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Review Article

A Brief Review about Microspheres

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Preparation of microspheres offers a multiplicity of opportunities to control aspects of drug administration. There are a variety of approaches in distribution a therapeutic substance to the intend site in a sustained controlled release fashion. This systems based on non effervescent approach. It is the reliable means to deliver the drug to the target site with specificity, Moreover the microspheres are micron size so they can easily fit into various capillary beds which are also having micron size. Among them microspheric drug delivery system has gained enormous attention due to its wide range of application as it covers targeting the drug to particular site to imaging and helping the diagnostic features Microspheres received much attention not only for long-lasting release, but also for objective of anticancer drugs. The purpose of the review is to accumulate various types of microspheres, altered methods to preparation, its function and also various parameters to evaluate their efficiency.

Keyword: Microspheres, Anticancer, Capillary beds

INTRODUCTION

Microspheres are small spherical particles, with diameters in the micrometer range (usually 1 μm to 1000 μm). Microspheres are from time to time referred to as microparticles. Microspheres be capable of manufactured from a range of natural and synthetic materials. polymer microspheres, Glass microspheres and ceramic microspheres are commercially obtainable. hard and hollow microspheres vary commonly in density and, consequently, are used for diverse applications. unoccupied microspheres are naturally used as additives to lower the density of a substance. hard microspheres have many applications depending on what material they are constructed of and what size they are Polyethylene and polystyrene microspheres are two most common types of polymer microspheres[1]. Polystyrene microspheres are usually used in biomedical applications due to their ability to facilitate procedures such as cell sorting and immuno precipitation. Ligands and Proteins adsorb on polystyrene readily and eternally, which make polystyrene microspheres appropriate for medical research and biological laboratory testing. Polyethylene microspheres are normally used as eternal or temporary filler. lesser melting temperature permit polyethylene microspheres to create porous structures in ceramics and other materials,[2]

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Types of Microspheres

Magnetic microspheres: This kind of delivery system is very much important

which localises the drug to the disease position. In this big amount of to all comers circulating drug can be replaced by smaller amount of magnetically beleaguered drug. Magnetic carriers obtain magnetic answer to a magnetic field from incorporated materials that are used for magnetic microspheres are chitosan, dextran etc.[3] The different type are Therapeutic magnetic microspheres: Are used to deliver chemotherapeutic agent to liver swelling. Drugs similar to proteins and peptides can also be targeted through this system.[4]Diagnostic microspheres: Can be used for imaging liver metastases and also can be used to distinguish bowel loops from other abdominall structures by forming nano size particles supra magnetic iron oxides.[5]

Bio adhesive microspheres

Adhesion can be defined as sticking of drug to the membrane by using the sticking property of the water soluble polymers. Adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc can be termed as bio adhesion. These kinds of microspheres exhibit a prolonged residence time at the site of application and causes intimate contact with the absorption site and produces better therapeutic action.[4]

Floating microspheres: In floating types the bulk density is less than the gastric fluid and so remains buoyant in Stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate, if the system is floating on gastric content and increases gastric residence and increases fluctuation in plasma concentration. Moreover it also reduces chances of striking and dose dumping. One another way it produces prolonged therapeutic effect and there fore reduces dosing frequencies. Drug (ketoprofen) given through this form[6]

Radioactive microspheres : Radio immobilisation therapy microspheres sized10-30 nm are of larger than capillaries and get stepped in first capillary bed when they come across. They are injected to the arteries that lead to tumor of interest. So all these conditions radioactive microspheres deliver high radiation dose to the targeted areas without damaging the normal surrounding tissues.[7]It differs from drug delivery system, as radio activity is not released from microspheres but acts from within a radioisotope typical distance and the different kinds of radioactive microspheres are α emitters, β emitters, γ emitters.[8]

Polymeric microspheres

The different types of polymeric microspheres can be classified as follows and they are biodegradable polymeric

microspheres and Synthetic polymeric microspheres.

