Micro balloons for drug delivery: Review

Korake S. P.

SVERI's College of Pharmacy (Poly.), Pandharpur

Micro balloons-

The purpose of this review on micro balloons is to accumulate the recent literature with special focus on the recent development on floatation to achieve gastric retention. Hollow microsphere promises to be a potential approach for gastric retention. The recent developments of floating drug delivery systems including approaches to design effervescent systems and non-effervescent systems, micro balloons and recent developments and future potential.

Hollow microspheres / microballoons loaded with drug in their outer polymer shelf were prepared by a novel solvent evaporation or solvent diffusion/ evaporation method to create a hollow inner core.

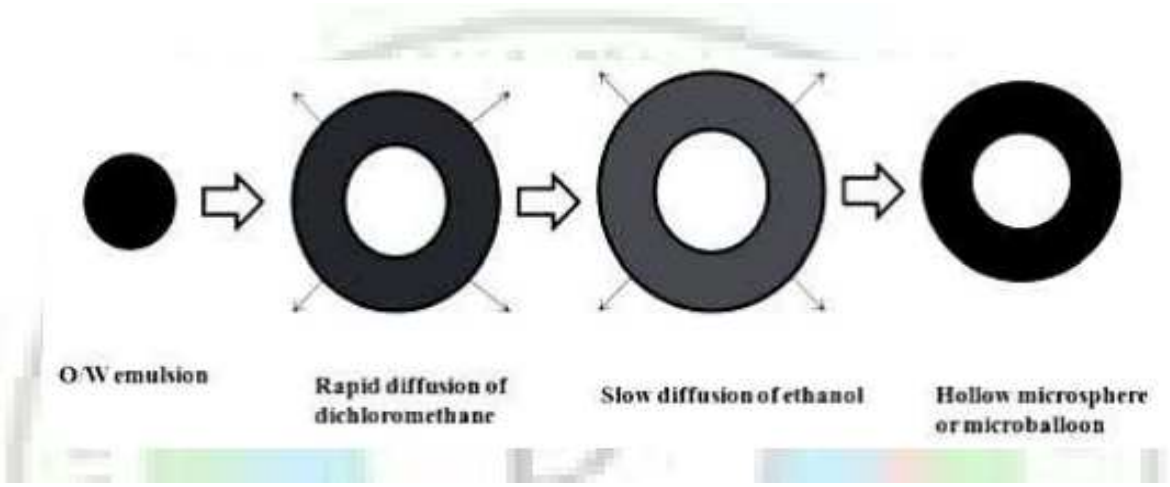

Fig 1 Formulation of floating hollow microsphere or microballoon

Advantages-

- **a)** Reduces the dosing frequency and thereby improve the patient compliance.
- **b)** Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects and despite first pass effect because fluctuations in plasma drug concentration is avoided, a desirable plasma drug concentration is maintained by continuous drug release.
- **c)** Hollow microspheres are used to decrease material density and Gastric retention time is increased because of buoyancy.
- **d)** Enhanced absorption of drugs which solubilise only in stomach
- **e)** Drug releases in controlled manner for prolonged period.

f) Site-specific drug delivery to stomach can be achieved.

g) Superior to single unit floating dosage forms as such microspheres releases drug uniformly and there is no risk of dose dumping.

h) Avoidance of gastric irritation, because of sustained release effect.

i) Better therapeutic effect of short half-life drugs can be achieved.

Limitation-

Some of the disadvantages were found to be as follows,

a) The modified release from the formulations.

b) The release rate of the controlled release dosage form may vary from a variety of factors like food and the rate of transit though gut.

c) Differences in the release rate from one dose to another.

d) Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the release characteristics of the dosage form may lead to potential toxicity.

e) Dosage forms of this kind should not be crushed or chewed.

Methods of Preparation-

1. Solvent Evaporation Method:

Floating multiparticulate dosage form can be prepared by solvent diffusion and evaporation methods to create the hollow inner core. The polymer is dissolved in an organic solvent and the drug is either dissolved or dispersed in the polymer solution. The solution containing the drug is then emulsified into an aqueous phase containing suitable additive (surfactants / polymer) to form oil in water emulsion. After the formation of a stable emulsion, the organic solvent is evaporated either by increasing the temperature under pressure or by continuous stirring. The solvent removal leads to polymer precipitation at the oil/water interface of droplets, forming cavity and thus making them hollow to impart the floating properties. The polymers studied for the development of such systems include cellulose acetate, chitosan, Eudragit, Acrycoat, Methocil, polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide and polycarbonate.

