HNUE JOURNAL OF SCIENCE
Natural Sciences 2025, Volume 70, Issue 2, pp. 91-101
This paper is available online at http://hnuejs.edu.vn/ns
DOI: 10.18173/2354-1059.2025-0024

PREPARATION AND CHARACTERIZATION OF CARRAGEENAN/ LOVASTATIN BIOMATERIALS

Vu Quoc Manh[1], Vu Thi Thuong[2], Doan Thi Yen[2], Le Tien Dat[2], Nguyen Ngoc Linh[1], Nguyen Thi Bich Viet[2], Nguyen Dang Dat[2] and Vu Quoc Trung[2,*]

[1]*Faculty of Pharmacy, Thanh Do University, Hanoi city, Vietnam*
[2]*Faculty of Chemistry, Hanoi National University of Education, Hanoi city, Vietnam*
[*]Corresponding author: Vu Quoc Trung, e-mail: trungvq@hnue.edu.vn

Received April 28, 2025. Revised May 6, 2025. Accepted June 30, 2025.

Abstract. Carrageenan is a natural, gel-forming polysaccharide widely used in pharmaceutical applications due to its biocompatibility and mucoadhesive properties. This study aimed to develop carrageenan/lovastatin (CAR/Lov) composite biomaterials, evaluate their potential to enhance the solubility of lovastatin (Lov), and investigate their controlled drug release behavior. The prepared CAR/Lov samples were characterized by Fourier-transform infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM), and differential scanning calorimetry (DSC) to examine the interaction between carrageenan and lovastatin and to assess the dispersion of the drug within the polymer matrix. The results indicated that the incorporation of lovastatin into the carrageenan matrix did not alter the chemical structure of the drug; however, it significantly improved its solubility and modulated its release profile. Among the tested samples, the CL15 formulation, with a Lov/CAR ratio of 1:15, demonstrated the most efficient drug release under simulated intestinal fluid (pH 7.4), achieving a release rate of 86.57%. In contrast, the release at pH 2.0 (simulating gastric conditions) was lower (33.57%). These findings highlight the potential of the CAR/Lov system for pH-responsive drug delivery, offering promising applications in the development of lipid-lowering drug formulations.

***Keywords*:** carrageenan, lovastatin, drug release, solubility, polymer gel system.

1. Introduction

Bioavailability is a critical parameter in pharmacokinetics, referring to the proportion and rate at which an active pharmaceutical ingredient (API) reaches the systemic circulation or its intended site of action after administration [1], [2]. Ensuring sufficient bioavailability is essential to achieve the desired therapeutic effect, particularly for orally administered drugs. However, a significant number of

pharmacologically active compounds, especially those developed in recent years, are classified as Biopharmaceutics Classification System (BCS) class II or IV drugs, characterized by poor aqueous solubility [3]. This intrinsic limitation results in suboptimal absorption and therapeutic performance.

One of the major challenges in modern pharmaceutical science is the development of delivery systems capable of enhancing the solubility, stability, and ultimately the bioavailability of poorly soluble drugs. Lipophilic compounds, in particular, tend to form crystalline structures that are resistant to dissolution in aqueous environments. Strategies to overcome this include physical or chemical modification of the drug, use of solubilizing agents, and incorporation into advanced drug delivery platforms designed to reduce particle size, increase surface area, or improve drug wettability [4].

Among these strategies, the fabrication of bio-based nanocomposite materials has gained significant attraction due to their ability to not only enhance the solubility and release kinetics of hydrophobic drugs, but also to address the increasing demand for sustainable, biodegradable, and biocompatible drug delivery systems [5]. Natural polymers, in particular, have shown great promise as matrix-forming agents due to their safety profiles, structural diversity, and functional adaptability.

Carrageenans are a family of linear sulfated polysaccharides derived from red seaweeds of the *Florideophyceae* class, such as *Agardhiella, Chondrus Crispus, Eucheuma, Furcellaria, Gigartina, Hypnea, Iridaea, Sarconema, and Solieria* [6]. Due to their biocompatibility, high molecular weight, high viscosity, and gel-forming ability, these polymers have gained considerable attention in recent decades not only in the food industry but also in medical, biotechnological, and pharmaceutical fields [5]. In drug delivery, carrageenans can function as both drug carriers and functional excipients capable of controlling drug release rates, enhancing solubility, and protecting drugs from premature degradation [5], [7], [8]. Furthermore, carrageenans have been reported to exhibit a wide range of biological activities, including antioxidants [9], antiviral, antibacterial [10], anticoagulant, and anti-inflammatory effects, further supporting their potential in therapeutic applications.

