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Chitosan and radiation chemistry

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ABSTRACT

Chitosan as a raw material with special properties has drawn attention of scientists working in the field of radiation processing and natural polymer products development, and also of specialists working in the field of radiation protection and oncologists. Especially the applications concern reduced molecular weight chitosan which still retain its chemical structure; such form of the compound is fostering biological, physical and chemical reactivity of the product. Chitosan degrades into fragments under γ-ray or electron beam irradiation. Antibacterial properties of the product are applied in manufacturing hydrogel for wound dressing and additional healing properties can be achieved by incorporating in the hydrogel matrix chitosan bonded silver clusters. Another possible application of chitosan is in reducing radiation damage to the radiation workers or radiation cured patients. In the case of radioisotopes oral or respiratory chitosan-based materials can be applied as chelators. Applications of chitosan in oncology are also reported.

1. Introduction

Chitin is one of the most abundant natural biopolymer derived from exoskeletons of crustaceans. It can be also obtained from cell walls of fungi which becomes a basis for biotechnological production of this material. Chitosan is a product derived from N-deacetylation of chitin in the presence of hot alkali. The degree of deacetylation and the degree of polymerization (DP), which in turn decides molecular weight of polymer, are two important parameters dictating the use of chitosans in many applications, in pharmaceutical, cosmetics, biomedical, biotechnological, agricultural, food, and non-food industries as well (water treatment, paper, and textile) (Mourya and Inamdar, 2008). Chitosan nanoparticles have shown promise as carriers of anticancer drugs, antitumor genes, and other novel therapeutic agents. In addition, chitosan nanoparticles by themselves appear toxic to various types of malignant cells. The paper reviews research on radiation-assisted development of materials based on chitosan and application of chitosan in radiation therapy and as an agent applied for radiological protection of the radiation workers and radiation-treated patients. This paper cover the well-known aspects of applications of radiation degraded chitosan and its derivatives and less known aspects of chitosan application of chitosan in radiooncology and radiological protection.

2. Chitosan modification by irradiation

Commercially available chitosan possesses high molecular weight and low solubility in most solvents and this fact limits its applications. The solubility of chitosan can be improved by diminishing molecular weight (Mao et al., 2004). Low molecular weight chitosan can be prepared by chemical, radiation or enzymatic degradation of high molecular weight polymer (Wasikiewicz et al., 2005). Radiation is one of the most popular tools for modification of polysaccharides. For decreasing the polymerization degree combined chemical-radiation methods can also be used. Chitosan oligomers were obtained through irradiation of chitosan dissolved in acetic acid (Choi et al., 2002). Popular method is also chemical degradation with H_2O_2 which even in small quantity reduces gradually molecular weight of chitosan (Tian et al., 2004)

2.1. Chitosan degradation by gamma ray irradiation

The gamma rays degradation of chitosan was investigated by Choi et al. (2002). Chitosans were irradiated in acetic acid solution with different doses (2–200 kGy) of Co-60 gamma rays to investigate the yields of chitosan oligomers. From the viewpoint of practical utilization of radiation techniques to produce depolymerized chitosan, irradiation with 100 kGy is enough in the use of γ-irradiation for degradation of chitosan (Zainol et al., 2009; Gryczka et al., 2009). Comparison of chitosan degradation and sodium alginate by gamma radiation (GD), sonochemical (USD) and ultraviolet (UVD) methods was performed by Wasikiewicz et al. (2005).Studies confirmed that the degradation

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proceeds by breakage of glycosidic bonds, but in the case of USD it is governed by mechanical forces, whereas GD and UVD involve radical scission mechanism. The crystallinity of chitosan decreases with degradation, and the crystalline state of water-soluble chitosan is entirely different from that of water-insoluble chitosan.(Kang et al., 2007).

2.2. Chitosan degradation by electron beam irradiation

Electron beam chitosan degradation was investigated by Chmielewski et al. (2007). Chitosan of average molecular weight M_w=710,000 was degraded using radiation and combined chemical-radiation methods. Chitosan powder was irradiated in plastic bags with electron beam within the dose range 20–250 kGy. The MW decreased remarkably with increase in the dose, up to 200 kGy. There was no significant change in molecular weight for higher doses. Using H_2O_2 in the first stage of degradation can decrease the required dose of radiation and the product with lower crystalline phase content is obtained.

