ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

RECENT ADVANCES IN SUSTAINED RELEASE FLOATING MICROSPHERE

Abhilasha Thakur, Ram Babu Sharma, Deepak Prashar*

LR Institute of Pharmacy, Jabeli Kyar, Solan (HP)-India

***Corresponding Author E-mail:** prashardeepak99@yahoo.in

ARTICLE INFO

Key words:
Microspheres, Patents, Commercial, Recent Advances

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

The present work tries to focus on the recent trends of microspheres therapeutically and commercially. In the recent scenario, the microspheres of variant types are being used as the drug delivery carrier. The numerous forms of microspheres provide an additional benefit to the researchers and commercial stakeholders. Currently the number of drugs for the treatment of prostate cancer, acromegaly, parkinsonism etc are being delivered through microsphere based drug delivery system. The work also signifies the patents that are being filed by the various companies and researchers in this field. Moreover, the commercially available preparations are also being highlightened

INTRODUCTION

Microspheres are multiparticulate drug delivery systems which are prepared to obtain prolonged or controlled drug delivery to improve bioavailability, stability and to target the drug to specific site at a predetermined rate. They are prepared from polymeric wax, natural, semi synthetic and synthetic polymers or other protective materials. Microspheres are normally free flowing powders having particle size ranging from 1-1000 micrometer consisting of synthetic polymers or proteins [1-5]. Numerous microspheres are available like polymeric microspheres, magnetic microspheres, floating microspheres, bioadhesive microspheres, radioactive microspheres, biodegradable polymeric microspheres, synthetic polymeric microspheres etc. There are numerous methods for the formulation of microspheres which includes double emulsion technique, phase separation coacervation technique, spray drying, solvent evaporation, Single emulsion technique, spray drying and spray congealing, solvent extraction [6-27]. They are being widely employed in the controlled and sustained release drug formulations.

Advances in Microsphere Based Technological Approaches [29-45]

Raj et al., 2021 suggested through a systemic review that mucoadhesion can be used for several drug candidates as a model for controlled drug delivery approaches. Microspheres have a variety of benefits, including safety and masking, reduced dissolution rate, and specific targeting of the active ingredient. Gavhane et al., 2021 suggested that, microsphere plays an integral role in tumor imaging, bimolecular interaction detection and treatment of cancer apart from its role in drug delivery. Kumar et al., 2021 carried

© Journal of Global Trends in Pharmaceutical Sciences

out the in vitro and in vivo studies on floating microsphere using various parameters to substantiate the gastroretensive nature. Patel et al., 2021 fabricated the floating microspheres of repaglinide using solvent evaporation technique. Further, prepared microspheres were characterized by production yield, particle size, in vitro buoyancy, entrapment efficiency, in vitro drug release, and in vivo floating behavior in albino rats. Moreover, the in vivo buoyancy behavior of the formulation was also investigated using albino rats. Uyen et al., 2020 fabricated the alginate based microspheres for the drug delivery. Alginate provided the merits over other raw materials such as inexpensiveness, nontoxic, biocompatible and biodegradability. Moreover, the review work also covers up the mechanism of action and drug release profile study too.

Satyanarayana and Sandeepthi 2018 formulated and evaluated the Atenolol tartrate floating microsphere by emulsification solvent diffusion technique. The aim of the study was to increase the gastric resident time of the drug formulation. The HPMC and Ethyl cellulose were used in different concentration for the development of formulation. Betala et al., 2017 formulated and evaluated the floating microsphere of Metformin hydrochloride. The drug is a hypoglycemic agent used for the treatment of non-insulin dependent Diabetes mellitus. It is a BCS class III drug having high solubility and poor permeability. Plasma half life ranges from 1.5 to 3 hours and oral bioavailability is 50 to 60 %. The formulation showed enhancement in the permeability and good bioavailability of drug. Floating microspheres were prepared using ionotropic gelation method. Ganesh et al., 2016 formulated the highly porous gastroretentive tablets of Dipyridamole by using sublimation method. The effect of amount of HPMC K4M on swelling and eroding of tablets were determined. The results suggested that the release profile of the drug was dependent on the polymer concentration. Nethaji et al., 2015 carried out the development and evaluation of gatro retentive floating microspheres of antibiotic ofloxacin. The in vitro drug release rate and stability studies of the formulation showed the good results with suitable potential therapeutic uses. Ganesh et al., 2015 formulated the floating gastroretentive tablets of quetiapine fumarate by using sublimation method. The effect of amount of HPMC K4M on swelling and eroding of tablets were determined. The results suggested that the release profile of the drug was dependent on the polymer concentration. Lin et al., 2014 developed the calcium silicate ($CaSiO_3$, CS) microspheres with diameter of 75–100 μm by a spray-drying method. The ionic extracts of CS microspheres promoted the proliferation of human osteoblast-like cells (MC3T3-E1).

