WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 11, 1128-1138. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF FLOATING MICROSPHERES CONTAINING SULFASALAZINE

Ariyan Dwivedi*, Dr. Arun Patel, Shailendra Patel and Neelesh Dwivedi

Shri Ram Group of Institute of Technology Jabalpur.

Article Received on
29 July 2020,

Revised on 19 August 2020,
Accepted on 09 Sep. 2020,

DOI: 10.20959/wjpr202011-18765

***Corresponding Author**
Ariyan Dwivedi
Shri Ram Group of Institute of Technology Jabalpur.

ABSTRACT

The main objective of any drug therapy is to achieve a desire concentration of the drug in blood or tissue which is therapeutically effective and nontoxic for extended period of time, and this goal can be achieved by proper design of sustain release dosage regimen. Microspheres have been widely accepted as a mean to achieve oral and parenteral controlled release. The microspheres require a polymeric substance as a coating material or carrier. A number of different substances biodegradable as well as non-biodegradable have been investigated for the preparation of microspheres. Of the various biodegradable polymers used for the development of sustained release formulations, poly(ϵ-caprolactone) has been reported to be advantageous since they are biocompatible. Poly (ϵ-caprolactone) is aliphatic polyester polymer, suitable for controlled drug delivery due to a high permeability to many drugs and at the same time being free from toxicity.

KEYWORDS: Floating Microspheres, Sulfasalazine, Poly (E-Caprolactone), Sustain Release, Permeability, Biodegradable.

INTRODUCTION: The modification of drug release is always performed to achieve a particular therapeutic aim, with which optimized bioavailability of API(s) can be reached by taking the physiological environment into consideration. In the cases of APIs with short elimination half-life, long acting preparations can be designed with the prolongation of API release and absorption. Modified drug delivery systems (MDDSs) can be classified based on the time and location of drug release. With per os administered medicines, the location of drug release in the gastrointestinal tract (GIT) may be in: the mouth (e.g. orodisperse, sublingual, buccal DDSs), the stomach (e.g. floating, expandable DDSs), the small intestine and/or the colon (e.g. intestinosolvent, enterosolvent, colon targeted DDSs). Thus the location

of drug release can be controlled with an appropriate modification of the preparation, with which site-controlled systems can be achieved. During drug release in the oral cavity or in the stomach, not only systemic but also local effects may be taken into consideration, while drug release in the small intestine may be expected to be predominantly systemic. In colon-specific therapy, mostly local effects may develop, since absorption is limited/ minimal. Those modified drug delivery systems, in which the modification is aimed at prolonging the residence time (GRT), are termed gastroretentive drug delivery systems (GRDDS).

MATERIAL AND METHOD

MATERIAL: The following materials that were procured from different sources some of which were analytical grade and best possible Laboratory Reagent were used as supplied by the manufacturer without further purification or investigation.

Table 1: List of drug and Excipients used.

S. No.	Materials Used	Grade	Gift sample
1	Sulfasalazine	Pharma	Alembic Pharma Vadodra.
2	HPMC	Pharma	Mapromax Life Sciences Pvt. Ltd., Dehradun
3	PVP	Pharma	Mapromax, Life sciences Pvt. Ltd. Dehradun
4	EC	Pharma	Mapromax, Life sciences Pvt. Ltd., Dehradun.
5	Dichloromethane	Pharma	Himedia Pvt. Ltd.

The following instruments that were installed and calibrated as per the SOP guidelines of the manufacturer as well as the guidelines given in the standard Monographs of the Indian Pharmacopoeia.

Table 2: List of instruments used.

S. No.	Instrument	Manufacturer
1.	Double beam UV Visible Spectrometer	LABINDIA 3000+
2	FT-IR	BRUKERS ALPHA
3.	Dissolution Apparatus	LABINDIA DS-8000
4.	Electronic Balance	Wencer
5.	Hot air oven	Labotech India
6.	Melting point apparatus	Chemline
7.	Particle Size Analyzer	Horiba Scientific

METHOD: Preparation of Floating Microsphere of Sulfasalazine

Floating microspheres containing aceclofenac were prepared using emulsion- solvent diffusion technique. The drug to polymer ratio used to prepare the different formulations was as shown in table 7.1. The drug polymer mixture dissolved in a mixture of ethanol (8 mL) and dichloromethane (8 mL) was dropped in to 0.2% sodium lauryl sulfate solution (400 ml).

