DEVELOPMENT AND CHARACTERIZATION OF ORAL MICRO-PARTICULATE DRUG DELIVERY SYSTEM

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ABSTRACT

The development and characterization of oral micro-particulate drug delivery systems are great strides in pharmaceutical science. This approach had thus been directed toward the improvement of the bioavailability of drugs and their therapeutic effects. The micro-particulate systems in question, which are mostly microparticles or microspheres, exhibit both controlled and sustained release of APIs, thus improving the patients' compliance by reducing dosing frequencies. These systems safeguard drugs from the gastrointestinal problems. Development is based on the selection of appropriate polymers and excipients that form the microparticles containing the active principle suitably entrapped within the matrix. Various methods, such as spray drying, solvent evaporation, and coacervation, can be employed for the preparation of these microparticles. Each of these techniques offers various advantages concerning particle size, drug-loading efficiency, and release profiles. The characteristics of the micro-particulate system are highly important, whereby techniques involve particle morphology through scanning electron microscopy, thermal properties through differential scanning calorimetry, and in vitro dissolution testing through release kinetics. Micro-particulate systems can also be engineered to deliver drugs in a site-specific manner that minimizes systemic side effects and optimizes therapeutic outcome.

KEYWORDS: - *Micro-particulate, Drugs, Oral micro-particulate, Drug delivery system etc.*

1. INTRODUCTION-1

Improvement of new medication particle is costly and time consuming. Further developing security viability proportion of "old" drugs has been endeavoured utilizing various techniques, for example, individualizing drug treatment, portion titration, and restorative medication observing. Conveying drug at controlled rate, slow conveyance, focused on conveyance are other exceptionally appealing strategies and have been sought after enthusiastically [(1)]. Drug conveyance framework is a connection point between the patient and the medication. It very well might be a definition of the medication to regulate it for a restorative reason or a gadget utilized to convey the medication [(2)]. Most of the DDS right now endorsed for parenteral organization fall into the classification of liposomal or lipid-based definitions or remedial particles connected to polyethylene glycol (PEG) [(3)]. In controlled drug conveyance frameworks (DDS) the medication is shipped to the spot of activity, hence, its impact on fundamental tissues and unfortunate aftereffects can be limited. This cutting-edge type of treatment is particularly significant when there is an inconsistency between a portion or grouping of a medication and its helpful outcomes or harmful impacts [(4)].

Microparticulate in the size scope of around 1-1000µm, comprising of biodegradable or bio erodible solids with exemplified helpful specialists; address a noticeable class of conveyance frameworks. For infusion purposes, microparticles more modest than 125µm are liked. Microparticles intended for parenteral medication conveyance can be made out of various materials with various actual qualities, for example, biocompatible, biodegradable, injectable, clean, viable with diluents, and chemically steady [(5)]. Microparticles are a kind of medication conveyance frameworks where the molecule size goes from one micron (one thousandth of a mm) to few mm.

This microencapsulation innovation permits insurance of medication from the climate, adjustment of delicate medication substances, disposal of contradictions, or covering of disagreeable taste [6]. The idea that cells shed little film vesicles from their plasma film was accounted for approximately 40 quite a while back, and for a long time this cycle was depicted as the arrival of "cell dust [7]. Oral medication conveyance definition and advances are predominantly cantered around the accompanying areas of gastro digestive (GIT). Different difficulties related with oral course include:

• Pill-gulping trouble.

• Aggravation and unpalatable medications are not given by this course.

• Gastrointestinal (GI) annihilation of labile particles.

• Slow beginning of activity [8].

Advantages of microparticles: [9]

1. It gives insurance to the exemplified drug against corruption, like enzymatic debasement.

2. It is not difficult to regulate.

3. This procedure assists in concealing with tasting.

4. They help in expanding the general bioavailability of drugs.

5. This strategy is adaptable in focusing on the conveyance of medication to explicit locales.

Disadvantages of microparticles:
1. Hazardous in the potential.
2.It is not recommended to chew or crush this dose form [10].

