

Development of sustained release biodegradable films aiming the use in the periodontal disease

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Introduction: Periodontitis is a worldwide highly prevalent disease that is characterized by an inflammatory process triggered by a bacterial overgrowth organized as a biofilm, which affects the support structures of the tooth. As a consequence, there is the formation of periodontal pockets that can lead to tooth loss if not treated. Conventional treatment consists of mechanical removal of plaque and calculus above the gum through scaling and root planning procedure, with or without the use of antimicrobials. The use of local drug delivery systems may avoid many side effects associated with systemic use of the antimicrobials. Pectin and sodium alginate are examples of biodegradable and biocompatible materials widely used in formulation development. They are also able to link to divalent metal ions providing an interesting matrix for controlling drug delivery

Objective: This study aims at developing biodegradable films to sustain the release of metronidazole inside periodontal pockets

Methods: Films based on pectin and sodium alginate containing metronidazole and pharmaceutical adjuvants such as hydroxypropylmethylcellulose (HPMC) and polyvinylpyrrolidone were developed (PVP). HPMC was added in order to improve tensile properties of the films while PVP was used in virtue of its capacity to inhibit drug crystallization during film drying. Glycerol and glycerol triacetate were evaluated as plasticizers. Formulations were characterized in terms of thickness, tensile and deformation properties, inhibition of drug crystallization, ability to cross-link with calcium in a range of calcium chloride concentration from 0.085 to 5.9 M, swelling properties and for their ability to sustain the release of the drug in a system that mimics the solvent flow and volume in the periodontal pocket. **Results:** The systems have appropriate visual characteristics and an average thickness of 200 μm . Alginate films showed higher tensile strength than the pectin films (35 mPa and 15 mPa respectively). Addition of HPMC reduced tensile strength of alginate films while pectin films were not affect by HPMC. Elongation at break showed the same tendency as tensile strength although values from alginate and pectin films were closer in this case. PVP was able to inhibit drug crystallization for both films, but in a smaller concentration in the case of alginate one. Pectin and alginate simple films were likely to be reticulated throughout all the range of calcium concentrations. Addition of HPMC caused higher influence upon pectin films. Pectin/HPMC could only be reticulated with calcium concentration higher than 1.35M. Degree of swelling of simple films was smaller for pectin films which showed lower water absorption for films cross-linked with a 2 to 3.5 M solution of calcium chloride. For alginate films lower water absorption occurred at a calcium chloride concentration of 0.3375 M. Addition of HPMC lead to a higher hydrosolubility of both alginate and pectin films. Films containing PVP, HPMC, pectin/glycerol and PVP, HPMC, alginate/glycerol triacetate were able to sustain the release of metronidazole for up to four days in a concentration equal or greater than the minimum inhibitory concentration for mouth pathogens related to periodontitis **Conclusion:** These films can be considered promising due to the sustained release of drug, easy availability and low cost of raw materials used.

Keywords: Periodontal disease, films, drug delivery, pectin, alginate, metronidazole.

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