Cosmeceutical Critique

Boldine

Boldo (*Peumus boldus* Mol.) is a slow-growing, shrubby evergreen tree native to the Chilean and Peruvian Andes. It is also found in Morocco and other parts of North Africa, and is cultivated in Europe. The plant has traditionally been used in South American folk medicine, particularly in Chile, Peru, and Brazil, to treat a wide range of conditions of the liver, bowel, and gallbladder (Pharmacol. Res. 1994;29:1-12).

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The primary active constituent identified in the tree is boldine, a simple aporphine alkaloid. Several aporphine alkaloids, which are secondary metabolites, are found in boldo leaves, with boldine being the most abundant (Curr. Med. Chem. Anticancer Agents 2005;5:173-82). Boldine is extracted from the leaves and bark of the tree (Phytother. Res. 2000;14:339-43; Pharmazie 2001;56:242-3).

In Germany and other European countries, the boldo plant is used as a medicinal. It is the subject of a German Commission E monograph that details the acceptable uses of the plant as an herbal drug for liver, gallbladder, and gastric conditions (Blumenthal M., et al. [eds.] The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines. Austin, Tex.: American Botanical Council and Boston: Integrative Medicine Communications, 1998, pp. 93-4).

Boldine is used worldwide in homeopathic and herbal medicine, and boldine extract is widely acknowledged as a viable herbal remedy in several pharmacopoeias (Chem. Biol. Interact. 2006;159:1-17; Pharmacol. Res. 1994;29:1-12). Indeed, boldine has been demonstrated to possess antioxidant activity in biologic as well as nonbiologic systems, and it has emerged as an ingredient of great interest for its potential in the treatment of free radical–mediated damage or conditions (Pharmacol. Res. 1994;29:1-12).

Antioxidant Actions

Boldine is now considered one of the strongest natural antioxidants (Chem. Biol. Interact. 2006;159:1-17).

In the early 1990s, the traditional use of *Peumus boldus* extract prompted a team of researchers to validate some of its therapeutic properties. They found that boldine imparted significant protection in vitro against *tert*-butyl hydroperoxide–induced toxicity in isolated rat hepatocytes, and in vivo against carbon tetrachloride–induced hepatotoxicity in mice. A test in rats with carrageenan-induced edema also revealed significant and dose-dependent anti-inflammatory effects (Planta Med. 1991;57: 110-5). The free radical–scavenging and hepatoprotective properties of this natural compound are now considered well established (Phytother. Res. 2000;14:254-60).

A 2001 study demonstrated that boldine imparts chemoprotective activity in murine liver, reducing the metabolic activation of drug-metabolizing enzymes as well as chemical mutagens (Pharmazie 2001;56:242-3).

Alkaloids semisynthesized from boldine have also been shown to inhibit activity against reactive oxygen species and are believed to represent a potential therapy for inflammatory disorders involving production of reactive oxygen species (Chem. Pharm. Bull. [Tokyo] 2004;52:696-9).

In a study in mice, boldine showed significant antioxidant activity, decreasing the oxidation of low-density lipoprotein. It also lessened atherosclerotic lesion formation in LDL receptor–deficient mice that were fed an atherogenic diet. The authors believe that antioxidant capacity, coupled with the traditional tolerance to boldine in humans, renders it a suitable alternative to vitamin E (Atherosclerosis 2004;173:203-10).

More evidence of boldine's antioxidant effects emerged from a study in which it protected intact red blood cells against hemolytic damage caused by the free radical initiator 2,2'-azobis-(2-amidinopropane) (AAPH). The effect was concentration dependent and occurred whether the herb was added simultaneously with, or 1 hour before, AAPH. Erythrocytes previously incubated with AAPH for 2 hours were largely unaffected by the addition of boldine. The investigators concluded that boldine had significant time-dependent cytoprotective as well as antioxidant activity (Phytother. Res. 2000;14:339-43).

It is noteworthy that boldine is found in plants other than the Chilean boldo. In a study of boldine and other aporphine alkaloids isolated from *Lindera angustifolia* Chen, a Chinese medicinal plant used for edema and rheumatic pain, the extract exhibited significant free radical–scavenging activity against 2,2-diphenyl-1-picrylhydrazyl. It also showed antinociceptive properties, which are thought to be associated with the capacity to scavenge free radicals (J. Ethnopharmacol. 2006;106:408-13).

Other Therapeutic Actions

Boldine has been shown to exert cytoprotective, anti–tumor promoting, anti-inflammatory, antidiabetic, and antiatherogenic activities, all of which may arise from its free radical–scavenging properties. This potent alkaloid also has been shown to confer significant pharmacologic benefit not related to oxidative stress, such as antitrypanocidal, vasorelaxing, immuno- and neuromodulatory, and cholagogic and/or choleretic activity (Chem. Biol. Interact. 2006;159:1-17).

In a study of carrageenan-induced edema in guinea pigs, boldine exhibited dose-dependent anti-inflammatory activity. It also acted against bacterial pyrogen-induced hyperthermia in rabbits. In addition, an in vitro arm of the same study revealed that boldine inhibited prostaglandin biosynthesis, to which investigators attributed the in vivo anti-inflammatory and antipyretic activities of boldine (Agents Actions 1994;42:114-7).

Boldine is contraindicated in people who have kidney disease, women who are pregnant or breast-feeding, and patients with liver bile duct obstruction or severe liver disease (Brinker F. Herb Contraindications and Drug Interactions. Sandy, Ore.: Eclectic Medical Publications, 1997, p. 26).

Photoprotective Action

In a recent study with the most direct dermatologic implications, boldine was shown to be photostable, with its antioxidative capacity remaining intact, thereby allowing the compound to confer photoprotection (J. Photochem. Photobiol. B 2005;80:65-9). Furthermore, in vitro tests of compounds extracted from lichens and the boldo tree revealed that their ultraviolet filtering power was similar to, or better than, that of octylmethoxycinnamate, suggesting their potential usefulness in sunscreen formulations (J. Photochem. Photobiol. B 2002;68:133-9).

Conclusions

Natural antioxidants are too plentiful, and the number under active investigation for medical and cosmetic uses too copious, to suggest that any one compound is the antioxidant du jour. That said, boldine has been studied with increasing frequency over the past 15 years, after a long history of use in folk medicine, and the evidence is ample enough to suggest that clinical trials are the next important step to determine the medical role of this natural botanical.

Direct applications in dermatology have not yet been seen, but given the antioxidant and anti-inflammatory activities exhibited by this aporphine alkaloid, there is cause to promote its use in research. Boldine is already being incorporated into several cosmeceutical moisturizers, anti-aging sera, eye and lip balms, and antioxidant masks available online. ■

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