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A NEW TREND IN DRUG DELIVERY SYSTEM: GASTRO-RETENTIVE FLOATING BEADS.

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Abstract: -

Recent scientific and patent literature came to the conclusion that there was a growing interest in innovative dosage forms that could be kept in the stomach for an extended period of time with some predictability. In order to address physiological variations such as short stomach residence times and unpredictable gastric emptying times employing gastro retentive drug delivery systems, numerous technological initiatives have been made in the research and development of rate regulated oral drug delivery systems. The therapeutic efficiency of many orally delivered medications is increased by the extended stomach retention period provided by gastroretentive controlled drug delivery devices. In the current inquiry, we looked at the cutting-edge techniques and polymers utilised to create efficient gastroretentive drug delivery systems. This paper discusses several floating dosage form strategies as well as recent and current innovations in floating drug delivery systems for gastro retention that are particular to the stomach.

Key words: - GRDDS, Effervescent and Non-effervescent Systems, evaluation of floating beads

INTRODUCTION: -

Oral administration is the most convenient and desirable method of delivering drugs into the systemic circulation. Recently, the pharmaceutical industry has become more interested in oral controlled release drug delivery to gain better therapeutic benefits, such as better patient compliance and to prevent repeated drug administration, extensive research has been done on extended-release and sustained-release dosage forms. Drugs that are highly soluble at acidic pH conditions and less soluble at pH levels higher than 7 have a smaller window of absorption from the intestine. The primary benefits of GRDDS are to increase drug bioavailability and provide site-specific drug administration for treating gastrointestinal disorders. The main disadvantage of

GRDDS is that it is incompatible with drugs that irritate the gastric mucosa as compared to conventional dose forms.(Birajdar, A.A. et al. 2021)

One of the gastro retentive dose forms that could enhance gastric retention time (GRT) and achieve adequate drug bioavailability is the gastro retentive drug delivery system (GRDDS). Due to its lower bulk density than an aqueous medium, this system floats in the gastric fluid. For medications that have an absorption window in the stomach or upper small intestine, FDDS is preferred. This technique is also helpful for medications that work locally in the proximal gastrointestinal (GI) tract, such as antibiotic delivery for the treatment of peptic ulcers caused by Helicobacter pylori and medications that are insoluble or unstable in intestinal fluid. (Rathod Sayali, P., 2021) Drug delivery methods for the stomach have numerous benefits; (I)Higher drug solubility and stomach absorption results in improved therapeutic impact for poorly soluble medicines. (ii) Drug dosage decrease and (iii) associated side effects reduction. (Kumar, A et al. 2021)

ANATOMY OF STOMACH: -

The stomach is separated into three anatomical regions: fundus, body, and antrum (pylorus). The stomach has a 1.12–1.5 L capacity, The normal stomach has a J shape. The pH of the napping stomach in young adult's ranges from 1.7 to 1.3 in the elder one. The fundus is in the proximal tube, the body stores undigested substances, and the pylorus is responsible for excretion. The mucus that forms on the epithelium is produced by mucous cells, which are controlling gastric acid. Gastric epithelium cells emit hydrochloric acid (HCl). Pepsinase is released by the zymogenic cells (enzyme). (Setia, M. et al. 2018, Nidhi, K.M et al.)

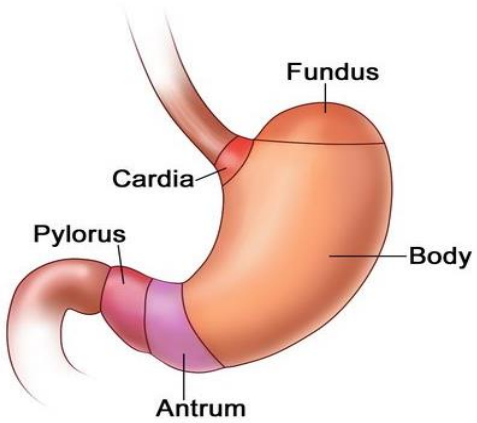

Figure 1: Anatomy of Stomach

Advantages: -

1. To improve intestinal absorption.
2. The GRDDS improves bioavailability.
3. The GRDDS improves patient compliance and reduces dosing frequency.
4. Develop a constant drug release.
5. A targeted drug delivery was facilitated by the GRDDS system.

6. Since there is no risk of dose dumping and floating microspheres make drug constant. (Pund, A.U. et al. 2020, Nidhi, K.M et al.)

Disadvantage: -

1. This method needed a large volume of fluid in the stomach for medication delivery to float, although this can be avoided by employing low density polymers.
2. More amount of water should be needed, for administered of dosage form (200-250 ml). (Setia, M, et al. 2018)
3. Incompatible with medications that have a GIT solubility or stability issue. (Nayak, B.S, et al. 2015).

