

COSMECEUTICAL CRITIQUE

Mahonia

Mahonia aquifolium, also known as Oregon grape root, belongs to the Berberidaceae or barberry family. This evergreen shrub, native to the American northwest and adjacent areas of Canada, has been used in folk medicine to treat chronic eruptions and various rashes, especially those containing pustules or resulting from consumption of fatty foods (Dermatol. Ther. 2003;16:106-13).

In numerous investigations, Oregon grape root has displayed a wide range of biologic activities, including antioxidant, antimicrobial, and antimutagenic properties. Although this column will focus on the Mahonia aquifolium species, it is worth noting that Mahonia bealei (also of the Berberidaceae family), native to China, exhibits anti-influenza effects in vitro (Zhong Yao Cai. 2003;26:29-30).

Research on the extract of the bark of Mahonia aquifolium has indicated that its primary bioactive characteristic is the inhibition of lipid peroxidation, and that its main constituents are the alkaloids berberine, berbamine, and oxyacanthine (Planta Med. 1994;60:421-4).

Mahonia aquifolium bark extract has been shown to inhibit keratinocyte growth. In one study, berberine was as effective as the mahonia extract at inhibiting cell growth, while berbamine and oxyacanthine, the benzyloquinoline alkaloid constituents of mahonia, were three times as effective at cell growth suppression (Planta Med. 1995;61:74-5).

Berberine-containing herbs have been used in folk medicine to relieve neonatal jaundice (Comp. Med. East West 1977;5:161-8), as anti-inflammatory agents (for lumbago and rheumatism), and as antinociceptive and antipyretic medications (Life Sci. 2002;72:645-57; J. Ethnopharmacol. 1998;59:211-5). Further, researchers studying the use of berberine as an antiacne medication in Japanese Kampoh (Japanese herbal medicine based on Chinese methods) found that the alkaloid inhibited lipogenesis in hamster sebaceous glands by 63% (Skin Pharmacol. 1993;6:56-60).

Antimicrobial Actions

In a study more than a decade ago, researchers screened 100 methanolic plant extracts for antifungal activity against nine species of fungi. In all, 81 of the extracts had some antifungal activity, and 30 extracts demonstrated activity against at least four of the fungal species assayed. Mahonia was one of six extracts showing the greatest antifungal activity (J. Ethnopharmacol. 1994;44:157-69).

In a more recent study, investigators evaluated the activity of Mahonia aquifolium stem bark extract and three of its constituents—berberine, palmatine, and jatrorrhizine—against various dermatophytes and two Candida species of human origin. Jatrorrhizine was the most effective against

all the fungi tested. Investigators concluded that this component of mahonia would be more suitable than berberine, palmatine, and the crude extract for further investigation as a potential antifungal agent (Phytother Res. 2003;17:834-7).

In vitro antimicrobial activity was also exhibited by the crude extract of Mahonia aquifolium stem bark and its two main protoberberine alkaloids, berberine and jatrorrhizine, in a wide-ranging evaluation of antibacterial and antifungal activity.



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The crude extract and key constituents displayed various levels of activity against 20 strains of coagulase-negative staphylococci, 20 strains of Propionibacterium acnes isolated from skin lesions of patients with severe acne, and 20 strains of Candida isolated from chronic vulvovaginal candidoses. Investigators concluded that

the results buttressed the traditional use of Mahonia aquifolium for the treatment of localized skin and mucosal infections, and that the herb warrants consideration for inclusion in formulations to treat acne and chronic yeast infections (Phytother Res. 2004;18:674-6).

Evidence of berberine's antimicrobial activity against several bacterial and fungal species has been gathering for several years (Folia Microbiol. 1999;44:164-6; Planta Med. 1997;63:196-8; J. Pharm. Sci. 1994;83:404-6; Canad. J. Microbiol. 1969;15:1067-76).

Antitumor Activity

Berberine has been shown to induce apoptosis in promyelocytic leukemia HL-60 and 3T3 fibroblast cells (Arch. Pharmacol. 1996;354:102-6; Cancer Lett. 1995;93:193-200), and protoberberines have exhibited significant toxicity against topoisomerases (Biochem. Pharmacol. 1998;56:1157-66).

Berberine, which is also the main alkaloid constituent of goldenseal, an herb used medically in eyewash and skin lotion formulations, was evaluated recently for its photochemical interactions with different solvents and potential phototoxicity to HaCaT keratinocytes. The alkaloid was a weak photosensitizer in water, but capable of generating superoxide anions and other radicals in a nonpolar setting. Significant reductions in cell viability and simultaneous elevation in DNA damage were observed in HaCaT keratinocytes exposed to UVA in the presence of berberine. The investigators concluded that exposure to the sun or to artificial UVA is contraindicated in people using topical products containing berberine (Chem. Res. Toxicol. 2001;14:1529-34).