Lovastatin (Lov) is a naturally occurring statin that effectively lowers blood cholesterol levels by competitively inhibiting the enzyme 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, thereby reducing hepatic cholesterol synthesis in the liver [11]. Clinical studies have demonstrated that Lov significantly reduces the incidence of coronary heart disease and related complications, even among individuals with average cholesterol levels but without prior cardiovascular events [12]. In addition to its lipid-lowering activity, Lov exhibits several pleiotropic effects such as endothelial protection, stabilization of atherosclerotic plaques, anti-inflammatory and antioxidant properties, and inhibition of platelet aggregation [12]. Despite these therapeutic benefits, lovastatin's clinical utility is limited by its short half-life, poor aqueous solubility, and low oral bioavailability (approximately 5%), primarily due to its hydrophobic structure and extensive first-pass metabolism.

To address these issues, numerous formulation strategies have been explored, including the use of nanoparticles, solid dispersions, liposomes, and polymeric carriers [5], [6], [8]. Biopolymer-based systems such as alginate/chitosan [13], [14], poly(lactic

acid) [15], and alginate [16] have been employed to encapsulate and control the release of Lov, with varying degrees of success. These systems aim to enhance drug stability, prolong circulation time, and achieve targeted or sustained release profiles.

In this study, carrageenan-based biomaterials loaded with Lov were developed using the ionic gelation method. Carrageenan served as a biopolymer matrix to disperse and encapsulate varying amounts of Lov. The physicochemical properties of the composites were characterized using spectroscopic, morphological, and thermal analysis techniques. Additionally, the drug release behavior under simulated gastrointestinal conditions was evaluated to determine the optimal carrageenan-to-lovastatin ratio for efficient and pH-responsive drug delivery. This research aims to provide a cost-effective, environmentally friendly, and biocompatible approach for improving the solubility and release performance of poorly water-soluble drugs such as Lov, thereby contributing to the development of oral drug delivery systems.

2. Content

2.1. Experiments

2.1.1. Chemicals

Lovastatin (Lov) (white powder, ≥ 98%) was purchased from Rhawn (China), Carrageenan (CAR) (ivory-white powder, moisture ≤ 12 %) was provided by Sigma Aldrich (USA). Other chemicals, including ethanol, HCl, NaOH, KOH, KH_2PO_4, and KCl, were supplied by Xilong Scientific Co. (China), and used as received without further purification.

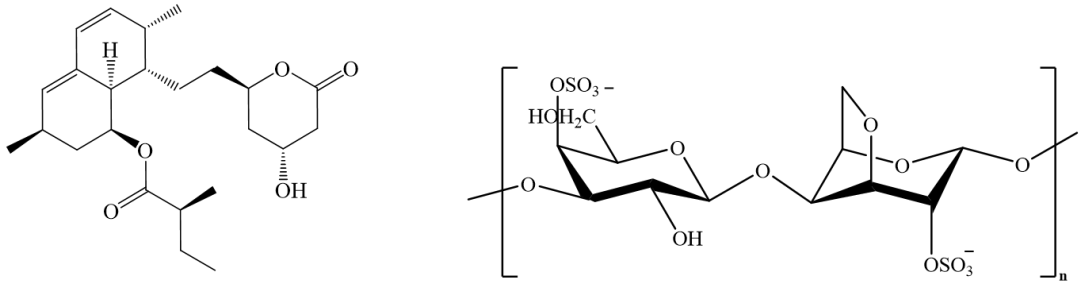

Figure 1. Structural formula of Lovastatin (Lov) and Carrageenan (CAR)

2.1.2. Preparation of CAR/Lov biomaterials

A specific amount of CAR was dissolved in 50 mL of distilled water by heating at 80 ºC for 15 minutes, then cooled to room temperature. Subsequently, a KCl solution was added to the mixture to obtain a final KCl concentration equivalent to 1 wt% of the CAR polymer. A Lov solution in ethanol was then gradually introduced into the CAR solution under continuous homogenization at a speed of 2.10^4 rpm to ensure uniform dispersion of Lov within the polymer matrix. The resulting mixture was further stirred at 400 rpm for 2 h to enhance homogeneity.

