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# A Review on Microballoons: A Better Approach for Gastro Retentive Drug Delivery System

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**ABSTRACT:** Oral route is generally best and broadly utilized route for the organization of drug in microballoons. Microballoons vows to be a probable approach for gastric retention. Microballoons drug delivery system is depend on non-effervescent system containing empty particles of spherical shape without center preferably having a size less than 200 micrometer. Microballoons become new technology in pharmaceutical field in the floating drug delivery for accomplishing the gastric retention. Microballoons are also known as hollow microspheres. Microballoons are permeable smooth in nature with good floating properties in gastric fluid. Microballoons are gastro retentive drug delivery system. It gives controlled release properties. Microballoons are spherical empty vehicles without core. That can remain buoyant in gastric region for prolong period of time without aggravation in gastrointestinal tract. The factor affecting physical properties in microballoons, GRDDS, advantages, disadvantages, methods of preparation of microballoons, application and various evaluation techniques are covered in detail.
**KEY WORDS:** Microballoons, Gastric retention, Hollow microspheres, Gastro retention drug delivery systems

## I. INTRODUCTION

Microballoons are gastro retentive drug delivery system with non-effervescent system. Microballoons or hollow microspheres are in empty particles of spherical shape without core. These microballoons are include some characteristics like free flowing powders containing proteins or synthetic polymers and having ideal size less than 200 micrometer.[1]

Microballoons are reflected as one of the appropriate buoyant systems with the unique advantages of floating properties because hollow space is central inside the microsphere. The various techniques involved in their preparation like simple solvent evaporation method, emulsion solvent diffusion method, solvent diffusion evaporation method, spray drying method, single emulsion technique, double emulsion technique, co-acervation phase separation method etc.[2]

**Gastro Retentive Drug Delivery System (GRDDS)**

Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper Gastro Intestinal Tract (GIT) for local or systemic effect. It is obtained by retaining dosage form into stomach and by releasing in the controlled manner.

To overcome physiological adversities such as short Gastric Residence Times (GRT) and unpredictable Gastric Emptying Times (GET). This dosage forms will be very much useful to deliver narrow absorption window drugs.

Oral route is most acceptable route for drug administration. Apart from conventional dosage forms several other forms were developed in order to enhance the drug delivery for prolonged time period and for delivering drug to a particular target site.

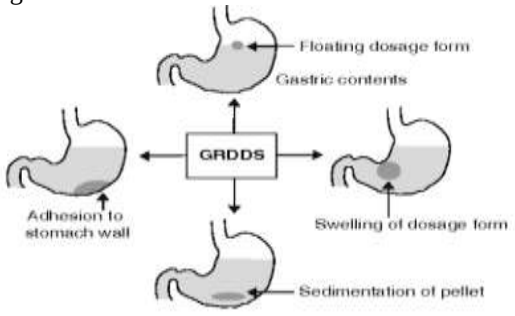


**Figure 1:** Gastro retentive drug delivery system

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**Factors affecting physicochemical properties of microballoons**

- Stirring rate
- Temperature of preparation
- Plasticizer
- Volume of aqueous phase
- Effect of solvent
- Amount of polymer and viscosity
- Solvent ratio
- Emulsifier concentration

**Application**

- For reduction of adverse effect of gastric irritation, gastro retentive floating microspheres are very effective.
- This system is stable in stomach for long period of time.
- Microballoons are effective method in delivery of drug with poor bioavailability.
- Dye to increase in gastric retention time the higher dose of drug is reduced because of low dose frequency.

**Advantages**

- Dosing frequency is decreases because of improvement in patient compliance.
- Maintain concentration of plasma drug.
- Increases gastric retention time.
- Controlled manner of prolonged period is release the drug.
- Dose dumping having no risk.
- For decreasing of material density microballoons are mostly used.
- Gastric retention time is increased cause of buoyancy by microballoons.

**Disadvantages**

- This kind of dosage forms should not be chewed or crushed.
- The release rate of controlled release dosage form may differ from the rate of transit though gut.
- The formulations are release modified.
- Higher drug load include in the controlled-release release formulations.
- In from one dose to another dose the release rate is different.

## II. METHODS OF PREPARATION

**Solvent evaporation method**

Improvement of the polymers, such systems include Eudragit, HPMC KM4 and ethyl cellulose etc. These polymers are mixed with the drug, than after the mixture is dissolved in solution of acetone and ethanol. The final solution is poured into 100 ml of liquid paraffin and then rotating at 1500 rpm. Finally emulsion is prepared and heated at 35°C temperature for 3hrs. After the emulsion is stable, acetone is completely evaporated and prepared microspheres are filtered using whattman filter paper. These microballoons are imparts the floating and sustained release properties.[3]