In addition, the porous structures of the CS microspheres resulted in favorable drug loading and sustained release property. The fabricated multifunctional CS microspheres are a promising drug delivery system as an injectable bioactive filling material for bone-regeneration. Hu et al., 2014 fabricated the modified composite microspheres of hydroxyapatite and poly(lactide-co-glycolide) own rich hydroxyapatite on the surface of composite microspheres. The modified composite microspheres have rough surface and high interfacial strength between hydroxyapatite and poly(lactide-co-glycolide). The results suggested that the modified composite microspheres clearly promoted osteoblast attachment, proliferation and alkaline phosphatase activity. Wu and Zreiqat 2010 developed bioceramic microspheres for bone regeneration having bioactive and degradable nature along with controlled drug-release ability. The diopside ($CaMgSi_2O_6$, DP) was used for the preparation of microsphere. The resulted microspheres have the potential to be used as bioactive filling materials for bone-tissue regeneration. Kumar et al., 2009 prepared the floating matrix drug delivery system of aceclofenac to prolong the gastric resident time and bioavailability.

© Journal of Global Trends in Pharmaceutical Sciences

Figure 1 Microsphere Based Drug Carrier [28]

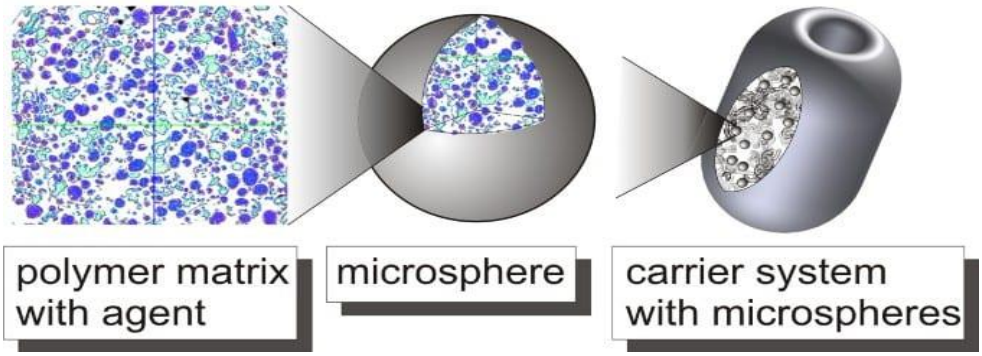

Table 1- Patent on Microsphere and Technologies

S. No.	Title of Patent	Patent ID	Inventor	Year	Current Assignee
1	Floating drug delivery composition	WO2001058424A1 WIPO (PCT)	Peter James WattsAlan SmithJohn Russell BondWilliam Columbus Ian Lafferty	2001	-------
2	Process for making multiparticulate gastroretentive dosage forms	EP2444064A1 European Patent Office	Joel Sylvain Michel Kirkorian	2012	Meliatys
3	Controlled-release floating pharmaceutical compositions	WO2010136739A2 WIPO (PCT)	Catherine Castan Philippe Caisse	2010	Flamel Technologies
4	Gastroretentive controlled release microspheres for improved drug delivery	US6207197B1 United States	Lisbeth Illum He Ping	2001	West Pharmaceutical Services Drug Delivery and Clinical Research Center Ltd
5	Bioadhesive microspheres and their use as drug delivery and imaging systems	WO1993021906A1 WIPO (PCT)	Edith Mathiowitz Donald Chickering Jules Serge Jacob	1993	Brown University Research Foundation
6	Coated microparticles with improved drug absorption	EP0635261A1 European Patent Office	José De Los Santos Garces Garces Angel Bonilla Munoz Jose Maria Garcia Anton	1995	Lipotec, S.A.
7	US20160338949A1 United States Stabilized gastroretentive tablets of pregabalin	US20160338949A1 United States 2016	Varinder Kumar Shavej AHMAD Romi Barat Singh Kaushal NAYYAR Mohan Prasad	Abandoned	Sun Pharmaceutical Industries Ltd
8	Gastric-retentive sustained release fomulation containing pregabalin and pva-peg graft copolymer	KR101317592B1 South Korea	Cho Il-hwan Hong Ilgi Shin Kyung-min Oh Da-won Hug, Noh Hyun-jung	2013	CJ CheilJedang Co., Ltd.