The final mixture was carefully poured into petri dishes and dried in a vacuum oven at 60 ºC for 24 hours to obtain the CAR/Lov biomaterial films. Samples with varying

Lov contents were prepared, as depicted in Table 1, to evaluate the influence of drug concentration on the physicochemical properties and release behavior of the biomaterials.

Table 1. Symbols and composition of CAR/Lov biomaterial samples

No.	Sample symbol	Sample composition		
		CAR (g)	*Lov (g)*	*KCl (g)*
1	CL5	0.5	0.025	0.005
2	CL7	0.5	0.035	0.005
3	CL10	0.5	0.050	0.005
4	CL15	0.5	0.075	0.005
5	CL20	0.5	0.100	0.005

2.1.3. Characterization

The primary functional groups in the CAR/Lov biomaterials were analyzed using Fourier Transform Infrared (FT-IR) spectroscopy. FT-IR spectra were recorded with a Thermo Nicolet Nexus 670 spectrophotometer (USA). The surface morphology of the biomaterials was examined using a high-resolution field emission scanning electron microscope (Hitachi S-4800 FESEM, Japan). Thermal properties were assessed by differential scanning calorimetry (DSC) using a DSC-60 instrument (Shimadzu, Japan).

To evaluate drug release, the *in vitro* release of Lov from CAR/Lov biomaterials was investigated using an RC-6 dissolution tester (Guoming, China). The concentration of Lov released over time was quantified with a YOKE UV1900 Double Beam UV-Vis Spectrophotometer (China).

2.1.4. Investigation of Lov release from CAR/Lov biomaterials in different buffers

The release behavior of lovastatin (Lov) from the CAR/Lov biomaterials was evaluated in buffer solutions at pH 2.0 and pH 7.4 to simulate gastric and intestinal environments, respectively. A measured amount of the biomaterial sample was immersed in 200 mL of the appropriate buffer solution and maintained at a constant temperature of 37.0 °C with gentle agitation at 200 rpm using a dissolution apparatus. At predetermined time intervals (every hour), a 5 mL aliquot was withdrawn for analysis, and an equal volume of fresh buffer solution was simultaneously added to maintain a constant total volume throughout the study.

The absorbance of each sample was measured at the maximum absorption wavelength (λ_{max}) specific to Lov using a UV-Vis spectrophotometer. The concentration of Lov released into the buffer solution at each time point was determined from standard calibration curves constructed for each pH condition, following the method described in [17]. All drug release experiments were performed in triplicate, and the average values were reported to ensure reproducibility.

The drug release study was carried out over a 30-hour period. The percentage of Lov released at time *t* was calculated using the following equation:

$$H\ (\%) = \frac{m}{m_o} \times 100\%$$

where H is the content of Lov released (%);

m is the mass of Lov (g) released at time t;

m_o is the initial mass of Lov (g) in the sample before the drug release test

2.2. Results and Discussion

2.2.1. Structure, morphology, and thermal properties of CAR/Lov biomaterials

**** Chemical structure of CAR/Lov biomaterials***

The FTIR spectra of pure CAR, Lov, and the CL biomaterial samples are presented in Figure 2 and summarized in Table 2. The spectroscopic results showed that both CAR and Lov were present in the biomaterials. Specifically, the stretching vibrations of saturated –CH groups were observed in the range of 2964–2865 cm^{-1}, while their bending vibrations appear between 1383 - 1373 cm^{-1} [8] (see Figure 2 and Table 2). Additionally, strong absorption bands corresponding to the stretching vibrations of the C–O functional groups are evident in the range of 1068 - 1036 cm^{-1}.

