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P-78

Rheological Studies of Hydrogels and Liposomal Dispersions: Factors Influencing the Viscoelastic Properties

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1. Introduction

Knowing the fact that the body fluids, such as human tears, synovial liquid and mucins possess viscoelastic character, the novel and innovative drug delivery systems - designed for the treatment in the area of viscoelastic body fluids - should also follow the viscoelastic rheological criterion. According to earlier results the viscoelastic behaviour can be achieved by the application of appropriate gelling agent. Novel literature data highlight the potential of vesicular systems for the design of viscoelastic systems. Viscoelastic systems exhibit high viscosity under low shear rate and low viscosity under high shear rate conditions [1]. Similarly, the rheological properties of intra-articular drug delivery systems should mimic the physiologic – viscoelactic – behaviour of synovial liquid. The use of viscoelastic formulations offer therapeutic advantages, among others facilitating the retention and permitting the easy spreading of the formulation – at the same time [2].

2. Methods

Multilamellar vesicles (MLV) were prepared using the thin-film hydration technique. From a stock solution of lipid (usually 10 mg/ml lipid in absolute ethanol) the appropriate volume was taken and the solvent was evaporated under nitrogen stream and held thereafter in a vacuum-desiccator for 24 hours. The hydration of the lipid films was carried out at about 50 °C, above the main phase transition temperature of liposomal samples used in the present study. Liposomal samples for rheological and size distribution measurements were hydrated with Milli-Q water, and hydroxyethyl-cellulose (0.5 %) gel. The final concentrations of lipids were 10.0 mg/ml.

1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC) were purchased from Sigma-Aldrich Ltd. (Budapest, Hungary). All the excipients used in our study (hydroxyethyl-cellulose, phenyl salicylate, caffeine) were purchased from Hungaropharma Ltd. (Budapest, Hungary). Deionized ultrafiltered water was produced by Milli-Q system (Millipore Inc., Budapest, Hungary).

Rheological measurements were carried out with Kinexus Pro rheometer (Malvern Instruments Ltd, UK). Measured data were registered with rSpace for Kinexus Pro 1.3 software. Preparations were measured using a cone and plate geometry. The gap between the cone and plate of sample placement was 0.15 mm. The temperature of the samples was set at 25.0 °C and controlled with an accuracy of ± 0.1 °C by Peltier system of the rheometer. Based on the results of preliminary amplitude sweep tests, a strain amplitude of 60 %

