

Formulation and Evaluation of Gastroretentive Tablet

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ABSTRACT :

biggest problem and delivery is low and eirotic drug bioavailability -the objective of present study was to develop a gastroretentive drug delivery system of propranolol Hydrochloride-One of the disadvantage in using propranolol is extensive First pass metabolism of drug and only 25%. Teaches systemk crulation. -propranolol is type of medicine called a betyblocker. like other beta blocker, propranolol Works by changing the way your body responds to some nerve impulses. including in the heart It sloins doinn. your heart rate and makes it easier For your heart to pump blood around your body, lowering blood pressure f heart rate, making it easier for your heart to pump blood. It treats conditions like High blood pressure, tremors and atrial Fibrillation-The paper aimed to progresssan Ideal gastraretentive drug delivery system in tended For directing action propranolol Hydrochloride as Fixed dose combination For antihypertensive therapy.gastroretentive Floating tablets (GRFT) were prepared by using asynthetic hydrophilic polymer polyethylene oxide of different grades such as PEO WSR N-12K and PED IR NF as release retarding polymerthe GRFT INere compressed by direct compression strategy and the tablets were evaluated For physico-chemical properties. •They were evoluated For physical prop. In vitro release as well as invivo behavior. In preliminary trials, tablet Formulated With HPC sodium alginate, Failed to produce matrix of required strength, Whereas Formulation containing xanthan gum showes good drug retaining abilities but Floating abilities were Found to be poor.

KEYWORDS : Superdisintegrants release-retarding polymers, Drug delivery, pharmaceutical science, Biomedical engineering. Floating delivery gastroret-entive Hydroxypropyl methylcellulose propranolol, Hydrochloride

I. INTRODUCTION :

Oral drug delivery has been known for decades as the most widely used route of administration among all the routes that have been explored for the systemic delivery. Oral route is the most convenient and extensively used route of drug administration. All controlled release systems have limited applications if the systems cannot remain in the vicinity of the absorption site. The controlled release drug delivery system possessing the ability of being retained in the stomach is called gastroretentive drug delivery system. They can help in optimizing the oral controlled delivery of drugs having “absorption window” continually releasing the drug prior to absorption window for prolonged period of time, thus ensuring optimal bioavailability

controlled release drug delivery systems (CDDS) owning the capacity to be engaged in the stomach remain entitled as Gastro Retentive Drug Delivery Systems (GRDDSs), then both retain aid in enhancing the oral precise release of medications through unremittingly discharging drug afore absorption window designed for an extended period. Further being capable to persistently and sustainably release medication towards the small intestinal absorption window, the enhancements delivered since GRDDSs embrace: attaining a further substantial then extended therapeutic outcome and consequently falling the incidence of management epochs, only if further effective management of resident stomach ailments, and curtailing equally lower-tract deactivation of the medication and impacts on the lower intestinal flora. Subsequently that, innumerable methodologies of this sort as floating, bioadhesive, swelling and escalating systems obligate remain advanced towards surge the gastric retaining period of dosage form

Physicochemical properties of GRDDS

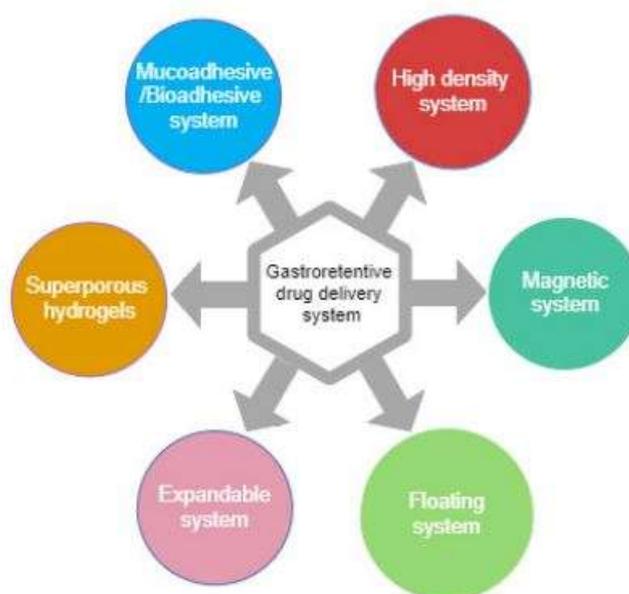
Physicochemical properties of GRDDS include density, size, and shape of the dosage form,

which play major roles in the formulation of GRDDS. The dosage forms having a density lower than the gastric contents can float to the surface, while high-density systems sink to the bottom of the stomach. For an ideal formulation, the density should be in the range of 1.0-2.5 g/cm³. Dosage forms having a diameter of more than 7.5 mm show better gastric residence time (GRT). Circular, spherical or tetrahedron-shaped devices show excellent gastroretentive properties.