Biodegradable polymeric microspheres:

Natural polymers such as starch are used with the concept that they are Bio degradable,bio compatible, and also bio adhesive in nature. Bio degradable polymers prolongs the residence time when contact with mucous membrane due toit's high degree of swelling property with aqueous medium, results gel formation. The rate and extent of drug release is controlled by concentration of polymer,[8] and the release pattern in a sustained manner. The main drawback is, in clinical use drug loading efficiency of biodegradable microspheres is complex and is difficult to control the drug release .However they provide wide range of application in microsphere based treatment.[9]

Synthetic polymeric microspheres

The interest of synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulk in agent, fillers, embolic particles, drug delivery vehicles etc and proved to be safe and biocompatible.[9] The main disadvantage of these kind of microspheres, are tend to migrate away from injection site and lead to potential risk,embolism and further organ damage.[10]

Method of Preperation

Incorporation of solid, liquid or gases into one or more polymeric coatings can be done by microencapsulation technique.[11] The different methods used for various microspheres preparation depends on particle size, route of administration, duration of drug release and these above characters related to rpm, method of cross linking, drug of cross linking ,evaporation time, co precipitation etc.[12]

Emulsion solvent evaporation technique

In this technique the drug is dissolved in polymer which was previously dissolved in chloroform and the resulting solution is added to aqueous phase containing 0 .2 % sodium PVP as emulsifying agent. The above mixture was agitated at 500 rpm then the drug and polymer (eudragit) was transformed into fine droplet which solidified into rigid microspheres by solvent evaporation and then collected by filtration and washed with demineralised water and desiccated at room temperature for 24hrs.[13]Aceclofenac microspheres were prepared by this technique.

Emulsion cross linking method

In this method drug was dissolved in aqueous gelatine solution which was previously heated for 1hr at 40ºC. The solution was added drop wise to liquid paraffin while stirring the mixture at 1500rpm for 10 min at 35ºC results in w/o emulsion then further stirring is done for

10 min at 15ºC.Thus the produced microspheres were washed respectively three times with acetone and Isopropyl alcohol which then air dried and dispersed in 5mL of aqueous glutaraldehyde saturated toluene solution at room temperature for 3 hrs for cross linking and then was treated with 100mL of 10 mm glyciene solution containing 0.1%w/v of tween 80 at 37ºc for 10min to block un reacted glutaraldehyde. Examples for this technique is Gelatin a microspheres.[14]

Co-acervation method

Co-acervation thermal change: Performed by weighed amount of ethyl cellulose was dissolved in cyclohexane with vigorous stirring at 80ºc by heating. Then the drug was finely pulverised and added with vigorous stirring on the above solution and phase separation was done by reducing temperature and using ice bath. Then above product was washed twice with cyclohexane and air dried then passed through sieve (sieve no. 40) to obtain individual microcapsule.[11]Co-acervation non solvent addition: Developed by weighed amount of ethyl cellulose was dissolved in toluene containing propyl isobutylene in closed beaker with magnetic stirring for 6 hr at500 rpm and the drug is dispersed in it and stirring is continued for 15 mins. Then phase separation is done by petroleum benzoin 5 times with continuous stirring.[11]After that the microcapsules were washed with n-hexane and air dried for 2 hr and then in oven at 50ºC for 4 hrs.[11]

Spray drying technique

This was used to prepare polymeric blended microsphere loaded with ketoprofen drug. It involves dispersing the core material into liquefied coating material and then spraying the mixture in the environment for solidification of coating followed by rapid evaporation of solvent.[15] Organic solution of poly (epsilon-caprolactone) (PCL) and cellulose acetate butyrate (CAB), in different weight ratios and ketoprofen were prepared and sprayed in different experimental condition achieving drug loaded microspheres. This is rapid but may loose crystalinity due to fast drying process.[15]

Emulsion-solvent diffusion technique

In order to improve the residence time in colon floating micro particles of ketoprofen were prepared using emulsion solvent diffusion technique. The drug polymer mixture was dissolved in a mixture of ethanol and dichloromethane (1:1) and then the mixture was added drop wise to sodium laury lsulphate (SLS) solution. The solution was stirred with propeller type agitator at room temperature at150 rpm for 1 hr. Thus the formed floating microspheres were washed and dried in a desiccators at room temperature.

