

TOPICAL DRUG DELIVERY SYSTEMS INCLUDED IN POLOXAMER 407 GEL: RHEOLOGICAL CHARACTERIZATION AND RELEASE STUDIES OF MODEL DRUG

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Poloxamer 407 copolymer is a versatile and widely used thermo-reversible material. Its use has many advantages, such as bio-adhesion, enhanced solubilization of poorly water-soluble drugs and many applications fields like oral, rectal, topical, nasal drug administration. Hydrogels made up of Poloxamer 407 are characterized by specific rheological features, which are affected by temperature, concentration and presence of other compounds. To make its topical application more interesting and functional, a strategic approach in topical therapeutic treatments may be the inclusion of drug delivery systems, such as ethosomes, transfersomes and niosomes, into hydrogel poloxamer formulation. The evaluation of the interaction between colloidal carriers and the Poloxamer 407 hydrogel network is essential for a suitable design of an innovative topical dosage form. For this reason, the Rheolaser Master™, based on diffusing wave spectroscopy, and a Kinexus Rotational Rheometer were used to evaluate the influence of nanocarriers on the microrheological features of hydrogels. The results provide evidence that vesicular systems do not influence the rheological features of the gel, supporting the possibility to encapsulate an innovative system into a three-dimensional network. Moreover, we evaluated the influence of poloxamer gel on percutaneous permeation of paclitaxel-loaded nanosystems. Paclitaxel permeation is slowed down in presence of poloxamer gel, but the combination of poloxamer gel with drug delivery systems does not prevent a better partitioning of the drug, in comparison with the hydro-alcoholic solution of paclitaxel, chosen as model drug. These findings suggest that nanosystems included in three-dimensional network of poloxamer gel could be used to achieve a long-time release of lipophilic drugs.