Physiological factors affecting retention of GRDDS in the stomach

The most important factors controlling the gastric retention time of dosage forms include

fed or unfed state, nature of the meal, caloric content, and frequency of feeding. In the case of a fasting environment, gastric retention time is less due to the increase in GI motility. Emptying of gastric content occurs due to peristalsis. If peristalsis coincides with dosage form administration, the gastric residence is short. However, after meals, peristalsis is delayed and may help increase the gastric residence of the formulation. A high-calorie meal containing proteins, fats, and fibrous compounds increases gastric retention time. In the case of multiple meals, the gastric retention is more than a single meal due to persistent inhibition of peristalsis.



Approaches of gastroretentive drug delivery system

AIM :

Propranolol has short half-life, high first-pass metabolism, presence of food increases the bioavailability, P-gp plays important role in the absorption, and the drug is acid-soluble basic drug which make it suitable for GRDDS.

Till today, no floating drug delivery system has yet developed for propranolol. So, it was decided to formulate propranolol floating tablets.

This approach develops a drug delivery system, which gets retained within gastric fluid, thereby releasing its active principles in the stomach.

Some methods used to achieve gastric retention of drugs include the use of effervescence

agents, mucoadhesive polymers, magnetic material, buoyancy enhancing.

OBJECTIVE :

Gastroretentive dosage forms release the drug in a controlled manner to their specific site of action.

They are formulated by intimate mixing of drug with a gel-forming hydrocolloid, which swells in contact with gastric fluid and maintains bulk density of less than unity.

These systems help increase the bioavailability of drugs that get metabolized in the upper part of the gastrointestinal tract, such as riboflavin and levodopa, etc.

PLAN OF WORK :

FORMULATION AND EVALUATION OF AN EFFERVESCENT, GASTRORETENTIVE DRUG-DELIVERY SYSTEM

Materials.

Methods.

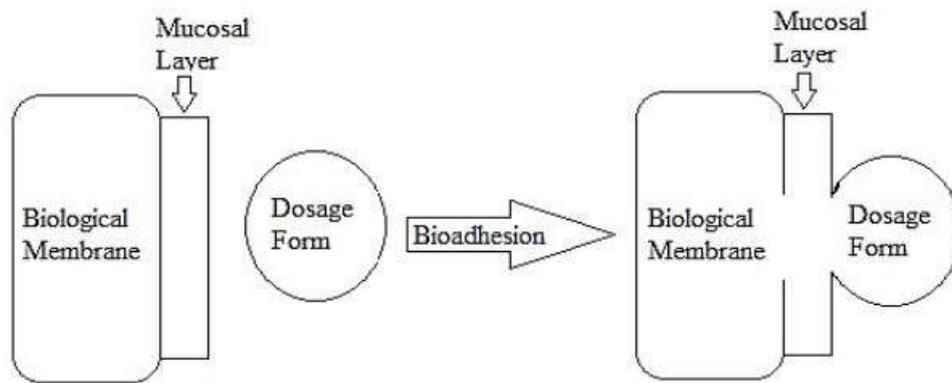
Formulation optimization. ...

Formulation trials. ...