The following micro particles were sieved and collected.[15]

Multiple emulsion method

Oral controlled release drug delivery of indomethacin was prepared by this system. In the establishment powder drug was diffuse in solution (methyl cellulose) followed by emulsification in ethyl cellulose solution in ethyl acetate. The primary emulsion was then re emulsified in aqueous standard. below optimized situation discrete microspheres were formed during this phase.[15]

Ionic gelation

Alginate/chitosan particulate system for diclofenac sodium release was prepared using this technique. 25%(w/v) of diclofenac sodium was added to 1.2%(w/v) aqueous solution of sodiumalginate.In order to get the complete solution stirring is continued and after that it was added drop wise to a solution containing Ca2+ /Al3+ and chitosan solution in acetic acid. Microspheres which were created were held in reserve in original solution for 24 hr for internal gellification followed by filtration for partition. The complete discharge was obtain at pH 6.4-7.2 but the drug did not liberate in acidic pH.[15]

Hydroxyl appetite (HAP) microspheres in sphere morphology

This was used to prepare microspheres with peculiar spheres in sphere morphology microspheres were prepared by o/w emulsion followed by solvent desertion. At primary o/w emulsion was primed by dispersing the organic phase (Diclofenac sodium containing 5% w/w of EVA and appropriate amount of HAP) in aqueous phase of surfactant. The untreated phase was diffuse in the form of tiny droplets which were surrounded by surfactant molecules this prevented the droplets from co solvencing and helped them to stay individual droplets .While stirring the DCM was slowly evaporated and the droplets solidify individual to become microspheres.[16]

Classification of Drug Delivery System

A. Single Unit Floating Dosage Systems

- Effervescent Systems (Gas-generating Systems)
- Non-effervescent Systems

B. Multiple Unit Floating Dosage Systems

- Non-effervescent Systems
- Effervescent Systems (Gas-generating Systems)
- Hollow Microspheres

C. Raft Forming Systems

A. Single Unit Floating Dosage Systems

a) Effervescent Systems *(Gas-generating Systems)* These buoyant systems utilized matrices prepared with swell able polymers similar to HPMC, polysaccha-rides similar to chitosan, aerated components like sodium bicarbonate, citric

acid and tartaric acid or chambers containing a liquid that gasifies at body temperature. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1. The ordinary approach for prepare these systems involves resin beads loaded with bicarbonate and coated with ethyl cellulose. The coating, which is insoluble but permeable, allow permeation of water. Thus, carbon dioxide is free, cause the beads to float in the stomach.[17] Excipients used most commonly in these systems contain HPMC, polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates.

b) Non-Effervescent Systems

This type of system, later swallowing, swells uncontrolled via inhibition of gastric fluid to an extent that it prevents their exit since the stomach. These system may be referred as the 'plug-type systems' since they have a tendency to remain lodged near the pyloric sphincter. The formulation methods of such dosage forms involves the mixing of drug with a gel, which swells in make contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than one within the outer gelatinous barrier. The air trapped by the enlarged polymer confers buoyancy to these dosage forms. Examples of this kind of FDDS contain colloidal gelbarrier microporous compartment system, alginate beads,[18] and hollow microspheres,[19] Another type is a Fluid- filled floating chamber,[20] which includes incorporation of a gas-filled floatation chamber into a micro porous component that houses a drug reservoir. Aperture or openings are found along the top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug. The other two walls get in touch with the fluid are sealed so that the un dissolved drug remnants therein. The fluid present possibly will be air, below partial vacuum or any previous appropriate liquid gas, or hard have an suitable specific gravity and an immobile performance. The appliance is of consume talented bulk, remains afloat within the stomach for a prolonged time and after the whole release the shell,[21] has a 3-layermatrix to control the drug release. This three-layer standard have improved by development of an asymmetric configuration drug delivery system in order to modulate the release extent and achieve zero-order release kinetics by initially maintaining a constant area at the diffusing front with subsequent dissolution/erosion toward the completion of the release process. Scheme was considered that it floated to prolong gastric

dwelling time in vivo, consequential in entire transit time the gastrointestinal tract environment with maximum absorptive capacity and consequently greater accessibility. This scrupulous attribute should be valid to drugs that encompass pH-dependent solubility, slim skylight of assimilation, as well as captivated by energetic convey from moreover the proximal or distal portion of the small intestine.

