Review Article

Integrative Therapies for Warts and Molluscum Contagiosum

Austin Hwang, BS[1], Andrea Rustad, BA[1], Melissa Nickles, MD[2], Peter Lio, MD[3] [a]

[1] Northwestern University Feinberg School of Medicine, Chicago, IL, [2] University of Illinois College of Medicine, Chicago, IL, [3] Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL

Keywords: warts, molluscum contagiosum, complementary medicine, alternative medicine, integrative therapy, verruca, essential oil, propolis, hypnosis, integrative dermatology

Journal of Integrative Dermatology

Warts and molluscum contagiosum (MC) are common viral skin infections that affect individuals of all age ranges, especially those who are immunocompromised and those in close contact with others. Conventional therapies for warts and MC include cryotherapy, curettage, imiquimod, and salicylic acid. However, evidence-based treatment guidelines for warts and MC are lacking. Considering that conventional therapies may be ineffective in some cases and limited by pain, especially in the pediatric population, clinicians and patients often seek complementary and alternative therapies. This review summarizes the clinical evidence surrounding the following integrative therapies for warts and MC: cantharidin; essential oils such as those from *Backhousia citriodora*, *Melaleuca alternifolia*, and *Santalum album*; propolis; *Echinacea*; heat therapy; garlic; and oral zinc. Anti-inflammatory, anti-proliferative, and/or immune-modulating effects of these modalities assist in clearing warts and MC. For children who tend to be more vulnerable to suggestion, hypnosis can be attempted as an alternative wart therapy.

INTRODUCTION

Warts and molluscum contagiosum (MC) are common viral skin infections that affect all age ranges, especially immunocompromised individuals and those who have close contact with others - such as physical intimacy or certain sports.[1,2] While estimates of their prevalence range from 5.1% to 11.5%, the greatest incidence of warts and molluscum are observed in children between the ages of 1 to 14 years old.[3,4] Transmission can occur through direct skin-to-skin contact or indirectly through fomites or the use of personal care items.[5] Major types of cutaneous warts include common warts, flat warts, and plantar warts.[6] Common warts present as irregularly surfaced, domed lesions with thrombosed capillaries upon paring of overlying hyperkeratotic debris, whereas flat warts are smooth, flat-topped variants often occurring on the face and extremities **(Figures 1-2)**.[6] Plantar warts resemble calluses on the plantar surface of the foot with a punctate pattern of multiple pinpoint blood vessels after paring (**Figure 3**).[6] In contrast, MC lesions appear as firm, dome-shaped pink or skin-colored papules with a central umbilication **(Figure 4**).[2] Their presentation is often in clusters or in a linear distribution.[7] MC may be more diffuse and symptomatic in areas affected by atopic dermatitis (**Figure 5**). In addition to distinct clinical appearances, the two conditions also hold different viral etiologies. Warts are caused by the human papillomavirus (HPV),[8] whereas MC is caused by the molluscum contagiosum virus, a poxvirus.[1] Commonly utilized therapies for warts and MC include cryotherapy, curettage, imiquimod, and salicylic acid.[9,10] However, given the lack of evidence-based treatment guidelines for warts and MC, the fact that they are sometimes refractory to conventional therapy, along with the benign nature of these conditions, patients and clinicians may be interested in trying complementary and alternative therapies. This review summarizes the clinical evidence surrounding the use of integrative therapies for warts and MC (**Tables 1-3**).

INTEGRATIVE THERAPIES

CANTHARIDIN

Cantharidin, a natural toxin produced by the blistering beetle, can treat warts and molluscum by inhibiting protein phosphatase and inducing vesiculation through acantholysis.[11,12] While often compounded specifically for this purpose, two commercial formulations of cantharidin currently exist. Canthacur (0.7% cantharidin) is indicated for common warts, periungual warts, and molluscum contagiosum. The second formulation Canthacur PS (1% cantharidin, 30%

a **Corresponding author:**
Peter Lio, MD
363 W Erie Street, Suite 350
Chicago, IL 60654
Phone: (312) 995-1955
Fax: (312) 995-1956
peterlio@gmail.com

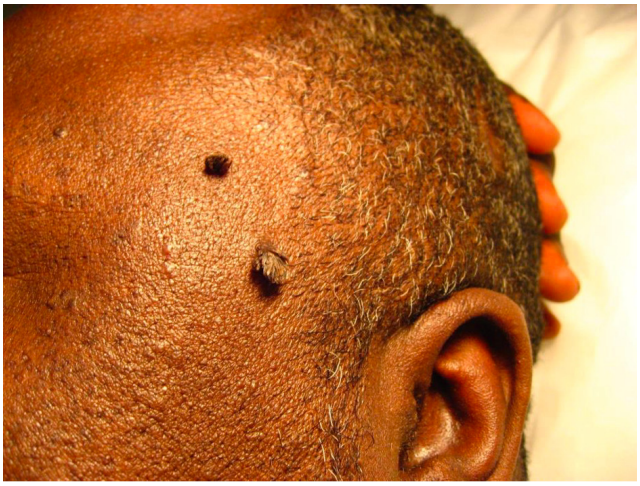

Figure 1. Filiform appearance of warts on the face.

Photo courtesy of Peter Lio, MD

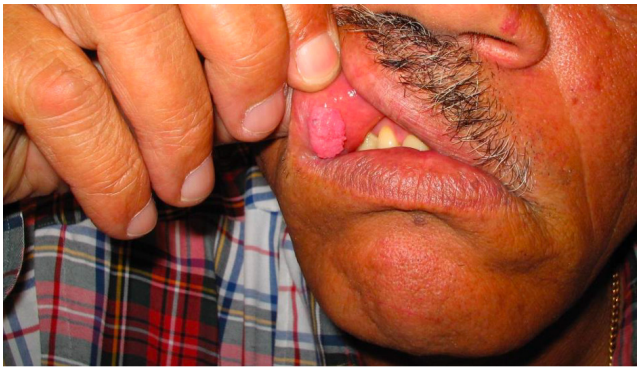

Figure 2: Oral mucosal wart.

