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(REVIEW ARTICLE)

Development and evaluation of biodegradable floating drug delivery for solubility enhancement of diclofenac sodium

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Abstract

Floating drug transport structures can lengthen gastric retention with the aid of using growing dose paper work with a decrease density than gut fluid. This lets in the machine to drift for an extended quantity of time over the contents of the belly with-out worrying the gastric emptying rate. The reason of this examine become to broaden a floating pill and take a look at it in vitro with diclofenac sodium because the version drug. The capsules have been synthetic making use of a dry granulation method primarily based totally on bubbling skill, wherein sodium bicarbonate become used for example a fueloline generator. In 1968, Davis provided FDDS for the primary time. These structures are recognized to have decrease densities than gastric fluid, letting them drift withinside the belly for an extended time. They're extensively mentioned as a vital aspect of forming most reliable belly retention and medicine bioavailability. Furthermore, they're appropriate transport structures for medicinal drugs with a slender absorption window withinside the higher small gut. Non-bubbling structures and bubbling structures were used to assemble FDDS due to the power mechanisms.

Keywords: Diclofenac sodium; Floating tablets; Gastric Residence Time (GRT); Gastro retentive

1. Introduction

Flotation is one of the most practical and hopeful ways to achieve drug retention in the gastrointestinal tract. A low mass floating drug delivery system (FDDS), otherwise a dynamically regulated system, is sufficient to float on the gastric contents and maintain flexibility in the stomach for extended periods of time without altering gastric emptying rates. A flexible, low density system. As a result, [1] the residence time in the stomach is increased, and the volatility of the plasma concentration of the drug is measured more appropriately. Increased gastric retention time improves the bioavailability of treatment by improving the solubility of poorly soluble drugs in high pH environments. The gastric retention system is an attractive candidate for drugs with a small absorption window, low water solubility, alkaline pH variability, and good absorption into the gut [2]. In humans and other animals, the gastrointestinal tract is an organ system that takes in, digests, absorbs nutrients, and excretes in the form of faces. Use of conventional non-steroidal anti-inflammatory drugs (NSAIDs) Decreased following the development of selective cyclooxygenase-2 therapy [3]. Nevertheless, the latter is still widespread. Due to its analgesic and anti-inflammatory properties, diclofenac is one of the most commonly optional NSAIDs. It may also be available as a commercial product. Like other NSAIDs, the use of diclofenac is connected with rare but serious and sometimes toxic gastrointestinal (GI) side effects, such as ulcers and bleeding, especially in the elderly [22,23].

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2. Basic GIT physiology

Figure 1 Gastrointestinal Tract

2.1. Upper GIT

2.1.1. Mouth

The tooth, tongue, and buccal mucous tissues, which comprise the salivary gland pointers and cowl to the gentle palate, mouth floor, and tongue bottom, are all included. To chunk nutrition, the tongue, cheeks, and tooth all paintings together, as do the decrease and higher lips.

2.1.2. Pharynx

The pharynx, that's enclosed withinside the neck and throat, is part of each the digestive and respiration systems. It prevents vitamins from getting into the lungs and trachea.

2.1.3. Stomach

This is wherein the famous of the digestion happens. The belly is a J-fashioned bag-like organ that briefly shops meals earlier than breaking it down, combining it with enzymes and different digestive fluids, and switch it to the small intestine [4].

2.2. Lower GIT

2.2.1. Small intestine

The famous of nutrient absorption takes place with inside the small gut, that's a 6 meter lengthy coiled skinny tube. Food is blended with enzymes from the liver and pancreas with inside the small gut. The surfaces of the small gut accumulate vitamins from food and bring them to the relaxation of the frame thru the blood circulation [5].

2.2.2. Large intestine

The massive intestine, frequently called the colon, is a thick tubular shape that wraps across the small intestine. Its number one characteristic is to digest waste objects and repair any closing vitamins and water returned into the body. The rest of the waste is then dispatched to the rectum, wherein it's far ejected as stool [24].

