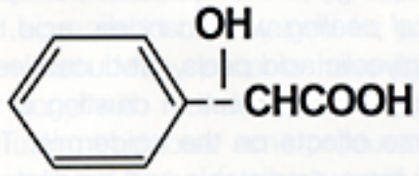
Summary of Mandelic Acid for the Improvement of Skin Conditions

Mark B. Taylor, MD

Over the past 3 years, mandelic acid, an alpha-hydroxy acid (AHA) named after the German *mandel* ("almond") and derived from the hydrolysis of an extract of bitter almonds,[1] has been studied extensively for its possible uses in treating common skin problems such as photoaging, irregular pigmentation, and acne. An open-trial investigation conducted at the Gateway Aesthetic Institute and Laser Center in Salt Lake City, Utah, has shown that mandelic acid is useful in suppressing pigmentation, treating inflammatory noncystic acne, and rejuvenating photoaged skin. Moreover, it has proven useful in preparing the skin for laser peeling and in helping the skin heal after laser surgery. This article discusses the characteristics of mandelic acid, its efficacy in the treatment of wrinkles, pigmentation, and acne, and its role in recovery following laser surgery.

Chemistry

Mandelic acid (alpha-hydroxybenzeneacetic acid) is an 8-carbon alpha-hydroxy acid with the chemical formula $HOCH(C_6H_5)COOH$ and structure[2]:



The mandelic acid molecule is larger than the glycolic acid molecule, a widely used AHA. In addition, mandelic acid, which has a pK of 3.41, is stronger than glycolic acid, which has a pK of 3.83 at 25°C. The acidity of AHAs may vary considerably with changes in temperature. Mandelic acid has a high melting point, is partially soluble in water, and is freely soluble in isopropyl and ethyl alcohol.[3] Mandelic acid occurs in two enantiomeric forms that may affect pharmaceutical activity.

Dr. Taylor is a clinical instructor in the Department of Dermatology at the University of Utah, and Director of the Gateway Aesthetic Institute and Laser Center in Salt Lake City, UT.

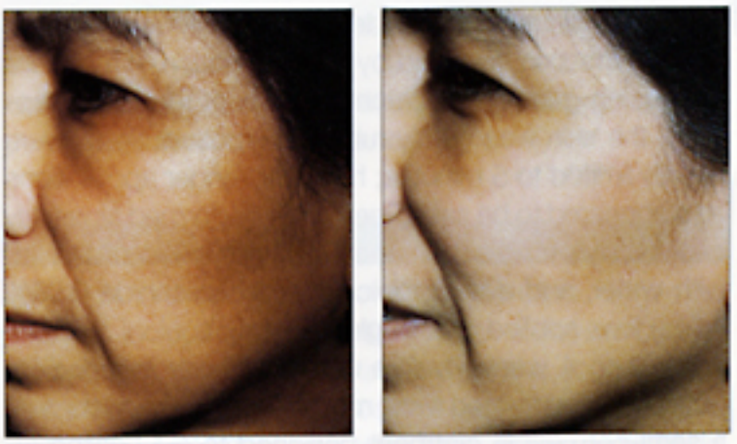


Fig. 1: Melasma in 45-year-old female (left) with hyperpigmentation caused by glycolic acid plus hydroquinone, and same patient (right) 9 months after use of mandelic acid BID.

Medical Uses

Mandelic acid has been used in medicine for many years as a urinary antiseptic. Methenamine mandelate (Mandelamine®, Parke-Davis, Morris Plains, NJ) has the urinary antiseptic action of both methenamine and mandelic acid. In concentrations of 35g to 50g/100L of urine, it inhibits *Staphylococcus aureus, bacillus proteus, escherichia coli,* and *aerobacter aerogenes.* Chemically, mandelic acid has a structure similar to that of other well-known antibiotics.[4] It is a nontoxic substance that, after being ingested orally, is excreted in the urine.

The author's interest in mandelic acid stems from its dual nature as an AHA with both potential cosmeceutical activity and well-established antibacterial activity. The earliest trials with mandelic acid had two aims: to determine whether it can produce antiaging effects on the skin similar to those produced by glycolic acid, and to assess the antibacterial action of mandelic acid in treating acne and preventing gram-negative bacterial infections after laser resurfacing.

