Triterpenoids, to which squalene is the immediate biologic precursor, and sesquiterpenoids, as well as, sterols, and represent the largest group of terpenoids, the most abundant group of botanical constituents and the most common ingredient class found in volatile oils. Consequently, triterpenoids appear in numerous botanical products with traditional and modern applications to dermatology, such as Cistella antica (gora kola) and propolis.

Indeed, the naturally occurring triterpenoids, oleanolic acid and ursolic acid, are known to confer antitumorogenic and anti-inflammatory effects in certain cells. In a study published in 2000, the principal natural triterpenoid, ecdysteroidol hydrocucurbitacin F, and natural triterpenoid hydrocucurbitacin F have also been found to be effective in a multiple-dose O-tetradecanoylphorbol-13-acetate (TPA) model of chronic dermal inflammation (Eur. J. Pharmacol. 1997;334:103-5).

Although triterpenoids are not as prevalent as many of the highly touted herbal sources as polyphenols, this group of compounds is gaining increased attention for its anti-inflammatory and anti-tumor-promoting capacity. In one trial, investigators studying the triterpenoids oleanolic acid and ursolic acid found that the former induced the differentiation of keratinocytes through peroxisome proliferator–activated receptor (PPAR)–α activation. In addition, topical application of oleanolic acid improved the recovery of epidermal permeability barrier function and increased ceramides in epidermis (Exp. Dermatol. 2006;15:66-73).

The preponderance of data on triterpenoids, though, points to the anti-tumor-promoting capacity of this copious botanical class of compounds.

Anti-Tumor-Promoting Actions

In a study designed to identify potential anti-tumor promoters, investigators screened 21 cucurbitane triterpenoids using an in vitro assay system, and found that several of the compounds significantly inhibited Epstein Barr virus (EBV) activation induced by the tumor promoter TPA. These compounds were scadienolide R6, 23,24-dihydrocucurbitacin F, 25-acetyl-23,24-dihydrocucurbitacin F, 2-oxo-d-phytyl-23,24-dihydro- cucurbitacin F, and cucurbitacin F. Two triterpenoids, 23,24-dihydrocucurbitacin F and 2-oxo-d-phytyl-23,24-dihydrocucurbitacin F also displayed significant activity against skin tumor promotion in an in vivo two-stage murine carcinogenesis model (Biol. Pharm. Bull. 1999;22:606-10).

In a study from Osaka (Japan) University of Pharmaceutical Sciences, seven serratane-type triterpenoids isolated from Picus species all exhibited potent inhibitory effects on 12-O-tetradecanoylphorbol-13-acetate-induced tumor promotion by TPA, and did so more strongly than oleanolic acid. In addition, 13α,14β-epoxy-3β-methoxyxyserratane-type triterpenoids had strong anti-inflammatory activity, as demonstrated in a two-stage carcinogenesis assay of mouse skin tumors induced by proinflammatory activator (initiator) and TPA (promoter).

The investigators concluded that these compounds may behave as potent tumor promoters as well as anti-tumor initiation and warrant consideration as significant cancer chemopreventive agents (Bioorg. Med. Chem. 2005;13:1403-8).

Protection Against UV

Four triterpenoids isolated from the stems of Styrax japonica were recently found to significantly inhibit matrix metalloproteinase-1 (MMP-1) in primary human skin fibroblasts induced by UV radiation. This finding is significant given the association between the upregulation of MMPs and chronic skin damage (Biol. Pharm. Bull. 2005;28:2003-6).

Previously, some of the same investigators identified the effects of 3,23-dihydro-20(29)/lupen-27-oyic acid, a triterpenoid derived from Tiarella polypophylla, on the regulation of MMP-1 and type 1 procollagen gene expression in UV irradiated skin where diminished collagen production has been associated with human dermal fibroblasts. The triterpenoid dose-dependently regulated expression of type 1 procollagen and diminished regulation of MMP-1 at the protein level (J. Pharm. Pharmacol. Res. 2004;27:1060-4).

Other Pharmacologic Actions

Triterpenoids also have been found in Boswellia serrata, an herb used in traditional medicine to treat inflammatory and arthritic conditions (and discussed in this column in November 2006, p. 17).

In a study published in 2000, the primary components and derivatives of Boswellia serrata exhibited anti-inflammatory activity that was significant in the dermal fibroblasts induced by UV radiation. This activity was significantly more potent than that of the triterpenoid sesquiterpenoids, to which the potent 7,12-dimethylbenz[a]anthracene (DMBA) for initiation and TPA for promotion, hopp-17(21)-ene and neohopp-13(18)-ene displayed significant anti-tumor-promoting effects on mouse skin (Biol. Pharm. Bull. 1996;19:962-5). Three years later, some of the same investigators, studying triterpenoids derived from Tarax- acum japonicum (Compositae) roots, found that taraxasterol and taxaroxol significantly inhibited the effects of TPA induced Epstein Barr virus early antigen (EBV-EA) induction, which is a preliminary in vitro screening approach to identifying anti-tumor-promoting agents. These compounds also exhibited potent anti-tumor-promoting activity in the in vivo two-stage murine carcinogenesis model (Cancer Lett. 2001;172:119-26).

The same lab subsequently studied 11 serratane-type triterpenoids isolated from Picus species and three synthetic analogues for their potential inhibitory effects on EBV-EA activation induced by TPA. That study yielded more informative findings, as several of the compounds showed potent inhibitory activity, again more strongly than the oleanolic control, including 21-episerratenediol, serratenediol, diospera- serratene-21beta-ol, 3β-hydroxyserratene-14-en-21-one, and 3α-methoxy-21β-hydroxyserratene-14-en-16-one. Furthermore, no cytotoxicity was associated with these compounds.

Of these triterpenoids, 21-episerratenediol was found to demonstrate significant inhibitory effects on skin tumor promoter TPA. That study yielded more informative findings, as several of the compounds showed potent inhibitory activity, again more strongly than the oleanolic control, including 21-episerratenediol, serratenediol, diospera-serratene-21beta-ol, 3β-hydroxyserratene-14-en-21-one, and 3α-methoxy-21β-hydroxyserratene-14-en-16-one. Furthermore, no cytotoxicity was associated with these compounds.

Conclusion

As we continue to explore botanical sources for medical and cosmetic purposes, we will learn more about the numerous triterpenoids found in plants. This class of biochemical compounds typically requires less attention than polyphenols in discussions of the most potent herbal ingredients used in dermatology, but the considerable potential of triterpenoids to be used in a broad range of cutaneous applications is gradually becoming appreciated.

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