require a large amount to maintain a prolonged effective dose. In this case, a broad therapeutic window is necessary to avoid toxicity; otherwise, the risk is unworthy to take and another mode of administration would be recommended.

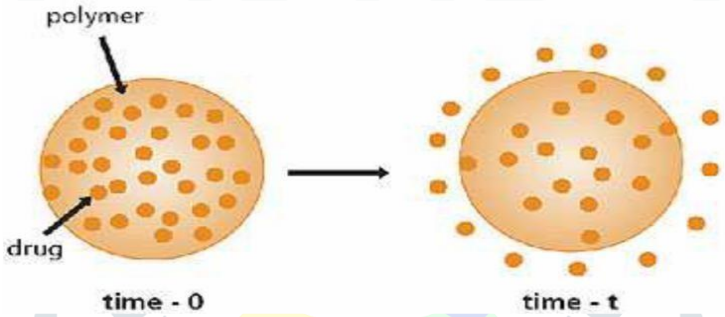

Fig: Schematic representation of diffusion sustained drug release: matrix system.

POTENTIAL ADVANTAGES OF SUSTAINED DRUG THERAPY

. 1) Improved patient convenience and compliance due to less frequent drug dosing.

✓ Employs minimum drug.

✓ Minimizes or eliminates local and systemic side effects.

✓ Obtain less potentiating or deduction in drug activity with chronicuse.

✓ Avoidance of night time dosing.

2) Reduction in fluctuation in steady-state levels and therefore-

✓ Better control of disease condition, and

✓ Reduced intensity of local or systemic side-effects.

✓ It minimizes drug accumulation with chronic dosing.

3) Improves efficacy in treatment Cure or control confirm more promptly.

✓ Improve control of condition thereby reducing fluctuation incirculating drug level.

✓ Improve bioavailability of some drugs.

✓ Make use of special effects, example- sustained release aspect formorning.

✓ More uniform effect.

4) Reduction in health care costs through-

✓ Improved therapy.

✓ Shorter treatment period.

✓ Lower frequency of dosing

✓ Reduction in personnel time to dispense, administer and monitorpatients.

5) Improved therapy-

✓ Sustained blood level- The dosage form provides uniform drug availability/blood levels unlike peak and valley pattern obtained by intermittent administration.

✓ Attenuation of adverse effects- The incidence and intensity of undesirable side effects caused by excessively high peak drug concentration resulting from the administration of conventional dosage form is reduced.

✓ It is seldom that a dose is missed because of non-compliance by the patient

6) Increased safety margin of high potency drugs due to better control ofplasma levels.

7) Maximum utilization of drug enabling reduction in total amount of drug administered. Disadvantages of sustained release dosage forms .

✓ They are costly.

✓ Unpredictable and often poor in-vitro in-vivo correlations, dose dumping, reduced potential for dosage adjustment and increased potential first pass clearance

. ✓ Poor systemic availability in general.

✓ Effective drug release period is influenced and limited by GI residence time. Factors governing the design of sustained/controlled release dosage form .

A) Drug related Factors

✓ Molecular size and diffusivity

✓ Aqueous solubility and pKa.

✓ Partition coefficient.

✓ Molecular size.

✓ Drug stability.

✓ Protein binding.

B) Biological factors

✓ Absorption.

✓ Distribution.

✓ Metabolism.

✓ Elimination.

✓ Elimination half-life.

✓ Therapeutic Index.

✓ Dose size.

✓ Duration of action.

✓ Plasma concentration response.

✓ Margin of safety.

✓ Side effects.

✓ Diseased state.

CLASSIFICATION OF ORAL SUSTAINED RELEASE SYSTEMS

1) Continuous release systems

a) Dissolution controlled release systems.

i) Matrix type.

ii) Reservoir type.

b) Diffusion controlled release systems.

i) Matrix type.

ii) Reservoir type.

c) Dissolution and diffusion controlled release systems.

d) Ion exchange resin drug complexes.

e) Slow dissolving salts and complexes.

f) pH dependent formulations.

g) Osmotic pressure controlled systems.

h) Hydrodynamic pressure controlled systems.

2) Delayed transit and continuous release systems

a) Altered density systems.

i) High density.

ii) Low density.

iii) Floating.

iv) Mucoadhesive systems.

v) Size based systems.