TYPES OF GRDDS: -

Based on the flotation mechanism, two distinct procedures were used in the development of FDDS. (Varshi, R. et al.2022)

Effervescent Systems (Gas-generating Systems)

In these formulations, release-retardant polymers, swellable polymers, polysaccharides like chitosan and effervescent compounds are included. (Pund, A.U. et al. 2020) Carbonates and other organic acids are used in effervescent compounds to produce carbon dioxide (CO2) gas, which lowers the density cycle and allows the stomach fluid to float over a time. Excipients such HPMC, polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide, and polycarbonates are most frequently utilised in this system. These are further classified into two categories. (Zubedi, S.S. et al. 2018)

a. Volatile liquid containing systems
b. Gas generating systems

Non-effervescent Systems.

In 1984, Sheth PR and Tossounlan J gave the first description on Non-effervescent Systems. The key benefits of non-effervescent systems include the stability of drugs that are acid- or base-labile and the unaffected pH of the stomach during floating lag times (Pund, A.U. et al. 2020)

Non-effervescent systems incorporate a sizable amount of matrix-formed polymers, polysaccharides, sodium carboxymethyl cellulose, and gel-forming, expanding, cellulosic hydrocolloids through tablets or capsules. These polysaccharides, polymers, and gel formers hydrate produce a colloidal gel barrier when they come into contact with stomach fluid, which controls the device's fluid stimulation level and the subsequent release of drug. (Varshi, R. et al.2022, Sato, Y. et al. 2003)

They are classified into the following categories:

a. Colloidal gel barrier systems
b. Microporous Compartment systems
c. Alginate beads
d. Hollow microspheres (Sato, Y. et al. 2003)

Evaluation Tests for Floating Beads: -

1) Percentage yield: - (Rathod Sayali, P., 2021)

The following formula was used to calculate the % yield for each prepared formulation of floating beads.

%Yield = actual weight of product ÷ total weight of excipient and drug ×100

2) Determination of drug content and drug entrapment efficiency (Amol ghare, et al. 2022)

In a mortar and pestle, 50 mg of beads were weighed, crushed, and then dissolved in 25 ml of 0.1 N hydrochloric acid. The solution was kept for 24 hrs. The volume of this solution was increased to 50 mL using mortar washings. Then it was filtered. The filtrate absorbance is given by using a UV spectrophotometer. The drug content and entrapment efficiency were calculated by using following formula.

%Drug entrapment = Calculated drug concentration ÷ Theoretical drug concentration × 100

3) Floating lag time or floating time (Baviskar, P. et al. 2019)

The prepared bead sample (n=20) was put in a beaker with 0.1N HCl solution (pH 1.2). The temperature was maintained at 37°C. The floating time of beads was examined over a period of 12 hours. Only after all of the beads floated in the test solution was the preparation judged to have buoyancy. The time the formulation took emerge on the surface of the medium (floating lag time) and the time for which the formulation remains floating on the surface of the medium (floating time) were noted.

4) Particle size analysis

a) Optical microscopy (Ranvirsingh, T.A et al. 2013)
   An optical microscope with a 4X magnification was used to study calcium alginate beads, and an average of 100 particles of bead were counted.
b) Scanning electron microscopy (Krishna, B.S. et al.)

   Scanning electron microscopy (SEM)has been used to investigate the morphology of cracked or sectioned surfaces, as well as to evaluate particle size distribution, surface topography, and texture. By using JEOL JSM-T scanning electron microscope (Japan).

5) In-Vitro Dissolution Study

In this analysis, USP dissolution devices were used at a specific speed. Dissolution fluid and distilled water are kept at 37±0.5°C. 900mL of 0.1N HCL dissolving media are used for the dissolution test, which is performed for the required amount of time at 100 rpm. samples that are periodically removed and replaced with the same amount of fresh medium. Plotting cumulative percentage drug release vs time was used to examine the dissolution patterns of the formulations. (Birajdar, A.A. et al. 2021, Gavini, V.2014)

6) Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR analysis was performed on both pure drug and a physical combination of drug and polymer. Samples were kept at room temperature for a month after the preparation of physical mixtures. Using a Fourier Transform spectrophotometer, the infrared absorption spectrum of the drug and physical mixture was measured over the range of wave numbers from 4000 to 400 cm^{-1}.

7) Differential Scanning Calorimetry (DSC)

All correctly weighed samples were placed in closed aluminium pans before being heated under nitrogen flow (10 ml/min) at a scanning rate of 100 degrees Celsius per minute from 25 to 3000 degrees Celsius. The reference as empty aluminium pan. (Baviskar, P. et al.2019)

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