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Safety Evaluation of Therapeutic Interventions for Plantar Warts (Kapasi): Psychodermatology, Stress-Mediated Immunity, and Regulatory Considerations

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ABSTRACT

Currently, there are more than 3 million people worldwide suffering from plantar warts (Kapsi). Possible ways of treatment include keratolytics, cryosurgery, lasers, and intralesional immunotherapy. However, many factors, including the high rate of treatment failure, local regulations, safety concerns, and self-medicating practices, complicate these methods. Some studies indicate that psychosocial stress may worsen the effect of therapy in the case of viral infections by decreasing immune function via the action of cortisol, thus contributing to increased susceptibility to HPV (Human Papillomavirus) infection and persistent lesions. Nevertheless, despite all these observations, the role of psychology in drug therapy remains underestimated in this area. This literature review integrates the perspectives of dermatologists, immunologists, psychoneuroendocrinologists, and specialists in pharmacovigilance. The analysis focuses on currently popular treatments, including nitric oxide patches, vitamin D3 injections, immunization based on the MMR vaccine, nanoparticle-based drugs, as well as off-label use of various acids, among others. Special attention is paid to the potential toxicity, safety, efficiency, regulatory approval, and risks of self-treatment. In addition, issues of chemical burns from uncontrolled wart medications, the need to improve post-marketing monitoring of safety, and the danger of HPV infection associated with laser treatment are covered. Some of the key gaps related to plantar wart treatment include a lack of psychodermatology protocols for managing patients with mental stress, inadequate prediction of the

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effectiveness of treatment in such cases, different OTC treatment regulations, and insufficient knowledge concerning the risks associated with immunotherapies. Possible future improvements include better regulation of medications, novel and safe treatments, and the development of artificial intelligence monitoring and adaptation systems.

Keywords: Plantar Warts; Drug Safety; Stress–Immunity; HPV; Psychodermatology

1. Introduction

Persistent, harmless lesions caused by some genotypes of the Human Papillomavirus [HPV] are known as plantar warts, or *Kapasi* in some regional languages. These lesions manifest on the parts of the foot that carry the brunt of our weight, and the mechanical pressure causes them to bleed more deeply and take longer to heal. Recurrence, treatment resistance, aesthetic concerns, and the extensive use of unregulated over-the-counter wart removers create a substantial clinical and public-health burden for plantar warts, even though they do not constitute a life-threatening risk. Plantar warts continue to be common, especially in children, teenagers, athletes, and those with impaired immune systems^[1]. Wart persistence has become better understood in recent years, and not only in the fields of dermatology and virology. Psychodermatology, the study of the role of the mind in the development of skin disorders, is gaining popularity. The hypothalamic-pituitary-adrenal [HPA] axis is activated by chronic psychological stress, which results in immunosuppression and high cortisol levels. This change in immunology makes the host less effective in eliminating HPV-infected keratinocytes, which could lead to plantar wart recurrence or treatment resistance^[2]. Although the impact of stress on the immune system is becoming more apparent, its role in treatment safety, therapeutic response, and recurrence rates has been understudied.

Additionally, there has been an expansion in the therapeutic landscape for plantar warts. Salicylic acid, cryotherapy, and trichloroacetic acid are among the more traditional methods, but they all come with their own set of risks, including the potential for burns, scarring, and accidental self-application. While newer techniques, including intralesional vitamin D3, various laser systems, nitric oxide-releasing patches, and mitochondrial reactive protein (MMR) immunotherapy, provide alternatives, they also raise questions about their long-term safety, regulatory ap-

proval, and potential side effects^[3]. The already high risk of harm is magnified by the prevalence of self-treatment, particularly with the help of uncontrolled chemical agents and internet recommendations.

There is a lack of literature that unifies dermatological pathology, psychoneuroimmunological pathways, therapeutic safety profiles, and regulatory criteria, even if there are various treatments out there. There is a lack of knowledge on pharmacovigilance data, consumer abuse trends, regulatory differences between worldwide agencies, and real-world adverse events because most existing studies concentrate on effectiveness rather than safety. To fill these gaps and understand how stress, immunity, and behavioral responses impact treatment success and safety, a thorough evaluation of current therapy methods is necessary.

From a biological, psychological, and pharmaceutical standpoint, plantar warts can be better understood with the conceptual groundwork laid out in this chapter. In line with current drug-safety concerns, it lays the groundwork for an approach that is safety-oriented and integrates Psychodermatology. This chapter establishes the groundwork for subsequent sections that concentrate on therapeutic assessment, regulatory factors, and future research paths by placing plantar warts within this multidimensional framework.

Search Strategy and Methodology

A systematic literature search was utilized to perform this narrative review across various electronic databases, such as PubMed, Scopus, Web of Science, and Google Scholar. Research on the treatment and prevention of plantar warts that was published between 2020 and 2025 was taken into account.

