Research Article

Design a Comprehensive Evaluation and Noval Approaches from Natural Source of Microspheres from Anti-hyperlipidimic Drug

Bendi Sri Venkateswarlu[1,*], Rajappa Margret Chandira[1], Palanisamy Pethappachetty[1], Naveeth Raffic[2]

[1]Department of Pharmaceutics, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation(Deemed to be University), Salem, Tamil Nadu, INDIA.
[2]Research Scholar, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation(Deemed to be University), Salem, Tamil Nadu, INDIA.

Submission Date: 15-06-2022; Revision Date: 23-06-2022; Accepted Date: 19-07-2022.

ABSTRACT

To deliver Atorvastatin orally, researchers developed bioadhesive controlled release microspheres utilising sodium alginate, guar gum, locust bean gum, and xanthan gum as copolymers. Atorvastatin microspheres may be effectively made using the ionotropic gelation process and the ionic cross-linking approach. Other procedures make use of higher volumes of organic solvents, which are more expensive and dangerous due to the risk of explosion, air pollution, toxicity, and the difficulty in removing all residues of organic solvent. The micrometric investigations showed that the produced microspheres had a mean particle size of 512-903m, which is acceptable for oral administration as bioadhesive controlled release microspheres. Percent yield, percent drug entrapment efficiency, particle size and swelling and mucoadhesion all increased as a result of an increase in polymer concentration. Microspheres of Atorvastatin utilising sodium alginate together with guar gum as a copolymer stuck to the mucus more strongly than those using sodium alginate combined with locust bean gum and xanthan gum as copolymers.

Keywords: Atorvastatin, Guar Gum, Xanthan Gum, Microspheres, Percentage of swelling and percentage of mucoadhesion.

Correspondence:
Prof. Dr. Bendi Sri Venkateswarlu,
Department of Pharmaceutics, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University), Salem-636308, Tamil Nadu, INDIA.

Email: svmanand@gmail.com

INTRODUCTION

Introduction to Microspheres[1-2]

There has been a long history of therapy for acute or chronic illness using different pharmaceutical dosage forms such as tablets and capsules as well as ointments and other emollients as carriers for the delivery of the drug to the patient. This sort of drug delivery system is commonly used many times a day to establish and maintain a therapeutically effective concentration of the drug delivered in the therapeutic range required for therapy. As a consequence, the toxicity and efficiency of the medicine are compromised. Controlled drug delivery systems are a result of this, as well as other issues including overdosing and unpredictability in absorption. If you're looking for a new medicine delivery method, the term "novel" implies that you're in a hurry to find anything. A well-designed continuous or controlled release medication delivery system might be a substantial improvement in tackling the current drug delivery system challenge. One of the goals of controlled release medication delivery is to distribute the medicine at a certain time and location. Targeting a particular organ or tissue, while modulating the rate of medication delivery to the target tissue, are two different concepts. Because of their many therapeutic benefits, such as simplicity of administration, patient compliance, and formulation flexibility, oral controlled release dosage forms have been developed during the last three decades. Although this approach has several physiological drawbacks, including the inability to

SCAN QR CODE TO VIEW ONLINE

www.ajbls.com

DOI: 10.5530/ajbls.2022.11.60

restrain and locate the controlled drug delivery system in a specific area of the GIT due to variable motility and the relatively brief gastric emptying time (GET) in humans, which normally averages 2-3 hr through the major absorption zone, i.e., the stomach and upper part of the intestine, can result in incomplete drug release from the drug delivery system.

MUCOADHESION / BIOADHESION[3]

Systems that leverage the bio-adhesion properties of certain polymers that become sticky when hydrated may be utilised to target medicine to a specific area of the body for long durations. The attachment of polymers to the mucosal layer's surface was dubbed "mucoadhesion," thus the word. Interfacial pressures hold together two materials, at least one of which is biological, to form bio adhesions. Bio is a term used in biology. adhesion can be classified into 3 types. They are Platelet aggregation and wound healing, for example, are examples of adhesion. For example, cell adherence to culture dishes and biofilm growth on prosthetic devices and inserts. Adhesion to a biological substrate, such as synthetic hydrogels on soft tissues and sealants on tooth enamel.

