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Warts Removal Gel By Keratolytic Agents: A Comprehensive Review Of Mechanism, Efficacy, And Safety Of Salicylic Acid And Lactic Acid

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ABSTRACT

Warts, or *verrucae*, are benign epidermal proliferations caused by the Human Papillomavirus (HPV) and are one of the most common dermatological conditions globally. This review examines the use of topical gels and solutions containing the keratolytic agents **salicylic acid (SA)** and **lactic acid (LA)** for the removal of warts, focusing on their mechanisms, clinical efficacy, and safety profile. Keratolytic therapy, particularly with SA, is widely considered the **first-line, over-the-counter (OTC) treatment** for common and plantar warts due to its low cost, ease of self-application, and favorable safety record. The combination of SA and LA enhances the destructive and desquamative effect on the hyperkeratotic tissue, leading to the gradual elimination of the virus-infected epidermis. Comparative clinical trials suggest that topical SA formulations offer an efficacy comparable to, or in some cases superior to, more invasive treatments like cryotherapy, particularly for common warts. This review synthesizes data from approximately 70 authentic sources to provide a detailed, evidence-based overview of this foundational treatment modality.

I. INTRODUCTION

A. History Of Warts and Etiology

Warts are common cutaneous lesions resulting from infection of the skin or mucous membranes by the **Human Papillomavirus (HPV)**. The infection causes unregulated proliferation of epidermal cells, leading to the characteristic rough, hyperkeratotic appearance of the lesions. The prevalence of warts in the general population is estimated to be between 7–12%, affecting hands and feet most frequently, though they can occur at any site. Although up to two-thirds of warts may resolve spontaneously within two years, patients frequently seek treatment due to pain, cosmetic concerns, and the risk of transmission.

B. Classification of Warts

Warts are broadly classified based on their location and morphology, which often dictates the appropriate treatment strategy:

1. **Verruca Vulgaris (Common Warts):** Firm, rough papules, most common on the hands, knees, and elbows.
2. **Verruca Plantaris (Plantar Warts):** Warts on the soles of the feet, often flat or growing inward due to pressure, and can be painful.
3. **Verruca Plana (Flat Warts):** Smooth, flesh-colored or light brown flat lesions, often found in clusters on the face, neck, and extremities.
4. **Filiform Warts:** Long, thin, finger-like projections, commonly found on the face or eyelids.

C. Purpose and Scope of the Review

The **Purpose** of this review is to provide an in-depth, evidence-based analysis of topical gels and solutions utilizing **salicylic acid (SA) and lactic acid (LA)** as keratolytic agents for wart removal.

The **Scope** is limited to a detailed examination of:

1. The specific biochemical mechanisms of SA and LA in wart destruction.
2. The compiled clinical efficacy data (cure rates) for SA/LA formulations compared to placebo and other destructive methods (e.g., cryotherapy).
3. Dosage, application regimen, and the associated safety and contraindication profiles.

II. KERATOLYTIC AGENTS: MECHANISM AND PROFILE

A. Mechanism of Action

Keratolytic agents function by promoting the softening and separation of the horny outer layer of the skin (stratum corneum). The **keratolytic gel** formulation, often incorporating a **collodion base** to form a water-resistant film, ensures prolonged contact of the active ingredients with the hyperkeratotic wart tissue.

B. Salicylic Acid (SA) Profile

Salicylic acid (SA) is a **beta-hydroxy acid (BHA)** and the cornerstone of keratolytic wart removal. Its mechanism is two-fold:

1. **Keratolysis and Desmolysis:** SA dissolves the intercellular cementing substance, a protein called **keratin**, which forms the bulk of the wart's hard skin. It acts as a desmolytic agent by weakening the attachments (corneodesmosomes) between the epidermal cells, causing the skin cells to shed more easily and unclogging pores.
2. **Immune Stimulation:** The mild irritation and inflammation caused by the acid application are thought to trigger a localized **immune response**, encouraging the body's immune system to recognize and attack the HPV-infected cells.

C. Lactic Acid (LA) Profile

Lactic acid (LA) is an **alpha-hydroxy acid (AHA)** that works synergistically with salicylic acid.

1. **Enhanced Keratolysis:** LA further breaks down the skin's surface and increases the **hydration** of the stratum corneum, allowing the SA to penetrate more effectively.
2. **Collodion Base Synergy:** The liquid formulation often uses a flexible collodion vehicle (a solution of pyroxylin in ether and alcohol), which forms a protective, occlusive, water-resistant film. This film keeps the active ingredients in contact with the wart, enhancing their penetration and efficacy.

D. Synergistic Effects of the Combination

The combination of SA (e.g., 16.7%) and LA (e.g., 16.7%) in a collodion base is highly effective because:

1. **Deeper Penetration:** The initial breakdown by LA and the hydrating effect allows the lipid-soluble SA to penetrate the waxy lipids of the skin more deeply into the infected tissue.
2. **Controlled Destruction:** The continuous, localized chemical destruction of the epithelial layer slowly eliminates the virus-infected cells while minimizing damage to the surrounding healthy tissue, making it a safe method for self-application.

III. CLINICAL EFFICACY AND COMPARATIVE STUDIES

A. Efficacy in Verruca Vulgaris (Common Warts)

Salicylic acid remains the most documented topical agent for common warts.

1. **Meta-Analytic Evidence:** A Cochrane systematic review, pooling data from six randomized controlled trials (RCTs), demonstrated that topical SA was **significantly more effective than placebo** for cutaneous non-genital warts at all sites. The pooled cure rate was reported to be around **75%** in the SA-treated group compared to **48%** in the control (placebo) group.
2. **Standard of Care:** Because of its consistent efficacy, minimal adverse effects, and low cost, SA in concentrations ranging from 5% to 60% (gel, solution, or plaster) is widely recommended as the **first-line therapy** for common warts.

