



## Editor's Choice

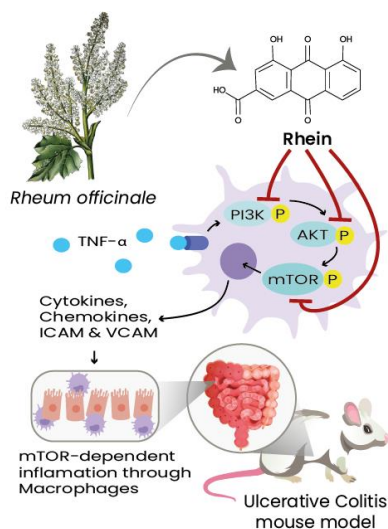
# Editor's Selection of the Important Research Investigations in the Field of Phytopharmacological Communications from Around the World

## Editorial Staff

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### Rhein Inhibits PI3K/Akt/mTOR Signaling Pathway to Show Efficacy in an Ulcerative Colitis Mice Model

Dong and his associates investigated the potential therapeutic effect of Rhein on ulcerative colitis (UC) and its mechanism in mouse models of human disease. Their results showed a decrease in the levels of TNF- $\alpha$ , IL-6, IL-1 $\beta$ , and other cytokines responsible for promoting inflammation. Moreover, both in-vivo and in-vitro mitigation of UC-associated symptoms such as colon shortening, weight loss, diarrhea, and hematochezia stimulated by dextran sodium sulfate was seen.



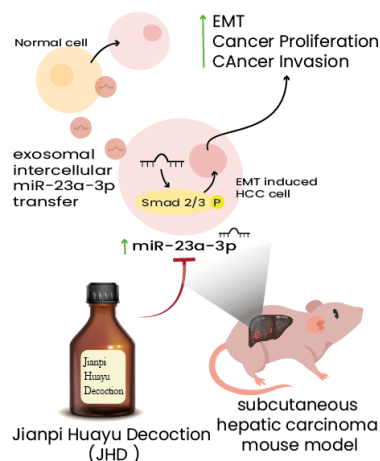
Through western blotting, decreasing phosphorylated protein levels of PI3K, Akt, mTOR, and p70S6K1 by Rhein was evident which indicates inhibition of the PI3K/Akt/mTOR signaling pathway. Rhein administration also partially reversed the gut

dysbacteriosis of mice induced by dextran sulfate sodium. A decrease in pathogenic bacteria (e.g., *Enterobacteriaceae* and *Turicibacter*) as revealed by 16sRNA gene sequencing was also observed. The authors conclude that Rhein possesses anti-UC activity as exhibited by alleviating the signs and symptoms of UC and diminishing gastrointestinal inflammation by blocking the PI3K/Akt/mTOR signaling pathway and modulating stomach microbiota. *Phytother Res.* 2022 May;36(5):2081-2094.

### A Traditional Chinese Remedy for Hepatocellular Carcinoma Functions by Suppressing Exosomal miR-23a-3p/Smad Signaling

A decoction of Jianpi Huayu (JHP) has been used traditionally in orthodox Chinese medicine to treat tumors such as hepatocellular carcinoma (HCC), however, the mechanism is still a mystery. Intercellular communication in the cancer cell microenvironment points toward a strong role of exosomes, but their contribution to HCC is still not well understood. Xie and colleagues investigated the anti-neoplastic effects of JHP and the possible function of exosomal signaling. Nude mice models with subcutaneous cancer were used to gauge the effects of JHP. Migration, invasion, proliferation, and epithelial-mesenchymal transition (EMT) of cultured HCC cells were mitigated by JHP. From the EMT-induced HCC cells, exosomes increased the invasion, migration, and EMT of other cultured HCC cells, whereas post-treatment of JHP, exosomes from EMT-induced HCC cells had little effect. Exosomal miR-23a-3p which is significantly upregulated in cancer cells as compared to normal cells

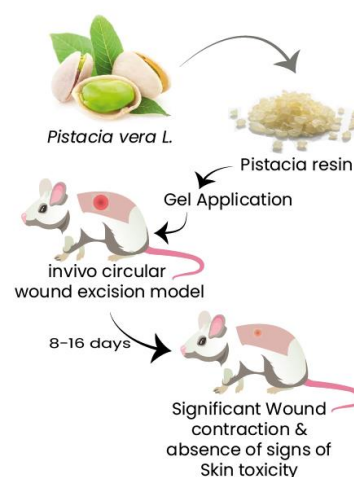
was reduced in JHD-treated cultured HCC cells. Post hepatectomy, patients with high miR-23a-3p levels had low survival rates. Smad signaling protein expression as well HCC cell proliferation was upregulated by miR-23a-3p.



More critically, miR-23a-3p overexpression countered the EMT and Smad signaling inhibition brought about by JHD treatment. In vivo examinations revealed that treatment with JHD additionally diminished the development of HCC-derived tumors in naked mice, and decreased the levels of miR-23a-3p in serum exosomes and the degree of EMT in cancer cells. The authors conclude that the anticancer properties of JHD partially if not completely are due to the downregulation of exosome-mediated intercellular miR-23a-3p transfer and subsequent blockade of Smad signaling. Disrupting this exosomal miR-23a-3p/Smad signaling pathway may be an effective treatment. *J Ethnopharmacol.* 2022 Aug 10;294:115360.

