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FORMULATION AND EVALUATION OF MODEL DRUG LOADED FLOATING MICROSPHERES

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ABSTRACT

Microspheres are characteristically free flowing powders having particle size ranging from 1-1000 µm consisting of proteins or synthetic polymers. The point of present work is to get ready floatng microspheres of Abacavir sulphate utilizing HPMC K100M and HPMC K4M as polymer. There are various approaches in delivering therapeutic substance to target site in sustained controlled release fashion. Abacavir sulphate is an enemy of HIV drug. The short half existence of Abacavir sulphate and different organization portion make Abacavir sulphate an excellent contender for formulation of floating drug delivery system. It is reliable means to deliver drug to target site with specificity, if modified and to maintain desired concentration at site of interest. Moreover microspheres are of micron size so they can easily fit into various capillary beds which are also having micron size. Floating microspheres of Abacavir sulphate were set up by dissolvable dissipation technique utilizing HPMC K100M and HPMC K4M as polymer. There are various departments of medicine like cancer, pulmonary, cardiology, radiology, gynecology, and oncology etc., numerous drugs are used and they are delivered by various types of drug delivery system. Purpose of review is to compile various types of microspheres, different methods to preparation, its applications and also various parameters to evaluate their efficiency.

KEYWORD: Microspheres, Abacavir Sulphate, Floating drug delivery system, Polymer.

I. INTRODUCTION

1.1 Introduction of Microspheres[1]

Microspheres are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature & ideally having particle size less than 200µm. There are two types of microspheres – microcapsules & micromatrices, which are described as, Microcapsules are those in which entrapped substance is dispersed throughout matrix. Microspheres are sometimes referred to as microparticles. Microsphere can be manufactured from various natural & synthetic materials. Microspheres play important role to improve bioavailability of conventional drugs & minimizing side effects. Controlled oral drug administration does not usually provide rate controlled release or target specificity. Microparticulate (Microsphere/Microcapsule) drug delivery system are considered & accepted as reliable one to deliver drug to target site of interest without untoward effects.

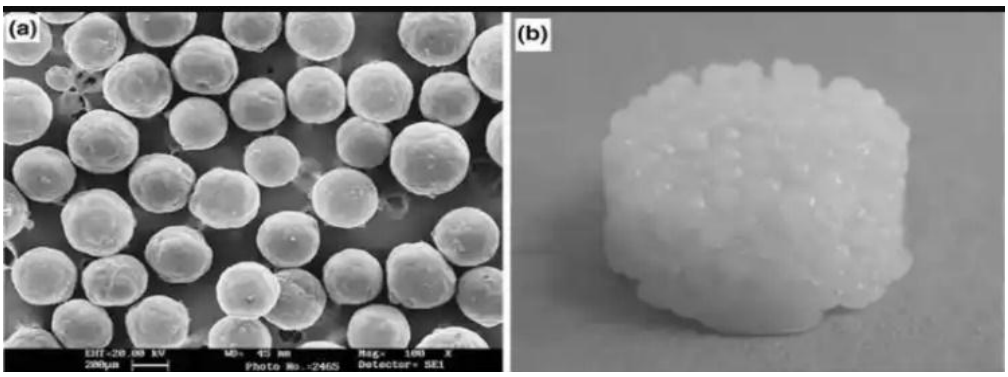


Figure 1: Microspheres.

1.2 Types of Microspheres

Microspheres can be manufactured from various natural & synthetic materials.

1) Glass microspheres

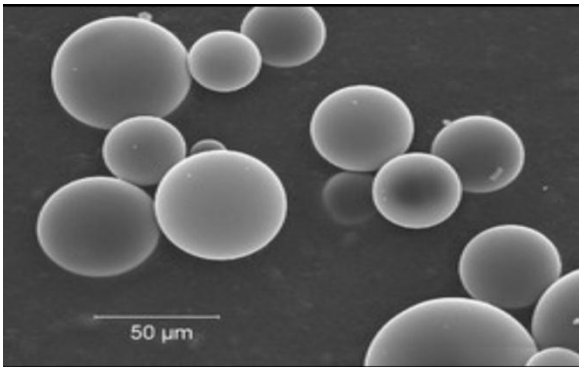


Figure 2: Glass microspheres.

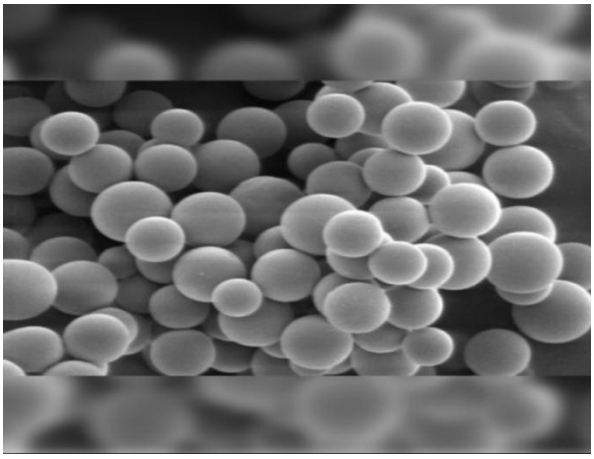


Figure 3: Hollow glass microspheres.

2) Polymer microspheres

3) Metal microspheres

4) Ceramic microspheres

Solid & hollow microspheres are typically used as additives to lower the density of a material.

During the most recent multi decade different evaluations have been performed concerning the maintained transport assessments kind of solutions, which have focused in on the prolongation of gastric emptying time (GET). The GET has been addressed to be from 2 to 6 hours in people in the fed state. In like manner orally, adequate bioavailability and prolongation of the astonishing plasma level irregularly can't be gotten.

Gastro retentive constructions can stay in the gastric locale several hours and consequently completely draw out the gastric home time of medications. Deferred gastric upkeep improves bioavailability, diminishes drug squander, and improves dissolvability for drugs that are less dissolvable in a high pH climate. It has applications additionally for neighborhood drug transport to the stomach and proximal little stomach related organs. Gastro support assists with equipping better accessibility of new things with new obliging prospects and great advantages for patients.