Photo courtesy of Peter Lio, MD

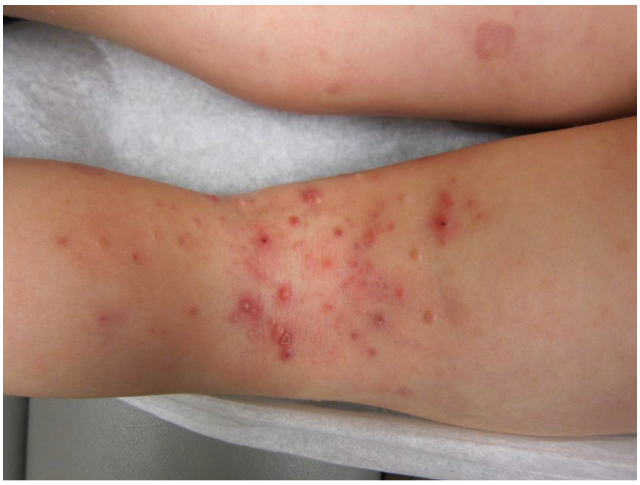

Figure 5. Diffuse molluscum contagiosum on the flexor surfaces of the legs in a patient with concomitant atopic dermatitis.

Photo courtesy of Peter Lio, MD

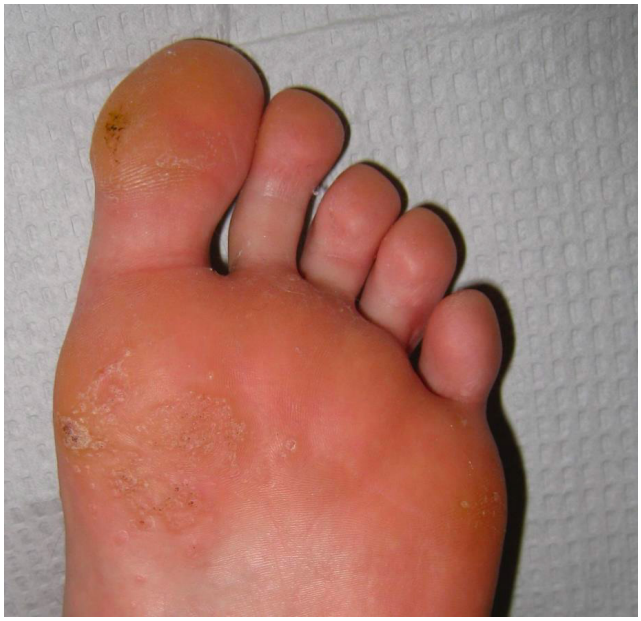

Figure 3. Plantar warts in clusters, often referred to as "mosaic warts".

Photo courtesy of Peter Lio, MD

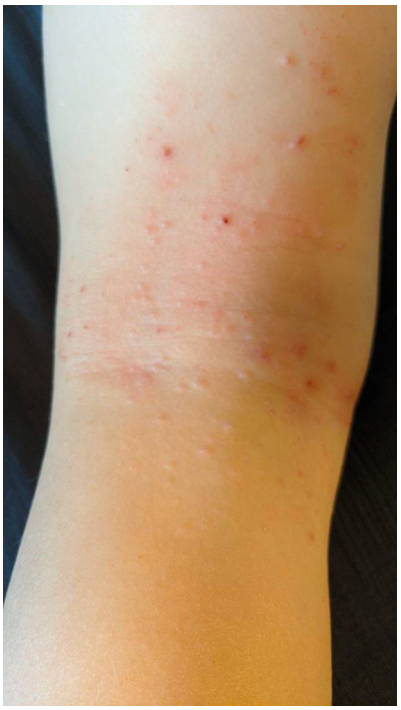

Figure 4. Molluscum contagiosum lesions with associated dermatitis in the popliteal fossa

Photo courtesy of Peter Lio, MD

salicylic acid, 2% podophyllotoxin) is indicated for plantar warts.[11,13] In a 6-week randomized double-blind, placebo-controlled trial (RDBPCT), 36.2% of pediatric patients (ages 2 to 17 years old; n=94) diagnosed with MC achieved complete clearance when treated with 0.7% cantharidin solution vs. 10.6% with placebo (P= 0.0065).[14] However, a systematic review of topical cantharidin treatment for warts

Table 1. Integrative Treatments for Warts Only

Treatment	Potential Mechanism	Main Outcomes	Adverse Events
Sandalwood album oil (SAO)	Anti-inflammatory, antimicrobial, and antiproliferative properties	≥18 y.o.: dose-dependent response, where SAO 10%, 20%, and 30% achieved a 75% reduction of warts in 9.5%, 11.1%, and 18.6% of patients, respectively, with topical SAO[18]	In some cases, allergic contact dermatitis
Propolis	Anti-bacterial, antifungal, antiviral, and anti-inflammatory properties	≥18 y.o. (n=135): complete clearance of common warts (73%), flat warts (75%), and plantar warts (17%) with oral propolis[20]	In some cases, allergic reactions at high oral doses (>15 g/d)
Echinacea	Antiviral and immune modulating properties	≥18 y.o. (n=135): complete clearance of common warts (20%) and flat warts (36%) with oral Echinacea[20]	None reported
Zinc	Micronutrient for normal cell function with immune-modulating effects	In three separate trials evaluating oral zinc (≥4 y.o.; n=13; n=23; n=32), complete clearance (53.8%; 86.9%; 59.3%)[45–47] Topical zinc oxide (≥12 y.o.; n=16): complete clearance (50%)[50]	Oral: nausea, copper deficiency at high doses Topical: swelling, scaling
Garlic	Antiviral properties	≥9 y.o. (n=23): with an aqueous garlic extract topical, complete clearance (100%)[62]	In some cases, blistering contact dermatitis or chemical burns when in contact with healthy skin
Hypnosis	Direct suggestion that treatment will clear warts	≤13 y.o. (n=9): complete clearance (55.6%)[56] ≥18 y.o. (n=33): complete clearance (80%)[57]	None reported

Table 2. Integrative Treatments for Molluscum Only

Treatment	Potential Mechanism	Main Outcomes	Adverse Events
Backhousia citriodora	Anti-inflammatory, antimicrobial, and antiproliferative properties	≤6 y.o. (n=31): reduction in lesions by ≥90% or complete clearance (56.3%) with topical treatment[15]	In some cases, allergic contact dermatitis
Melaleuca alternifolia (Tea tree oil)	Anti-inflammatory, antimicrobial, and antiproliferative properties	<12 y.o. (n=53): (+organically bound iodine) reduction in lesions by ≤90% or complete clearance (84.2%) with topical treatment[16]	In some cases, allergic contact dermatitis