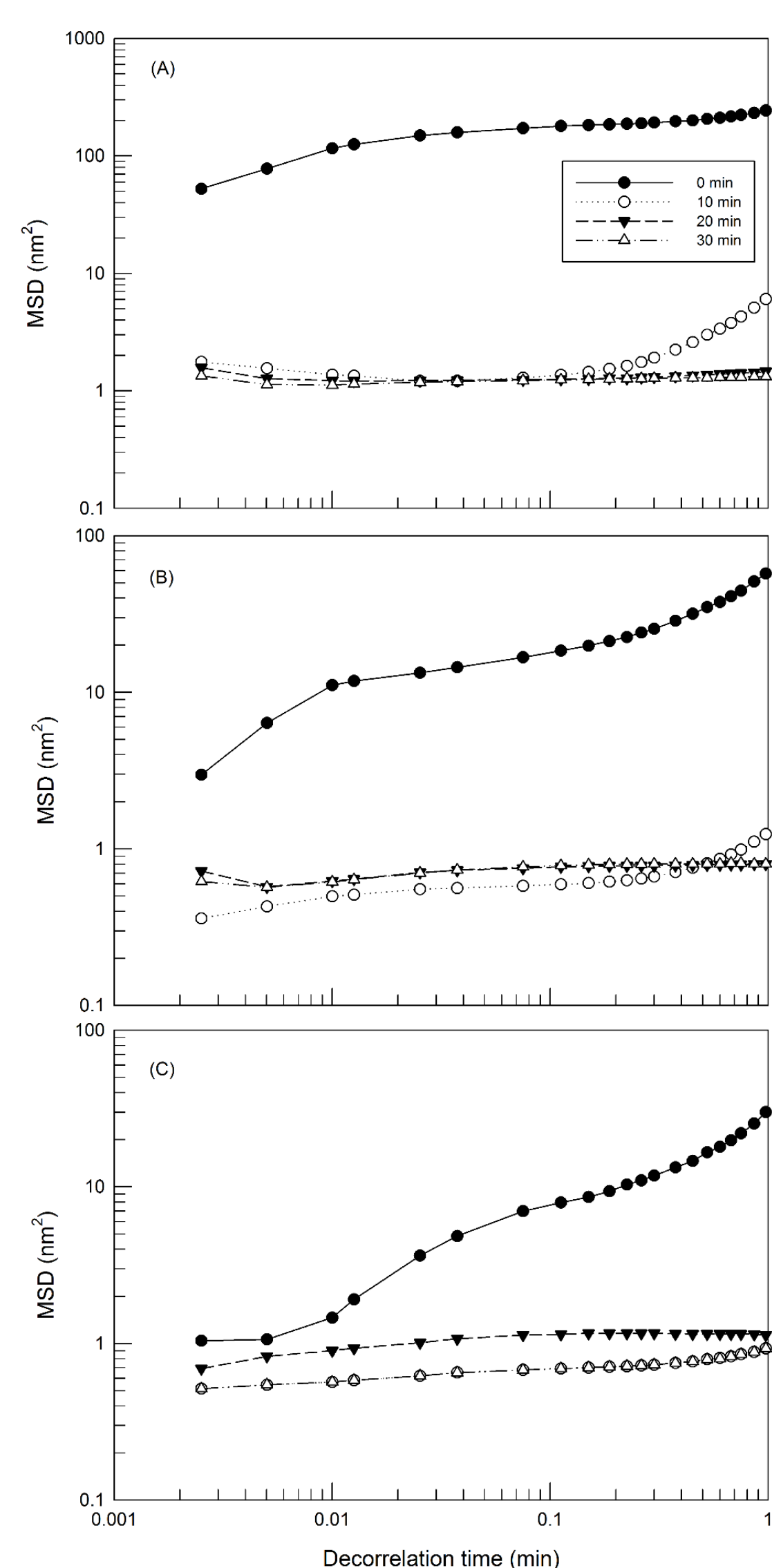


Figure 1. Mean square displacement MSD of hydrogel prepared with different concentrations of poloxamer 407: 20% (w/w) (A), 25% (w/w) (B) and 30% (w/w) (C), as a function of decorrelation time. The illustrated results were representative of three independent experiments.