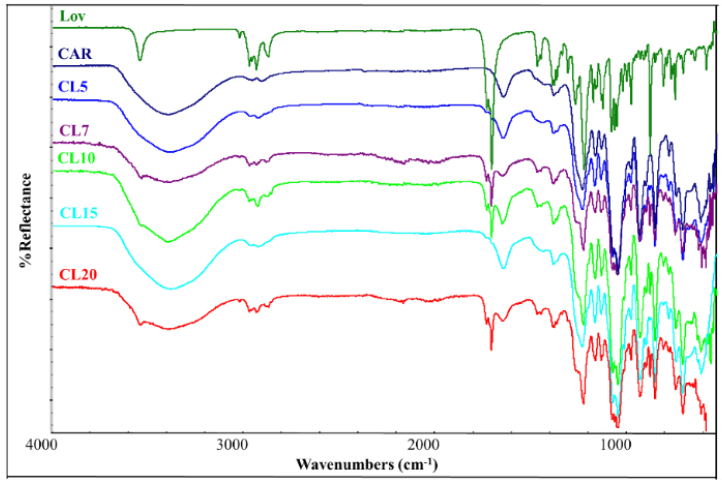

Figure 2. FTIR spectra of CAR, Lov, and CL samples

Table 2. Characteristic signals (cm^{-1}) of CAR, Lov, and CL samples

Sample	CAR	Lov	CL5	CL7	CL10	C15	CL20
ν_{OH}	3383.10	3537.36	3384.38	3376.29	3393.72	3377.56	3379.49
$\nu_{CH\ sat.}$	-	2964.39 2928.13 2865.29	2916.93	2964.53	2920.07	2913.71	2927.60
$\nu_{C=O}$	1633.78	1722.24 1696.93	1695.74	1697.43	1697.39	1697.63	1697.75
δ_{CH}	1373.27	1383.88	1374.45	1376.57	1376.04	1374.35	1377.03
ν_{C-O}	1036.25	1068.95	1026.23	1040.73	1037.87	1036.70	1040.92

For Lov, a distinct absorption band attributed to the stretching vibration of the carbonyl (C=O) group was observed in the range of 1696 - 1722 cm^{-1}, confirming the presence of the ester functionality. In the case of CAR, the characteristic C=O stretching band appears at approximately 1633 cm^{-1}, likely associated with carboxylate groups within the polysaccharide structure. Furthermore, a broad and intense absorption band centered around 3383 cm^{-1} corresponds to the O–H stretching vibrations, which is typical of the hydroxyl groups present in polysaccharide chains [5], [18], [19].

The infrared spectral data of the CAR/Lov biomaterial samples exhibit characteristic absorption bands corresponding to both carrageenan (CAR) and lovastatin (Lov), indicating the presence of these components within the composite matrix. Notably, the absorption bands associated with the stretching vibrations of the carbonyl (C=O) group appear at two distinct positions: approximately 1633 cm^{-1} (attributed to CAR) and within the range of 1696 - 1722 cm^{-1} (attributed to Lov). These peaks remain relatively stable across the samples, with only minor shifts observed. Such minimal changes suggest weak interactions, which may come from van der Waals forces or hydrogen bonding between the –OH groups of CAR and the C=O groups of Lov, rather than the formation of new covalent bonds.

The stability of these characteristic peaks across different Lov-to-CAR ratios indicates that the interaction between CAR and Lov is predominantly physical. No significant changes are observed in the chemical structure of either component. Accordingly, the incorporation of Lov into the carrageenan matrix does not compromise the integrity or therapeutic properties of the drug. This confirms the suitability of the CAR/Lov system as a biocompatible drug delivery material that preserves the original chemical identity of the active pharmaceutical ingredient.

