ORIGINAL ARTICLE

ScienZTech

INTERNATIONAL JOURNAL OF DRUG DELIVERY AND NANOTECHNOLOGY

Published by ScienzTech Publication Journal Home Page: www.scienztech.org/ijddn

Natural Microspheres: Versatile Carriers for Controlled Release of Active Compounds

Krishnamoorthy B*[1], Chanchal Navin Raj[2]

[1]Sanjivani College of Pharmaceutical Sciences, Rajota, Khetri (Raj)
[2]Sun Rise University, Bagd Rajput, Ramgarh, Alwar (Raj)

Article History:

Received on: 10 Feb 2023
Revised on: 05 Mar 2023
Accepted on: 07 Mar 2023

Keywords:

Venlafaxine Hydrochloride, microspheres, sustained release, ionotropic gelation, sodium alginate, chitosan, calcium chloride, characterization, entrapment efficiency, in vitro release, release kinetics

ABSTRACT

In this study, we aimed to develop microsphere systems for the sustained release of Venlafaxine Hydrochloride (HCl) using the ionotropic gelation method. Sodium alginate, chitosan, and calcium chloride were utilized as key components in the formulation. The prepared microbeads underwent comprehensive characterization, including size determination, shape analysis, and surface morphology assessment using scanning electron microscopy (SEM). The physical state of the drug in the formulations was investigated using X-ray powder diffraction analysis (X-RD), while the interaction between the drug and polymers was studied by Fourier-transform infrared spectroscopy (FTIR). Additionally, entrapment efficiency, in vitro release, and release kinetics were evaluated.The FTIR studies revealed the absence of any significant interaction between the drug and polymers, ensuring the stability of the formulation. The microspheres exhibited high entrapment efficiency, with up to 98.72% ± 0.79 being achieved. The in vitro release studies demonstrated the potential to finely control the release rate of Venlafaxine HCl over a wide time scale. The microspheres displayed superior performance in terms of providing prolonged release of the drug, making them an effective system for sustained drug delivery.

*Corresponding Author

Name: Krishnamoorthy B
Phone: +91 9666499784
Email: bkrishmoorthy2004@gmail.com

eISSN: 2455-2747

DOI: https://doi.org/10.26452/

Production and Hosted by

ScienzTech.org

© 2023 | All rights reserved.

INTRODUCTION

Microspheres made from natural products, particularly polysaccharides, have emerged as promising delivery carriers for controlled release of active compounds [1]. These microspheres can exist in the form of microparticles or microcapsules, offering numerous advantages. They can be tailored to various routes of administration and enable controlled and targeted release of drugs, resulting in enhanced efficacy, reduced toxicity, and improved patient compliance. In this article, we explore the potential of emulsification/internal gelation as an alternative method to extrusion/external gelation for encapsulating a wide range of compounds, including sensitive biological substances like anti-inflammatory drugs [2]. Additionally, we propose a novel emulsification/internal gelation technique for the production of small-diameter alginate microparticles in large quantities. Furthermore, we discuss the production procedure of chitosan microparticles through external gelation, involving the extrusion of a mixture of chitosan and the drug into a gelling bath containing divalent cations, resulting in the formation of gelated chitosan microparticles [3]. Venlafaxine HCl, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), is widely utilized as an antidepressant and anxiolytic agent in the management of various conditions, including Generalized

Anxiety Disorder, social phobia (social anxiety disorder), panic disorder with or without agoraphobia [4], as well as vasomotor symptoms in women with breast cancer and postmenopausal women [4]. Notably, it has demonstrated efficacy in improving both the frequency and severity of vasomotor symptoms. Given its therapeutic relevance and widespread use, Venlafaxine HCl has been selected as a model drug for the present study [5]. The primary objective of this research was to develop, optimize, and comprehensively characterize chitosan microspheres loaded with Venlafaxine HCl. Chitosan, a biocompatible and biodegradable polymer, offers several advantages as a carrier system for drug delivery.

Materials & Methodology

Venlafaxine HCl was received as a gift sample from Dr.Reddys Lab, Hyderabad; Chitosan powder was gifted from India Sea Foods, Cochin, Kerala; Sodium alginate procured from Fluka Chem, Buchs from Sigma, USA; Lactic acid from Merck Limited, Mumbai; and all other chemicals and solvents were of analytical grade satisfying pharmacopoeia specifications.