2. STRUCTURE:2

The size range of microparticles is 1 to 1000 µm, and their diverse structures are found in the well-known matrix or reservoir structure (Figure 1). The structure and form, in addition to the excipients employed, also influence the function. Microspheres, microgranules, micro pellets, microcapsules, micro sponges, and liposomal preparations are examples of multiarticulate drug delivery methods that garner interest due to their many advantageous technological properties.

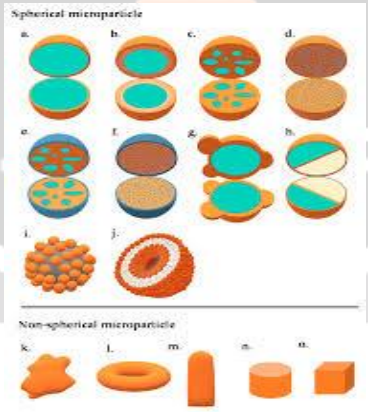
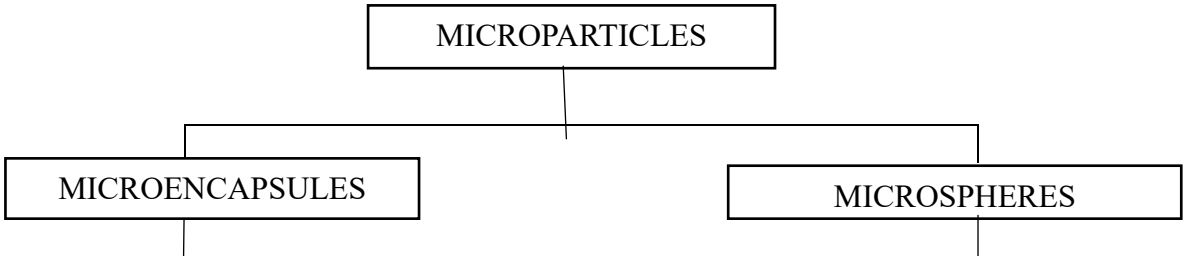
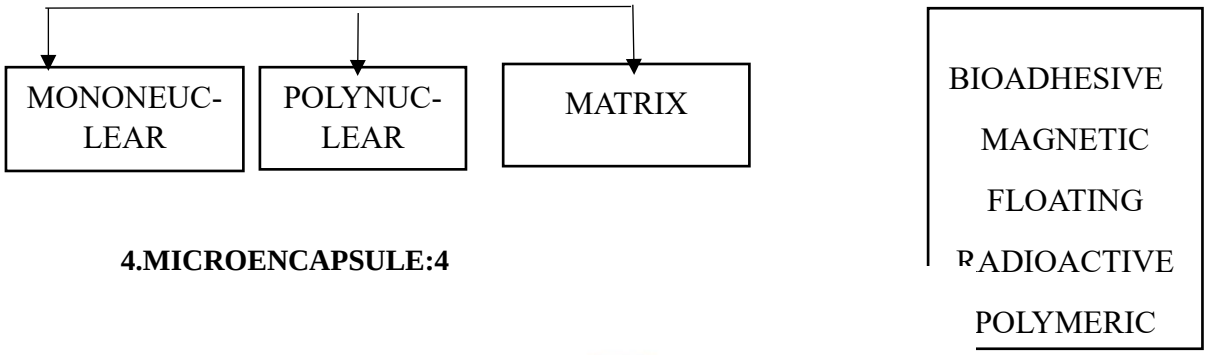


Fig.1: structure of microparticles

Based on how they are made and processed, microparticles can have a homogeneous or heterogeneous structure. The spheroid shape is typically chosen because it facilitates easier subsequent processing (like coating) [11].

