EFFECT OF CHITOSAN-MODIFIED FATTY ACID LIPOSOMES ON THE RHEOLOGICAL PROPERTIES OF THE CARBOHYDRATE-BASED GEL

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ABSTRACT:

Incorporation of liposome into gel is the most common approach for the preparation of topical and transdermal liposomal formulation, due to the ability of liposome to improve the drug deposition and permeation rate within the skin. In this study, the liposomal gel consisted of iota-carrageenan, carboxymethyl cellulose, and chitosan-coated-oleic acid liposome were prepared. The effect of liposomes on the rheological properties of the iota-carrageenan-carboxymethyl cellulose mix gel was evaluated. The rheological result indicated that the presence of the chitosan-coated-oleic acid liposomes in the gel had modified the viscoelastic and flow characteristics of the gel. The input energy from the oscillatory test could be stored more effectively in the elastic component of the liposomal gels, as compared to the original gel itself. This result showed that the liposomal gels exhibited greater elasticity and were more solid-like when compared with the original gel system. The complex viscosity of the liposomal gels was also found to decrease with increasing frequency, indicating the shear thinning behavior of the liposomal gels. The lower Power Law Index *PLI* of the liposomal gels indicated a greater shear thinning behavior and better spreadability.

KEY WORDS:

rheology, fatty acid vesicle, chitosan, carboxymethyl cellulose, *i*-carrageenan

1 INTRODUCTION

Polysaccharide-based gels play an important role in modern cosmetic and pharmaceutical formulations. This is mainly due to the characteristics of the polysaccharides, which are, biocompatible, biodegradable, edible, and are available from natural sources such as seaweeds [1]. The polysaccharide-based gels are commonly used as a matrix to disperse medicinal or cosmeticactive ingredients. The fluid-filling interstitial space within the gel network provides a continuous moisturizing effect to the skin [2-4]. Carboxymethyl cellulose (CMC) and ι -carrageenan (ι -C) are frequently used polysaccharides in food and pharmaceutical industries. CMC is a derivative of cellulose, with the carboxymethyl group bound to some of the hydroxyl groups of the glucopyranose monomer backbone [5]. In general, CMC is commonly used as binding, thickening, and stabilizing agent of various products in cosmetic and pharmaceutical industries [6, 7]. *ι*-C is a linear sulfated polysaccharide with alternating three-linked β -D-galactopyranose and four-linked 3,6-anhydro- α -pyranose residues [8]. ι -C has been used in the preparation of food stuff such as dairy products and jellies, due to its typical gelling strength [9, 10]. Besides the food industry, ι -C has also been used in the preparation of soft gel for the oral drug delivery system [11, 12].

The liposome drug carrier has been widely investigated since it was discovered by Bangham and co-workers (Figure 1a) [13]. However, single type, non-surface modified liposomes have been found to hardly survive in the blood stream, due to fast elimination by the mononuclear phagocyte system [14, 15]. The recognition and removal of the liposomes from the blood stream, as foreign particles, has been promoted by the adsorption of proteins that circulate from the blood stream onto the surface of the liposome [14]. This disadvantage inhibits the liposome's function as a drug carrier and reduces its circulation half-life [15]. In order to overcome this disadvantage, surface-modified lipo-

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somal gels were prepared by mixing the oleic acid, chitosan-coated oleic acid liposome, and acylated chitosan-coated oleic acid liposome into the 5:5G. The result demonstrated that the presence of liposomes in the gel matrix had increased the elastic property of the gel. This was explained by the rigidity of the loaded liposomes. The low *CE* value of liposomal gels is favorable because high *CE* will limit the transfer of liposomes from the gel matrix to the targeted site. Besides elastic properties, the higher complex viscosity of the liposomal gels when compared with 5:5G will enhanced the stability of the dispersed liposomes during storage. The presence of liposomes was also found to exhibit greater shear thinning behavior indicated higher spreadability of the liposomal gel when compared with 5:5G.

