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Recent Studies and Progression of Yin Chen Hao (茵陳蒿 Yīn Chén Hāo), a Long-term Used Traditional Chinese Medicine

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ABSTRACT

Yin Chen Hao (*Artemisia capillaris* Thunb; 茵陳蒿 Yīn Chén Hāo) is a traditional Chinese medicine for treating hepatic disorders. This review provides recent pharmacological studies of Yin Chen Hao as well as some chemical constituents isolated from Yin Chen.

Key words: *Artemisia capillaris*, Scoparone, Yin Chen

Yin Chen Hao (*Artemisia capillaris* Thunb, 茵陳蒿, Yīn Chén Hāo), also known as Yin Chen, Capillary or Oriental Wormwood belonging to Asteracea family, is a traditional Chinese medicine. Yin Chen Hao was first documented in The Divine Husbandman's Herbal Foundation Canon (神農本草經 shén nóng běn cǎo jīng) for treating hepatic diseases. According to Chinese Pharmacopoeia (中華藥典 Zhōng Huá Yào Diǎn), Yin Chen can be referred to two kinds of herbs: one is *Artemisia scoparia* Waldst et Kit and the other is *Artemisia Capillaris*. Yin Chen must be harvested for its aerial part in spring to exhibit pharmacologic effects. An old saying, "Yin Chen can be used as Yin Chen for treating diseases in February, but can only be used as lumber for burning in May (二月茵陳三月蒿,五月茵陳當柴燒)", indicates huge difference in bioactive component contents of Yin Chen Hao in different seasons.

Hepatic disorders

Yin Chen Hao traditionally was used to treat liver and choleretic disorders. Recently, Yin Chen was found to exhibit hepatoprotective effect by ameliorating murine concanavalin A (con A)-induced hepatitis via suppression of interferon (IFN)-g and interleukin (IL)-12 production.[1] In the following study, orally administrated Artemisiae Capillaris (AC) group (500, 1000, or 2000 mg/10 ml/kg) can decrease serum transaminases activities and IFN-g concentration *in vivo*.[1] Capillarisin, a flavonoid constituent of Yin Chen, is contained in the fraction and has potent hepatoprotective activity *in vivo*. *In vitro* IFN-g production was significantly suppressed by capillarisin in con A-stimulated splenocyte culture and nitrite release from IFN-g-stimulated macrophages was also decreased. Another study also showed that Yin Chen may prevent the EtOH-induced cytotoxicity on human hepatoma cell line and Hep G2 cell.[2] Aqueous extract of AC (0.5–5 μg/mL) inhibited the secretion of EtOH-induced interluekin-1α (IL-1α) and tumor necrosis factor-α (TNF-α). AC also inhibited the EtOH-, IL-1α, and TNF-α-induced cytotoxicities. Furthermore, AC was found to inhibit the EtOH-induced apoptosis of Hep G2 cells. Water extract of Artemisia capillaries (ACWE) was capable of ameliorating the 2,2¢-azobis(2-amidinopropane) dihydrochloride (AAPH)-induced hepatic injury by catechin antioxidant activ-

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ity *in vivo*.[3] ACWE (7.5 g/kg) was orally administered for 7 days before AAPH treatment (60 mg/kg). The treated group significantly reduced hepatic damage by lowering the levels of enzyme markers, such as glutamic oxaloacetic transaminase and glutamic pyruvic transaminase and attenuating the accumulation of thiobarbituric acid-reactive substances (TBARS) in both plasma and liver tissues compared with AAPH alone. High-performance liquid chromatography results showed that catechin composition in the ACWE are 28% (–)-epigallocatechin gallate, 49% (–)-epigallocatechin, and 23% other catechins. Another study also indicated ethyl acetate fraction of AC (100 mg/ml) protected Chinese hamster lung fibroblasts (V79) cells against oxidative stress and increased cell viability by enhancing the antioxidative activity.[4] The ethyl acetate fraction of AC scavenged intracellular reactive oxygen species (ROS) and increased the activities of cellular antioxidant enzymes like superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), and glutathione (GSH) content, resulting in preventing lipid peroxidation by inhibiting TBARS formation. Interestingly, the antihepatofibrotic effects of water extract of AC and Artemisia iwayomogi (AI), both long-term been used for hepatotherapeutic medicine in Korea, were comparatively analyzed using a carbon tetrachloride (CCl4)-induced liver fibrosis rat model.[5] The results showed that AI exerts greater hepatoprotective and antifibrotic effects as compared with AC via enhancing antioxidant capacity and down-regulating fibrogentic cytokines. Besides, scientific evidence was found to account for Yin Chen's effect on treating jaundice.[6,7] The constitutive androstane receptor (CAR, NR1I3) was identified as a key regulator of bilirubin clearance in the liver. Treatment of wild-type and humanized CAR transgenic mice with AC for 3 days accelerates the clearance of intravenously infused bilirubin, but this effect is absent in CAR knockout animals. Expression of bilirubin glucuronyl transferase and other components of the bilirubin metabolism pathway was induced by Yin Chen treatment of WT mice or mice expressing only human CAR, but not CAR knockout animals.