Preparation of chitosan coated alginate beads:

Sodium alginate was dissolved in distilled water at various concentrations ranging from 1% to 4% (w/v), as indicated in Table 1. Venlafaxine hydrochloride was pre-dissolved in double distilled water. The solution was slowly added to the sodium alginate solution while maintaining constant stirring. To eliminate any air bubbles that might have formed during mixing, the solution was subjected to sonication for 30 minutes. The gelation medium was prepared by thoroughly mixing equal proportions of calcium chloride solution (0.5% to 2% w/v) with different concentrations of chitosan solution (0.5% to 2%). The chitosan solution had previously been prepared with 2.4% lactic acid, and the pH of the medium was adjusted to 4.5 $\pm$ 0.1. The mixture was stirred continuously for 2 hours and kept at room temperature (25ºC) until further use. Using a 5 ml hypodermic syringe equipped with a #21 needle, the homogenous mixture of sodium alginate drug solution was added drop-wise into the gelation medium. The addition was performed under constant stirring at room temperature (25ºC). The beads formed in the gelation medium were left to cure for 4 hours. Subsequently, they were washed with distilled water to remove any excess gelation medium. The beads were then air-dried at room temperature (25ºC) in a dust-free chamber until they reached a constant weight. The prepared beads were carefully stored in an airtight container at room temperature (25ºC) to ensure their stability and integrity for further analysis and evaluation [6].

IR Spectral and DSC Study

To investigate and predict any physiochemical interaction between different excipients, I.R spectroscopy was utilized. Spectra matching approach was employed to detect potential chemical interactions between the drugs and polymer. A physical mixture consisting of the drug, polymer, and other excipients was prepared. The mixture was then combined with an appropriate quantity of potassium bromide. This mixture was compressed under 15 tons of pressure using a hydraulic press to form a transparent pellet. The resulting pellet was scanned in the range of 4000 to 400 cm-1 using an FTIR spectrophotometer (FTIR 8400 S, Shimadzu). The obtained IR spectrum of the physical mixture was compared with those of the pure drug and polymers. Peak matching analysis was performed to identify any appearance or disappearance of peaks, indicating potential chemical interactions between the components as well as other excipients [7]. The thermal behaviors of the pure drug(s), polymer(s), physical mixture of drug(s) and polymer(s), as well as the drug-loaded beads, were studied using a Pyris Diamond TG/DTA model no. instrument from PerkinElmer, Singapore. The analysis was carried out in a nitrogen atmosphere with a flow rate of 150 ml/min and a platinum crucible was used, and alpha alumina powder served as the reference material. Thermograms were recorded with a scanning speed of 10ºC/min, covering a temperature range from 30ºC to 300ºC.

X-Ray Powder Diffractometry [X-RD] Analysis

In order to investigate the physical state of the drug within the formulations, X-ray diffraction patterns of the pure drug, polymer(s), physical mixture of drug and polymer(s), blank microspheres, and drug-loaded microspheres were recorded using a Miniflex goniometer operating at a scanning speed of 1º/min. The analysis covered a 2θ angle range of 10-70 [8].

Surface Morphology Investigations and Particle Size Analyses

Particle size analysis of the microspheres was conducted using optical microscopy. The instrument was calibrated, with one unit of the eyepiece micrometer equivalent to 17.5 μm. Approximately 50 microspheres were measured for each sample to determine their sizes. The shape and surface morphology of the drug-loaded microspheres were examined using Scanning Electron Microscopy

Table 1: Formulation design for the preparation of venlafaxine hydrochloride loaded chitosan coated alginate beads

Formulation code	Sodium alginate (in % w/v)	$CaCl_2$ (in % w/v)	Chitosan (in % w/v)	Drug : Alginate ratio	Gelation time (in h)
VA1	3	2	-	1:4	4
VA2	3	2	0.5	1:4	4
VA3	3	2	1	1:4	4
VA4	3	2	1	1:3	4
VA5	3	2	1	1:2	4
VA6	3	2	1	1:4	2
VA7	2	2	1	1:4	4
VA8	3	1	1	1:4	4
VA9	3	2	2	1:4	4
VA10	3	2	1	1:4	8
VA11	4	2	1	1:4	4
VA12	3	-	1	1:4	4

Table 2: Percentage drug loading and Entrapment efficiency (%) and particle size (μm) of Venlafaxine hydrochloride loaded chitosan coated alginate beads (Mean ± SD, n=3)

