A Review: Floating Microsphere System

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Abstract- *Recent advance in novel drug delivery system to enhance the safety and efficacy of the drug molecule by formulating the dosage form being convenient for administration. Gastric emptying is a complex process, one that is highly inconstant and makes an in vivo performance of drug delivery system indeterminate. Several difficulties are faced in designing controlled released system for better absorption and enhanced the bioavailability. conventional oral dosage forms such as tablet, capsules provide specific drug concentration in systemic circulation without offering any control over drug delivery and also cause great fluctuation in plasma drug level. Hollow microsphere are gaining curiosity due to their wide ranging applicability in directing of drugs to the stomach. They distribute uniformly over the gastric fluid to avoid the vagaries of gastric emptying and release the drug for prolonged period of time. The purpose of this review is to bring together the recent literature with respect to the method of preparation and various other parameter affecting the performance and characterization of floating microsphere.*

Aim and objective

1. *Floting microspheres are especially effective in the delivery of sparingly soluble and insolubal drugs*
2. *Floting microspheres to improve patient compliance.*

Keywords- Floating microsphere, Conventional and Gastro retentive drug delivery system

I. INTRODUCTION

Oral drug route administration is by far the most preferable route for taking medications. Microspheres are small spherical particles, with diameter 1µm to 1000µm.They are free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature. There are two types of microsphere, microcapsules and micromatrices. conventional oral dosage form such as tablets, capsules provide specific drug concentration in systemic circulation without offering any control over drug delivery and also cause great fluctuations in plasma drug levels. floating drug delivery system (FDDS) promises to be a potential approaches for gastric retention. The controlled gastric retention of solid dosage forms may be archived by the mechanism of mucoadhesion, floatation, sedimentation, expansion, modified shape systems, or by the simultaneous administration of pharmacological agents that delay gastric emptying. The main objectives of these new drug delivery systems are:

1. It would be single dose which release the active ingredient over a extended period of time.
2. It should deliver the active entity directly to the site of action thus minimizing or eliminating the side effects

Table no 1: Conventional v/s Gastro retentive drug delivery system.

Conventional drug delivery system	**Gastroretentive drug delivery system**
1.High risk of toxicity	**1**.Very low risk of toxicity
2. No risk of dose dumping	**2**.Possibility of dose dumping
3. Drug having rapid absorption through GIT	**3**.Drugs acting locally in the stomach
4.Drug which degrade in stomach	**4**. Drug which degrade in stomach

Ideal characteristics of floating microsphere:

1. To incorporate reasonably high concentration of the drug.
2. Dispersability in aqueous vehicle for injection.
3. Control particle size in aqueous vehicle for injection.
4. Release of active reagent with good control.
5. Susceptibility to chemical modification.

Advantages of floating microsphere:

1. enhancing solubility of poorly soluble drug by particle size reduction.
2. It cause prolonged therapeutic effect.
3. It can dose and toxicity.
4. It can provide constant drug concentration in systemic blood circulation.
5. As the drug is protected from enzymatic and photolytic cleavage so it is best for drug delivery.

The floating system can be based on the following approaches:
1 **Effervescent system**: Sodium bicarbonate and other gas generating agents carbonate like citic acid and tartaric acid are used and they produce carbon dioxide in the formulation.

2 **Mucoadhesive system**: These system permits given DDS (Drug delivery system) incorporate with mucoadhesive agent which adhere to device stomach walls can cause gastric emptying.

3 **Hydrodynamically balanced system**: It includes incorporate buoyant materials to enable to device to float.

4 **Raft system incorporate alginate gels**: Carbonate component is include in these sytem and upon with gastric acid, bubbles form in the gel.

5 **High density system**: Depending upon on the density and diameter of pellets the GI transit time can be extended over 5.8 – 25 hrs. Barium sulphate, zinc oxide, titanium dioxide and iron powder these all excipients are used in the system and these materials increase the density upto the 1.5-2.4gm/cm3.