Table 3. Integrative Treatments for Both Warts & Molluscum

Treatment	Potential Mechanism	Main Outcomes	Adverse Events
Cantharidin	Inhibits protein phosphatase and induces vesiculation	2-17 y.o. (n=94): 36.2% achieved complete clearance with topical treatment (36.2%)[13] (+podophyllotoxin+salicylic acid), complete clearance of plantar warts (81-100%) with topical treatment[12]	Pain, blistering, and hyper-/hypopigmentation
Heat Therapy	Promote immune response by upregulating antiviral proteins and cytokines	Varies by regimen Targeted hyperthermic device (radiofrequency-generated heat): 6-59 y.o. (n=39); 9-41 y.o. (n=27); complete clearance of warts (53.6%-86%)[37,39,40] Controlled infrared device: 20-54 y.o. (n=2); 49 y.o. (n=1); ≥21 y.o. (n=13) complete clearance of warts (n=3, 100%);[42] complete clearance of molluscum (3-28 y.o.; n=21; 57%)[44]	In some skin types, scarring

and MC by Vakharia et al. suggests variable clearance rates ranging from 15.4 to 100% when treating MC with topical cantharidin. When topical cantharidin is used in combination with podophyllotoxin and salicylic acid, clearance rates improve to a range of 81-100%, with four studies noting 100% clearance.[13] Pain (7-85.7%), blistering (10-100%), and hyper-/hypopigmentation (1.8-53.3%) are the most common adverse effects of cantharidin treatment.[13] Notably, hyper-/hypopigmentation is common in patients with skin of color after both cantharidin and cryotherapy treatment, so this should be considered in patient care and counseling.[10] Despite its efficacy and safety, cantharidin has yet to receive FDA approval, but this may change in the near future with VP-102.

VP-102 is a drug-device combination that contains a Good Manufacturing Practice (GMP)-controlled formula-

tion of cantharidin (0.7% w/v) intended to treat common warts, external genital warts, and molluscum contagiosum. While it is currently under FDA evaluation, VP-102 has demonstrated potential in phase 2 and phase 3 clinical trials. In two identical phase 3 trials (CAMP-1 and CAMP-2; ≥ 2 years old, n=582), topical application of VP-102 or vehicle once every 21 days (for a maximum of 4 treatments) resulted in complete clearance of lesions by 46.3% (CAMP-1) and 54.0% (CAMP-2) of patients with VP-102 vs. 18% (CAMP-1) and 13% (CAMP-2) with placebo.[15] The most common adverse events included moderate application site vesicles (43.5% and 20.0% in the VP-102 and placebo groups, respectively), pain (28.0% and 9.3%), pruritus (11.2% and 3.3%), erythema (23% and 18.7%), and scabbing (9.9% and 7.3%).

ESSENTIAL OILS

Some essential oils, such as those from *Backhousia citriodora* (lemon myrtle), *Melaleuca alternifolia* (tea tree), and *Santalum album* (sandalwood), have demonstrated anti-inflammatory, anti-microbial, and anti-proliferative properties that make them appropriate candidates for topical treatment of warts and MC with potentially minimal side effects. In a 3-week randomized controlled trial (RCT), children (mean age 4.6 ± 2.1 years; n=31) with MC were treated with once daily topical application of 10% solution of essential oil of Australian lemon myrtle leaf (*B. citriodora*) or vehicle control (olive oil).[16] By day 21, complete clearance or reduction in lesions by at least 90% was achieved by 56.3% of patients treated with essential oil of *B. citriodora* vs. 0% in the control group ($P < 0.05$).[16] No adverse events were reported from this study. Although the essential oil of Australian lemon myrtle appears moderately efficacious and safe in treating MC, further work is needed to identify the active ingredient(s) responsible for these clinical effects.

Essential oils of *M. alternifolia* (tea tree essential oil) have also demonstrated potential for treating MC. In a 4-week RCT, children (mean age 6.3 + 5.1 years; n=53) with MC were treated with twice daily topical application of a combination of essential oil of *M. alternifolia* and organically bound iodine (TTO-I), essential oil of *M. alternifolia* (TTO) only, or iodine only.[17] By day 30, complete clearance or reduction in lesions by at least 90% was achieved by 84.2%, 16.7%, and 6.3% of patients treated with TTO-I, TTO, and iodine respectively ($P<0.01$).[17] Although no adverse events were observed in this study, tea tree essential oil can cause allergic contact dermatitis in some cases.[18]

Sandalwood album oil (SAO), also known as East Indian sandalwood oil (EASO) derived from the *S. album* tree, may be beneficial in treating multiple skin conditions such as acne, psoriasis, atopic dermatitis, common warts, and MC.[19] In a 12-week Phase 2 RDBPCT, adult patients (n=183) with common warts were treated with twice daily topical application of placebo, 10%, 20%, or 30% East Indian Sandalwood Oil (EISO). After 12 weeks, a reduction in warts by at least 75% was achieved by 9.5%, 11.1%, and 18.6% of patients treated with EISO 10%, 20%, 30%, respectively, vs. 4.7% of patients treated with placebo.[19,20] No adverse events were observed in this study.