Formula	VA1	VA2	VA3	VA4	VA5	VA6	VA7	VA8	VA9	VA10	VA11	VA12
Drug loading	11.05 ± 0.95	16.88 ± 1.92	18.82 ± 0.16	19.04 ± 0.07	21.57 ± 1.32	20.78 ± 0.19	16.42 ± 0.46	18.63 ± 1.07	15.73 ± 2.24	13.47 ± 0.12	12.36 ± 0.20	10.31 ± 1.2
Entrapment efficiency(in %)	70.73 ± 0.52	89.65 ± 2.09	98.72 ± 0.79	95.21 ± 2.25	80.57 ± 1.82	94.85 ± 1.99	79.04 ± 2.42	90.90 ± 0.89	94.63 ± 2.68	90.54 ± 1.18	82.78 ± 1.55	55.01 ± 3.00
Particle size (μm)	596.45 ± 1.04	624.86 ± 0.98	703.55 ± 0.75	712 ± 0.150	784.60 ± 1.08	688.56 ± 1.25	716.80 ± 0.96	743.20 ± 1.44	724.40 ± 0.34	764.55 ± 1.06	880.10 ± 1.23	708.10 ± 0.86

Table 3: Release kinetics behavior of different formulations of Venlafaxine hydrochloride -loaded chitosan coated alginate beads

Formulation code	VA1	VA2	VA3	VA4	VA5	VA6	VA7	VA8	VA9	VA10	VA11	VA12
Zero-Order [r2]	0.35	0.63	0.44	0.49	0.34	0.48	0.52	0.44	0.58	0.76	0.74	0.73
First-Order [r2]	0.954	0.98	0.94	0.96	0.93	0.97	0.97	0.98	0.98	0.99	0.98	0.95
Higuchi-Matrix[r2]	0.90	0.97	0.93	0.95	0.90	0.92	0.95	0.93	0.96	0.99	0.99	0.99

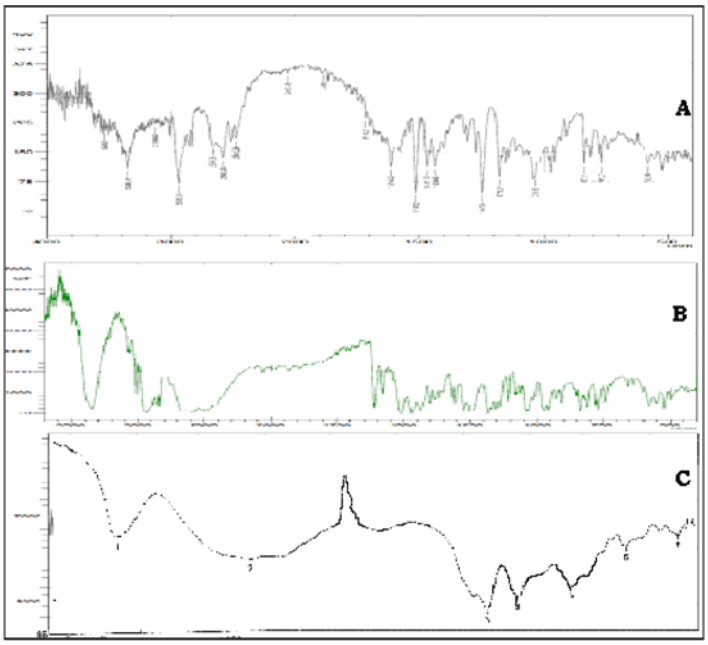

Figure 1: FT-IR spectra of A) Venlafaxine hydrochloride loaded chitosan coated alginate beads; B) pure Venlafaxine hydrochloride; C) unloaded blank chitosan coated alginate beads

