

Inhibitory effect of a formulated extract from multiple citrus peels on LPS-induced inflammation in RAW 246.7 macrophages

Tadahiro Etoh¹, Yong Pil Kim¹, Masahiko Hayashi¹, Michiko Suzawa², Shiming Li³, Chi-Tang Ho³, and Kanki Komiyama^{4*}

¹Faculty of Pharmacy, Iwaki Meisei University, Iino, Chuo-dai, Iwaki, Fukushima 970-8551, Japan; ²Miyauchi Citrus Research Center, Shigoka-Machi, Takasaki, Gunma, 370-0845, Japan

³Department of Food Science, Rutgers University, New Brunswick, NJ 08901, USA;

⁴Kitasato Research Center for Environmental Sciences, Kitasato, Sagamihara, Kanagawa, 252-0329, Japan

Corresponding author: Kanki Komiyama, Kitasato Research Center for Environmental Sciences, Kitasato, Sagamihara, Kanagawa, 252-0329, Japan

Submission date: April 28, 2013; Acceptance date: June 20, 2013; Publication date: June 26, 2013

ABSTRACT:

Background: Formulated Citrus Peel Extract (GL) made from the peels of six citrus fruits available in Japan, namely *navel oranges*, *citrus hassaku*, *citrus limon*, *citrus natsudaidai*, *citrus miyauchi* and *satsuma*, was initially developed as a cosmetic product to protect skin from UV irradiation. Anecdotal evidences of anti-cancer property of GL have been reported by consumers based on the cases such as topical application for melanoma, and oral ingestion for prostate, lung and liver cancers.

Those anecdotal reports stimulated us to investigate anti-tumorigenesis activity of GL. In the previous study, we reported that the topical application of GL inhibited DMBA/TPA-induced skin tumor formation by decreasing inflammatory gene parameters.

Objective: In this study, we mainly investigated the effect of GL on translocation of NF- κ B together with production of nitric-oxide and TNF- α induced by LPS in RAW 264.7 cells.

Results: This investigation showed that GL decreased the release of TNF- α and nitric oxide from macrophage RAW264.7 cells stimulated by LPS in a dose-dependent manner. In addition, GL suppressed the expression of iNOS and nuclear translocation of NF- κ B in RAW264.7 cells, inhibited the degradation of I κ B- α , and scavenged hydroxyl radicals (DMPO/OH adduct) *in vitro*.

Conclusions: Our findings suggest that GL suppresses the inflammation *in vitro*, and exerts chemopreventive activity through the inhibition of production of TNF- α and iNOS proteins due to the inhibition of nuclear translocation of NF- κ B and oxidative stress. GL appears to be a novel functional natural product capable of preventing inflammation and inflammation-associated tumorigenesis.

Keywords: GL, Citrus peel extract, anti-inflammation, Nitric oxide, iNOS, NF- κ B, TNF- α