3. Floating drug delivery system

Since abdominal FDDS has a lower substance mass than gastric juice, it floats in the stomach for a long time without impairing gastric emptying. While the stomach is floating, the drug can be easily removed from the device at low cost. When dosing is started, the rest of the abdominal device will be empty. As a result, GRT is increased and changes in plasma drug perception are better managed. The bureaucracy of the floating sustained-emission dose maintains a low apparent density at the same time as the polymer hydrate, and the bureaucracy can maintain a gelled barrier on the outer surface, resulting in a hydrodynamically balanced system (HBS) is recognized. The drug is a mile with the largest hydrophilic matrix, so it is phased out of the source matrix. These papers have a lower bulk density than the stomach contents, so they need to proceed for 3-4 hours in the flow of the stomach contents without interfering with the self-load of emptying [6]. The most recommended hydrophilic colloid for buoyant forms of the formulation is cellulose ether polymers, especially hydroxy propyl methyl cellulose. Adipose tissue with a bulk density much less than 1 can be introduced into the system to reduce water consumption and improve buoyancy [25].

3.1. Classification of FDDS

3.1.1. Non effervescent system

Such structures are usually composed of polycarbonate, polystyrene, polymethacrylate, or polyacrylate, as well as surprisingly swellable hydrophilic colloids in the matrix-forming polymer. Usually, polysaccharides or cellulose compounds are used for the swelling moiety. Upon contact with gastric juice, the hydrophilic colloid hydrates, forming a low-density gel community that can trap air and float above body fluids in the abdomen. Drug launches are carried out using the beneficial and useful resources of using these colloidal gels. Hydrophilic drugs are mainly introduced with useful and useful resources that use diffusion mechanisms, and hydrophobic drugs are introduced with useful and useful resources that use the wear of the outer bottom of the system.

3.1.2. Effervescent system

This is a matrix-primarily based totally system. Swellable polymers like methylcellulose and Chitosan, in addition to severa bubbling chemicals, are used to make this drink. Sodium bicarbonate, tartaric acid, and citric acid are examples. These are designed such that once they arrive into touch with gastric material, co2 is launched and imprisoned in a swelling hydrocolloid, which offers the dosage shape buoyancy. The distribution approach became created the usage of a swellable uneven triple layer pill design [2].

Advantages of FDDS

- Improved drug absorption.
- Controlled shipping of medicine.
- Delivery of medicine for neighborhood motion withinside the stomach.
- Minimizing the mucosal irritation.
- Treatment of gastrointestinal disorders.
- Simple and traditional device for manufacture.
- Site-particular drug shipping.
- Ease of management and higher affected person compliance.

Disadvantages of FDDS

- They are not suitable for drug applicants that have gastric stability or solubility issues.
- FDDS requires a high enough level of fluid in the stomach for the system to float, so you need an enough amount of water (200-250 mL) to ingest with the floating drug delivery system.
- Drugs that irritate the gastric mucosa are not applicants for floating drug delivery system.
- Drugs that are absorbed throughout the gastrointestinal tract and undergo passes of metabolism may be adverse. Nifedipine.

3.2. Names of drugs for various FDDS forms

3.2.1. Tablets

Oedema et al., 2000 created a controlled-release bilayer floating tablet for furosemide. Using the compounding approach, the poor drug solubility can be increased by combining the solid dispersion in a 1:1 ratio with -cyclodextrin (Singh and Brahma, 2000). Drug and the polymers Hydroxypropyl methylcellulose K4M, **Hydroxypropyl**

methylcellulose K100M, and CMC (used for regulated drug release) were both present in one layer. A sodium bicarbonate and citric acid combination that bubbled up from the second layer. According to an in vitro flotation research, the commencement of flotation occurs more quickly the lower the compression force is. The time required for the tablets to float increased from 20 minutes when squeezed at a force of 15 MPa to 45 minutes when the strain was 32 MPa. X-ray analysis of a blood analysis research conducted on 6 healthy male volunteers revealed that the floating pills stayed in the stomach for 6 hours, and that their bioavailability was lower than that of traditional tablets. It was determined that it was 1.8 times more effective than the pill. When urine volume was assessed, the floating dose form had a lower and extended peak diuretic impact compared to the traditional tablet [29].

3.2.2. Capsules

Sodium alginate and sodium bicarbonate are combined to create floating capsules. Because of the creation of CO2 trapped in the hydrated gel network when exposed to an acidic environment, the system was demonstrated during in vitro tests to float [29].