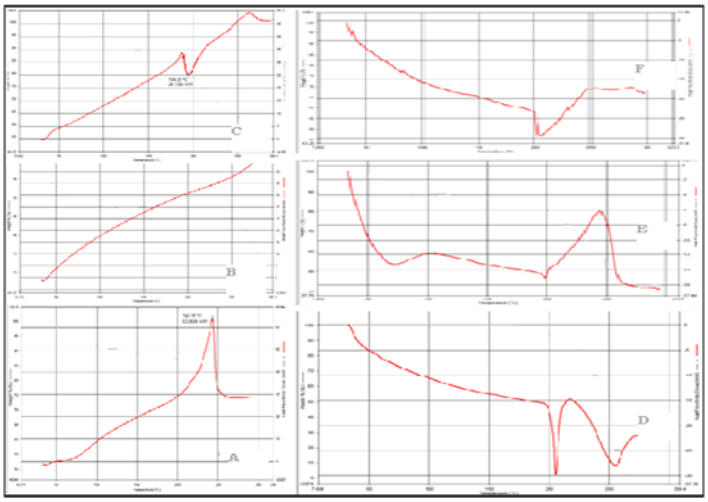

Figure 2: DSC thermograms of A) sodium alginate; B) chitosan; C) unloaded blank beads; D) pure venlafaxine hydrochloride; E) physical of Venlafaxine hydrochloride andsodium alginate and chitosan polymers; F) Venlafaxine hydrochloride loaded chitosan coated alginate beads

(SEM) with Vega © Tescan, USA [9].

Determination of Drug loading and Entrapment efficiency

For each batch, a total of fifty milligrams of venlafaxine hydrochloride loaded chitosan-coated alginate beads were placed in 100 ml of distilled water. The mixture was allowed to stand for 24 hours with intermittent shaking to ensure complete dissolution of the drug from the beads. Following the dissolution period, the solution was filtered through Whatman filter paper to remove any undissolved particles or impurities. An aliquot of the filtered solution, appropriately diluted, was subjected to spectrophotometric analysis using a UV-Visible spectrophotometer (Shimadzu 1800, Japan). The spectrophotometric assay was conducted at a wavelength of 274 nm, which corresponds to the specific absorption peak of venlafaxine hydrochloride. The absorbance of the aliquot was measured and recorded, allowing for the quantification of the released drug concentration.

Drug Loading was calculated using the formula in Equation 1 [10].

Drug Loading in % = W/W_t x 100 ..... (Equation 1)

Where,

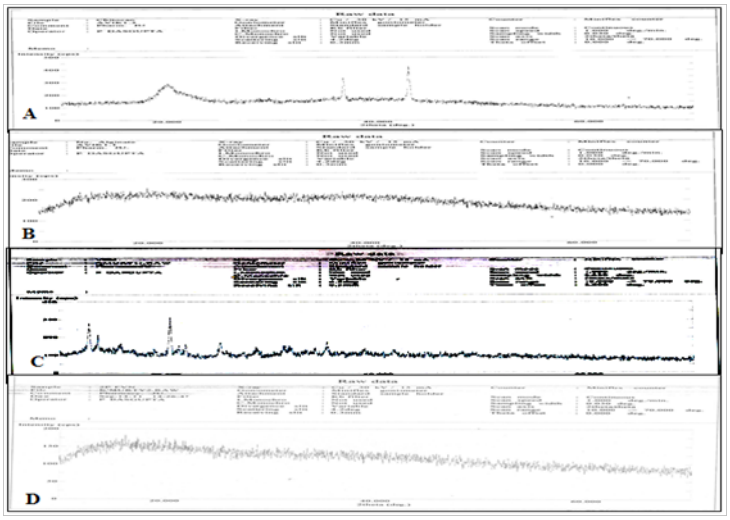

Figure 3: X-ray diffractograms of A) sodium alginate; B) chitosan; C) pure venlafaxine hydrochloride D) Venlafaxine hydrochloride loaded chitosan coated alginate beads

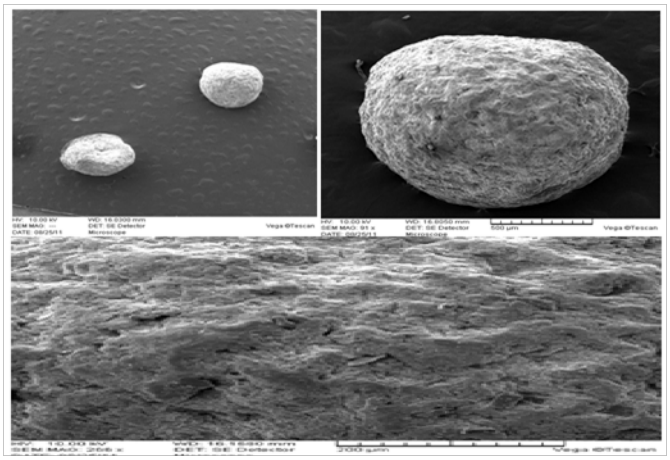

Figure 4: Scanning electron micrographs of Venlafaxine hydrochloride loaded chitosan coated alginate beads (VA11)

W = Drug content of the beads

W_t = Weight of the beads

Theoretical drug loading was determined by calculation assuming that the entire drug present in the polymer solution gets entrapped in beads and no loss occurs at any stage of preparation of the beads. The unloaded beads did not interfere with the spectrophotometric determination of drugs, which was checked before performing the drug loading studies.