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REFERENCES

- Klein S: Polysaccharides in oral drug delivery recent applications and future perspectives, in: Edgar KJ, Heinze T, Buchanan CM (Ed.), Polysaccharide materials: Performance by design, American Chemical Society, Washington DC (2009).
- [2] Kumar JA, Pullakandam N, Prabu SL, Gopal V: Transdermal drug delivery system: An overview, Int. J. Pharma. Sci. Rev. Res. 3 (2009) 49-54.
- [3] Kwon HJ, Gong JP: Negatively charged polyelectrolyte gels as bio-tissue model system and for biomedical application, Curr. Opin. Colloid Interface Sci. 11 (2006) 345–350.
- [4] Saha D, Bhattacharya S: Hydrocolloids as thickening and gelling agents in food: A critical review, J. Food. Sci. Technol. 47 (2010) 587–597.
- [5] Heinze T: New ionic polymers by cellulose functionalization, Macromol. Chem.Physic. 199 (1998) 2341 - 2364.
- [6] Weiner ML: Taxicological properties of carrageenan, Agent. Action. 32 (1991) 46-51.
- [7] Srokova I, Talaba P, Hodul P, Balazova A: Emulsifying agents based on o-(carboxymethyl)cellulose, Tenside Surfact. Det. 35 (1998) 342-344.
- [8] Millane RP, Chandrasekaran R, Arnott S: The molecular structure of kappa-carrageenan and comparison with iota-carrageenan, Carbohyd. Res. 182 (1988) 1–17.
- [9] Gupta RK, Hariharan M, Wheatley TA, Price JC: Controlled-release tablets from carragennans: Effect of formulation, storage and dissolution factors, Eur. J. Pharm. Biopharm. 51 (2001) 241–248.
- [10] Gobet M, Mouaddab M, Cayot N, Bonny J, Guichard E, Le Quéré J, Moreau C, Foucat L: The effect of salt content

on the structure of iota-carrageenan systems: 23na dqf nmr and rheological studies, Mag. Reson. Chem. 47 (2009) 307-312.

- [11] Miyazaki S, Ishitani M, Takahashi A, Shimoyama T, Itoh K, Attwood D: Carrageenan gels for oral sustained delivery of acetaminophen to dysphagic patients, Biol. Pharm. Bull. 34 (2011) 164–166.
- [12] Thrimawithana TR, Young S, Alany RG: Effect of cations on the microstructure and in-vivo drug release of κ - and ι -carrageenan liquid and semi-solid aqueous dispersions, J. Pharm. Pharmacol. 63 (2011) 11–18.
- [13] Bangham AD, Hill MW, Miller GA: Preparation and use of liposomes as models of biological membranes in Methods in membrane biology, Plenum Press, New York (1974).
- [14] Maurer N, Fenske DB, Cullis PR: Developments in liposomal drug delivery systems, Expert Opin. Biol. Ther. 1 (2001) 923-947.
- [15] Immordino ML, Dosio F, Cattel L: Stealth liposomes: Review of basic science, rationale, and clinical applications, existing and potential, Int. J. Nanomed. 1 (2006) 297–315.
- [16] Klibanov AL, Maruyama K, Torchilin VP, Huang L: Amphipathic polyethyleneglycols effectively prolong the circulation time of liposomes, FEBS Lett. 268 (1990) 235–237.
- [17] He SJ, Zhu JB, Xie FM: Preparation and characterization of tramadol eg-coated multivesicular liposomes for sustained release, Pharmazie 6 (2010) 467–470.
- [18] Takeuchi H, Kojima H, Yamamoto H, Kawashima Y: Evaluation of circulation profiles of liposomes coated with hydrophilic polymers having different molecular weights in rats, J. Control. Release 75 (2001) 83–91.
- [19] Parabaharan M: Review paper: Chitosan derivatives as promising materials for controlled drug delivery, J. Biomater. Appl. 23 (2008) 5-36.
- [20] Yuan ZH, Cheng DW, Zhang ST, Zheng ZD: Preparation, characterization and evaluation of docetaxel-loaded, folate-conjugated peg-liposomes, Yakugaku Zasshi 130 (2010) 1353–1359.
- [21] Torchilin VP: Recent advances with liposomes as pharmaceutical carriers, Nat. Rev. Drug Discov. 4 (2005) 145–160.
- [22] Gabrijelčič V, Šentjurc M: Influence of hydrogels on liposome stability and on the transport of liposome entrapped substances into skin, Int. J. Pharm. 118 (1995) 207–212.
- [23] Pavelić Ž, Škalko-Basnet N, Schubert R: Liposomal gels for vaginal drug delivery, Int. J. Pharm. 219 (2001) 139–149.
- [24] Mura P, Maestrelli F, González-Rodríguez ML, Michelacci I, Ghelardini C, Rabasco AM: Development, characterization and in-vivo evaluation of benzocaine-loaded liposomes, Eur. J. Pharm. Biopharm. 67 (2007) 86–95.
- [25] Dew N, Edwards K, Edsman K: Gel formation in systems composed of drug containing catanionic vesicles and oppositely charged hydrophobilically modified polymer, Colloid Surf. B. 70 (2009) 187–197.
- [26] Mourtas S, Haikou M, Theodoropoulou M, Tsakiroglou C, Antimisiaris SG: The effect of added liposomes on the rheological properties of a hydrogel: A systematic study, J. Colloid Interf. Sci. 317 (2008) 611–619.