© Journal of Global Trends in Pharmaceutical Sciences

			Kang Hyun-ah Crimson, Seong Bo-hyeon		
9	Gastroretentive Dosage Forms Of GABA Analogs	US20130078290A1 United States	Pratibha Sudhir Pilgaonkar Maharukh Tehmasp Rustomjee Anilkumar Surendrakumar Gandhi	2013	Rubicon Research Private Limited
10	Gastric resistant pharmaceutical composition comprising rifaximin	JP4827915B2 Japan	Giuseppechi. Viscomi, Villiam Tsamboni, Ernesto Palazzini, Maria Rosalia Pantaleo	2011	-----
11	Biodegradable Polymer Microsphere Compositions for Parenteral Administration	US Patent # 10,874,612	N. Dormer and C. Berkland	2020	Adare Pharmaceuticals USA, Inc., NJ
12	Gastro-Retentive Dosage Forms for Sustained Drug Delivery	US Patent # 10,857,098	K. Meghpara, J. Vaghashiya, N.H. Shah, D. Desai, W. Phuapradit, H.K. Sandhu, S.R.K Vaka, N.B. Shelke, and A. Chatterji	2020	Kashiv Biosciences LLC, NJ

Table 2 Some Marketed Formulations of Microspheres

S. No.	Drug	Commercial Name	Company	Method of Preparation	Therapeutic Uses	Delivery Route
1	Bromocriptine	PARLODEL LAR™	Novartis	Spray drying	Parkinsonism	Subcutaneous & Intra muscular
2	Buserelin	SUPRECUR MP	Sanofi-Aventis	--------	Endometriosis	Intra muscular
3	Recombinant bovine somatropin	POSILAC	Monsanto	--------	Increases milk production in cattles	Subcutaneous/ Intra muscular
4	Goserelin acetate	ZOLADEX	I.C.I	--------	Prostate cancer	Subcutaneous
5	Minocycline	ARESTIN	Orapharma	---------	Periodontitis	Subgingival
6	Triptorelin	TRELSTAR DEPOT/ DECAPEPTYL SR	Pfizer/ Ferring	Phase separation	Prostate cancer	Intra muscular
7	Lanreotide	SOMATULINE LA	Ipsen-Beafour	Phase separation	Acromegaly	Intra muscular
8	Somatropin	NUTROPIN	Genentech/Alkerm	Cryogenic	Growth	Subcutaneou

© Journal of Global Trends in Pharmaceutical Sciences

		DEPAT	es	Spray-drying	deficiency	s
9	Leuprolide	ENANTONE DEPOT/ LUPRON DEPOT/TRENANTONE	Takeda/TAP/Takeda	Double emulsification	Prostate cancer & Endometriosis	Intra muscular
1	Octreotide	SANDOSTATIN LAR	Novartis	Phase separation	Acromegaly	Intravenous/ Subcutaneous
1	Risperidone	RISPERDAL / CONSTA	Janssen/ Alkermes. Inc	Double emulsification	Bipolar disorder & Schizophrenia	Intra muscular
1	Naltrexone	VIVITROL	Alkermes	Double emulsification	Alcohol dependence	Intra muscular