Entrapment efficiency was determined by using the following relationship:

$$Entrapment\ \ Efficiency = (Experimental\ Drug\ Content / Theoretical\ Drug\ Content) \times 100 \quad \text{... (Eqn 2)}$$

Invitro Drug Release and Its Release Behavior Studies

In vitro drug release studies were conducted using drug-loaded beads weighing 100 mg from each batch. The studies were performed using a USP XXI dissolution rate test apparatus, in 350 ml of double distilled water at a temperature of 37 $\pm$ 0.5ºC. The apparatus was set to operate at a stirring speed of 50 rpm.At predetermined time intervals, 3 ml of the dissolution medium was sampled, and an equal volume of fresh dissolution medium was replenished to maintain a constant volume. The collected samples were filtered through Whatman No. 1 qualitative filter paper and analyzed for drug content at a wavelength of 274 nm using a Shimadzu 1800 UV spectrophotometer from Japan.Statistical analysis was carried out using GraphPad Prism 5 software. Each parameter was repeated three times (n=3) to ensure the reliability and reproducibility of the results. To analyze the release kinetics of the drug, data obtained from in vitro drug release studies were fitted into three different kinetic models: zero order, first order [11], and Higuchi's model [12,

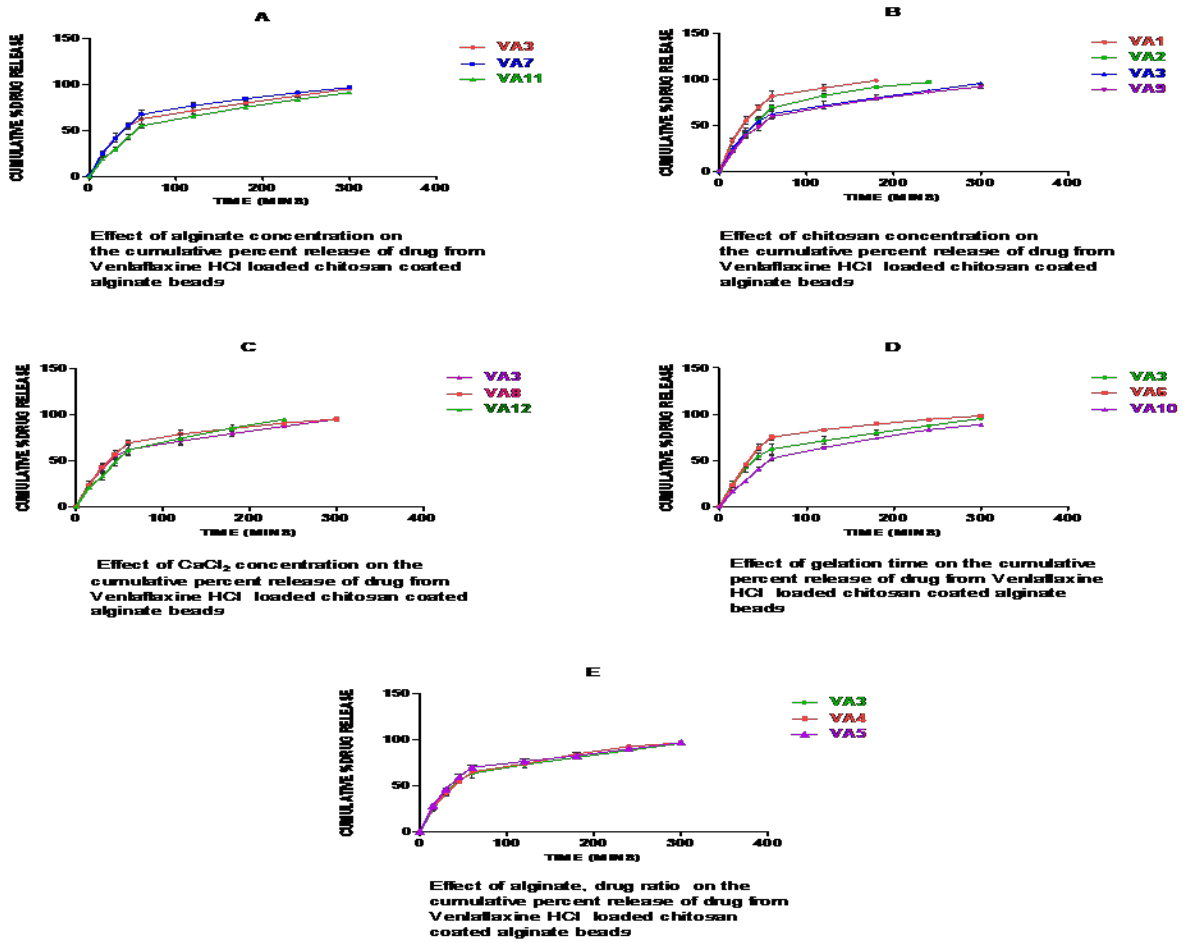

Figure 5: Effect of experimental variables on the cumulative drug release of Venlafaxine hydrochloride loaded chitosancoated alginate beads: A) alginate concentration; B) chitosan concentration; C) Calcium chloride concentration; D) gelation time and E) alginate drug ratio

13]. The zero-order model involved plotting the cumulative amount of drug released against time. The first-order model involved plotting the logarithm of the cumulative percentage of drug remaining against time. Higuchi's model involved plotting the cumulative percentage of drug released against the square root of time. By fitting the release data to these kinetic models, valuable insights into the release behavior and kinetics of the drug from the formulation were obtained.

Stability Studies

The prepared microspheres were packed securely in aluminum foil and subjected to stability studies for a period of three months, following the guidelines provided by the International Council for Harmonisation (ICH). Stability testing was conducted at two different temperature and relative humidity (RH) conditions [14]:

1. 25ºC and 65% RH
2. 40ºC and 75% RH

To maintain the desired humidity levels, a saturated solution of sodium chloride was used. By subjecting the microspheres to these temperature and humidity conditions, their stability and potential changes over time were evaluated in accordance with ICH guidelines.

RESULTS AND DISCUSSION