Polymers used for Mucoadhesive System[2,4-5]

The delivery of active drugs to a specific place via mucoadhesive systems is being investigated. Systems that enhance the period that an active drug stays in a specific region have been made possible in part because of polymers. Swellable networks of polymers, linked together by cross-linking agents, are the basis of mucoadhesive polymers. To provide adequate wetting by mucus and optimum fluidity to allow for the mutual adsorption and interpenetration of polymer and mucus, these polymers have ideal polarity and have the best fluidity. Characteristics of an excellent polymer for a bioadhesive drug delivery system should be as follows. Toxic, irritating, and non-absorbable polymer breakdown products should be avoided at all costs. Cationic Polyelectrolyte's, Non-Ionic Polymers, Hydrogels, Thiolated polymers and Lectin-based polymers.

Iontropic gelation technique[6-9]

Polysaccharides (alginate, gellatin, and pectin) are dissolved in water or mild acidic solution in the ionotropic gelation process (chitosan). Dropwise, under steady stirring, the solutions containing various counter ions are added to these solutions. Polysaccharides undergo ionic gelation and precipitation to produce spherical particles as a result of complexation between species with opposing charges. Filtration removes the beads from the solution, which is then rinsed with distilled water and dried. The allaqueous system used in this procedure eliminates the need for microspheres to contain any remaining solvents. There are two main groups of ionotropic gelation counterions: Inorganic counter ions with low molecular weights (e.g., calcium chloride, magnesium chloride, zinc chloride, tin chloride, copper chloride, chromium chloride, boron chloride, iron chloride, copper sulphate, tin sulphate, chromium sulphate, tin oxide, and copper sulphate). Ions with a high molecular weight (e.g. Octylsulphate, laurylsulphate, hexadecylsulphate, cetylstearylsulphate). This process of ionotropic gelation is easy and safe. Reversible physical crosslinking through electrostatic contact, rather than chemical crosslinking, eliminates the potential toxicity of reagents and other undesired side effects.

MATERIALS AND METHODS

Atorvastastin was purchased from natco Labs Pvt. Ltd, Xanthan Gum was purchased from Signet Chemical Corporation, Mumbai, India., Guar Gum was purchased from Merck Specialties Pvt Ltd, Mumbai, India, Locust Bean Gum was purchased from Merck Specialities Pvt Ltd, Mumbai, India, Methanol and Calcium chloride was purchased from are obtained from mercury scientific lab, Salem, India.

UV Spectroscopic Studies (Determination of λ_{max})[10-11]

The standard solution of atorvastastin was scanned between scanned in the range of 200nm to 400nm on a UV-Visible spectrophotometer. The drug exhibited a λ_{max} at 246nm and 248nm.in 6.8 pH phosphate buffer. 10 mg of Atorvastatin was accurately weighed and dissolved in 10ml of methanol (Stock Solution I) to get a concentration of 1000 µg/ml. From the stock solution- I, 1ml of aliquots was taken and suitably diluted with 0.1N HCl (Stock Solution-II) to get concentrations of 100µg/ml. From the stock solution- II, aliquots were taken and suitably diluted with 0.1N HCl (pH 1.2) to get concentrations in the range of 2 to 10µg/ml. The absorbance of these samples was analyzed by using a UV-Visible Spectrophotometer at 246nm against reference solution 0.1N HCl (pH 1.2). The same procedure is repeated with 6.8pH phosphate buffer. The results are shown in the Table 1, 2 and Figure 1.

Table 1: Prepared formulation of Atorvastatin Microcapsules.

Sl. No	Formulation code	Ratio	Polymers
1	F1	1:2.5	Atrovastastin yeast :Na alginate : Guar Gum
2	F2	1:1:3	Atrovastastin yeast :Na alginate : Guar Gum
3	F3	1:3.5	Atrovastastin yeast :Na alginate : Guar Gum
4	F4	1:1:4	Atrovastastin yeast :Na alginate : Guar Gum
5	F5	1:2.5	Atrovastastinyeas :Na Locust Bean Gum alginate:
6	F6	1:1:3	Atrovastastin yeast Locust Bean Gum :Na alginate:
7	F7	1:3.5	Atrovastastin: yeast Locust Bean Gum :Na alginate:
8	F8	1:1:4	Atrovastastin yeast Locust Bean Gum :Na alginate:
9	F9	1:2.5	Atrovastastin yeast Xanthan gum :Na alginate:
10	F10	1:1:3	Atrovastastin yeast Xanthan gum :Na alginate:
11	F11	1:3.5	Atrovastastin yeast Xanthan gum :Na alginate:
12	F12	1:1:4	Atrovastastin yeast Xanthan gum Na alginate:

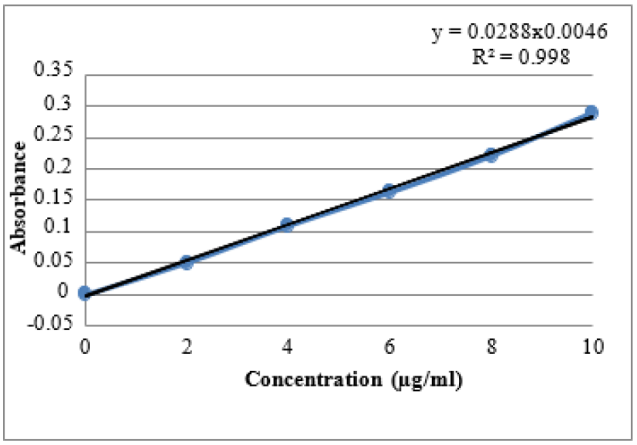

Figure 1: Data of Standard Calibration Curve of Atorvastastin.

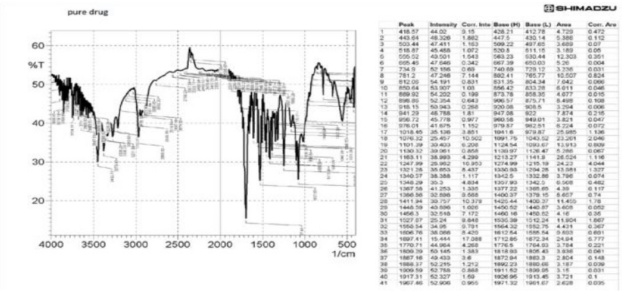

Figure 2: FT-IR spectrum of the pure drug atorvastatin.

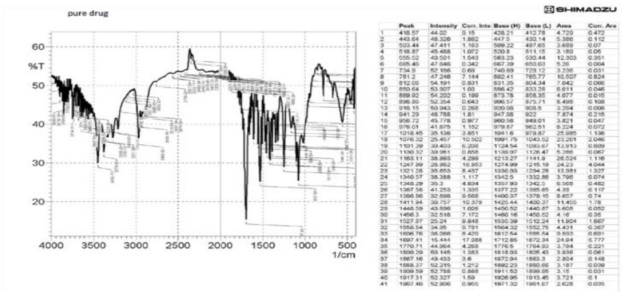

Figure 3: FT-IR spectrum of pure drug atorvastatin and all excipients.

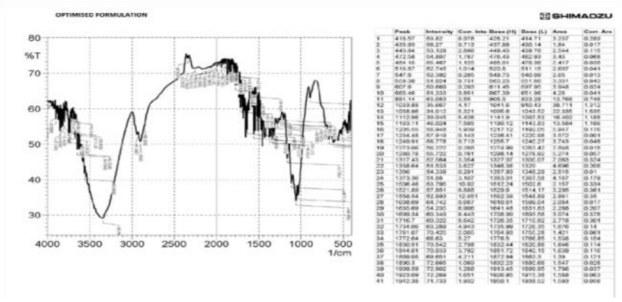

Figure 4: FT-IR spectrum of atorvastatin loaded microsphere F4 optimized.

FT-IR Spectra Analysis[12-14]

FT-IR spectroscopic was recorded on Shimadzu's fourier transform infrared spectrometer japan with a frequency range of 4000-500cm^{-1} The FT-IR spectroscopic analysis of both the control and treated sample of each drug was carried out to evaluate the studies. The results are shown in the Figure 2, 3, 4.

Determination of Solubility

The solubility of atorvastatin powder (approximately 1gm) in Dichloromethane, methanol and water was studied in the test tube.

Drug and Excipients Compatibility Studies

Compatibility must be established between the active ingredient and other excipients to produce a stable, efficacious, attractive and safe product particular

excipient with an active ingredient is available, then compatibility studies are of paramount importance.

Formulation Development of Microspheres[15-17]

Preparation of microspheres by using ionotropic gelatin method

Batches of microcapsules were prepared by ionotropic gelation method which involved a reaction between sodium alginate and polycationic ions like calcium to produce a hydrogel network of calcium alginate. Sodium alginate and the microspheres polymer were dispersed in purified water (10 ml) to form a homogeneous polymer mixture. The API, Atorvastatin (100 mg) were added to the polymer premix and mixed thoroughly with a stirrer to form a viscous dispersion. The resulting dispersion was then added through a 22G needle into calcium chloride (4% w/v) solution. The addition was done with continuous stirring at 200rpm. The added droplets were retained in the calcium chloride solution for 30 min to complete the curing reaction and to produce rigid spherical microcapsules. The microcapsules were collected by decantation, and the product thus separated was washed repeatedly with purified water to remove excess calcium impurity deposited on the surface of microcapsules and then air-dried. The preparation procedure is shown in the Table 1.