Research Methods

Preliminary trials were open and uncontrolled, and included more than 1,100 patients over the past 3 years. Some patients were followed with photographic documentation and global evaluations, and were monitored for improvement and adverse effects—methods typical of the evaluation of a new cosmetic product. Patients

were evaluated for improvement in acne, skin texture, wrinkles, lentigenes, and melasma.

Mandelic acid is prepared in an algae extract (Mandelic Marine Complex™, NuCelle, a division of North American Medical, Idaho Falls, ID) gel or lotion base in 2% to 10% concentration for topical use. Additional preparations were combined with topical vitamins (including vitamins A, C, E, D3) and sunscreen with SPF 15. Patients were instructed to use the products twice daily.

Chemical peels were performed with 30% and 50% mandelic acid. A 2% mandelic acid wash was used to cleanse the skin, followed by the application of mandelic acid using gauze applicators. As the product was applied, the skin was gently rubbed. Exposure times were usually limited to 5 minutes; however, longer applications also appeared to be safe. Peels were performed at weekly or biweekly intervals. After the peel, the skin was cleansed with water, and a mild topical steroid (desonide 0.05% lotion) was applied in a single application.

For 2 to 4 weeks before and after laser resurfacing, patients were treated with mandelic acid products and a semi-permeable ointment designed to aid healing after laser surgery. Patients were evaluated for the following: time to reepithelialization, incidence of gram-negative infections, duration of postresurfacing erythema, postinflammatory pigmentation, milia, and other postoperative complications.

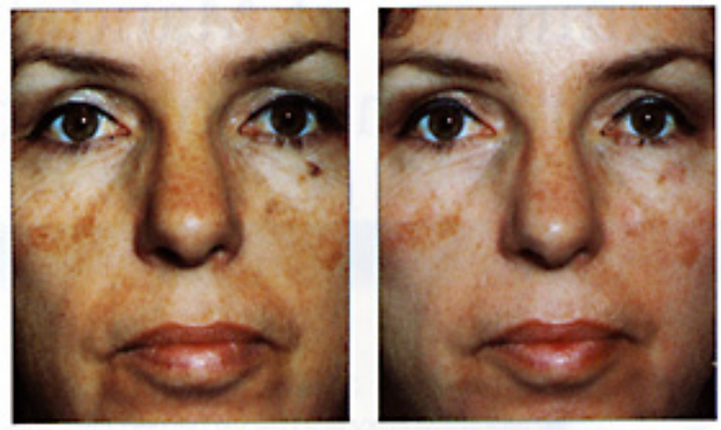


Fig. 2: Melasma and lentigenes in 48-year-old female (left), and same patient one month after use of mandelic acid (dark lesion under left eye removed with liquid nitrogen).

Fig. 3: 29-year-old female with 11-year case of melasma (left), and same patient after one month of mandelic acid BID (right).

Results

Preliminary results from the open clinical trials using these products are encouraging in several diverse areas related to skin care:

1. *Fine wrinkles and lines* appear to improve, much like photoaged skin does with the use of 10% glycolic acid preparations. Skin texture improves quickly within days or weeks in characteristic AHA therapeutic fashion. A notable difference between glycolic acid and mandelic acid products is the lack of skin irritation and erythema that often accompanies skin treatments with glycolic acid in 30% to 70% preparations used for peeling. As with glycolic acid, the effect is sustained over months and years of treatment, with gradual and continued improvement in fine lines and wrinkles being the characteristic benefit.

It is noteworthy that a remarkable difference was seen in the treatment of darkly pigmented skin types. Improvement can be seen in fine wrinkles and lines in patients with Fitzpatrick skin types I through VI without any postinflammatory hyperpigmentation. This includes Asian skin types, which have universally been able to use mandelic acid products without any postinflammatory hyperpigmentation.

In contrast, the author has observed in his dermatology practice a large number of darkly pigmented patients who have developed irritation, erythema, and subsequent postinflammatory hyperpigmentation while treating the skin with 5% to 10% glycolic acid, tretinoin, or hydroquinone.