The FTIR spectra of both the pure drug and the beads were compared, and any significant deviations between their respective peaks were examined to determine the occurrence of interactions between the drug and the excipients used in the formulation.Upon analyzing the IR spectroscopic tracings, it was observed that there were no substantial variations between the peaks observed in the pure drug and those detected in the beads. This finding suggests that there was no discernible interaction between venlafaxine hydrochloride and the excipients employed in the formulation of the beads. The absence of significant peak deviations in the FTIR

spectra implies that the drug and excipients did not undergo any chemical reaction or form new compounds during the preparation of the beads. This is a desirable outcome, as it ensures the stability and integrity of the drug within the formulated beads. Furthermore, it suggests that the chosen excipients were compatible with venlafaxine hydrochloride, thereby allowing for a successful drug encapsulation process.These results are presented in Figure 1, illustrating the comparison of the FTIR spectra of the pure drug and the beads.

The DSC analysis revealed the characteristic melting point of pure venlafaxine hydrochloride at 207ºC [106]. Sodium alginate exhibited an exothermic decomposition peak around 240ºC, while chitosan did not exhibit any significant peaks. Interestingly, the DSC thermogram of the blank beads differed from that of the polymer (sodium alginate), indicating potential interaction between sodium alginate and calcium ions [15]. Notably, the absence of the exothermic peak at 207ºC in the DSC thermogram of the drug-loaded beads suggests that the venlafaxine hydrochloride existed in an amorphous state as a molecular dispersion within the polymeric matrix [Figure 2].

The X-ray diffraction (XRD) analysis of venlafaxine hydrochloride exhibited distinct sharp peaks, which were absent in the XRD pattern of the drug-loaded beads. This observation suggests that the drug loaded within the polymer matrix is present in a non-crystalline state, indicating the amorphous nature of the venlafaxine hydrochloride in both chitosan coated alginate beads [Figure 3].

The surface morphology of venlafaxine hydrochloride-loaded beads, namely chitosan-coated alginate beads was examined using scanning electron microscopy (SEM). The results revealed that beads exhibited a spherical shape. Additionally, the dried regions of the beads appeared flat, indicating successful drying during the preparation process. Furthermore, the drug was found to be uniformly dispersed within the polymeric matrix of the beads, without any discernible core or coat structure. The average particle size of the venlafaxine hydrochloride beads, optical microscopy was employed to determine. The analysis showed that the mean particle size ranged from 596.45 μm to 880.10 μm for the chitosan-coated alginate beads loaded with venlafaxine hydrochloride [Table 2].

