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The Enhancing Effect of γ-Cyclodextrin Inclusion on γ-Tocotrienol-dependent Negative Growth Control of Mesothelioma Cells in a Xenograft Model

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ABSTRACT

Background: Malignant mesothelioma is an aggressive cancer with no effective treatment options. Of phytochemicals, tocotrienol (T3), a member of vitamin E, is one of the most potent anti-mesothelioma agents, but the effectiveness *in vivo* is quite limited, due to its low bioavailability. In this study, we investigated if the oral treatment of γ-T3 inclusion with γ-cyclodextrin (CD) could improve the bioavailability and anticancer activity of the T3.

Findings: Using nude mice bearing MSTO-211H cells (a human malignant mesothelioma cell line), the effect of γ-T3 inclusion with γ-CD on γ-T3 level in tumor tissues, tumor growth, and its related mRNA levels were examined. The difference of tumor growth between the two groups had no statistical significance, but the latter showed a lower tendency compared with the former. In linked with this observation, the level of vascular endothelial growth factor mRNA required for *in vivo* tumor growth in γ-T3 inclusion with γ-CD group was lower than that in γ-T3 group, on the contrary, the level of γ-T3 level showed an opposite tendency.

Conclusion: Our study demonstrated that the bioavailability of γ-T3 was improved by an oral administration of a novel γ-T3 inclusion complex with CD. Furthermore, the improvement of

the bioavailability contributed to the increase of anticancer activity of γ-T3 *in vivo*.

Key words: Anti-cancer agent, bioavailability, cyclodextrin, mesothelioma, tocotrienol.