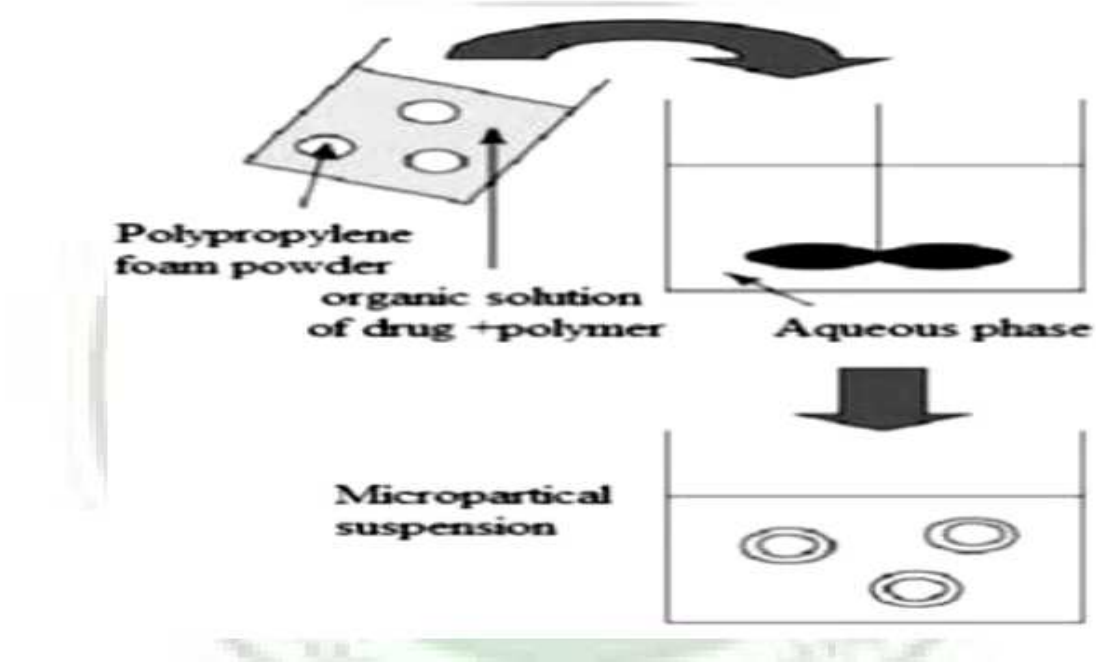

Fig.2 solvent evaporation method

b. Emulsion Solvent Diffusion Method:

In the emulsion solvent diffusion method the affinity between the drug and organic solvent is stronger than that of organic solvent and aqueous solvent. The drug is dissolved in the organic solvent and the solution is dispersed in the aqueous solvent producing the emulsion droplets even though the organic solvent is miscible (Figure 3). The organic solvent diffuse gradually out of the emulsion droplets in to the surrounding aqueous phase and the aqueous phase diffuse in to the droplets by which drug crystallizes