B. Multiple Unit Floating Systems

In spite of extensive research and development in the area of HBS and other buoyant remedy, these systems undergo from an significant problem of high variability of gastrointestinal transit time, when verbally administer, as their all-or-nothing gastric empty environment. Direct to triumph over the on top of difficulty, numerous element buoyant system be residential, which decrease the inter-subject unpredictability in absorption and lower the probability of dose-dumping. Information have been establish on the progress of both non-effervescent and effervescent multiple unit systems,[22] Much research has been focused and the scientists are still exploring the field of hollow microspheres, competent of buoyant on the gastric solution and having improved gastric retention properties.

a) Non-effervescent Systems No much report was found in the literature on non-effervescent multiple unit systems, as compared to the sparkling system. But few workers has report the opportunity of developing such system containing indomethacin, using chitosan as the polymeric excipient. A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried

b) Effervescent Systems (Gas-generating Systems)

There are information of sustained release floating granules containing tetracycline hydrochloride, The granules are a mixture of drug granulates of two stages of which A contain 60 parts of HPMC, parts of poly acrylic acid and 20 parts of drug and B contains 70 parts of sodium bicarbonate and 30 parts of tartaric acid. 60 parts by weight of granules of stage A and 30 parts by weight of granules of stage B are mixed along with a lubricant and filled into capsule. In dissolution media, the capsule shell dissolves and liberates the granules, which showed a floating time of more than 8 hrs and sustained drug release of 80% in about 6.5 hrs. Floating mini capsules of pepstatin having a diameter of 0.1-0.2 mm has been reported by Umezawa. These mini capsules contain a central core and a coating. The central core consists of a granule composed of sodium bicarbonate, lactose and a binder, which is coated with

HPMC. Pepstatin is coated on the top of the HPMC layer. The system floats because of the CO2 release in gastric fluid and the pepstatin resides in the stomach for prolonged period. Alginates have received much attention in the development of multiple unit systems. Alginates are non-toxic, biodegradable linear copolymers composed of L-glucuronic and L-mannuronic acid residues. comprises of calcium alginate core and calcium. Presence of water, and increases the membrane permeability.[23] Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The non-floating beads had a shorter residence time with a mean onset emptying time of 1h. A new multiple type of floating dosage system had developed having a pill in the core, composed of effervescent layers and swell able membrane layers coated on sustained release pills. The inner layer of effervescent agents containing sodium bicarbonate and tartaric acid was divided into 2 sub layers to avoid direct contact between the 2 agents. These sub layers were surrounded by a swell able polymer membrane containing polyvinyl acetate and purified shellac. When this system was immersed in the buffer at 37°C, it settled down and the solution permeated into the effervescent layer through the outer swell able membrane. CO2 was generated by the neutralization reaction between the 2 effervescent agents, producing swollen pills (like balloons) with a density less than 1.0 g/.[24]

c) Hollow Microspheres

Hollow microspheres are considered as one of the most promising buoyant systems, as they possess the unique advantages of multiple unit systems as well as better floating properties, because of central hollow space inside the microsphere. The general techniques involved in their preparation include simple solvent evaporation and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation. Polymers such as polycarbonate, Eudragit Sand cellulose acetate were used in the preparation of hollow microspheres, and the drug release can be modulated by optimizing the polymer quantity and the polymer-plasticizer ratio.