Various combinations of keywords were used in the search, including: “plantar warts,” “HPV,” “wart treatment,” “drug safety,” “cryotherapy,” “immunotherapy,” “psychodermatology,” “stress and immunity,” and “wart management safety.”

Papers that had been peer-reviewed, as well as clinical trials, systematic reviews, and pertinent regulatory reports that dealt with therapeutic interventions and safety issues, were eligible for inclusion. Items that were either not relevant to safety outcomes or did not have an English version were not considered. Though not a systematic review, we did our best to present the most recent findings in a balanced and thorough manner. This study does not use a sample size because it is a narrative review; nonetheless, it does provide a thorough summary by combining results from several studies.

2. Etiology, Transmission, and Clinical Complexity of Plantar Warts

The most prevalent forms of Human Papillomavirus [HPV] that cause plantar warts are 1, 2, 4, 27, 57, and 63, which are not carcinogenic. These viruses have a strong preference for keratinized epithelium and can infect plantar skin through tiny abrasions brought on by friction, pressure, or light trauma. The virus replicates as keratinocytes migrate toward the surface, taking advantage of their natural differentiation cycle once it has entered the basal layer. Because mechanical forces push the lesion deeper into the dermis, which contributes to discomfort and delayed resolution, the thick, pressure-bearing plantar surface is an excellent setting for viral persistence^[4].

In humid shared spaces like gyms, pool areas, and locker rooms, plantar warts can spread from person to person or from infected surfaces to bare skin. HPV is able to withstand wet environments and can infect surfaces for long periods of time. People are much more likely to get sick if they wander barefoot in these kinds of places. Additional factors that make it easier for viruses to enter the body include perspiration, cuts, and broken skin barriers. As a result of differences in immune response and exposure patterns in behavior, the most afflicted demographics are children, teens, and athletes^[5].

Both the location of the warts on the foot and the amount of mechanical stress they are subjected to greatly affect how they appear clinically. In most cases, lesions manifest as hyperkeratotic papules with a rough surface and a callus-like border. In deeply buried lesions, the typ-

ical small black dots—representing thrombosed capillaries—may not be apparent. When warts grow endophytic in weight-bearing areas, they can make walking extremely painful, sometimes even agonizing. Athletes and the elderly are at increased risk for diminished physical activity due to changed gait patterns, secondary musculoskeletal strain, and pain^[6].

The clinical course can be complicated by comorbid health issues. Multiple, bigger, or treatment-resistant lesions are common in immunocompromised patients, such as those with HIV infection or receiving immunosuppressive therapy. Reduced peripheral feeling, decreased wound healing, and increased susceptibility to secondary infections are additional risks that patients with diabetes encounter. It is particularly crucial to take safety into account when dealing with these groups because even a small amount of trauma from cryotherapy or topical treatments can cause ulceration or deeper tissue damage. Careful medication selection and monitoring are essential in high-risk populations due to these complications.

There is still a lack of understanding on various clinical and epidemiological aspects of plantar warts, despite their prevalence. Information regarding the long-term natural history of HPV in various age groups, regional differences in HPV strains, and genotype-specific pathogenicity is scarce. Also, there is a lack of research comparing clinical severity with stress levels, behavioral risk factors, or markers of the immune system's state, despite mounting evidence that these factors play a substantial role in persistence and recurrence. These blind spots show how crucial it is to combine virological, immunological, and psychological viewpoints in order to create safer and more effective methods of treating plantar warts.

Many different forms of human papillomavirus (HPV) are responsible for causing plantar warts, and these different genotypes have different symptoms and recurrence rates. Types 1, 2, 4, 27, 57, and the newly-emerging type 63 all play distinct roles in the depth and durability of plantar skin lesions, according to recent investigations^[1-5]. Understanding variance in illness severity requires recognition of these genotype-specific behaviors. **Table 1** provides a synopsis of the main human papillomavirus types that cause plantar warts.

Table 1. HPV Types Associated With Plantar Warts and Their Clinical Characteristics.

HPV Type	Common Clinical Presentation	Depth/Severity Pattern	Recurrence Tendency	Supporting Studies
1	Deep, endophytic plantar lesions	Painful, pressure-driven	Moderate	DermNet NZ ^[7]
2	Raised keratotic papules	Mild–moderate	High	Redzic et al. ^[8]
4	Small, superficial plantar lesions	Low severity	Moderate	Bruggink et al. ^[9]
27 & 57	Mosaic or clustered patterns	Persistent, extensive	High	Villares et al. ^[10]
63	Atypical plantar morphology	Variable	Unknown	Hogendoorn et al. ^[11]

3. Stress, Immunity, and Psychodermatology in Wart Persistence

An infection that was once thought to be solely skin-related now has a complicated immunological and behavioral component: psychological stress. This aspect plays a significant role in the persistence and recurrence of plantar warts. Elevated cortisol levels, which inhibit several components of cell-mediated immunity, are a consequence of stress activating the hypothalamic-pituitary-adrenal [HPA] axis. Since strong T-cell activity, antigen presentation, and local cytokine signaling are necessary for efficient clearance of infected keratinocytes, this type of immunosuppression is especially pertinent to HPV infections. These immune responses are dampened when cortisol stays high for long periods of time, which allows HPV-infected cells to hide and stay in the skin ^[12].