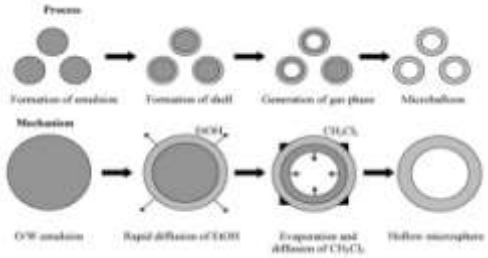

**Figure 2:** solvent evaporation method

**Emulsion solvent diffusion method**

Prepared solution of ethanol: dichloromethane and dissolved the drug polymer mixture in the above solution. This mixture is adding drop by drop in polyvinyl alcohol solution and rotating at 1500 rpm for 1 hr. and at different temperature.[4]

In this method, the affinity between the organic solvent and drug is stronger than the organic solvent and aqueous solvent. This drug is dissolved in organic solvent. Then the solution is distributed in the aqueous solvent developing the emulsion droplets though the organic solvent. This organic solvent is diffuse out of emulsion droplets in the aqueous phase. The drug crystallizer is diffuse the aqueous phase into the droplets.[3,5]

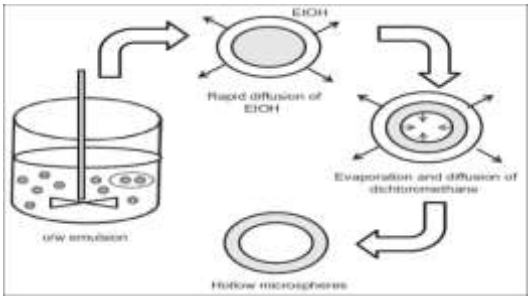


**Figure 3:** emulsion solvent diffusion method

**Solvent diffusion evaporation technique**

This technique is mixture of both emulsion solvent evaporation method and emulsion solvent diffusion method. These two drug polymers and 0.1% of surfactant like PEG are mixed with the solution of ethanol: dichloromethane (1:1) at normal temperature. This prepared solution is slowly dissolved into 80 ml of 0.46% w/w of polyvinyl alcohol as emulsifier. The propeller

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agitator stirrer is using for 1 hr. for evaporation of organic solvent. The resulting solution is filtered.[6]

The optimizer result of various processes like polymer ratio, stirring speed, concentration of emulsifier and drug: polymer ratio based on the selection of best formulation.[6]

**Spray drying**

This method is most active industrial process for drying and formation of particle. It is a best process where the required bulk density, particle size distribution and particle shape can be obtain.[7]

The polymer is dissolved in organic solvent like dichloromethane and acetone etc. to production of slurry. Then the slurry is sprayed into the drying chamber and concentration gradient of solvent form. This process is used because the time of the solute diffusion is longer than the solvent during the drying process in the droplet evaporation.[8]