3. TYPES OF MICROPARTICLES:3





4.MICROENCAPSULE:4

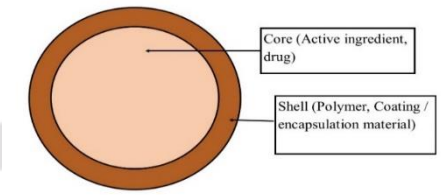


Fig.: 2 Microencapsule

The method of micro-encapsulation involves enclosing microscopic particles or droplets in a covering to create tiny capsules. The physical and chemical characteristics of the material to be enclosed determine the microencapsulation process. Among the many uses for these microcapsules is the conversion of liquids to solids, eliminating reactive substances, safeguarding the environment, and enhancing material handling capabilities. The microcapsule might possibly have more than one wall [(12)].

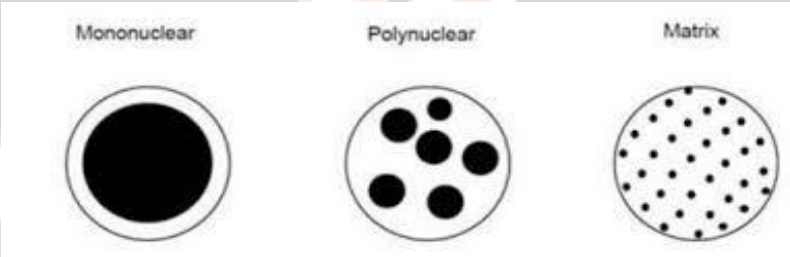


Fig.: 3

4.1 MICROSPHERE:

Microsphere is little circular molecule having the molecule size range 0.1-200µm, and comprised of biodegradable and non-biodegradable material and can be infused by 18 or 20 number of needles. A few Medications that are effectively consumed by the G.I.T. what's more, having short t1/2 are wiped out rapidly from the blood course. Controlled Medication conveyance Framework can stay away from the issues of ordinary medication conveyance framework by delivering the medication gradually into the G.I.T. furthermore, keep a steady medication fixation in the serum for longer timeframe 1 [(13)].

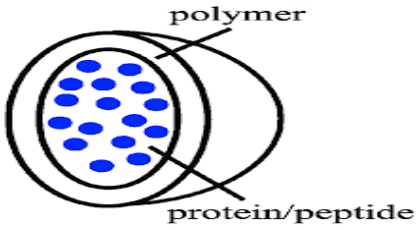


Fig.:4 Microsphere

4.1.1 Bio adhesive:

Drugs can be delivered to a specific area of the body for extended periods of time using bio adhesive drug delivery systems, which take advantage of the bio adhesion of some polymers, which become adhesive upon hydration. Adhesion between a polymer and a biological membrane is an example of bio adhesion, an interfacial phenomenon in which two materials, at least one of which is biological, are kept together by means of interfacial forces between an artificial material and biological substrate. "Bio adhesion" refers to the bonding of a polymer to the mucin layer of a mucosal tissue. The mucosal layer is found in the gastrointestinal tract, urogenital tract, ear, nose, and eye, among other parts of the body [14].

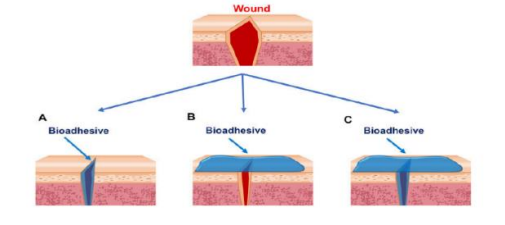


Fig.: 5 Bioadhesive

4.1.2 Magnetic:

Magnetic microspheres are supramolecular particles that are ferromagnetic enough to be drawn into micro vessels and pulled into neighbouring tissues by magnetic fields of 0.5 to 0.8 tesla, but small enough to flow through capi llaries without causing embolic occlusion. By binding a medication or therapeutic radioisotope to a magnetic component and injecting it into the patient's bloodstream, magnetic targeting stops the drug's movement in the target area with a strong magnetic field. Incorporated minerals like magnetite, iron, nickel, cobalt, neodymium-iron-boron, or samarium cobalt provide magnetic carriers their magnetic responsiveness to a magnetic field. The development of magnetic microspheres reduced renal clearance [15].