The effects of sodium bicarbonate on drug release profile and floating properties were investigated. The formulation was optimized on the basis of acceptable tablet properties, floating lag time, total duration of floating and in vitro drug release. The formulations F1 to F9 showed the good results with positive feedback. Shashikanth et al., 2009 prepared the floating microspheres of ketorolac trometamol. The drug is employed in the short-term management of moderate to severe acute post-operative pain requiring gatro retentive behaviour for better bioavailability. Tanwar et al., 2007 carried the preparation and evaluation of floating microspheres of verapamil hydrochloride for improving the drug bioavailability by prolongation of gastric residence time. Cellulose acetate, acrycoat S100 and eudragit S100 microspheres loaded with verapamil hydrochloride were prepared by solvent diffusion-evaporation method. The microspheres had smooth surfaces, with free-flowing and good-packing properties. Dandangi et al., 2004 carried out the formulation of verapamil hydrochloride micropellets using inotropic gelation technique. The result of the study suggested that the prolonged release rate can be achieved for verapamil using the inotropic gelation technique. The invitro and stability study of the formulation was too carried out.

Microsphere Patents [46-56]

Patents are one of the requirements of the present scenario. Every new formulation, drug moiety and any advanced formulation technique require to be patented to get it commercialized. The reason behind the filing up of patents is to get it marked for company and economically too company can rent it to generate some financial asserts. In recent the numerous patents have been filled by the researchers as per the advancement in sustained release floating microsphere.

Commercialization of Microsphere

The applicability of any formulation can only authenticated when it is being accessible commercially. The market utilization of the microsphere is of utmost importance. In the present scenario numbers of formulation are being offered by the companies based on different types of microspheres [60-61]

CONCLUSION

The present work suggested that the applicability of the microsphere is increasing in the present scenario. The availability of the different types of microspheres and various methodologies to develop and formulate it provides an edge over the other drug carriers. The gastro retentive

© Journal of Global Trends in Pharmaceutical Sciences

applicability of the microsphere is being explored a lot. On the therapeutic frontage too the microsphere are being considered of immense importance. All these prospects are being clearly highlightened through the current review work. In future the microsphere can be utilized on different fields such as medical, dental and vetinary too.

REFERENCES

1. Jamini M, Rawat S. A review on microsphere. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2013; 4(1): 1223-1233.
2. Patel NR, Patel DA, Microsphere as a novel drug delivery. International Journal of Pharmacy and Life Sciences 2011; 2(8): 992-997.
3. Singh C, Purohit S, Singh M, Pandey BL. Design and evaluation of microspheres: A Review. Journal of Drug Delivery and Research 2013; 2(2): 18-27.
4. Prasanth VV, Moy AC, Mathew ST, Mathapan R. Microspheres: An overview. International Journal of Research in Pharmaceutical and Biomedical Sciences 2011; 2: 3328.
5. Prasad SGB, Microspheres as drug delivery system – A review. Journal of Global Trends in Pharmaceutical Sciences 2014; 5(3): 1961 -1972.
6. Mohan M, brief review on mucoadhesive microspheres. International Journal Of Research And Reviews In Pharmacy And Applied Sciences 2014; 4(1): 975-986.
7. Kumar A, Jha S, Rawal R, Chauhan PS, Maurya SD. Mucoadhesive microspheres for novel drug delivery system. A Review. American Journal of Pharmtech Research 2013; 3(4): 197-213.
8. Senthil A, Narayanaswamy, VB, Ajit I, Galge DS, Bhosale RS. Mucoadhesive microspheres. International Journal of Research in Ayurveda and Pharmacy 2011; 2(1): 55 -59.
9. Smart JD. The basic and underlying mechanisms of Mucoadhesion. Advanced Drug Delivery Reviews 2005; 57: 1556 – 1568.
10. Andrew GP, Laverty TP, Jones DS. Mucoadhesive polymeric for controlled drug delivery. European Journal of Pharmaceutics and Biopharmaceutics 2009; 71(3):505-518.
11. Thummar AV, Kyada CR, Kalyanvat R, Shreevastva B. A review on mucoadhesive microspheres as a novel drug delivery system. International Journal for Pharmaceutical Research Scholars 2013; 2(2): 188-200.
12. Mukherjee S, Bandyopadhyay P. Magnetic microspheres: A latest approach in novel drug delivery system. Journal of Pharmaceutical and Scientific Innovation 2012; 1(5): 21-25.
13. Batra D, Kakar S, Singh R, Nautiyal U. Magnetic microspheres as a targeted drug delivery system: An overview. Journal of Drug Delivery Research 2012; 1(3): 1-17.
14. Gupta R, Pathak K. Optimization Studies on Floating Multiparticulate Gastroretentive Drug Delivery System of Famotidine. Drug Development and Industrial Pharmacy 2008; 34(11): 1201-1208.
15. Dutta P, Sruti J, Patra CN, Rao MEB. Floating microspheres: Recent trends in the development of gastrorententive floating drug delivery system. International Journal of Pharmaceutical Sciences and Nanotechnology 2011; 4(1): 1296-1306.
16. Mukund JY, Floating microspheres: A review. Brazilian Journal of Pharmaceutical Sciences 2012; 48(1): 17-30.
17. Kawatra M, Jain U, Ramana J. Recent advances in floating microspheres as gastroretentive drug delivery system: A review. International Journal of Recent

