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Formulation and Evaluation of Floating Microspheres

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Abstract: *Gastro-retentive dosage forms have potential for use as controlled- release drug delivery systems. Gastro retentive floating drug delivery systems have a bulk density lower than that of gastric fluids and thus increase residence time of drug in stomach and providecontrolled delivery of many drugs. The aim of the present study is formulation and characterization of floating microspheres usingmodel drug. Floating microspheres were prepared by oil-in-water emulsion solvent evaporation technique using ethyl cellulose as release retarding polymers. The floating microspheres were evaluated for percentage yield (%), particle size, drug content, drug entrapment efficiency, in-vitro floating ability and in-vitro drug release studies. The surface morphology of prepared microspheres was characterized by scanning electron microscopy. The microspheres were found to be spherical in shape and porous in nature. Compatibility studies were performed by fourier transform infrared (FTIR) technique. The prepared microspheres showed prolonged drug release of 12 h and remain buoyant for more than 12 h. In-vitro release kinetics were studied in different release kinetics models like zero order, first order model. It was concluded that developed floating microspheres offers a suitable and practical approach forprolonged release of drug over an extended period of time and thus oral bioavailability, efficacy and patient compliance is improved*

Keywords: Gastro retentive drug delivery, Floating drug delivery system, Emulsion solvent evaporation method, FloatingCapability

I. INTRODUCTION

Floating microspheres are gastro retentive drug delivery systems based on non-effervescent approach. They are spherical empty particles without core. These microspheres are characteristically free flowing powders consisting of protein or synthetic polymers with diameters 1 µm to 1000 µm. Hydro dynamically controlled drug delivery systems (Floating drug delivery system) are low density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.[1]

The sustained release of drug from floating systems improves the gastric retention of drugs and reduces the fluctuations in plasma drug concentration. Commonly used polymers to prepare floating microspheres include polycarbonate, HPMC, cellulose acetate, calcium alginate, Eudragit S, chitosan etc. Thus floating microspheres are considered as one of most promising buoyant systems. They possess the unique advantages of multiple unit systems and in addition better floating properties.[2]

The general techniques involved in their preparation include emulsion solvent evaporation and emulsion solvent diffusion. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvent employed for the preparation. [3]

Oral route is considered to be highly suitable route and frequently used for delivery of drug due to ease of administration, patient compliance and flexibility of formulation. The success of oral controlled delivery system depends on the fact that the drug can be better absorbed from GI tract. But the main problem with conventional delivery is to maintain the drug concentration within the therapeutic effective concentration level, which can be achieved only when taken several times a day.[4]

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Although attempts have been made to develop controlled release delivery systems for oral route but various limitations like variable drug absorption, uncontrolled gastric transit time have established the need of more intelligent drug delivery systems, which can prolong the transit time of drug, or provide effective concentration locally. The gastro retentive drug delivery system can be retained in the stomach and help in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the GI tract. [5]

Various methods have been designed to increase the gastric residence time (GRT) which include: floating drug dosage systems (FDDS), swelling or expanding systems, muco-adhesive systems and high-density systems. These system give advantage in improving bioavailability of drugs that have a narrow absorption window, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It also has applications for local drug delivery to the stomach and proximal small intestines. [6]

Most preferred route for drug delivery is the oral route due to its patient compliance and easiness of ingestion and cost-effectiveness. Many different techniques have been developed like tablet capsule syrups etc for delivery of a significant amount of drug at a specific site and time prearranged and systematic manner but this route has numerous physiological problems, like-easily bypass through GIT at major absorption zone (stomach and upper part of intestine) due to high density and low density retention time resulting incomplete drug release and low efficacy of drug unpredictable absorption due to degradation of drug by stomach acid and enzyme, hence the site specific drug delivery for diabetic through oral route is also most challenging task for researchers. [7]

So these difficulties provoked the investigators to develop a DDS known as gastro retentive floating microspheres which performs its actions i.e. its therapeutically active plasma concentration of drug for prolonged period of time, by minimizing the dosing criteria and minimizing the fluctuations in plasma concentration of drug by the pharmacological effect of the drug in a systemic and controlled way. After oral delivery of gastro retentive floating microspheres, the drug reserved in to the stomach and performs the action of drug release in a well-ordered manner, so that the delivery of drug is continuous at its absorption sites in GIT (gastrointestinal tract).[8,9]

