COSMECEUTICAL CRITIQUE

Rosmarinic Acid

Rosmarinic acid (alpha-*o*-caffeoyl-3,4-dihydroxyphenyl lactic acid) is a naturally occurring hydroxylated compound and analogue of caffeic acid (3,4-dihydroxycinnamic acid).

Caffeic acid, which is one of the main hydroxycinnamic acids (a major class of phenolic compounds), confers antioxidant activity, protects human skin from ultraviolet C–induced erythema, and exhibits considerable anticarcinogenic potential (J. Nutr. 2001;131:66-71; Folia Biol. [Praha] 2003; 49:197-202; Int. J. Pharm. 2000;199:39-47; Nutr. Cancer 1998;32:81-5).

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Caffeic acid and its derivatives, such as rosmarinic acid, carnosol, and carnosic acid—all of which manifest antioxidant activity—are thought to be the key constituents of rosemary. Caffeic acid also is found in coffee, several grains, fruits, and vegetables, including white grapes, olives, spinach, cabbage, and asparagus, as well as white wine and olive oil (Phytother. Res. 2003;17:987-1000; Indian J. Exp. Biol. 1999;37:124-30).

Notably, rosmarinic acid is a common component of some fern and hornwort species, as well as species of the Boraginaceae family and, particularly, the Lamiaceae family (Phytochemistry 2003; 62:121-5). The Lamiaceae family includes common culinary herbs such as basil, lavender, lemon balm, marjoram, oregano, peppermint, perilla, sage, savory, thyme, and rosemary.

A dimer of caffeic acid, rosmarinic acid is well absorbed through the gastrointestinal tract and the skin, and has been shown to augment prostaglandin E2 production and reduce leukotriene B4 production in human polymorphonuclear leukocytes (Indian J. Exp. Biol. 1999;37:124-30).

Rosmarinic acid is versatile, and it is used in food preservatives, cosmetics, and medical applications by dint of its antimicrobial, antiviral, antioxidant, anti-inflammatory, and immunomodulatory properties (Indian J. Exp. Biol. 1999; 37:124-30; Phytochemistry 2003;62:121-5; J. Agric. Food Chem. 2001;49:5165-70; J. Dermatol. 2008;35:768-71; Photochem. Photobiol. 2006;82:1668-76).

This column will briefly discuss the research and potential dermatologic applications of this phenolic compound.

Anti-Inflammatory Actions

Twenty years ago, rosmarinic acid was identified as a nonsteroidal anti-inflammatory agent.

In a 1989 study, researchers intravenously and topically administered the antioxidant polyphenol to rats to assess how different routes of administration affect absolute bioavailability and related tissue distribution.

They found absolute bioavailability to be high for both IV and topical administration (60% for topical administration), with a longer lag time associated with percutaneous administration, suggesting that rosmarinic acid is well absorbed from the gastrointestinal tract as well as the skin.

The investigators concluded that rosmarinic acid has potential as a therapeutic nonsteroidal anti-inflammatory agent (Methods Find. Exp. Clin. Pharmacol. 1989;11:345-52).

During the ensuing 2 decades, a variety of beneficial activities were associated with rosmarinic acid, suggesting medical indications. In 2004, Osakabe et al. determined that oral supplementation with the polyphenol was an effective treatment for seasonal allergic rhinoconjunctivitis, due to inhibition of the inflammatory response and the scavenging of reactive oxygen species exhibited by the compound (Biofactors 2004;21:127-31).

Antitumorigenic Actions

The same year, Osakabe et al. reported on the antitumorigenic effects of a rosmarinic acid–rich *Perilla frutescens* extract in a two-stage murine skin cancer model. They noted significant suppression of tumorigenesis as a result of the topical application of 2 mg/mouse of the extract following tumor initiation with 7,12-dimethylbenz[*a*]anthracene (DMBA).

Tumor promotion was achieved by the use of 12-tetradecanoylphorbol 13-acetate (TPA). The researchers noted that anti-inflammatory activity 5 hours after TPA treatment was equivalent between a perilla extract containing 68% rosmarinic acid and a commercially available rosmarinic acid.

In addition, TPA-induced increases in myeloperoxidase activity, as well as the production of certain chemokines, were significantly reduced by pretreatment with perilla extract or rosmarinic acid, as were expression levels of intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 mRNA. Furthermore, pretreatment with the extract or with commercial rosmarinic acid significantly reduced reactive oxygen radical synthesis (of 8-hydroxy-2-deoxyguanosine) induced by double treatment of TPA.