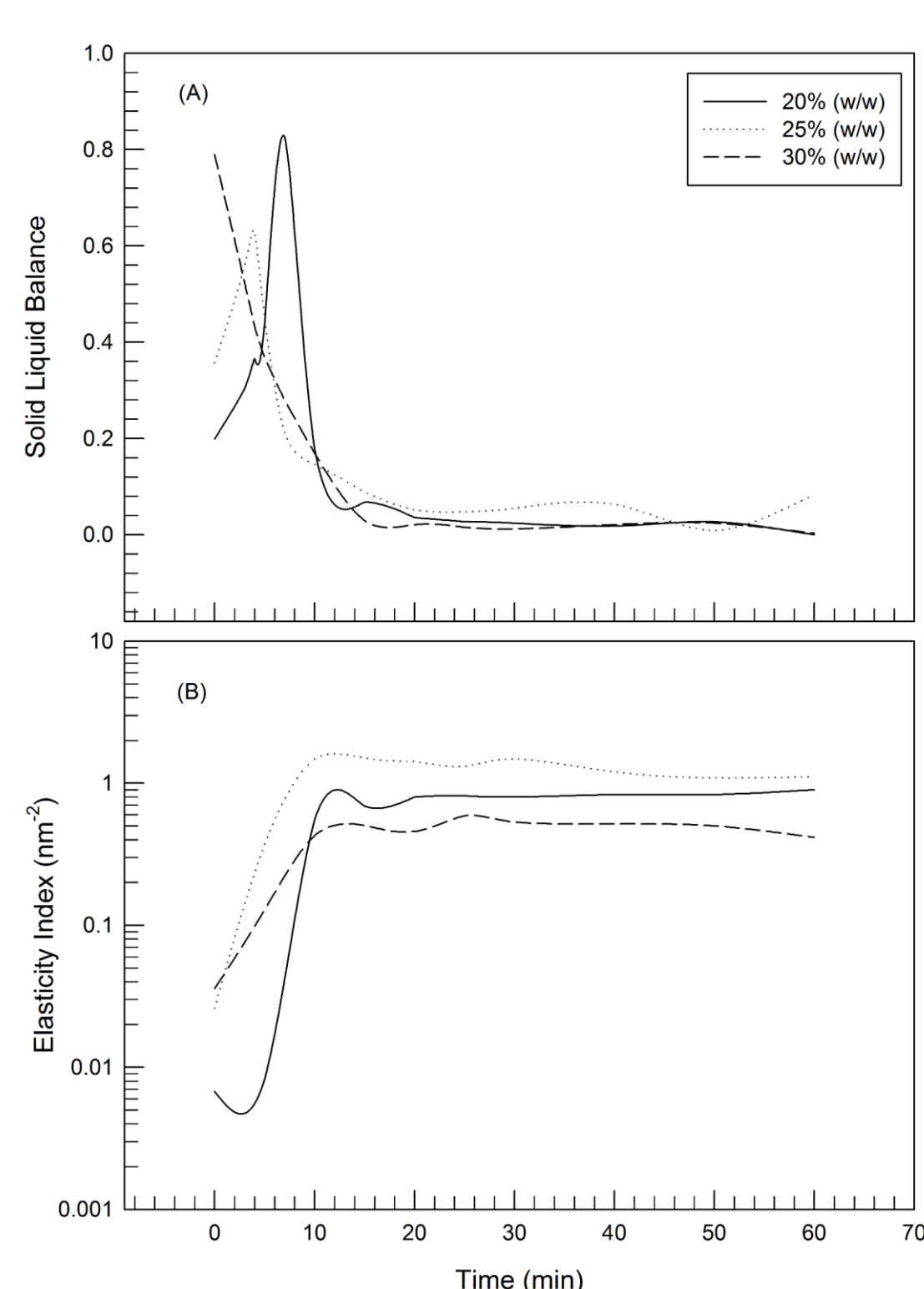


Figure 2. Elasticity Index (EI) (A) and Solid Liquid Balance (B) profiles versus time for 20% poloxamer 407, 25% poloxamer 407 and 30% poloxamer 407 samples.