The solution was stirred with a propeller-type agitator at room temperature for 1 h at 500 rpm. The formed floating microspheres were filtered, washed with water and dried at room temperature in a desicator. The various batches of floating microsphere were prepared as follows.

Table 3: Formulations of the Floating Microspheres Prepared.

Sr. No	Formulation Code	Sulfasalazine (mg)	EC(mg)	HPMC(mg)	PVA(mg)
1	**F1**	250	50	250	-
2	**F2**	250	100	250	-
3	**F3**	250	150	250	-
4	**F4**	250	200	250	-
5	**F5**	250	-	250	50
6	**F6**	250	-	250	100
7	**F7**	250	-	250	150
8	**F8**	250	-	250	200

RESULTS AND DISCUSSION

Evaluation of Sulfasalazine Floating Microspheres

Particle size analysis

Particle size was determined by Optical microscopy method. It plays important role in floating ability and release of drug from Microsphere. If size of Microspheres is less than 500 μm release rate of drug will be high and floating ability will reduce, white Microspheres ranging between 400μm - 600μm, the floating ability will be more and release rate will be in sustained manner.

The mean particle size of Sulfasalazine microsphere was in range 479.2 – 589.8 μm as shown in Table -4.

Mean particle size of Different Batches of Sulfasalazine microsphere

Table 4: Mean particle size of Different Batches of Sulfasalazine microsphere.

S. No	Formulation code	Mean particle size (μm)
1.	F1	479.2±15
2.	F2	495.8±45
3.	F3	490.2±32
4.	F4	498.5±23
5.	F5	512.2± 15
6.	F6	545.6±22
7.	F7	589.8±12
8.	F8	521.2±21

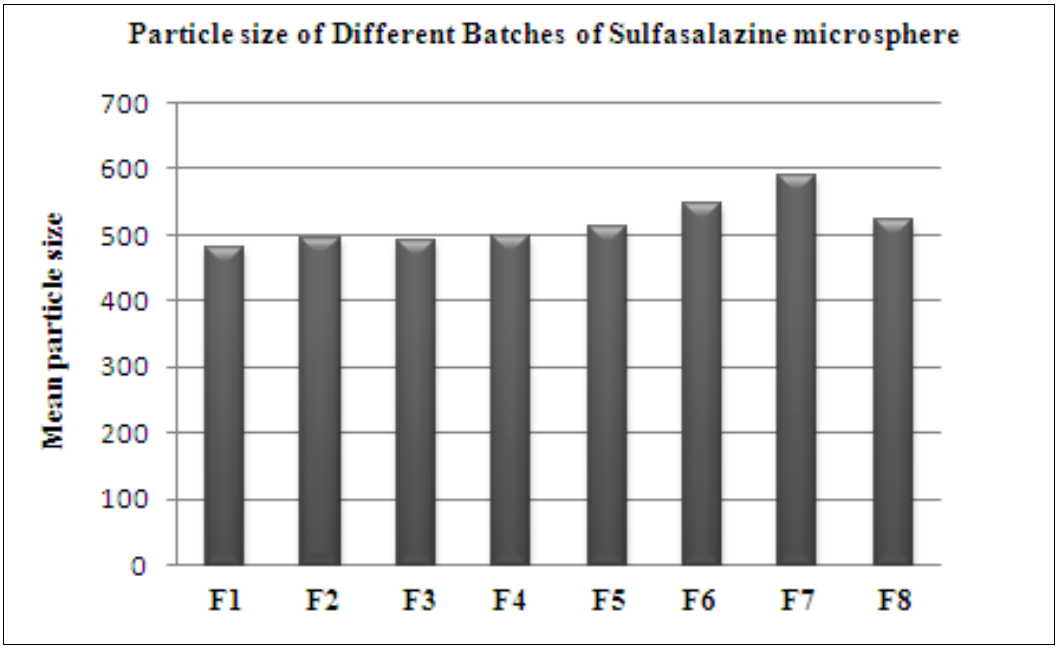

Figure 1: Mean particle size of Different Batches of Sulfasalazine microsphere.