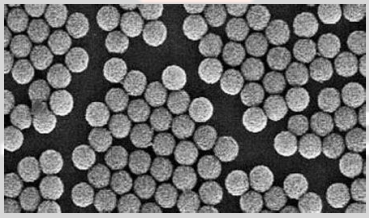


Fig.: 6 Magnetic

4.1.3 Floating:

Using a non-effervescent method, floating microspheres are a gastroretentive medication delivery device. Floating microspheres are also referred to as hollow microspheres, micro balloons, or floating microparticles. Strictly speaking, floating microspheres are spherical, empty particles devoid of a centre. These particles move freely and range in size from 1 to 1000 µm. Kawashima et al. (1992) used an emulsion solvent evaporation technique to create non-effervescent hollow polycarbonate microspheres. When the medicine is released gradually at the intended pace, there are less variations in the plasma drug concentration and more stomach retention [16].

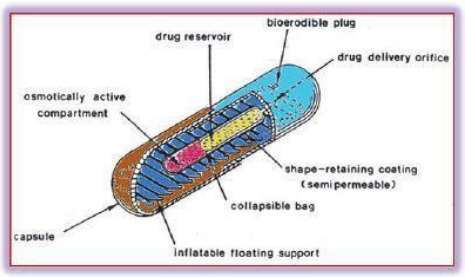


Fig.: 7 Floating

4.1.4 Radioactive:

One benefit of employing radioactive microspheres is that they can deliver a high concentration of radioactivity to the intended region without endangering the organs or tissues nearby. For alpha emitters, the effective treatment range is up to 90 mm; for beta emitters, it is not greater than 12 mm; and for gamma emitters, it is up to several centimetres [17].

4.1.5 Polymeric:

Oral medication administration by conventional methods typically does not offer target specificity or rate-controlled release. Modern drug delivery techniques include implanted biodegradable polymers with dispersed medication or rate-controlling membranes that provide desired drug release [18] these are of two types:

I. **Biodegradable Polymeric Microsphere**: The idea behind the use of natural polymers like starch is that they are biodegradable, biocompatible, and naturally bio adhesive. The polymer concentration and the sustained release pattern regulate the drug's release rate and extent.
II. **Synthetic Polymeric Microspheres**: These have shown promise as drug delivery vehicles, bulking agents, fillers, and embolic particles in clinical applications. They are also frequently employed in this regard [19].

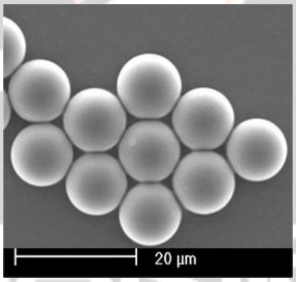


Fig.: 8 Polymeric

5. TECHNIQUES USED FOR MICROPARTICLES PREPARATION: 5

A) Physical methods:
- solvent evaporation
- Coacervation phase suspension
- Spray drying
- Fluidized bed coating

B) Chemical methods:
- Emulsion polymerization
- In-situ polymerization
- Interfacial polymerization (IFP)

A) Physical method:

a) **Solvent evaporation:** The continuous phase's capacity in this procedure is insufficient to dissolve the whole volume of the disperse phase solvent. As a result, the dispersion's surface evaporatively loses solvent, resulting in hardened microspheres [20]. Using an agitator, this process entails emulsifying an organic solvent comprising dissolved polymer and dissolved dispersion drug in an excess of continuous phase. Particle size and form are influenced by the emulsifier content in the aqueous phase. The stirring rate is lowered and the organic solvent evaporates at the proper temperature and atmospheric or decreased pressure once the required

droplet size has been created by filtering, centrifuging, or lyophilizing the suspension, the solid microparticles are extracted. There are essentially two methods for
solvent evaporation technique: single and multiple emulsion solvent evaporation techniques [21].