In a study of the antimutagenic activity of crude extract fractions of the bark of Mahonia aquifolium against the common direct-acting mutagen acridine orange, investigators found that while antimutagenic properties were associated with both bis-benzyloquinoline and protoberberine alkaloid fractions, only the protober-

berine derivatives, jatrorrhizine and berberine, exhibited significant concentration-dependent inhibitory activity against the mutagen.

This was particularly true of berberine, which was threefold stronger than jatrorrhizine. In fact, even at very low doses, berberine suppressed the acridine orange-induced mutagenicity and consistently demonstrated the highest cytotoxicity among the mahonia components tested (BMC Complement Altern. Med. 2002;2:2).

Other Actions

In a chemical structural study of three alkaloids isolated from Mahonia aquifolium (berberine, jatrorrhizine, and magnoflorine), the free phenolic group-bearing alkaloids (jatrorrhizine and magnoflorine) exhibited a greater capacity to scavenge peroxy radicals, which the investigators attributed to higher lipophilicity (Bioorg. Med. Chem. 2004;12:4709-15). Nevertheless, berberine is one of the primary active ingredients in mahonia that is consistently identified for study.

Photochemical reactions and sensitivity are particularly relevant, as a recent study showed that irradiation of berberine in oxygenated dimethyl sulfoxide solvent generated the formation of superoxide anion radicals and singlet oxygen.

Other protoberberinium salts—palmatine and jatrorrhizine—were associated with significantly less photochemical generation of reactive oxygen species. Nevertheless, the investigators concluded that UVA-induced photochemical reactions of protoberberinium salts, which have been shown to exhibit antibacterial, antimalarial, and antitumor activity, warrant attention, particularly in their use for treating skin disorders (Phytother Res. 2004;18:640-6).

Psoriasis

By far, psoriasis is the dermatologic condition most associated with treatment using Mahonia aquifolium. Traditional and alternative treatments, as well as a growing body of research, bear this out.

In one study, investigators tested four protoberberine alkaloid extracts of Mahonia aquifolium (berberine, oxyberberine, jatrorrhizine, columbamine), as well as two aporphine alkaloid extracts of the herb (magnoflorine and corytuberine), for their ability to inhibit lipoxygenase, the metabolism of which contributes to psoriasis pathogenesis.

Oxyberberine, corytuberine, and columbamine were significantly better inhibitors than the remaining alkaloids. Lipoxygenase inhibition was found to be commensurate with lipid antioxidant activity. The authors concluded that the efficacy of Mahonia aquifolium for the treatment of psoriasis can be at least partially ascribed to the lipoxygenase inhibition imparted by the herb's alkaloid constituents (Planta Med. 1995;61:372-3).

In another study evaluating the capacity of Mahonia aquifolium compounds to inhibit lipoxygenase, the same team of in-

vestigators tested six bis-benzyloquinoline (BBIQ) alkaloid constituents (oxyacanthine, armoline, baluchistine, berbamine, obamagine, and aquifoline) and found that berbamine and oxyacanthine were the most potent inhibitors, also significantly hampering lipid peroxidation. The researchers again suggested that the inhibition of lipoxygenase by these Mahonia aquifolium components may account for therapeutic effects of the plant extract, particularly when it is used to treat psoriasis (Pharmazie. 1996;51:758-61).

In a monograph published in 2005, three open-label clinical trials of Mahonia aquifolium 10% topical cream for treatment of psoriasis were discussed. The first study, which evaluated the safety of the herb in 39 patients treated for 12 weeks, revealed statistically significant increases in Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) scores after 4 weeks of treatment that continued up to 1 month after treatment ended.

The second study examined 32 psoriasis patients with mild to moderate bilateral presentations treated for up to 6 months with mahonia on one side of the body and a standard psoriasis formulation, i.e., calcipotriene ointment (Dovonex), on the other. The herbal treatment was considered effective, with 84% of patients reporting a good to excellent response and 63% of patients rating Mahonia aquifolium equal to or better than the standard preparation.

Similarly, the third trial, an observational study of 33 patients with mild to moderate bilateral psoriasis treated for 1 month, showed that patients improved after 1 week of therapy, with mahonia performing as well as or better than the vehicle-treated side.

The authors suggested that these findings by numerous researchers in several countries show Mahonia aquifolium to be safe and effective as a treatment for mild to moderate psoriasis (Am. J. Ther. 2005;12:398-406).

Conclusions

In addition to a long history of traditional folk use of Mahonia aquifolium, there is an expanding track record of modern use of this dynamic herb for several dermatologic indications, especially psoriasis. Mahonia's reputation as a long-time natural remedy, as well as its status in the sanctioned dermatologic armamentarium, positions this botanical as an important ingredient in a broad array of accepted medications and over-the-counter preparations.

In terms of psoriasis treatment, Mahonia aquifolium appears to belong among the various treatments considered for the mild to moderate manifestation of this recalcitrant condition. ■

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