Psychoneuroimmunology studies show that people with chronic stress have different cytokine profiles, less lymphocyte proliferation, and lower natural killer cell activity, all of which lend credence to the idea that stress contributes to wart chronicity. Some individuals may develop numerous warts, have a poor response to treatment, or have fast recurrence after treatment because these immunological alterations hinder viral clearance. Additionally, clinical data indicate that lesions that are more difficult to treat tend to be associated with stressful life events, scholastic expectations, and sleep difficulties. Similar trends have been shown in other viral dermatologic diseases, which supports the possibility of a shared mechanism, although these connections have not been thoroughly quantified in plantar wart-specific research yet ^[13].

Additional factors that contribute to the persistence of warts are the behavioral effects of stress. People experiencing high levels of stress may put off getting help, be

less consistent with their treatment plans, or even utilize harmful self-treatment methods, such as buying corrosive substances online, to alleviate their symptoms. Damage to the skin, scarring, and subsequent infections are all made more likely by these methods. In addition, the plantar skin can become macerated due to stress-induced hyperhidrosis, which can weaken the epidermal barrier and make it easier for viruses to spread or reinfect. Both the molecular and behavioral components that dictate the development of a disease are impacted by stress, and these indirect channels highlight this ^[14].

The effects of psychodermatological factors on plantar warts have not been thoroughly investigated, even though the body of evidence is mounting. Stress biomarkers such as salivary cortisol, C-reactive protein, or pro-inflammatory cytokines are understudied in clinical trials examining wart therapies, and few of these trials even consider psychological aspects. Consequently, there is a lack of consensus on how to assess stress levels in relation to wart care, and it is difficult to quantify the role of stress in treatment outcomes. This void prevents the creation of tailored treatment plans that may combine dermatological treatments with stress-reduction techniques. There is an urgent need to investigate the relationship between patients' psychological health, immunological function, and therapeutic safety in relation to plantar warts, as there is a lack of integrated research on the topic.

There is still a lack of direct clinical data in patients with plantar warts that links psychological stress to treatment success, despite these molecular insights. The majority of the results are derived from larger studies on viral infections and dermatology. Hence, to confirm these correlations in populations of plantar warts, more clinical studies are necessary.

4. Current Therapeutic Modalities and Drug-Safety Considerations (2020–2025)

Although there are several options for treating plantar warts, no one method ensures full eradication, and there are risks associated with each method. Size, location, age, comorbidities, immunological state, and pain or side effect tolerance are some of the factors that go into treatment selection for warts. Consumer access to powerful topical treatments and online self-treatment methods has been on the rise in recent years, making it all the more vital to evaluate the safety profiles of these new treatment alternatives. Dermatologists, family doctors, pharmacists, and public health officials can all benefit from this chapter's overview of important therapeutic categories and emphasis on safety issues.

The accessibility and low cost of topical keratolytics like salicylic acid have kept them among the most popular therapies globally. Chemical burns, tissue maceration, and ulceration can result from the abuse of high-concentration preparations. This is especially true for patients with diabetes, peripheral neuropathy, or impaired circulation. Many products are sold over the counter without medical supervision, which increases the danger of overapplication, even though they are normally safe when used carefully. There is a notable lack of long-term toxicity data for these newer systems, which highlights a critical gap in safety evaluation^[15]. However, recent studies examining changed formulations, such as lipid-based carriers and nanoparticle vehicles, indicate greater penetration and perhaps higher efficacy. One common method for treating infections on the skin is cryotherapy, which involves rapidly freezing and destroying the affected epidermal tissue using liquid nitrogen. Pain, blistering, color changes, and, in extremely rare instances, nerve damage are side effects of cryotherapy, despite the fact that treatment helps many patients. Sites that bear more of the body's weight are more likely to experience adverse effects, and the continual mechanical stress there may make healing more sluggish. While there have been a number of studies examining response rates in relation to patient immunity and lesion depth (spanning 2020–2024), very few have looked at the long-term effects of many cryotherapy treatments. How repetitive freeze-

thaw injury impacts plantar tissue over years of use is not well understood due to the absence of long-term safety monitoring^[16].

Caustic compounds, such as trichloroacetic acid (TCA), are commonly utilized in various situations, including clinical and non-clinical ones. Although TCA is an efficient keratolytic due to its speedy protein coagulation, serious chemical harm can occur from using it at the wrong concentration or by someone without proper training. Additional hazards are posed by the widely available, unlicensed wart-removal products that contain strong acids. Burns, infections, and permanent scarring caused by self-treatment attempts have been documented in recent case reports. These cases disproportionately affect adolescents and individuals who rely on unverified online advice. Stronger regulation of consumer-level items and better public education about safe usage are urgently needed, as these developments show^[17].