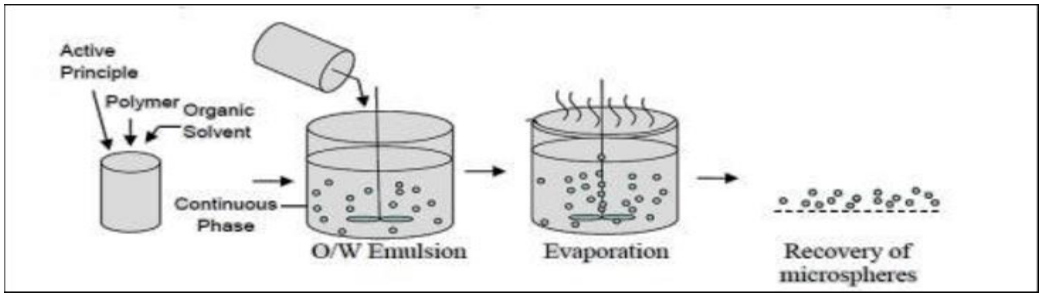


Fig.:9 solvent evaporation

b) Coacervation phase separation: When a coacervating chemical is added to a polymer solution, it causes polymer phase separation, which is generally referred to as coacervation [22].

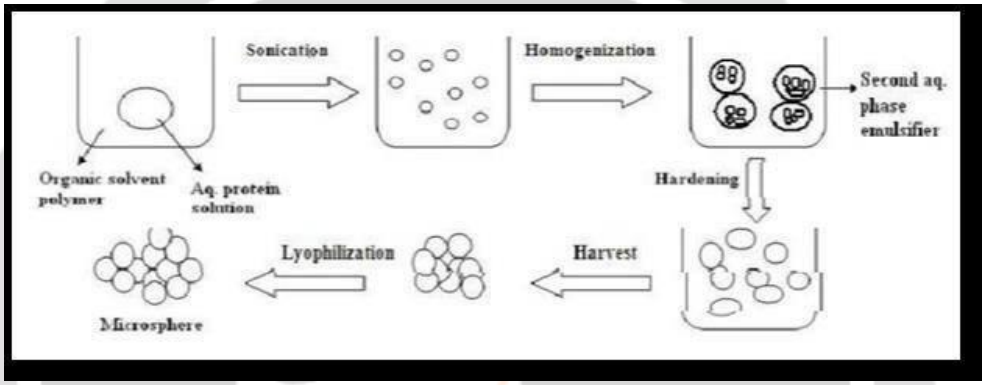


Fig.:10 coacervation phase separation

c) Spray drying: The spray dryer had a two-fluid nozzle and ran in a co-current mode, which directed the flow of both the drying air and the feeding suspension in the same direction. To keep the suspended cellulose fibers from sedimenting, the feeding suspension was constantly stirred with a magnetic stirrer during the drying process [23].

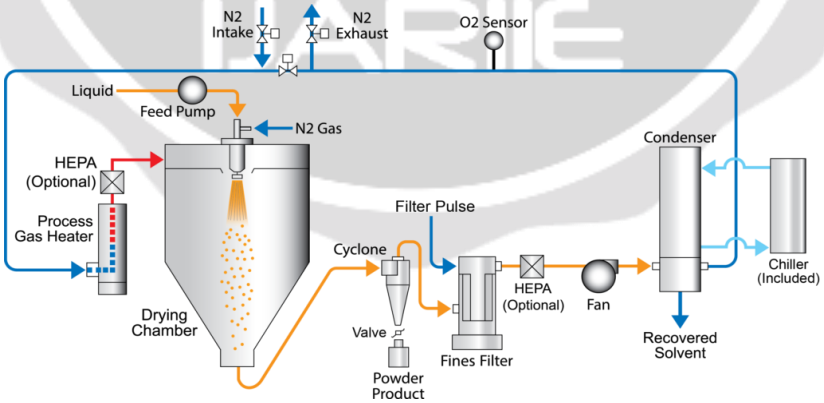


Fig.:11 spray drying

d) Fluidized bed coating: One encapsulating technique is fluidized bed coating, which involves spraying coating material over the fluidized core material. Three distinct techniques for fluidized bed coating are:

(a) tangential spray
(b) bottom spray
(c) top spray.