B. Efficacy in Verruca Plantaris (Plantar Warts)

Plantar warts often present a treatment challenge due to the thickness of the stratum corneum and inward growth from pressure.

1. **Comparative Trials:** While the efficacy of SA for plantar warts is considered comparable to cryotherapy in many studies, cure rates for plantar warts can be lower than those for common warts.
2. **Trial Data:** One RCT comparing 50% Salicylic Acid self-treatment with cryotherapy for plantar warts found **no evidence of a significant difference in complete clearance** at 12 weeks (SA: 14% vs. Cryotherapy: 14%). However, another study noted cure rates of 66.7% for cryotherapy versus 80% for 40% Salicylic Acid in plantar warts. This variability highlights the importance of patient compliance and correct application.

C. Comparison with Cryotherapy

Cryotherapy (freezing the wart with liquid nitrogen) and topical SA are the two most common first-line treatments. Head-to-head trials often show parity, especially for plantar warts.

Treatment Modality	Average Cure Rate (Range)	Advantages	Disadvantages
Salicylic Acid (Topical)	≈61% (40-84%)	Inexpensive, OTC, self-applied, minimal pain, no scarring	Requires long treatment duration (weeks/months), patient compliance
Cryotherapy (Liquid Nitrogen)	≈45.6% (30-70%)	Administered in-office, fewer sessions needed	Painful, blistering, scarring risk, higher cost per cured patient

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D. Comparison with Other Topical Agents

Keratolytic agents are often the standard against which other destructive and immune-modulating therapies are measured.

Agent	Mechanism	Key Comparison Data
Cantharidin	Vesicant (causes blister formation)	Often used in combination with SA (e.g., Cantharidin-Podophyllin-SA formula, with high reported cure rates up to 97.8%).
Imiquimod	Immune response modifier	Used for genital warts, but also effective for flat warts by stimulating T-cell immunity. Longer clearance time.
Podophyllotoxin	Antimitotic (inhibits cell proliferation)	Effective for genital warts, with clearance rates of 36–83%. Systemic side effects possible.

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IV. SAFETY PROFILE, DOSAGE, AND ADMINISTRATION

A. Dosage and Administration Regimen

Successful treatment relies heavily on the correct application technique and adherence to the regimen.

1. **Preparation:** The wart should be soaked in warm water for 5 to 10 minutes to soften the keratin. The hardened, dead surface tissue should then be gently filed down using a pumice stone or emery board before application.
2. **Application:** The keratolytic solution (typically 10% to 27% SA in a collodion base) is applied directly to the wart, taking care to avoid contact with the surrounding healthy skin. The area is then often covered with a non-porous bandage or duct tape to maintain an occlusive environment and enhance penetration.
3. **Duration:** Treatment is typically applied **daily** and continued for an average of **8 to 12 weeks**, or until the wart is completely removed and the normal skin lines are restored. Treatment may be continued for up to 3–6 months for recalcitrant warts.

B. Adverse Effects

The side effects of topical SA and LA are generally localized and mild.

1. **Common Local Side Effects:**
   - Skin irritation, redness (*erythema*), or itching.
   - Burning or stinging sensation upon application.
   - Localized peeling (*desquamation*) and dryness.
2. **Rare Systemic Effects (Salicylism):** Systemic absorption, leading to salicylate toxicity (salicylism), is rare but possible, especially when applied to very large areas, broken skin, or in patients with poor renal/hepatic function. Symptoms include confusion, dizziness, ringing in the ears (*tinnitus*), and rapid breathing.

C. Contraindications and Precautions

To ensure safety, specific patient populations and wart types should avoid this treatment.

1. **Medical Conditions:**
   - **Diabetes Mellitus:** Due to the risk of nerve damage (neuropathy) and poor circulation, which can impair healing and lead to severe ulceration or infection, especially on the feet.
   - **Poor Blood Circulation** or peripheral vascular disease.
2. **Specific Wart Types and Areas:**
   - Warts on the **face, genitals, moles, birthmarks, or warts with hair growing from them**.
   - Areas of **broken, irritated, infected, or inflamed skin**.
3. **Pediatric Concerns:** Salicylic acid should not be used in children or teenagers who have the **flu or chickenpox** due to the potential, though very low, risk of developing **Reye's syndrome**.

V. FUTURE PERSPECTIVES AND CONCLUSION

A. Future Perspectives

Future research should focus on optimizing combination therapies and delivery systems. Advancements include:

1. **Enhanced Delivery:** Developing microencapsulated or transfersomal gel systems to improve penetration of keratolytic agents into the deeper epidermal layers while minimizing irritation.
2. **Combination with Immunotherapy:** Exploring the synergistic effect of combining chemical destruction with topical immunomodulators (e.g., 5-Fluorouracil or Imiquimod) for recalcitrant warts.
3. **Cost-Effectiveness Studies:** Given the high cost associated with physical methods, more large-scale RCTs are needed to confirm the long-term cost-effectiveness and sustained cure rates of keratolytic agents versus cryotherapy and laser therapies.

B. Conclusion

The topical application of **keratolytic gels containing salicylic acid and lactic acid** remains a gold-standard, first-line, and self-applicable treatment for common and plantar warts. Its mechanism—the dual action of chemical debridement by Salicylic Acid and synergistic enhancement by Lactic Acid—makes it highly effective and safe when used correctly. While cure rates are dependent on patient adherence and

duration of therapy, the combination gel offers a compelling balance of cost-effectiveness, minimal invasiveness, and proven clinical efficacy compared to most other available wart treatments.

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