© Journal of Global Trends in Pharmaceutical Sciences

Advances in Pharmaceutical Research 2012; 2(3): 5-23.
18. Ramteke KH, Jadhav. Microspheres: As carriers used for novel drug delivery system. IOSR Journal of Pharmacy 2012; 2(4): 44-48.
19. Alagusundaram M, Sudana CM, Umashankari K, Badarinath A, Lavanya C, Ramkanth S. Microspheres as a novel drug delivery sysytem - A review. International Journal of Chem Tech Research 2009; 3: 526-534.
20. Lokwani P, Goyal A, Gupta S, Songara R, Singh N, Rathore K. Pharmaceutical Applications of Magnetic Particles In Drug Delivery System. International Journal of Pharmaceutical Research and Development 2011; 147 – 156.
21. Prasanth V, Moy A, Mathew S, Mathapan R. Microspheres - An Overview. International Journal of Research in Pharmaceutical and Biomedical Sciences 2011; 2(2): 332-338.
22. Mohan M, brief review on mucoadhesive microspheres. International Journal Of Research And Reviews In Pharmacy And Applied Sciences 2014; 4(1): 975-86.
23. Kumar A, Jha S, Rawal R, Chauhan PS, Maurya SD. Mucoadhesive microspheres for novel drug delivery system: A Review. American journal of PharmTech Research 2013; 3(4): 197-213.
24. Dupinder K, Seema S, Gurpreet S, Rana AC: Biodegradable microspheres: A review International Research Journal of Pharmacy 2012; 3(12): 23-27.
25. Saralidze K, Koole LH, Knetsch MLW. Polymeric microspheres for medical applications. Materials 2010; 3: 3537-3564.
26. Sahil K, Akanksha M, Premjeet S, Bilandi A, Kapoor B. Microsphere: A review. International Journal of Research in Pharmacy and Chemistry 2011; 1: 1184-1198.
27. Kumar BP, Microparticulate drug delivery system: A Review. Indian Journal Of Pharmaceutical Science And Research 2011; 1(1): 19-37.
28. https://www.advancedsciencenews.com/polymer-microspheres-for-drug-delivery-to-the-bladder/
29. Raj H, Sharma A, Sharma S, Verma K, Chaudhary A. Mucoadhesive Microspheres: A Targeted Drug Delivery System. Journal of Drug Delivery and Therapeutics 2021; 11(2-S):150-155.
30. Gavhane P, Deshmukh M, Khopade AN, Kunjir VV, Shete RV. A Review on Microsphere. Journal of Drug Delivery and Therapeutics 2021; 11(1):188-194.
31. Krishna, Kumar A, Srivastava R. In Vitro In Vivo Studies On Floating Microspheres For Gastroretentive Drug Delivery System: A Review. Asian Journal of Pharmaceutical and Clinical Research 2021; 14(1): 13-26. doi:10.22159/ajpcr.2021.v14i1.39183.
32. Patel AK, Guar gum based floating microspheres of repaglinide using 32 factorial design: Fabrication, optimization, characterization and invivo buoyancy behavior in albino rats. ASSAY and Drug Development Technologies. 2021: 63-74. http://doi.org/10.1089/adt.2020.1006
33. Uyen NTT, Hamid ZAA, Tram NXT, Ahmad N. Fabrication of alginate microspheres for drug delivery: A review, International Journal of Biological Macromolecules 2020; 153: 1035-1046. https://doi.org/10.1016/j.ijbiomac.2019.10.233.
34. Satyanarayana L, Sandeepthi N. Formulation and evaluation of Atenolol floating microspheres. Indo American Journal of Pharmaceutical Science 2018; 05 (01): 135-140.
35. Betala S, Varma MM, Abbulu K. Formulation and evaluation of floating microspheres of metformin