3.2.3. Pills

The device comprises of a double layer around a slow-release tablet known as a seed. A blowing agent makes up the inner layer, while a swellable membrane layer makes up the outside layer. The system sinks right away when submerged in dissolving fluid at body temperature and produces a balloon-shaped pill that floats because of its low density. The system's CO2 generation and capture are to blame for this density decline [30].

3.3. Polymers used in FDDS

3.3.1. Diclofenac sodium

Active pharmaceutical ingredient the elements in medications known as active ingredients are those that cause the positive health effects that patients report.

3.3.2. Hydroxypropyl methylcellulose (HPMC)

HPMC is used as a basic material to create coatings with a range of characteristics, including elasticity, transparency, resistance to oil and fat, and moderate strength, moisture, and oxygen barrier capabilities.

3.3.3. Microcrystalline cellulose (MCC)

Microcrystalline cellulose (MCC) is a time period for delicate timber pulp and is used as a texturizer, an anti-caking agent, a fats substitute, an emulsifier, an extender, and a bulking agent in meals production. The maximum not unusualplace shape is utilized in diet dietary supplements or tablets

3.3.4. Citric acid

Citric acid is used as an excipient in pharmaceutical arrangements because of its antioxidant properties. It continues balance of energetic elements and is used as a preservative. It is likewise used as acidulate to manipulate pH and acts as an anticoagulant via way of means of chelating calcium in blood.

3.3.5. Sodium bicarbonate

Sodium bicarbonate at the extent of 20 mg in step with pill confirmed a floating lag time of eighty three to 106 seconds. This cost is near the bring about the examine with the aid of using kata et al. [11] Hence, sodium bicarbonate (20 mg in step with pill) was critical to acquire most appropriate in vitro buoyancy.

3.3.6. Mg. Stearate

It has been widely used for many decades in the food industry as an emulsifier, binder and thickener, as well as an anticaking, lubricant, release, and antifoaming agent.

3.3.7. Talc

In the pharmaceutical industry, talc is primarily used as a lubricant to improve powder flow during tablet compression. Of course, talc is also used in the personal care industry as an adsorbent in talcum he powders and in the cosmetic industry in other types of powders and blushes.

3.3.8. Polyvinylpyrrolidone (PVP)

In pharma, PVP is commonly used as a tablet binder, disintegrate, pore former and solubilizer.

3.4. Factor affecting FDDS

3.4.1. Density

GRT is a density-dependent dose shape buoyancy characteristic. Size: Dosage form devices with a diameter more than 7.5 mm are advised to increase GRT in comparison to those with a 9.9 mm diameter.

3.4.2. Shape

In comparison to previous designs, tetrahedron and ring-shaped devices are said to have a greater GRT and 90%–100% retention at 24 hours. These devices' flexural moduli are 48 and 22.5 kilograms per square inch (KSI). Formulas that incorporate one or more units: When compared to single unit dosage forms, multiple unit formulations show more predictable launch profiles and no overall performance degradation due to unit failures. Additionally, they provide a greater margin of safety in the event that a dosage form fails and permit the co-management of devices with specific launch profiles or those composed of incompatible materials.

3.4.3. Size

Dosage form units with a diameter more than 7.5 mm are reported to increase GRT compared with those with a diameter of 9.9mm [26,27].

3.4.4. Content of the meal

Inability to digest polymers or salts of fatty acids can cause the stomach's motility pattern to shift to a fed state, slowing down gastric emptying and extending the time that drugs are released from the stomach [28].

3.4.5. Gender

No matter the weight, peak, or body floor area, the mean ambulatory GRT in men (3.4 0.6 h) is significantly lower than that in women (4.6 1.2 h).

3.4.6. Age

Old people, particularly the ones over 70, have an extensively longer GRT.

3.4.7. Posture

GRT may be used to both supine and upright ambulatory patient situations. Concomitant medication administration: The FDDS is affected by anticholinergics, such as atropine and propantheline, opiates, such as codeine, and pro-kinetic marketers, such as metoclopramide and cisapride.

