induces the aggregation of lipid raft components coupled with NADPH oxidase enzymes, in which rVvhA increased the interaction of NADPH oxidase 2(NOX2, gp91phox) with a cytosolic protein NCF1 (p47phox) to facilitate the production of reactive oxygen species (ROS). rVvhA uniquely stimulated aconventional PKC isoform PKCa and induced the phosphorylation of both ERK and JNK, which are responsible for the activation of transcription factor NF-kB. rVvhA induced an NF-kB-dependent imbalance of the Bcl-2/Bax ratio, the release of mitochondrial cytochrome c, and caspase-3/-9 activation during its promotion of apoptotic cell death. In addition, rVvhA has the ability to inhibit the expression of cell cycle-related proteins, such as CDK2, CDK4, cyclin D1, and cyclin E.

Conclusions: Our results suggest that rVvhA induces NF-κB dependent mitochondrial cell death via the production of lipid raft-dependent ROS. Thus highlighting the signaling pathways involved in the rVvhA-stimulated apoptosis pathway may provide potential targets for strategic modulations during *V. vulnificus* infections. In conclusion, rVvhA acting on lipid rafts induces NOX2-mediated ROS production, with this being necessary for PKC/ERK/JNK activation in intestinal epithelial cells.

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Lycopene Inhibits Nicotine-induced Embryo Anomalies Via Antioxidative, Anti-apoptotic, and Anti-inflammatory Activities

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Introduction: Maternal nicotine exposure during pregnancy causes various diseases. Lycopene, a major carotenoid in tomatoes, red fruits, and vegetables, is associated with decreased risk of chronic diseases via dietary intakes[1-3]. In this study, it was to investigate whether lycopene has a beneficial effect on nicotine-induced malformation in mouse embryos using a whole embryo culture system.

Materials and Methods: Mouse embryos (embryonic day 8.5) were exposed to nicotine (1mM) in the presence or absence of lycopene (1×10^{-6} or 1×10^{-5} μM) for 48 hours, and then morphological scoring, real-time PCR and western blotting for antioxidant enzymes, apoptotic, and anti-inflammatory genes, lipid peroxidation, and SOD activity were performed.

Results: Nicotine induced significant decreases in embryonic growth (yolk sac diameter, crown-rump length, head length, and somite number) and developmental factors (yolk sac circulatory, allantois, heart, hind-, mid-, and fore brains, otic, optic, and olfactory systems, branchial bars, maxillary and mandibular processes, and forelimb and hind limb) compared with those of control group ($P < 0.05$). However, morphological scores were significantly recovered in embryos co-treated with nicotine (1mM) in the presence of lycopene ($P < 0.05$). Moreover, nicotine reduced the SOD activity and the mRNA levels of SOD1, GPx1, and bcl-x_L, but increased the lipid peroxidation level and the mRNA levels of bax, caspase3, TNF-α, and NF-κB. However, co-treatment with lycopene improved all of the parameters related to antioxidant, anti-apoptotic effects as compared to nicotine-treated embryos.

Conclusions: These results suggest that lycopene inhibits nicotine-induced embryo damage via the antioxidative, anti-apoptotic and anti-inflammatory activities, indicating that lycopene might be a potent agent for new medicine designed to protect embryo from smoking-induced risks in pregnancy.

References

[1] Herber *et al.*, 2002, Exp Biol Med; 227:920-3.
[2] Nkondjock *et al.*, 2005, J Nutr; 135:592-7.
[3] Comhair *et al.*, 2002, Am J Physiol ; 283:L246-L255.

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4-O-methylhonokiol Attenuates Oxidative Stress that Triggers Teratogenesis of Embryos in Cultured Mouse Embryos Exposed to Nicotine

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Introduction: In order to search an effective preventive agent against embryotoxicity induced by harmful nicotine, the potential effects of 4-O-methylhonokiol, an active compound isolated from *Magnolia officinalis,* were investigated in mouse embryos maintained for 48 h in a whole embryo culture system[1-4].

Materials and Methods: The mouse embryos were cultured on embryonic day 8.5 with nicotine 1mM and/ or 4-O-methylhonokiol (1×10^{-4} or 1×10^{-3} μM). After 48 hours, the embryos were taken out for morphological parameters, oxidative damage, antioxidant status, and the expression of nicotine-responsive genes by morphological scoring, lipid peroxidation measurement, quantitative real-time PCR and superoxide dismutase(SOD) activity, respectively.

Results: Embryos exposed to 1 mM nicotine developed not only severe morphological anomalies, increased expressions of TNF-α, IL-1β, and caspase 3 mRNAs; and elevated levels of lipid peroxidation, but also decreased levels of SOD, cytosolic glutathione peroxidase, phospholipid hydroperoxide, hypoxia inducible factor 1α, and Bcl-x_L mRNAs, and reduced SOD activity. However, these parameters were significantly improved when embryos exposed to the nicotine were concurrently treated with 4-O-methylhonokiol (1×10^{-4} or