### Wound Healing by Italian and Algerian Resins

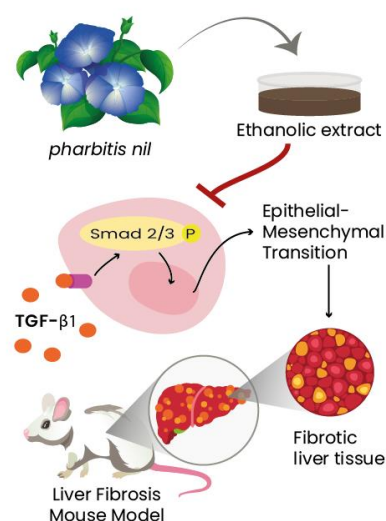
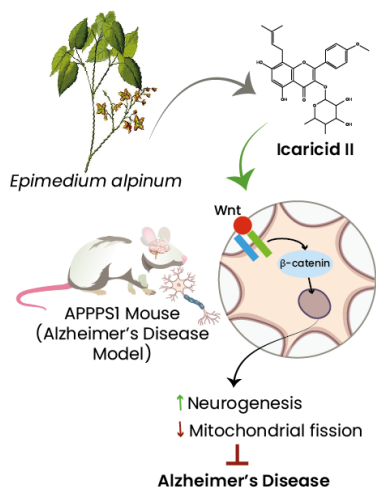
One of the most common traditional medicine remedies used for wound healing is the oleoresin preparation of *Pistacia vera*. However, no scientific rationale has been provided for the wound healing properties of the plant and its resins. Boudjelal and associates using a circular wound healing model assessed the ability of the plant collected from Algeria and Italy for in-vivo wound healing. Their results exhibited a high terpenoid content in the plant and significant healing effects.



From day 8 to day 16 significant wound contraction was seen upon application of Algerian and Italian oleoresin ointment preparation. The results were comparable to the standard drug used, Cicatryl. Histological tissue results corroborated the in vivo results. The lack of toxicity was confirmed by applying the ointments to the skins of rabbits. The authors argue that their investigation supports the traditional practice of using *Pistacia vera* as an effective remedy for healing wounds and injuries. *Fitoterapia.* 2022 Jun;159:105197.

### Activation of Wnt/ $\beta$ -Catenin Pathway by Icarisid II Improves Cognition

Reestablishing the impaired neurogenesis in Alzheimer's disease (AD) patients can lead to improved cognitive function. Xiao and colleagues investigated whether the natural product icarisid II (ICS II) which possesses strong neuroprotective properties can restore physiological neurogenesis in APP/PS1 mice. After oral administration of ICS II, APP/PS1 mice showed hippocampal neuronal generation alongside the activation Wnt/ $\beta$ -catenin signal pathway as exhibited by the stimulation of Wnt-3a, phosphorylated glycogen synthase kinase-3 $\beta$  (p-GSK-3 $\beta$ ) and  $\beta$ -catenin. Their data also showed inhibition of phosphorylated dynamin-related protein 1 (p-Drp), mitochondrial fission factor (Mff), and mitochondrial fission 1 protein (Fis1). However, upregulation of Mitofusin 1 (Mfn 1) and Mitofusin (Mfn 2) suggested a depression in mitochondrial fission.



These effects of ICS II were canceled by XAV-939, a Wnt/ $\beta$ -catenin signaling pathway inhibitor. The authors concluded that ICS II can mitigate mitochondrial fission through the Wnt/ $\beta$ -catenin pathway and alleviate cognitive damage through neurogenesis in an AD mouse model. *Phytother Res.* 2022 May;36(5):2095-2108.

### Amelioration of Liver Fibrosis by Pharbitis nil Through TGF $\beta$ 1-SMAD2/3 Pathway

In the regions of Eastern Asia, traditional remedies of the seeds of the medicinal herb Choisy, scientifically known as *Pharbitis nil* (*L.*) have been used to treat hepatic diseases such as cirrhosis of the liver, fatty liver, and obesity. In chronic inflammatory hepatic disorders such as non-alcoholic steatohepatitis, fibrosis of the liver is the leading cause of morbidity and mortality. However, efficacious pharmaceutical products to treat liver fibrosis are awaiting approval. Jung and colleagues investigated whether alleviation of hepatic fibrosis is possible with *Pharbitis nil* ethanolic extract (PNE).

Two different pre-clinical models were used in this investigation. C57BL/6 male mice that were 6 weeks old were given CCl<sub>4</sub> as intraperitoneal injections two times a week for 6 weeks after which they were subjected to daily administration of 5 or 10 mg/kg PNE from the third week onwards. For 41 weeks the mice were given a high-fat diet (HFD) and at week 35 they were given 5mg/kg PNE every day for the final 6 weeks. The antifibrotic effects of PNE were further evaluated in primary mouse hepatic stellate cells and LX-2 cells. In both CCl<sub>4</sub>-treated mice and mice subjected to HFD, PNE successfully mitigated liver fibrosis, inflammation, and hepatic necrosis as well as inhibited the liver fibrosis progression. Reduced levels of fibrosis markers such as SMAD2/3 activations in mouse livers and in TGF $\beta$ 1-treated primary mouse hepatic stellate and LX-2 cells show that PNE attenuates liver fibrosis by downregulating TGF $\beta$ 1-induced SMAD2/3 activation. *J Ethnopharmacol.* 2022 Aug 10;294:115370.

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