2.3. Chitosan grafting

Chitosan has also been found to be a good candidate as a support material for gene delivery, cell culture and tissue engineering. For a breakthrough in utilization, graft copolymerization onto chitosan will be a key point, which will introduce the desired properties and enlarge the field of the potential applications of chitosan by choosing various types of side chains. such as grafting percentage and grafting efficiency, and the properties of grafted chitosan. The graft copolymerized chitosans find its potential applications in the field of drug delivery, tissue engineering, antibacterial, biomedical, metal adsorption and dye removal. Grafting of polystyrene onto chitin and chitosan using ^{60}Co γ-irradiation at room temperature was investigated. The effects of various conditions such as adsorbed dose, solvent and oxygen on grafting were investigated. It was found that the grafting yield increased with increase in the absorbed dose. Others have also reported the radiation grafting of chitosan with *N*,*N*-dimethylaminiethylmethacrylate (DMAEMA) (Yilmaz et al., 2007). Studies were reported on graft polymerization of butyl acrylate onto chitosan by using γ-irradiation (Yu et al., 2004). In this study, increasing grafting percentage was observed when the monomer concentration and total dose were increased or when the chitosan concentration and reaction temperature were increased. Review of the R&D works is presented by Jayakumara et al. (2005).

3. Medical and health care applications

Medicine, human health care and food safety are the most promising applications of chitosan. The foreseen or implemented products cover different fields of man health-related areas from food preservation, through cosmetics to drugs to radiopharmaceuticals manufacturing.

3.1. Health care products

Controlled drug release: Graft copolymerization of acrylic acid (AA) and acrylamide (AAm) onto chitosan (CS) was carried out using gamma irradiation. The ability of the prepared copolymer intended to be used as gastric antibiotic delivery system was estimated using amoxicillin trihydrate as a model drug. Release of amoxicillin trihydrate from these investigated hydrogels was studied. For non-ionized drugs, such as amoxicillin trihydrate, the electrostatic polymer/ polymer interactions take place between the cationic groups from CS and the anionic ones from PAA resulting in entrapping of the drug into the mesh space of the hydrogel. The non-ionized amoxicillin release was controlled by the swelling/eroding ratio (Taleb, 2008).

With the purpose of obtaining a biocompatible and microbiologically safe matrix that could be simultaneously used as wound dressing material and controlled drug release system, membranes with different thicknesses and different contents in chitosan and hydroxyethyl methacrylate (HEMA) have been prepared by γ-irradiation from a ^{60}Co source. The amount of released drug was shown to be dependent on membranes network crosslinking due to composition, radiation and membrane thickness (Casimiro et al., 2007).

Diet supplement: The influence of average molecular weight of chitosan in its fat-binding ability in vitro has been studied by using a biopharmaceutical model of the digestive tract. It was found that reduction in molecular weight leads to a significant increase in the amount of fat bound by 1 g of chitosan. Three physical methods of chitosan degradation, irradiation in dry state, irradiation in aqueous solution and sonication in aqueous solution, were tested. Radiation- or sonochemical treatment may be useful in improving fat-binding properties of chitosan as an active component of dietary food additives (Czechowska-Biskup et al., 2005).

Artificial models of organs: Synthetic membranes as dermal equivalent can be applied in in vitro studies for developing new transdermal drugs or cosmetics. These membranes could be composed to mimic the dermis and seed cultivated keratinocytes as epidermal layer on it. The endothelial cells in growth to promote neovascularization and fibroblasts in growth to promote the substitution of this scaffold by natural components of the dermis. As, they can mimic the scaffold function of dermis, the membranes with biological interaction could be used for in vivo studies as dermal equivalent. For this application, poly(vinyl alcohol) (PVA) membranes crosslinked by gamma radiation were swelled with chitosan solution. PVA do not interact with the organism when implanted and is intended to mimic the mechanical characteristics of the dermal scaffold. The chitosan as a biocompatible biosynthetic polysaccharide was incorporated into PVA membranes to improve the organism response. Degradation of chitosan by the organism occurs preferably by hydrolysis or enzymatic action, for example, by lysozyme. For this purpose the swelling kinetic of PVA membranes with chitosan solution was performed and their degradation in vitro was verified (Rodas et al., 2005).

Wound dressing: With the purpose of obtaining a biocompatible and microbiologically safe matrix that simultaneously could be used as wound dressing material and as a controlled drug release system, membranes with different thickness and different contents in chitosan and hydroxyethyl methacrylate (HEMA) have been prepared by γ irradiation from a ^{60}Co source. Antibiotic release experiments were performed before or after irradiation over amoxicillin loaded chitosan/pHEMA membranes in physiological saline solution. Results pointed out a fast amoxicillin release with similar release profile in all the studied membranes. The amount of released drug was shown to be dependent on membranes network crosslinking due composition, radiation and membrane thickness (Casimiro et al., 2007).

In other studies, two-layer hydrogels which consisted of polyurethane membrane and a mixture of polyvinyl alcohol (PVA)/poly-*N*-vinylpyrrolidone(PVP)/glycerin/chitosan were made for a wound dressing. Polyurethane was dissolved in solvent; the polyurethane solution was poured on the mould, and then dried to make a thin membrane. Hydrophilic polymer solutions were poured on the polyurethane membranes. They