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Development of an Implantable Matrix from Biodegradable Polymer for Prolonged Release of Active Substance Physico-Chemical and Biopharmaceutical Characterization

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ABSTRACT

The aim of this study is to create a hydrophilic matrix from a biopolymer: chitosan, so that it can be used as a biodegradable implant. The selection of this matrix is motivated by the possibility of using a simple technology to manufacture direct compression mini compresses, in order to obtain a prolonged release of the active ingredient, Diclofenac

Keywords: hydrophilic matrix, chitosan, biodegradable implant mini tablets prolonged release

1 Introduction

There are many methods for the release of drugs from implantable systems, using passive release from degradable or non-degradable reservoir consisting of monolithic matrix, micro- or Nano spheres or an active programmed release through osmotic systems. But the use of monolithic matrices based on biopolymers remains more advantageous due to the low cost of industrial manufacture, but also due to their bio-erosion in the organism after the exhaustion of the active substance [1]. There is a very wide variety of bio-polymers from marine products, including the family of polysaccharides such as chitosan. These bio-polymers are an interesting alternative in the manufacture of polymer matrices, because they possess very interesting physico-chemical properties allowing to modify the release, pharmacokinetics and distribution of active substances in the body [2]. The objective of this work is to formulate a hydrophilic matrix based on a biopolymer: chitosan, for use as a biodegradable implant. The choice of such a matrix due to the possibility of the use of a simple technology of making mini compresses by direct compression, in order to obtain a prolonged release of the active ingredient diclofenac.

2 Experimental

The chitosan used was extracted from seach bone (Sepia officinalis l) according to the method [3] and then characterized physico-chemically to determine these intrinsic and structural properties such as yield, molecular weight, water content, solubility, degrees of deacetylation (DDA) and characterization by infrared spectroscopy.. For the formulation of chitosan matrix we proceeded by two methods: the first is based on a simple physical mixture between the dry powders of the polymer and active ingredient .The second technique is based on trapping the active ingredient in the polymer during its alkalization (change of solubility) in order to promote the interaction between active ingredient and chitosan. Both types of matrices were characterized on the pharmaco-technical properties (weight, hardness) disintegration time and biopharmaceutical by a study of kinetics of release in the gastric medium simulated at pH 1.2 and phosphate medium pH 6.8, in order to clarify the mechanisms involved in the release of active ingredient.

3 Results and Discussion

The extraction mass yield obtained according to the equation R m = mf/mi x100 is 50.6%, which is acceptable, the water content calculated by the loss at drying is 7.70%, while the solubility is high in acidic

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medium and very low in alkaline medium due to the large protonation of chitosan in acid medium. The degree of deacetylation of chitosan determined by potentiometry is 97.8% which indicates that chitosane obtained and highly desacetillated. The spectral analysis of the extracted chitosan reveals characteristic absorption bands at 3300 cm-1 attributed to the hydroxyl group (-OH), at the 1550 cm-1 band attributable to the amide bond (N-H) of the amine group and at 1150 cm-1, attributing to the glycosidic bond (C-O-C) characteristic of the glucosamine units of the chitosane. (Fig1)

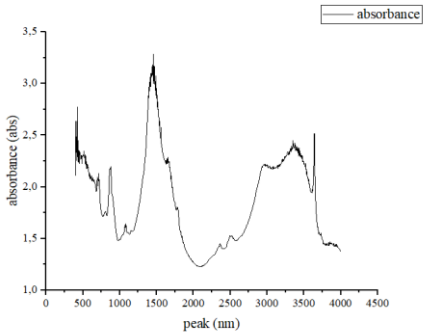

Fig 1: IR spectrum of extracted Chitosane

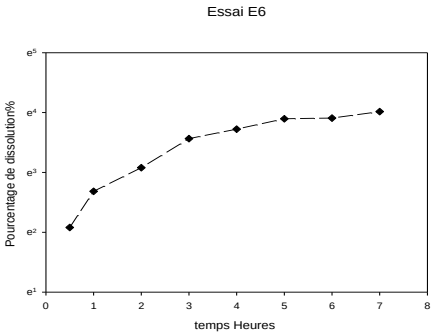

Fig 2: Diclofenac release profile in pH 6.8 Medium

The results of pharmacological characterization revealed tablets of medium weight equal to 500mg10mg with a diameter of 8mm and thickness of 5mm. The decaying kinetics of tablets in phosphate pH 6.8 medium is of a slow type with an erosion percentage of 40% at 3Hours, and a dissolution rate of 56% in 6 hours for the E6 test (Fig2), which suggests that the release mechanism is of diffusional type associated with prolonged erosion of the matrix which is in favour of prolonged release of diclofenac from this matrix.

4 Conclusion

The extraction of chitosan with a very interesting degree of desacetylation was obtained by the technique of depolymerisation in acidic medium. The application of extracted chitosan in the preparation of active-substance matrices was done by direct compression of the PA-chitosan mixture in different proportions. The results demonstrated the ability of the chitosan-based matrix to release the active substance according to a prolonged type profile combining a mechanism of erosion and slow diffusion.

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