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Effect of Diethylaminoethyl-dextran Coated Liposomes on the Rheological Properties of Carbopol Gel

Premanarayani Menon, Yin Yin Teo* and Misni Misran

Department of Chemistry, Faculty of Science, University of Malaya,
Lembah Pantai, 50603 Kuala Lumpur, Malaysia

*Corresponding author: yinyinteo@um.edu.my

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Abstract:
Liposomal gel has played an important role in administration of drugs via topical and transdermal routes. Incorporation of liposome into gel not only has overcome the liquid nature of liposomal dispersion but also helped to preserve the original structure of liposome. In this study, we formulated a liposomal gel consisting of Carbopol gel and a diethylaminoethyl dextran (DEAE-DX) coated liposome. The effect of coated and non-coated liposomes on the rheological properties of Carbopol gel was investigated. The rheological results indicated that incorporation of liposomes into Carbopol gel modified the viscoelastic and flow behaviour of the gel significantly. Apart from that, liposomal gel consisting of DEAE-DX coated liposomes exhibited more solid-like behavior compared to the non-coated liposomal gel. Incorporation of DEAE-DX coated liposomes increased the yield stress of liposomal gel compared to non-coated liposomes. This supports the findings obtained from the amplitude and frequency tests whereby addition of DEAE-DX enhanced the rigidity of the gel so that the resultant gel was more resistant to flow.

Key words:
Diethylaminoethyl dextran, liposome, carbopol

1 INTRODUCTION

Carbopol is a gelling agent that is commonly used in the preparation of topical gels. Carbopol is composed of acrylic acid polymers crosslinked with divinyl glycol [1]. They are approved for pharmaceutical use by several different administration routes which include topical, oral and intravenous. They also exhibit good rheological properties resulting in a stable gel system. Also, Carbopol gels are anionic with good buffering capacity, which may contribute to the maintenance of the desired pH. It has been confirmed that liposomes are fairly compatible with Carbopol by other researchers [2, 3]. Due to the afore-mentioned advantages of Carbopol gels, liposomes were incorporated into Carbopol gel in this study. Liposomes are artificially constructed spherical vesicles of a few nanometres to micrometres in diameter. They are composed of phospholipids or amphipathic molecules enclosing water or an aqueous buffer (Figure 1). Throughout the years, liposomes have made substantial advancements in medical applications, particularly as anticancer agents for chemotherapeutics owing to their excellent properties such as biodegradability, non-toxic and flexibility. Furthermore, liposomal formulations provide innovative systems for vaccination, gene therapy and radiopharmaceuticals. Liposomes have attracted much attention among the colloidal drug carrier systems proposed for site-specific drug delivery [4–8]. Apparently, liposome also can be functionalized through topical administration route. In the dermatological field, liposomes were initially preferred as a drug carrier due to their moisturizing and restoring properties. Later, the potential of liposomes to encapsulate various types of drugs as well as the administration of these drugs to the epidermal cells and to deeper cell layers was explored [9].

The most common problem related to liposomes is their stability. Unmodified liposomes result in aggregation of the vesicles. Subsequently, the aggregation of particles causes leakage of encapsulated material [10]. As stability is a general problem with lipid vesicles, we have incorporated a polycationic polymer Diethylaminoethyl Dextran (DEAE-DX) into the formulation in order to promote the stability of liposomes. Diethylaminoethyl-Dextran (DEAE-DX) was used in this study because of its excellent properties such as biodegradability and biocompatibility [11]. Positively charged DEAE-DX is similar to chitosan and also may interact