3.4.8. Single or multiple unit formulation

When compared to single unit dosage forms, multiple unit formulations provide a more predictable release profile, allows the co-administration of units with various release profiles or containing incompatible substances, and allow for a greater margin of safety against dosage form failure.

3.4.9. Concurrent drug administration

Pro-kinetic drugs like metoclopramide and cisapride, opiates like codeine, anticholinergics like atropine and propantheline, and anticholinergics like atropine can all have an impact on floating time [31].

4. New approaches on floating drug delivery system [FDDS]

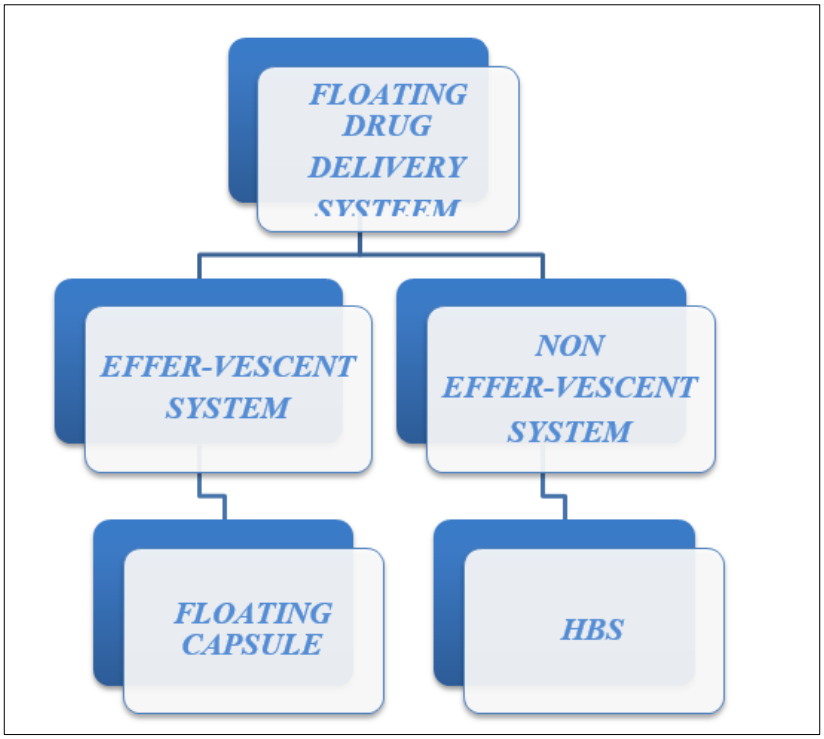


Figure 2 Types of Floating drug delivery system

4.1. Hydrodynamically balanced system [HBS]

HBS containing gel-forming hydrophilic polymers is a unit dosage form. Hydroxypropyl methylcellulose (HPMC) is no longer a rare excipient, but sodium carboxymethyl cellulose (NaCMC), carrageenan, hydroxyl ethyl cellulose (HEC), hydroxypropylcellulose (HPC), and alginic acid are also used. In particular, administration of the drug-blended polymer is carried out in gelatin capsules that dissolve rapidly in gastric juice. Floating lumps are made of useful resources that utilize the hydration and swelling of polymer soil. Delayed release HBS pills (including hydrophilic-hydrophilic colloids) were first superior due to Sheth and Tossounian techniques. After contact with gastric juice, a light mass of gelatin forms on the bottom of the tablet, forming an impermeable barrier. The active ingredient slowly released from the ground gelatin mass maintained buoyancy in gastric juice. Liquid paraffin, lactose, HPMC K4M, and polyvinylpyrrolidone K30 (PVP K30) were used to compose ofloxacin HBS tablets. The tablets circulated without delay for more than 6 hours. A sustained drug launch is expected during this period, the price of which depends on the PVP K30, HPMC K4M, and liquid paraffin content.

4.2. Floating system based on polypropylene foam power

Use polypropylene foam powder to organize buoyant particles and study their major normal overall performance in vitro. An oil-in-water solvent extraction approach was used to assemble buoyant particles of polypropylene foam powder. Verapamil hydrochloride has been used as a drug in combination with sustained release polymers. All formulations showed adequate buoyancy behavior with a wide range of dissolution profiles. Researchers are also looking at airborne drugs that are entirely based primarily on polypropylene foam powder in matrix-forming polymers. The surprisingly porous foam powder resulted in an essentially low density structure that could float on 0.1N HCl at 37°C for at least 8 hours. The starting site is strongly associated with drug chemistry and can be modified to match the ratio of polymer matrix to foam powder.

