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Subacute Oral Toxicity of Chitosan Oligosaccharides on Sprague Dawley Rats

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Introduction

Chitosan is derived from chitin by deacetylation in the presence of alkali, which is a copolymer consisting of β-(1→4)-2-acetamido-D-glucose and β-(1→4)-2-amino-D-glucose units with the latter usually exceeding 80% (Arvanitoyannis et al., 1998). Chitosan has been developed as new physiological material since it possesses antibacterial activity, hypocholesterolemic activity and antihypertensive action. However, even though chitosan has very strong functional properties in many areas, its high molecular weight and high viscosity may restrict the use in vivo. In addition, there is little doubt that such properties will influence absorption in the human intestine. Recently, studies on chitosan have attracted interest for converted chitosan to oligosaccharide, because the oligosaccharide possesses not only water-soluble property but also versatile functional properties such as antitumor activity, immuno-enhancing effects, enhancement of protective effects against infection with some pathogens in mice, antifungal activity, calcium absorption accelerating effect (Jeon et al., 1999) and antimicrobial activity. There is, however, little information on the toxicity of chitosan oligosaccharide.

In the present study, we investigated subacute toxicity of chitosan oligosaccharide when orally administered to Sprague Dawley rats.

Materials and Methods

Animals: Thirty-six Sprague-Dawley rats (SPF grade) of male (161.5±12.8 g) and female (148.6±7.7 g), 4 weeks old, were purchased, and acclimated to laboratory conditions for one week prior to exposure.

Test substance: Chitosan oligosaccharide (below MW 1,000 Da) was donated by R&D Center of Kitto Life Co. (Korea), and stored at 4℃ until use.
Experiments: Nine rats per group of male and female were treated at doses of 0 (control), 500 (group L), 1,000 (group M) and 2,000 mg/kg/day (group H) for 4 weeks in a stainless-steel chambers. The behavior and external appearance of the rats were observed daily. Body weight was measured once a week, and the quantity of food left by individual rats was recorded on a daily basis throughout the experimental period. In addition, the following estimations were performed ; urinalysis, hematological and biochemical examinations, necropsy and histopathological examination.

Results

Animal observations: No significant differences in behavior or external appearance were observed between control and exposed rats.

Body weight and food consumption: There were no significant differences in body weight and food consumption between control and exposed rats.

Urinalysis: All urine of rats had normal color, and glucose, ketone body, urobilinogen and bililubin in the urine of control and exposed rats were shown to be normal or negative.

Hematology: The hematological values in the all tested rats were not significantly different between control and exposed rats.

Blood biochemistry: There were no generalized changes in rat parameters, although the decrease of alanine aminotransferase was observed in the rats of the middle dose group.

Organ weights: There were no significant differences in organ weights between control and exposed rats.

Histopathology: No exposure-related changes were observed in the lungs and kidneys, and there were no differences the testes of control and exposed rats.

References

Arvanitoyannis I.S., A. Nakayama and S. Aiba. 1998. Chitosan and gelatin edible films. Carbohydr. Polym. 37: 371-382.
Jeon Y.J., G.H. Kim, P.J. Park and S.K. Kim. 1999. Calcium absorption accelerating effect of chitosan oligosaccharides prepared by ultrafiltration membrane enzymatic reactor. J. Korean Fish. Soc. 32: 247-251.