**** Structural morphology of CAR/Lov biomaterials***

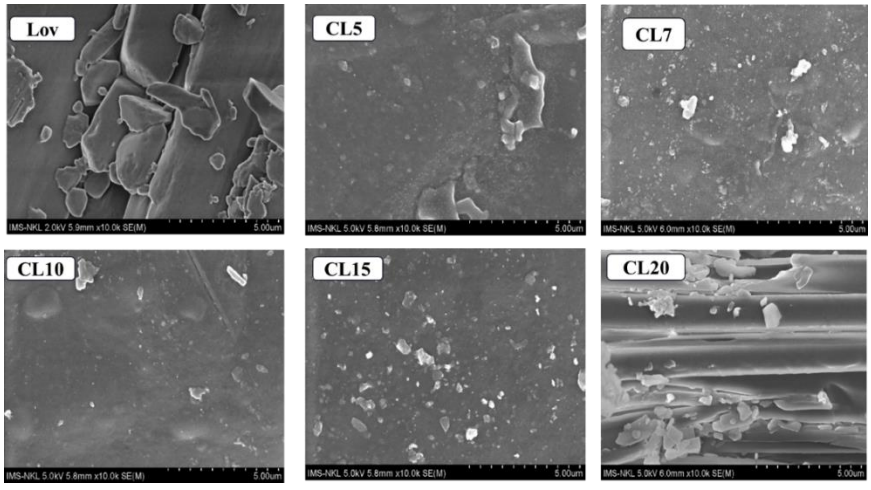

Figure 3. SEM images of Lov and CL samples

The SEM images shown in Figure 3 reveal the morphological differences between pure Lov and the CL biomaterial samples. In its pure form, Lov appears as rod-shaped crystals with dimensions ranging from approximately 5 to 10 μm. Upon incorporation into the CAR matrix, Lov is initially dissolved in ethanol-. Its morphology transforms

into a more spherical attributed to enhanced dispersion and the homogenization process during synthesis.

The morphology and distribution of Lov within the CL samples vary with the drug-to-polymer ratio. Among the formulations, the CL15 sample demonstrates the most favorable morphology, with Lov uniformly dispersed throughout the CAR matrix as spherical particles approximately 0.5–1 μm in diameter. This enhanced dispersion is attributed to hydrogen bonding interactions between the carbonyl (C=O) groups of Lov and the hydroxyl (–OH) groups of the CAR polymer, facilitating the integration of Lov into the matrix.

In contrast, other samples exhibit less favorable dispersion. In these formulations, Lov particles either remain as large, rod-shaped crystals or appear as aggregated clusters, indicating incomplete incorporation into the polymeric network. These observations suggest that both the solvent-mediated dispersion and the specific drug-to-polymer ratio play crucial roles in determining the morphology and uniformity of drug distribution within the biomaterial system [20].

**** Thermal properties of CAR/Lov biomaterials***

The thermal behavior of the CAR/Lov biomaterials was evaluated using differential scanning calorimetry (DSC), and the results are presented in Figure 4 and summarized in Table 3. The DSC thermogram of pure lovastatin (Lov) shows a sharp endothermic peak at 174.6 °C, which corresponds to its melting point. This melting process begins at approximately 172 °C and ends at 177 °C, in good agreement with values reported in previous studies [21], [22].

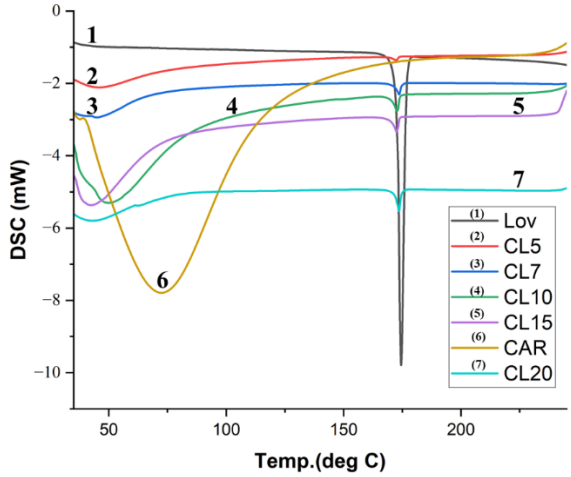

Figure 4. DSC curves of Lov and CL samples

When Lov is incorporated into the carrageenan (CAR) matrix, a noticeable decrease in its melting point is observed across all composite samples. This reduction in melting temperature suggests that Lov probably exists in a more amorphous state within the polymeric system. Such a transformation is typically associated with improved drug dispersion and reduced crystallinity. Among the samples, CL15 exhibited the most pronounced decrease in melting point, with an endothermic peak observed at 170.8 °C. This result is consistent with the SEM observations, where the CL15 sample showed the smallest and most uniformly dispersed Lov particles.

Table 3. DSC parameters of Lov and CL samples

Sample	1st endothermic peak (°C)	2nd endothermic peak (°C)
Lov	-	174.6
CAR	64.6	-
CL5	45.2	174.5
CL7	44.9	173.8
CL10	42.1	173.2
CL15	40.9	170.8
CL20	43.9	173.7

In addition to the melting peaks of Lov, all samples exhibit a broad endothermic peak in the range of 40.9–64.6 °C, corresponding to the gelation of CAR with KCl in the preparation process. Notably, the enthalpy of hydration decreased with increasing Lov content [23]. The CL15 sample, which contains 15% Lov, displayed the lowest hydration peak at 20.9 °C, suggesting that the incorporation of Lov reduces the water-binding capacity of the CAR matrix.

