Development of new biomaterials based on chitosan as a vehicle for medical purpose

Background

According to the IUPAC Recommendation (2012), the term "biomaterial" means material exploited in contact with tissues, organisms, or microorganisms.

In recent years, a variety of metallic components, polymer or composite was used for medical application. Biomaterials in medical device perform, augment, or replace a natural function of whole or part of a living structure.

At present time biomaterials use for joint and cochlear replacements, as a bone plates, bone cement, artificial ligaments and tendons, dental implants for tooth fixation, blood vessel prostheses, heart valves, skin repair devices (artificial tissue), contact lenses, breast implants, drug delivery systems, vascular grafts, and stents etc.

Due to contact with living systems the main properties of biomaterials are biocompatibility, non-toxicity, non-allergenic and biodegradable (for in-graft only). Besides, the desirable properties of biomaterials can be the presence of the stimulating action on living systems, antibacterial and satisfactory mechanical properties.

A lot of natural and artificial materials use in biology and medicine as biomaterials. We would like to focus on chitosan as natural course for biomaterial synthesis. Chitosan is a linear polysaccharide obtained by the deacetylation of chitin, which is a structural biopolymer present in the exoskeletons of crustaceans and mollusks as well as the cell wall of fungi [Belgacem, M. N., 2008] and it is the second most abundant polysaccharide found in nature after cellulose. Chitosan has been found to be nontoxic, biodegradable, biofunctional, biocompatible in addition to having antimicrobial characteristics [Jayakumar, R., 2007; Jongrittiporn, S., 2001]. Previous studies have shown that chitin and chitosan-based dressings can accelerate repair of different tissues facilitate contraction of wounds and regulate secretion of the inflammatory mediators such as interleukin 8, prostaglandin E, interleukin 1 β, and others [Bottomley K, 1999]. During the last few decades, as a source of bioactive material, chitosan and chitooligosaccharides, which are degradation products of chitin or chitosan produced by enzymatic or acidic hydrolysis, were introduced into a variety of biomedicals including wound healing, bone and dura mater replacement, drug and gene delivery, tissue engineering and other [Agnihotri S., 2004; Kumar M., 2004].

Our previous results.

Our group has created three types of materials: films, porous chitosan-apatite and chitin-chitosan composites. We used chitosan films as a wound healing agent; chitosan-apatite for bone replacement and chitin-chitosan composite for duraplasty.

Low and medium molecular weight chitosans were used to prepare films (200 kDa, 500 kDa and 700 kDa, the degree of deacetylation 82 % and 80.5 %, respectively). The films were prepared by casting 2 % solution of low or average molecular weight chitosan in 1 % acetic acid on a substrate, followed by evaporation of the solvent at room temperature. After removing the solvent, the films were treated with 5 % NaOH solution for 3 min. Finally, the films were rinsed with distilled water and then treated with 1:10 glycerol-water mixture for half an hour. The excess of the plasticizer was removed by filter paper.

The chitosan-apatite composites were obtained by adding aqueous solutions of CaCl2 and NaH2PO4 (keeping Ca/P ratio equal to 1.67) into 0.2 % solution of chitosan in 1 % acetic acid. The necessary pH level was maintained by adding NaOH. Products of the synthesis were aged, rinsed thoroughly, and then dried. Water content and chitosan-to-apatite ratio were estimated by weighing the samples before and after annealing in air at the temperature of 130 ^{0}C and 900 ^{0}C for 45 min. To obtain porous materials, a lyophilization procedure was applied to wet (not dried completely) substances by using the vacuum chamber. The frozen samples were dried under 10^{-3} Pa overnight.

The chitin-chitosan film was made out of 3 % solution of chitosan (molar mass – 200 kDa, deacetylation 80–90 %). Firstly, we poured 10 ml of 3 % solution of chitosan in 1 % acetic acid on a round teflon support (with diameter – 8 cm, thickness of solution layer – 5 mm). Secondly, we evaporated the solvent at room temperature for 48–72 h. The obtained film was treated with NaOH for 2 h, washed frequently with distilled water and then it glycerinated for 30 min in order to enhance elasticity and softness. Chitin particles (1–2 mm) were added into the chitosan solution to enhance mechanical properties and decrease degradation rate of the film. Chitosan and chitin were 50/50 and 80/20 in the ratio. By stirring, the chitin particles were dispersed within the volume of viscose solution to form homogeneous solution.

We have studied physical and chemical properties of these materials and noticed satisfactory rate of biodegradation and water absorption for chitosan films and chitin-chitosan materials. Moreover, these materials have satisfactory mechanical properties similar to skin and dura mater. XRD patterns of the chitosan-apatite materials suggest the presence of nanocrystalline apatite with the average crystallite size of 20 nm. The similar size of crystallites is characteristic for natural bone bioapatite.

Our next step was to investigate the interaction between biomaterials and living tissues, so we conducted certain experiments on the animal models. The experiments proved material biocompatibility and non-toxicity as well as stimulatory effect on tissue regeneration (bones, skin and dura mater). However, the best way for biological investigation of new materials is cell culture experiment that can reduce the number of experimental animals and decrease the time of experiment. Apart from these, a cell culture experiment provides information that can improve even material quality.