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Commentary on the Development and Application of Chitosan in Immunochemistry

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Abstract

Chitosan has attracted much interest due to its special physical and chemical properties related to immunochemistry. The aim of this commentary is to appraise chitosan as an attractive functional polymer for medicine applications, which contributes to the development of chitosan for the immunochemistry. As reported, Chitosan has been used for immunochemistry purpose, such as functional food for enhancement of immune ability, immunostimulant and bio-remediating agent, nanoparticles antigen delivery systems, coating or gel vehicle for drug delivery, composites for intracellular delivery, wound healing medicine, enhance immune responses to virus, as well as other immunochemical materials. The further chemical modifications in chitosan will further assist the scientists for reaching new applications in immunochemistry based on chitosan.

Keywords: Chitosan; Immunochemistry; Antigen delivery systems; Drug delivery; Immune responses

Introduction

Recently, chitosan have been applied to various fields like pharmaceutical, biomedical, biomaterials, and biotechnological field [1]. Chitosan is composed of 1,4-β linked glucose amine and N-acetyl glucosamine units, and its properties depend on its molecular weight, degree of deacetylation, which in turn depend on the production process and the source [2]. Chitosan has received great attention in medical engineering, especially in immunochemistry [3]. Due to its positive charge, chitosan is a good drug delivery vehicle. Chitosan's biological properties, particularly its nontoxicity, biodegradability, anti-microbial activity, and biocompatibility, resulted in smoother scars and faster healing process [4]. Therefore, chitosan became a widely studied immunochemical material [5]. In this commentary, chitosan had been introduced to produce functional food for enhancement of immune ability, immunostimulant and bio-remediating agent, nanoparticles antigen delivery systems, coating or gel vehicle for drug delivery, composites for intracellular delivery, wound healing medicine, enhance immune responses to virus, as well as other immunochemical materials.

Immunostimulant and Bio-Remediating Agent

It was reported that chitosan was used as an immunostimulant to assess its antibacterial/aquatic bio-remediating effects [6]. Results achieved by feeding 1% chitosan as preventive/therapeutic regimes have revealed a remarkably enhanced several innate immunological parameters, increased resistance against *A. hydrophila* and strikingly improved water quality compared to the 0.5 and 2% chitosan containing diets. Conclusively, experimental results suggest the commercial usage of chitosan as an efficient immunostimulant and bio-remediating agent in aquaculture.

Antigen Delivery Systems

Nanoparticles delivery systems from antigen are a promising approach in the struggle against disease. It is reported that the obtainment and the characterization of antigen by Infrared spectroscopy as well as molecular modeling and computational chemistry studies of the chitosan-antigen interaction through theoretical models [7]. The Molecular Modeling studies presented the best conformation and binding site on the nanoparticle chitosan-antigen in models proposed. Interactions were observed between O-Acetyl and N-Acetyl groups the antigen and hydroxy, amino and methyl groups the Chitosan.

Coating or Gel Vehicle for Drug Delivery

The excellent properties offered by chitosan provide it a significant edge for nanoparticle formation over other nanocarrier materials [8]. Some strategies have been used to increase the adhesion and penetration of drugs through the vaginal mucosa. Two of them are the development of mucoadhesive semisolid formulations and the development of polymeric nanocarriers. It is hypothesized that the combined use of these two strategies results in a better performance of the formulation to retain imiquimod into the vaginal tissue. Thus, when considered the integrative indexes for the formulations, our results show that chitosan based nanocarrier presents the best performance for the treatment of HPV [9].

Composites for Intracellular Delivery

According to previous report, a novel CpG oligodeoxynucleotides delivery system was developed based on graphene oxide-chitosan nanocomposites. CpG oligodeoxynucleotides activate innate and adaptive immune responses, and show strong potential as immunotherapeutic agents against various diseases [10]. Graphene oxide-chitosan nanocomposites were prepared by self-assembly of both components via electrostatic interactions. Compared with graphene oxide, graphene oxide-chitosan nanocomposites possessed smaller size, positive surface charge and lower cytotoxicity. Graphene oxide-chitosan nanocomposites can serve as efficient nanocarriers for enhancing the delivery efficiency of CpG oligodeoxynucleotides.

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Enhancement of Immune Ability in Digestive System

Suthongsa reported the effects of dietary levels of chito-oligosaccharide on ideal digestibility of nutrients, and proved that the chito-oligosaccharide supplements may enhance intestinal function after weaning [11]. The effect of chito-oligosaccharide supplementation on growth performance, nutrient digestibility and small intestinal functions as an effective alternative to antibiotic addition in post-weaning diets was examined. These data suggest that chito-oligosaccharide might be a useful dietary supplement to promote nutrient absorption and digestibility efficiency.

Wound Healing Activity

In a comparative study by Marei, primary cell cultures of neonatal mice skin tissue were seeded onto locust chitosan based scaffold and shrimp chitosan based scaffold [12]. Wound healing activity progress of locust chitosan based scaffold and shrimp chitosan based scaffold was tested *in vivo* using histopathology, and it was revealed that locust chitosan based scaffold accelerated healing in contrast to shrimp chitosan based scaffold. The data demonstrated that locust chitosan based scaffold shows a high degree of biocompatibility *in vivo*. These results suggest that chitosan is a potential substitute for the development of low cost implantable materials to accelerate wound healing.

Enhance Immune Responses to Influenza Virus

Approaches based on combined use of delivery systems and adjuvants are being favored to maximize efficient delivery of antigens [13]. The efficacy of methylglycol chitosan was evaluated for improving systemic and mucosal immune responses to a monovalent detergent-split fluvirus vaccine. Sublingual vaccination of mice with split-flu vaccine formulated with methylglycol chitosan resulted in specific serum IgG and mucosal IgA titers that were significantly greater than titers from non-adjuvanted vaccination. The results demonstrate that vaccination utilizing methylglycol chitosan as adjuvants is a viable alternativeroute of vaccination for flu which can elicit systemic immune responses equivalent to or greater than IM vaccination with the added benefit of stimulating a robust specific mucosal immune response. Furthermore, the coating of modified liposomes with methylglycol chitosan produced the most effective flu-specific immune response. These results demonstrate efficient sublingual vaccine delivery utilizing a combination of a muco-adhesive and surface neutral liposomes to achieve a robust mucosal and systemic immune response [14]. A novel delivery system was described comprised of chitosan-functionalized gold nanoparticles and saponin-containing botanical adjuvant, which established the possible role of immunomodulatory adjuvants in particulate delivery systems for mucosal delivery of vaccines [15].

Tissue Engineering

A representing study explored the first ever fabrication of graphene oxide–chitosan–hyaluronic acid based bioactive composite scaffold containing an osteogenesis-inducing drug simvastatin for bone tissue engineering application [16]. Porosity, density, swelling, degradation and biomineralization studies favored the simvastatin loaded graphene oxide–chitosan–hyaluronic acid scaffold in comparison to the conventional chitosan based scaffolds. The *in vitro* results showed that the drug simvastatin also offers a significant influence on osteogenesis and biomineralization and it possess excellent biocompatibility to be used as a bone tissue engineering scaffold, which is able to persuade osteogenesis and mineralization.

The current reports on the properties of chitosan attached great importance for the immunochemistry related applications. Further understanding and validation of the observed immune modulatory effects of chitosan to realize the full potential of chitosan for a broad range of treatments is essential and will influence the science of immunology enormously.

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