Diabetes

Besides hepatic disorders, AC also showed effect on diabetic studies. ß-Cell destruction by cytokines is important event in insulin-dependent diabetes mellitus.[8] Nitric oxide synthase (iNOS) expression and nitric oxide (NO) production, stimulated by cytokines, lead to insulin insufficiency. ACWE (100–500 mg/ml) completely and dose-dependently protected IL-1ß and IFN-γ-mediated cytotoxicity on RINm5F (RIN) rat insulinoma cells.[9] Reduction of IL-1ß and IFN-γ-induced NO production correlated well with reduced levels of the iNOS mRNA and protein, which molecular mechanism involved the inhibition of nuclear factor kappa B (NF-κB) activation.[9] Another study also reported that AC demonstrated the highest advanced glycation endproducts (AGE) inhibitory activity among several indigenous Artemisia species.[10] Glycation can lead to the onset of diabetic complications due to chronic hyperglycemia. An acylated flavonoid glycoside, along with 11 known flavonoids, 6 coumarins, and 2 phenolic derivatives were obtained from Yin Chen and evaluated their AGE inhibitory activity to establish structure-activity relationship (SAR). Presence of hydroxyl group at C-7 and a glucosyl group instead of a methoxyl group at C-6 may play a crucial role in AGE inhibition (coumarin structure, Figure 1).

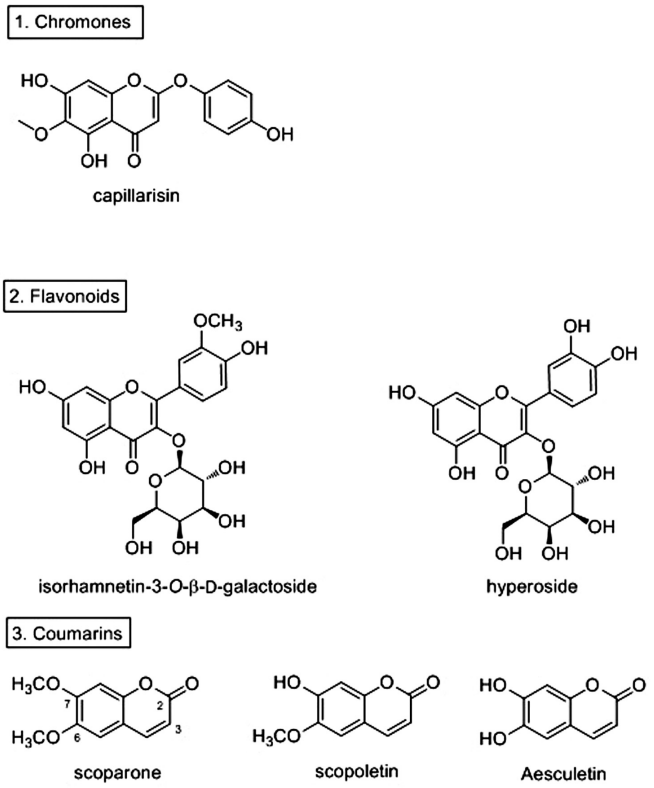

Figure 1. Structures of chemical constituents from *Artemisia capillaries*

Lipid metabolism

Lipid metabolism disorders are observed in metabolic syndromes. A study reported the increased lipid metabolism effect of the AC ethyl acetate (ACEA) fraction (0.1 g/kg bw) on high fat diet-induced obesity.[11] *In vitro* the ACEA fraction treatment decreased the leptin level, fat accumulation, and peroxisome proliferator-activated receptor-gamma (PPAR-g) expression in cultured 3T3-L1 adipocytes. Lipid-lowering effect was found in high-fat and ACEA-treated group via increased mitochondrial β-oxidation by increasing the activity of the rate-limiting enzyme, carnitine palmitoyl transferase I. Also, the activity of fatty acid synthase and glycerol-3-phosphate dehydrogenase, related to adipogenic differentiation, were markedly suppressed in the high-fat and ACEA-treated group, as compared with the high-fat group. Moreover, lowered hepatic lipid droplet accumulation and adipose tissue weight and size were seen in the ACEA-treated group.

Skin inflammation

Yin Chen has been reported to treat skin inflammatory conditions in traditional Chinese medicine. Since several allergic and skin inflammatory disorders are involved 5-LOX products, ethanol extract (70%) of the aerial parts of AC was prepared