As doctors look for ways to get patients' immune systems to attack and destroy HPV-infected cells, immunotherapeutic techniques have come to the fore. Studies performed after 2020 have demonstrated promising outcomes for intralesional injections of Candida antigen, measles vaccination, and vitamin D3. Swelling, fever, widespread eruptions, and, extremely rarely, hypersensitivity reactions are some of the hazards associated with these treatments. The majority of immunotherapy medicines are also utilized off-label, which means that there is a lack of consistency in the regulatory guidelines for dosing, administration, and contraindications. Widespread use is impeded by gaps in safety knowledge caused by the lack of thorough pharmacovigilance systems that record adverse events associated with these treatments^[18].

Targeted tissue destruction is accomplished quickly and efficiently with laser-based treatments, such as pulsed-dye lasers and CO₂ lasers. Although it is usually safe when done by skilled individuals, vaporizing tissue that is infected with HPV can release aerosols that contain virus particles. Research has shown that laser ablation could release HPV into the air, which is a cause for concern for both patients and doctors. Many low-resource clinics do not have sophisticated smoke evacuation systems, even if protective gear might lessen exposure. These restrictions show how important it is to have standardized procedures in place to

reduce the dangers of HPV aerosolization in the workplace during laser therapy^[19].

One of the most recent innovations in medicine is nitric oxide-releasing patches. A non-invasive approach that increases immune activation and prevents viral replication is provided by these systems. Preliminary safety data show encouraging results, with most patients reporting just mild annoyance. Unfortunately, there hasn't been enough research on the long-term safety, relapse rates, and interactions of these drugs with comorbid diseases since they are still relatively new. Some customers choose unregulated chemical treatments due to cost concerns, putting themselves at greater risk than necessary.

Various available medications offer different approaches to treating plantar warts, but it's important to carefully assess the safety of each option. Maximizing

patient outcomes is still hindered by gaps in long-term safety data, insufficient regulation of consumer products with high risks, and a lack of pharmacovigilance reporting. These problems show how current methods of wart treatment lack essential components: patient education, regulatory monitoring, and safety monitoring.

Plantar warts can be treated in a variety of ways, but all modalities have different safety concerns that doctors take into account when deciding which one to use. Lasers, cryotherapy, immunotherapy, keratolytics, and nitric oxide patches all carry different hazards, according to recent reviews^[6-11]. It is crucial to understand these safety profiles in order to choose the right therapy, especially for fragile patients. **Table 2** provides a comparative review of various treatments, along with their main safety concerns.

Table 2. Major Treatment Modalities for Plantar Warts and Key Safety Considerations.

Treatment Modality	Mechanism	Common Side Effects	Serious Risks	Special Precautions	Safety Evidence
Salicylic acid	Keratolysis	Irritation, peeling	Chemical burns	Avoid in diabetic patients; risk of burns with overuse	Kwok et al. ^[15]
Cryotherapy	Tissue freezing	Blistering, pain	Scarring, nerve injury	Painful; caution in children and neuropathy patients	Bruggink et al. ^[6]
Trichloroacetic acid	Chemical cautery	Burning, redness	Deep tissue injury	Risk of deep tissue injury if misused	Cengiz et al. ^[17]
Intralesional immunotherapy [MMR/Candida/Vit D3]	Immune activation	Swelling, fever	Hypersensitivity	Monitor for hypersensitivity reactions	Awal and Kaur ^[20]
CO ₂ laser	Tissue vaporisation	Redness	HPV aerosol exposure	Risk of HPV aerosol exposure; use protective equipment	Bennardo et al. ^[21]
Nitric oxide patch	Antiviral, immune modulation	Mild irritation	Unknown long-term risks	Limited long-term safety data	Schumacher et al. ^[22]

5. Self-Medication Practices and Public-Health Risks

The widespread availability of over-the-counter wart removers, instruction content online, and the impression that plantar warts are minor diseases that do not require medical care have all contributed to the rise in self-medication for plantar warts. Nevertheless, individuals often fail to adequately consider the myriad of safety problems brought about by these techniques. Beyond specific injuries, there are larger public-health concerns related to chemical misuse, diagnostic delays, and the strain on healthcare systems. In order to create safer management strategies and regulatory controls, it is crucial to identify the hazards of self-directed care, espe-

cially as treatment alternatives become more numerous and potent.