4.3. Formulation chamber packed with air or innocent gas

The microporous compartment structure is built on the principle of drug encapsulation into a compartment with pores in the partitions (top and bottom) connected to the chamber containing air. The peripheral partitions within the tool were completely sealed to eliminate the interaction of undissolved drug with gastric mucus. A low density microporous chamber allows transport devices with floats to bypass gastric juice. When a limited amount of gastric fluid enters the pores, the drug dissolves and exits the dosage form and is always introduced into the intestine at some point.

4.4. Floating capsule

Effervescent including Li et al. Floating capsules consisting of effervescent mixture, carbopol 934, and HPMCs of different viscosities were prepared. They found that the presence of carbopol, HPMC viscosity, and polymer-polymer interactions had a significant effect on the buoyancy and release properties of the dosage form.

5. NSAIDS

(Nonsteroidal anti Inflammatory medicines) are one of the maximum broadly prescribed drugs. Some are over the counter and are in all likelihood to be misused. With the advent of selective and centered COX-2 inhibitors and misoprostol, extreme gastrointestinal facet outcomes had been reduced. However, the more recent NSAIDs are nonetheless nephrotoxic withinside the identical manner that older NSAIDs are [16].NSAIDS-associated nephrotoxicity has been studied withinside the past. 2-eight acute tubular necrosis, acute tubulointerstitial nephritis, glomerulonephritis, renal papillary necrosis, continual renal failure, salt and water retention, and high blood pressure are all examples of nephrotoxicity. NSAIDs had been connected to subclinical renal impairment. The challenge of NSAID-precipitated continual renal failure remains up for debate.[17,18,19,20] Due to its quick organic half-life, this remedy calls for common dosage, that can reason fluctuations in plasma drug concentrations and failure to launch the drug withinside the required amount, ensuing in bad affected person compliance and useless therapy [14,15].

- Diclofenac
- Griseofulvin
- p-nitro aniline
- 0Ibuprofen
- Ketoprofen
- Piroxicam
- Verapamil
- Cinnarizine

Are examples of suitable applicants that may be created the usage of shipping methods? For neighborhood and systemic activities, oral management has validated to be the maximum suitable, versatile, and extensively used technique of drug shipping [7].

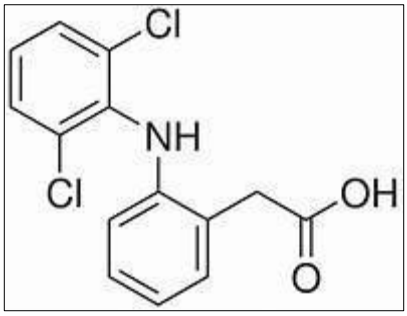
5.1. Diclofenac sodium

Diclofenac sodium is an over-the-counter (OTC) non-steroidal anti-inflammatory drug (NSAID) that relieves mild to mild pain caused by arthritis in the short term. As a topical gel, diclofenac sodium functions like an oral NSAID (including ibuprofen). Or naproxen sodium) does this by suppressing the era of pain signaling molecules known as prostaglandins. It penetrates the skin and leaves it on for up to 7 days to relieve the pain of arthritis on the skin.

5.1.1. About diclofenac sodium

Diclofenac is a non-steroidal anti-inflammatory medicine this is derived from phenylacetic acid (NSAID). NSAIDs, frequently called nonsteroidal anti-inflammatory drugs (NSAIDs), block the enzymes COX-1 and COX-2, which can be accountable for the manufacturing of prostaglandins (PGs). Inflammation and ache signalling are each aided via way of means of PGs. Diclofenac, like different NSAIDs, is often used as a first-line remedy for acute and continual ache and infection due to quite a number conditions. The rational drug layout of diclofenac turned into primarily based totally at the systems of phenylbutazone, mefenamic acid, and indomethacin. Two chlorine businesses on the ortho role of the phenyl ring lock the hoop in most torsion, which seems to be connected to better potency. To keep away from NSAID-brought about belly ulcers, it is often used with misoprostol. Diclofenac turned into authorized via way of means of the FDA for the primary time in July 1988 [21].