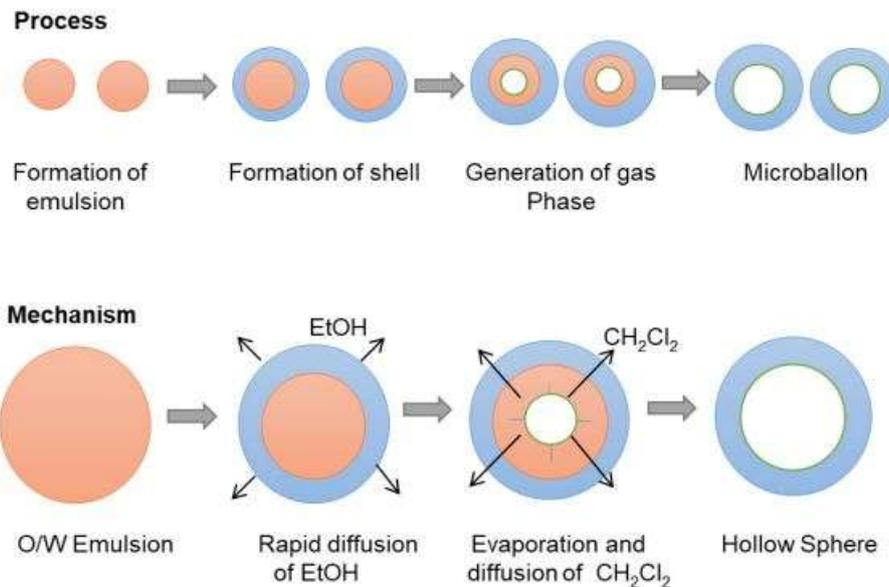
Optimization of tablet batches on the basis of floating behavior. ...

Physical evaluation of the optimized tablet formulation. ...

Determination of density. ...



Approaches of gastroretentive drug delivery system



Preparation technique and mechanism of microballoons formation

DRUG PROFILE :

DRUG NAME : Propranolol Hydrochloride

Molecular formula:- C₁₆H₂₂ClNO₂

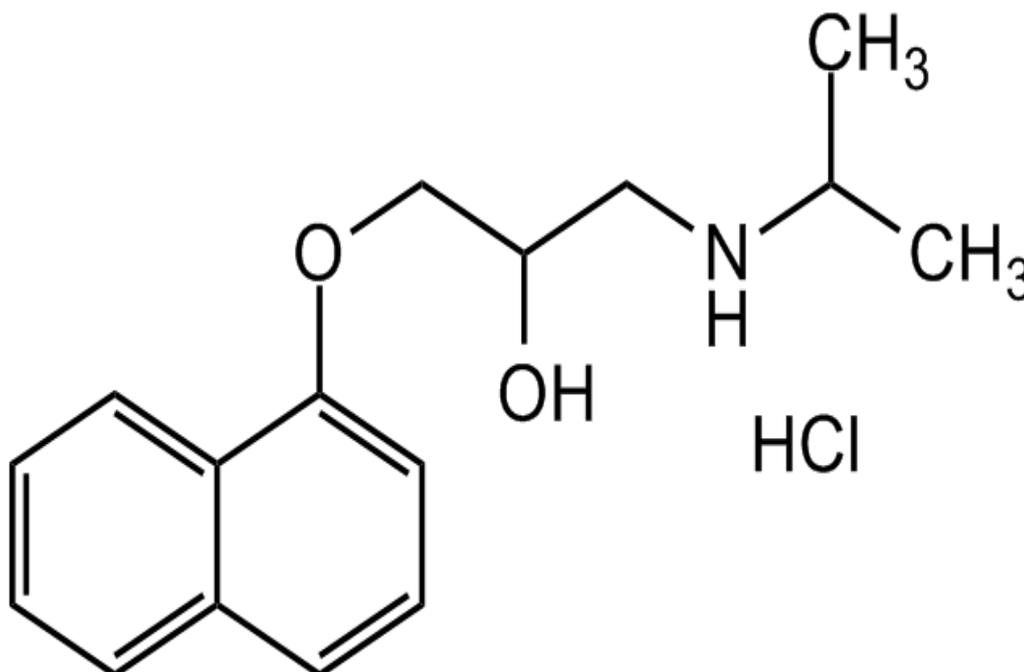
Molecular weight :-295.80

IUPAC:-(RS)-1-(1-methylethylamino)-3-(1-naphthyloxy)propan-2-ol

Solubility :Both propranolol free base and propranolol hydrochloride are water soluble. Propranolol hydrochloride is considered to be readily biodegradable and there is evidence to support its rapid degradation in both surface waters and water-sediments systems.

