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Improved Efficiency and Inhibition of *Salmonella* spp. Growth in Poultry by Using a Synergistic (Acetic Acid)

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ABSTRACT: Oral administration of medications in the form of microballoons is the most prevalent and preferred method. Microballoons are suggested as a viable alternative for gastric retention. The microballoon drug delivery method is founded on non-effervescent systems that consist of hollow spherical particles without a center, with a preferred diameter of less than 200 micrometers. The pharmaceutical industry has recently discovered a promising new topic in the form of floating medication delivery using microballoons. Hollow microspheres, or microballoons, are known by a variety of other names. A smooth, permeable material that floats well in gastric fluid is known as microballoons. The microballoons are responsible for the retention of the medication in the stomach. It is capable of gradually and consistently releasing its contents. Unfilled spherical vehicles are known as microballoons. That is capable of maintaining its buoyancy in the stomach for an extended period without causing irritation to the intestines. The physical characteristics of microballoons, as well as their benefits, drawbacks, production methods, applications, and assessment procedures, are all thoroughly examined in relation to GRDDS.

KEY WORDS: Gastro-retention drug delivery devices such as microballoons, gastric retention microspheres, and hollow microspheres

I. INTRODUCTION

Drugs may be delivered to the stomach with the help of microballoons, which do not need an effervescent mechanism. Microballoons, also known as hollow microspheres, are tiny, hollow sphere-shaped particles. Some of the features of these microballoons include the presence of proteins or synthetic polymers in freely flowing powder form and a size of fewer than 200 micrometers.¹

Due to its hollow construction and inherent buoyancy, microballoons are considered to be one of the most promising buoyant systems of the future.

Within the microsphere, space plays a key role. Methods such as simple solvent evaporation, emulsion solvent diffusion, solvent diffusion evaporation, spray drying, single emulsion, double emulsion, co-acervation phase separation, etc.² are all used in their production.

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.

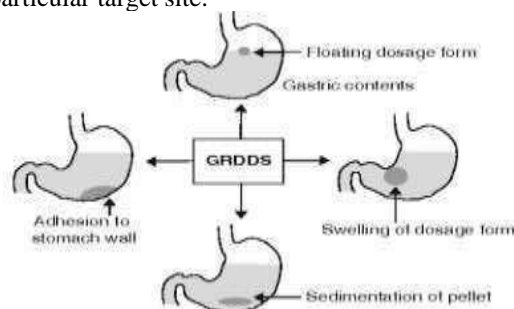


Figure 1: Gastro retentive drug delivery system

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

Systems like Eudragit, HPMC KM4, ethyl cellulose, etc., are used to enhance polymers like these. The medication is combined with the polymers, and then the whole thing is dissolved in an acetone and ethanol solution. After the solution has been mixed, 100 ml of liquid

paraffin is added and rotated at

1500 rpm. After the emulsion has been made, it is heated for three hours at 35 degrees Celsius. The acetone is then evaporated until only the microspheres remain, and the whattman filter paper is used to separate them. The floating and prolonged release qualities are bestowed onto these microballoons.³

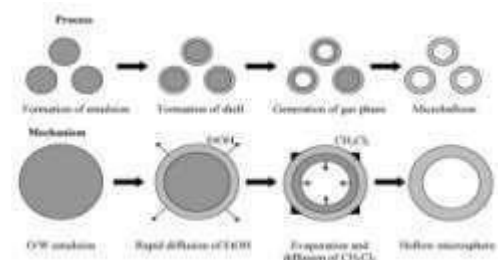


Figure 2: solvent evaporation method

Emulsion solvent diffusion method

The drug polymer combination was dissolved in an ethanol:dichloromethane solution. Polyvinyl alcohol solution is being rotated at 1500 rpm for 1 hour while this combination is being added drop by drop.⁴

In this technique, the organic solvent has a higher affinity for the drug than the aqueous solvent does. Organic solvent is used to dissolve this medication. The organic solvent is used to disperse the solution throughout the aqueous phase, where the emulsion droplets are formed. Emulsion droplets in the aqueous phase disseminate this organic solvent. Diffusion of the drug's aqueous phase into droplets is performed by the crystallizer.^{3,5}

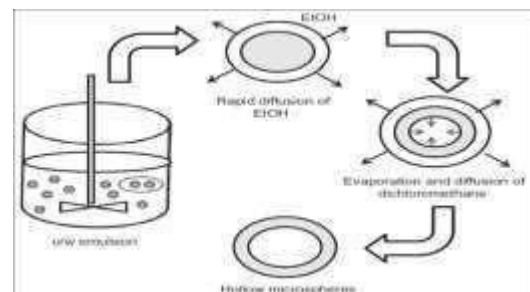


Figure 3: emulsion solvent diffusion method

Solvent diffusion evaporation technique

This approach combines elements of both the evaporation and diffusion of the emulsion solvent. At room temperature, a mixture of ethanol and dichloromethane (1:1) containing these two drug

polymers plus 0.1% of a surfactant such PEG is prepared. The 80 ml of produced solution is diluted gradually with the 0.46% w/w polyvinyl alcohol used as an emulsifier. a propeller Organic solvent is being evaporated using an agitator stirrer for 1 hour. The solution is then filtered.⁶

The selected optimal formulation is based on a number of processes, including polymer ratio, stirring speed, emulsifier concentration, and drug: polymer ratio.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

Double emulsion techniques

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

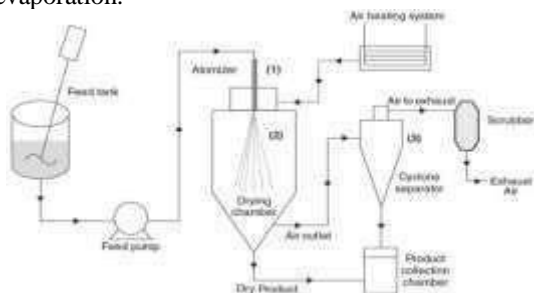


Figure 4: spray drying

1. Bulk density

Bulk density is calculated by following equation:-
Bulk density = mass of microspheres / bulk volume

2. Tapped density

It is calculated by following equation:-
Tapped density = mass of microspheres / tapped volume

3. Hausner's ratio

Hausner's ratio is calculated by following equation:-
Hausner's ratio = tapped density / bulk density

4. Carr's index

It is calculated by following equation:-
Carr's index = (bulk density – tapped density / tapped density) x 100

5. 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 (%) = $[W_f / (W_f + W_s)] \times 100$
Where, W_f = weight of floating microsphere

W_s = 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}

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III.

SUMMARY

A type of gastro-retentive medication delivery device, microballoons have the ability to levitate above gastric contents and remain in the stomach for an extended period of time as a result of their high buoyancy and low density. Our medication delivery technology is superior to the status quo, as evidenced by this analysis. Microballoons are essential in the areas of cell sorting, diagnostics, innovative medication administration, and efficient in vivo distribution. The preparation methods for microballoons are restricted to those that involve emulification.

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