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FILE: ▪ Neem (*Azadirachta indica*)
▪ Gastric Hyperacidity
▪ Ulcer

HC 020695-377

Date: May 29, 2009

RE: Review of Neem Shows Potential of Bark Aqueous Extract for Preventing and Healing Gastric Ulcers

Maity P, Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. The use of neem for controlling gastric hyperacidity and ulcer. *Phytother Res*. Jan 12, 2009. [Epub ahead of print].

The neem (*Azadirachta indica*) tree is a well-known Indian medicinal plant with antiulcer and antisecretory activities. Pre-clinical research has demonstrated that neem possesses anti-inflammatory, antiseptic, and immunomodulatory properties. Around 180 chemical compounds have been isolated from neem, but few have been studied pharmacologically. In this review, the authors examine "the pharmacological, biochemical and clinical evidence for the therapeutic potential of Neem extracts and their mechanism of action for the prevention and treatment of gastric ulcer and related conditions."

The first scientific evidence of neem's potential for treating gastric ulcers was uncovered in a 1984 in vivo study that found that the neem seed oil constituent nimbidine blocks gastroduodenal lesions. Over the last 15 years, several studies have indicated that both neem bark and leaf extracts have antiulcer and antisecretory properties. Pre-clinical in vivo research has shown that neem bark aqueous extract dose-dependently prevents gastric lesions and decreases gastric acid secretion. Aqueous extracts of neem leaves have been shown to prevent gastric lesions, reduce the severity of gastric ulcers, and stimulate ulcer healing. Research has shown that the bark extract is superior to the leaf extract in the prevention of stress- and indomethacin-induced gastric ulcers, while the leaf extract is better at preventing ethanol-induced gastric ulcers. Compared to current antiulcer drugs with exposure to stress and indomethacin, when given intraperitoneally (IP) the bark extract is equivalent in potency to omeprazole in preventing ulcers, while the leaf extract is less potent than omeprazole, but more potent than ranitidine. The biological activity differences between the bark and leaf extracts are apparently due to their distinct chemical

compositions, since the bark and leaf phytochemical profiles appear for the most part to be very different. A few known compounds are held in common.

One small clinical study has examined the therapeutic effects of neem bark extract on patients with illnesses related to gastric acid, as well as gastroduodenal ulcers. Patients taking 30 mg of neem bark extract twice daily a half hour before meals for 10 days showed 77% decreased gastric acid production and 63% decreased total gastric secretion volume. Patients who took 30-60 mg neem bark extract for 6-10 weeks experienced esophageal and gastric ulcer healing. No killing effect on *Helicobacter pylori* was detected. There were no adverse effects observed during the study.

Neem bark and leaf extracts possess antioxidant effects that protect the gastric mucosa against oxidative damage caused by ethanol, indomethacin, and stress. The bark extract has also been shown to prevent apoptosis during indomethacin-induced ulceration. In vivo models have shown that neem leaf and bark extracts possess antisecretory effects, inhibiting gastric acid production. The gastric acid inhibitory effects from IP injection of neem bark and leaf extract are approximately equivalent to those of the drugs ranitidine and omeprazole, and they have the same mechanism of action as omeprazole – proton pump inhibition involving inhibition of H^+-K^+-ATPase. This activity is more potent for neem bark extract. Neem bark's anti-inflammatory effect and its inhibitory effect on the activation of neutrophil leukocytes "might contribute to the prevention of inflammation and activated neutrophil-mediated damaged [sic] observed during ulceration." In addition, flavonoids from neem bark and leaf extracts may also prevent ulceration through maintaining prostaglandin levels by stopping prostaglandin synthetase inhibition caused by stress, ethanol, and indomethacin. A neem bark phenolic glycoside "tentatively called neemoside" has been shown to be a potent proton pump inhibitor. Other antiulcer compounds isolated from neem include nimbidine and salanin, but these are found in the seed oil. Toxicity studies have indicated that neem bark extract is safe with no adverse effects on vital organs in vivo. Neem leaf extract has been shown to cause genotoxicity in male mice germ cells at 0.5-2.0 g/kg/day for 6 weeks, and the dry leaf powder at 20-60 mg daily for 24 days in rats caused adverse effects in the male reproductive system.

The authors conclude "on the existing evidence, Neem has a tremendous potential for the development of novel nontoxic antiulcer products." They write that the "bark extract has an additional advantage in that it is nontoxic and effective in patients," but further clinical trials and toxicology studies are needed of this preparation to "establish its full potential for therapeutic use in humans."

—Marissa Oppel, MS

The American Botanical Council has chosen not to reprint the original article.