Control of the hydrophilic/hydrophobic interaction balance in the processing of chitosan physical hydrogels for tissue engineering

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INTRODUCTION: Chitosan, a natural glycosaminoglycan fully absent in mammals, exhibits the rare property of bioactivity. We developed a new family of biomaterials based on chitosan physical hydrogels for tissue repair and tissue engineering[1] (skin, cartilage, blood vessels, bone..). The polymer network of such hydrogels results only from intermolecular physical cross-links (hydrogen bonding, hydrophobic interactions, nanocrystallites) without any toxic chemical crosslinking agent. To obtain such hydrogels, a control of the hydrophilic /hydrophobic (H/H) interaction balance in chitosan solutions had to be achieved.

METHODS: The initial chitosan, produced from squid pens, had a low content of N-acetyl-D-glucosamine residues, *i.e.* a degree of acetylation DA=(1.5±0.1)%, and a high weight-average degree of polymerisation: DP_w = 3106±64. After a first step of purification, chitosans of different DAs were prepared from the reacetylation under soft conditions of the initial chitosan. Polyelectrolyte chitosan acetate solutions were obtained by stoechiometric protonation of the amine moieties.

RESULTS: The detailed study of the so-called "polyelectrolyte peak", revealed by Small Angle Synchrotron X-Ray Scattering diagrams for aqueous solutions of different concentrations allowed the identification of two organization regimes[2,3].

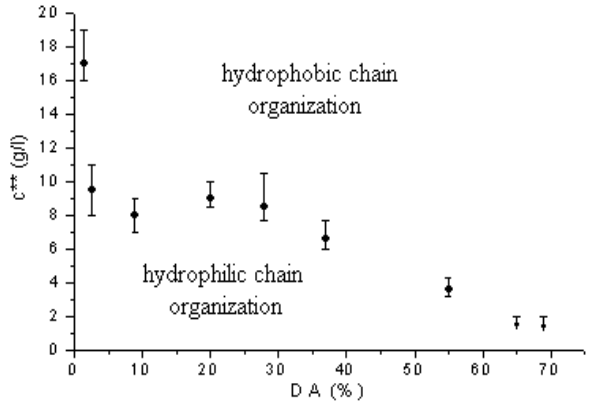

*Fig. 1: Law of variation of the crossover concentration c** as a function of DA in chitosan acetate solutions (ESRF D2AM)*

In the hydrophilic regime at low polymer concentration, the polymer exhibits the conformation of a highly charged polyelectrolyte. In the hydrophobic regime, interchain interactions are favored and then nano-aggregates are present. The crossover concentration (*c***) associated to this structural transition is then considered as a way to characterize the H/H interaction balance[3]. Gelation takes place at a critical value of the H/H interaction balance, either by solvent exchange or by neutralisation of the NH_3^+ moieties. Therefore, if nano-aggregates are present in the initial solution then, during the gelation stage, they collapse to form a nanostructured gel.

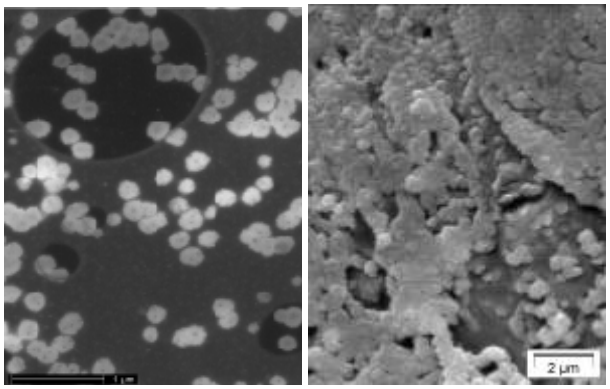

Fig. 2: Nano-domains of aggregated chains in chitosan solutions (left) and hydrogels (right).

DISCUSSION & CONCLUSIONS: The control of the H/H interaction balance in chitosan solutions and during gelation allowed the processing of physical hydrogels with a wide range of mechanical properties, offering promising results in the regeneration of tissue like skin or cartilage[3].

REFERENCES: [1]A. Montembault *et al.* (2006), Biochimie **88**: 551-64 [2]N. Boucard *et al.* (2007), *Biomacromolecules* **8**: 1209-17. [3]S. Popa-Nita *et al.* (2008) *To be published.*

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