Fighting *Pseudomonas aeruginosa*-prevalent wound infections by means of natural-origin compounds

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Abstract: Pseudomonas aeruginosa-derived infections are considered a public health problem once that *P. aeruginosa* is stated as a human pathogen highly resistant to antibiotics. Recently, essential oils (EOs) have been reported as an alternative to antibiotics. Polymeric microcapsules can include antimicrobial agents at the core and be surrounded by a polymeric shell, usually made of polysaccharides like chitosan (CS), aiming to work as drug carriers and protecting the encapsulated biomolecule from the surrounding environment. Hydrogel-like films are commonly produced to incorporate microcapsules because of their high porosity, that enables a high permeability of oxygen, nutrients and metabolites. Sodium alginate (SA) and gelatin (GN) are polymers that are frequently applied in the production of films. In this study, a delivery platform was developed for the controlled release of cinnamon leaf oil (CLO) entrapped in CS microcapsules produced via ionotropic gelation. CS solution was prepared without pH adjustment (CS1) and with pH adjusted to 5.0 (CS4), which according to the literature improves the polymer stability for microencapsulation. The microcapsules were then incorporated in hydrogel-like films, composed of a combination of SA and GN. Results confirmed an effective incorporation of CS microcapsules, containing CLO, within SA/GN films, as well as a continuous release of the entrapped CLO during 24h. Time kill kinetics tests showed that during the first hour of interaction with the CLO-containing films bacteria continued to grow. However, as the CLO release from the films increased, its action against the bacteria also improved with a >99% elimination. CS1 microcapsules were deemed more effective, due to their enhanced CLO release profile and antimicrobial action. All qualitative and quantitative antimicrobial tests proved the potential of CLO loaded films for the inhibition of multi-drug resistant bacteria.

<u>Keywords</u>: bio-based polymers; drug delivery platform; natural extracts; trigger-based release; bactericidal effects