JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

GENERAL REVIEW ON FORMULATION AND EVALUATION OF NOVEL FLOATING *IN SITU* GEL FOR GASTRORETENTIVE DRUG DELIVERY

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Abstract:

The objective of the study was to develop floating *in situ* gel formulations. These formulations increase the targeted action on bacteria for a longer time that can be used in the treatment of various gastric diseases. Floating drug delivery system comes with the advantage of sustained release of drugs over a prolonged period of time thereby maximizing the oral absorption of drugs with narrow absorption window, it overcomes the challenges of conventional oral drug delivery system. *In situ* gel formulations were prepared by varying concentrations of sodium alginate as *in situ* gel forming bio-degradable polymer and calcium carbonate as a cross-linking agent. The formulations were evaluated for Physical appearance, pH, *in vitro* drug release, viscosity, *in vitro* floating behaviour, *in vitro* gelling capacity and drug content.

Keywords: *in-situ* gel, Floating drug delivery system, drug delivery systems, sol to gel form.

Introduction:

Drug delivery system (DDS) is becoming increasing sophisticated as pharmaceutical scientists acquire a better understanding of physiochemical and biological parameters pertinent to their performance.Oral administration is the most convenient and preferred means of drug delivery to the systemic circulation. Oral controlled release drug delivery has recently been of increasing interest to achieve improved therapeutic advantages, such as ease of administration, patient compliance, and flexibility in formulation. Oral controlled release drug delivery has recently

gained lots of interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of administration, patient compliance and flexibility in formulation.In the *in-situ* type of drug delivery system, the preparation is in a solution form before administration in body, but it converts into a gel form after administration. An *in-situ* gel is made of polymer materials that have a solution or semisolid state that responds to external stimuli at the administration site. These gels also have conformations that can undergo reversible conversion to form a semisolid or solid preparation. For ex Clarithromycin is a macrolide antibiotic hence it can be used to treat gastric diseases.(1) Floating *in situ* gel drug delivery systems have been used to deliver many drugs which are used either for their systemic or for their local effects in the stomach. A major constraint in the oral controlled drug delivery is that not all drug candidates are absorbed uniformly throughout the gastrointestinal tract (GIT), and some drugs are absorbed only in a particular portion of GIT or absorbed to a different extent in various segments of the GIT. The pH-dependent solubility and stability levels of a drug play an important role in its absorption.

In situ gel forming systems –

In situ gel-forming polymeric formulations is in sol form before administration undergo gelation in situ to form a gel . These in situ solutions are liquid at room temperature but undergo gelation when in contact with body fluids or change in ph. These have a characteristic property of temperature dependent, pH-dependent and cation induced gelation. Compared to conventional controlled release formulations, in situ forming drug delivery systems possess potential advantages like simple manufacturing process, ease of administration, reduced frequency of administration, and improved patient compliance and comfort .Oral in situ gel forming system also known as stomach specific or raft forming systems have provided a suitable way of providing the controlled drug delivery within stomach with enhanced gastro-retention Drugs that are easily absorbed from gastro intestinal tract (GIT) and have short half life are eliminated quickly from systemic circulation. Frequent dosing of these drugs is required to achieve therapeutic activity.

Classification of floating drug delivery systems:

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in the development of Floating Drug Delivery Systems.

1. Effervescent systems -

These buoyant delivery systems utilize matrices prepared with swellable polymers such as Methocel or polysaccharides, e.g., chitosan, and effervescent components, e.g., sodium bicarbonate and citric or tartaric acid or matrices containing chambers of liquid that gasify at body temperature. Gas can be introduced into the floating chamber by the volatilization of an organic solvent (e.g., ether or cyclopentane) or by the carbon dioxide produced as a result of an effervescent reaction between organic acids and carbonate–bicarbonate salts This produces an upward motion of the dosage form and maintains its buoyancy.

2. Non-effervescent systems-

Non-effervescent floating drug delivery systems are normally prepared from gel-forming or highly swellable polysaccharides or matrix forming polymers like polyacrylate, polycarbonate, polystyrene and polymethacrylate. In one approach, intimate mixing of drug with a gel forming hydrocolloid which results in contact with gastric fluid after oral administration and maintain a relative integrity of shape and a bulk density less than unity within the gastric environment. The air trapped by the swollen polymer confers buoyancy to these dosage forms. examples-HPMC, Carbopol etc.