Mean Particle size of Optimized Batch F1

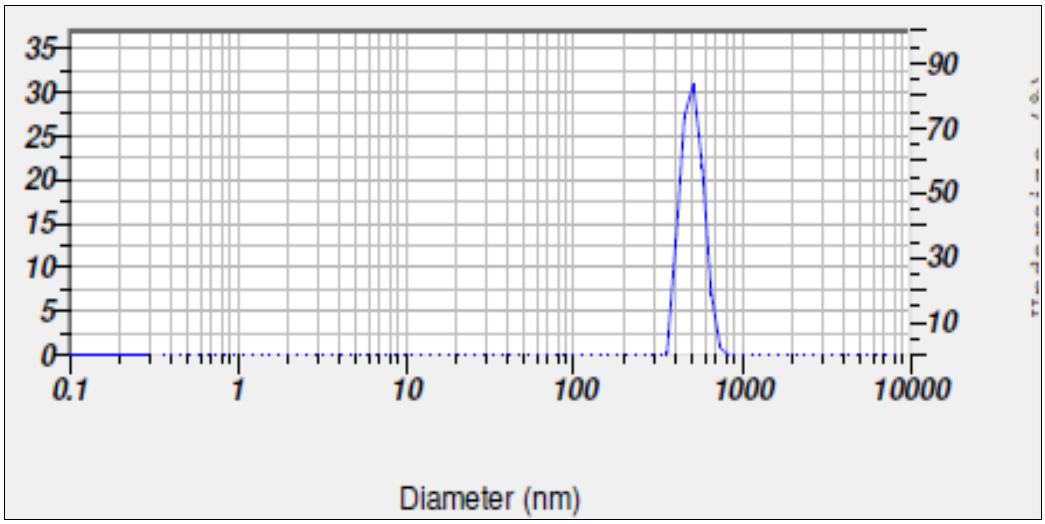

Figure 2: Mean Particle size of Optimized Batch.

Floating behavior of microsphere

Sulfasalazine Microsphere was dispersed in 0.1 HCl as simulate gastric fluid. Floating ability of different formulation was found to be differed according to EC and HPMC ratio. F_1-F_4 formulations showed best floating ability (91.47-72.97%) in 6 hours. F_5-F_8 formulation showed less floating ability (66.12-45.09%) as showed in Table-8.2.

Percentage buoyancy for different formulation

Table 5: Percentage Buoyancy for Different Formulation.

Formulation	1 hour	2 hours	4 hours	6 hours
F1	98.41	97.08	93.23	91.47
F2	98.11	95.58	92.17	87.34
F3	98.54	95.64	85.34	78.45
F4	99.54	92.49	80.57	72.97
F5	98.72	91.95	73.49	66.12
F6	98.45	86.62	65.14	57.76
F7	88.34	75.41	56.04	45.09
F8	82.25	74.56	55.25	40.56

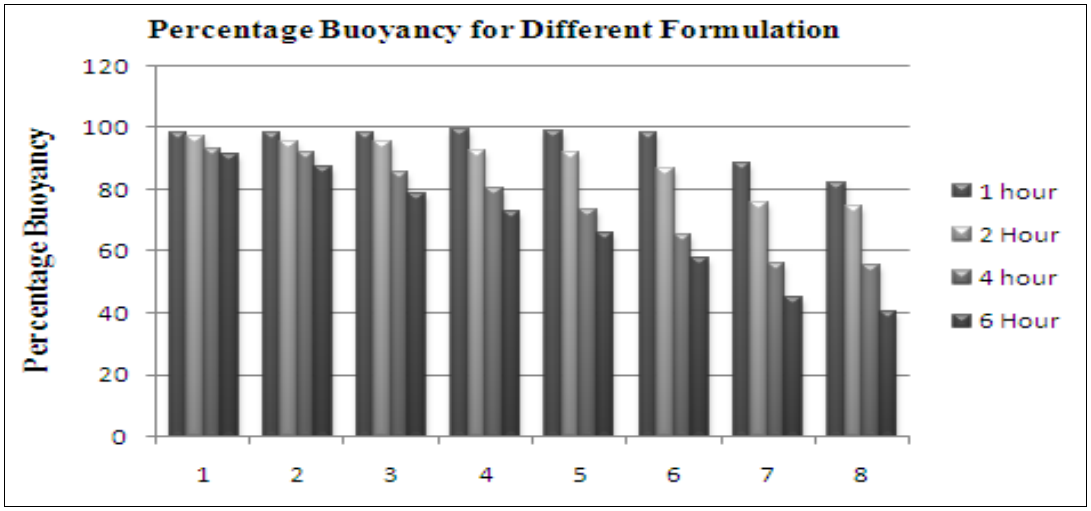

Figure 3: Percentage Buoyancy for Different Formulation.