ORAL PROPOLIS AND *ECHINACEA*

Propolis is a resinous material from bees and plant buds/exudates that has demonstrated anti-bacterial, anti-fungal, anti-viral, and anti-inflammatory properties, thereby improving natural resistance to infection.[21] When added to ointments, propolis has been suggested to promote healing of genital herpes lesions and reduce local symptoms.[21] Another immunomodulator with antiviral properties, *Echinacea* (purple coneflower), also holds potential for treating warts.[21] In a single-blind, randomized, 3-month trial, 135 patients with flat, plantar, or common warts were treated with 500 mg/day single oral dose of propolis, 600 mg/day oral *Echinacea purpurea*, or placebo.[21] Complete clearance of common warts, flat warts, and plantar warts was achieved by 73%, 75%, and 17% of patients, respectively, when treated with propolis, compared to 20%, 36%, and 0% of patients treated with *Echinacea purpurea*.[21] A significant difference was observed in the treatment of common and plantar warts by both propolis vs. *Echinacea* compared to placebo groups ($p<0.05$). More notably, by six months, none of the patients who achieved complete cure developed recurrent or new lesions.[21] Though this particular trial reported no adverse events, other studies have reported significant side effects such as allergic reactions and skin or mucous membrane irritations from propolis when given at doses greater than 15 g/day.[22] Caution should be taken with propolis when treating patients with asthma or eczema.[22] At lower doses, however, the side effects of propolis were limited to isolated cases of allergy and contact dermatitis.[23,24] In a separate RCT with adults and adolescents (n=172), the addition of nutraceutical oral supplementation (OS) with *Echinacea* to conventional standard therapy (CST) significantly reduced the number of warts at 6 months compared to CST alone.[25] Complete remission was achieved in 86% vs. 54.5% of patients given CST or CST+OS treatments, respectively ($P<0.001$).[25] No adverse events were observed in either trial nor with either medication. Furthermore, to the best of our knowledge, no English-language study has been published using propolis or *Echinacea purpurea* for MC.

HEAT THERAPY

While cryotherapy is a standard of care in wart and molluscum treatment, heat therapy, or hyperthermia, has also been widely used, albeit to a lesser degree. In a RCT of 52 adult patients, one hyperthermic treatment exhibited a higher clearance rate of warts when compared to cryotherapy; however, the result was not statistically significant. Notably, there was a higher rate of post-treatment scarring with hyperthermia, with all incidents occurring in patients with skin phototypes IV or V and forearm or hand dorsum warts.[26] In most cases, however, hyperthermia is advantageously non-destructive and can be delivered via a variety of treatment methods, including thermal water immersion, topical patches, and targeted devices.

The mechanism whereby elevated temperature may improve the clearance of warts or molluscum is still undetermined, although investigation has demonstrated multiple possibilities. Heat is thought to either inactivate or slow the

spread of HPV to adjacent tissue, allowing the skin's natural repair and shedding process to take place. Local hyperthermia has been shown in *in vitro* studies to lead to the upregulation of certain anti-viral proteins and cytokines, while downregulating those involved in cellular metabolism, protein translation, and keratinocyte differentiation.[27,28]

THERMAL WATER IMMERSION

Dating as far back as Greek mythology, the therapeutic benefits of thermal mineral water have been well-known around the world for centuries.[29] Balneotherapy (BT) refers to treating disease by bathing in thermal mineral water, generally with patient immersion in baths or pools, and has a long history of use in inflammatory skin and rheumatologic diseases.[30] When BT is combined with ultraviolet radiation phototherapy, augmenting the proposed anti-inflammatory effect, it is termed balneophototherapy (BPT). In the 1800s, BT first emerged as a treatment in Europe, soon followed by use in the United States.[31] Its use decreased in the 20th century as more pharmacologic treatments became available. However, over recent decades, renewed interest has emerged in BT as an alternative or complementary treatment option with minimal side effects.

Skin inflammation may be decreased by the qualities of thermal waters,[32] although there is a paucity of robust clinical evidence for BT and BPT. Treatment regimens lack standardized protocol, as factors including the chemical composition, hydrogeologic origin, duration of immersion, and temperature of thermal spring water used vary widely.[32,33] Such heterogeneity in regimens complicates the ability to extrapolate and generalize the efficacy of BT and BPT in dermatology, and thus far, no randomized, placebo-controlled trials have been conducted.

Thermal spa bathing for 3 days was associated with complete clearance of recalcitrant warts in an organ transplant patient in one case.[34] Warts are often recalcitrant in immunosuppressed patients, such as those with organ transplants, making BT/BPT an appealing option. However, when investigators attempted a study comparing thermal to hyperthermic tap water treatment between the right and left hand of five organ transplant patients with hand warts, no significant improvement in size or number of warts was noted after 12 sessions over one month. It was concluded that neither thermal spa nor hyperthermic tap water is effective in the treatment of resistant hand warts in organ transplant patients, while again noting that this cannot be generalized without testing thermal water from differing geographic sources.[34]

TARGETED HYPERTHERMIA

In addition to aqueous immersion, hyperthermic wart therapy has been effectively applied in multiple cases as a targeted treatment. This allows for greater localization of heat to the wart compared to aqueous submersion of a larger anatomic area. However, notable variability exists in methods. Hyperthermic sources included microwave, radiofrequency, and thermal patches; temperatures range from 40°C to more than 50°C; and timing protocol has varied from seconds to hours of administration.[35–38] Despite the inconsistencies in methodology, both adhesive epicutaneous patches and patented hyperthermic devices have demonstrated efficacy in multiple studies.

TOPICAL HEAT PATCHES

Exothermic patches deliver lasting and continuous heat over a period of time, and can be placed and managed by the patient. The self-administered design is very convenient and cost-effective for patients, necessitating fewer medical visits and expenses. Patients with recalcitrant warts experienced clearance of warts with such patches for at least 2 hours daily over 4-6 weeks at a safe temperature of 42-43ºC in five reported cases.[36,39]

TARGETED DEVICES

Targeted hyperthermic devices use radiofrequency-generated heat, with some designs making direct contact with the skin and others acting locally without direct contact. Subjects should experience a tolerable sensation of burning or some pain, with tolerance being generally higher on the feet.[40] Older devices were often used with local lidocaine anesthesia,[38] while in more recent studies, effective temperatures were titrated to subject tolerability without anesthesia. Multi-subject studies over 3 months using such devices reported resolution of warts in 53.6% to 86%, compared to 11.5% and 41% of controls in these studies, respectively.[38,40,41] All patients remained clear of warts at later follow-up. Patients with load-bearing pain secondary to plantar warts also experienced benefit from localized hyperthermia, with 80% reporting decreased pain by 3 months.[42]

Regular local hyperthermia for 30 minutes at 44°C delivered with a controllable infrared device has also been used successfully for the treatment of disfiguring facial warts and extensive flat warts. Two cases of facial common warts successfully resolved in 10 and 12 weeks after treatment once a day for three consecutive days, and a repeat session two consecutive days a week later.[43] In a case report of multiple warts present for over one year, lesions completely cleared over 2 months of treatment, with initial regression evident within the first week of treatment. The patient had no recurrence at 15 months of follow-up.[44] Molluscum also has been demonstrated to respond to targeted hyperthermia although no data were found regarding other types of heat therapy for molluscum. Infrared device treatment at 44ºC for 30 minutes once a week led to total clearance of MC lesions in 57% of 21 patients ranging from ages 3 - 28 years old by 12 weeks, with no recurrence at 3 month follow-up.[45]

ORAL AND TOPICAL ZINC

Zinc, a micronutrient required for normal cell functioning, is commonly used as a treatment for a variety of medical illnesses due to its immune-modulating effects and lack of serious complications. As a wart treatment, zinc has shown positive results in several clinical trials, although its efficacy has not been well-established.

