DABCO-functionalized nanoemulsions with antimicrobial properties for potential treatment of ocular myasthenia gravis

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Ocular myasthenia gravis (OMG) is an autoimmune disease in which Ab is produced against proteins at the neuromuscular junction in the ocular district, causing inability to contract extraocular and eyelid muscles and thus leading to muscle weakness, diplopia, ptosis, and therefore difficulty in vision[1]. In cases where treatment with acetylcholinesterase inhibitors fails, oral corticosteroids are used. One way to avoid the side effects of systemic administration of these drugs is their local administration[2]. However, by topical administration, the percentage of drug absorbed in the eye is less than 5%[3]. The use of oil-in-water nanoemulsions (NEs) to deliver corticosteroids increases their bioavailability and improves their absorption[4]. The use of DABCO as a cationic surfactant for the formulation of the NEs allows a controlled drug release over time, through electrostatic interaction with the negatively charged mucins in the tears[2]. DABCO's antibacterial properties also allow it to act as a preservative, making it possible to avoid the use of preservatives in the formulation, which are often responsible for allergic reactions[2]. In this work, DABCO S2-NEs were produced and characterised, leading to the definition of a delivery system akin to ocular delivery, supporting the hypothesis of their use in the treatment of OMG. It is also possible to consider functionalising NEs with monoclonal antibodies (one of the latest treatments in the cure of the disease) to achieve a synergistic effect.

Preparation Two formulations of NEs were produced, with the same ingredients but different amounts of DABCO S2. Both formulations consist of sunflower oil (2%), Tween 80 (0.2%), Poloxamer 188 (0.01%), glycerol (1.5%). F8 contains DABCO S2 0.12% and F9 0.08%.

The two control formulations (F8C and F9C) were also prepared, in which CTAB was used instead of DABCO S2 in the same quantities. Formulations and controls were analysed in a 56 days period to define some of the basic physico-chemical characteristics such as particle size (PS, Fig.1), polydispersity index (PDI, Fig.2), rheological behaviour (Fig.3) and DSC.

Particle size and polydispersity index The size for a NEs suitable for ocular delivery is between 20 and 500 nm; as can be seen from the PS chart, all formulations maintain sizes between 200 and 300 nm (however always below 400nm) over the period analysed. PDI values close to zero testify to a monodisperse and homogeneous NEs, as well as being stable over time.

Figure 1

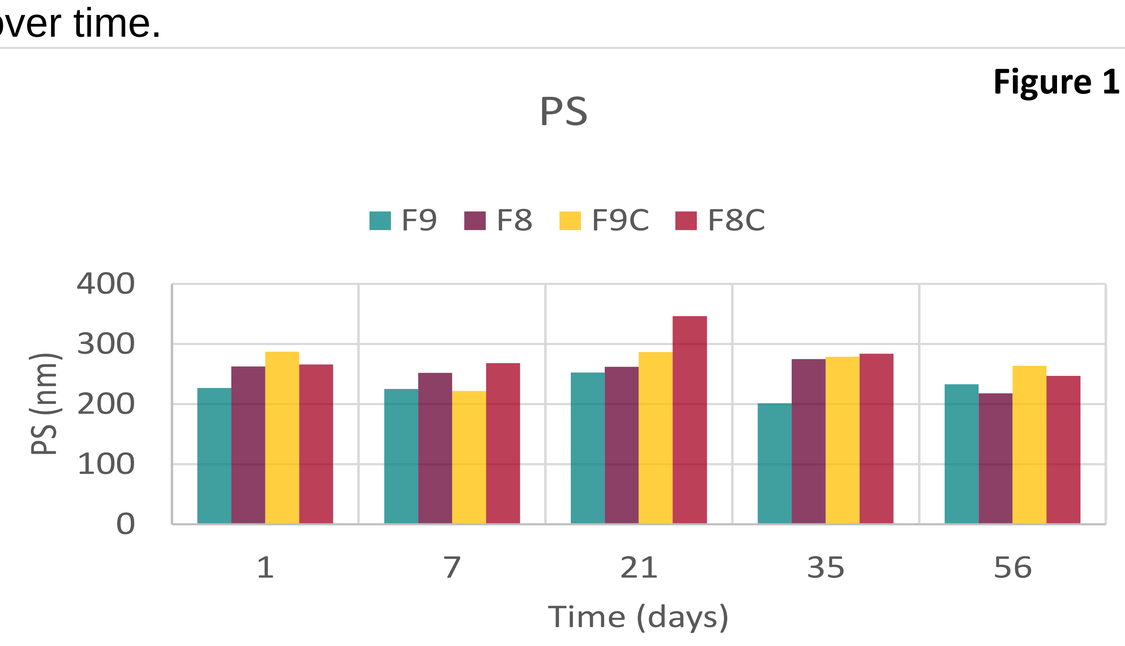
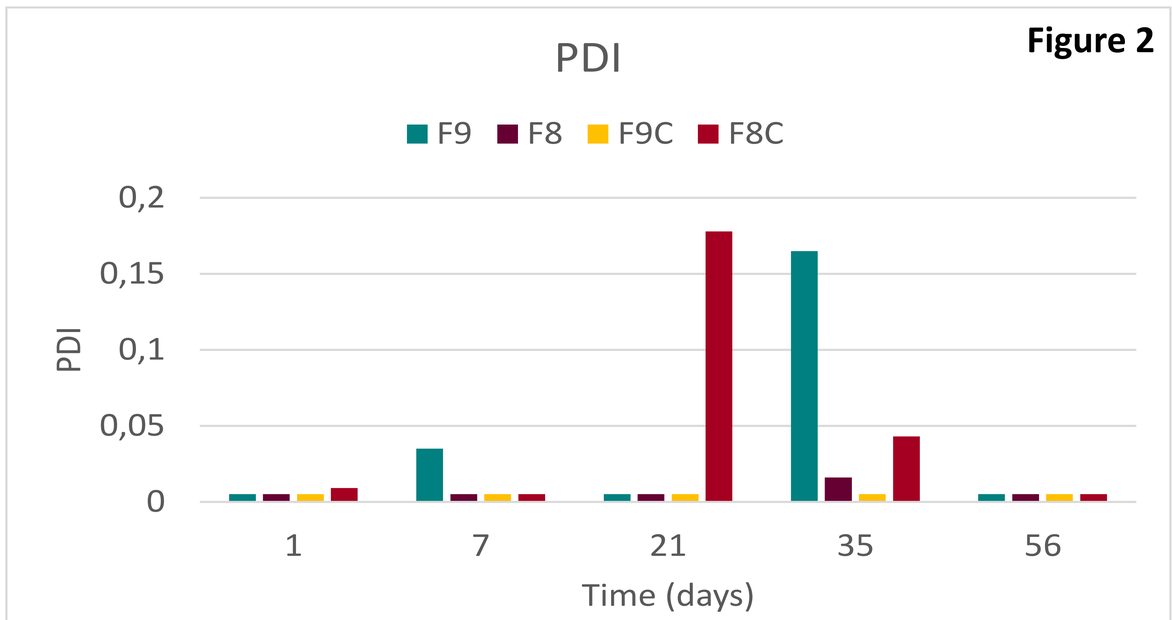