The availability of high-strength keratolytic drugs, such as salicylic acid and trichloroacetic acid, without proper supervision raises serious concerns about their potential misuse. People may use these products in very wide areas, on skin that is already sensitive or fragile, or in excessive amounts. Incorrect use has been documented in clinical studies to cause burns, ulcers, cellulitis, and subsequent bacterial infections. People with decreased sensitivity, such as diabetic neuropathy, are more vulnerable to these kinds of damage. The increased danger associated with these items is due, in part, to the lack of clear labeling, the fact that product concentration varies, and the fact that consumer education is inadequate^[23].

Misinformation, unfettered availability of powerful medicines, and a lack of knowledge about proper treatment methods all contribute to the problem of people trying to cure their plantar warts by self-medicating. People frequently cause avoidable harm and postpone healing by following unproven internet advice, choosing harmful cor-

rosive products, or misdiagnosing their lesions. Anxieties, excessive medication use, and skin injuries all contribute to an already high risk of viral transmission and recurrence. **Figure 1** shows the interplay between these factors and the increasing cascade of events that might make self-treatment of warts worse.

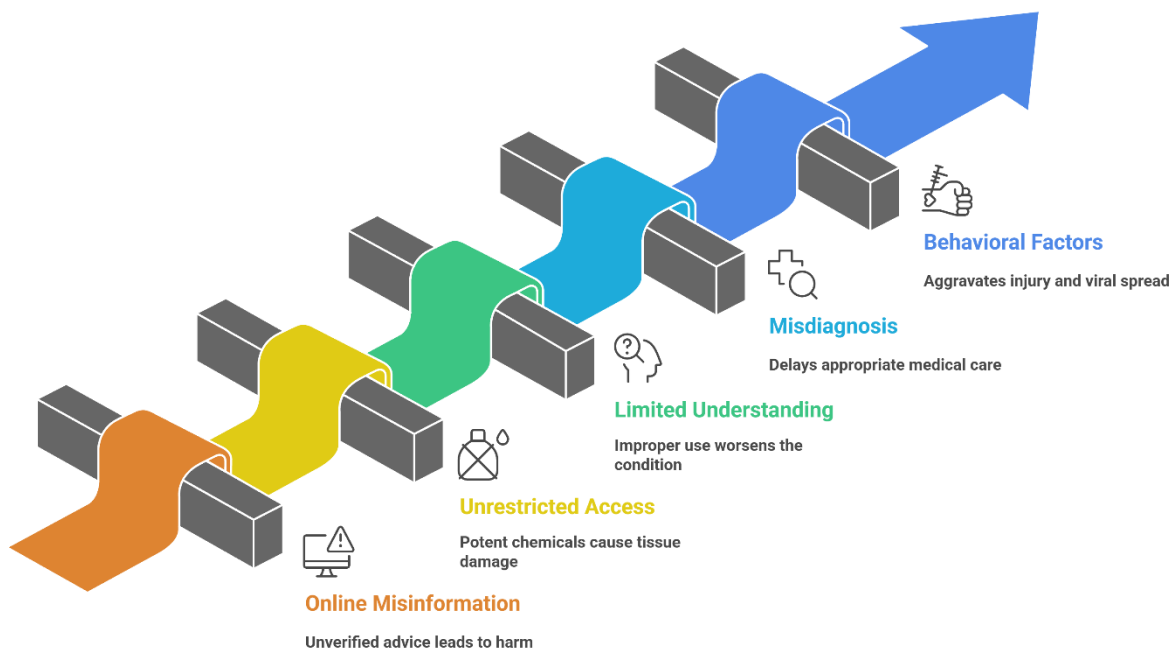


Figure 1. Pathway Demonstrating How Self-Medication Worsens Plantar Warts Through Misinformation, Misuse, and Behavioural Feedback.

Online resources have made matters worse by encouraging people to try unproven home cures, such as using harsh chemicals, improvised cryotherapy, or sharp objects to remove lesions. Significant risks are associated with a few of these methods. Avoid frostbite and nerve damage by utilizing only medical-grade refrigerants and avoiding homemade equipment when trying to freeze warts. Similarly, using blades for self-debridement raises the possibility of secondary infection, inoculation of neighboring tissues, or excessive bleeding. The fact that these approaches are so popular among young adults and teenagers is a result of their lack of knowledge, their perception of how convenient they are, and their unwillingness to seek professional help^[24].

Delayed manifestation of complex or unusual lesions is another issue with public health. People who try to treat themselves may mistake warts for other illnesses like calluses, foreign-body granulomas, or even early stages of

skin cancer. Delaying essential medical evaluation and obfuscating diagnostic symptoms can result from prolonged self-management. Even though malignant transformation is uncommon, there could be serious repercussions if diagnoses are overlooked. These diagnostic problems are made worse by the absence of organized consumer assistance, which highlights the necessity for manufacturers and health authorities to communicate more clearly.