These thermal analysis results support the successful incorporation of Lov into the CAR matrix and further confirm the morphological changes observed in SEM imaging, particularly in the case of CL15.

2.2.2. Investigation of Lov release from the CAR/Lov samples

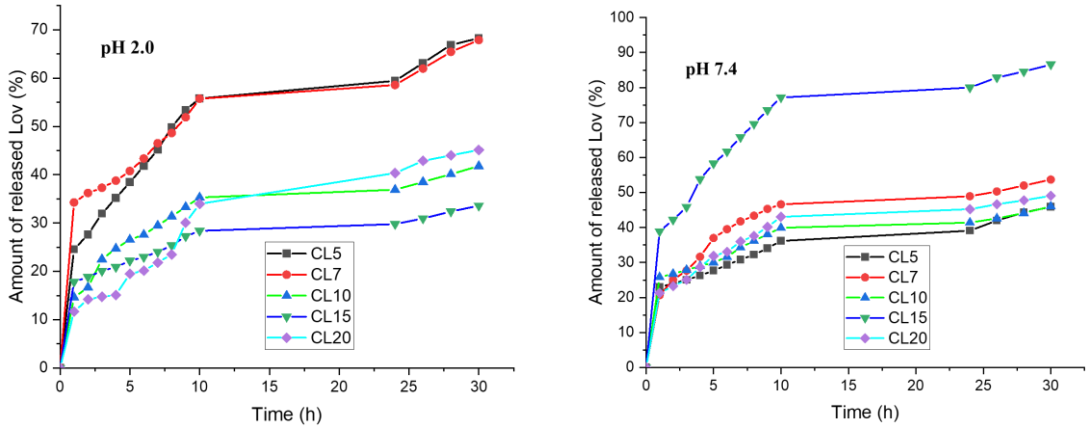

Figure 5. Drug release behaviors of Lov from the biomaterials in pH 2.0 solution (left), and in pH 7.4 solution (right)

The release profile of lovastatin (Lov) from CAR/Lov biomaterials was investigated over a 30-hour period under two distinct pH conditions to simulate physiological environments: gastric fluid (pH 2.0), representing the stomach, and intestinal fluid (pH 7.4), simulating the small intestine. During the initial phase, Lov release occurred primarily at the surface of the biomaterials, where Lov particles were loosely bound or superficially embedded. Subsequently, the erosion of the matrix by the aqueous medium induced swelling of the CAR hydrogel, thereby facilitating the diffusion of Lov into the surrounding solution [8].

In the acidic environment (pH 2.0), the cumulative release of Lov ranged from 11.7% to 68.2%. Among the samples, CL5 and CL7 exhibited the highest release percentages, with 68.25% and 67.86% of the drug released after 30 hours, respectively. In contrast, the CL15 sample showed the lowest release at pH 2.0, with only 33.58% of Lov released during the same time frame. These findings suggest that the CL15 formulation provided improved protection for Lov in the gastric environment, thereby reducing premature drug release and enhancing potential delivery to the intended site of absorption.

In the simulated intestinal environment (pH 7.4), the release behavior differed significantly. The more neutral conditions promoted increased swelling of the CAR matrix, enhancing drug diffusion. Additionally, the absence of competitive ion exchange, particularly the replacement of K^+ ions used in gelation by H^+ ions used in gelation, enabled greater matrix expansion and drug release. Under these conditions, the CL15 sample showed the highest drug release efficiency, with 86.57% of Lov released after 30 hours, compared to 45.91–53.70% for the other samples.

Overall, the CL15 formulation with a Lov/CAR ratio of 1:15 demonstrated optimal performance. It provided minimal release in the acidic gastric environment, thus preserving drug integrity, while enabling controlled and enhanced release under intestinal conditions. These characteristics make CL15 a promising candidate for site-specific delivery of Lov, facilitating its absorption in the small intestine, where systemic uptake is more effective.

3. Conclusions

This study successfully developed carrageenan/lovastatin (CAR/Lov) biomaterials with enhanced drug dispersion and controlled release properties. Analytical characterization using FTIR, SEM, and DSC confirmed that Lov was effectively incorporated into the carrageenan matrix through physical interactions, without altering the chemical structure of the active pharmaceutical ingredient. Among the various formulations, sample CL15 prepared with a Lov/CAR ratio of 1:15 exhibited the most favorable characteristics, including uniform particle distribution, reduced crystallinity, and optimal drug dispersion within the polymeric network.