Non-effervscent system: Swelling of poymer or bioadhesion to mucosal layer in GI tract is main mechanism in these system. Hydrocolloids, polysaccharides are gel forming agent and polymethacrylate, polyacrylates are mostly used in the formulation. Types of these system are as

Single layer floating tablet:

It is formulated by intimate mixing of drug with a gel forming hydrocolloid, which swells in contact with gastric fluid

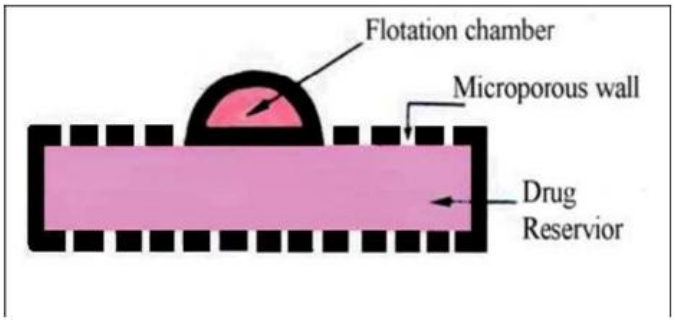


Figure 1: Intra Gastric Floating Gastrointestinal Drug Delivery System

Bilayer floating tablet:

These contain two layer one is immediate release layer and another one is sustained release. Bilayer dosage form contain bilayer formulation in which one layer is drug release consist misoprostor and other is hydrocolloide gelling agent such as HPMC.

Hollow microsphere:

Microballons (microsphere) loaded drug in the outer polymer shells prepared by the emulsion solvent diffusion technique.

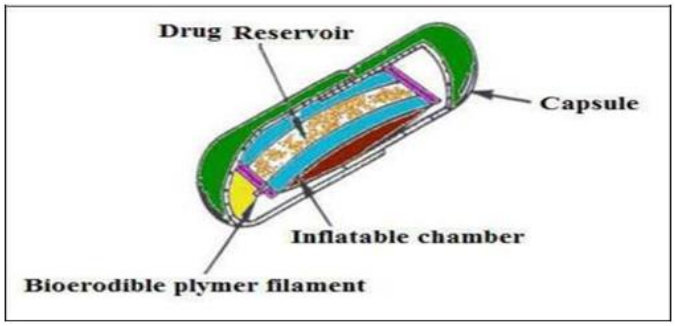


Figure2: Inflatable Gastrointenstinal Delivery System

Types of microspheres:

1. Bioadhesive microspheres
2. Magnetic microsphere
3. Floating microsphere
4. Radioactive microsphere
5. Polymeric microsphere

Sticking of drug to the membrane by using the sticking property of the water soluble polymers is called as adhesion. These types of microsphere exhibit a prolonged residence time at the site of of application and produce therapeutic effect.adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc.

1. Magnetic microsphere:

Drug is localised at the disease site and these system is important. Larger amount of drug is replaced by smaller amount of magnetically targeted drug. therapeutic magnetic microsphere are used to deliver chemotherapeutic agent to liver tumour. Proteins and peptides can also be targeted through this system.

2. Floating microsphere:

In this system bulk density is less than the gastric fluid so remains buoyant in stomach. It produces prolonged therapeutic effect and therefore reduces dosing frequencies. Keto profen is given in the form of floating microsphere.

3. Radioactive microsphere:

Microsphere size is 10-30nm are of larger than capillaries. As radio activity is not released from microsphere but acts from within a radioisotope typical distance , so it is differs from drug delivery system.

4. Polymeric microsphere:

Starch is used as bio-degradable , biocompatibility and bioadhesive in nature. Synthetic polymeric microsphere widely used in clinical application. Used as bulking agent , filters, embolic particles, vehicle etc.

Methods of prepration of floating microsphere:

1 .Spray Drying

- Solvent Evaporation
- Single emulsion technique
- Double emulsion technique
- Phase separation coacervation technique
- Spray congealing
- Solvent extraction
- Quassi emulsion solvent diffusion

Spray Drying:

polymer and suitable organic solvent are firstly mixed with each other. Dichloromethane and acetone are used as organic solvent. With the help of high speed homogenization solid drug is then dispersed in the polymer solution. After that this dispersion is atomized in a stream of hot air. The atomization leads to the formation of the small droplets from which solvent evaporates instantaneously leading the formation of microsphere. With the help of cyclone separator micro particles are separate from hot air. Trace of solvent is removed by vacuum drying. Feasibility of operation under aseptic conditions is one of the advantages of this method.