5.1.2. Structure of diclofenac sodium



Chemical formula: >C14H11Cl2NO2

Molecular Wt.: >296.1

5.1.3. Mode of action

The analgesic, anti-inflammatory, and antipyretic effects are controlled by diclofenac. Diclofenac, like many NSAIDs, inhibits cyclooxygenase (COX-1 and COX-2), however the exact mechanism of action is not usually known in practice. In vitro, diclofenac has been shown to be a potent inhibitor of prostaglandin production. In vitro, diclofenac has been shown to be a potent inhibitor of prostaglandin production. The diclofenac dosage achieved sooner or later after cure determined the in vivo impact. In animal models, prostaglandins boost bradykinin's impact on pain generation and sensitise afferent neurons. Prostaglandins are mediators of inflammation. Because diclofenac suppresses the formation of prostaglandins, its movement may be caused by low prostaglandin levels in peripheral tissues.

5.1.4. Side effect

Diclofenac may also have positive unsightly aspect results similarly to its useful advantages. Although now no longer all of those aspect results are probably to occur, in the event that they do, clinical remedy can be required.

- Acid or bitter stomach
- Belching
- Bleeding gums
- Blood with inside the urine or stools
- Bloody or black, tarry stools
- Chest pain

6. What is the maximum amount of diclofenac sodium you can take?

It is important to examine and obey the Drug Facts label in any respect instances. Topical diclofenac sodium is an over the counter medicinal drug that need to be taken 4 instances a day, each day. The FDA has authorized OTC topical diclofenac sodium to be used for as much as 21 days except in any other case informed with the aid of using a physician. It's vital now no longer to use topical OTC diclofenac sodium to greater than frame places at once [7].

7. What is diclofenac sodium safety information?

When used in keeping with the Drug Facts label, diclofenac sodium has been accredited with the aid of using the FDA as secure and effective. Unless your medical doctor or some other healthcare professional advises you to, you must by no means take extra diclofenac sodium or for an extended time period than the label suggests. If you operate extra or for longer than recommended, a few fitness risks, which includes as coronary heart attack, stroke, liver damage, or gastrointestinal bleeding may also growth. Sustained launch drug shipping structures are the maximum normally prescribed dosage bureaucracy nowadays due to the fact they have got many benefits over conventional dosage bureaucracy, which includes higher affected person compliance because of much less common drug management, reduced fluctuation in steady-country drug levels, maximal drug use, and a discount in healthcare expenses because of higher remedy and shorter remedy periods[6,8].For sustained launch structures, the oral path of management has attracted loads of interest and progress, due to the fact gastrointestinal body structure lets in for extra flexibility in shipping device layout than different routes[9].Several elements have an effect on the drug bioavailability of medicinal dose bureaucracy. Gastric residency time is one in every of them (GRT) [12]. The gastric mptying procedure, which

connects the belly and the small intestine, can take everywhere from a couple of minutes to twelve hours. Because of this heterogeneity, the bioavailability of an orally taken dose shape is variable[12].Furthermore, Because of the quick gastric emptying period, the medication from the dose shape might not be launched completely. The Floating Medication Delivery System (FDDS) is a gastroretentive dosage shape that may assist to increase GRT and growth drug bioavailability [14].

8. Conclusion

The process of a medicine being absorbed in the gastrointestinal system is extremely varied, and the lengthening of stomach retention of the dosage form increases the amount of time the drug will be absorbed. In order to increase the bioavailability and manage the distribution of numerous medications, gastro-retentive floating drug delivery devices have become more popular. In order to maximize the delivery of molecules that display an absorption window, limited bioavailability, and substantial first pass metabolism, an increase in the number of gastroretentive drug delivery will be developed. Gastric retention may be addressed with FDDS. Many businesses are working to commercialize this approach, despite the fact that there are still a number of issues that need to be resolved in order to accomplish sustained gastric retention.

Compliance with ethical standards

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All the author suggests there is no conflict of interest.

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