Drug Entrapment

The drug entrapment efficacies of different formulations were in range of 48.47 - 76.19 % w/w as shown in Table No- 8.3. Drug entrapment efficacy slightly decreases with increase EC content in Microspheres. This is due to the permeation characteristics of that could facilitate the diffusion of part of entrapped drug to surrounding medium during preparation of Sulfasalazine microspheres.

Drug entrapment for different formulation

Table 6: Drug Entrapment for Different Formulation.

Formulation	Drug entrapment (% w/w)
F1	75.56±0.21
F2	70.12±0.32
F3	70.21±0.54
F4	68.89±0.41
F5	65.56±0.25
F6	63.25±0.38

F7	62.25±0.25
F8	58.98±0.24

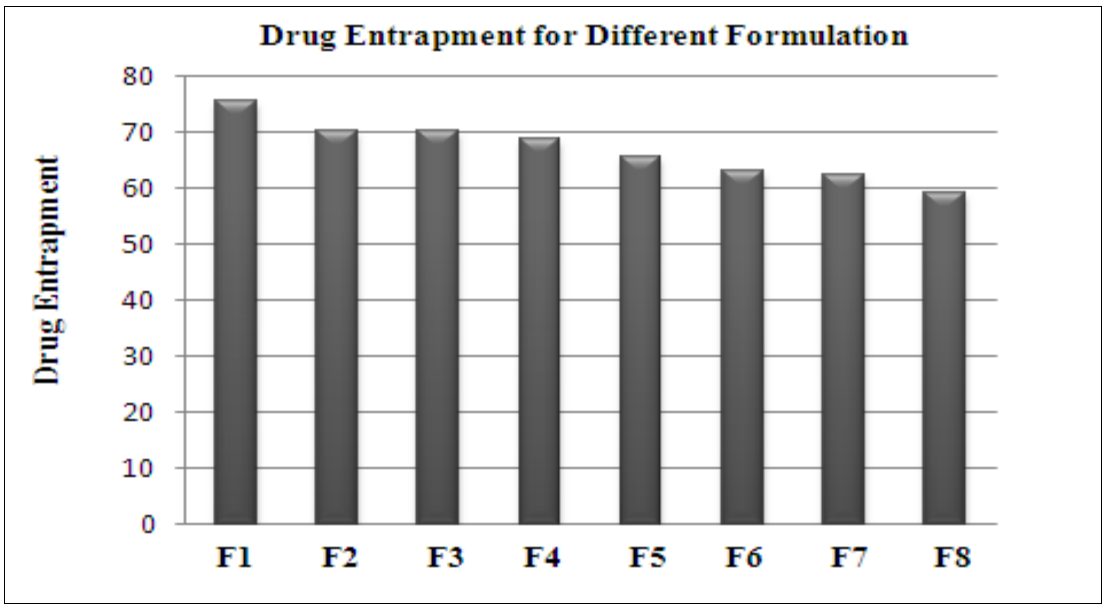

Figure 4: Drug Entrapment for Different Formulation.

8.1.4 Percentage Yield

Percentage yield of different formulation was determined by weighing the Microspheres after drying. The percentage yield of different formulation was in range of 56.84 - 82.87% as shown in Table-8.4.

Percentage yield for different formulation

Table 7: Percentage Yield for Different Formulation.

Formulation	Percent Yield (%)
F1	82.87
F2	78.53
F3	76.47
F4	71.56
F5	69.31
F6	66.03
F7	56.84
F8	52.25