Factors affecting the floating drug delivery system:

- Density
- Size and Shape
- Fed or Unfed State
- Nature of the meal
- Caloric Content
- Gender
- Age
- Posture
- Concomitant drug administration

Need of floating drug delivery system:

Oral dosage forms pose low bioavailability problems due to their rapid gastric transition from stomach, especially in case of drugs which are less soluble at alkaline pH of intestine. Similarly, drugs which produce their local action in stomach get rapidly emptied and do not get enough residence time in stomach. So, frequency of dose administration in such cases is increased. To avoid this problem floating drug delivery system has been developed. Oral in situ gel forming system also known as stomach specific or raft forming systems have provided a suitable way of providing the controlled drug delivery within stomach with enhanced gastro-retention. The tablet/capsule floating dosage forms are stable as compare to liquids but the problem with them is that they are needed to swallow as whole unit. In case of dosage adjustment these cannot be broken in halves as these are also designed for controlled release and floating ability also depends on dimensions of tablets. In this technique, a solution of low viscosity is used which on coming in contact with the gastric fluids, undergo change in polymeric conformation and a viscous gel of density lower than the gastric fluids is produced. This low-density gel formation called as raft not only provide the much-desired gastro retention to prolong the contact time, but also produce the continuous and slow drug release.

Evaluation tests:

1. **Appearance:** Gel formulations were visually inspected for clarity, color and homogeneity.
2. **Surface pH:** The pH values of different formulations were measured using a calibrated digital pH meter at room temperature in triplicate.
3. **Viscosity:** Viscosity of the samples was determined using Brookfield *Digital Viscometer*. The formulation (100 ml) was taken in a beaker and maintained at room temperature. For determination of viscosity, spindle no. 5, 6 was used in plate and cone viscometer.(3)
4. ***In-vitro* Gelling Capacity:** To evaluate the formulations for their *in-vitro* gelling capacity by visual method. The gelling capacity of the solution was evaluated on the basis of stiffness of formed gel and time period.(1)
5. **Determination of Drug Content:** drug concentration was determined by using a UV-visible spectrophoto-meter
6. ***In-vitro* Drug Release Studies:** The drug release study was carried out using USP Type II paddle-type apparatus.
7. **Stability Studies:** The stability studies were carried out according to ICH and WHO guidelines to determine the physical and chemical stabilities of prepared formulations.

Recent advances-

One of the challenges facing today's pharmaceutical industry centers on coming up with efficient treatment options that are readily acceptable to physicians and patients. Delivery systems must also contribute to a better therapeutic outcome if they are going to provide viable alternatives to pharmaceuticals currently delivered by other routes. In situ gel formulations are one of the challenging drug delivery systems. The recent advancement of biotechnologies has led to the development of labile macromolecular therapeutic agents that require complex formulations for their efficient administration. N-stearoyl L-alanine(m)ethyl esters when mixed with a vegetable oil and a biocompatible hydrophilic solvent led to the formation of injectable, in situ-forming organogel. Following subcutaneous injection, leuprolide- loaded organogel degraded and gradually released leuprolide for 14 to 25d.

Future prospects –

Herbal drug delivery is the emerging field in the pharmacy. The use of floating drug delivery system for herbal medicament is the novel approach for the better delivery of drugs. For this purpose there is a great opportunity to work on GI transit profiles. This has given rise to new products with substantial benefits to the patients. Now with the advent of FDDS the products have been designed which could release drug for upto 24 hrs.

Conclusion:

In conclusion, the primary requirement of a successful controlled release product focuses on increasing patient compliance which the in situ gels offer. Exploitation of polymeric in- situ gels for controlled release of various drugs provides a number of advantages over conventional dosage forms. Sustained and prolonged release of the drug, good stability and biocompatibility characteristics make the in situ gel dosage forms very reliable. Use of biodegradable and water soluble polymers for the in situ gel formulations can make them more acceptable and excellent drug delivery systems. In-situ drug delivery provides a great potential for development of liquid orals for their sustained drug release. This floating in-situ gel approach is suitable for drugs having narrow absorption window in stomach or drugs showing local effect in stomach. These types of drugs which are currently present in market as their solid dosage forms (tablets or capsules) will be available as their floating in-situ gels.

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