A treatment regimen commonly used in published studies for oral zinc is 10 mg/kg (maximum dosage 600 mg)

for 1-2 months. In patients with or without signs or symptoms of zinc deficiency, this regimen in three separate studies demonstrated improved wart regression to be associated with a rise in serum zinc levels.[46–48] Patients in studies with long-term follow-up were observed to remain wart-free at 6-month follow-up in multiple studies.[47,49] The most notable side effect was nausea, with between 16-100% of zinc-treated patients reporting nausea,[48–50] occasionally significant enough to cause patient drop-out. Oral zinc may be a promising wart treatment, particularly for stubborn warts in children due to its painless and self-administered nature. However, nausea may limit its practice use. For this reason, oral zinc administration can be divided into three separate doses throughout the day with meals to ameliorate nausea.[50]

Zinc has also been used topically for warts, circumventing the side effect of nausea. In a randomized, double-blind controlled trial of 44 patients, 50% of patients treated with topical zinc oxide 20% ointment experienced complete cure of warts within three months, compared to 42% of controls, without any noteworthy side effects.[51]

Zinc, both oral or topical, is a cost-effective and relatively safe treatment, yet additional robust research is necessary to further evaluate its use in wart therapy. A 2021 systematic review reported that zinc therapy was found to be effective in 13 of 16 evaluated studies; six of these investigated isolated oral zinc supplementation, two explored oral zinc as an adjuvant therapy, five looked at intralesional zinc sulfate, and three examined topical zinc treatment.[52] Overall, zinc holds its appeal as a wart treatment. Importantly, however, long-term ingestion of high-dose zinc may lead to copper deficiency and copper co-administrated should be considered in long-term use.[53] To the best of our knowledge, no English-language study has been published using zinc for MC.

HYPNOSIS

Using hypnosis as a treatment method for warts dates back to the 1940's.[54,55] Over the years, multiple case reports and series have been published supporting a potential role for psychotherapy and hypnosis in the treatment of viral warts, particularly in children.[56,57] In one case series, nine children under the age of 13 with warts on the hands, feet, and/or face were treated with simulated x-ray sessions.[57] Patients were placed in front of an x-ray tube and the cooling unit was turned on but no voltage was set and thus no x-rays were produced. Parents were informed of the harmless nature of the treatment. Experimenters suggested to the patients that the x-rays would work on their warts and that they may feel a warmness in and around the wart later. Each "radiation" lasted 1 minute and therapy was repeated every 1-3 weeks. Five of the patients completely cleared their warts and three of them partially cleared them after an average of three treatment sessions. This is an example of a direct suggestion in hypnosis, in which a patient is told that they will feel a certain way. It has been suggested that children will almost always respond to direct suggestion in hypnosis, whereas adults will not.[58]

Hypnoanalysis, in which hypnosis is incorporated into psychoanalysis and psychotherapy, may work better for teens and adults.[56,58] One case report found that five treatment sessions of psychotherapy with hypnosis spanning over seven weeks completely cleared a wart on the hand of a 16-year-old girl.[56] The therapy focused on guided imagery and suggestions for optimizing the patient's immune system. Another case series of 41 adults with warts found that 33 participants (80%) were cured with hypnoanalysis.[58] Considering that warts may spontaneously resolve, it can be difficult to prove the true efficacy of hypnosis. However, since it is safe and noninvasive, hypnosis could be considered as an additional therapy for warts, particularly in children who may be more susceptible to suggestion. To the best of our knowledge, no English-language study has been published using hypnosis in the treatment of MC.

GARLIC

Garlic has been used to treat warts in traditional Chinese medicine[59] and has demonstrated *in vitro* antiviral properties.[60,61] In a case series of five children, garlic was demonstrated to be an effective treatment method for palmar warts.[62] Parents were instructed to rub the cut surface of a raw garlic clove onto their child's wart, then cover with a bandage or waterproof tape overnight. All five children experienced clearing of their wart with improvement seen at an average of 3.2 weeks and complete clearance seen at an average of 9 weeks. One child reported itching, but the therapy was otherwise well-tolerated. In a larger study of both children and adults, 28 patients with 2–96 warts, nine patients with 1–2 corns, and a control group of five patients with 7–35 warts were treated with twice-daily aqueous garlic extract, lipid garlic extract, or a control solution.[63] Authors found the lipid garlic extract to be more effective than the aqueous garlic extract, with near-complete clearance being achieved in all patients after 1-2 weeks of treatment with the lipid garlic extract versus only partial clearance after a treatment period of over 2 months in those applying aqueous garlic extract. No participant in the control group demonstrated any signs of clearance.

Patients using garlic therapy for warts should be counseled to avoid placing garlic on the healthy surrounding skin because garlic can cause a blistering contact dermatitis and chemical burns.[64,65] To prevent such reactions, patients can coat the area around the warts with zinc oxide paste to protect the surrounding skin.[63] If counseled on correct application, garlic offers a safe and cost-effective alternative therapy for the treatment of warts. To the best of our knowledge, garlic has not been explored in the literature as a treatment for MC.

SPECIAL CONSIDERATIONS IN TREATMENT

Wart or molluscum treatment in certain populations such as children, pregnant patients, and those with diabetes mellitus can present additional challenges. Children tend to have significantly lower thresholds for pain and discomfort, making standard treatments such cryotherapy, laser, or surgical removal particularly challenging - especially for warts located in the genitalia or other sensitive areas. These same three treatment modalities are generally contraindicated for genital warts in pregnancy. In diabetes mellitus, defec-

tive immune responses lead to more extensive and persistent warts.