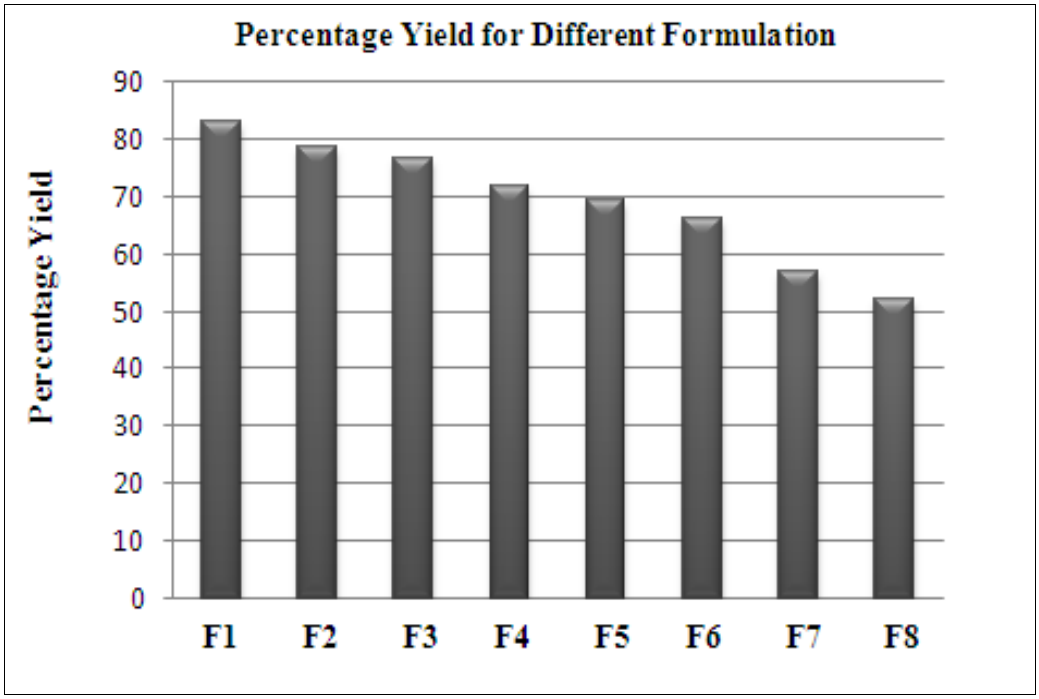

Figure 5: Percentage Yield for Different Formulation.

8.1.5 Scanning Electronic Microscopy

Shape and surface characteristic of Sulfasalazine microspheres examine by Scanning Electronic Microscopy analysis. Surface morphology of formulation examines at different magnification, which illustrate the smooth surface of floating Microspheres.

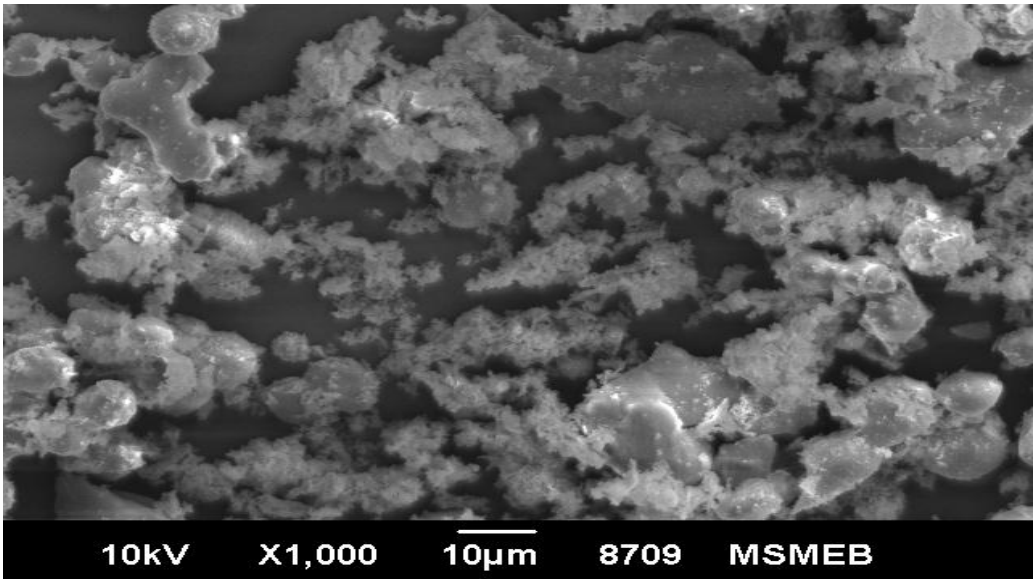

Figure 6: Scanning Electronic Microscopy Image of Optimized Formulation F-1.

8.1.6 *In-Vitro* Drug release study

Table 8.12: Comparative Release Study data of formulation F1-F7.