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- [27] Nishinari K: Some thoughts on the defination of a gel, in: M Tiokita, Nishinari K (Ed.) Gels: Structures, properties, and functions: Fundamental and applications, Springer-Verlag Berlin Heidleberg, German (2009).
- [28] Brummer R, Godersky S: Rheological studies to objectify sensations occuring when cosmetic emulsions are applied to the skin, Colloid. Surf. A. 152 (1999) 89–94.
- [29] Ilg P, del Gado E: Non-linear response of dipolar colloidal gels to external fields, Soft Matter 7 (2011) 163–171.
- [30] Garg A, Aggarwal D, Garg S, Singla AK: Spreading of semisolid formulations: An update, Pharm. Technol. (September 2002) 84–105.
- [31] Ueda CT, Shah VP, Derdzinski K, Ewing G, Flynn G, Maibach H, Marques M, Rytting H, Shaw S, Thakker K, Yocobi A: Topical and transdermal drug products, Pharmacopeial Forum 35 (2009) 750-764.
- [32] Jelvehgari M, Rashidi MR, Mirza MSH: Adhesive and spreasing properties of pharmaceutical gel composed of cellulose polymer, Jundishapur, J. Nat. Pharm. Prod. 2 (2007) 45-58.
- [33] Ivens UI, Steinkjer B, Serup J, Tetens V: Ointment is evently spread on the skin, in contrast to creams and solutions, Brit. J. Dermatol. 145 (2001) 264–267.
- [34] Le-Tien C, Lacroix M, Ispas-Szabo P, Mateescu MA: N-acylated chitosan: Hydrophobic matrices for controlled drug release, J. Control. Release 93 (2003) 1–13.
- [35] Tan HW, Misran M: Characterization of fatty acid liposome coated with low molecular weight chitosan, J. Liposome Res. 22 (2012) 329–335.
- [36] Tan HW, Misran M: Polysaccharide-anchored fatty acid liposome, Int. J. Pharm. 441 (2013) 414–423.
- [37] Moghadam SH, Saliaj E, Wettig SD, Dong C, Ivanova MV, Huzil JT, Foldvari M: Effect of chemical permeation enhancers on stratum corneum barrier lipid organizational structure and interferon alpha permeability, Mol. Pharm. 10 (2013) 2248-2260.
- [38] Nakauma M, Tanaka R, Ishihara S, Funami T, Nishinari K: Elution of sodium caseinate from agar-based gel matrix-

es in simulated gastrc fluid, Food Hydrocolloid. 27 (2012) 427–437.

- [39] Sohm R, Tadros ThF: Viscoelatic properties of sodium montmorillonite (gelwhite h) suspensions, J. Colloid Interf. Sci. 132 (1989) 62–71.
- [40] Kästner U, Hoffmann H, Dönges R, Hilbig J: Structure and solution properties of sodium carboxymethyl cellulose, Colloid Surf. 123–124 (1997) 307–328.
- [41] Benchabane A, Bekkour K: Rheological properties of carboxymethyl cellulose (cmc) solutions, Colloid Poly. Sci. 286 (2008) 1173–1180.
- [42] Rodríguez-Hernández AI, Tecante A: Dynamic viscoelastic behavior of gellan-ι-carrageenan and gellan-xanthan gels, Food Hydrocolloid. 13 (1999) 59ν64.
- [43] Jones RA, Staples EJ: A study of the helix-coil transition of ι-carrageenan segments by light scattering and membrane osmometry, J. Chem. Soc. Perkin Trans. 2 12 (1973) 1608–1612.
- [44] Norton IT, Goodall DM: Dynamics of cation-induced conformational ordering in solutions of segmented ι-carrageenan, J. Chem. Soc. Faraday Trans. 179 (1983) 2501–2515.
- [45] Grillet AM, Wyatt NB, Gloe LM: Polymer gel rheology and adhesion in Rheology, in: Juan De Vicente (Ed.), Rheology, InTech, Croatia (2012).
- [46] Gu YS, Decker EA, McClements DJ: Influence of ph and ι -carrageenan concentration on physicochemical properties and stability of β -lactoglobulin-stabilized oil-inwater emulsions, Agr. Food Chem. 52 (2004) 3626 – 3632.
- [47] Barnes HA: A handbook of elementary rheology, The University of Wales Institute of Non-Newtonian Fluid, Wales (2000).
- [48] Mourtas S, Duraj S, Fotopoulou S, Antimisiaris SG: Intergrity of liposomes in presence of various formulation excipients, when dispersed in aqueous media and in hydrogels, Colloid. Surf. B. 61 (2008) 270–276.
- [49] Chieng YY, Chen SB: Rheological study of hydrophobically modified hydroxymethyl cellulose and phospholipid vesicles, J. Colloid Interf. Sci. 349 (2010) 236–245.



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