The floating systems are low-density systems that have sufficient buoyancy to float over the gastric content and remain buoyant the stomach without affecting the gastric emptying rate for a prolonged period of time which causes the inadequate release of drug at the absorption site . Over the last minority decades, several gastro-retentive drug delivery systems being intended, including high- density systems that is retain in the lower part of the stomach , lower density which cause buoyancy in gastric-juice , muco-adhesive systems that cause a bio-adhesion to stomach mucosa , un-foldable, extendible, or swell-able systems which can restriction of the emptying dosage forms through the pyloric sphincter , super porous hydrogel system , magnetic system , etc.[10,11,12]

II. MATERIALS AND METHOD

MATERIALS

CHEMICALS :- Ethyl Cellulose, Isopropyl Alcohol ,Acetone, Liquid Paraffin , Alcohol, Eudragit

EQUIPMENTS:- Mechanical Stirrer, Beaker (50ml&500ml), Magnetic Stirrer, Three Propellor Stirrer

METHOD USED :- SOLVENT EVAPORATION TEST

1. Firstly to weigh the amount of drug or API as per our Dose ex 250mg
2. Then weigh all remaining excipients one by one.
3. Add all the excipients keep aside for short period in Butter paper.
4. Now take 500ml beaker and add 300ml liquid paraffin in it.
5. Now add 250mg of drug & Polymer in 50ml size beaker & dissolve drug and polymer in the solvent.
6. Now immerse magnetic stirrer in 500ml beaker of liquid paraffin
7. Start the mechanical stirrer which is already immersed in liquid paraffin then add drop by drop drug & polymer solution from 50ml size beaker, we have to add whole solution from 50ml size beaker slowly into the liquid paraffin
8. Now both solutions are moving in 500ml size beaker and due to rotation of paddle, Alcohol evaporate from liquid paraffin will and finally solid particulate will appear in liquid paraffin
9. That appeared solid particle can be filter by using filter paper
10. Then filter solid particles are wash with same other solvent to move foreign particle and some ions which are attached to it.

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11. Then the cleaned microsphere are kept in dessicator for storage