Time	% of Drug Release							
(hr)	F1	F2	F3	F4	F5	F6	F7	F8
0.5	16.429	15.000	14.286	14.286	17.857	16.429	14.286	11.21
1.0	26.536	18.607	18.571	18.571	28.036	25.821	22.857	21.47
1.5	30.679	27.357	27.321	27.321	34.393	31.357	33.964	32.32
2.0	57.107	32.929	32.893	32.893	43.857	43.536	39.143	34.61
3.0	71.214	60.143	40.821	40.821	61.571	54.821	58.786	52.00
4.0	81.607	77.214	52.643	52.643	71.500	78.000	56.464	42.28
6.0	95.214	85.714	72.107	72.107	78.214	93.643	66.036	53.21
8.0	100.036	90.179	86.714	86.714	95.107	99.893	95.250	81.93

Graph of release study of formulation F1-F8

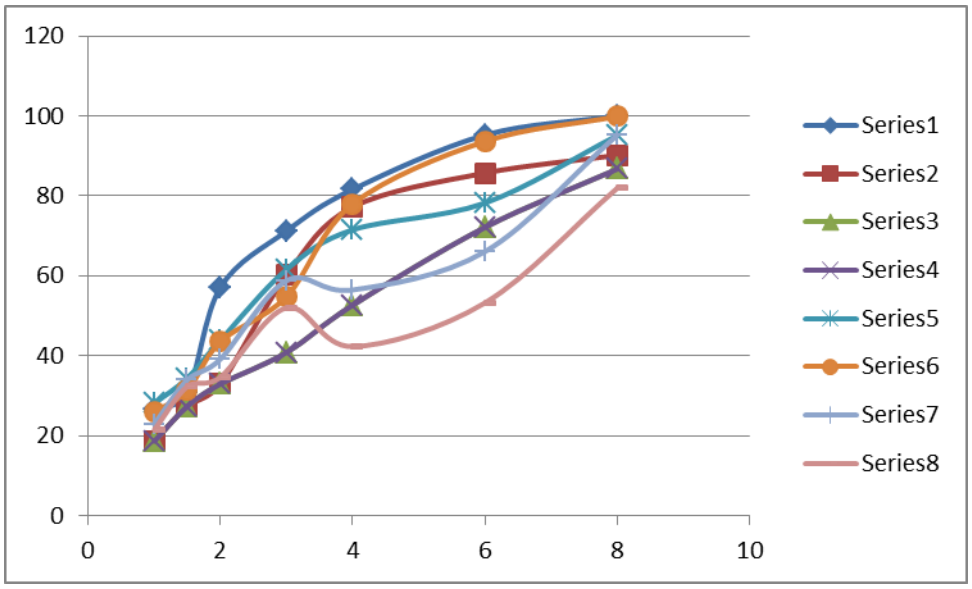

Figure 7: Graph of release study of formulation F1-F7.

Table 8.14: Comparative study of regression coefficient for selection of optimize Formulation F-7.

Zero order		First order	Higuchi	Korsmayer
r2	0.862	0.831	0.942	0.616

The In vitro drug release data of the optimized formulation was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, Higuchi's and Korsmeyer's models in order to determine the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r' values of **Higuchi** was maximum i.e 0.942 hence indicating drug release from formulations was found to follow **Higuchi** kinetics.

CONCLUSION

Floating microspheres of Sulfasalazine were prepared by the solvent evaporation technique. Sulfasalazineis a slightly water soluble drug which has good absorption in gastric pH. Sulfasalazine suffers from poor oral bioavailability since it is less soluble in water and shows poor absorption in lower GIT. Hence, such a drug requires a novel gastroretentive drug delivery system which can provide an extended period of time in stomach and improve oral bioavailability. Microspheres are the suitable drug delivery system for the drugs that have poor absorption from lower GIT. PCL microspheres were studied for characterization, compatibility study, particle size and shape, *in vitro* drug release, entrapment efficiency, and buoyancy time. The formulation using Ethyl cellulose and HPMC showed a constant rate of release. Thus, prepared floating microspheres of Sulfasalazine may prove to be potential candidates for a drug delivery.