The investigators attributed part of the anticarcinogenic activity of *P. frutescens* to the independent mechanisms associated with rosmarinic acid, free radical scavenging, and inflammatory response suppression (Carcinogenesis 2004;25:549-57).

Antimicrobial Actions

In 2006, Moreno et al. investigated *Rosmarinus officinalis* extracts to identify their bioactive constituents and properties, as well as the distribution and levels of antioxidants. They found a strong correlation between antioxidant activity and total phenol content, with all rosemary extracts displaying significant radical scavenging activity.

A methanol extract that contained 30% carnosic acid, 16% carnosol, and 5% rosmarinic acid was substantially more effective as an antimicrobial agent against gram-positive bacteria, gram-negative bacteria, and yeast than was a water extract containing 15% rosmarinic acid.

The investigators concluded that the antimicrobial activity of rosemary extracts was linked to their phenolic composition, and that carnosic acid and rosmarinic acid are probably the primary antimicrobial components of rosemary (Free Radic. Res. 2006;40:223-31).

Photoprotection

Later that year, Psotova et al. examined the protective effects of *Prunella vulgaris* and rosmarinic acid, its primary phenolic constituent, against alterations induced by UVA exposure in a human keratinocyte cell line. For 4 hours, human keratinocytes exposed to UVA (10-30 J/cm^2) were treated with 1-75 mg/L of *P. vulgaris* extract or 0.9-18 mg/L of rosmarinic acid.

Rosmarinic acid acts as an exogenous photoprotective agent by scavenging free radicals and as an endogenous photoprotector by activating the body's defense mechanisms.

Both *P. vulgaris* extract and rosmarinic acid mitigated UVA-induced loss of cell viability and significantly inhibited the production of free radicals engendered by UVA exposure. DNA damage also was lessened as a result of postexposure treatment with both compounds.

The investigators, who noted that *P. vulgaris* and rosmarinic acid are used in cosmetics, concluded that both botanicals exhibit concentration-dependent photoprotection and have potential as supplementary photoprotective agents in dermatologic formulations (J. Photochem. Photobiol. B 2006;84:167-74).

Also in 2006, investigators topically applied caffeic acid and its analogues, such as rosmarinic acid, to the abdomens of live hairless mice, and found that the polyphenols inhibited the production of reactive oxygen species upon exposure to UVA. They achieved similar results through oral administration of the polyphenols (Photochem. Photobiol. 2006;82:1668-76).

In 2007, Lee et al. conducted several experiments with B16 melanoma cells to identify the effects of rosmarinic acid on melanogenesis. They found that the polyphenol elevated melanin content and tyrosinase expression in a concentration-dependent fashion, and that protein kinase A was involved in and mediated the melanogenesis spurred by rosmarinic acid (Biochem. Pharmacol. 2007;74:960-8).

Early in 2009, Sánchez-Campillo et al. performed in vitro and in vivo experiments that showed rosmarinic acid acts as an exogenous photoprotective agent by scavenging free radicals. The researchers also found that rosmarinic acid acts as an endogenous photoprotector by activating the body's defense mechanisms through the regulation of tyrosinase activity and the initiation of melanin synthesis.

In particular, in vivo experiments showed that UVA-exposed mice orally treated with rosmarinic acid displayed only slight dysplasia (in 30% of cases), whereas UVA-exposed mice fed a control diet exhibited severe or moderate dysplasia in all cases (Food Chem. Toxicol. 2009;47:386-92).

Atopic Dermatitis

In 2008, Lee et al. assessed the effects of rosmarinic acid on mild atopic dermatitis in 21 patients (14 females, 7 males) aged 5-28 years. Twice daily, a 0.3% rosmarinic acid emulsion was topically applied to elbow flexures for 8 weeks. Erythema on the antecubital fossa was significantly diminished at 4 and 8 weeks, and transepidermal water loss from the antecubital fossa was significantly lower at 8 weeks than at baseline, according to local Severity Scoring of Atopic Dermatitis index results.

Xerosis, pruritus, and general symptoms all improved, according to the results of self-administered questionnaires. The investigators concluded that rosmarinic acid warrants consideration as a therapeutic agent for atopic dermatitis (J. Dermatol. 2008;35:768-71).

Rosmarinic acid can be obtained through the diet or as an oral supplement pill, and it is used in cosmetic formulations with numerous other ingredients.

Conclusion

Rosmarinic acid is a significant polyphenol with an apparently wide range of potential and realized dermatologic applications.

The direction of current research is promising, but much more work is still required to determine how important this antioxidant will be in the dermatologic armamentarium. To date, atopic dermatitis may be the indication for which this herbal ingredient is best suited. ■

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