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#### ABSTRACT

A new optimized delivery vector with biomedical applications was designed in this study. The aim was to obtain and characterize drug delivery system which has the capacity to incorporate large quantities of hydrophilic and lipophilic active principles, protect them from degradative reactions and ensure delivery of the drugs. Curcumin was selected as a model drug. The system consists of grapeseed oil used as the oily phase, a surfactant blend and ethanol as the solvent. Three different water soluble polymers were selected: Carbopol® 980 NF, chitosan and sodium hyaluronate salt, in order to increase the viscosity of the final formulation, required by the considered applications. The used ingredients are safe, biocompatible and biodegradable. All obtained systems were physico-chemically characterized in terms of electrical conductivity, dynamic light scattering and rheometric measurements. Evaluation of the cytotoxicity was determined by MTT test. In the final phase of the study, the release behaviour of the curcumin from the delivery vectors was evaluated. Some mathematical models were applied to establish the kinetic release mechanism.

#### MATERIALS & METHODS

The optimized delivery system, namely microemulsion T4b was prepared using **Grapeseed oil** obtained by the cold pressing method as oily phase and **distilled water** for second phase. A blend of surfactants (Smix): **Tween 80 and Polyglyceryl-3-diisostearique**, was used as emulsifying agents and **ethanol** was used as solvent. The microemulsion's components were homogenized using a vortex equipment, and then the mixtures were left 24-48 h at 25 °C to allow for the necessary equilibration time.

The microemulsion was analyzed using dynamic light scattering equipment, conductivity meter, rheometer and cross-polarized light microscopy, to establish the internal structure of the system.

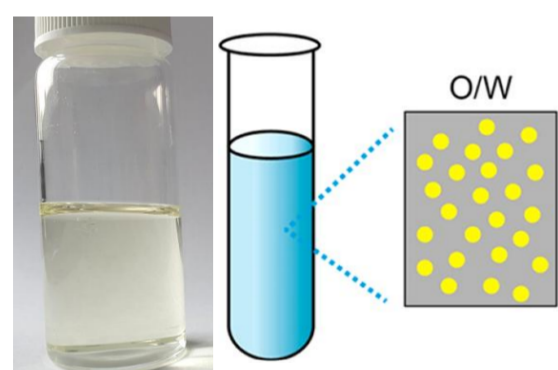
Preparation of microemulsion gels using Carbopol® 980 NF and hyaluronic acid sodium salt, were carried out by adding the polymer to the previously prepared T4b microemulsion (the reference) under magnetic stirring, for 24-48 h, until the complete dissolution of the polymer. For preparation of chitosan microemulsion gels, the chitosan solution was previously prepared and used as the aqueous phase of the microemulsion.

Curcumin encapsulation was carried out by adding it to the reference T4b microemulsion and also to the prepared microemulsion gels. All samples were magnetically stirred for 24-48 h, until complete dissolution of curcumin.

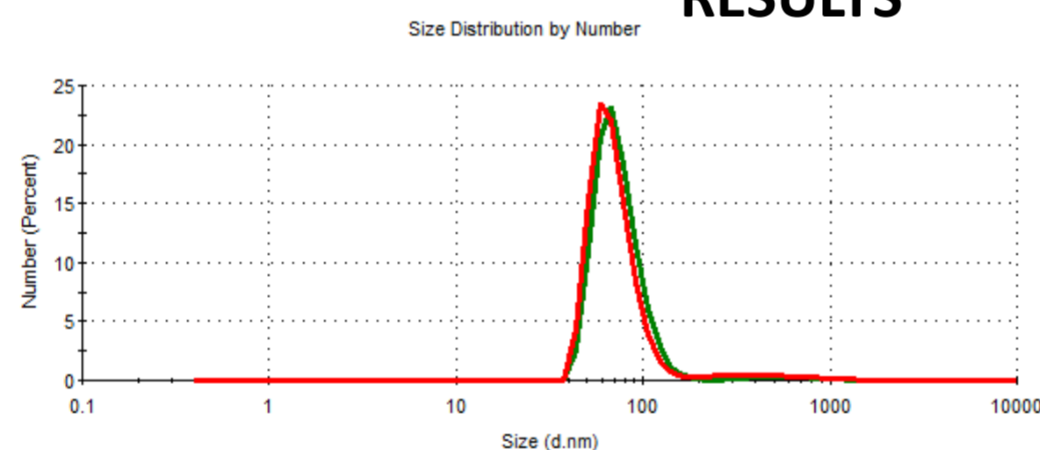
The release behavior of the curcumin was evaluated from 3 different systems: i) the microemulsion T4b; ii) the microemulsion gel with 0.3 wt.% hyaluronate acid Na salt in T4b and iii) the microemulsion gel with 0.34 wt.% chitosan in T4b. For the *in vitro* release experiment a Spectrum™ Spectra/Por™ regenerated cellulose dialysis membrane tubing (12,000 to 14,000 Dalton MWCO) was used.