Multiple studies suggest that oral zinc may be an effective, safe, and painless wart treatment for children.[46,47,49,50] Essential oils are also promising areas of investigation for painless molluscum treatment in children.[12,13] Local hyperthermia has been successfully used to treat perianal and genital warts in both children and pregnant women in case reports, as a much more comfortable and less risky treatment option.[66,67] In patients with diabetes, local hyperthermia also appears promising as a safe and effective treatment modality, with complete clearance within about 1-2 months in a case report.[68]

CONCLUSION

Despite the prevalence of warts and MC, no evidence-based treatment guidelines currently exist. As a result, some patients may turn to complementary and alternative therapies for relief. Promising data exists for many modalities of such integrative therapies. Cantharidin; essential oils such as those from *Backhousia citriodora*, *Melaleuca alternifolia*, and *Santalum album;* propolis; *Echinacea;* heat therapy; garlic; and zinc are examples of treatments with proposed anti-inflammatory, anti-proliferative, and/or immune-modulating effects that assist in clearing warts and MC. For children who tend to be more vulnerable to suggestion, hypnosis can be attempted as an alternative wart therapy. While additional research is required to understand the mechanism and true efficacy, the integrative therapies reviewed herein offer practical and relatively safe alternatives for the treatment of warts and MC.

CONFLICTS OF INTEREST

Dr. Lio reports research grants/funding from AOBiome, Regeneron/Sanofi Genzyme, and AbbVie; is on the speaker's bureau for Regeneron/Sanofi Genzyme, Pfizer, Incyte, Eli Lilly, LEO, Galderma, and L'Oreal; reports consulting/advisory boards for Almirall, ASLAN Pharmaceuticals, Bristol-Meyers, UCB, Dermavant, Regeneron/Sanofi Genzyme, Merck, Pfizer, LEO Pharmaceuticals, AbbVie, Eli Lilly, L'Oreal, Pierre-Fabre, Johnson & Johnson, Menlo Therapeutics, IntraDerm, Exeltis, AOBiome, Realm Therapeutics, Galderma, and Verrica.

The other authors report no conflict of interest.

FUNDING SOURCES

No funding sources were secured for this study.

Submitted: March 30, 2022 PDT, Accepted: May 31, 2022 PDT

REFERENCES

1. Chen X, Anstey AV, Bugert JJ. Molluscum contagiosum virus infection. *Lancet Infect Dis*. 2013;13(10):877-888. doi:10.1016/s1473-3099(13)70109-9

2. Meza-Romero R, Navarrete-Dechent C, Downey C. Molluscum contagiosum: an update and review of new perspectives in etiology, diagnosis, and treatment. *Clin Cosmet Investig Dermatol*. 2019;12:373-381. doi:10.2147/ccid.s187224

3. Olsen JR, Gallacher J, Finlay AY, Piguet V, Francis NA. Time to resolution and effect on quality of life of molluscum contagiosum in children in the UK: a prospective community cohort study. *Lancet Infect Dis*. 2015;15(2):190-195. doi:10.1016/s1473-3099(14)71053-9

4. Basdag H, Rainer BM, Cohen BA. Molluscum contagiosum: to treat or not to treat? Experience with 170 children in an outpatient clinic setting in the northeastern United States. *Pediatr Dermatol*. 2015;32(3):353-357. doi:10.1111/pde.12504

5. Phan S, Wyant C, Huynh C, Joaquin C, Hassan O. Efficacy of topical treatments for molluscum contagiosum in randomized controlled trials. *Clin Dermatol*. 2021;39(6):1005-1013. doi:10.1016/j.clindermatol.2021.07.002

6. Stulberg DL, Hutchinson AG. Molluscum contagiosum and warts. *Am Fam Physician*. 2003;67(6):1233-1240.

7. Leung AKC, Barankin B. Molluscum contagiosum: an update. *IAD*. 2017;11(1). doi:10.2174/1872213x11666170518114456

8. Al Aboud AM, Nigam PK. Wart. In: *StatPearls*. StatPearls Publishing; 2021.

9. Lio P. Warts, molluscum and things that go bump on the skin: a practical guide. *Arch Dis Child Educ Pract Ed*. 2007;92(4):ep119-124. doi:10.1136/adc.2007.122317

10. Eichenfield L, Hebert A, Mancini A, Rosen T, Weiss J. Therapeutic Approaches and Special Considerations for Treating Molluscum Contagiosum. *J Drugs Dermatol*. 2021;20(11):1185-1190. doi:10.36849/jdd.6383

11. Al-Dawsari NA, Masterpol KS. Cantharidin in Dermatology. *Skinmed*. 2016;14(2):111-114.

12. Silverberg NB, Sidbury R, Mancini AJ. Childhood molluscum contagiosum: experience with cantharidin therapy in 300 patients. *J Am Acad Dermatol*. 2000;43(3):503-507. doi:10.1067/mjd.2000.106370

13. Vakharia PP, Chopra R, Silverberg NB, Silverberg JI. Efficacy and Safety of Topical Cantharidin Treatment for Molluscum Contagiosum and Warts: A Systematic Review. *Am J Clin Dermatol*. 2018;19(6):791-803. doi:10.1007/s40257-018-0375-4

14. Guzman AK, Schairer DO, Garelik JL, Cohen SR. Safety and efficacy of topical cantharidin for the treatment of pediatric molluscum contagiosum: a prospective, randomized, double-blind, placebo-controlled pilot trial. *Int J Dermatol*. 2018;57(8):1001-1006. doi:10.1111/ijd.14079

15. Eichenfield LF, McFalda W, Brabec B, et al. Safety and Efficacy of VP-102, a Proprietary, Drug-Device Combination Product Containing Cantharidin, 0.7% (w/v), in Children and Adults With Molluscum Contagiosum: Two Phase 3 Randomized Clinical Trials. *JAMA Dermatol*. 2020;156(12):1315. doi:10.1001/jamadermatol.2020.3238

16. Burke BE, Baillie JE, Olson RD. Essential oil of Australian lemon myrtle (Backhousia citriodora) in the treatment of molluscum contagiosum in children. *Biomed Pharmacother*. 2004;58(4):245-247. doi:10.1016/j.biopha.2003.11.006

17. Markum E, Baillie J. Combination of essential oil of Melaleuca alternifolia and iodine in the treatment of molluscum contagiosum in children. *J Drugs Dermatol*. 2012;11(3):349-354.

