## 半夏瀉心湯の抗炎症作用の解明から口腔粘膜炎への未病対策を考察する

## 王 宝禮\*

要旨:7種類の生薬(半夏、黄芩、乾姜、人参、甘草、大棗、黄連)を含有する半夏瀉心湯の抗炎症作用の細胞生物学的解明に着手した。半夏瀉心湯は歯周病原因菌  $Porphyromonas\ gingivalis$  由来の lipopolysaccharides (P.g.LPS) 誘導性の extracellular signal-regulated kinase (ERK) リン酸化を抑制した。次に cytosolic phospholipase  $A_2$  (cPL $A_2$ ) および LPS 誘導性 cyclooxygenase-2 (COX-2) 発現の抑制及び COX-2 活性の阻害、さらに cPL $A_2$ のリン酸化とその活性化の阻害によって、prostaglandin  $E_2$  (PG $E_2$ ) 産生を減少させ、炎症性サイトカインである interleukin (IL)-6、8 の産生も抑制した。これらの結果は アラキドン酸カスケード中での抗炎症作用の半夏瀉心湯の作用点を示唆している。その後、生薬における分子レベルで抗炎症作用、フリーラジカル消去作用、抗菌作用、鎮痛作用、組織修復促進作用などが報告され、口内炎改善メカニズムが解明され続けている。これらの薬理作用から、がん薬物療法や放射線療法による頭頚部がん治療の副反応として重要な問題である口腔粘膜炎治療に発展してきた。現在のがん診療における半夏瀉心湯の位置づけと抗炎症作用、未病改善作用を考察した。

索引用語:半夏瀉心湯, 抗炎症作用, 口腔粘膜炎, がん支持療法, 未病

## PAIN AND KAMPO MEDICINE Vol.33 (2024)

Exploring presymptomatic disease strategies against oral mucositis through the Elucidation of anti-inflammatory effects of hangeshashinto  ${\rm Hourei\ OH}^*$ 

**Abstract**: We have initiated a cellular biological elucidation of the anti-inflammatory effects of hangeshasinto, which contains seven crude drugs (pinellia tuber, scutellaria root, processed ginger, ginseng, glycyrrhiza, jujube, and coptis rhizome). Hangeshashinto inhibited the phosphorylation of extracellular signal-regulated kinase (ERK) induced by lipopolysaccharides (LPS) derived from the periodontal pathogen Porphyromonas gingivalis (P.g.LPS). Hangeshashinto also inhibited the expression of cytosolic phospholipase A<sub>2</sub> (cPLA<sub>2</sub>) and LPS-induced cyclooxygenase-2 (COX-2), along with the activity of COX-2. Futhermore, it inhibited the phosphorylation and activation of cPLA2, leading to reduced production of prostaglandin E2 (PGE2) and suppression of the production of inflammatory cytokines Interleukin (IL)-6 and IL-8. These findings indicate a site of action for the anti-inflammatory action of hangeshashinto within the arachidonic acid cascade. Subsequently, the effects of crude drugs, such as anti-inflammatory action, free radical scavenging action, antibacterial action, analgesic action, and tissue repair promoting action, have been reported at the molecular level, and the mechanism for improving stomatitis is continuously being elucidated. Based on these pharmacological actions, hangeshasinto has been increasingly utilized as a treatment for oral mucositis, a significant complication of chemotherapy and radiotherapy in anticancer therapy and head and neck cancer radiation therapy. In this paper, we investigated the role of hangeshashinto and its anti-inflammatory effects in current cancer treatment, and discussed its potential for the improvement of presymptomatic diseases.

**Key words**: hangeshashinto, anti-inflammatory action, oral mucositis, supportive care for toxicities arising from cancer treatment, presymptomatic disease

<sup>\*</sup>The Center of Innovation in Dental Education, Osaka Dental University Hourei OH, The Center of Innovation in Dental Education, Osaka Dental University. 8-1 Kuzuha Hanazono-cho, Hirakata-shi, Osaka 573-1121, Japan