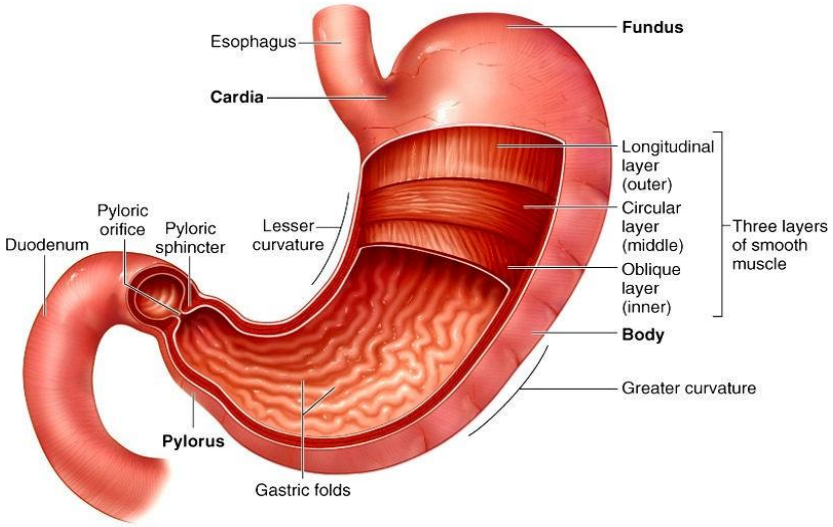


Figure 4: Internal structure of stomach.

1.3 APPROACHES (gastro retentive)[2,3,4]

Several approaches have been attempted in the preparation of gastro-retentive drug delivery systems. This include,

1. Floating systems
2. Bioadhesive systems
3. Swellable systems
4. High density systems
5. Modified-shape systems

- **Floating systems**

➢ Floating frameworks have low mass thickness so they can glide on the gastric juice in the stomach without influencing gastric emptying.

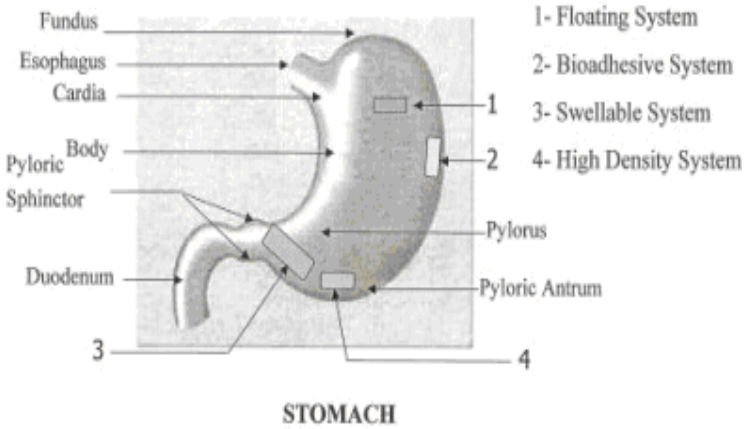


Figure 5: Gastro retentive dosage forms.

1.4 Floating Drug Delivery Systems[3,4,5,6,7]

Floating drug delivery system have a mass thickness not really gastric fluids(less than 1.004 g/ml) in like manner stay light in the stomach without influencing the gastric emptying rate for a drawn out timeframe. While the system is floating on the gastric substance, the drug is passed on constantly at the ideal rate from the system. After appearance of drug, the overabundance system is delivered from the stomach, this outcome in an all encompassing GRT and an unparalleled control of changes in plasma drug focus.

The floating maintained delivery parcel structures present by a long shot a large portion of the credits of hydrophilic networks and are known as 'hydrodynamically changed systems' ('HBS') since they can keep up their low clear thickness, while the polymer hydrates and builds up a gelled block at the external surface. The drug is passed on constantly from the swollen design, as in view of standard hydrophilic associations. These developments are relied upon to stay light upon the gastric substance without influencing the intrinsic speed of emptying considering how their mass thickness is lower than that of the gastric substance.

Figure 6 Floating Tablets.

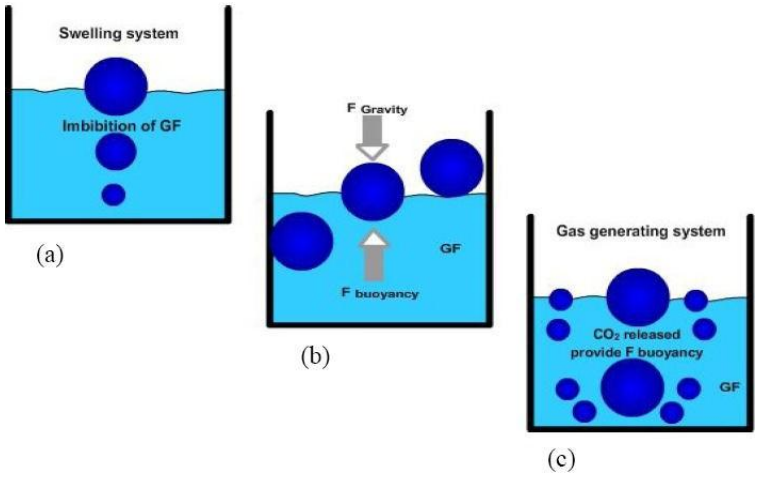


Figure 7 Mechanism of floating systems.

GF= Gastric fluid

1.5 Advantages of Fdds[8]

- Floating segment structures, for example, tablets or compartments will stays in the reaction for conceded time even at the corrosive neutralizer pH of the stomach related system.
- FDDS are invaluable for drugs induced for neighborhood development in the stomach eg Antacids
- FDDS divide structures are useful if there should be an occasion of enthusiastic intestinal unforeseen development and in free guts to keep the drug in floating condition in stomach to improve reaction.
- Acidic substance like headache medicine causes disturbance on the stomach divider when related with it thusly; HBS/FDDS nuances might be valuable for the relationship of ibuprofen and other close to drugs.
- The FDDS are helpful for drugs eaten up through the stomach eg: Ferrous salts, destructive neutralizers.

1.6 Disadvantages of Fdds[8]

- Floating systems are not reasonable for those drugs that have dissolvability or security issues in gastric fluids.
- Drugs like Nifedipine, which is particularly burned-through along the entire GI plot and which go through significant first-pass assimilation, may not be proper opportunities for FDDS since the slow gastric voiding may influence diminished systemic bioavailability. Similarly there are limitations to the meaning of FDDS for drugs that are aggravation to gastric mucosa.
- One of the damages of floating systems is that they require a pleasingly essential level of fluids in the stomach, so the drug appraisals structure coast in that and work capability.
- These systems in like manner require the presence of food to concede their gastric emptying.
- Single unit floating DDS show all or none gastric emptying considers.

II. MATERIAL METHODOLOGY

2.1 Preformulation

- Preformulation testing is an examination of physical and compound properties of a drug substance alone and when joined with excipients. It is the initial phase in the objective advancement of dose structures.

