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FLOATING DRUG DELIVERY SYSTEM: AN UPDATED REVIEW

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ABSTRACT

The purpose of writing this article regarding floating drug delivery system point out the principle mechanism of FDDS to achieve gastric retention. The present review addresses briefly explain about the Gastric retention, Suitable drugs and excipients, Different approaches, Characterization. The review also summarizes the application of FDDS. Efforts are made on the controlled drug delivery (floating drug delivery) to fulfill the complex task of gastric emptying and effective for more than 12hours and thus by increasing the patient compliance.

Key words: Floating drug delivery system, Gastric emptying time, Technologies on floating drug delivery, Applications.

INTRODUCTION

Floating systems or Hydrodynamically controlled systems 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]. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal[2]. Floating drug delivery system is capable of achieving more predictable and increased bioavailability of drugs. However, the development process is often facing several physiological difficulties, inability to restrain and localize the DDS within desired regions of the gastrointestinal (GI) tract and the variable nature of gastric emptying process. It can last from a few minutes to 12 h. This variability, in turn, may lead to unpredictable bio-availability and times to achieve peak plasma levels, since the majority of drugs are preferentially absorbed in the upper part of the small intestine [3]. Thus, placement of a DDS in a specific region of the GI tract offers numerous advantages, especially for drugs exhibiting an absorption window in the GI tract or drugs with a stability problem. Overall, the intimate contact of the DDS with the absorbing membrane has the potential to maximize drug absorption and may also influence the rate of drug absorption [4-5]. These considerations have led to the development of oral controlled- release (CR) dosage forms possessing gastric retention capabilities. As the first part in this series of reviews on contemporary gastroretentive systems, the current technological developments in FDDS, including patented and clinically available products, formulation development strategy, and their advantages and future potential for oral controlled drug delivery are discussed.

BASIC PHYSIOLOGY PROBLEMS & APPROACHES

Stomach anatomy

Anatomically the stomach is divided into three regions: Fundus, body, and antrum (pylorus). The proximal part made of fundus and body act as reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as pump for gastric emptying by propelling actions [6].

Gastric emptying and problems

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The stomach may be used as a 'depot' for sustained-release (SR) dosage forms. The process of gastric emptying occurs both during fasting and fed states; however, the pattern of motility differs markedly in the two states. In the fasted state, it is characterized by an interdigestive series of electrical events which cycle both through the stomach and small intestine every 2–3 h. This activity is called the interdigestive myoelectric cycle or migrating myoelectric complex (MMC), which is often divided into four consecutive phases [7].

Phase 1: (Basic phase)-last from 30-60 minutes with rare contractions.

Phase 2: (Preburst phase)-last for 20-40 minutes with intermittent action potential and contractions.

Phase 3: (Burst phase) - last for 10-20 minutes which includes intense and regular contractions for short period.

Phase 4: last for 0-5 minutes and occurs between Phase 2 and 1 of 2 consecutive cycles [8].

FACTORS AFFECTING GASTRIC RESIDENCE TIME OF FDDS

Formulation factors

Size of tablets

Retention of floating dosage forms in stomach dep ends on the size of tablets. Small tablets are emptied from the stomach during the digestive Phase, but la rge ones are expelled during the house keeping waves [9-10].

It was found that floating dosage units remained b uoyantregardless of their sizes on the gastric contents throu ghout their residence in the gastrointestinal tract.

Density of tablets

A buoyant dosage form having a density less than that of the gastric fluids float, A density of less than 1.0 g/ ml i.e. less than that of gastric contents has been reported [11].

Shape of tablets

Six shapes (ring tetrahedron, cloverleaf, string pell et, and disk) were screened in vivo for their gastric retentio n Potential [12].

Viscosity grade of polymer

Drug release and floating properties of FDDS are greatly affected by viscosity of polymers and their interacti on. Low viscosity polymers (e.g, HPMC K100 LV) were fo und to be more beneficial than high viscosity polymers (e.g., HPMC K4M) in improving floating properties [13].

Idiosyncratic factors

Gender

Women have slower gastric emptying time than do men. Mean ambulatory GRT in meals (3.4±0.4 hours) is less compared with their age and race matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface [14].

Age

Low gastric emptying time is observed in elderlyth an in younger subjects. Elderly people, especially those over 70 years have a significantly longer GRT. Intrasubject and intersubject variations also are observed in gastric and intestinal transit time [15].

SUITABLE DRUGS FOR GASTRORETENTION

Appropriate candidates for controlled release gastr oretentive dosage for molecules that have poor colonic abso rption but are characterized by better absorption properties at upper parts of the GIT [8].