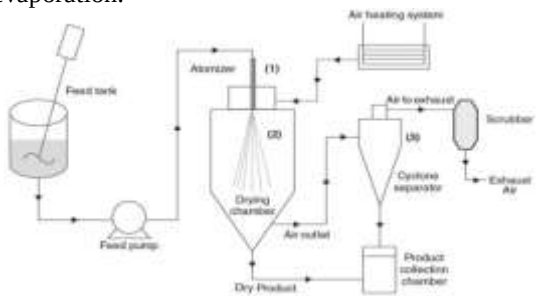


**Figure 4:** spray drying

**Single emulsion techniques**

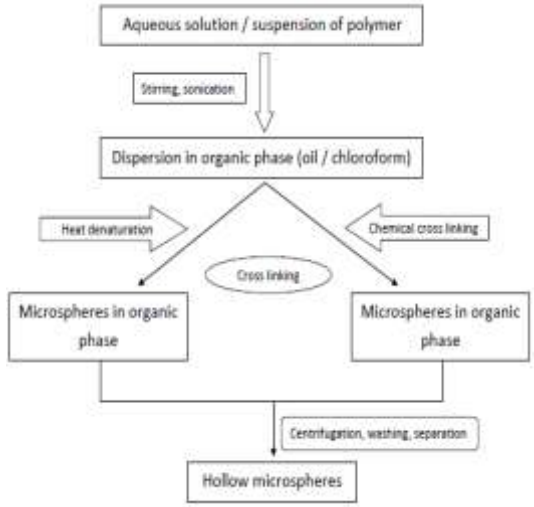


**Figure 5:** Single emulsion techniques[9]

**Double emulsion techniques**

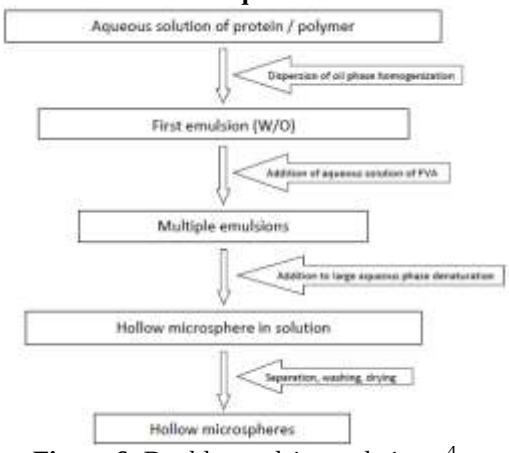


**Figure 6:** Double emulsion techniques[4]

**Co-acervation phase separation technique**

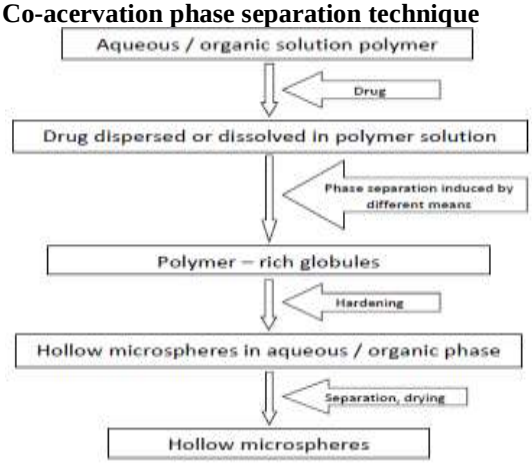


**Figure 7:** Co-acervation phase separation technique[6]

## III. EVALUATION OF MICROBALLOONS

**Percentage yield**

The actual yield is amount of product that is actually formed when the reaction is carried out in the laboratory. Percentage yield of microballoons is resulted for drug & it is calculated using the following equation.[10,11,12]

Percentage yield = M/Mo x 100

Where M = weight of beads

Mo = total expected weight of polymer & drug

**Micromeritic properties**

The microballoons are evaluated by following micromeritics properties:

**1. Particle shape & size**

The most widely used procedure to visualize microparticle is conventional light microscopy and SEM.

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**2. Bulk density**

Bulk density is calculated by following equation:-

Bulk density = mass of microspheres / bulk volume

**3. Tapped density**

It is calculated by following equation:-

Tapped density = mass of microspheres / tapped volume

**4. Hausner's ratio**

Hausner's ratio is calculated by following equation:-

Hausner's ratio = tapped density /bulk density

**5. Carr's index**

It is calculated by following equation:-

Carr's index = (bulk density – tapped density / tapped density) x 100

**6. Angle of repose**

The powder mass is allow to flow through the funnel orifice kept to a plane paper kept on the horizontal surface, giving a heap angle of paper

The angle of repose is calculated by following equation:-

$\tan \Theta = h/r$

**In vitro buoyancy**

Suitable quantity of microballoons is placed in 900 ml of 0.1N HCl. This mixture is rotating at 100 rpm for 8-10 hrs. in dissolution apparatus. After this rotation the layer of buoyant microballoons are separated by filtration. Particles which is including in the layer of sinking particulate are separated.

Particles of both types (buoyant microspheres and settled microspheres) are dried until constant weight is reached. The fractions of microballoons are weighed.[13]

Buoyancy is calculated by following equation:-

Buoyancy (%) = [Wf / (Wf + Ws)] x 100

Where, Wf = weight of floating microsphere

Ws = weight of settled microsphere

**Scanning electron microscopy**

Dry microballoons are placed on electron microscope brass stub a coated. The spectro-random canning of the stub is taking pictures of microballoons. The microballoons are viewed at a voltage of 20KV of microscope.[14]

**In vitro drug release studies**

The release rate is determined by microballoons in United States Pharmacopoeia XXIII basket type dissolution apparatus.

Weighed microballoons are equivalent to dose of drug and place in the basket of apparatus. The maintained temperature and rotation speed by dissolution fluid. Addition of 5 ml of dissolution fluid maintained initial volume of the dissolution fluid.[15]

**Data analysis of release studies**

This type of study include five kinetic models like Zero order, First order, Higuchi matrix, Peppas-Korsmeyer and Hixon-Crowell release equations are used to process the in vitro release data.[16,17]

**Swelling studies**

These types of studies are used for calculation of molecular parameters of polymers. Determination of swelling studies takes place using optical microscopy, dissolution apparatus and other techniques. These techniques are including CLSM, Cryo-SEM, and LSI etc. For the swelling studies, dissolution apparatus is used and it is calculated as following equation:[18]

Swelling ratio = weight of wet formulation / weight

**In vivo studies**

To performed the in vivo studies, use the suitable animal models examples like rat and beagle dogs etc. the radio graphical studies investigate the floating behavior using sulphate microballoons.[19,20]

## IV. CONCLUSION

Microballoons are gastro retentive drug delivery system which has low-density, sufficient buoyancy to float over gastric contents and stay in stomach for prolonged period in gastro intestinal tract. From the review we proved as the most promising drug delivery than conventional drug delivery system. Microballoons find the central place in particularly in diseased cell sorting, diagnostics, novel drug delivery and effective in vivo delivery. In microballoons all methods of preparations are depend on the emulsification.

## V. FUTURE SCOPE

Various new products expected that the new technologies may increase this possibility using gastro retentive drug delivery. In future, further market research may concentration on microballoons models:

- The design of gastro retentive drug delivery system having narrow GRT for clinical need, example: dosage & state of disease.
- Development of gastro retentive drug delivery system is beneficial for the treatment of Parkinson's disease, gastric and cancers.

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