© Journal of Global Trends in Pharmaceutical Sciences

hydrochloride. Indo American Journal of Pharmaceutical Science 2017; 4 (11): 4190-4199.
36. Ganesh, Development of Highly Porous gastroretentive Dipyridamole Tablets Using A Sublimation Method. Indo American Journal of Pharmaceutical Science 2016; 3(6): 662-671.
37. Nethaji, Development and Evaluation Gastro-Retentive Floating Microspheres of Ofloxacin. Asian Journal of Pharmaceutical and Health Sciences 2015; 5(1): 1193-1202.
38. Ganesh, Preparation of highly porous gastroretentive quetiapine fumarate tablets by using a sublimation method. Indo American Journal of Pharmaceutical Science 2015; 2 (8): 1154-1166.
39. Lin K, Zhang DZN, Kawazoe N, Chen G, Chang J. Fabrication and characterization of bioactive calcium silicate microspheres for drug delivery. Ceramics International 2014; 40(2): 3287-3293. https://doi.org/10.1016/j.ceramint.2013.09.106.
40. Hu X, Shen H, Yang F, Liang X, Wang S, Wu D. Modified composite microspheres of hydroxyapatite and poly(lactide-co-glycolide) as an injectable scaffold. Applied Surface Science 2014; 292: 764-772. https://doi.org/10.1016/j.apsusc.2013.12.045.
41. Wu C, Zreiqat H. Porous bioactive diopside (CaMgSi2O6) ceramic microspheres for drug delivery. Acta Biomaterialia 2010; 6(3): 820-829.https://doi.org/10.1016/j.actbio.2009.09.025.
42. Kumar R, Patil S, Patil BM, Patil SR, Paschapur MS. Design and in-vitro evaluation of oral floating matrix tablets of Aceclofenac. International Journal of Chem Tech Research. 2009; 1(4):815- 825.
43. Shashikanth DB, Rupnar YS, Sonvane RM. Formulation and evaluation of floating microspheres of ketorolac trometamol. International Journal of Pharma Research and Development 2009; 1(9):1-8.
44. Tanwar YS, Development and Evaluation of Floating Microspheres of Verapamil hydrochloride. Brazilian Journal of Pharmaceutical Science 2007; 43(4): 529-534.
45. Dandangi PM,. Microencapsulation of verapamil hydrochloride by Ionotropic gelation technique. Indian Journal of Pharmaceutical Sciences 2004; 66(5): 631-635.
46. https://patents.google.com/patent/WO2001058424A1/en
47. https://patents.google.com/patent/EP2444064A1/en
48. https://patents.google.com/patent/WO2010136739A2/en
49. https://patents.google.com/patent/US6207197B1/en
50. https://patents.google.com/patent/WO1993021906A1/en
51. https://patents.google.com/patent/EP0635261A1/en
52. https://patents.google.com/patent/US20160338949A1/en
53. https://patents.google.com/patent/US20160338949A1/en
54. https://patents.google.com/patent/US20130078290A1/en
55. https://patents.google.com/patent/JP4827915B2/en
56. https://www.americanpharmaceuticalreview.com/Featured-Articles/574645-Pharmaceutical-P-I-N-Points-Patent-Innovation-News/
57. Susan DS, Jabar DS, Jabar AF, Patrick AF, Patrick PD, Deluca P. A model-dependent approach to correlate accelerated with real-time release from biodegradable microspheres AAPS PharmSciTech 2005; 6(4):E553-564.
58. Bari H. A prolonged release parenteral drug delivery system – An overview. International Journal of Pharmaceutical Sciences Review and Research 2010; 3(1): 1-11.

© Journal of Global Trends in Pharmaceutical Sciences