- Preformulation considers identify with drug and logical examination did in supporting detailing improvement endeavors of the dose structures.
- The accompanying preformulation reads were performed forgot test of drug.

2.1.1 Organoleptic Properties

1. Color and nature

- Moved little amount of the example on a white piece of paper spreaded the powder and inspected outwardly.

2. Taste and Odor

- Exceptionally less amount of Abacavir sulfate was utilized to get taste with the assistance of tongue just as smelled to get the scent.

2.1.2 Physical Characteristics

1. Flow properties

- The flow properties of powder are basic for a proficient microsphere getting ready. In the event that the drug is recognized at pre plan stage to be "inadequately flowable" the issue can be addressed by choosing suitable excipients. Point of rest is characterized as the most extreme point conceivable between the outside of a heap of the powder and the even plane.

2. Bulk density

- Bulk density is the ratio of mass of powder to the bulk volume. Bulk density generally relies upon specific shape as the molecule become more round fit as a fiddle, bulk density is increments.
- Bulk density is controlled by estimating the volume of a known mass of a powder test that has been gone through a screen into a graduated chamber.

3. Tapped density

- Tapped density is the ratio of mass of powder to the tapped volume.

4. Estimation of powder compressibility

- The compressibility list is proportions of the penchant of a powder to be compacted. In that capacity, they are measures relative significance of bury particulate connections. In a free flowing powder, such connections by and large less and tapped densities will be nearer in esteem. For less fortunate flowing materials, there are much of the time more

noteworthy bury particulate cooperation, and a more prominent distinction among bulk and tapped densities will be noticed. These distinctions are reflected in the compressibility file determined by the equation.

5. Hausner's ratio

- It is the ratio of volume of tapped volume is tapped density to bulk density

$$\textbf{Hausner's ratio} = V_t/V_b \text{ or } \rho_b/\rho_t$$

6. Melting point

- It is one of the boundaries to pass judgment on the immaculateness of rough drug. In the event of unadulterated synthetic compounds, liquefying focuses are sharp and steady.

2.1.3 Solution Properties

1. pH of the solution

- Gauged and moved precisely about 1.0 g of test in a 200ml spotless and dried measuring glass, dissolved in carbon dioxide let loose water and made the volume to 100ml with same dissolvable, blended. Peruse the pH of newly arranged arrangement by utilizing pre-calibrated pH meter. The outcomes are appeared in outcomes and conversation.

2. Solubility

- A semi quantitative assurance of the solubility was made by adding dissolvable in little steady add up to a test tube containing fixed amount of solute of the other way around. After every expansion, the system is vivaciously shaken and analyzed outwardly for any undissolved solute particles. The solubility is communicated regarding ratio of solute and dissolvable. The outcomes are appeared in outcomes and conversation.

2.1.4 Dentification of Drug and Compatability Study

1. Drug excipient compatibility studies

- In the tablet dose structure the drug is in personal contact with at least one excipient; the last could influence dependability of the drug. Information on drug-excipient communications is in this manner valuable to the formulator in choosing fitting excipients. This data is now being in presence for known drugs. For new drugs or new excipients, the pre details researcher should create the required data.

2.2 Evaluation[1]

1. **Particle size & shape**

- The most widely used procedures to visualize microparticles are conventional light microscopy (LM) & scanning electron microscopy (SEM).

2. **Particle size analyzer**

- Microsphere (50 mg) was suspended in distilled water (5mL) to prevent microsphere aggregation, above suspension is sonicated in water bath and particle size was expressed as volume mean diameter in micrometer.

3. **Optical microscopy**

- This method was used to determine particle size by using optical microscope (Meizer OPTIK) measurement was done under 450x (10x eye piece and 45x objective) and100 particles were calculated.

4. **Degradation behavior**

- The surface chemistry of microspheres can be determined using electron spectroscopy for chemical analysis (ESCA).

5. **Angle of repose**

- The powder mass was allowed to flow through funnel orifice kept vertically to plain paper kept on horizontal surface, giving heap angle of powder on paper. Angle of repose was calculated by following equation.

$$\tan \theta = h/r$$

- Where, h & r is height band radius of powder cone.

6. **Bulk density**

- Bulk density was obtained by dividing mass of powder by bulk volume in cm^3. It was calculated by using equation

Bulk density = mass of microspheres / bulk volume

7. **Tapped density**

- It is ratio of total mass of powder to tapped volume of powder. It is expressed in g/ml and is given by

Tapped density = mass of microspheres/Tapped volume

8. Drug entrapment efficiency

- It is percentage of drug that is successfully entrapped with in microspheres. Drug entrapment efficiency can be calculated using following equation,

% Entrapment = Actual content / Theoretical content x 100

9. Swelling index

- It is conducted in phosphate buffer of pH 6.8. Their diameter is measured periodically by using laser particle size distribution analyzer until they were decreased by erosion & dissolution.

Swelling index = (mass of swollen microspheres – mass of dry microspheres/mass of dried microspheres) 100

10. In vitro methods

- Release studies for different type of microspheres are carried out by using phosphate buffer pH 7.4, mostly by rotating paddle apparatus. Agitated with 100 rpm, samples were collected at specific time intervals & replaced by same amount & analyzed.

11. Adhesion property

- Freshly cut piece of pig intestine is used, clean and wash it with isotonic saline solution. Accurate weight of microspheres was placed on mucosal surface, phosphate buffer of pH 6.8 is warmed at 37°C was peristaltically pumped at rate of 5 ml/min over tissue. Duration of complete washing of microspheres from pig intestine was recorded.

12. Buoyancy Lag Time

- Buoyancy lag time (BLT): The time taken for dose structure to arise on surface of medium called floating lag time (FLT) or buoyancy lag time (BLT).
- Buoyancy time: The time during which the dose structure stays light were estimated.

13. Floating Time

- Test for buoyancy is normally acted in (SGF) Simulated Gastric Fluid kept up at 370˚C. The time for which the measurements structure ceaselessly skims on the disintegration media is named as floating time.

III. METHOD OF PREPARATION

3.1 Method of Preparation[1]

Planning of microspheres ought to fulfill certain standards:

a. The capacity to fuse sensibly high concentrations of medication.
b. Stability of arrangement after blend with clinically adequate shelf life.
c. Controlled molecule size and dispersability in watery vehicles for infusion.
d. Release of dynamic reagent with great power over wide time scale.
e. Biocompatibility with controllable biodegradability and
f. Susceptibility to substance alteration.