Sustained release floating microspheres using polycarbonate were developed employing solvent evaporation technique. Aspirin, griseofulvin and p-nitroaniline were used as model drugs. Dispersed

phase containing polycarbonate solution in dichloromethane, and micronized drug, was added to the dispersion medium containing sodium chloride, polyvinyl alcohol and methanol. The dispersion was stirred for 3-4hrs to assure the complete solvent evaporation, and the microspheres obtained were filtered, washed with coldwater and dried. The spherical and hollow nature of the microspheres was confirmed by Scanning electron microscopic studies. The microspheres showed a drug payload of more than 50%, and the amount of drug incorporated is found to influence the particle size distribution and drug release. The larger proportion of bigger particles was seen at high drug loading, which can be attributed to the increased viscosity of the dispersed phase.

C. Raft Forming Systems

Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The raft floats because of the buoyancy created by the formation of CO_2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the esophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids.[25]

Mechanism of Floating Systems

There are various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas-generating systems and swelling or expanding systems, mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices and co-administration of gastric-emptying delaying drugs. Among these, the floating dosage forms have been most commonly used. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

While the system is floating on the gastric contents the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric

content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature.

The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intra gastric buoyancy capability variations F = F buoyancy - F gravity = (Df - Ds) gv Where, F= total vertical force Df = fluid density Ds = object density v = volume and g = acceleration due to gravity.[26]

Advantages of FDDS[27]

1. The gastro retentive systems are advantageous for drugs absorbed through the stomach, e.g. ferrous salts, antacids.

2. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence, HBS formulation may be useful for the administration of aspirin and other similar drugs.

3. Administration of prolongs release floating dosage forms, tablet or capsules, will result in dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid would be available for absorption in the small intestine after emptying of the stomach contents. It is therefore expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine.

4. The gastro retentive systems are advantageous for drugs meant for local action in the stomach. e.g. antacids.

5. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhea, poor absorption is expected. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.

6. FDDS improves patient compliance by decreasing dosing frequency.

7. Bioavailability enhances despite first pass effect because fluctuations in plasma drug concentration are avoided; a desirable plasma drug concentration is maintained by continuous drug release.

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

9. Gastric retention time is increased because of buoyancy.

10. Enhanced absorption of drugs which solubilize only in stomach.

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

12. Avoidance of gastric irritation, because of sustained release effect, floatability and uniform release of drug through multi particulate sys-tem.

REFERENCE

1. Kataria Sahil1, Middha Akanksha1, Sandhu Premjeet1, Ajay Bilandi and Bhawana Kapoor IJRPC 2011; 1(4): 2231-78

2. Kutmalge M. D, Ratnaparkhi M. P⋆, Wattamwar M. M, Chaudhari S. P Department of Pharmaceutics, Marathwada Mitra Mandal's College of Pharmacy, Theragaon(Kalewadi), Pune.

3. Li, S.P., Kowalski C.R., Feld K.M., Grim W.M., Recent Advances in Microencapsulation Technology and Equipment, Drug Dev Indian Pharm.1988; 14: 353-76.

4. Patel JK,Patel RP, Amin AF, Patel MM, www.pharmainfo.net/reviews/bioadhesive microspheres- review, 2010 4(6).

5. Shanthi N.C., Gupta R., Mahato K.A., Traditional and Emerging Applications of Microspheres: A Review, International Journal of Pharm Tech Research. 2010; 2(1):675-681.

6. Najmuddin M., Ahmed A., Shelar S., Patel V., Khan T., Floating Microspheres of Ketoprofen :Formulation and Evaluation, International Journal Of Pharmacy and Pharmaceutical sciences. 2010; 2(Suppl2):83-87.

7. www.springerlink.com /content/ r883r 91q17576vx6/, 25th Nov 2010, DOI: 10.1007/0-306-46891-3_9, Hafeli U, Physics and Chemistry Basic of Biotechnology. Focus on biotechnology. Review. Radioactive Microspheres for Medical Application, 2002; 7:213-48.

8. Yadav AV., Mote HH., Development of Biodegradable Starch Microspheres for Intranasal Delivery, Indian J. of pharma. Sciences. 2008; 70 (2):170-4.

