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Chitosan-based hydrogels as biomaterials for controlled release

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Because of its favorable properties chitosan has been studied as a biomaterial and as a pharmaceutical excipient in drug formulations. For this, chitosan has to be crosslinked either chemically using covalent agents, or physically with ionic agents. The use of crosslinking agents is imposed by the properties of the non-crosslinked gels, such as lack of shape and mechanical stability. It is well-known that the covalent crosslinking agents present a certain toxicity leading to cytotoxic formulations. To reduce this toxicity original concepts were developed. The first one to be described was double-crosslinking consisting in a mixture of covalent (glutaraldehyde was used in a minimum amount to ensure the system stability) and ionic (sodium or magnesium sulphate, sodium tripolyphosphate) crosslinking agents. A second concept is the use of natural non-toxic crosslinking agents such as tannic acid. Due to hydrogen interactions able to form with the polysaccharides, tannic acid is able to prepare hydrogels able to load and deliver drugs or biologically active matter. These materials can be prepared under different forms such as hydrogels, particles and capsules. Their properties depend on some initial preparation parameters, the aqueous solution concentration, the process conditions, etc. Specific tests were performed in order to prove the ability of these biomaterials to be used in different areas of medicine. But drug release studies on these materials show, in many cases, a burst effect phenomenon. A great quantity of active principle is released in the first minutes before release rate stays constant. This effect leads to a great initial drug concentration in the body and decreases the lifetime of the system. According to applications it may be desired (wound dressing) or, very often, negative. To overcome this problem liposomes dispersed in the hydrogel were used playing the role of supplementary barrier against early drug release. Complex systems capable of prolonged and controlled drug release kinetics were prepared based on chitosan hydrogels and drug loaded liposomes. Calcein release from polymeric hydrogels has been retarded from several days to weeks after calcein inclusion in small phosphatidylcholine unilamellar and multilamellar vesicles entrapped subsequently in hydrogels. The calcein release kinetics of complex systems was compared to simple systems (control hydrogels) and important changes were observed proving that the mechanism of the process increases in complexity. Kinetic constants obtained from Higuchi or Korsmeyer-Peppas models were compared and discussed. Moreover, it is demonstrated that liposomes' stability can be greatly improved by inclusion in polymer matrices.

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