Evaluation Studies of Micro Capsules[18-21]

Percentage yield

The percentage of production yield was calculated from the weight of dried microspheres recovered from each batch and the sum of the initial weight of starting materials. The percentage yield was calculated using the following formula: Practical mass (Microcapsules). The results are shown in the Table 3.

$$\% \text{ Yield} = \frac{\text{Practical yield}}{\text{Theoretical mass (polymer + Drug)}} \times 100$$

Drug entrapment efficiency

Atorvastatin microcapsules with a potency of 100 milligrammes were used in the study. Microcapsules were crushed to determine how much medication was within. An amount of the powder was added to the volumetric flask of 100 millilitres, and 10 millilitres of methanol were used to dissolve the solution. Whatmann filter paper was used for 24 hr to filter out the solution before it was spectrophotometer-measured at 246 nm for its absorbance. The results are shown in the Table 3.

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Experimental Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

UV-Spectroscopic Studies

Standard Calibration Curve of Atorvastatin

Table 2: Data of Standard Calibration Curve of Atorvastatin.

Parameters	Value
R^2	0.998
SLOPE	0.0288
INTERCEPT	0.998

Evaluation and Characterisation of Microspheres

Percentage yield and drug entrapment efficiency

Table 3: Evaluation of microspheres formulation F1-F12.

Sl. No.	Formulation code	% yield	% Drug entrapmentefficiency
1	F1	80	82.66
2	F2	83.33	84.4
3	F3	85	84.66
4	F4	88	88.66
5	F5	62.22	53.2
6	F6	80	55
7	F7	80	68.86
8	F8	87	76.66
9	F9	80	66.73
10	F10	86	70
11	F11	86.66	75
12	F12	87.5	79.2

Particle Size Analysis

Optic microscopy was used to measure the particle size in the microparticle samples. The eyepiece micrometre was calibrated and found to be equivalent to 12.5 micrometres per unit. Using a 45x magnification, about 100 microparticle sizes were determined.

Swelling Study

Using a pH 1.2 simulated stomach fluid, the swelling ratio of several dried microcapsules was evaluated gravimetrically. Removed microcapsules were wiped to remove excess liquid and weighed on a scale at regular intervals. The following equation was used to calculate the percentage of w/v swelling. The results are shown in the Table 4.

Scanning Electron Microscopy

Gold–palladium coating in an argon atmosphere at ambient temperature may be employed by SEM to analyse the shape and surface topography of drug microspheres and the product (drug/microspheres complex). The presence of inclusion complexes may be

Percentage Swelling of Prepared Microspheres

Table 4: Data of Percentage swelling.

Sl. No.	Formulation code	Percentage swelling
1	F1	28
2	F2	42
3	F_3	62
4	F4	85
5	F5	24
6	F6	39
7	F7	55
8	F8	64
9	F9	31
10	F10	53
11	F11	67
12	F12	85

SEM Studies

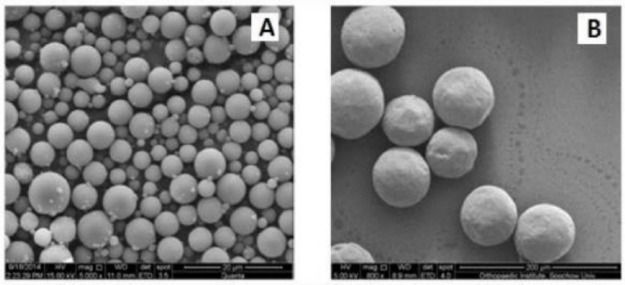

Figure 5: SEM of atorvastatin microspheres optimized formulation

seen under an electron microscope by comparing the crystallisation states of the source components with the final result. The results are shown in Figure 5.

Evaluation of Microspheres Property

The wash-off technique was used to examine the microspheres property of microcapsules in an *in vitro* adhesion testing method. Cotton thread was used to attach fresh goat stomach mucus to glass slides. USP II tablet disintegration test was performed on the prepared glass slides with around 20 microcapsules scattered on each slide. When the device was activated, the sample was exposed to gradual up and down movement in the pH 1.2 simulated gastric fluid contained in the 1-litre tank. The machine is stopped and the number of microcapsules remaining to stick to the mucosal surface is counted at intervals of 1 hr up to 8 hr. The results are shown in Table 5.

$$\% \text{ Mucoadhesion} = \frac{\text{Number of microcapsules adhered}}{\text{Number of microcapsules applied}} \times \text{umb}$$

In-vitro Mucoadhesion

Table 5: Data of Percentage Mucoadhesion.