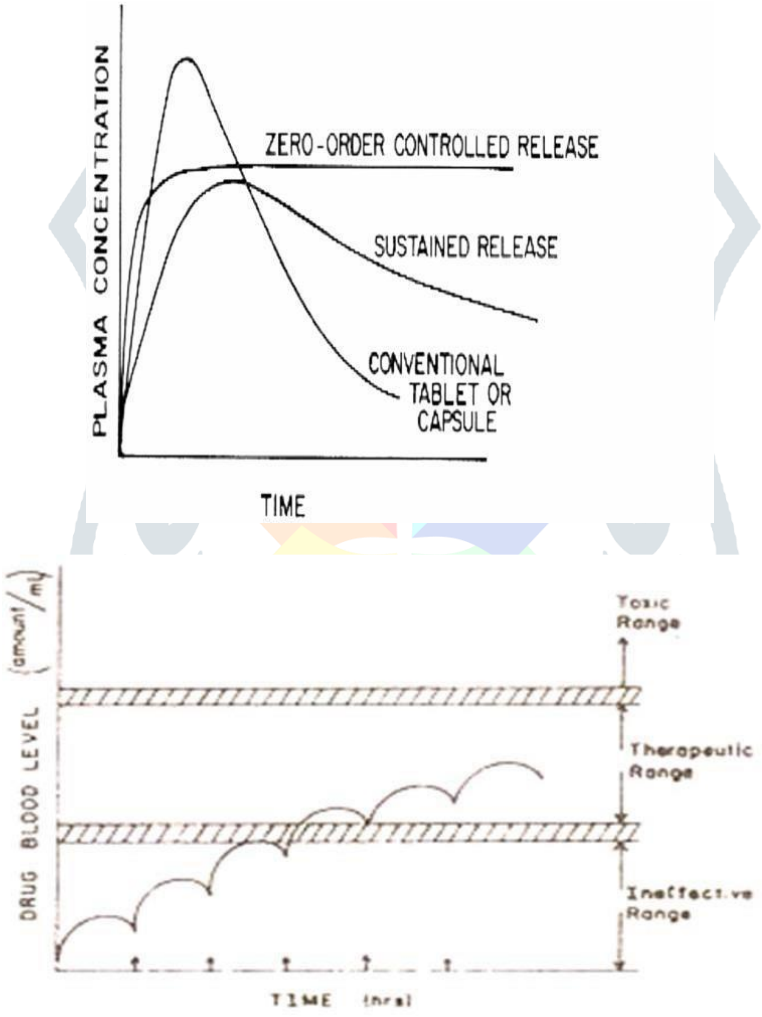

Figure: typical drug blood level versus time profiles following oral multiple dose therapy

An alternative approach is to administer the drug repetitively using a constant dosing interval, as in multiple-dose therapy. This is shown in Figure **2** for the oral route. In this case the drug blood level reached and time required to reach that level depend on the dose and dosing interval. There are several potential problems inherent in multiple-dose therapy. If the dosing interval is not appropriate for the biological half-life of the drug, large peaks and valleys in the drug blood level may result. For example, drug with short half-life requires frequent dosing to maintain constant therapeutic levels. The drug blood level may not be within the therapeutic range at sufficiently early times, an

important consideration for certain disease state. Patient noncompliance with the multiple-dosing regimen can result in failure of this approach.

HYDROXY METHYL,PROPYL CELLULOSE USED IN SUSTAIN RELEASE MATRIX TABLETS HYDROXY ETHYL CELLULOSE (HPMC) ALONE, OF TWO DIFFERENT VISCOSITY GRADES OF HYDROXYPROPYL METHYL CELLULOSE (HPMC K4M & HPMC K15M.).

(HPMC)K4MPROPYL

METHOCE K4M is a **medium–molecular weight**, hydroxypropyl methylcellulose (HPMC) thickener. It will yield a viscosity of 4,000 cPs at 2% in water and is typically used in coatings, adhesives, and ceramics. Fulfilled by ChemPoint. Manufacturer: DuPont. Product Line: METHOCEL Cellulose Ethers

(HPMC)K15M

Hydroxypropylmethylcellulose (HPMC) K15M is **a high purity, water-soluble cellulose derivative designed to perform many functions in processed foods** - including reversible hot water gelation, water binding and retention, oil barrier formation, thickening, suspending and stabilizing, and film formation.

DIFFERENT GRADES OF HPMC

The composite formulations comprising polyethylene glycol (PEG) 3350 and hydroxypropyl methylcellulose (HPMC) of ten different grades (**K100 LV, K4M, K15M, K100M, E15 LV, E50 LV, E4M, F50 LV, F4M and Methocel VLV**) at various concentrations were prepared and their viscosities at different temperatures determined.

ADVANTAGES OF HPMC

HPMC is an extensive hydrophilic polymer used in many pharmaceutical dosage forms, including as a hydrophilic matrix form with prolonged drug release.

Hydroxypropyl methylcellulose:
Hydroxypropyl methylcellulose (HPMC or hypromellose) is a partly *O*-methylated and *O*-(2- hydroxypropylated) cellulose ether derivative.

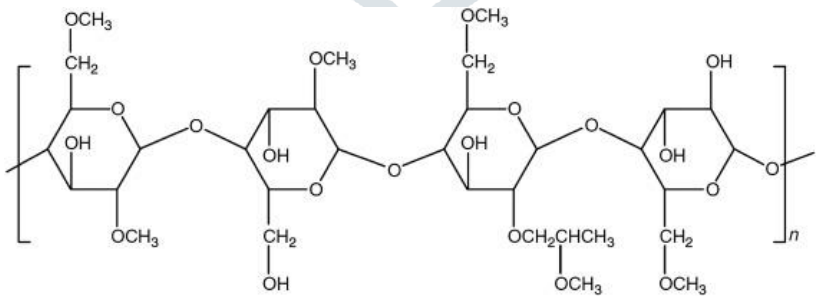

Figure - Typical structure for HYDROXYPROPYL methylcellulose. This is an example of a mixed DERIVATIZED cellulosic containing both HYDROXYPROPYL and METHOXYL functionality. The specific system shown has a HYDROXYPROPYL DS of 0.25 (~9.6 wt.%) and METHOXYL DS of 1.5 (~23 wt.%).

COCLUSION

The article discussed overview OF HYDROXY ethyl cellulose (HPMC) alone, of two different viscosity grades of HYDROXYPROPYL methyl cellulose (HPMC k4m & HPMC k15m.).

By considering above facts, the present study was aim to formulate and evaluate the sustained release matrix tablets of Zidovudine to prolong the release of drug for extended period of time in order to; Improve patient compliance, Reduce dosing frequency Reduce side effects, Minimum plasma fluctuation, Increase bioavailability of the drug.
Keeping this in view, the present investigation has been aimed at designing suitable sustained release matrix tablets using polymers like HPMC ,Guar gum and Ethyl cellulose.

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