2. *Chemical peeling* with mandelic acid, when compared with glycolic acid peels, produced less erythema, and was less likely to result in crusting or blistering or other adverse effects on the epidermis. The onset of erythema is more predictable and gradual, and there is less likelihood that "hot spots" will develop in dry areas of the face (e.g., on the cheek lateral to the commissure). Repeated, weekly peeling with 5-minute exposure times, followed by washing with water, was well tolerated by most patients. Repeated peeling is useful for treating acne, melasma, lentigenes, and fine photoaging damage (e.g., wrinkles, dullness, skin texture changes).

3. *Abnormal pigmentation,* including melasma, postinflammatory hyperpigmentation, and lentigenes, improved quickly when treated with mandelic acid products. In many patients, melasma improved up to 50% after 1 month of treatment using 10% mandelic acid lotion. Faintly pigmented lentigenes respond much more slowly—a result characteristic of treatment with other AHA products—with gradual fading over a period of weeks or months. Mandelic acid products used with prescription-strength bleach-

ing agents containing hydroquinone or kojic acid also showed excellent fading with no adverse effects, and may hasten the benefits of treatment.

Dermal melasma has often been resistant to topical treatments, but marked improvement was seen in patients who had failed other topical treatments with tretinoin, hydroquinone, and steroids. Many of these patients were of darker skin types, and had experienced postinflammatory hyperpigmentation from other topical products. This was especially true of tretinoin and hydroquinone. No adverse darkening of the melasma was seen when these patients were treated with mandelic acid products. Dermal melasma responded much more slowly than epidermal melasma (as determined by Wood's light examination). A sustained, gradual improvement over a period of months is characteristic of patients treated with mandelic acid products. One notable patient of Italian descent had severe melasma on the forehead that was resistant to prescription bleaching agents and to tretinoin. Over 6 months, almost complete clearing of the melasma with the use of mandelic acid was seen. Some patients were treated with mandelic acid products plus PhotoDerm® (ESC Medical, Yokneam, Israel). Combination therapy may yield faster improvement.

4. *Acne improvement* is remarkable in many patients treated with inflammatory pustular, comedonal, and papular acne. Patients with gram-negative folliculitis also showed improvement while using mandelic acid products. Many acne patients who are resistant to antibiotics given both systemically and topically have responded very well to the mandelic acid. Patients with acne at grade III or below responded most positively.

Initial research on mandelic acid was predicated on its antibiotic nature. It was hoped that an improvement in wrinkles and acne could be obtained for patients who suffered from both. Many patients have been able to control their acne with mandelic acid products alone (i.e., without using traditional acne products). Mandelic acid has been found to be especially useful in treating adult female patients suffering from both photoaging and acne. Some acne rosacea patients were also treated, and their conditions also showed improvement.

5. *Laser skin resurfacing* patients have been treated over the past 11 months before and after the resurfacing procedure. Immediately after laser resurfacing and until reepithelialization, patients were treated with a semipermeable ointment. The most notable result of using mandelic acid after laser peels was the lack of postoperative gram-negative infections in more than 100 cases. Patients used these products for 2 to 4 weeks before laser resurfacing and, after reepithelialization, started using maintenance products also containing mandelic acid. A semipermeable ointment allowed easy cleansing of the skin without occluding bacteria and dead-skin fragments. When mandelic acid products were used preoperatively and postoperatively, postinflammatory hyperpigmentation rarely occurred.

Impressions have been sustained over the course of the study that mandelic acid products, used alone or in tandem with antioxidant vitamins, have multiple beneficial effects as a skin treatment.

Conclusion

Although this study was not a double-blind, controlled study, it included many patients over a 3-year period. Impressions have been sustained over the course of the study that mandelic acid products, used alone or in tandem with antioxidant vitamins, have multiple beneficial effects as a skin treatment—including antibacterial effects and improvement in photoaged skin, acne, abnormal pigmentation, and skin texture. Safe use in darkly pigmented skin types was also a major difference seen when the mandelic acid products were compared with glycolic acid and tretinoin. ■

Disclosure of Interest: The author is a member of the Board of Directors of North American Medical, manufacturer and producer of NuCelle Mandelic Marine Complex products.

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