Sl. No.	FormulationCode	Percentage Mucoadhesion
1	F1	65
2	F2	70
3	F3	75
4	F4	85
5	F5	60
6	F6	65
7	F7	70
8	F8	75
9	F9	60
10	F10	70
11	F11	75
12	F12	80

In vitro Drug Release Study

The USP type – I rotating basket technique was used in simulated gastric fluid with a pH of 1.2 in a fully calibrated eight-station dissolving test setup (37± 0.50C, 50 rpm) (900ml). All dissolution investigations used microcapsules weighing precisely 100mg of Atorvastatin per formulation. At predefined intervals, aliquots of material were taken and the absorbance at 246nm was measured to check for drug release. A new pre-warmed stomach fluid pH 1.2 was replaced promptly at each time interval to maintain sink conditions throughout the experiment, as shown in the Figure. The results are shown in Table 6 and Figure 6.

In-vitro Drug Release Kinetics

Various mathematical models were fitted with the observed release data. The Korsmeyer-Peppas equation was used to estimate the parameters n and time component k, the release rate constant and 'R', the regression coefficient to better understand the process of release. Peppa's equation was used to study the release mechanism of Atorvastatin from the microcapsules. The results are shown in the Table 7.

Stability Studies

The optimized nanosponge formulation for stability determination accelerated stability conditions at (40°C/75%RH). Every 30 days for three months, it is taken and examined for load efficiency and *in-vitro* drug release. All of these variables are compared to the initial sample and evaluated to see if it meets the requirements. If so, the batch has passed the test. The results are shown in the Table 8.

Table 6: Data of *in-vitro* drug release of Atorvastatin microspheres Capsule F1 – F12

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Time in hrs	% drug release											
0	0	0	0	**0**	0	0	0	0	0	0	0	0
0.5	21.12	23.33	31.40	**19.11**	20.36	21.44	23.36	30.21	27.33	24.40	22.45	26.63
1	31.62	28.22	38.36	**29.03**	31.48	33.55	35.45	42.54	37.44	31.15	36.36	35.45
3	38.34	42.45	47.48	**38.17**	40.59	47.62	46.26	51.43	49.43	49.35	51.48	49.55
6	46.48	52.26	59.55	**45.21**	69.32	64.48	59.51	67.51	58.53	52.45	63.69	58.36
12	59.28	60.69	69.31	**58.04**	71.47	73.36	68.48	72.62	63.26	68.52	70.59	71.49
24	67.65	71.26	78.21	**78.13**	83.55	80.64	73.45	81.35	75.88	78.64	79.55	80.59
48	79.78	82.49	84.36	**94.01**	90.89	92.26	89.68	90.26	91.26	90.85	89.33	91.45

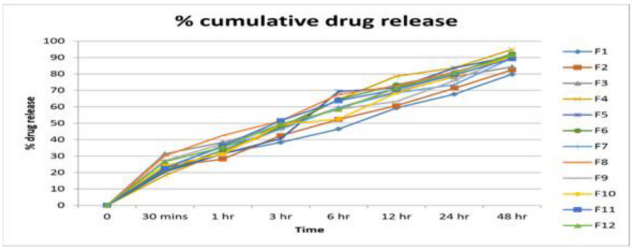

Figure 6: Data of *in-vitro* drug release of Atorvastatin microspheres Capsule F1 – F12

Statistical Analysis

As previously established in prior investigations, the experiment is not complete without statistical methods to convey data. In addition, the current analysis comprised several inter-batch comparisons of various parameters observed. MS Excel 20013 was used to collect data and perform the necessary mathematical computations and statistical analyses. The data were presented as mean SEM, with statistical significance determined by comparing two means in Microsoft Office Excel 20013. In each of the aspects, p=0.05 was considered significant.

RESULTS AND DISCUSSION[22-23]

UV-Spectroscopic Studies

Standard Calibration Curve of Atorvastastin

Atorvastatin 10 mg/ml solution was scanned in the 200-400nm range. In simulated stomach fluid pH 1.2, the medication had a max of 246nm and high repeatability. In this study, we discovered a correlation between the absorbance and concentration that was almost perfect, with an intercept that was 0.0046. Based on the results It was determined that the substance agreed with the preliminary identification. Furthermore, the maximal wavelength of the drug was determined to be 246nm and showed that the drug obeys to Beer-Lamberts law.

