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CAM use in dermatology. Is there a potential role for honey, green tea, and vitamin C?

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A B S T R A C T

Complementary and alternative medicine (CAM) is a group of non-traditional medical practices that includes natural products, manipulations, and mind and body medicine. CAM use has grown and become popular among patients. In dermatology, honey, green tea, and vitamin C have been used as topical treatments for a variety of diseases. We performed a systematic review to explore the cutaneous effects of each of these three products. Honey's unique antibacterial, anti-inflammatory, and antioxidant properties were shown to contribute to wound healing, especially in ulcers and burns. Green tea, among many health benefits, demonstrated protection from ultraviolet-induced events, such as photoimmunosuppression and skin cancer growth. Vitamin C, known for its antioxidant properties and key role in collagen production, has been shown to produce positive effects on skin hyperpigmentation and aging. Future large well-designed clinical trials are needed in order to further investigate the potential of these agents as dermatological therapies.

1. Introduction

Complementary and alternative medicine (CAM) is a broad field defined by a group of health care practices and products that are usually not considered part of the traditional western medicine. When used in place of conventional medicine, it is referred to as "alternative medicine," while when used in combination with conventional medicine, it is called "complementary medicine." Categories of CAM include natural products, mind and body medicine, manipulations, and body-based practices [1].

The use of CAM is wide and continuously growing in the United States. In 2007, the National Health Interview Survey (NHIS) estimated that about 38% of adults in the U.S. utilized CAM [1]. Further analysis of the 2007 NHIS revealed that among people reporting skin problems in the previous year, approximately 84.5% had used CAM [2]. Vitamin, mineral and herbal supplements were found to be the most common modalities used for skin problems [2]. Another survey conducted in 2010 at a dermatology department of a tertiary care center reported that 82% of respondents had used CAM for their skin in the previous year and 78% stated that physicians should incorporate CAM into their treatment plans [3].

With the goal of enhancing awareness of CAM in dermatology, we performed a systematic review of three popular products topically used for cutaneous conditions: honey, green tea, and vitamin C.

2. Methods

Article search was done using PubMed, Medline, and The Cochrane Database. Limit was placed for English language and full text. Controlled trials with animals and humans and in vitro studies were included. Three different searches were done, one for each CAM category. For honey, search terms were "honey", "skin" and "complementary and alternative medicine." For green tea, terms included "green tea", "skin" and "complementary and alternative medicine." For vitamin C, terms used were "vitamin C" or "ascorbic acid", "skin" and "complementary and alternative medicine." Reference lists were also explored. Articles presenting a clearly defined cutaneous effect of the specific CAM modality were considered.

3. Honey

Honey is a sugar rich product derived from floral nectars and prepared by the bees in the wax cells of the hive [4,5]. In its processing, the water content of honey is reduced and glucose is oxidized into gluconic acid, lowering honey's pH and leading to

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hydrogen peroxide production [5]. Honey has been used as a medicine in a variety of cultures. It is believed to be first used in ancient Egypt for wound care between 2600 and 2200 BCE [6].

3.1. Wound healing

Many studies have shown honey to be effective in wound healing especially due to its antibacterial, anti-inflammatory, and antioxidant properties [4,7]. The high osmolarity, low pH, hydrogen peroxide content, and the presence of antioxidant components (phenolic acid and flavonoids) are responsible for honey's acceleration of wound healing, decrease of inflammation, and free radical protection [4,8]. Honey's hyperosmolar medium and hydrogen peroxide prevent bacterial growth. Due to its high viscosity, it forms a physical barrier and creates an ideal moist environment for healing [9].

Subrahamanyan (1998) compared clinical and histological outcomes of burn wounds treated with honey dressing vs. silver sulfadiazine (SSD). By day 7, histological evidence of reduced inflammation and signs of repair were present in 80% of honey treated wounds compared to 52% of SSD treated wounds. By day 21, 100% of honey treated wounds had clinically healed compared to 84% in the SSD treated group [9].

Güneş & Eşer (2007) evaluated the efficacy of honey dressings for stage II and III pressure ulcers (PU) compared to a control group treated with ethoxy-diaminoacridine plus nitrofurazone dressings [10]. PU stage II is defined as a partial thickness loss of dermis presenting as a shallow open ulcer, while PU stage III is a full thickness skin loss where subcutaneous fat may be visible [11]. At 5 weeks, there was a 56% reduction in ulcer size in the honey treated group vs. 13% reduction in the control. They concluded honey dressings to be well tolerated, effective, and safe for PU stage II and III likely due to its acidity and antimicrobial activity [10].