Another area of concern is the potential for chemical harm caused by unregulated wart-removal kits. You can find items with acid concentrations or blended ingredients that are higher than what is considered safe for use on internet marketplaces. Consumers are exposed to potentially dangerous formulations due to the fact that regulatory control of these products differs significantly across regions. Misuse is more likely to occur because these kits may not always provide the necessary instructions, cautions, or contraindications. There are significant logistical hurdles

to regulating these products because of how easily they may be delivered across borders^[25].

From a community health standpoint, the risk of viral persistence and transmission is increased when people self-medicate. The infectivity of plantar sores can be prolonged by ineffective or inconsistent treatment, especially in contexts where people walk barefoot. Patients need to be educated about both safety and transmission, because the virus could continue to spread in shared spaces like gyms, hostels, or swimming pools. Many people do not understand how their actions impact their own healing and the healing of their communities because there is a lack of coordinated public-health messaging.

Despite these hazards, there is a lack of empirical evidence on how often plantar warts occur and how effective self-medication is. There is a lack of data on the frequency of chemical burns and other injuries caused by wart self-treatment in epidemiological research, and nearly no national pharmacovigilance systems record adverse events related to wart removers sold to consumers. The inability of regulatory bodies to establish safety standards based on evidence is a direct result of the data gap that exists in the policymaking process. In order to better direct future public-health measures, it would be beneficial to strengthen monitoring systems and perform population-based studies.

6. Regulatory Considerations and Safety Compliance

Protecting consumers from wart-removal methods that are inappropriate, dangerous, or ineffective is a key function of regulatory monitoring. However, there is still a lack of uniformity in the regulation of plantar wart therapies across jurisdictions, which causes issues with product quality, safety, and post-marketing monitoring. With the proliferation of powerful topical treatments and internet wart-removal kits, which may not adhere to recognized safety standards, these discrepancies are becoming increasingly noticeable. Evaluating the wider safety implications of plantar wart management requires an understanding of the regulatory framework.

A wart treatment's active ingredients and intended use determine how it is classified by regulatory agencies, including the FDA, EMA, and CDSCO in India. There

are no restrictions on who can buy keratolytic treatments containing salicylic acid because they are generally considered over-the-counter medications. Despite the fact that this categorization makes things easier to find, it also leads to their frequent misuse because people buy them without consulting experts. The concentration and risk characteristics of chemicals like trichloroacetic acid and some cryotherapy equipment determine whether they are regulated as medical devices or require expert administration. Consistent safety standards are difficult to achieve due to the absence of national norms^[26]. How off-label medicines are handled by regulators adds another level of complexity. For stubborn plantar warts, immunotherapeutic treatments are being employed more and more in clinical practice. These therapies include intralesional *Candida* antigen, the measles-mumps-rubella vaccination, and vitamin D3. Nevertheless, these medicines were not initially intended for the treatment of warts, and their usage is mostly dictated by the clinician's experience rather than established regulatory guidelines. Although dermatology frequently uses off-label prescriptions, there are concerns over the reporting and monitoring of adverse responses due to the lack of official safety standards or dose recommendations. This void is especially important for children, people with impaired immune systems, and those with preexisting autoimmune diseases because their reactions to immune-stimulating drugs might be unpredictable^[27].

Complication rates from wart treatments are under-reported in post-marketing surveillance systems that aim to record side effects from authorised medications. Many individuals self-treat and wait to seek medical attention until problems develop, which leads to under-reporting. Customers may not know where to find reporting information or may not be aware that they are required to do so even when injuries have occurred. Consequently, authorities in charge of regulating products on the internet may not get enough information to spot harmful trends, particularly those involving unregulated internet goods. Because of this deficiency in monitoring, authorities are unable to revise safety standards, issue warnings, or recall potentially dangerous goods from circulation^[28].

An additional regulatory hurdle arises from online sales. People can buy powerful chemical agents or medical

gadgets online without going through the usual channels of regulation. These unlicensed goods can have acid concentrations higher than allowed, incorrectly listed components, or insufficient directions for proper usage. There has been inconsistent implementation of the regulations that certain nations have put in place to prevent the sale of medical items online. The worldwide reach of e-commerce adds another layer of complexity to regulation, as products might come from regions with lax monitoring and be sent all over the world without quality checks. This event highlights the importance of regulatory cooperation across borders to improve consumer safety.

Disparities in consumer knowledge and safe usage are exacerbated by the fact that labeling standards differ greatly among regions. Clear directions, cautions, contraindications, and advice on when to seek medical care are essential components of effective labeling. However, comprehensive warning labels are missing from many products, particularly those marketed online. People with several health conditions, such as diabetes or peripheral vascular disease, are more likely to experience negative side effects from using caustic agents or unsupervised cryotherapy machines, which is a major concern due to inadequate labeling. These dangers could be reduced and safer self-care habits could be supported by standardized labeling requirements among regulatory authorities.

