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Chemoprotective effects of the formulated extract DA-9601 of *Artemisia asiatica* against experimentally induced oxidative and inflammatory tissue damage

Jeong-Sang Lee[1], Tae-Young Oh[2], Byung-Ok Ahn[2], Hyun Cho[2], Ki-Baik Hahm[3], and Young-Joon Surh[1]

[1]College of Pharmacy, Seoul National University, Seoul, [2]Dong-A Pharmaceutical Research Institute, Yong-In, and [3]Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

Gastroesophageal reflux disease (GERD) is multifactorial in etiology and is characterized by movement of acid and other noxious substances from the stomach into the esophagus. The most severe histologic consequence of chronic gastroesophgeal reflux is Barrett's esophagus, which has been considered as a premalignant condition often leading to the formation of adenocarcinoma of esophagus. Oxidative DNA damage appears to contribute to oncogenesis related to GERD. In order to clarify the role of oxidative stress in pathogenesis of GERD and Barrett's esophagus, we developed an animal model and investigated the possible protective effects of selected antioxidative substances.

For this purpose, Sprague-Dawley rats were subjected to duodenal ligation using a small-lumen ring to provoke acute GERD. Two days after the operation, the malondialdehyde formation in GERD esophagus was significantly increased, which correlated well with histologic severity. Increased levels of inducuble nitric oxide synthase and cyclooxygenase-2 were also observed. Nuclear extracts from the esophagus of GERD rats exhibited dramatic activation of the nuclear transcription factor, NF-κB, which was subsequently associated with increased IκBα degradation. Oral administration of the anti-secretory drug ranitidine (10mg per kg) or of DA-9601 (100mg per kg) derived from the medicinal plant *Artemisia asiatica* markedly attenuated not only histologic abnormalities and formation of reactive oxygen species but also activation of NF-κB in GERD animals. DA-9601 also restored the tissue glutathione levels which were lowered in GERD animals.

In the experimentally induced chronic GERD, DA-9601 administration also preserved the proliferating cell nuclear antigen (PCNA) expression at a normal level and prevented the metaplasia development compared with the chronic GERD.