

Yuniardini Septorini Wimardani¹
Dewi Fatma Suniarti²
Hans-Joachim Freisleben¹
Septelia Inawati Wanandi³
Masa-Aki Ikeda⁴

¹Graduate Study Program in
Biomedical Science, Faculty of
Medicine, Universitas Indonesia,
Indonesia

²Department of Oral Biology, Faculty
of Dentistry, Universitas Indonesia,
Indonesia

³Department of Biochemistry and
Molecular Biology, Faculty of
Medicine, Universitas Indonesia,
Indonesia

⁴Section of Molecular Embryology,
Graduate School of Medical and Dental
Sciences, Tokyo Medical and Dental
University, Japan

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Corresponding author:

Yuniardini Septorini Wimardhani, Graduate Study Program in Biomedical Science, Faculty of Medicine, Universitas Indonesia
Jl. Salemba Raya No. 6 Jakarta 10430 Indonesia, email: yuniardini@ui.ac.id

Cytotoxic effects of chitosan against oral cancer cell lines is molecular-weight-dependent and cell-type-specific

Abstract

The elucidation of the anticancer mechanisms of many anticancer agents from natural sources with minimal toxicity to normal cells are still being performed. Chitosan is a polycation polysaccharide, which is an N-deacetylated derivative of chitin. It is naturally and abundantly present in crab and shrimp shells, and has been widely used as a multipurpose biomaterial. Antitumor activity is one of many attractive biological properties of chitosan. Report of its antitumor activities on oral squamous cell carcinoma (SCC) cells is scarce despite many *in vitro* and *in vivo* reports on other cancer types. Physical characteristics of chitosan have been reported to influence its antitumor activity, the effects of which vary depending on cell types. Therefore, this study examined whether cytotoxic effects and doses of chitosan are affected by its molecular weight (MW) in oral SCC and non-cancer cell line. Cytotoxic effects of two types of chitosan with different MWs (average 50 - 190 kDa and 310 - >375 kDa) were tested on three oral SCC (HSC-3, HSC-4 and Ca9-22) cell lines and a keratinocyte cell line (HaCaT) using MTT assay. However, chitosan had opposite effects on HaCaT cells at certain concentrations. Both types of chitosan induced proliferation of HaCaT cells at concentrations that showed cytotoxic effects on HSC-3 and Ca9-22 cells (200 - 300 µg/ml). In particular, HaCaT cells treated with the high MW chitosan exhibited 2-fold stronger proliferative activity compared to untreated cells (300 µg/ml, $p < 0.01$). In contrast, neither type of chitosan induced proliferation of oral SCC cell lines. HSC-3 and Ca9-22 cells were more sensitive to both types of chitosan, which inhibited cell proliferation in a dose-dependent manner, while HSC-4 cells were resistant to the both types. The low MW chitosan exerted stronger cytotoxic effects on all cancer cells than the high MW one, indicating that the cytotoxic activity of chitosan negatively correlates with its MW. Although cytotoxic properties of chitosan against oral SCC cells are varied among the cell lines tested, chitosan exerts selective toxicity to oral SCC cells and even the opposite effects on non-cancer keratinocytes.

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