POLYMERS AND OTHER INGREDIENTS USED

Polymers

The following polymers used to preparations of floating drugs: HPMC K4 M, Calcium alginate, Eudragit S100 Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, polymethyl meth acrylate, Methocel K4M, Polyethylene oxide, ß Cyclodextrin, HPMC 4000, HPMC 100, CMC, Polyethylene glycol, polycarbonate, PVA, Polycarbonate, Sodium alginate, HPC-L, CP 934P,HPC, Eudragit S, HPMC, Metolose S.M. 100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4 M and Carbopol [17].

Inert fatty materials (5%-75%)

Edible, inert fatty materials having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. E.g. Beeswax, fatty acids, long chain fatty alcohols, Gelucires [18].

Effervescent agents

Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine) [18].

TECHNOLOGICAL DEVELOPMENTS IN FDDS

Based on the mechanism of buoyancy, two distinctly different technologies, i.e., non-effervescent and effervescent systems have been utilized in the development of FDDS. The various approaches used in and their mechanisms of buoyancy are discussed in the following subsections.

Non-effervescent FDDS

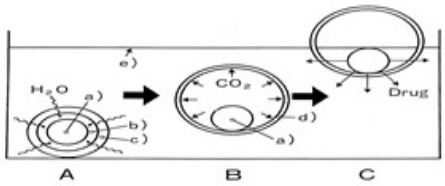
The most commonly used excipients in non-effervescent FDDS are gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides, and matrix forming polymers such as, Polyacrylates, polymethacrylate and polystyrene, polycarbonate One of the approaches to the formulation of such floating dosage forms involves mixing of drug with a gel-forming hydrocolloid, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier

[19]. The air trapped by the swollen polymer confers buoyancy to these dosage forms. In addition, the gel structure acts as a reservoir for sustained drug release since the drug is slowly released by a controlled diffusion through the gelatinous barrier [20].

Effervescent FDDS

These buoyant delivery systems utilize matrices prepared with swellable polymers such as Methocelor polysaccharides, e.g., chitosan, and effervescent components, e.g., sodium bicarbonate and citric ortartaric acid [21] or matrices containing chambers of liquid that gasify at body temperature [22-24]. The matrices are fabricated so that upon arrival in the stomach, carbon dioxide is liberated by the acidity of the gastric contents and is entrapped in the gellified hydrocolloid. (figure 1) .This produces an upward motion of the dosage form and maintains its buoyancy. A decrease in specific gravity causes the dosage form to float on the chime [21]. The carbon dioxide generating components may be intimately mixed within the tablet matrix, in which case a single-layered tablet is produced, or abilayered tablet may be compressed which contains the gas generating mechanism in one hydrocolloid containing layer [25] and the drug in the other layer formulated for a SR effect [26].

Figure 1. Effervescent FDDS



EVALUATION OF FLOATING DRUG DELIVERY SYSTEMS

Various parameters that need to be evaluated in Gastroretentive formulations include floating duration, dissolution profiles, specific gravity, content uniformity, hardness, and friability in case of solid dosage forms. In the case of multiparticulate drug delivery systems, differential scanning calorimetry (DSC), particle size analysis, flow properties, surface morphology, mechanical properties and X-ray diffraction studies are also performed

APPLICATIONS OF FLOATING DRUG DELIVERY Systems Enhanced Bioavailability

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non GRDFCR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act absorption. concomitantly to influence the magnitude of Drug.

Sustained Drug Delivery

Oral CR formulations are encountered with problems such as gastric residence time in the GIT. These problems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited.

Site –Specific Drug Delivery Systems

These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine .The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency. Eg: Furosemide and Riboflavin.

Absorption Enhancement

Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, there by maximizing their absorption.

Minimized Adverse Activity at the Colon

Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented.

Reduced Fluctuations of Drug Concentration

Continuous input of the drug following CRGRDF administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented [27].

CONCLUSION

The currently available polymer-mediated Non effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles, appear to be an effective and rational approach to the modulation of controlled oral drug delivery. This is evident from the number of commercial products and a myriad of patents issued in this field. The FDDS become an additional advantage for drugs that are absorbed primarily in the upper segments of GI tract, i.e., the stomach, duodenum, and jejunum. Finally, with an increasing understanding of polymer behaviour and the role of the biological factors mentioned above, it is suggested that future research work in the floating drug delivery systems should be aimed at discovering means to accurately control the drug input rate into the GI tract for the optimization of the pharmacokinetic and toxicological profiles of medicinal agents.

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