As a whole, the regulatory framework for plantar wart therapies is still not well-prepared to deal with new safety concerns that may arise. There are ongoing gaps in consumer protection due to factors such as product classification differences, insufficient post-marketing surveillance, a lack of oversight of off-label therapies, and the abundance of unregulated online products. A more effective and safety-oriented approach to controlling plantar warts requires more regulatory coordination, better data collection, and enhanced public education.

7. Integrating Psychodermatology with Drug Safety and Clinical Decision-Making

It is important to know the patient's mental health, behavioral habits, and treatment safety capabilities when managing plantar warts; this goes beyond just choosing the

right therapeutic substance. A more holistic approach that takes into account the impact of psychological stress, coping mechanisms, and treatment behaviors on therapeutic results and safety is provided by incorporating psychodermatology into clinical decision-making. With the advent of new medicines, the rise of self-medication, and the fact that clinicians deal with patients who have varying expectations and health literacy levels, this viewpoint is becoming more important.

The effectiveness of treatment is highly dependent on biological and behavioral pathways, both of which are impacted by psychological stress. From a scientific perspective, it is worth noting that high cortisol levels can hinder the immune responses needed to eliminate HPV-infected keratinocytes. This, in turn, can have an impact on the efficacy of immunomodulatory therapy and the rate at which lesions heal. Stressed people may act erratically, such as skipping treatments, using excessive amounts of topical drugs to get better faster, or trusting unproven solutions found online. Burns, infections, and scarring are more likely to occur as a result of these acts. Clinicians can better identify patients who may need extra assistance or other treatment approaches by incorporating stress assessment—through short questionnaires, conversations about lifestyle choices, or biomarker evaluation^[29].

Additionally, patient adherence is improved using a psychodermatology-informed strategy. Applying keratolytics for an extended period of time or scheduling numerous appointments for cryotherapy or immunotherapy are common methods for treating plantar warts. Patients experiencing mental health issues may fail to account for the required time or become disheartened when they do not see immediate results. Adherence and the reduction of risky behaviors can be enhanced by the provision of reasonable expectations, emotional support, and organized follow-up. One way to lessen the chances of unpleasant responses is to provide patients with clear instructions regarding dose and application procedures. This way, patients are less likely to apply therapies to healthy skin nearby or abuse acids^[30]. Treatment results for warts may be improved even further by adding stress-reduction techniques to their care. Interventions like cognitive-behavioral therapy, relaxation techniques, and mindfulness training have been linked to higher immune function and better coping with chronic

diseases, according to broader dermatological research. While there is a lack of data specifically related to plantar warts, the fact that similar treatments have been successfully used to treat other stress-sensitive skin disorders suggests that they may be worth investigating further in clinical practice. A reduction in stress-related immunosuppression, which in turn aids virus clearance and decreases recurrence, may be as easy as suggesting better sleep hygiene or including short daily relaxation sessions^[31].

Vulnerable populations' safety must also be considered in decision-making. To keep burns and delayed healing to a minimum, patients with neuropathy, immunosuppression, peripheral vascular disease, diabetes, or both need to have their treatment programs adjusted. Psychodermatological evaluation is useful in these situations because it allows physicians to spot patterns of behavior that can put patients at risk when they self-administer therapies. Clinicians can enhance safety outcomes and decrease the incidence of complications requiring medical intervention by customizing recommendations and choosing lower-risk therapy.

Messages about public health and patient education can also be effectively integrated. In order to decrease avoidable injuries, it is important to communicate clearly about the hazards of self-treatment, how to use over-the-counter medications correctly, and whether symptoms need medical assistance. Clinicians should advise their patients to avoid unregulated items and to check information with reputable sources due to the abundance of false information online. Home safety decision-making should be further reinforced by instructional materials that include stress-management guidance. To manage plantar warts more comprehensively, psychodermatology should be part of drug safety and therapeutic decision-making processes. Patient safety is emphasized as a major feature of effective treatment in this approach, which acknowledges the interconnectedness of biological, psychological, and behavioral aspects. Clinicians can create safer, more successful, and individualized treatment programs by taking into account stress, treatment understanding, lifestyle factors, and individual vulnerability.

8. Future Directions

Problems with safety, effectiveness, and regulatory

consistency persist in the treatment of plantar warts, despite several new therapeutic options. Incorporating new technology, insights from psychoneuroimmunology, and more thorough safety evaluations into future research is essential, going beyond conventional dermatologic methods. If we want better patient outcomes and less stress from recurrent or resistant lesions, we need to do this. There are a number of prominent areas that warrant more study and the formulation of new policies.