The coating efficiency of the wall material in this encapsulation method depends on a number of factors, including the wall material's feed rate, the nozzle's atomization pressure, the temperature and velocity of the incoming air,

etc. Fluidized bed coating was used by Coronel-Aguilera & San Martín-González (2015) to encapsulate spray-dried beta carotene with hydroxypropyl cellulose [24].

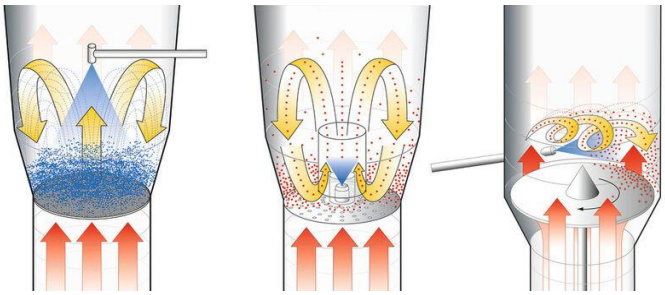


Fig.:12 Fluidized bed coating

B) Chemical method:

a) Emulsion polymerisation:

Using this method, the agitated aqueous polymerization medium containing the material to be encapsulated (core material) and an appropriate emulsifier is mixed with the monomer (alkyl acrylates) dropwise. Drug loading can also be achieved by incubating cyanoacrylate nanocapsules, or empty nanocapsules, with the dissolved or finely dispersed drug in addition to the drug being entrapped during microcapsule creation [25].

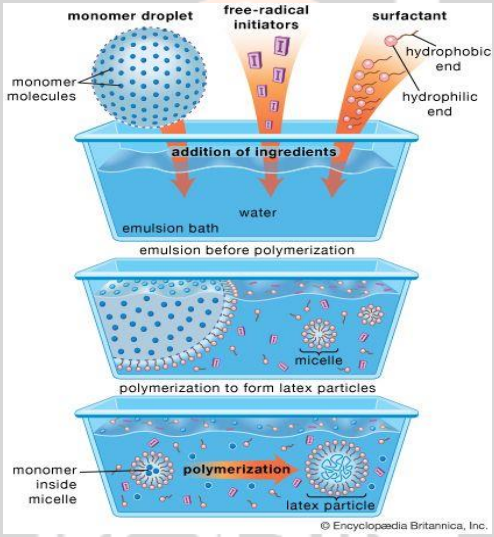


Fig.:13 Emulsion polymerization

b) In-situ polymerization: In situ polymerization is firmly connected with interfacial polymerization in that shell arrangement happens by means of polymerization responses inside the epitome blend. As the polymer develops, it stores onto the outer layer of the center material, where cross connecting responses might happen close by polymer chain development, ultimately framing a strong container shell [26].

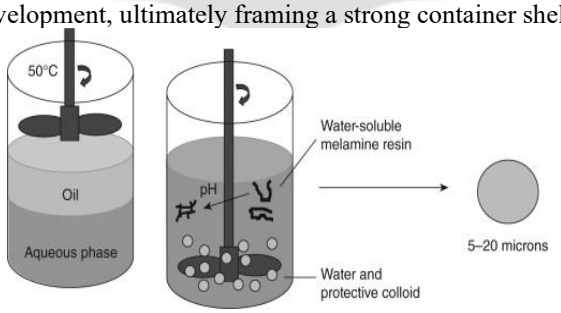


Fig.:14 In situ polymerization

c) Interfacial polymerization: In this method the shell case is shaped at or on the surface of the drop or on the molecule by polymerization of the responsive monomers. The substances utilized as a shell are multifunctional 11 monomers. The multifunctional monomer is broken up in fluid center material and it will be scattered in fluid

stage containing a scattering specialist. For the most part, utilized shell shaping material incorporates co-reactant multifunctional reagent like diamines, isocyanates and diacid chlorides [27].