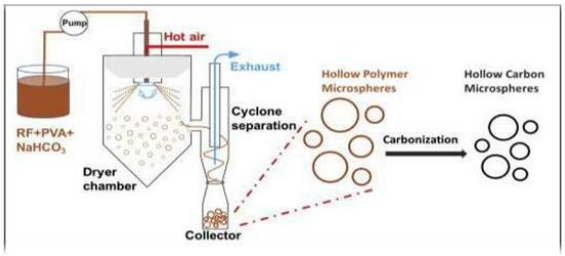
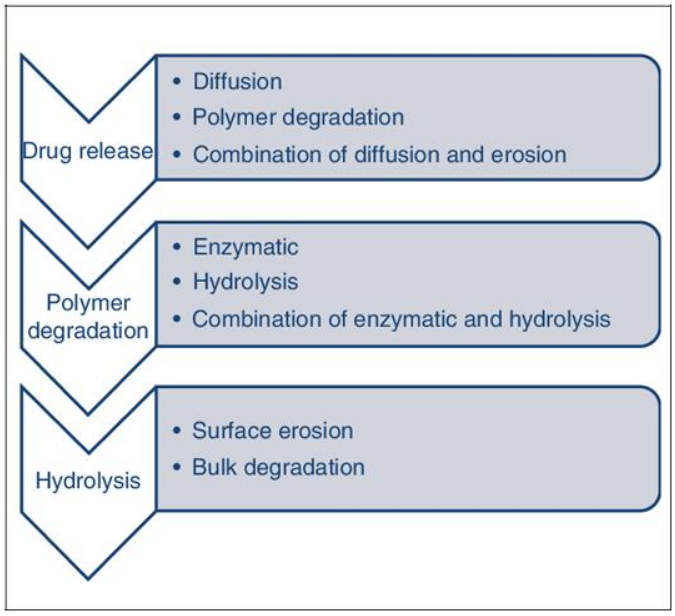


Fig 4 : spray drying

Mechanism of drug release from the microsphere:



The mechanism of drug release from multiparticulates can occur in the following steps:

Diffusion :

On contact with aqueous fluids in the GIT , water diffuses into the interior of the particles.
Dissolution of drug occur and the drug solutions diffuse across the release coat to the exterior.

Erosion:

Some coating can be designed to erode gradually with time, thereby releasing the drug contained within the particle.

Osmosis:

In allowing water to enter under the right circumstances, an osmotic pressure can be built up withing the interior of the particle. The drug is forced out of the particle into the exterior through the coating.

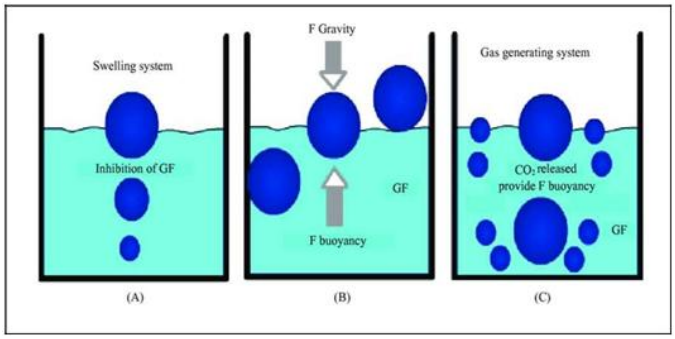


Fig 7: mechanism of floating system: (A) Swelling system (B) Force of gravity (C) Gas generating system

Characterization of floating microsphere:

1.Particle size: the particle size of microsphere was determined by the optical microscopic method and mean microsphere was calculated by measuring 100 particles with the help of a calibrated ocular micro meter.