The decision of method relies on nature of polymer also nature of medication and term of treatment. Most significant physical substance factors that might be controlled in microsphere make are:-

- The molecule size necessity
- Molecular weight of polymer
- Polymer to sedate proportion
- No soundness issue
- Final item ought to be non-harmful.
- Total mass of medication and polymer
- Reproducibility
- Controlled molecule size and dispersability in watery vehicles for infusion
- Release of dynamic reagent with great power over wide time scale

3.2 Techniques For Microsphere Preparation

1. Single emulsion techniques
2. Double emulsion techniques
3. Polymerization

A. Normal polymerization

a) Bulk
b) Suspension
c) Emulsion

B. Inter-facial polymerization

4. Phase separation co-acervation technique
5. Spray drying
6. Emulsion solvent evaporation tech.
7. Solution-enhancement dispersion method
8. Wax coating Hot-melt method

1. **Single emulsion technique**

- There are a few Proteins and sugars, which are set up by this method. In which characteristic polymers are disintegrated in watery medium and followed by scattering in oil stage for example non-fluid medium.
- That is initial phase in Next advance cross linking is done by 2 techniques:-

1. Cross linking by heat: by including scattering into warmed oil, however it is inadmissible for thermo labile medications.
2. Chemical cross linking operators: - by utilizing specialists for example formaldehyde, di corrosive chloride, and glutaraldehyde and so on however it is having disservice of unreasonable presentation of dynamic fixing to synthetic compounds whenever included a season of arrangement and afterward exposed to centrifugation, washing and detachment. Chitosan arrangement (in acidic corrosive) by adding to Liquid paraffin containing surfactant coming about development of w/o emulsion. Metformin hydrochloride microspheres are plan by utilizing gluteraldehyde 25% arrangement as cross linking operator.

2. **Double emulsion technique**

- It is development of numerous emulsions for example W/O/W is planning by pouring essential w/o emulsion into watery arrangement of poly vinyl liquor. This w/o/w emulsion put t steady mixing for 30 min. gradually add some water to emulsion over time of 30 min. gather Microcapsules by filtration and dry under vacuum. It is most appropriate to water solvent medications, peptides, proteins and antibodies. Common just as engineered polymer can use for this strategy. Watery protein arrangement is scattered in lipophilic natural nonstop stage. This protein arrangement may contain dynamic constituents. Scatter in oil/natural stage homogenization/energetic for example arrangement of first emulsion then expansion to watery arrangement of PVA (Poly Vinyl Alcohol) for example different emulsion framed now by expansion to enormous watery stage denaturation/solidifying after this detachment, washings' and drying and assortment of microspheres genistein chitosan microsphere were set up by o/w/o numerous emulsion strategy by Wu and Li (2002).

3. **Polymerization techniques**

- Basically two procedures are utilizing for readiness of microsphere are named:

a) Normal polymerization

- In mass polymerization, monomer or combination of number of monomers alongside initiator or impetus is typically warmed to start polymerization. Polymer so acquired might be formed as microspheres. Medication stacking might be finished by including drug during cycle of polymerization. It is unadulterated polymer development procedure however it is exceptionally hard to disperse warmth of response which influences thermo labile dynamic fixings. Suspension polymerization is completed of lower temperature and furthermore alludes to as pearl polymerization in which warming monomer blend with dynamic medication as beads scattering in constant fluid stage. Microsphere size acquired by suspension procedures is less 100 µm. Emulsion polymerization is vary from suspension as due presence of initiator in watery eliminate but at the same time is conveyed at low temperature as suspension outside stage regularly water in last two strategies so through which warmth can undoubtedly disperse arrangement of higher polymer at quicker rate is conceivable by these methods however relationship of polymer with un responded monomer and different added substances can happen.[2]

b) Interfacial polymerization

- It includes response of different monomers at interface between two immiscible fluid stages to shape film of polymer that basically encompasses scattered stage. In this procedure two responding monomers are utilized; one is break down in ceaseless stage while other is scatter in nonstop stage (fluid in nature) all through which second monomer is emulsified. Two conditions emerge due to solvency of framed polymer in emulsion bead. That is arrangement is solid kind of transporter if polymer is solvent in bead. Capsular sort framed if polymer is insoluble in bead.

4. Spray drying and spray congealing

- Idea of spray drying method (fig 8) contingent on expulsion of dissolvable or cooling of arrangement two cycles are spray drying and spray hardening. Dissipation is essential system in spray drying, though in spray congealing it is that of stage reversal from fluid to strong. The two cycles are comparative, aside from energy stream. Spray drying is most generally utilized modern cycle including molecule development and drying. Thusly, spray drying is ideal cycle where finished result must conform to exact quality norms with respect to molecule size circulation, lingering dampness content, mass thickness, and molecule shape.

- Principle: Three stages associated with spray drying

1. Atomization: of fluid feed change into fine beads.
2. Mixing: it includes passing of hot gas stream through spray beads which bring about dissipation of fluids and abandoning dried particles.
3. Dry: Dried powder is isolated from gas stream and gathered.

- In this method polymer is first disintegrated in appropriate unstable natural dissolvable, for example, dichloromethane, $(CH_3)_2CO$, and so on drug in strong structure is then scattered in polymer arrangement under rapid homogenization. This scattering is then atomized in stream of hot air, this structure little beads or fine fog, from which dissolvable vanishes quickly driving development of microspheres. Size reach is 1-100 µm. By utilizing hot air separate of Microparticle by methods for typhoon separator while hints of dissolvable are eliminated by vacuum drying. Favorable circumstances of cycle are practicality of activity. This strategy is exceptionally helpful to embody different penicillin's. Thiamine mononitrate and sulpha ethylthiadizole are embodied in combination of mono-and diglycerides of stearic corrosive and palmitic corrosive utilizing spray hardening. Exceptionally fast dissolvable vanishing anyway prompts development of permeable microparticles.
- The sprays are creates by either revolving (wheel) or spout atomizers. Dissipation of dampness from beads and development of dry particles continue under controlled temperature and wind stream conditions.
- The microsphere size is controlled by pace of spraying, spout size, temperature (in drying and gathering chambers.) and feed pace of polymer drug arrangement. Nature of item is improved by expansion plasticizer spray stream rate should kept steady around 6ml/min.
- Spray drying strategy is likewise helpful for planning chitosan microsphere [9], In 1999 He et.al. Utilized formaldehyde as cross linking and furthermore detailed novel technique in which cimetidine and famotidine were ensnared in microspheres arranged by spray drying of numerous emulsion (o/w/o or w/o/w). They found that release of medications from microspheres by this novel technique was altogether sustained when contrasted with those readied by traditional spray drying or o/w emulsion strategy. In 1994 Giunchedi et al. was utilized spray drying utilized for arrangement of PCL microspheres of ketoprofen. He utilized natural arrangement of medication and two polymers, cellulose acetic acid derivation butyrate and PCL was made in combination of dichloromethane and chloroform (1:1). Arranged arrangement was sprayed through spout in spray drier under

various exploratory conditions. Strong microspheres were gathered into definite base vessel spray drier.