18. de Groot AC, Schmidt E. Tea tree oil: contact allergy and chemical composition. *Contact Dermatitis*. 2016;75(3):129-143. doi:10.1111/cod.12591

19. Moy RL, Levenson C. Sandalwood Album Oil as a Botanical Therapeutic in Dermatology. *J Clin Aesthet Dermatol*. 2017;10(10):34-39.

20. A Trial of a Botanical Drug Containing East Indian Sandalwood Oil (EISO) for Treatment of Common Warts. Accessed February 2, 2022. https://clinicaltrials.gov/ct2/show/study/NCT01286441

21. Zedan H, Hofny ERM, Ismail SA. Propolis as an alternative treatment for cutaneous warts. *Int J Dermatol*. 2009;48(11):1246-1249. doi:10.1111/j.1365-4632.2009.04184.x

22. Castaldo S, Capasso F. Propolis, an old remedy used in modern medicine. *Fitoterapia*. 2002;73:S1-S6. doi:10.1016/s0367-326x(02)00185-5

23. Silvani S, Spettoli E, Stacul F, Tosti A. Contact dermatitis in psoriasis due to propolis. *Contact Dermatitis*. 1997;37(1):48-49. doi:10.1111/j.1600-0536.1997.tb00387.x

24. Callejo A, Armentia A, Lombardero M, Asensio T. Propolis, a new bee-related allergen. *Allergy*. 2001;56(6):579. doi:10.1034/j.1398-9995.2001.056006579.x

25. Cassano N, Ferrari A, Fai D, et al. Oral supplementation with a nutraceutical containing Echinacea, methionine and antioxidant/immunostimulating compounds in patients with cutaneous viral warts. *G Ital Dermatol Venereol*. 2011;146(3):191-195.

26. Izadi Firouzabadi L, Khamesipour A, Ghandi N, Hosseini H, Teymourpour A, Firooz A. Comparison of clinical efficacy and safety of thermotherapy versus cryotherapy in treatment of skin warts: A randomized controlled trial. *Dermatol Ther*. 2018;31(1). doi:10.1111/dth.12564

27. Sun YZ, Li JF, Wei ZD, et al. Proteomic and bioinformatic analysis of condyloma acuminata: mild hyperthermia treatment reveals compromised HPV infectivity of keratinocytes via regulation of metabolism, differentiation and anti-viral responses. *Int J Hyperthermia*. 2019;36(1):383-393. doi:10.1080/02656736.2019.1578420

28. Yang Y, Wang H, Zhang X, et al. Heat Increases the Editing Efficiency of Human Papillomavirus E2 Gene by Inducing Upregulation of APOBEC3A and 3G. *J Invest Dermatol*. 2017;137(4):810-818. doi:10.1016/j.jid.2016.06.635

29. Jackson R. Waters and spas in the classical world. *Med Hist Suppl*. 1990;34(10):1-13. doi:10.1017/s0025727300070952

30. Huang A, Seité S, Adar T. The use of balneotherapy in dermatology. *Clin Dermatol*. 2018;36(3):363-368. doi:10.1016/j.clindermatol.2018.03.010

31. Benedetto AV, Millikan LE. Mineral water and spas in the United States. *Clin Dermatol*. 1996;14(6):583-600. doi:10.1016/s0738-081x(96)00089-2

32. Matz H, Orion E, Wolf R. Balneotherapy in dermatology. *Dermatol Ther*. 2003;16(2):132-140. doi:10.1046/j.1529-8019.2003.01622.x

33. Seite S. Thermal waters as cosmeceuticals: La Roche-Posay thermal spring water example. *Clin Cosmet Investig Dermatol*. 2013;6:23-28. doi:10.2147/ccid.s39082

34. Güleç AT. Natural thermal spa water versus hyperthermic tap water for treatment of recalcitrant hand warts in organ transplant recipients: A patient-blinded, comparative preliminary study. *Exp Clin Transplant*. 2018;16 Suppl 1(Suppl 1):189-193.

35. Pfau A, Abd-el-Raheem TA, Bäumler W, Hohenleutner U, Landthaler M. Nd:YAG laser hyperthermia in the treatment of recalcitrant verrucae vulgares (Regensburg's technique). *Acta Derm Venereol*. 1994;74(3):212-214.

36. Dvoretzky I. Hyperthermia therapy for warts utilizing a self-administered exothermic patch. Review of two cases. *Dermatol Surg*. 1996;22(12):1035-1038; discussion 1038-9. doi:10.1111/j.1524-4725.1996.tb00657.x

37. El-Tonsy MH, Anbar TED, El-Domyati M, Barakat M. Density of viral particles in pre and post Nd: YAG laser hyperthermia therapy and cryotherapy in plantar warts. *Int J Dermatol*. 1999;38(5):393-398. doi:10.1046/j.1365-4362.1999.00719.x

38. Stern P, Levine N. Controlled localized heat therapy in cutaneous warts. *Arch Dermatol*. 1992;128(7):945-948. doi:10.1001/archderm.1992.01680170077010

39. Schuller-Levis G, Levis W, Dvoretzky I. Treatment of recalcitrant warts with occlusive warming patches. *J Drugs Dermatol*. 2014;13(10):1194-1196.

40. Gao XH, Gao D, Sun XP, et al. Non-ablative controlled local hyperthermia for common warts. *Chin Med J*. 2009;122(17):2061-2063.