FT-IR Spectra Analysis

Based on the results of the study, it is possible to conclude that no additional peaks were observed in the physical mixture and that all of the excipients are API compatible. The compatibility study was performed at ATR-FTIR and revealed that excipients have no interaction with API.

Evaluation and Characterisation of Microspheres

percentage yield and drug entrapment efficiency

The product yield was found to rise in direct proportion to the polymer ratio used in the formulation. For sodium alginate microspheres with GUAR GUM copolymer, the yield ranged from 80 to 88 %; for sodium alginate microspheres with LOCUST BEAN GUM copolymer, the yield varied from 62.22 to 87 %; and for sodium alginate microspheres with XANTHAN GUM copolymer, the yield varied from 80 to 87.5 %. The entrapment efficiency of microspheres ranged from 82.66 to 88% of Atorvastatin, 53.2 to 76.66% of microspheres that contained sodium alginate together with Locust Bean Gum as copolymer, and 66.73% to 78% of microspheres that contained sodium alginate along with the Xanthan Gum.

SEM Studies

These microspheres were examined using Scanning Electron Microscope in order to determine the surface morphology of the microspheres. Images of microspheres containing sodium alginate with Guar gum and Locust Bean Gum as copolymers are visible at 75x, 50x, 40x and 11x magnifications in this SEM study for F4 formulation. Microspheres that contained sodium alginate with Xanthan Gum as copolymer had

Table 7: *In vitro* Kinetic data of Atorvastatin microspheres Capsule F1 – F12.

Code	Zero-order		First-order		Higuchi		Hixson crowell		Peppas	
	R2	Slope	R^2	Slope	R^2	Slope	R^2	Slope	R^2	N
F1	0.696	1.296	0.886	0.012	0.904	10.536	0.829	0.033	0.979	0.277
F2	0.677	1.339	0.884	0.013	0.895	10.98	0.821	0.036	0.988	0.281
F3	0.582	1.271	0.814	0.146	0.824	10.78	0.741	0.367	0.969	0.818
F4	0.803	1.656	1.000	0.000	0.964	12.93	0.954	.053	0.987	0.334
F5	0.615	1.529	0.861	0.020	0.851	12.83	0.780	0.047	0.936	0.329
F6	0.625	1.503	0.905	0.020	0.861	12.57	0.819	0.048	0.947	0.309
F7	0.647	1.408	0.905	0.017	0.869	11.64	0.831	0.042	0.960	0.276
F8	0.567	1.342	0.857	0.018	0.810	11.44	0.765	0.042	0.958	0.230
F9	0.667	1.407	0.938	0.019	0.876	11.49	0.868	0.044	0.980	0.247
F10	0.681	1.487	0.934	0.019	0.896	12.17	0863	0.046	0.980	0.288
F11	0.597	1.404	0.918	-0.02	0.838	11.865	0.781	0.043	0.932	0.284
F12	0.644	1.455	0.918	-0.02	0.873	12.08	0.838	0.046	0.983	0.268

Table 8: Data of Stability studies of Atorvastatin microspheres.

Time	40°C±2°C/75% RH±5%RH Accelerated stability study	Room Temperature stability study	40°C±2°C/75% RH±5%RH Accelerated stability study	Room Temperature stability study	Swelling index (%)
	Entrapment Efficiency (%)		*In vitro* release studies (%)		
Initial	88.66	88.66	94.88	94.88	85
15 days	88.45	88.45	94.13	94.32	85
30 days	88.01	88.12	93.80	94.01	85
45 days	87.98	88.01	93.61	93.97	84
60 days	87.67	87.93	93.01	93.23	84
90 days	87.45	87.88	92.90	93.11	83

a size range of 664 to 903 micrometres. Increases in polymer concentration enhanced particle size and percent drug entrapment effectiveness of microspheres. Formulation F4 SEM photos may be seen in the gallery below.

Percentage of Swelling Index

The amount of polymer directly affects the swelling ratio. As the polymer to drug ratio increased, the percentage of swelling increased from 28 to 85% for microspheres containing sodium alginate along with GUAR Gum as copolymer, 24 to 64% for microspheres containing sodium alginate along with Locust Bean Gum as copolymer and 31 to 85 for microspheres containing sodium alginate along with Xanthan Gum as copolymer.

