



Floating Drug Delivery System for Analgesic - A Review

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ABSTRACT

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. An analgesic or painkiller is any member of the group of drugs used to achieve analgesia, relief from pain. Analgesic drugs act in various ways on the peripheral and central nervous systems. They are distinct from anaesthetics, which reversibly eliminate sensation. Drugs like ibuprofen, ketoprofen, aspirin, piroxicam etc., are also delivered through this method. The source of the analgesic drug delivered through this system has a good prolong effect and bioavailability and are reviewed in this article.

Keywords: Floating drug delivery system, analgesics, ketorolac, and oral route.

INTRODUCTION

The oral route of drug administration is most commonly used for the therapeutic drugs because of its cost efficiency and easy administration leads to good patients compliance.¹ Floating drug delivery system is also called hydrodynamically controlled system. It has low density which gives the drug highest buoyancy to float in gastric content in the stomach and remain buoyant in the stomach without affecting the gastric emptying rate for prolonged period of time. It floats over the gastric contents, the drug is released slowly at the desired rate, prolonging the gastric retention time in the stomach and reducing the variations of drug concentration in plasma.² Usually these types of drugs have very less adverse side effects and have good bioavailability with Long action.¹ Drugs that are formulated with this system are Aspirin, Griseofulvin, p-nitroaniline, Ibuprofen, Ketoprofen, Piroxicam, Verapamil, Cholestyramine, Theophylline, Nifedipine, Nicardipine, Dipyridamol, Tranilast, Diclofenac sodium, Indomethacin, Prednisolone, Cinnarizine and Albendazole. In this article floating drug delivery system for analgesics are examined reviewed with their advantages and disadvantages.

Floating Drug Delivery System

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

Different types of floating drugs are effervescent and non-effervescent floating drugs. Effervescent systems include use of gas generating agents, carbonates like Sodium bicarbonate and organic acid like citric acid and tartaric acid present in the formulation to produce carbon dioxide gas, thus reducing the density of system and

making it float on the gastric fluid. These effervescent systems further classified into two types are Gas generating systems, Volatile liquid/vacuum systems.¹

The non-effervescent System based on mechanism of swelling of polymer or bioadhesion to mucosal layer in gastrointestinal tract. The most commonly used are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bio-adhesive polymer such as chitosan and carbopol. Types of non-effervescent drug system: Single layer floating tablets, Bilayer floating tablets, Alginate beads and Hollow microspheres.¹

Advantages

- Improved drug delivery
- Control in the amount of drug to be delivered
- Have a local action on stomach
- Minimize mucosal irritation
- Easy administration
- Convenient equipment for manufacturing
- Target/site specific drug delivery.³

Disadvantages

- Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be assured
- Drugs that cause irritation and lesion to gastric mucosa are not good to be formulated as floating drug delivery
- High variability in gastric emptying time due to its all or non-emptying process
- Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size.³



Factors affecting floating drug delivery system

- Density
- Age
- Posture
- Gender
- Shape of dosage form
- Nature of the meal
- Fed or unfed state
- Calori content
- Size of the tablet.³

A Floating Drug Delivery System for An Analgesic-

An analgesic or painkiller is any member of the group of drugs used to achieve analgesia, relief from pain. Analgesic drugs act in various ways on the peripheral and central nervous systems.⁴ Types of analgesics used are classified into opioid, non-opioid and miscellaneous drugs. Analgesics are one of the commonly and extensively used drugs for pain. Analgesics that are given in the form of floating drug delivery system are ketorolac, aspirin, diclofenac sodium, ibuprofen, tapendadol and aspirin calcium carbonate.

Aspirin

Aspirin, acetylsalicylic acid, is non-steroidal anti-inflammatory drug often used to treat pain, fever, and inflammation. Aspirin is also used long-term, at low doses, to help prevent heart attacks, strokes, and blood clot formation in people at high risk of developing blood clots. bioavailability of the drug is 80-100% and the protein binding capacity is 90-100%. The half-life is 2-3 hours in low dose and 13-30 hours in high dose. In oral route it does not reflect the inhibition of platelet.⁵ The floating aspirin tablet is prepared by Aspirin, Methocel, Ethocel, Aerosil, Dicalcium phosphate anhydrous according to this study the physical properties of floating tablet is much better than the normal tablet.⁶

Ketorolac

Ketorolac or ketorolac tromethamine is a non-steroidal anti-inflammatory drug, used as an analgesic. This drug has 100% bioavailability.⁷ It is metabolised in liver with biological half-life of 3.5 to 9.2 hours and is excreted via renal and biliary. The route of administration is oral, i.v, i.m. The Ketorolac Tromethamine solution is added to 95 ml sodium alginate solution, containing methyl cellulose, hydroxypropylcellulose, sodium carboxymethyl cellulose, and pectin as co-polymers was used as composition for floating tablets which had more biological half-life of more than 8 hours when compared to normal composed tablets.⁸