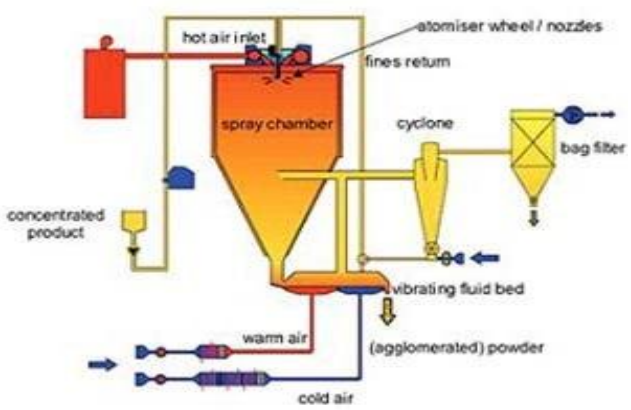


Figure 8: Spray drying method for preparation of microspheres.

- **Advantages and disadvantages**

➢ Spray drying is very useful for pulmonary drug delivery as well as for oral dosages form and it is remarkable versatility of technology, and wide range of product can be obtained by this technique. It is very flexible and reproducible method that, why number of industries use this technique for drying operation. It can be designed to virtually any capacity required easily. Can be used with both heat-resistant and heat sensitive products. Powder quality remains constant during dryer. Particles which produced uniform in size and frequently hollow thus reduce bulk density of product. But there are some drawbacks in technique; equipment is very bulky and expensive. Overall thermal efficiency is low, as large volumes of heated air pass through chamber without contacting particle.

5. Wax Coating and Hot Melt

➢ In this method polymer is scatter in appropriate scattering medium and gradually cooled to frame microspheres. Polymers which having low liquefying point manufactured into microspheres by this strategy without any problem.[10] For coating and coring of molecule wax is use generally. In which exemplify drug by scattering in shed wax. Wax suspension is scattered by rapid blending into cold answer for instance fluid paraffin. Unsettle blend for 60 minutes. At that point emptied outside stage and suspended microspheres gather from dissolvable. Also, permit drying it in air. It is economic strategy as correlation with others and medication release is quicker. Generally Carnauba wax and beeswax can be utilized as coating materials and these can be blended so as to accomplish wanted attributes.

6. Emulsion Solvent Evaporation Technique

- In this strategy drug is broken down in polymer which was recently disintegrated in chloroform and coming about arrangement is added to watery stage containing 0.2% sodium of PVP as emulsifying operator. Above blend was fomented at 500 rpm at that point medication and polymer (eudragit) was changed into fine bead which set into inflexible microspheres by dissolvable vanishing and afterward gathered by filtration and washed with demineralised water and dried up at room temperature for 24 hrs.

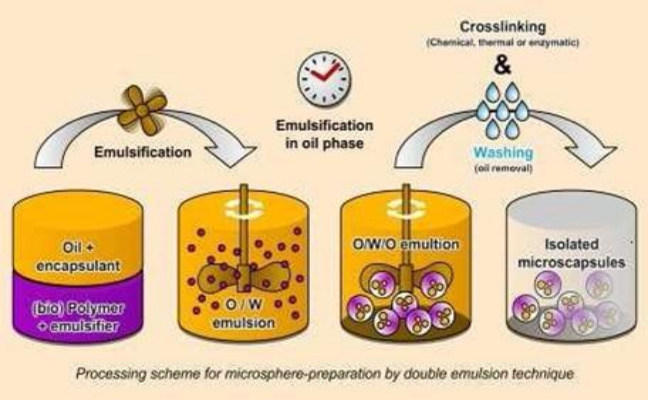


Figure 9: Microspheres by Double Emulsion Technique.

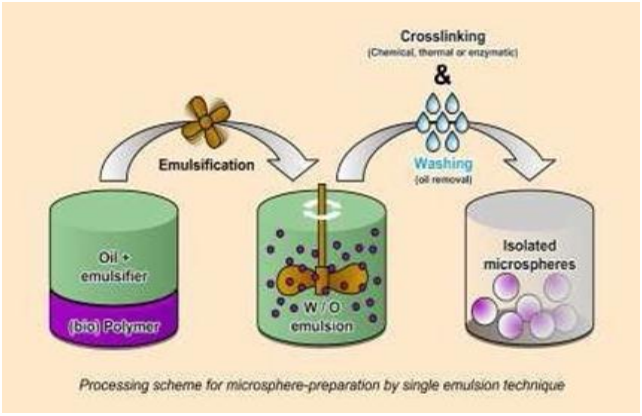


Figure 10: Microspheres by Single Emulsion Technique.

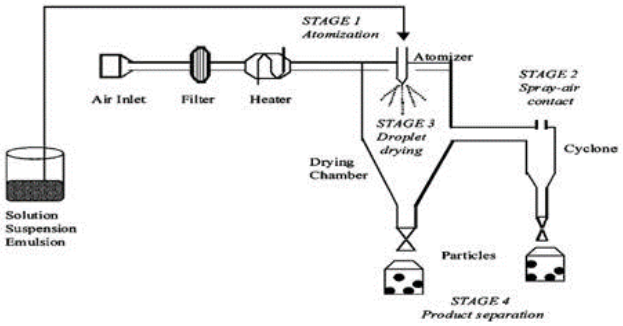


Figure 11: Microspheres by Spraying Drying Technique.

7. Phase separation co-acervation technique

- It is straightforward separation of micromolecular arrangement into two immiscible fluid phases. In this cycle, polymer is solubilized to for arrangement. This cycle is intended for getting ready store type framework for example exemplify water solvent medications for example peptides, proteins and so forth. Guideline of co-acervation is diminishing solvency of polymer in natural phase to influence arrangement of polymer rich phase called co-acervates. In this technique, arrangement of scattering of medication particles in arrangement of polymer and contradictory polymer is added to framework which makes first polymer to phase isolate and immerse drug particles. Matrix type's arrangements can likewise be set up by this cycle for hydrophilic medication for example steroids, Addition of non-dissolvable outcomes in cementing of polymer. Poly lactic corrosive (PLA) microspheres have been set up by this strategy by utilizing butadiene as inconsistent polymer.