One encouraging path is to use digital health technologies and artificial intelligence to track how treatments are working and spot any dangers. Machine learning algorithms have the potential to examine lesion images, monitor their evolution, and identify precursors to problems like chemical damage or secondary infections. In addition, there are smartphone apps that can help with adherence by sending out notifications when treatment is over- or under-applied, as well as reminders and detailed instructions. In order to reduce the hazards of self-treatment, these digital tools could be particularly helpful for communities that do not have easy access to dermatologic care^[32]. Creating less hazardous formulations for topical treatments is another critical area for further investigation. Recent developments in nanotechnology hold great promise for the amelioration of drug delivery issues and the eventual lowering of therapeutically effective doses of caustic agents. While early trials with lipid-carrier systems and nanoparticle-based salicylic acid demonstrated enhanced penetration and regulated release, the long-term safety profiles of these systems are still mostly unknown. These products must undergo thorough toxicological testing before they may be authorized for general use. Biodegradable microneedle patches could be a safer alternative to harmful treatments like cryotherapy or chemical cauterization; they deliver focused therapy with minimal disturbance to the skin and should be investigated further.

There is also a need for more individualized approaches to treatment. In the future, therapy selection may be guided by biological markers like HPV genotype, local immune response, and stress-related biochemical markers. Patients with abnormal cytokine patterns or elevated cortisol levels, for instance, may benefit more from immune-enhancing treatments than from keratolytics or destructive procedures. One way to lessen the likelihood

of treatment toxicity and recurrence is to personalize treatment plans according to patients' stress levels and immunological markers. In order to develop evidence-based algorithms for individualized treatment, longitudinal studies combining psychological evaluations with biomarker analysis are required^[33].

Regulatory framework enhancement should also be a subject of future research. One way to lessen the dangers of using unregulated formulations is for wart treatments, especially over-the-counter ones, to have their safety criteria standardized globally. Online marketplaces selling medical products might be better supervised; regulatory bodies could establish more transparent concentration restrictions, and labeling standards could be more stringent. To further aid clinician decision-making, standardized protocols for the safe administration of immunotherapies and new laser technologies should be established. To better understand real-world safety and respond quickly to new dangers, pharmacovigilance systems should actively record adverse events from medications administered at both the clinical and consumer levels^[34].

Finally, there is unrealized potential in incorporating psychosocial therapies into wart management. Studies on many types of skin and immune disorders have shown that behavioral counseling, sleep optimization, and stress-reduction methods can help boost immune function and improve the effectiveness of treatments. The effectiveness of these methods in treating plantar warts has not been tested in randomized controlled trials. Patients with chronic or recurring lesions affected by psychological stress would benefit greatly from a safer and more comprehensive care paradigm if their clinical worth could be proven.

The use of machine learning methods for wart treatment outcome prediction has recently been investigated. One example is the utilization of classifiers like Naïve Bayes and k-nearest neighbors [KNN] to aid in the prediction of therapeutic effectiveness and the selection of optimal wart treatment procedures. The promise of AI in dermatology for improving clinical decision-making and personalizing treatment regimens is demonstrated by these approaches.

In sum, a multidisciplinary strategy integrating psychodermatological principles, regulatory refinement, personalized medicine, and technological innovation will be

necessary for the future of plantar wart treatment. Clinicians and legislators can advance toward a safer and more successful framework for treating plantar warts by filling in existing gaps and incorporating these new viewpoints.

9. Conclusions

Plantar warts are an ostentatiously straightforward skin ailment that actually exposes a web of interconnected factors, including viral biology, host immunity, psychological stress, clinical safety, and regulatory supervision. There are a variety of treatment methods available, but no one modality offers 100% clearance, and each has its own set of risks and advantages that need to be considered. Clearer safety standards and more consumer protection are needed since self-medication is on the rise, and because powerful over-the-counter medicines and unregulated internet concoctions are easily accessible.

One aspect of plantar wart treatment that is frequently disregarded is the importance of understanding the function of psychological stress. Biologically, stress affects treatment outcomes through immunosuppression mediated by cortisol. Behaviorally, it shapes patient adherence and self-care routines. Safer and more effective treatment techniques can be supported by incorporating psychodermatological principles into clinical decision-making, which provides a more holistic and patient-centered framework.

Collaboration between different fields is crucial for future advancements in this area. The potential for fewer treatment-related dangers and better outcomes is high in light of recent developments in digital technology, nanomedicine, biomarker-driven personalised therapy, and unified regulatory requirements. No less critical will be the endeavors to fill up the existing gaps in safety data, especially in regards to real-world monitoring systems and long-term studies. Improving the treatment landscape for plantar warts will require a shift in focus toward patient safety, education, and mental health in order to create a system that is both effective and fair.

Author Contributions

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ysis, S.G.; investigation, S.G.; resources, S.S.B. and S.B.; data curation, S.G.; writing—original draft preparation, S.G.; writing—review and editing, S.S.B. and S.B.; visualization, S.G.; supervision, S.S.B.; project administration, S.S.B. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare that there are no conflicts of interest associated with the preparation or publication of this manuscript.

AI Use Statement

The authors confirm that artificial intelligence tools

(ChatGPT) were used only for language refinement and structuring purposes. All scientific content, interpretation, and conclusions are the original work of the authors and have been critically reviewed and validated to ensure accuracy and integrity.

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