Importantly, CL15 formulation demonstrated a pH-responsive drug release profile: limited release in acidic conditions (simulating gastric fluid) and significantly higher release in a mildly alkaline environment (simulating intestinal fluid). This pH-dependent release behavior enhances the protection of Lov in the stomach and promotes its absorption in the intestine, thereby improving its bioavailability.

These findings underscore the potential of carrageenan-based biomaterials as promising candidates for the development of controlled-release drug delivery systems. Specifically, they offer a viable approach for improving the therapeutic efficacy of poorly water-soluble drugs such as Lov.

REFERENCES

[1] Currie GM, (2018). Pharmacology, Part 2: Introduction to pharmacokinetics. *Journal of Nuclear Medicine Technology*, 46(3), 221-230, DOI: 10.2967/jnmt.117.199638.

[2] Chow SC, (2014). Bioavailability and bioequivalence in drug development. *WIREs Computational Statistics*, 6(4), 304-312, DOI: 10.1002/wics.1310.

[3] Ramu S, Jithendra C & Sathish K, (2022). Emerging role of biopharmaceutical classification and biopharmaceutical drug disposition system in dosage form development: A systematic review. *Turkish Journal of Pharmaceutical Sciences*, 19(6), 706-713, DOI: 10.4274/tjps.galenos.2021.73554.

[4] Wu C, Wang J, Hu Y, Zhi Z, Jiang T, Zhang J & Wang S, (2012). Development of a novel starch-derived porous silica monolith for enhancing the dissolution rate of poorly water soluble drug. *Materials Science and Engineering C*, 32(2), 201-206, DOI: 10.1016/j.msec.2011.10.019.

[5] Ha MH, Vu QM, Vu TTT, Dao TPT, Pham TD, Nguyen TBV, Duong KL, Nguyen NL, Doan TYO, Nguyen TC, Thai H & Vu QT, (2022). Evaluation of the effect of the chitosan/carrageenan ratio on lovastatin release from chitosan/carrageenan based biomaterials. *Vietnam Journal of Chemistry*, 60(S1), 72-78, DOI: 10.1002/vjch.202200078

[6] Zia KM, Tabasum S, Nasif M, Sultan N, Aslam N, Noreen A & Zuber M, (2017). A review on synthesis, properties and applications of natural polymer based carrageenan blends and composites. *International Journal of Biological Macromolecules*, 96, 282-301, DOI: 10.1016/j.ijbiomac.2016.11.095.

[7] Yegappan R, Selvaprithiviraj V, Amirthalingam S & Jayakumar R, (2018). Carrageenan based hydrogels for drug delivery, tissue engineering and wound healing. *Carbohydrate Polymers,* 198, 385-400, DOI: 10.1016/j.carbpol.2018.06.086.

[8] Vu QM, Nguyen TC, Dam DMN, Vu QT, Le TL, Hoang TD, Tran TKN, Nguyen TA, Nguyen PH & Thai H, (2021). A novel method for the preparation of carrageenan/fish scale collagen/allopurinol biocomposite film. *International Journal of Polymer Science*, 2021, 9960233, DOI: 10.1155/2021/9960233.

[9] Gómez-Ordóñez E, Jiménez-Escrig A & Rupérez P, (2014). Bioactivity of sulfated polysaccharides from the edible red seaweed *Mastocarpus stellatus*. *Bioactive Carbohydrates and Dietary Fibre*, 3(1), 29-40, DOI: 10.1016/j.bcdf.2014.01.002.

[10] Inic-Kanada A, Stein E, Stojanovic M, Schuerer N, Ghasemian E, Filipovic A, Marinkovic E, Kosanovic D & Barisani-Asenbauer T, (2018). Effects of iota-carrageenan on ocular *Chlamydia trachomatis* infection *in vitro* and *in vivo*. *Journal of Applied Phycology,* 30(4), 2601-2610, DOI: 10.1007/s10811-018-1435-0.