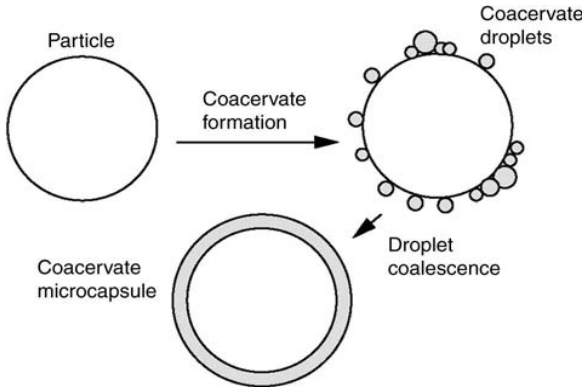


Figure 12: Schematic diagram of formation of co-acervate around core material.

- Be that as it may, this strategy isn't reasonable for natural solvents and glutaraldehyde which are harmful in nature. Berthold et al. (1996a) arranged prednisolone sodium phosphate stacked chitosan microspheres utilizing sodium sulphate as precipitant. Expansion of sodium sulphate to arrangement of chitosan in acidic corrosive brought about diminished dissolvability of chitosan, prompting precipitation of chitosan as ineffectively solvent subsidiary.

8. Solvent extraction

- In this strategy readiness of microparticles, includes evacuation of natural phase by extraction of natural solvent. Isopropanol can be utilized as water miscible natural solvents. By extraction with water, Organic phase is eliminated. Solidifying season of

microsphere can be decline by this technique. One variety of cycle includes direct expansion of medication or protein to polymer natural arrangement. Pace of solvent evacuation by extraction technique relies upon temperature of water, proportion of emulsion volume to water and dissolvability profile of polymer.

9. Emulsification method

- Multiple emulsions may also be formed for instance; warmed watery medication arrangement can be scattered in liquid wax to shape water-in-oil emulsion, which is emulsified in warmed outer fluid phase to frame water-in-oil-in-water emulsion. Framework is cooled and microcapsules gathered. For profoundly fluid dissolvable medications, non - aqueous phase can be utilized to forestall loss of medication to outside phase. Another option is to quickly diminish temperature when essential emulsion is set in outside watery phase.

IV. RESULT AND DISCUSSION

4.1 Pre Formulation Studies

1. Organoleptic properties

- These tests were preceded as strategy given, Preformulation part. The outcomes are delineated in after table.

Table 1: Organoleptic properties.

Test	Specifications/limits	Observations
Color	White to off white	Off White powder
Odor	Odorless	Odorless

The results complies as per specifications

2. Angle of repose

- It was resolved according to methodology preformulation in material and technique part.
- The outcomes are represented in after table.

Table 2: Flow properties.

Material	Angle of repose
Abacavir sulphate	29.26”

The result shows that drug having poor flow

3. Bulk density and tapped density

- It was resolved according to methodology given preformulation in material and technique part. The outcomes are delineated in table.

Table 3: Density.

Materials	Bulk Density(gm/ml)	Tapped density(gm/ml)
Abacavir sulphate	0.17	0.24

4. Powder compressibility

- It was resolved according to methodology given in preformulation in material and technique part. The outcomes are outlined in table.

Table 4: Powder compressibility.

Material	Compressibility index	Hausner's ratio
Abacavir sulphate	28.02%	1.32

The results shows that drug having poor flow property

5. Melting point

- It was resolved according to technique given in preformulation in material and strategy part. The outcomes are represented in after table.

Table 5: Melting point.

Material	Material point range	Result
Abacavir sulphate	163 °C	Complies

The result complies as per specification.

4.2 SOLUTION PROPERTIES

1. pH of the solution

- It was resolved according to system given in preformulation in material and strategy part. The outcomes are represented in after table.

Table 6: pH.

Material	Test	Specification	Observation
Abacavir sulphate	pH	7.3	7.3

The result complies as per specification

2. Solubility

- It was determined as per procedure given in preformulation in material and method part. The results are illustrated in following table.

Table 7: Solubility.

Test	Specification	Result
solubility	Freely soluble in water, Sparingly soluble in DMSO, ethanol, methanol	Complies

The result complies as per specification.

4.3 DRUG-EXCIPIENT COMPATABILITY STUDIES

Discussion

- Medication excipient associations accept a fundamental part with respect to appearance of medication from detailing among others. FTIR methods have been used here to inspect the physical and substance correspondence among drug and excipient used.