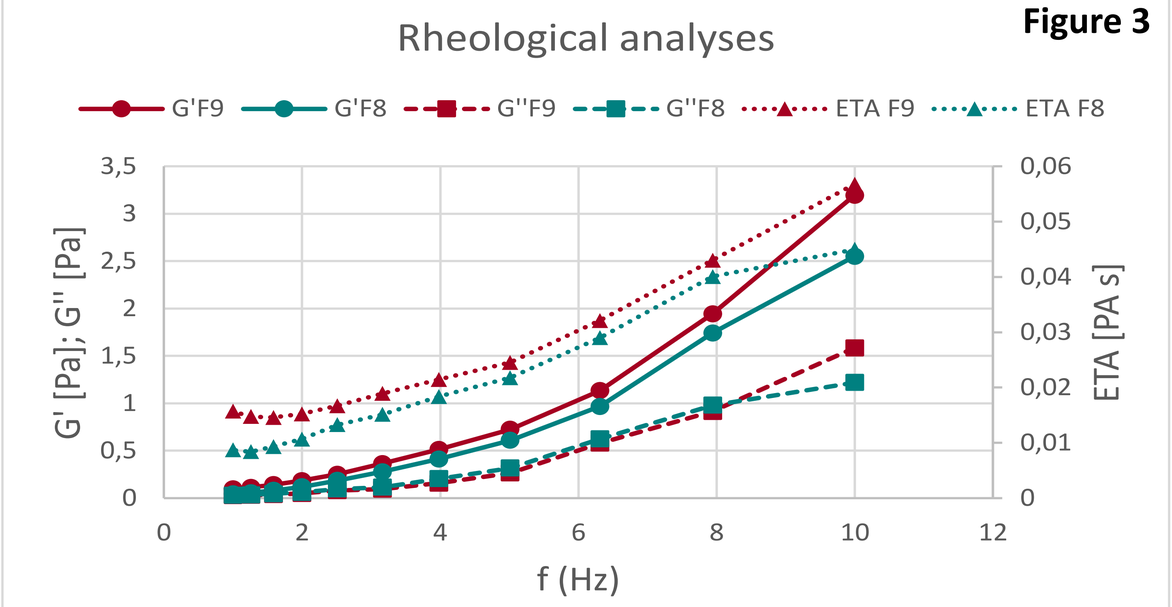
Figure 2



Rheological behaviour For both formulations, G' (elastic modulus) takes on values higher than G'' (viscous modulus) and both increase with increasing frequency. The two formulations behave as viscoelastic fluids.

DSC By DSC, the dissolution of DABCO S2 in sunflower oil was observed; in fact, the mixture of the two subjected to heating does not show the presence of solids. On the other hand, analysis of the thermograms obtained by testing the two formulations F8 and F9 shows the presence of solid components.

Figure 3



Conclusion This work is an pioneering the production and characterization of DABCO NEs as potential delivery systems of drugs to ameliorate symptoms of ocular myasthenia gravis. The developed systems showed promising results for solubilizing lipophilic drugs (e.g. corticosteroids) in their inner oily phase, with suitable rheological behaviour for the eye route.

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