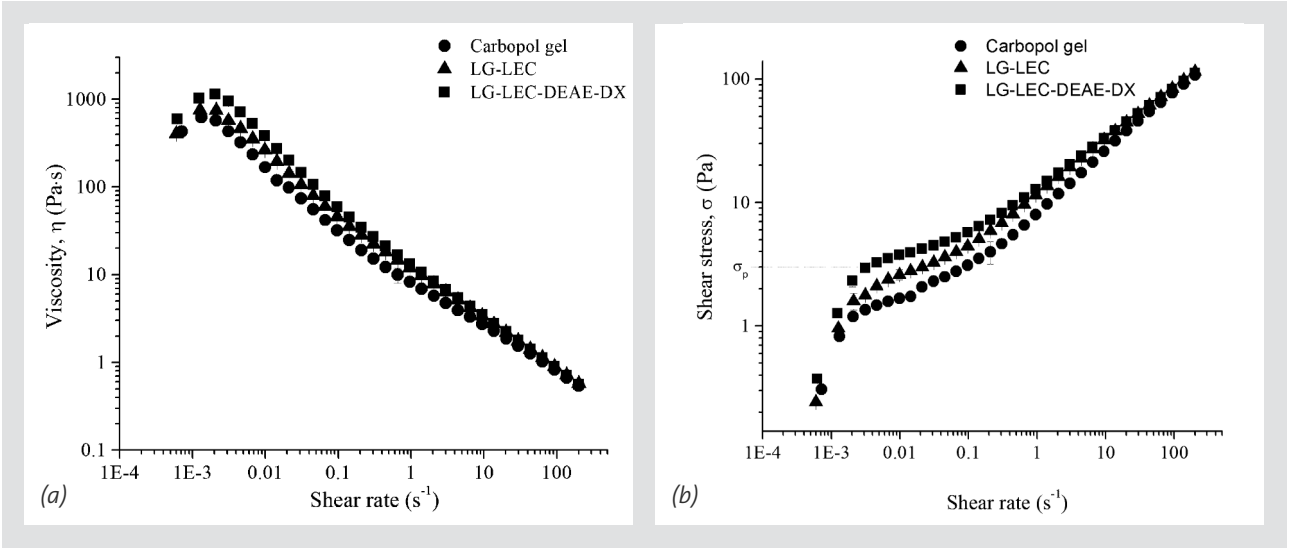

Figure 4: The flow behavior of the gel where (a) is the shear viscosity profile with increasing the shear rate and (b) is the shear stress versus shear rate profile.

After analysing the linear viscoelastic region for all the liposomal gels, a frequency sweep was performed in order to provide more information on the forces or interactions in the gel system [20]. The frequency sweep profile exhibited *G'* larger than *G''* over the selected frequency range for all liposomal gels. This result further supports the fact that addition of liposomes into Carbopol gel could maintain the solid like behaviour of 0.25 %w/v Carbopol gel (Figure 3b). However, the slope of *G'* of the liposomal gel was found to decrease and show lower frequency dependence compared to the pure Carbopol gel. The decrease in slope implied that the liposomal gel has more solid-like behaviour than pure Carbopol gel. In this case, sedimentation is unlikely to occur.

3.2.2 Flow behavior

Generally, polymeric gel systems are non-Newtonian and exhibit shear thinning behaviour. Similar to Carbopol gel, the liposomal gel also exhibited shear thinning behaviour. The spreadability and flowability of the liposomal gels were studied by measuring shear viscosity as a function of shear rate and shear stress [21]. At low shear rate, the shear-viscosity profile of all the liposomal gels was found to be slightly higher than Carbopol gel (Figure 4). Also, the yield stress σ_p of the liposomal gel was found to be larger than pure Carbopol gel. Yield stress σ_p is the stress applied in order to make the structured fluid flow (Table 3). The value of yield stress is significant as it indicated the degree of deformation of a structured fluid. Furthermore, higher viscosity at low shear rate is desirable for topical gel during storage [22]. The results which show that liposomal gels have higher shear viscosity and yield stress σ_p might be attributed to the presence of liposomes which have increased the rigidity of the formulation as discussed in the previous section whereby the liposomal gel exhibited larger storage modulus *G'*. As a result, the gel is more resistant to flow. Results of flow behaviour also indicated that there is a significant increase in yield stress of liposomal gel upon incorporation DEAE-DX coated liposomes compared to non-coated liposomes. This result supports the findings obtained from the amplitude and frequency sweep tests whereby addition of DEAE-DX enhanced the rigidity of the gel; therefore the resultant gel was more resistant to flow.

Name	Yield stress,σ_p (Pa)
0.25 % Carbopol gel	1.35
LG-LEC	1.78
LG-LEC-DEAE-DX	2.96

Table 3: Yield stress σp of liposomal gels which was determined from the steady rheological behavior.

3.3 MORPHOLOGY OF LIPOSOMAL GEL

DEAE-DX coated liposomes were incorporated into Carbopol gel at a concentration 0.25 %w/v (Figure 5). In this research, all the liposomes were found to be entrapped in the 3-dimensional network of the gel. The entrapped liposomes in the gel matrix showed spherical morphology. Also, all the particles exhibited a particle size of less 200 nm. This shows that incorporation of liposomes into the gel matrix did not significantly alter the size of the liposomes

4 CONCLUSION

The viscoelastic properties and the flow behaviour of gels are important because they give an overall prediction on the deformability, spreadability and stability of topical gel formulations. We found that incorporation of liposome into gel had a significant influence on its rheological properties. Presence of liposome in the gel

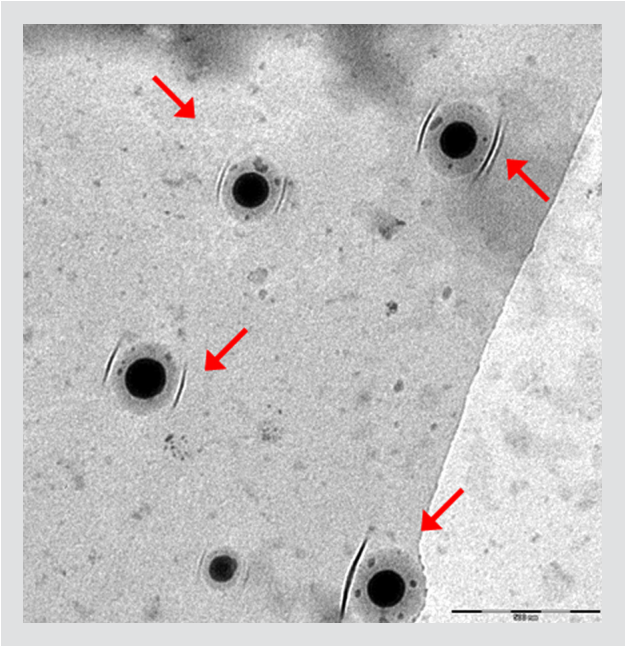

Figure 5: TEM micrograph of LG-LEC-DEAE-DX at the scale of 500 nm.