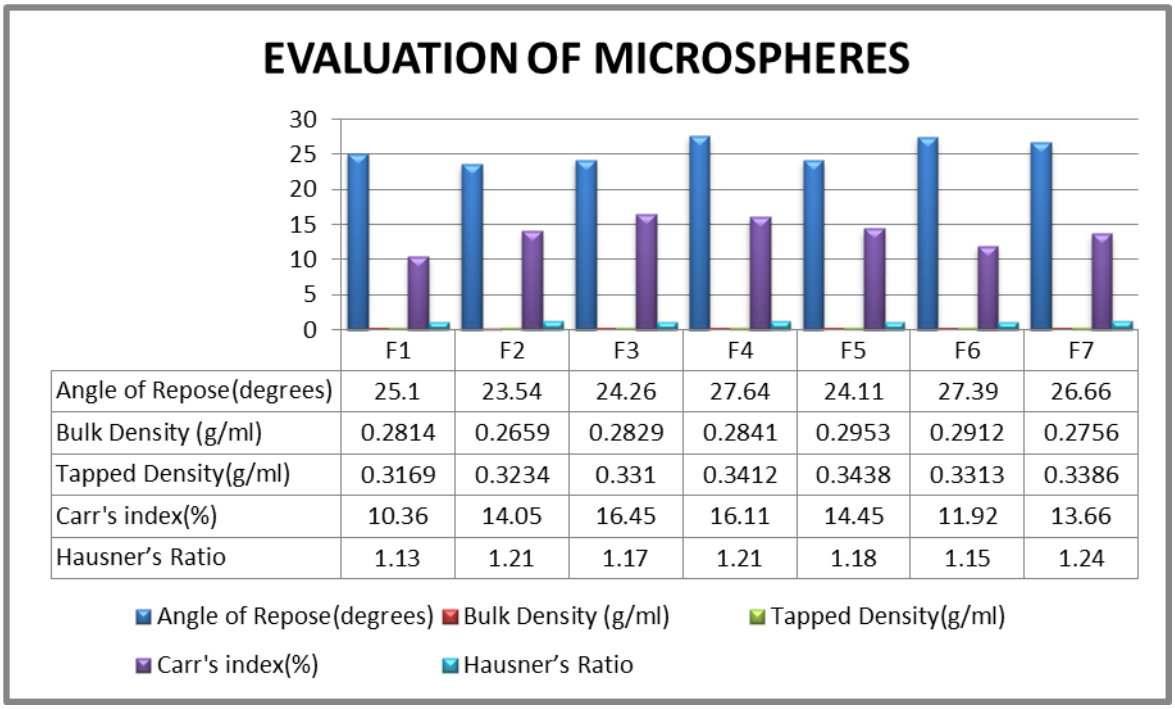
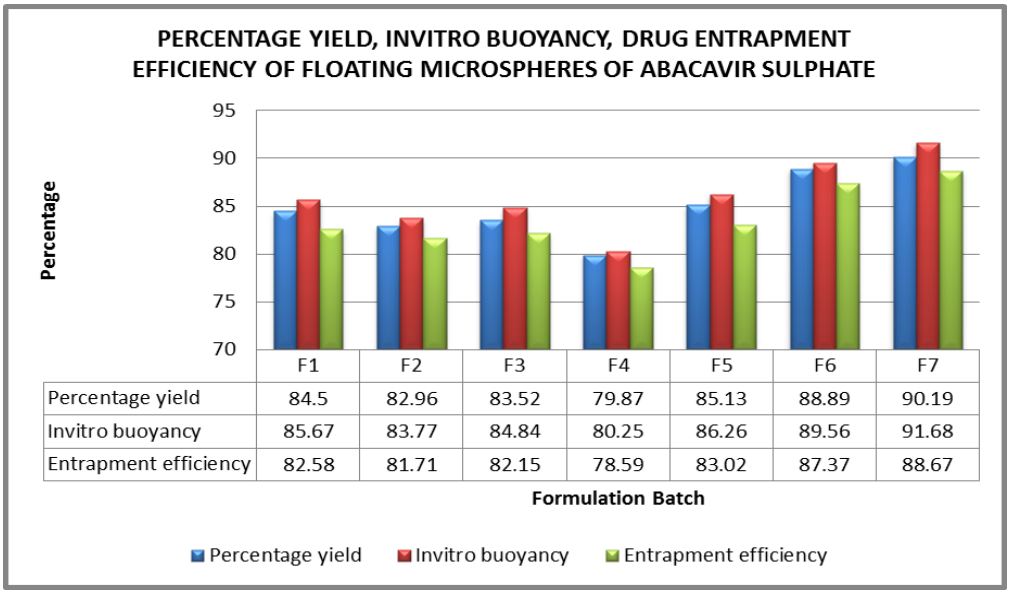


Figure 13: Evaluation of Microspheres.

Discussion

- Angle of repose for the formulations F1-F7 was found to be in the range 23.54º to 27.64º shows excellent flow property.
- Carr's index for the formulations F1-F7 found between 10.36% and 16.11% representing the good flow property.



	F1	F2	F3	F4	F5	F6	F7
Percentage yield	84.5	82.96	83.52	79.87	85.13	88.89	90.19
Invitro buoyancy	85.67	83.77	84.84	80.25	86.26	89.56	91.68
Entrapment efficiency	82.58	81.71	82.15	78.59	83.02	87.37	88.67

Figure 14: Percentage yield, In-vitro Buoyancy, Drug Entrapment efficiency of Floating Microspheres of Abacavir sulphate.

1. **Percentage yield**

- The most limit percentage yield was found in F7 formulation and was noted to be 90.19% among all formulations.
- The floating microspheres were set up with different and mix of two polymer of HPMC K4M, HPMC K100M, Sodium Alginate and Sodium CMC to explore the effect of epitome capability and were used to choose its impact on floating behavior.

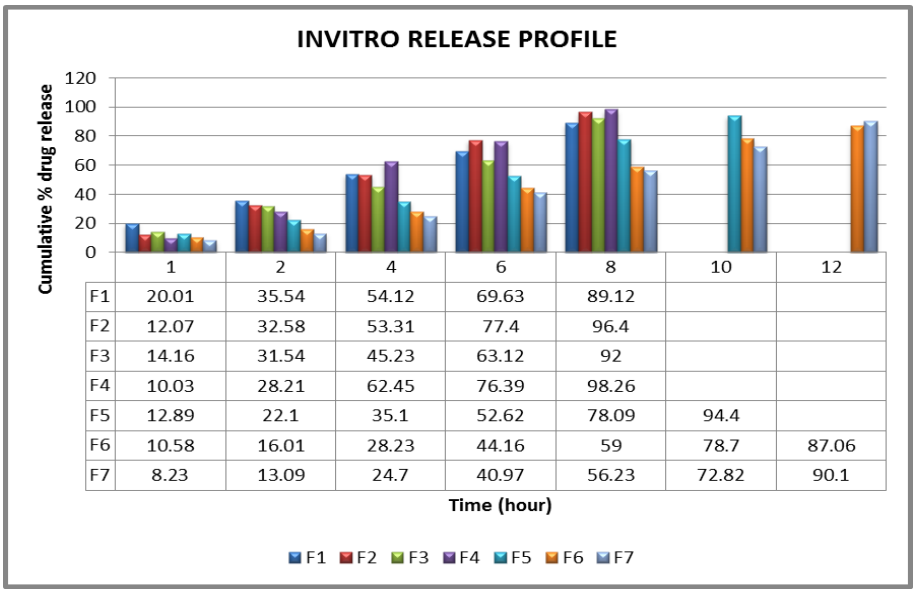
2. **In-vitro Buoyancy Discussion**

- The various polymers with same ratios of formulation were picked for upgrade of their buoyancy property. The formulations where mix of HPMC K4M, HPMC K100Mare giving the better results.
- The formulations are picked as the best formulations depending on their buoyancy, epitome capability. From the delayed consequences of the overall large number of ten formulations, it is asserted that the change of polymers of Sodium Alginate, Sodium CMC, HPMC K4M, and K100M impacts the properties of the formulations. The formulation F7 with drug and mix of two polymer 1:1 ratio, is giving the best result of buoyancy property.
- The microspheres, having lower densities (having an unfilled focus) showed buoyancy and are needed to be held in gastric environment for more than 12 hrs. This may be credited to a reducing in thickness of microspheres with an augmentation in polymer concentration.

Figure 15: Buoyancy Study of Floating Microspheres.

