PP 13 - Studies on the Mechanism of Thermal Gelation of Chitosan-Glycerol Phosphate Solutions

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Chitosan-glycerol phosphate (GP) solutions reveal a sol-gel transition upon heating and can be used as cell and drug delivery carriers or as tissue engineering scaffolds in part due to this property and their physiological characteristics. These hydrogels can be injected or applied to specific local sites and offer therapeutic properties for the local repair of damaged tissues such as cartilage, bone and chronic wounds. The unique ability of some formulations to be liquid at room temperature and gel at body temperature offers a particular advantage. In order to elucidate the molecular mechanism of gelation of chitosan-GP solutions, potentiometric titration of chitosan and GP and temperature ramp experiments on diluted chitosan-GP solutions were performed. The experiments indicated that the transition from liquid to solid is the result of a proton transfer from chitosan to GP induced by heating. Chitosan intermolecular electrostatic repulsion is thus reduced by this progressive and homogeneous neutralization until the chitosan charge state reaches a specific value at which precipitation or phase separation is initiated (sol-gel transition in concentrated solutions). We found this proton transfer to occur due to a significant decrease of the pKa of chitosan upon heating combined with a pKa of GP that is not sensitive to temperature and the fact that these two pKa values (chitosan and GP) are closely matched. Experiments also showed that the temperature of the transition can be adjusted in a predictable manner by changing the chitosan/GP ratio and thereby tailored to cover the range 0-100°C. We also found that the temperature of the phase transition is accurately modelled by a macroscopic theory using acid-base equilibria and electroneutrality.