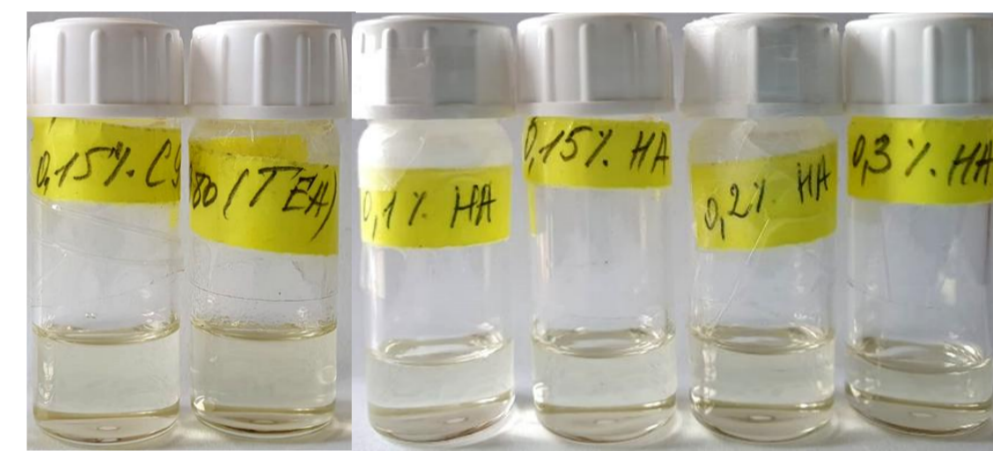
#### RESULTS



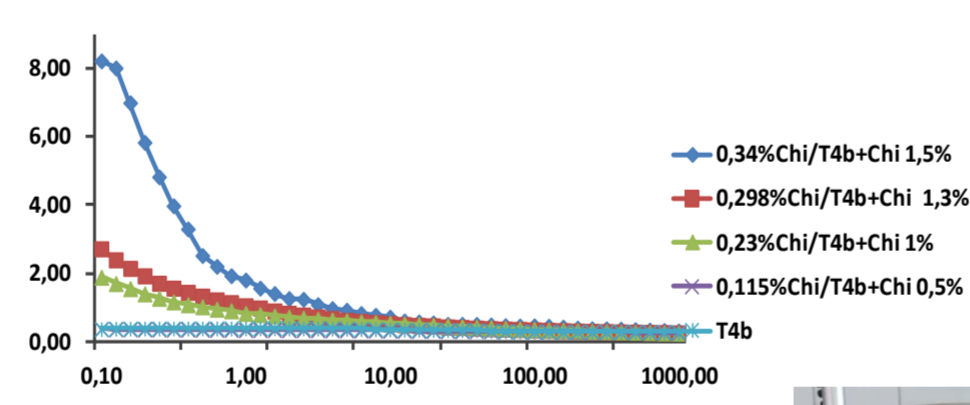
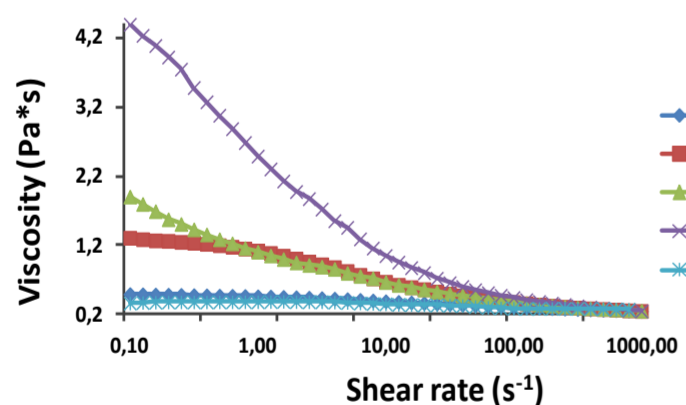
Appearance of the optimized microemulsion.