(±)-Propranolol (hydrochloride) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of (±)-

propranolol (hydrochloride) in these solvents is approximately 11, 16, and 14 mg/ml, respectively.



II. MATERIALS AND METHODS

Propranolol hydrochloride was obtained as gift sample from Concept Pharmaceuticals, Aurangabad. HPMC (Methocel K4 M and E 15 LV, Colorcon Asia Ltd., Goa, India), HPC (Klucel HF, Aqualon, Signet Chemical Corporation), xanthan gum, and sodium alginate were obtained from Nulife Pharmaceuticals, Pimpri, Pune, India. All other chemicals used were of reagent grade.

EVALUATION OF TABLET

NON OFFICIAL TEST

1. General appearance
2. organoleptic
3. size & shape
4. Hardness
5. Friability

OFFICIAL TEST

1. Neight variation
 2. content uniformity (API)
 3. Dissolution
 4. Disintegration.
- . General Appearance
- A. size and shape

compressed tablets shapes and dimensionare determined by the during the compression, process. crown thickness of tablet measured by micrometer. Total crown thickness is measured by veinio calliper.

Tablet thickness should be controlled with +5% OF std.value

B.colour

Non-uniformity of colour over the tablet (mottling) colour qualification is determined by

Reflectance spectrophotometry

• Tristimulus colorimetry

Micro-reflectance photometry.

C. Tablet Hardness -Devices used

It's the Force required to break the tablet in diametric compressiontest Hardness of tablet af Fects - Dissolution behavior.

Hardness also called as crushing strength.

Device use standard Hardness - should be minimum 4 kg fuperator

Monsento Tester

Gives strength in kgs

strong-cobb Tester

Folle applied by hydraulic pressure and later air pressure.

Pfizer Tester

Forle applied by hydraulic pressure f Later air pressure.t

Ernleka tester

Gives strength in kgs.

scheluniger but Tester

Gives strength in kgs & strong cobb

D. Friability

- Uncoated compressed tablet

useful For determination of drug loss during transportation. and is determined by Roche Friabilator, shock and abrasion: evaluation (0)

Take 20 tablet.

Tablet Falls From - 6 inch distance smrib ni

✓ speed 25 rpm dor

Time 24 min

Total revolution - 100 minim ad

. Acceptance - Not more than 19. CIA

TAB Initial weight: 1 = 25 rpm

6 TAB Final Weight Gmin=100rpm.

Friability = F.IN -FIN -X 100 - 0,5-11

Bluor

1. Weight variation

Twenty tablets were selected at randomly and weighed individually for the determination of weight variation of tablets. The mean and standard deviation were determined (Indian Pharmacopoeia, 2007).

2 . Hardness test

Five tablets were selected at random and the hardness of each tablet was measured on Monsanto hardness tester.

3. Friability test

The friability test was carried out in Roche Friabilator. Twenty tablets were weighed (X₀) initially and put in a rotating drum. They were subjected to 100 falls of 6 inches height (25 rpm for four minutes). After complete rotations the tablets were dedusted by using camel hairbrush and weighed (X). The percent loss in weight or friability (f) was calculated by the formula given in the following equation: (Carr, 1965)

FORMULATION OF FLOATING TABLETS OF PROPRANOLOL HYDROCHLORIDE

Dissolution of all the formulations in Table I (preliminary formulations) was carried out.

It was observed that drug release is controlled by the polymer type and its concentration. Many of the polymers used were found to be unsuitable for formulating floating tablets because of their lack of abilities to form matrix and control the release of drug or poor buoyancy shown by the formulations containing those particular polymers

Formulation of Propranolol Hydrochloride Floating Tablets (Preliminary Trials) In preliminary studies, effect of various polymers on the release of drug was studied by formulating tablets with polymers in concentrations of 30%, 40%, and 50%. Total weight of tablet was 200 mg (Table I). The tablets were directly compressed in 16 station rotary tablet press with oval flat-faced die punches of 8.5 mm diameter.