[11] Choi OS, Park SJ, Seo SW, Park CS, Cho JJ & Ahn HJ, (2005). The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor, lovastatin (statin), ameliorates CCK-induced acute pancreatitis in rats. *Biological and Pharmaceutical Bulletin,* 28(8), 1394-1397, DOI: 10.1248/bpb.28.1394.

[12] Liao JK & Laufs U, (2005). Pleiotropic effects of statins. *Annual Review of Pharmacology and Toxicology*, 45(1), 89-118, DOI: 10.1146/annurev.pharmtox.45.120403.095748.

[13] Thai H, Tran DL, Thach TL, Le DG, Do TMT, Vu QT, Nguyen TA, Nguyen DT & Nguyen TC, (2019). Effect of both lovastatin and ginsenoside Rb1 on some properties and *in vitro* drug release of alginate/chitosan/lovastatin/ginsenoside Rb1 composite films. *Journal of Polymers and the Environment,* 27(12), 2728-2738, DOI: 10.1007/s10924-019-01550-8.

[14] Nghiem DT, Nguyen TC, Do MT, Nguyen TH, Tran DL, Tran HD, Le VQ, Vu QT, Nguyen DT & Thai H, (2020). Influence of the preparation method on some characteristics of alginate/chitosan/lovastatin composites. *Advances in Polymer Technology,* (1), 7879368, DOI: 10.1155/2020/7879368.

[15] Guan Q, Chen W & Hu X, (2015). Development of lovastatin-loaded poly(lactic acid) microspheres for sustained oral delivery: *in vitro* and *ex vivo* evaluation. Drug Design, Development and Therapy*,* 10(9), 791-798, DOI: 10.2147/DDDT.S76676.

[16] Vo AQ, Nguyen TC, Nguyen QT, Vu QT, Truong CD, Nguyen TL, Ly TNL, Bach LG & Thai H, (2021). Novel nanoparticle biomaterial of alginate/chitosan loading simultaneously lovastatin and ginsenoside Rb1: Characteristics, morphology, and drug release study. *International Journal of Polymer Science,* (1), 1-14, DOI: 10.1155/2021/5214510.

[17] Nguyen TBV, Vu QM, Tran TKG, Doan TY, Vu TT, Ha MH, Nguyen DD, VU QT & Nguyen NL, (2024). Release of lovastatin drug from poly(lactic acid) biomaterial. *Vietnam Journal of Chemistry and Applications*, 3B,(71), 23-30.

[18] Nguyen TC, Vu QM, Thai H, Kavitha R, Clastinrusselraj IS, Vu QT, Tran TKN & Ajayan V, (2022). Optimizing the component ratio to develop the biocomposites with carrageenan/collagen/allopurinol for the controlled drug release. *Journal of Drug Delivery Science and Technology,* 68, 102697, DOI: 10.1016/j.jddst.2021.102697.

[19] Hung LD & Huong DT, (2020). Characterization of kappa-carageenan from the red alga Kappaphycus striatum. *Vietnam Journal of Biotechnology,* 18(2), 321-329, DOI: 10.15625/1811-4989/18/2/15196.

[20] Thai H, Nguyen TC, Thach TL, Tran TM, Mai DH, Nguyen TTT, Le DG, Can VM, Tran DL, Bach LG, Kavitha R, Clastinrusselraj IS & Le VQ, (2020). Characterization of chitosan/alginate/lovastatin nanoparticles and investigation of their toxic effects *in vitro* and *in vivo*. *Scientific Reports,* 10(1), 909, DOI: 10.1038/s41598-020-57666-8.

[21] Vu TTT, Nguyen THN, Vu QM, Nguyen NL, Nguyen TBV & Vu QT, (2023). Synthesis and characterization of chitosan/carrageenan/polyaniline-based biocomposite as lovastatin carrier and its drug release ability in buffer solutions. *HNUE Journal of Science: Natural Sciences,* 68(3), 64-74.

[22] Verma R, Nagpal M, Singh TG, Singh M & Aggarwal G, (2020). Improved efficacy of lovastatin from soluplus-peg hybrid polymer-based binary dispersions. Current Bioactive Compounds*,* 16(8), 1164-1171, DOI: 10.2174/1573407216666191218142852.

[23] Horinaka J & Hara K, (2025). High-concentration hydrogels of κ-carrageenan prepared using subcritical water. *Carbohydrate Polymers,* 352, 123137, DOI: 10.1016/j.carbpol.2024.123137.