The drug loading of the prepared venlafaxine hydrochloride beads was influenced by various experimental variables, including sodium alginate concentration, calcium chloride concentration, and chitosan concentration. The highest percentage of drug loading was achieved in formulation VA5, with a value of 21.57%. Conversely, formulation VA12 exhibited the lowest drug loading at 10.31%. An increase in sodium alginate concentration from 2% to 3% w/v resulted in an improvement in the percentage of drug loading, as observed in formulations VA7 and VA3. However, when the sodium alginate concentration was further increased to 4% w/v (as in formulation VA11), a decrease in drug loading was observed. Similarly, an increase in chitosan concentration up to 1% w/v led to an enhancement in drug loading, as demonstrated by formulations VA2 and VA3. However, subsequent increments in chitosan concentration did not yield further improvements in drug loading.The entrapment efficiency of the venlafaxine hydrochloride-loaded chitosan alginate beads ranged from 55.0% to 98.75%. This indicates that the formulation process successfully encapsulated the drug within the beads, with varying degrees of efficiency depending on the specific formulation. These findings demonstrate the influence of different experimental variables on the drug loading and entrapment efficiency of the venlafaxine hydrochloride beads. The optimal formulation (VA5) achieved a high drug loading percentage, highlighting the importance of carefully selecting the concentrations of sodium alginate and chitosan. In the case of the dissolution profiles of the venlafaxine hydrochloride-loaded chitosan-coated alginate beads (formulations VA3 to VA11) exhibited varying drug release percentages. At the end of 5 hours, the drug release percentages were found to be 95.33 $\pm$ 1.3, 96.52 $\pm$ 1.26, 97.03 $\pm$ 1.24, 98.07 $\pm$ 0.09, 95.29 $\pm$ 0.70, 95.28 $\pm$ 1.25, 91.67 $\pm$ 1.75, 88.68 $\pm$ 0.38, and 86.67 $\pm$ 1.38% for VA3 to VA11, respectively. Formulations VA1, VA2, and VA12 achieved 95% drug release at the end of 3 and 4 hours, respectively. Among all the formulations, VA11 exhibited the highest sustaining effect, with 86.67% of venlafaxine hydrochloride released over the 5-hour period. Figure 4 represents the influence of different polymers and calcium chloride concentration on the cumulative percentage of drug release from the chitosan-coated alginate beads. The beads prepared using a sodium alginate concentration of 4% w/v demonstrated a prolonged drug release compared to those prepared with 2% and 3% w/v sodium alginate. Additionally, an increase in calcium chloride concentration resulted in a delay in the drug release. However, since calcium chloride was used at a lower concentration of 2% w/v, its effect on the drug release was less pronounced. Furthermore, an increase in chitosan concentration led to retardation in the release of the drug.These findings highlight the impact of

different variables on the drug release behavior of the chitosan-coated alginate beads loaded with venlafaxine hydrochloride. The formulation with 4% w/v sodium alginate (VA11) exhibited the maximum sustained drug release, while variations in calcium chloride concentration and chitosan concentration affected the release kinetics. This information is valuable for optimizing the formulation parameters and tailoring the drug release characteristics of the venlafaxine hydrochloride-loaded beads for specific therapeutic applications [Table 3] [Figure 5].

The suitability of different mathematical models for describing the in vitro release data of venlafaxine hydrochloride-loaded chitosan-coated alginate beads was assessed based on their correlation coefficients. A higher correlation coefficient indicated a more appropriate model for the release data. Linear regression analysis of the zero-order and Higuchi's plot models demonstrated lower correlation coefficients compared to the first-order model. The first-order model exhibited a higher correlation coefficient, suggesting a linear relationship between the logarithm of the percent drug remaining to be released from the beads and time. Therefore, the release of venlafaxine from the chitosan-coated alginate beads followed a first-order kinetic model. These findings provide valuable insights into the release behavior of venlafaxine from the formulated beads and support the use of the first-order model for describing the release kinetics in vitro.

The short-term stability study conducted on all optimized batches revealed no significant changes in the cumulative release profiles. This indicates that the formulation remained stable under the specified conditions of the stability study.