Tapentadol

Tapentadol is an opioid analgesic.⁹ It is usually use to moderate severe pain from injury and surgeries etc. The route of administration of the drug is oral route. The bioavailability of the drug is 32% and the protein binding capacity of the drug is 20%. The excretion is through urine

and faeces. The biological half-life is nearly 4 hours. Combination of 20% sodium bicarbonate and 10% citric acid shows optimum floating ability whereas the formulation containing 20% Xanthan gum and 28% Locust bean gum shows optimum sustained drug release pattern. This study concludes that High floating ability of the formulation is likely to increase its gastrointestinal residence time and improve the extent of bioavailability. Thus it is much better than the regular formulation.¹⁰

Ibuprofen

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID).¹¹ It is a propionic acid derivative.¹² It is used for treating pain, fever, and inflammation. This used in painful menstrual periods, migraines, and rheumatoid arthritis. The bioavailability of the drug is 87-100% and the protein binding capacity is 98%. It is metabolised by liver and the biological half live is 13.-3 hours. It is excreted through urine. The ibuprofen floating tablets were prepared by blending the drug (ibuprofen), polymer s(HPMCK4M) and Carbopol940 to this sodium bicarbonate, lactose, citric acid were added. Floating systems have low bulk density so that they can float on the gastric juice in the stomach.¹³

Gabapentin

Gabapentin, is an antiepileptic agent and is a analog of GABA.¹⁴ It is a medication used to treat epilepsy, neuropathic pain, hot flashes, and restless leg syndrome. The bioavailability of the drug is 27%-60% and the half-life of the drug is 5-7 hours and it is excreted through renal route. The protein binding capacity of the drug is less than 3%. The Route of administration of this drug is oral route. it is absorbed slowly orally.¹⁵ Gabapentin's anticonvulsive and analgesic mechanisms of action are thought to involve the inhibition of neurotransmitter release within the peripheral and central nervous system through interaction with the alpha-2-delta accessory subunit of voltage-gated calcium channels.¹⁶ Floating microspheres of gabapentin is prepared by using Gabapentin, carbopol 934 and polyvinyl alcohol which was dissolved in emulsion solvent. The study results says that the microspheres of gabapentin had life for more than 12 hours than the normal dosage.¹⁷

Diclofenac sodium

An analgesic-antipyretic- anti-inflammatory drug, it used in rheumatoid, osteoarthritis, bursitis, ankylosing spondylitis, toothache, dysmenorrhoea, renal colic, post-traumatic and postoperative inflammatory conditions—affords quick relief of pain and wound edema. It is well absorbed orally, 99% protein bound, metabolized and excreted both in urine and bile. The plasma t_{1/2} is 2 hours. it has good tissue penetrability and concentration in synovial fluid is maintained for 3 times longer period than in plasma, exerting extended therapeutic action in joints.¹⁸ The floating tablet for diclofenac sodium is prepared with



Amberlite IRA 900, diclofenac sodium, ethylcellulose 100 cPs, Eudragit RS-100 and dibutyl phthalate. This study shows that more reproducible drug absorption and reduces the risk of local irritation, compared with single-unit dosage forms.¹⁹

Ketoprofen

Ketoprofen, propionic acid is a non-steroidal inflammatory drug which usually has an analgesic and antipyretic effect.²⁰ This is usually taken through oral route and has high bioavailability.²¹ It has 2-2.5 hours of bioavailability, it under goes first pass metabolism. The floating tablet of ketoprofen is prepared by using individually with HPMC K₁₅M and HPMC K₁₀₀M polymers. According to the study done the modified ketorolac was floating in stomach for 12 hours.²² Another study was done floating tablets for ketoprofen with the preparation of Ethyl cellulose (EC), sodium carboxymethyl cellulose (SCMC) and hydroxypropylmethylcellulose (HPMC K4M) are used. Tablet containing HPMC K4M released approximately 99% of drug in 12 h and showed good buoyancy with very short lag time (20 s) and long floatation time of more than 24 h.²³

Verampil

Verapamil is a calcium channel blocker.²⁴ It is not an analgesic. It is used to treat migraine, cluster headaches, angina pectoris etc. the bioavailability of the drug is 30-35% and plasma half-life is 2-4 hours. It is metabolized through liver and excreted through renal. The floating form of verapamil is prepared by using Verapamil HCl, hydroxypropylmethylcellulose, hydroxyl propyl methylcellulose, and xanthan gum BP, Polyvinyl pyrrolidone, carbopol, carbopol, sodium bicarbonate, and anhydrous citric acid were used in the preparation of floating drug delivery system. This study showed that floating version of verapamil had short buoyancy lag time, total buoyancy time more than 24 h and controlled drug released up to 24 h.²⁵ Another study was done on floating form of verapamil was formulated by Verapamil HCl, HPMC K15M and sodium alginate, Citric acid, sodium bicarbonate, hydrochloric acid, magnesium stearate and microcrystalline cellulose and according to this study showed the desirable form of drug release which was better than normal oral tablets.²⁶

CONCLUSION

Oral route of drug delivery is one of the oldest and safest methods of drug delivery system. But it has its own disadvantages too. To overcome this some of the disadvantage a modified drug release system was introduced-floating drug delivery system. This system has many advantages over the other drugs in path of analgesics. Analgesics are usually given for pain so if the drug has long action and less side effects that may act as good analgesics with this modified delivery system the delivery and action of analgesics have been impressed with good bioavailability.

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