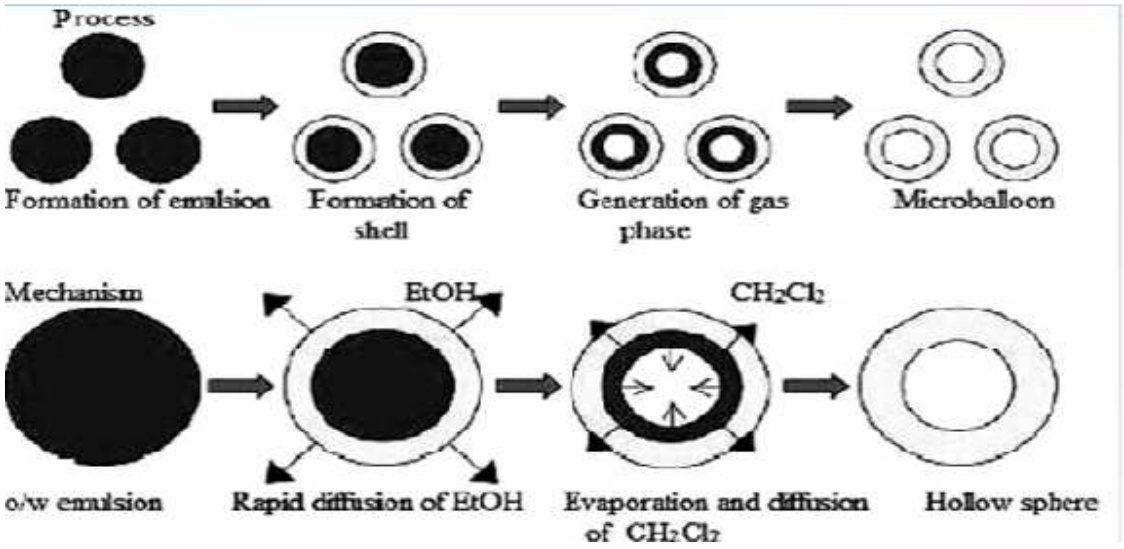

Figure 3: Preparation technique (emulsion-solvent diffusion method) and mechanism of microballoon

Applications –

a. Solid and hollow microspheres vary widely in density and, therefore, are used for different applications. Hollow microspheres are typically used as additives to lower the density of a material. Solid microspheres have numerous applications depending on what material they are constructed of and what size they are.

b. Hollow microspheres can greatly improve the pharmacotherapy of the stomach through local drug release, leading to high drug concentrations at the gastric mucosa, thus eradicating helicobacter pylori from the submucosal tissue of the stomach and making it possible to treat stomach and duodenal ulcers, gastritis and oesophagitis.

c. These microspheres systems provide sustained drug release behavior and release the drug over a prolonged period of time. Hollow microspheres of tranilast are fabricated as a floating controlled drug delivery system.

d. The drugs recently reported to be entrapped in hollow microspheres include Prednisolone, Lansoprazole, Celecoxib, Piroxicam, Theophylline, Diltiazem hydrochloride, Verapamil hydrochloride and Riboflavin, Aspirin, Griseofulvin, Ibuprofen, Terfenadine.

e. Floating microspheres can greatly improve the pharmacotherapy of stomach through local drug release. Thus, eradicating Helicobacter pylori from sub-mucosal tissue of the stomach are useful in the treatment of peptic ulcers, chronic gastritis, gastro esophageal reflux diseases etc. Floating bio adhesive microspheres of aceto hydroxamic acid are formulated for treatment of Helicobacter pylori infection. Hollow microspheres of ranitidine HCl are also developed for the treatment of gastric ulcer.

f. Floating microspheres are especially effective in delivery of sparingly soluble and insoluble drugs. It is known that as the solubility of a drug decreases, the time available for drug dissolution becomes less adequate and thus the transit time becomes a significant factor affecting drug absorption. For weakly basic drugs that are poorly soluble at an alkaline pH, hollow microspheres may avoid chance for solubility to become the rate-limiting step in release by restricting such drugs to the stomach. The positioned gastric release is useful for drugs efficiently absorbed through stomach such as Verapamil hydrochloride. The gastro-retentive floating microspheres will alter beneficially the absorption profile of the active agent, thus enhancing its bioavailability.

g. Polymer granules having internal cavities prepared by de acidification when added to acidic and neutral media are found buoyant and provided a controlled release of the drug prednisolone. Floating hollow

microcapsules of melatonin showed gastroretentive controlled-elease delivery system. Release of the drug from these microcapsules is greatly retarded with release lasting for 1.75 to 6.7 hours in simulated gastric fluid. Most of the mucoadhesive microcapsules are retained in the stomach for more than 10 hours e.g., Metoclopramide and glipizide loaded chitosan microspheres.

h. The floating microspheres can be used as carriers for drugs with so-called absorption windows, these substances, for example antiviral, antifungal and antibiotic agents (Sulphonamides, Quinolones, Penicillins, Cephalosporins, Aminoglycosides and Tetracyclines) are taken up only from very specific sites of the GI mucosa. i. Hollow microspheres of non-steroidal anti inflammatory drugs are very effective for controlled release as well as it reduces the major side effect of gastric irritation; for example floating microspheres of Indomethacin are quiet beneficial for rheumatic patients.