REFERENCES

1. N. Narang, An updated review on: Floating drug delivery system, Int J Appl Pharm, 2010; 3: 1-7.
2. Y.H. Bae, K. Park, Targeted drug delivery to tumors: myths, reality and possibility, J Control Release, 2011; 153: 198-205.
3. E.A. Klusner, E. Lavy, M. Friedman, A. Hoffman, Expandable gasrtroretentive dosage forms, J Control Release, 2003; 2: 143-162.
4. E.A. Klusner, E. Lavy, D. Stepensley, M. Friedman, A. Hoffman, Novel gasrtroretentive dosage form: evaluation of gastroretentivity and its effect on riboflavin absorption in dogs, Pharm Res, 2002; 19: 1516-1523.
5. G.M. Clarke, J.M. Newton, M.D. Short, Gastrointestinal transit of pellets of differing size and density, Int J Pharm, 1993; 100: 81-92.
6. Y. Huang, W. Leobandung, A. Foss, N.A. Peppas, Molecular aspects of muco-and bioadhesion: tethered structures and site-specific surfaces, J Control Release, 2000; 65 63-71.
7. B.N. Singh, K.H. Kim, Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention, J Control Release, 2000; 63: 235-259.
8. S.A. Elkheshen, A.E.B. Yassin, S. Alsuwayeh, F.A. Alkhaled, In vitro and in vivo evaluation of floating controlled release dosage forms of verapamil hydrochloride, Pharm Ind, 2004; 66: 1364-1372.

9. K.N. Amit, M. Ruma, D. Biswarup, Gastroretentive drug delivery systems: a review, Asian J Pharm Clin Res, 2010; 3: 2-10.
10. S.U. Zate, P.I. Kothawade, G.H. Mahale, K.P. Kapse, S.P. Anantwar, Gastroretentivebioadhesive drug delivery system, Int J PharmTech Res, 2010; 2: 1227-1235.
11. M. Camilleri, Integrated upper gastrointestinal response to food intake, Gastroenterology, 2006; 131: 640-658.
12. C. Marriott, N.P. Gregory, Mucus physiology and pathology, Bioadhesive Drug Delivery Systems, CRC Press Florida, 1990; 1-24.
13. Allen, W.J. Cunliffe, J.P. Pearson, C.W. Venables, The adherant gastric mucus gel barrier in man and changes in peptic ulceration, J Intern Med, 1990; 732: 83-90.
14. J.D. Smart, The basics and underlying mechanisms of mucoadhesion, Advanced drug delivery reviews, 2005; 57: 1556-1568.
15. Wilson CG and Washington N: The Stomach: its role in oral drug delivery. In: Rubinstein, M.H., (Ed.). Physiological pharmaceutics: biological barriers to drug absorption. Ellis Harwood. Chechester, 1989; 47-70.
16. Desai S: A novel floating controlled release drug delivery system based on a dried gel matrix network [master's thesis]. 1984 Jamaica, NY, St John's University.
17. Prajapati S and Dharamsi A: Floating drug delivery for prolonging gastric retention of dosage form. Indian Journal of Novel Drug Delivery, 2013; 5: 15-27.
18. Sharma N, Agarwal D, Gupta M and Khinchi M: A comprehensive review on floating drug delivery system. International Journal of Research in Pharmaceutical and Biomedical sciences, 2011; 2: 428-441.
19. Swetha S, Allena RT and Gowda DV: A comprehensive review on gastroretentive drug delivery systems. International Journal of Pharmaceutical and Biomedical Research, 2012; 3: 1285-1293.
20. Kawatra M, Jain U and Ramana J: Recent advances in floating microspheres as gastro-retentive drug delivery system: A review. International Journal of Recent Advances in Pharmaceutical Research, 2012; 2: 5-23.
21. Bhowmik D: Floating drug delivery system- A review. Der Pharmacia Lettre., 2009; 1: 199-218.
22. Pandey A, Kumar G, Kothiyal P and Barshiliya Y: A Review on current approaches in gastro retentive drug delivery system. Asian Journal of Pharmacy and Medical Science, 2012; 2: 60-77.

23. Makwana A, Sameja K, Parekh H and Pandya Y: Advancements in controlled release gastroretentive drug delivery system: A review. Journal of Drug Delivery and Therapeutics, 2012; 2: 12-21.
24. Nayak KP and Upadhyay P: Gastroretentive drug delivery systems and recent approaches: A review. Journal of Pharmaceutical Research and Opinion, 2012; 2: 1-8.
25. Kagan L and Hoffman A: Selection of drug candidates for gastroretentive dosage forms: Pharmacokinetics following continuous intragastric mode of administration in a rat model. European Journal of Pharmaceutics and Biopharmaceutics, 2008; 69: 238–246.
26. Reddy BV, Navaneetha K: Gastroretentive drug delivery system- A review. Journal of Global Trends in Pharmaceutical Sciences, 2013; 4: 018-1033.
27. Vasa S and Banji D: Approaches for gastrotentive drug delivery systems. International Journal of Applied Biology and Pharmaceutical Technology, 2010; 1: 589-6.