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Antitumour Activity of Chitosan Hydrogen Selenites

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Abstract: Chitosans reacted with selenious acid to prepare chitosan hydrogen selenites, which were found to be growth-inhibitory against sarcoma 180 solid tumor. The results indicated that the activity also depended on the molecular weight of chitosan supports.

Keywords: Chitosan hydrogen selenites, antitumour activity.

Selenium is a biologically important element and essential for life[1]. Selenium deficiency causes severe degenerative disease, such as Kesan cardiomyopathy, and has been implicated in increasing the incidence of human cancer and some chronic ailment as well as ageing. Administration of selenium compounds such as sodium selenite protects animals against carcinogens and markedly reduces the incidence of various neoplasms in human[2]. Chitosan is one of the most abundant glycans in nature and its cationic charge is unique. The nontoxic, biodegradable and biocompatible aminopolymer and its degradation products of chitosan have specific biological activities[3] such as antibacterial action, antitumor activity, immuno-enhancing effects. Here we report the preparation of chitosan hydrogen selenites with different molecular weights, and their antitumor activities.

Chitosans with low molecular weight were prepared by hydrolysis of chitosan (degree of deacetylation 86%) with cellulase[4]. The reaction mixture was separated, using ultrafiltration membranes of 10 KDa, 3 KDa and 1 KDa, respectively. The filtrates were neutralized to pH 9 and precipitated by adding ethanol. The residues (CS1, CS2 and CS3) were finally collected by filtration, washed with ethanol and dried. The molecular weights (*Mw* and *Mn*) were determined by gel permeation chromatography (TOSOH TSK-G 3000 PW, TOSOH pullulan standards). The resulting chitosans reacted with aqueous solution of SeO_2 to prepare chitosan hydrogen selenites CS1-Se, CS2-Se and CS3-Se, respectively. The structure of chitosan hydrogen selenite was confirmed by FT-IR[5], UV and ^{13}C-NMR spectra, which were compared with that of the corresponding chitosan and its hydrochloride salt.

Acute toxicity of chitosan hydrogen selenites by oral administration (LD_{50} > 15.0 mg selenium/kg) was lower than sodium selenite (LD_{50} 6.0 mg selenium/kg).

Antitumor effects on sarcoma 180 were observed in normal and young female

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Kunming mice weighing 18 ± 2 g. Ten mice were used in each group. Sarcoma 180 ascites cells (1×10^7 cells/mice) were inoculated subcutaneously into the groin of mice. After 24 h of the tumor implantation, the tested samples dissolved in saline were provided once 50 mg/kg daily by oral administration (p.o) or intraperitoneal injection (i.p) for 10 days. After that, the animals were sacrificed and tumors were excised and weighted. The tumor growth inhibition ratio was calculated by using the formula: Inhibition (%) = [(C-T)/C] × 100, where C is the average weight of the control group and T is the weight of the tested sample groups. The Student′s *t*-test for statistical analysis of data was used.

Table 1 shows the growth-inhibitory effect of samples on sarcoma 180 in mice. It indicates that chitosan hydrogen selenite (CS2-Se) significantly inhibited the growth of the tumor. Its tumor growth-inhibition ratio is higher than corresponding chitosan (CS2) and acetate (CS2-Ac). The activity of chitosan hydrogen selenites (1% selenium content) is correlated with the molecular weight of chitosan supports, and a maximum of inhibition was found around *Mw* of 3300.

Table 1 Antitumor activities of chitosan and its selenites

Sample	Mw	*Mw/Mn*	Inhibition (%)	
			(p. o)	(i. p)
CS2	3300	1.79	29.1	41.0*
CS2-Ac	3300	1.79	18.5	34.2*
CS1-Se	17000	2.35	33.2*	34.4*
CS2-Se	3300	1.79	41.5**	65.3**
CS3-Se	1078	1.40	22.4	48.7**

*P < 0.05; **P < 0.005

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