9. Saralidze K., Leo H., Koole., Menno L., Knetsch W., Polymeric Microspheres for Medical Applications, Materials. 2010; 3:3357- 3564.

10. Trivedi P., Verma A.M.L., Garud N. Preperation and Charecterization of Acclofenac Microspheres,Asian Journal of pharmaceutics. 2011; 2(2): 110-115.

11. Rajkumar K, SainathGoud R, SaiSowjanya P, AnushaP,LavanyaAdavi S, E.R Reddy.Floating microsheres: a novel approach in drug delivery.Journal of Drug DeliveryResearch2012; 1(4):1-17.

12. Mathew Sam T., Devi Gayathri S., Prasanth V.V., Vinod B; NSAIDs as

microspheres, The Internet Journal of Pharmacology .2008;6(1).

13. Mathew Sam T., Devi Gayathri S., Prasanth V.V., Vinod B; NSAIDs as microspheres, The Internet Journal of Pharmacology .2008;6(1).

14. Trivedi P., Verma A.M.L., Garud N. Preperation and Charecterization of Acclofenac Microspheres,Asian Journal of pharmaceutics. 2011; 2(2): 110-115.

15. Dandagi MP., Masthiolimath S.V., Gadad P.A., Iliger R.S., Mucoadhesive Microspheres of PropanalolHcl for Nasal Delivery, Indian Journal of pharmaceutical Sciences. 2007;69 (3):402-407.

16. Pradesh T.S., Sunny C.M., Varma K.H., Ramesh P., Preperationn of microstuctured hydroxyapatite micro-spheres using oil in water emulsion, Bull Matter.Sci. 2005; 28(5):383- 390.

17. Rubinstein A., Friend D.R. (1979). U.S. Patent no. 4140755. Whitehead, L., .Fell, J., Sharma, H.L. Floating dosage forms: an in vivo study demonstrating prolonged gastric retention, J. cont. Rel. 1998; 55: 3-12.

18. Sato, Y., Kawashima, Y. Physicochemical properties to determine the buoyancy of hollow microspheres (microballoons) prepared by the emulsion solvent diffusion method, Eur. J. Pharm. Sci., 2003;55: 297-304

19. Joseph, N.H., Laxmi, S., Jayakrishnan, A. A floating type oral dosage form for piroxicam based on hollow microspheres: in vitro and invivo evaluation in rabbits, J. Cont. Rel., 2002; 79: 71-79. DOI

20. Abhishek Chandel, Kapil Chauhan, Bharat Parashar, Hitesh Kumar, Sonia Arora Department of Pharmacy, Manav Bharti University, Solan -173229, Himachal Pradesh, India.

21. Iannuccelli, V., Coppi, G., Bernabei, M.T., Cameroni, R. Air compartment multiple-unit system for prolonged gastric resi-dence. Part I. Formulation study, Int.J.Pharm. 1998;174: 47-54.

22. Stops, F., Fell, J.T., Collett, J.H., Martini, L.G. Floating dosage forms to prolong gastroretention the characterisation of calcium alginate beads, Int. J. Pharm., 2008; 350: 301-11.

23. Ichikawa, M., Watanabe, S., Miyake, Y. A new multiple unit oral floating dosage system. I: Preparation and in vitro evaluation of floating and sustained-release kinetics, J. Pharm. Sci. 1991; 80: 1062-66.

25. Paterson, R.S., Foster, J.E., O'Mahony, B., Stevens, H.N.E., Eccleston, G.M., Murray, J.G. . An assessment of floating raft formation in man using magnetic resonance imaging (MRI). J Pharm Phar-macol., 2000; 8: S2

26. Garg S. and Sharma S. Gastroretentive Drug Delivery System, Business Briefing:

Pharmatech., 2003; 160-66.

27. Babu, V.B.M., Khar, R.K. . In vitro and In vivo studies of sustained release floating dosage forms containing salbutamol sulphate. Pharmazie. 1990; 45: 268-70.