In-vitro Mucoadhesion

As the polymer to drug ratio increased, microspheres containing sodium alginate along with Guar Gum as copolymer exhibited % mucoadhesion ranging from 65 % to 85%, microspheres containing sodium alginate along with Locust Bean Gum as copolymer exhibited % mucoadhesion ranging from 60 % to 75% and microspheres containing sodium alginate along with Xanthan Gum as copolymer exhibited % mucoadhesion ranging from 60 % to 80%.

In-vitro Drug Release Studies

After 9 hr, the formulations F1, F2, F3, and F4 containing Sodium alginate and guar gum as copolymer exhibited maximal release of 92.66 %, 90.66 %, 90.6 %, and 94.66 %, respectively. F5, F6, F7, and F8 included Sodium alginate combined with Locust Bean Gum as a copolymer, which resulted in maximal release of 92.22 % after 9 hr, 90.66 % after 11 hr, and 89.55 % after 12 hr accordingly. Sodium alginate and Xanthan Gumas copolymer in formulations F9, F10, F11, and F12 resulted in a maximum release of 92.6% after nine hours, 91.3 % after ten hr, 90 % after 11 hr, and 92.44 % after 12 hr, respectively. The drug's release has been regulated via a device that monitors swelling. In

addition, the reduced surface area caused by the bigger particle size at greater polymer concentrations resulted in a delayed-release.

In-vitro Drug Release Kinetics

The optimized formulation F4 had an appreciable correlation with the Zero-order plot (R^2=0.628) and was simultaneously apparent to the Higuchi drug release profile (R^2=0.865) thus, presenting a conventional release pattern as a capsules. The data fitting with Korsmeyer Peppas model and value of 0.932 for the variable n calculated for each batch including F4, confirms that the release kinetics followed non-Fickian drug release mechanism.

Stability Studies

According to ICH guidelines, the amended formulation was subjected to a three-month stability assessment (Accelerated stability study) at 40°C±2°C/75% RH±5 percent RH and (Room Temperature) at 25°C±2°C/60% RH±5% RH stability study. The results indicated a marginally significant difference between the entrapment efficiency and *in vitro* release testing

CONCLUSION

The stability studies for the optimized F4 formulation were conducted for three months. The study results indicated negligible levels of changes were observed in appearance, entrapment efficiency and *in vitro* drug release during storage at accelerated temperature and the room temperature was observed. The results don't show major variances during storage for optimized formulation. After 3 months the entrapment efficiency showed 91.6% and *in vitro* drug release showed 95.17% it could be assumed that the temperature was an optimum condition for the storage of the formulation. Thus, based on these findings, it is possible to conclude that the microsphere capsule formulation, particularly the F4 formulation, exhibited improved release behaviour, which would assist in reducing dose frequency and providing an effective route of administration and improved the Bio-availability.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

FTIR: Fourier Transform Infrared; **HCl:** Hydrochloric acid; **N:** Normality; **RH:** Relative Humidity; **UV:** Ultra Violet.