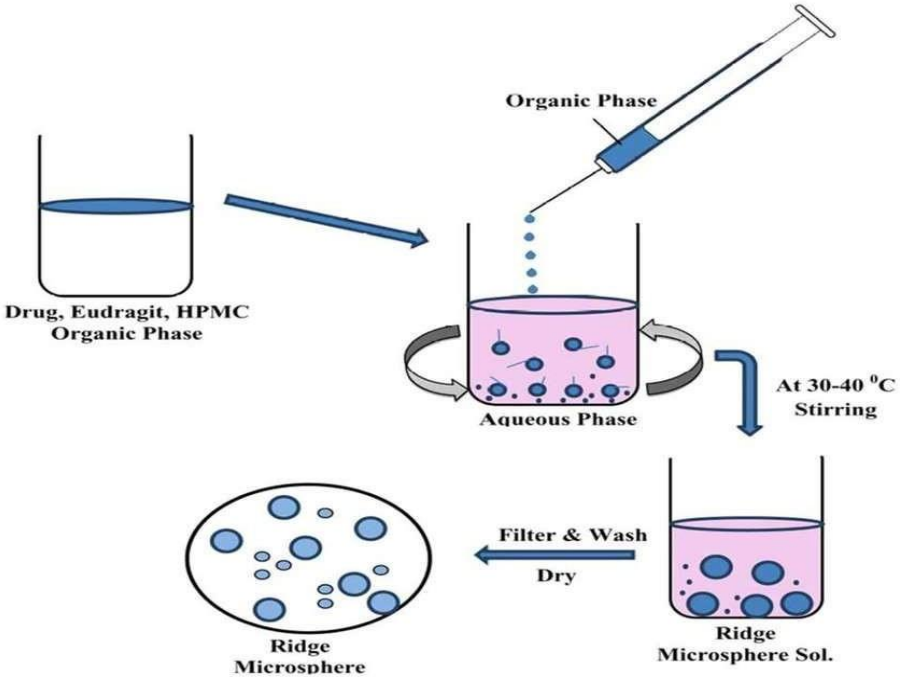

Fig.1:- Preparation of floating microspheres

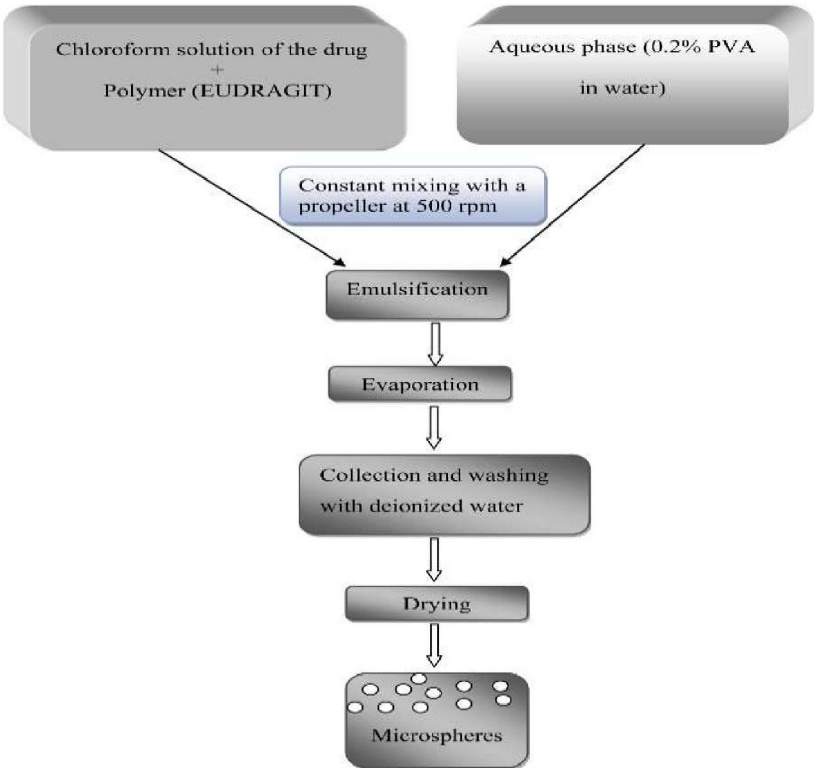

Fig.2:- Flow chart of preparation of floating Microspheres

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III. SIZE, SHAPE AND SURFACE ANALYSIS

Size distribution of the prepared microspheres was studied by optical microscope. Surface morphology of the microspheres was examined by Scanning electron microscopy (SEM).The coated microspheres were then, observed for morphological characteristics and to confirm the spherical nature of microsphere with a Scanning electron microscope.[13,14]

IV. MICRO-MERITIC PROPERTIES

Tapped density of the prepared microspheres was determined by using tap density tester and % carr index and hausner ratio was calculated. Angle of repose was assessed to know the flow ability of microspheres by a fixed funnel method [14,15]

V. ADVANTAGES

- Extended time over critical (effective) concentration ¼ less inter and intra-Subject variability.
- Improved receptor activation selectivity.
- Better therapeutic effect of short half-life drugs can be achieved. The ¼ Gastric retention time is increased because ofbuoyancy.

VI. CONCLUSION

Floating microspheres of were prepared by solvent evaporation technique, using various biodegradable polymers such as ethyl cellulose in order to retain drug in body for longer period of time. It is insoluble in water and has short half-life of 1.5 h. It requires frequent dosing before meals due to short half-life and thereby imposing side effects. The drug requires a novel gastro-retentive drug delivery system which can provide an extended period of time in stomach and improve oral bioavailability.

Floating microspheres were characterized for floating ability, compatibility study, particle size and shape, drug content, in vitro drug release, entrapment efficiency. Due to their low density, these multi particulate drug delivery systems showed good floating ability and remained in gastric environment for more than 12 h. The microspheres showed its buoyancy for more than 15 h, required for sustained therapeutic activity in comparison to Ethyl cellulose based microspheres.

Major advantages of the system include ease of preparation, good floating ability, high encapsulation efficiency and sustained drug release over several hours. From this study it was concluded that formulation of floating microspheres offers prolonged gastric residence time and continuous release of the medication over an extended period of time thus oral bioavailability of the drug and subsequent efficacy is improved.

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