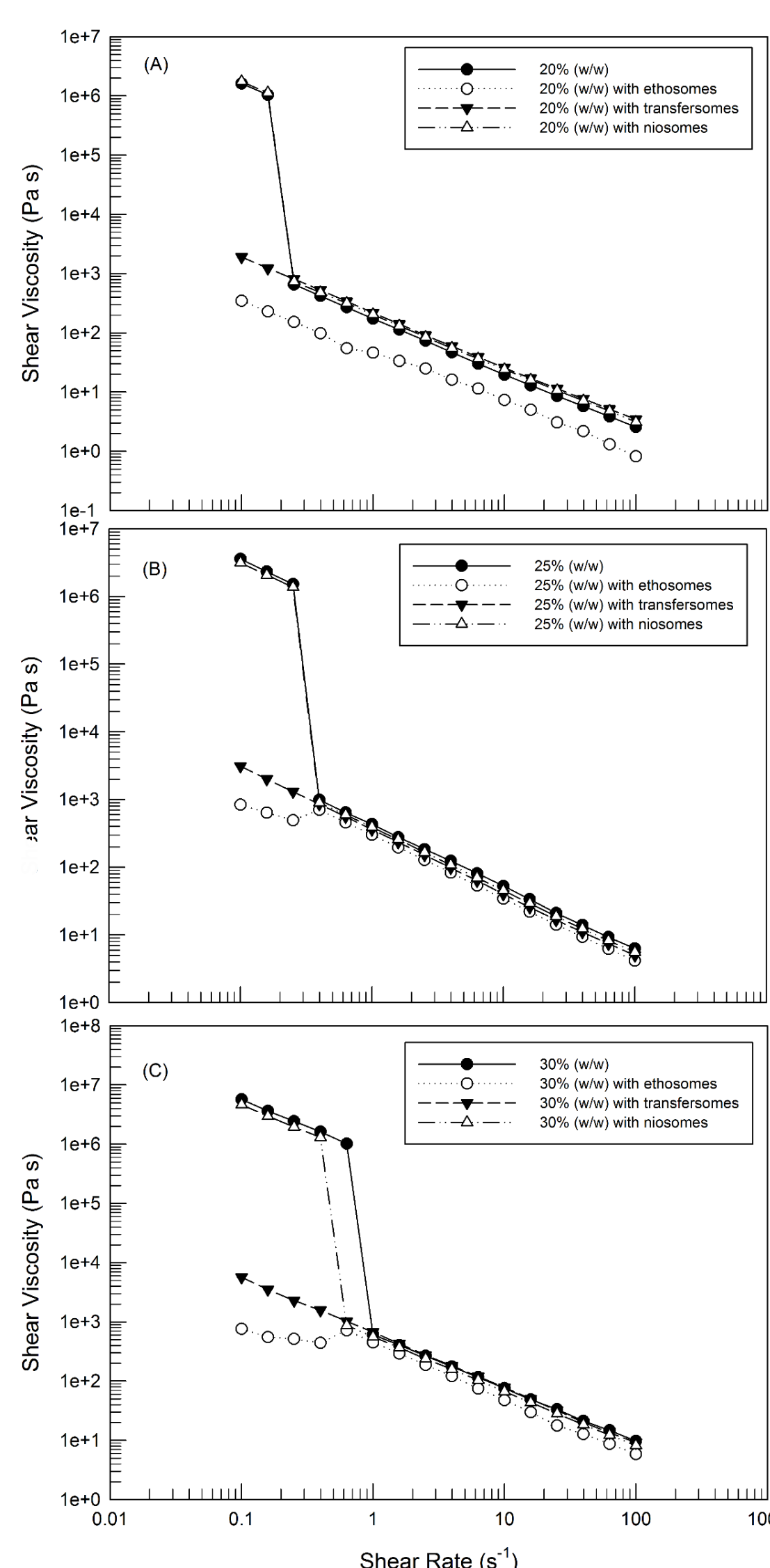


Figure 5. Flow curves (shear viscosity versus shear rate) of (A) 20% Poloxamer 407, (B) 25% Poloxamer 407 and (C) 30% Poloxamer 407, with and without carriers. The illustrated results were representative of three independent experiments.

