Nanoencapsulation strategies for improved delivery of xanthone-based compounds with antiviral activity

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Background: Xanthones are widely available natural compounds, with various biological activities due to their core structure that facilitates chemical substitutions (1). Recent emergence of viruses such as SARS-CoV-2 reinforced the need for effective antiviral compounds, and hydroxy-xanthones have shown promise in this field (2). However, their strong hydrophobicity leads to generally poor bioavailability, limiting their therapeutic potential (1). Here, we present the development of solvent-free oil-in-water nanoemulsions (O/W NEs) to improve the effect of hydroxy-xanthones against coronavirus infection.

Methods: Design of Experiments (DoE) was used to develop O/W NEs with squalene or isopropyl tetradecanoate (IPTD) as oils, and soy lecithin and Span 80 as co-surfactants. Surfactants were dissolved in each oil at room temperature and this phase was mixed with water using a pipette or syringe and needle, under magnetic stirring. Particle size, polydispersity index (PdI) and zeta potential were measured using a Liteziser 500, following sample dilution with water. The formulations were stored at 4 ^{o}C for stability assessment, and physicochemical parameters were measured at predetermined times.

Results: Preliminary results showed that, in the proportions selected, it was not possible to form nanoemulsions with squalene, with all formulations separating into both phases soon after mixing. However, with IPTD, three formulations showed appropriate formation of a homogenous nanoemulsion population, with particle size ranging from 140 to 400 nm and PdI below 0.35. In terms of surface charge, the NEs showed strong negative zeta potential values (ranging from -45 to -66 mV), as expected. This is aligned with our future goal of further coating these nanoemulsions with a cationic polymer such as chitosan, that has shown immunomodulatory properties. We also observed that the method used to mix both phases did not significantly influence their final characteristics. The formulations showed good stability at 4 ^{o}C, maintaining their size and PdI for up to 3 days.

Conclusions: We successfully developed O/W NEs without using any solvents, which could affect stability and efficacy of drug molecules. The formulations showed appropriate physicochemical characteristics and preliminary stability in storage conditions. Ongoing studies include further stability assessment, encapsulation of hydroxy-xanthone derivatives, assessment of encapsulation efficiency and drug release, and evaluation of antiviral activity against coronavirus.

(1) Gomes AS et al, Curr Med Chem, 2016:3654. (2) Dean B et al, Bioorg Med Chem Lett, 2023:129211.