2.Bulk density: it is defined as the mass of powder divided by bulk volume. 10gm of sample was placed in 25ml measuring cylinder and note down the and it is calculated with the help of following equation.

$$\frac{Bulk\ density}{Volume\ of\ sample} = Weighr\ of\ sample$$

3.Tapped density: the volume of weighed quantity of microspheres was determined after 100 taps using tapped density apparatus

$$Tapped\ density = \frac{Weight\ of\ sample}{Tapped\ volume}$$

4.Compressibility index and hausner ratio: This was determined by the following formula's

$$Compressibility\ index = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100$$

$$Hausner\ ratio = \frac{Tapped\ density}{Bulk\ density}$$

5.Angle of repose: The angle of repose of the microscope which measure the resistance to particle flow, was calculates as below.

tan^{o} = (h\r)

Table 2: Carr's index as an indication of powder flow

Carr's index	Types of flow
5–15	Excellent
12–16	Good
18–21	Fair to passable
23–35	Poor
33–38	Very poor
>40	Extremely poor

Application of microsphere in pharmaceutical industry:

1.Opthalmic drug delivery: Microsphere developed using polymer exhibit favourable biological behaviour such as bioadhesion, permeability-enhancing properties and intresting physico- chemical characteristics, which make it a unique material for the design of ocular drug delivery vehicles. Eg. Chitosan , Alginate, Gelatine

2. Oral drug delivery: Microsphere containing polymer having the ability to form the film. The pH sensitivity, coupled with the reactivity of the primary amine groups, make microspheres more suitable for oral drug delivery application. Eg. Chitosan, Gelatin

II. CONCLUSION

Floating microspheres can be Suitable altenative to the conventional formulation, by localizing the drug at upper GIT thereby, improving the bioavailability and reducing the dosing frequency.

REFERENCES

[1] **Aulton M E. Pharmaceutics**; "The science of dosage form design" Churchill Livingstone; 1989;113-114.

[2] Bhowmik D. Chiranjib B, Chandria M, Jayakar B, Sampath Kumar K.P.Floating Drug Delivery System-A Review, Scholars Research Library. Der Pharmacia Lettre**. 1(2):** 199- 218(2009).

[3] Chawla C, Gupta P, Koradia V, Bnasal A K. Gastroretention: A Means to Address Regional Variability in intestinal drug Absorption. Pharmaceutical technology**. 27(2):** 50-68(2003).

[4] Praveen Nasa, Sheefali Mahant, Deepika Sharma, "Floating Systems: A Novel Approach Towards Gastroretentive Drug Delivery System," Int J Pharmcy and Pharm Sci, 2010; 2(3); 27.

[5] Brahamankar D. M; Jaiswal S. B; "Biopharmaceutics and Pharmacokinetics: A treatise" 1st edition, 1995,pp. 399.

[6] Jain SK, Awasthi AM, Jain NK, Agrawal GP, Calcium silicate based microspheres of repaglinide for gastroretentive floating drug delivery: preparation and in vitro characterization. J Control Release 2005;107:300-309.

[7] Hoffman A. Adv. Drug Deliv. Rev, Expandable gastro retentive dosage forms, 1998;33: 185- 199.

[8] Mojaverian P, Vlasses PH, Kellener PE, Rocci ML. Floating drug delivery system; An innovative acceptable approach in gastroretentive drug delivery, Pharm. Res, 1988; 10: 639- 64.

[9] Jamini M., and Rawat S., A review on microsphere, Res. Jpharm. Boil. Chem. Sci. 2013; 4,(1): 1223- 33.
[10] Pavan Kumar B., Chandiran I.S., Bhavya B., Sindhuri M., Microparticulate drug delivery system: A Review, Indian journal of pharmaceutical science & research, 2011;1(1): 19-37.
[11] Gupta S. Udit U, Omray L, Reetesh Y, Soni V(2010) Prepration and characterization of floating drug delivery system of acyclovir Int J Appl Pharma2: 7-10.
[12] Santini J, Rechards A, Sheidt R, Cima M, Langer R(2000) Microchips as controlled released drug delivery devices. Chem Int Ed 39:2396-2407.
[13] Atyabi F, Mohammadi A, Dinarvand R(2005) Prepration of nimodipine loaded microspheres: Evaluation of parameters. Iran J Pharm Sci 1: 143-152.