REFERENCES

1. Durgavale AA, Dhole AR, Mohite SK, Magdum CS. Formulation and evaluation of floating microsphere of captopril using different gas forming agents. Am J PharmTech Research. 2012;2(2):565-75.
2. Diyya AS, Kumar VR. Formulation and *in vitro* evaluation of floating microspheres of glipizide.
3. Moussa RA, Osman R, Awad GA, Mortada N. Montelukast spray dried microparticles: Preparation, excipients selection and *in vitro* pulmonary deposition. Int J Pharm Pharm Sci. 2015 Nov 1:233-40.
4. Arul B, Kothai R, Sangameswaran B, Jayakar B. Formulation and evaluation of chitosan microspheres containing isoniazid. Indian J Pharm Sci. 2003;65(6):640.
5. Haznedar S, Dortunç B. Preparation and *in vitro* evaluation of Eudragit microspheres containing acetazolamide. Int J Pharm. 2004;269(1):131-40. doi: 10.1016/j.ijpharm.2003.09.015, PMID 14698584.
6. Katstra WE, Palazzolo RD, Rowe CW, Giritlioglu B, Teung P, Cima MJ. Oral dosage forms fabricated by three Dimensional Printing™. J Control Release. 2000;66(1):1-9. doi: 10.1016/s0168-3659(99)00225-4, PMID 10708873.
7. Abbasiliasi S, Shun TJ, Tengku Ibrahim TA, Ismail N, Ariff AB, Mokhtar NK, *et al*. Use of sodium alginate in the preparation of gelatin-based hard capsule shells and their evaluation *in vitro*. RSC Adv. 2019;9(28):16147-57. doi: 10.1039/c9ra01791g, PMID 35521410.
8. Senthilkumar SK, Jaykar B, Kavimani S. Formulation, characterization and *in vitro* evaluation of floating microsphere containing rabeprazole sodium. Jitps. 2010;1(6):274-82.
9. Kishore VS, Rao BT, Pavani K, Nagasen D, Varma KR, Gowtham D. *Plantago ovata* seeds and bhringaraj leaves as superdisintegrants: Formulation and evaluation of sotalol hydrochloride orodispersible tablets. Int J Pharm Chem Biol Sci. 2013;3(4).
10. Kumar S, Chand T. Formulation and development of floating and mucoadhesive microspheres of clarithromycin. J Pharm Innov. 2013 Jul 1;2(5).
11. Ratnaparkhi MP, Dhiwar SB, Dhage KE, Bhore SS, Kadam PM, Patil PS. Formulation and *in-vitro* characterization of floating microspheres of Metfomin HCl. Scholars Research Library. Pharm Lett. 2012;4(5):1390-400.
12. Lee JH, Park TG, Choi HK. Development of oral drug delivery system using floating microspheres. J Microencapsul. 1999;16(6):715-29. doi: 10.1080/026520499288663, PMID 10575624.
13. Gladziwa U, Klotz U. Pharmacokinetics and pharmacodynamics of H2-receptor antagonists in patients with renal insufficiency. Clin Pharmacokinet. 1993;24(4):319-32. doi: 10.2165/00003088-199324040-00005, PMID 8098275.
14. Martin A, Bustamante P, Chun AH. Physical pharmacy. Lea and Febiger; 1993.
15. Pharmacopoeia I. The Indian pharmacopoeia commission. Cent Indian Pharmacopoeia Lab Minist Health Fam Welf Govt India Sect. 2007;23.
16. Kalaiselvan V, Kumar R, Singh GN. Indian Pharmacopoeia commission's partners for promoting public health. Adv Pharmacoepidemiol Drug Saf. 2015;4(181):2167-1052.
17. Prakash J, Srivastava S, Ray RS, Singh N, Rajpali R, Singh GN. Current status of herbal drug standards in the Indian pharmacopoeia. Phytother Res. 2017;31(12):1817-23. doi: 10.1002/ptr.5933, PMID 29027278.

18. Shabir GA. Validation of high-performance liquid chromatography methods for pharmaceutical analysis. Understanding the differences and similarities between validation requirements of the US Food and Drug Administration, the US Pharmacopeia and the International Conference on Harmonization. J Chromatogr A. 2003;987(1-2):57-66. doi: 10.1016/s0021-9673(02)01536-4, PMID 12613797.
19. Battu SK, Repka MA, Majumdar S, Madhusudan RY. Formulation and evaluation of rapidly disintegrating fenoverine tablets: Effect of superdisintegrants. Drug Dev Ind Pharm. 2007;33(11):1225-32. doi: 10.1080/03639040701377888, PMID 18058319.
20. Basu SK, Adhiyaman R. Preparation and characterization of nitrendipine-loaded Eudragit RL 100 microspheres prepared by an emulsion-solvent evaporation method. Trop J Pharm Res. 2008 Sep 11;7(3):1033-41. doi: 10.4314/tjpr.v7i3.14688.
21. Sun ZF. Numerical simulation of flow in an array of in-line blunt boards: Mass transfer and flow patterns. Chem Eng Sci. 2001;56(5):1883-96. doi: 10.1016/S0009-2509(00)00464-4.
22. Nappinnai M, Kishore VS. Formulation and evaluation of microspheres of diltiazem hydrochloride. Indian J Pharm Sci. 2007;69(4):511. doi: 10.4103/0250-474X.36935.
23. Gupta R, Prajapati SK, Pattnaik S, Bhardwaj P. Formulation and evaluation of novel stomach specific floating microspheres bearing famotidine for treatment of gastric ulcer and their radiographic study. Asian Pac J Trop Biomed. 2014;4(9):729-35. doi: 10.12980/APJTB.4.201414B73.

Cite this article: Venkateswarlu BS, Chandira RM, Pethappachetty P, Raffic N. Design a Comprehensive Evaluation and Noval Approaches from Natural Source of Microspheres from Anti-hyperlipidimic Drug. Asian J Biol Life Sci. 2022;11(2):442-50.