elevated its viscoelasticity. Furthermore, the higher values of critical strain and yield stress that were obtained for liposomal gel compared to the plain gel indicates that the former gel is more resistant to deformation. Furthermore, there was also variation observed in the rheological properties between a gel containing coated and non-coated liposomes. Liposomal gel containing DEAE-DX coated liposome exhibited even higher values of elastic modulus, critical strain, yield stress and cohesive energy. This phenomenon indicated a special interaction between DEAE-DX and Carbopol that could promote the internal forces holding the polymers to become stronger. This improved the adhesiveness of the resultant gel due the presence of the oppositely charged polymers. Overall, LEC-DEAE-DX liposomes in gel has potential for use as drug carriers.

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REFERENCES

[1] Puoci F: Advanced polymers in medicine Springer International Publishing, Berlin, Germany (2014).
[2] Gupta PN, Pattani A, Curran RM, Kett VL, Andrews GP, Morrow RJ, Wolfson AD, Malcolm RK: Development of liposome gel based formulations for intravaginal delivery of the recombinant hiv-1 envelope protein cn54gp140, Eur. J. Pharm. Sci. 46 (2012) 315–322.
[3] Pavelić Ž, Škalko-Basnet N, Schubert R: Liposomal gels for vaginal drug delivery, Int. J. Pharm. 219 (2001) 139–149.
[4] Dass CR, Walker TL, Burton M, Decruz EE: Enhanced anticancer therapy mediated by specialized liposomes, J. Pharm. 49 (1997) 972–975.
[5] Harasym TO, Bally MB, Tardi P: Clearance properties of liposomes involving conjugated proteins for targeting, Adv. Drug Deliv. Rev. 32 (1998) 99–118.
[6] Kim S: Liposomes as carriers of cancer chemotherapy, Drugs 46 (1993) 618–638.
[7] Lasic DD: Novel applications of liposomes, Trends Biotechnol. 16 (1998) 307–321.
[8] Storm G and Crommelin DJ: Liposomes: Quo vadis?, Pharm. Sci. Technol. Today 1 (1998) 19–31.
[9] Patel HK, Shah CV, Shah VH, Upadhyay UM: Factorial designing, development and in-vitro evaluation of liposomal gel for topical delivery of quetiapine, Asian J. Pharm. Sci. 7 (2012) 290–302.
[10] Park SN, Jo NR, Jeon SH: Chitosan-coated liposomes for enhanced skin permeation of resveratrol, J. Ind. Eng. Chem. 20 (2014) 1481–1485.
[11] Abioye AO, Kola-Mustapha A, Chi GT, Ilya S: Quantification of in situ granulation-induced changes in pre-compression, solubility, dose distribution and intrinsic in vitro release characteristics of ibuprofen-cationic dextran conjugate crystanules, Int. J. Pharm. 471 (2014) 453–477.
[12] Wasankar SR, Faizi SM, Deshmuk AD: Formulation and development of liposomal gel for topical drug delivery system, Int. J. Pharm. Sci. Res. 3 (2012) 4461–4470
[13] Paveli E, Skalko-Basnet N, Jalsenjak I: Liposomal gel with chloramphenicol: Characterisation and in vitro release, Acta Pharm. 54 (2004) 319–330.
[14] A-sasutjarit R, Sirivat A, Vayumhasuwan P: Viscoelastic properties of carbopol 940 gels and their relationships to piroxicam diffusion coefficients in gel bases, Pharm. Res. 22 (2005) 2134–2140.
[15] Ikeda S, Foegeding EA, Jersey US: Measurement of gel rheology: Dynamic tests, Current protocols in food analytical chemistry ,New John Wiley Sons Inc. (2003).
[16] Troy DB, Remington JP, Beringer P: The science and practice of pharmacy, Lippincott, Williams & Wilkins (2006)
[17] Tan HW, Misni M: Effect of chitosan-modified fatty acid liposomes on the rheological properties of the carbohydrate-based gel, Appl. Rheol. 24 (2014) 34839.
[18] 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 Interface Sci. 317 (2008) 611–619.
[19] López YA, Villafuerte-Robles L: Functional performance of chitosan/carbopol 974p nf matrices in captopril tablets, J. Pharm. 2016 (2016) 1–9.
[20] Franck A: Understanding rheology of structured fluids, TA instruments (2004).
[21] Garg A, Aggarwal D, Garg S, Singla AK: Spreading of semisolid formulations: An update, Pharm. Technol. 26 (2002) 84–105.
[22] Yang Y, Wang S, Xu H, Sun C, Li X, Zheng J: Properties of topically applied organogels: Rheology and in vitro drug release, Asian J. Pharm. Sci. 3 (2008) 175–183.

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