IN VITRO ASSESSMENT

For GRDDS, in vitro assessment is very essential to predict gastric transit behavior. Following are the parameters, which should be considered for designing novel gastroretentive formulations.

i. Buoyancy lag time

It is the time taken for gastroretentive formulations to move onto the surface of the dissolution medium. It is determined using a USP dissolution apparatus containing 900 mL of 0.1 N HCl solution as a testing medium maintained at 37°C. The time required to float different dosage forms noted as floating lag time.⁵⁰

ii. Floating time

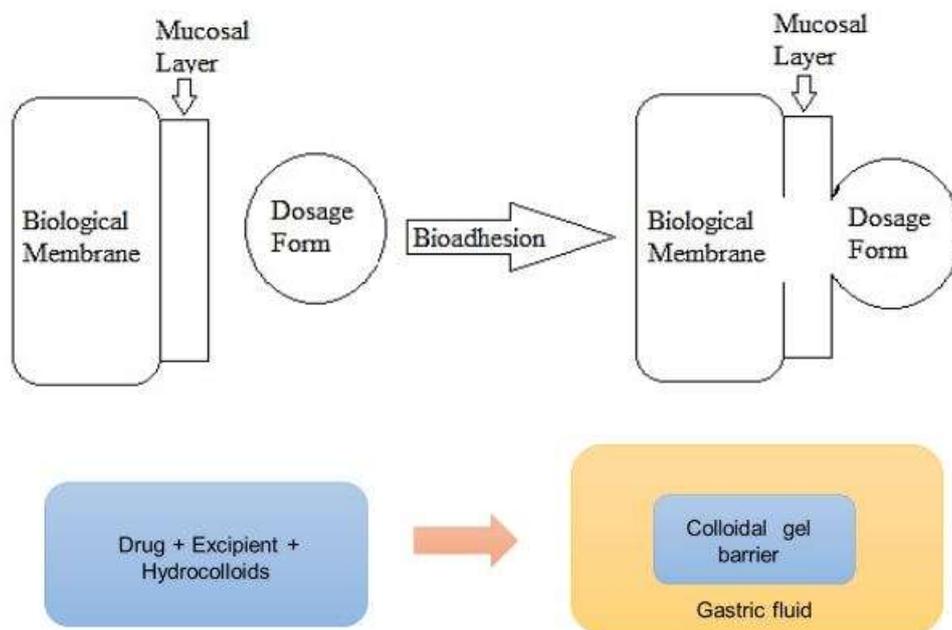
This determines the buoyancy of dosage form. In this test, a specific dissolution apparatus is used depending upon the type of dosage form with 900 mL of dissolution medium kept at 37°C. The floating time or floating duration of the dosage form is determined by visual observation.^{51,52}

iii. Specific gravity/density

Specific gravity estimates are essential for both low-density and high-density GRDDS. Specific gravity is determined using the displacement method.⁵³

iv. Swelling index

Swelling index is determined by immersing the tablets in 0.1 N HCl at 37°C and their periodic removal



III. RESULT AND CONCLUSION

GRDDS are unique systems and have become important in the last three decades. It offers various advantages, viz., sitespecific, slow, and controlled release of drugs from different types of gastroretentive dosage forms, thus improving patient compliance and reducing the side effects by minimizing dosing frequency. Therefore, it is expected that in the future, various pharmaceutical companies will come forward to initialize gastroretentive drug delivery technology to create excellent advantages, prolonging patents, and a better outcome for their marketed formulations. Ethics

Peer-review: Externally peer-reviewed. Authorship Contributions Concept: K.V., S.M., P.D., Design: K.V., S.M., J.S., P.D., Data Collection or Processing: K.V., S.M., P.D., Analysis or Interpretation: K.V., S.M., Literature Search: K.V., S.M., Writing: K.V., S.M., M.A.K., D.K.M.

Conflict of Interest: No conflict of interest was declared by the authors.

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Propranolol hydrochloride floating tablets were prepared by blending drug, HPMC, HPC, gas generating agent, and diluents followed by direct compression. The matrix tablets swelled while in

contact with the aqueous medium. Tablets formulated with HPC, sodium alginate, and HPMC E 15 LV failed to produce matrix of required strength. The formulations containing xanthan gum showed good drug retaining abilities but floating abilities were found to be poor. It was concluded formulation V containing HPMC K4 M gave the best in vitro release of 92% in 18 h. In vivo evaluation by X-ray technique showed that tablet was retained in the stomach for 4 h.

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