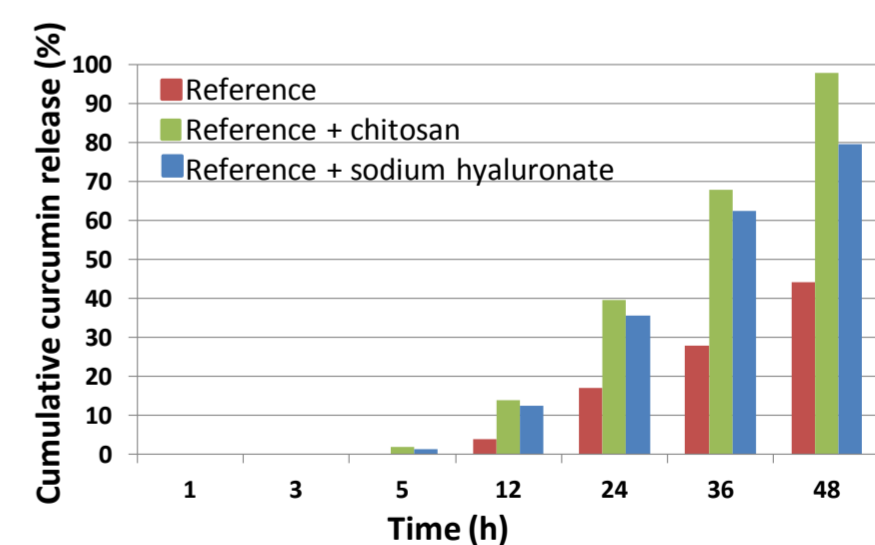
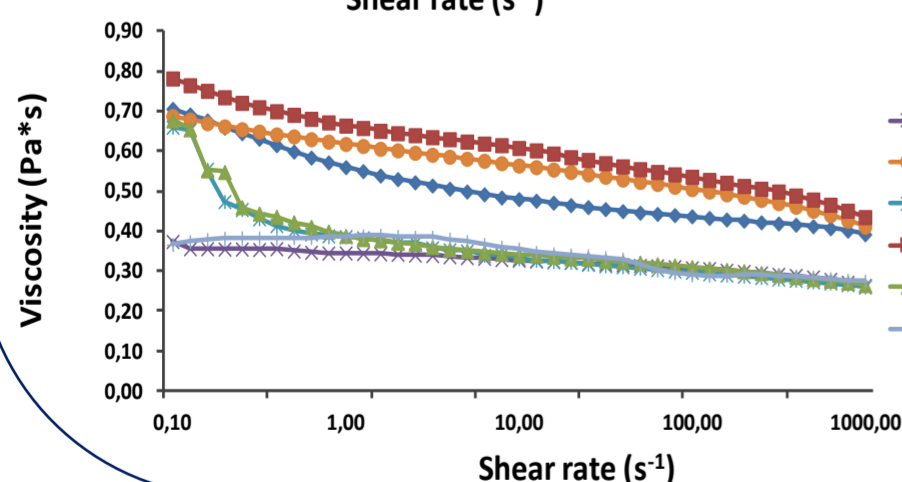
Droplet size distribution for the optimized microemulsion, at 24h - red, at 1 year - green.



Appearance of the obtained gel microemulsions.



Flow curves indicating rheological behaviour of the optimised microemulsion and gel microemulsions.



Release profile of the curcumin from delivery systems.



#### ACKNOWLEDGEMENT

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#### CONCLUSIONS

Due to the physico-chemical characteristics, the microemulsion represents a system that improves the degree of penetration of the active principles in the skin and increases the encapsulation capacity for the active principles.

In this study, an important amount of curcumin was encapsulated, as a model active principle, in the optimized microemulsion and gel microemulsions, approximately 1.7 (w / w)%.

The characteristic of chitosan to improve the penetration into the skin, of the formulations in which it is included, represents an important advantage for topical applications.

Taking into account the fact that the highest viscosity was obtained for gel microemulsions with chitosan and their high biocompatibility with the skin, the 0.34% chitosan sample in T4b would be the most suitable as a system of transport and controlled release of hydrophobic active principles in skin.