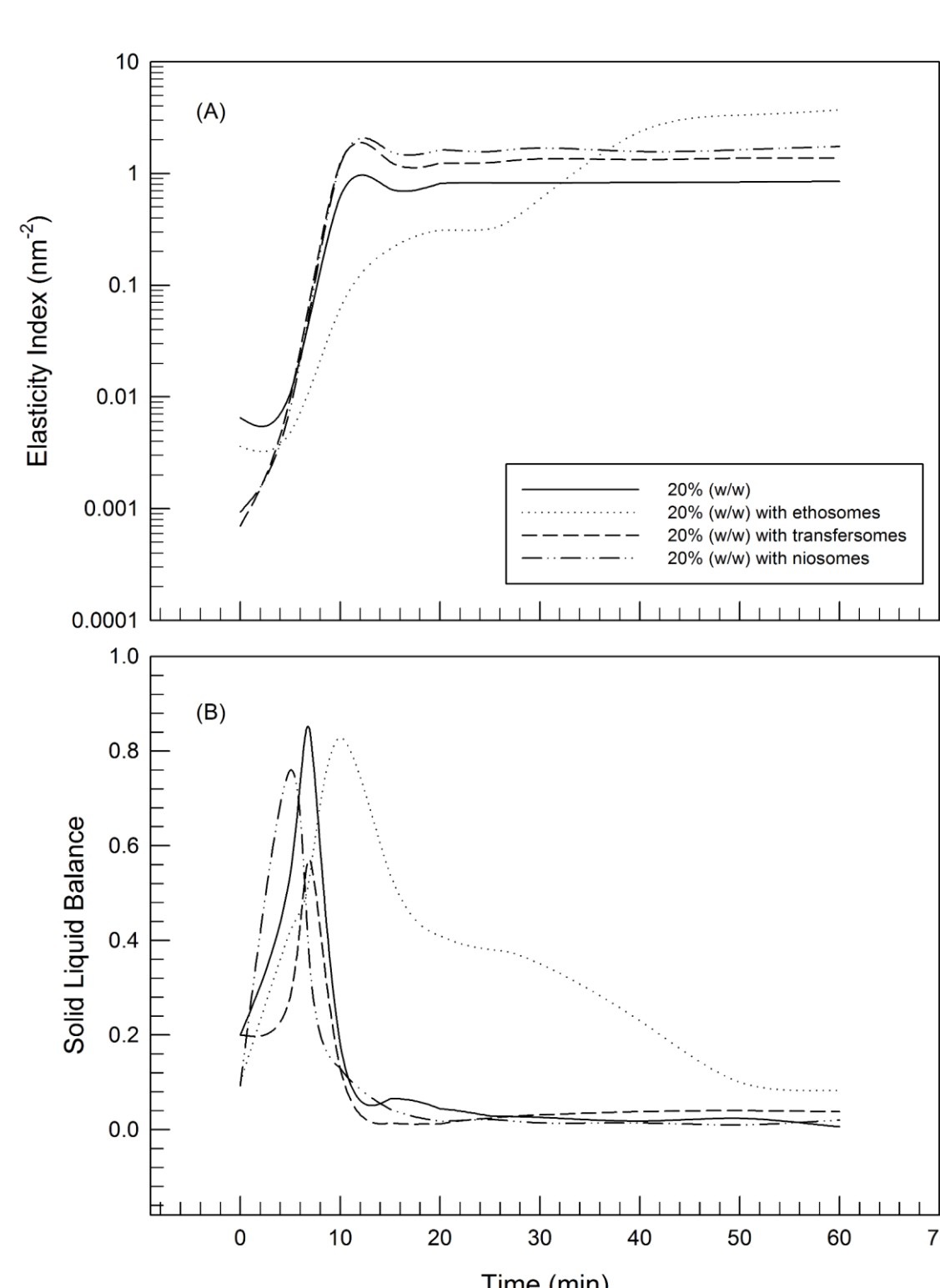


Figure 3. Elasticity Index (EI) (A) and Solid Liquid Balance profile (B) versus time for 20% poloxamer 407 with and without TDDSs.

