

Semi-interpenetrated Hydrogels Composed of PVA and Hyaluronan or Chondroitin Sulphate: Chemico-Physical and Biological Characterization

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Physical hydrogels based on poly (vinyl alcohol) (PVA) were synthesized in the presence of natural polysaccharides, either hyaluronan or Chondroitin sulphate, in order to obtain versatile biomaterials with enhanced performances. The physical network is obtained by the freeze thawing technique, a simple method widely used for structuring PVA blends. The chemico-physical characterization of resulting materials consisted of swelling studies and mechanical analysis. Furthermore the release of embedded polysaccharides from the network was evaluated to improve understanding of the strength of hydrogen bonding between the different polymeric chains, and the effect of the sulphate groups on the interaction promoting network formation and stability. Biological response in terms of cytotoxicity, adhesion and cell vitality of murine fibroblast and human keratinocytes showed that the addition of glycosaminoglycans to a PVA polymer leads to a biomaterial with potential applications in biomedical fields. Hydrogels, highly hydrated polymer networks, are formed by chemical or physical crosslinking of the hydrophilic polymers. The characteristics of hydrogels, including sensitivity to the environment, tissue-like water content and elasticity, grant the potential for biomedical application.

Poly (vinyl alcohol) (PVA) is a semi-crystalline synthetic polymer with good mechanical properties, that proved biocompatible. These characteristics make this hydrogel particularly suitable for pharmaceutical, biomedical, and cosmetic applications. Its structure presents some features that make it an excellent candidate for biomaterial synthesis. In fact it is non-toxic, non-carcinogenic, easy to be processed and bioadhesive. PVA is produced by the polymerization of vinyl acetate to poly (vinyl acetate), followed by hydrolysis of PVAc to PVA. The molecular weight distribution, the degree of deacetylation and the initial concentration of PVA are the main parameters that affect hydrogel properties such as crystallizability, adhesion, mechanical strength, and diffusivity. Because of its high degree of swelling in water and in biological fluids and its rubbery and elastic nature, PVA is capable of simulating natural tissue and can be accepted into the body. PVA must be crosslinked in order to remain insoluble in solution, the crosslink may be accomplished by chemical agents (glutaraldehyde, acetaldehyde, formaldehyde), by the use of electron beam or γ -irradiation, under alkaline conditions and, by physical methods, such as repeated freeze-thawing cycles. The last method, avoiding the presence of crosslinking agents, overcomes toxicity issues. Moreover, such physical crosslinked materials exhibit higher mechanical strength than

PVA gels structured by common techniques due to the presence of crystalline regions. Different applications have been proposed for PVA hydrogels: they have been used as intervertebral disc nuclei and artificial articular cartilage; for drug delivery vehicles, alone as well as in combination with other polymers in order to obtain desirable release profiles (slow release). In particular Oka et al. examined aspects such as lubrication, load bearing, biocompatibility, and attachment of the material to the bone to look at the overall biomechanics of the material. Microsphere of PVA interpenetrated with poly (acrylic acid) were used to deliver a model anti-inflammatory drug, diclofenac sodium, to the intestine. PVA and methacrylate based interpenetrated polymer network (IPN) was synthesized from Darwis and co-worker, using formaldehyde as crosslinker, in order to obtain a hydrogel with physico-chemical properties resembling those of the artificial spinal disc. A typical physical crosslinking involved repetitive freezing and thawing of PVA aqueous solution. This technique promotes the formation of ordered microcrystalline domains as a result of enhanced intra- and inter-polymer interaction in the unfrozen regions of the PVA-water system. Many studies have been carried out on the effect of addition of other components to PVA. PVA has been associated also with natural polysaccharide such as GAGs. Hydrogels made of Chondroitin sulphate and poly (vinyl alcohol) systems were introduced to obtain new bioartificial materials that have excellent mechanical properties, biocompatibility and enhanced rheological properties. Furthermore Liu and collaborators, showed that PVA hydrogels are potential candidates for artificial blood vessels, when physically crosslinked with chitosan, gelatin and starch. In fact there was an improvement in cell adhesion without compromising the appropriate mechanical properties of PVA suitable for vascular system development. Composites based on PVA and PLGA by freeze-thawing technique were proposed as drug delivery systems of dexamethasone. The latter is considered a model pharmaceutical active principle for its inflammatory capability, because exhibits an approximately zero-order controlled release profile over a period of one month.

Concerning this topics, two well-known, glycosaminoglycan, Hyaluronic acid (HA) and Chondroitin sulphate (CS), both component of extracellular matrix, were employed for the synthesis of novel PVA based biomaterials. CS plays a key role in biomaterials field: it is a widely distributed glycosaminoglycan in the human body, structurally present in cartilage and other tissues such as eye, aorta, skeletal muscle,

lung and brain. In biomedical applications, CS has shown in vivo anti-inflammatory effect. It also regulates metabolism in vitro, in fact CS can stimulate the production of Chondroitin sulphate proteoglycans over the entire period of culture in monolayer cultured chondrocytes. It can be used for treating autoimmune and joint disease, for instance VISCOAT® (3% Chondroitin sulphate (aq) and 3% v/v sodium hyaluronate (aq), is used as a surgical aid in cataract extraction and lens implantation. CS is also a component of the dermal layer of the FDA-approved skin substitute for treating burns. However the most commonly exploited natural polysaccharide in scaffold assembly for tissue engineering and as component for implant materials is hyaluronic acid. HA, in fact, present a high capacity

for lubrication, is very hydrophilic and influences several cellular functions such as migration, adhesion and proliferation. It has a high molecular mass, up to millions of Daltons, and interesting viscoelastic properties influenced by its polymeric and polyelectrolyte characteristics. HA is ubiquitary in almost all biological fluids and tissues. In clinical practice, it is used as a diagnostic marker for many diseases including cancer, rheumatoid arthritis and liver pathologies, as well as for supplementation of impaired synovial fluid in arthritic patients by means of intra-articular injections. It is also used in certain ophthalmological and othological surgical techniques, in reconstruction of soft tissue, and in cosmaceutical regeneration protocols.