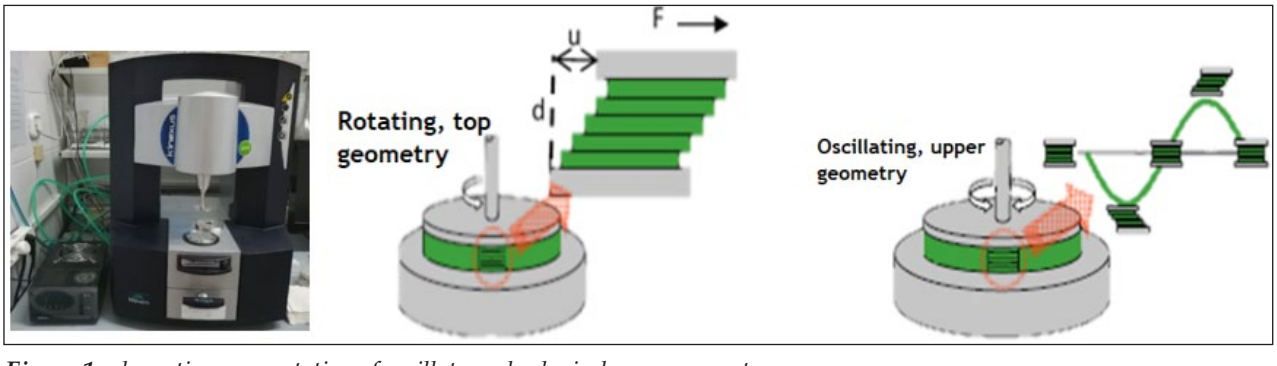

Figure 1 *schematic representation of oscillatory rheological measurements.*

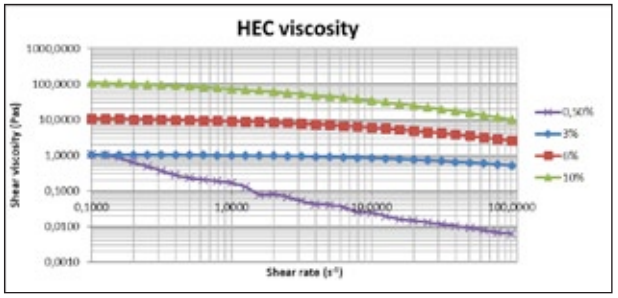

Figure 2 *change in viscosity of HEC as a function of gel concentration*

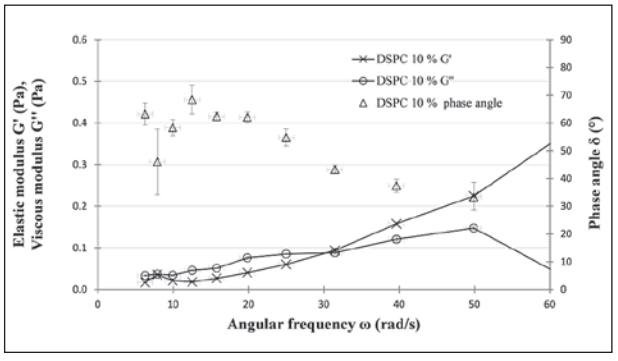

Figure 3 *Oscillation rheology of DSPC (90/10) MLV sample with 10.0 mg/ml lipid concentration hydrated with HEC gel*

was used for all of frequency sweep tests to provide linear viscoelastic behavior. In all measurements a cylindrical cover made of stainless steel was placed over the samples, in order to create a closed, saturated volume round the sample and to prevent evaporation of the sample. In case of each sample three parallels were analysed.

3. Results

Carrying out dynamic oscillation measurements in the linear viscoelastic range (LVR) the measured parameters such as phase angle δ (°), loss modulus or viscous modulus G″ (Pa) and storage modulus or elastic modulus G′ (Pa) vary with the angular frequency ω (rad/s) employed [3].

Frequency sweeps were conducted in order to investigate the viscoelastic behaviour of prepared liposomal compositions. In case of a viscoelastic material the value of phase angle (δ) crosses 45° at which point G′ = G″. The cross-over point of G′ and G″ assigns the transition point of viscoelastic materials which characterizes the transition from viscous type behaviour into elastic type behaviour in case of viscoelastic liquid [3-4]. Elastic behaviour is present, if the material restores its original shape when the external force is removed, and

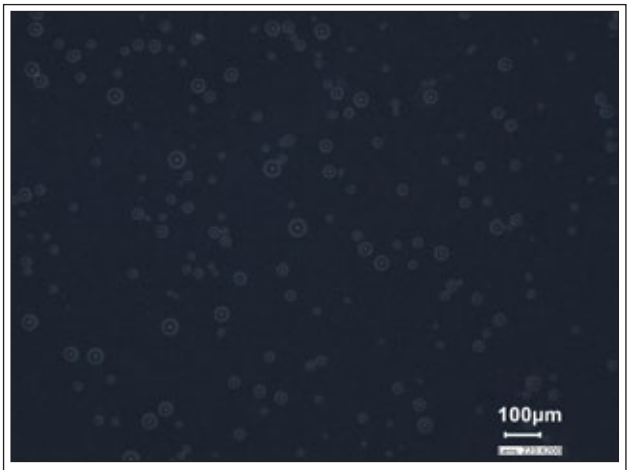

Figure 4 *Microscopic image of HEC DSPC liposomal dispersion*

viscous behaviour, if deformation ceases and the material does not regain its original shape when the applied force is removed [5].

4. Conclusions

Viscoelastic property as an advantageous and in many case required rheological character of drug delivery systems can be ensured by the presence of liposomes. On the basis of our dynamic oscillation measurements the multilamellar vesicles prepared from DSPC (lipid concentration 10.0 mg/ml) possess viscoelastic character. The lamellarity and/or size of vesicles can have a significant effect on disappearance of the viscoelasticity of liposomal dispersions. Similarly, the addition of drug molecules may lead to the disappearance of viscoelastic character of liposomal dispersions, too.

5. Acknowledgements

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