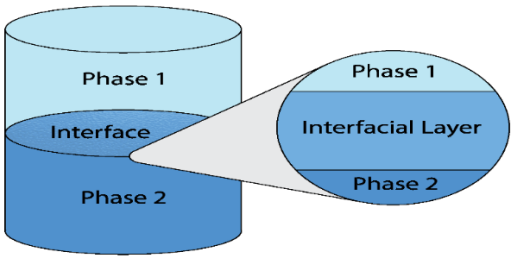


Fig.:15 Interfacial polymerization

6. EVALUATION PARAMETERS:6

1. Microscopic yield
2. Drug entrapment
3. Surface morphology
4. In-vitro release study

Microscopic yield:

Completely dried microspheres were gathered and gauged precisely. The rate yield was then determined utilizing formulae given below [28].

Percentage Yield = Weight of obtained microspheres X100
Total weight of drug and polymer

Drug entrapment:

Ensnarement productivity addresses the extent of the underlying measure of medication integrated/related into/with the microparticles. This boundary was not set in stone by applying the accompanying condition [29].

Entrapment efficiency (%) = Qty of drug encapsulated
Qty of drug added for encapsulation

Surface morphology:

SEM

The kafirin microparticles were mounted onto carbon tabs and covered with platinum to a thickness of roughly 10 nm utilizing a Baltec Drug 020 falter coater.The tests were seen at 5 kV and a working distance of 8 mm utilizing a field discharge checking electron magnifying instrument [30]. Cross-segments were made to notice the center and inward construction of the microparticles [31].

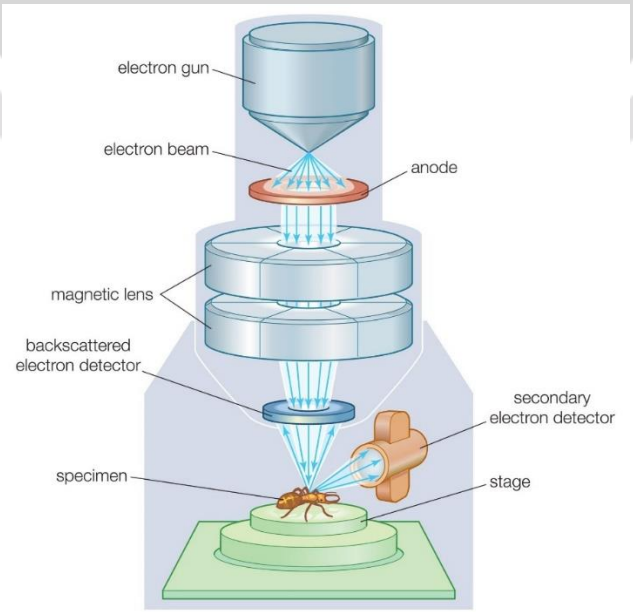


Fig.:16 SEM

In- vitro release study

I. **Dissolution apparatus:** Three distinct techniques were used to study the release profiles of aerodynamically categorized particles of Substance A in its many forms, budesonide, and felorol: USP apparatus (paddle apparatus), USP apparatus flow through cell and modified Franz diffusion cell. HPL C was used to determine concentrations in each experiment, which carried out in triplicate. Degassed P BS buffer with a pH of 7.4 was used as the dissolution medium for the 37°C dissolution experiments [(32)].

II. **Dialysis method:** The dialyzer was filled with 50 mg of peptide-loaded microspheres that were suspended in 5 mL of release fluid (0.1 M PBS pH 7.4) at 37°C. After that, the dialyzer was added to a 50 mL glass cylinder filled with release media, and the mixture was shaken with a magnetic stir bar at 300 rpm. By periodically taking one millilitre (1 mL) sample of the outer media's contents, drug release was evaluated. The buffer was changed right away following the sampling [(33)].

CONCLUSION:

The conclusion is that the development and characterization of oral micro-particulate drug delivery systems represent key advances in modern therapeutics and are finally offering a real solution to many of the problems presented by conventional oral dosage forms. Micro-particulate systems can also be engineered to deliver drugs in a site-specific manner that minimizes systemic side effects and optimizes therapeutic outcome.

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