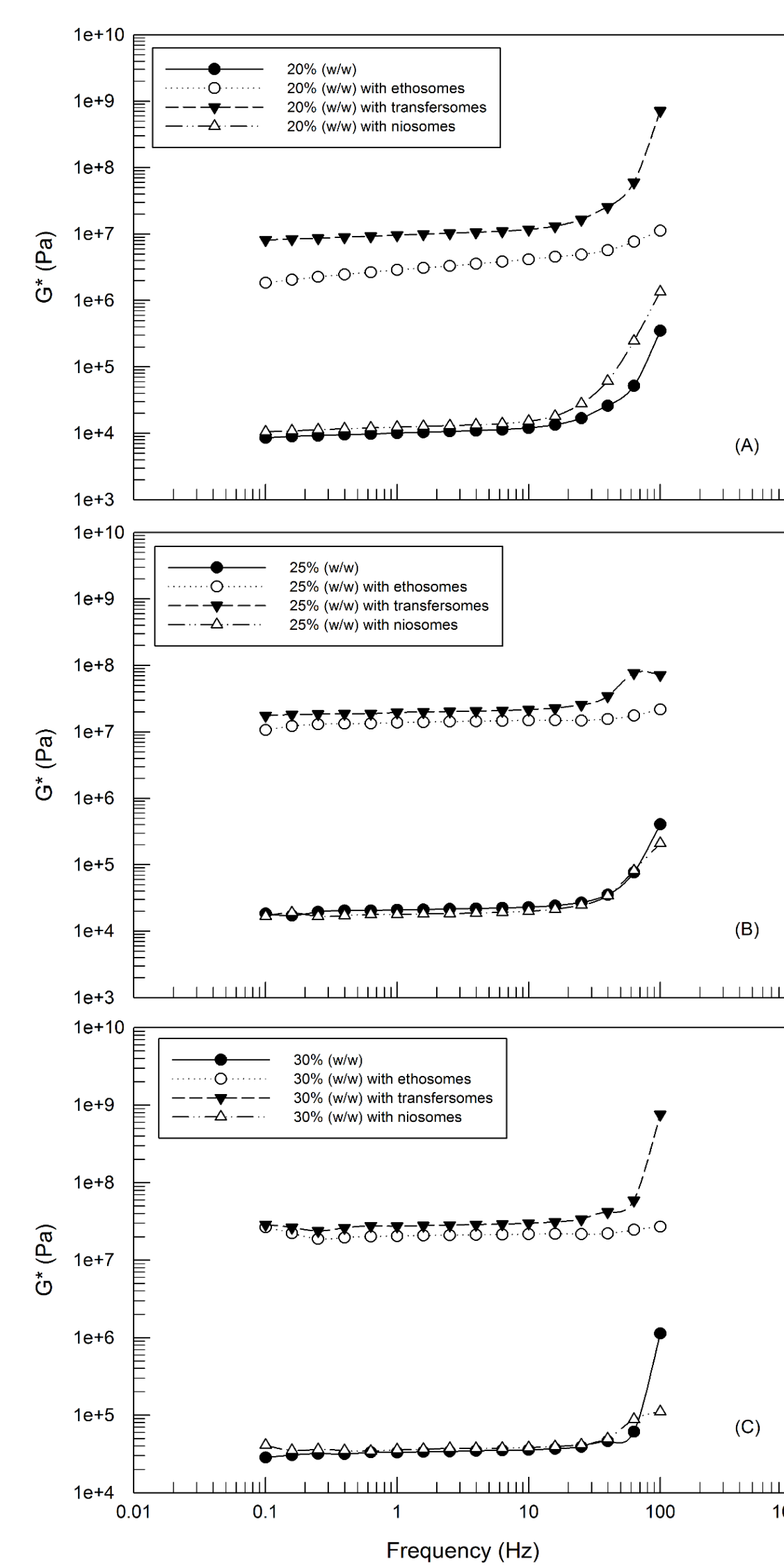


Figure 6. Complex shear modulus (G^*) versus Frequency for 20% Poloxamer 407 (A), 25% Poloxamer 407 (B) and 30% Poloxamer 407 (C) with and without TDDSs. The illustrated results were representative of three independent experiments.

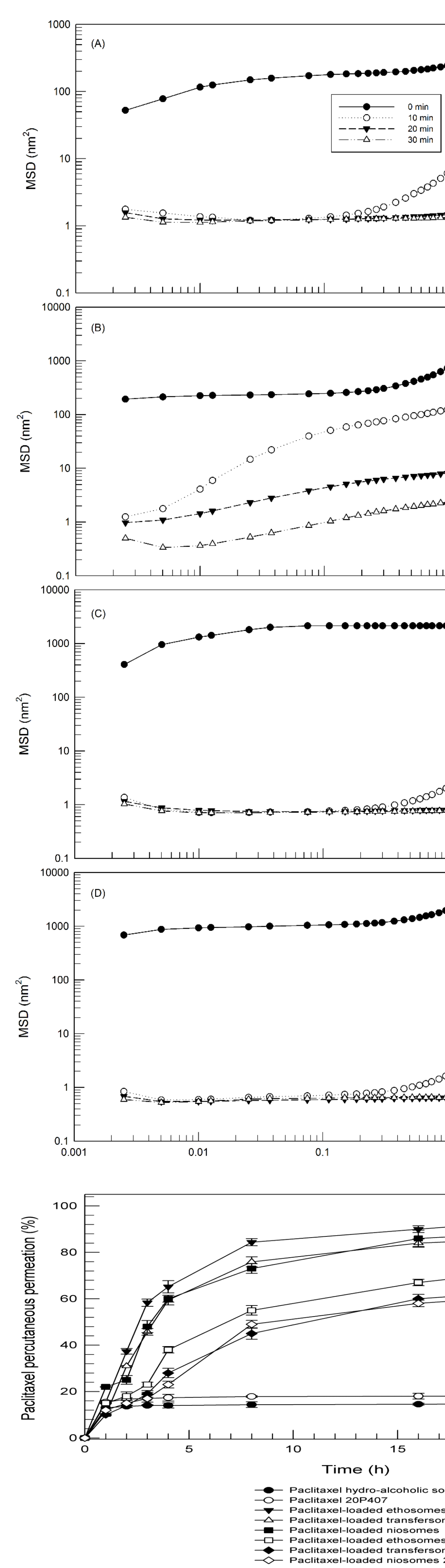


Figure 7. In vitro percutaneous permeation of paclitaxel from different formulations through SCE membranes, in comparison with a hydroalcoholic drug solution (as the control). Values represent the mean of three different experiments \pm standard deviation.

Figure 4. Mean square displacement of hydrogels made up of poloxamer 407 at 20% (w/w) alone (A) or in the presence of ethosomes (B), transfersomes (C) and niosomes (D) as a function of decorrelation time. The illustrated results were representative of three independent experiments. The same experiments were carried out for evaluating the effects of nanosystems on poloxamer gel characterized by 25% and 30% of poloxamer 407. The effects of nanocarriers on microrheological features of hydrogels were modulated by the amount of poloxamer used for the preparation. In fact, no effect on the microrheological features was observed at 25% (w/w) and 30% (w/w) poloxamer 407 concentrations (data not shown), probably because the greatest concentrations of poloxamer hid the TDDSs effects.