3.2. Antibacterial

Honey has a broad-spectrum activity that has been shown to inhibit over 80 species of bacteria, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and *Pseudomonas aeruginosa* [12–14]. The antibacterial effects are mostly attributed to honey's high osmolarity, hydrogen peroxide (H_2O_2), and methylglyoxal (MGO) [12].

With the goal of identifying all bactericidal factors in honey, Kwakman et al. (2010) successively neutralized individual honey bactericidal components (low pH, bee defensin-1, MGO, and H_2O_2) and measured their antibacterial activity. Bee defensin-1 peptide was identified in this study as a contributor to honey's antimicrobial activity, probably by protecting it against spoilage. All bacterial species tested, including *S. aureus*, *Escherichia coli*, *P. aeruginosa*, and vancomycin-resistant *Enterococcus faecium* were susceptible to different combinations of bactericidal components, emphasizing the importance of the multifactorial nature of honey for its broad-spectrum activity. Simultaneous neutralization of H_2O_2, MGO, and bee defensin-1 annulled all of honey's antibacterial activity [15].

Maddocks et al. (2012) in vitro studies showed that Manuka honey was able to inhibit *Streptococcus pyogenes* biofilms development as well as disrupt existing biofilms through cell death and dissociation. In addition, they first showed that Manuka honey impaired adherence of bacteria to fibronectin, a host tissue ligand highly expressed in damaged tissues, such as wounds. It is thought that this would result in decrease colonization of wounds by bacteria [12].

3.3. Conclusion

Therapeutic topical honey has been extensively used by diverse cultures, especially for wound healing and burns. Honey is a safe, widely accessible, and non-expensive product. Various clinical and in vitro studies have shown honey to be effective in wound healing, mainly due to its antibacterial, anti-inflammatory, and antioxidant properties. Data revealed that honey components can lead to tissue growth and epithelialization.

The antibacterial activity of honey has also been attributed to its osmolarity, low pH, presence of hydrogen peroxide, and MGO. Honey has proven activity against over 80 bacterial species, including MRSA, VRE, and *P. aeruginosa*. Taking into consideration the several types of honey and the variables involved in its production, activity against pathogens cannot be generalized. Further research is needed in order to classify specific activity of individual honeys and identify which ones should be used as standard therapy.

4. Green tea

Tea is a highly consumed beverage worldwide, with green tea being a popular choice well-known for its extensive health benefits. Green tea contains high levels of natural polyphenolic compounds (catechins) and antioxidants that can reduce reactive oxygen species (ROS) and prevent harmful ultraviolet (UV) radiation effects [16,17]. The major catechins found in green tea are epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin gallate, and epicatechin [17,18].

Studies exploring the dermatological benefits of topical green tea have shown protective effect on photoaging, photoimmunosuppression, skin cancer growth and invasion, and keloid proliferation.

4.1. Photoprotection

Exposure to UV radiation is known to cause detrimental cutaneous events. These include creation of ROS, DNA damage, immunosupression (through migration of Langerhans cells from the epidermis to local lymph nodes), and upregulation of extracellular matrix metalloproteinases (MMPs) [16,19].

Topical green tea has been shown to reduce erythema, decrease DNA damage, and inhibit Langerhans cells depletion subsequent to exposure to UVA and UVB [16,20,21]. In a study by Elmets et al. (2001), 6 human volunteers had green tea extract (concentration ranging from 0.25%–10%) applied to their backs 30 min before being exposed to UV radiation. Application of green tea resulted in a dose-dependent inhibition of erythema with a 2.5% solution providing excellent protection in all subjects. Biopsy specimens had 66% less sunburn cells (an initial finding of epidermal cell apoptosis), and stains revealed 58% reconstitution of epidermal Langerhans cells [20].

Similarly, Li et al. (2009) exposed 20 human volunteers to solar-simulated UVR on the upper back 30 min after application of vehicle and 2%–5% green tea extract (GT). They found that the GT blocked the increase of total epidermal thickness (TE) and prevented over expression of MMP-2 and MMP-9, which are metalloproteinases central to the degradation of the extracellular matrix [16].

4.2. Skin cancer

Green tea has been reported to protect against skin cancers by interfering with a variety of well-known mechanisms that participate in carcinogenesis. These include immune system stimulation,