CONCLUSION

The developed microparticulate drug delivery system using a blend of natural polymers for venlafaxine hydrochloride holds great promise for oral administration. This system is characterized by its simplicity and reproducibility. The chosen polymers, namely chitosan and sodium alginate, serve as effective carriers due to their easy availability and biocompatibility. Based on the data obtained, it can be concluded that the formulation of chitosan-coated alginate beads loaded with the drug is a suitable sustained drug delivery system for venlafaxine hydrochloride. However, for further extended release, the incorporation of other suitable natural polymers into the delivery system may be considered to retard the drug release to some extent.

ACKNOWLEDGEMENTS

Authors are thankful to the Secretary,Sanjivani College of Pharmaceutical Sciences, Rajota, Khetri (Raj) for providing necessaryfacilities to complete this work.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

REFERENCES

[1] Qiu A, Wang Y, Zhang G, Wang H. Natural Polysaccharide-Based Nanodrug Delivery Systems for Treatment of Diabetes. Polymers (Basel). 2022;14(15):3217–3217.

[2] Ahmed MM, El-Rasoul A, Auda S, Ibrahim SH. Emulsification/internal gelation as a method for preparation of diclofenac sodium-sodium alginate microparticles. Saudi Pharmaceutical Journal. 2013;21(1):61–69.

[3] Valle J, Valle R, Bierhalz A, Bezerra FM, Hernandez AL. Chitosan microcapsules: Methods of production and use in textile finishing. Journal of Applied Polymer Science. 2021;138:50482–50482.

[4] Mokale V, Naik J, Wagh P, Khairnar G. Preparation and Evaluation of Sustained Release Venlafaxine HCl Microspheres. J Pharm Sci. 2014;13(1):83–91.

[5] Madhavi B, Kamal ZN, Kusum B, Srikanth V, Ramalingam R, Vinod KR, et al. Formulation and evaluation of Venlafaxine HCl microspheres. Hygeia JDMed. 2011;3(1):64–70.

[6] Mandal S, Kumar SS, Krishnamoorthy B, Basu SK. Development and evaluation of calcium alginate beads prepared by sequential and simultaneous methods. Brazilian Journal of Pharmaceutical Science. 2010;46(4):785–793.

[7] Atram SC, Nikure Y. Formulation and evaluation of natural polymer-based sustained release microspheres. International Journal of Creative Research Thoughts (IJCRT). 2022;10(8):705–711.

[8] Aranaz I, Paños I, Peniche C, Heras A, Acosta N. Chitosan Spray-Dried Microparticles for Controlled Delivery of Venlafaxine Hydrochloride. Molecules. 1980;22.

[9] Sahoo SK, Mallick AA, Barik BB, Senapati PC. Preparations and in-vitro evaluation of ethyl

cellulose microspheres containing Stavudine by the double emulsion method. Pharmazie. 2006;62:117–121.

[10] Jianxian C, Saleem K, Ijaz M, Ur-Rehman M, Murtaza G, Asim MH. Development and in vitro Evaluation of Gastro-protective Aceclofenac-loaded Self-emulsifying Drug Delivery System. International Journal of Nanomedicine. 2020;15:5217–5226.

[11] Danbrow M, Samuelov Y. Zero order drug delivery from double-layered porous films: release rate profiles from ethyl cellulose, hydroxypropyl cellulose, and polyethylene glycol mixtures. J Pharm Pharmacol. 1980;32:463–470.

[12] Higuchi T. Rate of release of medicaments from ointment bases containing drugs in suspension. J Pharm Sci. 1961;50:874–875.

[13] Higuchi T. Mechanism of sustained-action medication: theoretical analysis of the rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1973;52:1145–1149.

[14] Kashappagoud H, Desai TM, Kumar P. Preparation and Evaluation of a Novel Buccal Adhesive System. AAPS PharmSciTech. 2004;5:35–35.

[15] Jeyanthi R, Mehta C, Thanoo BC, Deluca PP. effect of processing parameters on the properties of peptide-containing polylactic-co-glycolic acid (PLGA) microspheres. J Microencapsulation. 1997;14:163–174.

Copyright: This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Cite this article: Krishnamoorthy B, Chanchal Navin Raj. **Natural Microspheres: Versatile Carriers for Controlled Release of Active Compounds**. Int. J Drug Deliv. 2023; 1(1): 8-16.

© 2023 ScienzTech.org.