41. Huo W, Gao XH, Sun XP, et al. Local hyperthermia at 44 C for the treatment of plantar warts: a randomized, patient-blinded, placebo-controlled trial. *J Infect Dis*. 2010;201(8):1169-1172. doi:10.1086/651506

42. Huo W, Gao XH, Sun XP, et al. Local Hyperthermia at 44°C for the Treatment of Plantar Warts: A Randomized, Patient-Blinded, Placebo-Controlled Trial. *J Infect Dis*. 2010;201(8):1169-1172. doi:10.1086/651506

43. Ma Y, Huo W, Hong YX, Chen HD, Gao XH. Successful clearance of facial common warts by local hyperthermia: report of two cases. *Dermatol Ther*. 2012;25(4):386-388. doi:10.1111/j.1529-8019.2012.01470.x

44. Chen JL, Zheng S, Yang Y, Gao XH, Qi RQ, Chen HD. Successful treatment of extensive flat warts with local hyperthermia: A case report. *Dermatol Ther*. 2020;33(6):e14525. doi:10.1111/dth.14525

45. Gao YL, Gao XH, Qi RQ, et al. Clinical evaluation of local hyperthermia at 44 °C for molluscum contagiosum: pilot study with 21 patients. *Br J Dermatol*. 2017;176(3):809-812. doi:10.1111/bjd.14849

46. Sadighha A. Oral zinc sulphate in recalcitrant multiple viral warts: a pilot study. *J Eur Acad Dermatol Venereol*. 2009;23(6):715-716. doi:10.1111/j.1468-3083.2009.03169.x

47. Yaghoobi R, Sadighha A, Baktash D. Evaluation of oral zinc sulfate effect on recalcitrant multiple viral warts: a randomized placebo-controlled clinical trial. *J Am Acad Dermatol*. 2009;60(4):706-708. doi:10.1016/j.jaad.2008.09.010

48. Al-Gurairi FT, Al-Waiz M, Sharquie KE. Oral zinc sulphate in the treatment of recalcitrant viral warts: randomized placebo-controlled clinical trial. *Br J Dermatol*. 2002;146(3):423-431. doi:10.1046/j.1365-2133.2002.04617.x

49. Mun JH, Kim SH, Jung DS, et al. Oral zinc sulfate treatment for viral warts: an open-label study. *J Dermatol*. 2011;38(6):541-545. doi:10.1111/j.1346-8138.2010.01056.x

50. Stefani M, Bottino G, Fontenelle E, Azulay DR. Efficacy comparison between cimetidine and zinc sulphate in the treatment of multiple and recalcitrant warts. *An Bras Dermatol*. 2009;84(1):23-29. doi:10.1590/s0365-05962009000100003

51. Khattar JA, Musharrafieh UM, Tamim H, Hamadeh GN. Topical zinc oxide vs. salicylic acid-lactic acid combination in the treatment of warts. *Int J Dermatol*. 2007;46(4):427-430. doi:10.1111/j.1365-4632.2006.03138.x

52. Song D, Pan L, Zhang M, Wang S. Clinical use of zinc in viral warts: a systematic review of the clinical trials. *J Dermatolog Treat*. Published online June 16, 2021:1-23. doi:10.1080/09546634.2021.1942420

53. Duncan A, Yacoubian C, Watson N, Morrison I. The risk of copper deficiency in patients prescribed zinc supplements. *J Clin Pathol*. 2015;68(9):723-725. doi:10.1136/jclinpath-2014-202837

54. Vollmer H. Treatment of warts by suggestion. *Psychosom Med*. 1946;8(2):138-142. doi:10.1097/00006842-194603000-00011

55. McDOWELL M. Juvenile warts removed with the use of hypnotic suggestion. *Bull Menninger Clin*. 1949;13(4):124-126.

56. Phoenix SL. Psychotherapeutic intervention for numerous and large viral warts with adjunctive hypnosis: a case study. *Am J Clin Hypn*. 2007;49(3):211-218. doi:10.1080/00029157.2007.10401583

57. Meineke V, Reichrath J, Reinhold U, Tilgen W. Verrucae vulgares in children: successful simulated X-ray treatment (a suggestion-based therapy). *Dermatology*. 2002;204(4):287-289. doi:10.1159/000063360

58. Ewin DM. Hypnotherapy for warts (verruca vulgaris): 41 consecutive cases with 33 cures. *Am J Clin Hypn*. 1992;35(1):1-10. doi:10.1080/00029157.1992.10402977

59. Zhang S, Zhang M, Xing Y, Zhao L, Wang J. Treatment of 119 cases of verruca vulgaris and verruca plana by external application of pulvis pepper alba. *J Tradit Chin Med*. 1996;16(2):127-128.

60. Guo NL, Lu DP, Woods GL, et al. Demonstration of the anti-viral activity of garlic extract against human cytomegalovirus in vitro. *Chin Med J*. 1993;106(2):93-96.

61. Tsai Y, Cole LL, Davis LE, Lockwood SJ, Simmons V, Wild GC. Antiviral properties of garlic: in vitro effects on influenza B, herpes simplex and coxsackie viruses. *Planta Med*. 1985;51(5):460-461. doi:10.1055/s-2007-969553

62. Silverberg NB. Garlic cloves for verruca vulgaris. *Pediatr Dermatol*. 2002;19(2):183. doi:10.1046/j.1525-1470.2002.00038.x

63. Dehghani F, Merat A, Panjehshahin MR, Handjani F. Healing effect of garlic extract on warts and corns. *Int J Dermatol*. 2005;44(7):612-615. doi:10.1111/j.1365-4632.2004.02348.x

64. Rafaat M, Leung AK. Garlic burns. *Pediatr Dermatol*. 2000;17(6):475-476. doi:10.1046/j.1525-1470.2000.01828.x

65. Filobbos G, Chapman T, Gesakis K. Iatrogenic burns from garlic. *J Burn Care Res*. 2012;33(1):e21. doi:10.1097/bcr.0b013e3182335a29

66. Huo W, Di ZH, Xiao BH, Qi RQ, Weiland M, Gao XH. Clearance of genital warts in pregnant women by mild local hyperthermia: a pilot report. *Dermatol Ther*. 2014;27(2):109-112. doi:10.1111/dth.12066

67. He CC, Sun YZ, Qi RQ. Successful treatment of perianal warts in children with local hyperthermia: A case report. *Dermatol Ther*. 2020;33(4):e13634. doi:10.1111/dth.13634

68. Huo W, Li GH, Qi RQ, et al. Clinical and immunologic results of local hyperthermia at 44 °C for extensive genital warts in patients with diabetes mellitus. *Int J Hyperthermia*. 2013;29(1):17-20. doi:10.3109/02656736.2012.758874