3. Entrapment efficiency Discussion

- The percentage entrapment efficiency of various formulation limits of the prepared microspheres were showed up in table. The entrapment efficiency changed from 78.59 to 88.67.
- The formulation F7 is having high embodiment efficiency of 88.67% and F4 is having low encapsulation efficiency of 78.59%.
- The low representation is a consequence of using single polymer of HPMC K100M than the medicine concentration where the measure of HPMC K100M is deficient to trap the drug. The high embodiment efficiency is an immediate aftereffect of using mix of polymers of HPMC K100M, HPMC K4 where the augmentation in the HPMC concentration structures greater microspheres embodying more proportion of medicine.



	1	2	4	6	8	10	12
F1	20.01	35.54	54.12	69.63	89.12		
F2	12.07	32.58	53.31	77.4	96.4		
F3	14.16	31.54	45.23	63.12	92		
F4	10.03	28.21	62.45	76.39	98.26		
F5	12.89	22.1	35.1	52.62	78.09	94.4	
F6	10.58	16.01	28.23	44.16	59	78.7	87.06
F7	8.23	13.09	24.7	40.97	56.23	72.82	90.1

Figure 16: In-vitro Release Profile.

Discussion

- From the starting of In-vitro dissolution study of all formulations (F1-F7), formulation F7 discharge approximately 90.10% of drug at the end of 12 hours for a sustained release and the formulation F7 selected as the most excellent formulation from all seven batches.

4. Scanning Electron Microscopy (SEM)

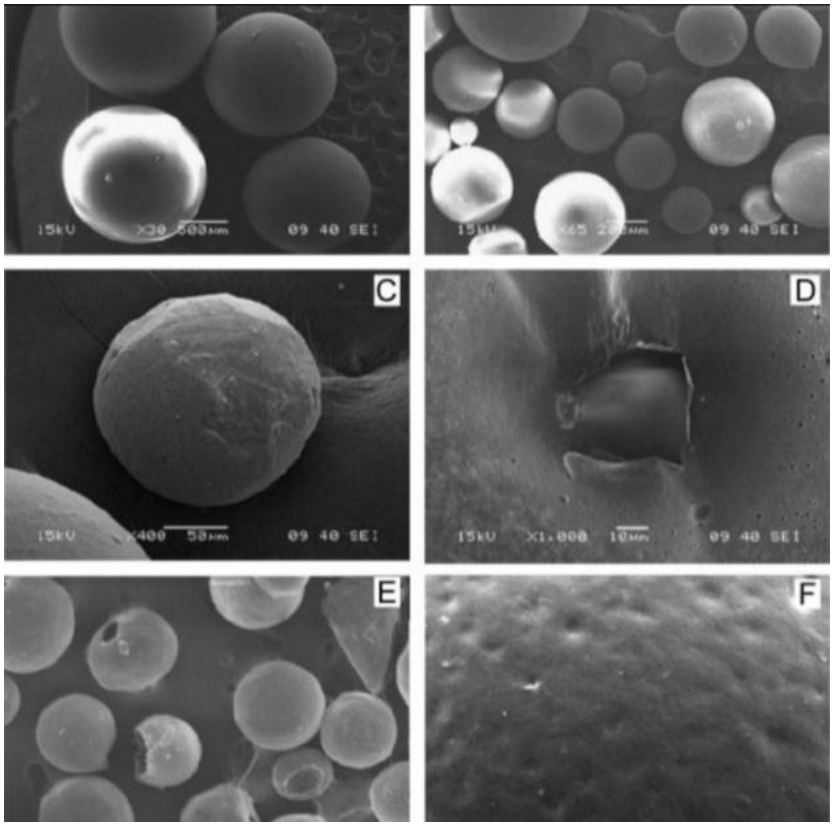


Figure 17: Scanning electron microscopy.

Discussion

- Morphology of floating microspheres was dissected by scanning electron microscopy. The viewpoint on the microspheres showed void development with a smooth surface morphology showed extent of sizes inside each bunch. The outer surface of microspheres was smooth and thick, while the inside surface was penetrable. The shell of microspheres also showed some penetrable development it may be achieved by evaporating of dissolvable caught inside the shell of microsphere in the wake of outlining smooth and thick layer.

V. CONCLUSION

- It has been observed that microspheres are better choice of drug delivery system because it is having advantage of target specificity and better patient compliance. Number of methods has been devised to prepare microspheres of desired size shape and surface. A complete goal for sustained drug release is to help healing activity while restricting the negative manifestations of the drug. In such way, floating microspheres have emerged as a novel drug delivery system to treat HIV with Abacavir sulfate.
- The sort of polymer influences the drug discharge rate and the mechanism. In this examination sustained delivery Floating Microsphere approach for Abacavir sulfate purposes that with hydrophilic polymers the GI maintenance can be upgraded and decrease recurrence of dosing, consequently limiting the event of results, site particularity, increment the adequacy of the drug and better persistent consistence.
- At the point when these floating microspheres diverged from other floating dosage forms like floating tablets have mass thickness not by and large gastric fluid consequently stay light in the stomach for deferred time period. So in feature; microspheres will have important role to play in advancement of medical field.

VI. SUMMARY

- In this study of Microspheres were prepared successfully using solvent evaporation method and also include formulation & evaluation of sustained delivery floating microspheres of Abacavir sulfate. Formulation was found to be efficient with good recovery yield, percentage drug entrapment.
- Preformulation studies including Organoleptic properties like Bulk density, Tapped density, Angle of Repose, Carr's index, Hausner's ratio, Melting point range, pH, Solubility.
- Microspheres are promising pharmaceutical dosage forms by providing better drug delivery systems and avoiding dose related side effects in entire physiological region.
- Various polymers like sodium carboxy methyl cellulose, sodium alginate, HPMC K4M, HPMC K100M were used in the preliminaries. All the evaluations are approved in preformulation studies were used by utilization of three polymers.
- Evaluation of Abacavir Sulphate Floating Microspheres includes Micromeritics properties, Buoyancy studies, SEM and Drug entrapment efficiency.
- Delivery considers were done in 0.1N HCL for 12 hours and studied tests for all the four polymer system. Results showed that specifying F7 submits 90.10% delivery to 12 hrs

which is portrayed with HPMC K100M and HPMCK4M blend. Dissect was refined for plan F7 and was discovered to be 88.67%. The portion of drug discharge from microspheres follows Non-Ficknian discharge.

- The formulation F7 selected as the most excellent formulation from all seven batches of Abacavir Sulphate floating Microspheres.

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