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

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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-κB 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-κB in RAW264.7 cells, inhibited the degradation of IκB-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-κB 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-kB, TNF-α