

REVOLUTIONIZING SKIN THERAPY: HERBAL GEL-BASED DRUG DELIVERY SYSTEMS FOR DERMATOLOGICAL DISORDERS

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ABSTRACT

Herbal medicine has been widely recognised as a safe, economical, and effective approach for the management of various skin disorders due to its therapeutic potential and minimal adverse effects. The skin, being the largest organ of the human body, serves as a protective barrier against environmental hazards and is frequently affected by infections, inflammation, wounds, acne, eczema, and other dermatological conditions. Herbal formulations have gained considerable attention in topical drug delivery because of the presence of bioactive phytochemicals with antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties. Among the various topical dosage forms, gels are preferred owing to their non-greasy nature, ease of application, better patient compliance, enhanced drug release, and cooling effect. This review provides a comprehensive overview of herbal medicine in dermatological applications, including the anatomy and physiological functions of the skin, common skin disorders, and the significance of topical gel formulations. The article discusses the concept of gels, their advantages, and classification based on the number of phases, colloidal systems, hydrogel types, and rheological behavior. Furthermore, it highlights the therapeutic importance of medicinal plants commonly used for treating skin diseases and summarizes the pharmacological activities of selected herbal drugs employed in topical formulations. In addition, the review presents an overview of commercially available polyherbal gel formulations and their applications in managing various skin conditions. The compiled information emphasizes the growing importance of herbal gels as promising alternatives to conventional topical therapies. The review concludes that polyherbal gel formulations offer synergistic therapeutic benefits, improved patient acceptability, and significant potential for future research and development in the field of herbal dermatological drug delivery.

KEYWORDS: Herbal medicine, Topical gel, Skin diseases, Polyherbal formulations, Hydrogels.

1. INTRODUCTION TO HERBAL MEDICINE

In contemporary society, 80% of individuals utilise herbal remedies to address prevalent dermatological issues. Acne vulgaris is a prevalent inflammatory dermatological disorder that impacts 85% of adolescents. This developmental period predominantly impacts those aged 18 to 25.^[1] Individuals between the ages of 35 and 40 often exhibit reduced prevalence of acne vulgaris, an inflammatory disorder affecting the sebaceous glands.^[2] Symptoms of this sickness include pain, erythema, and inflammation, with occasional formation of pus. Herbal cosmetics are increasingly gaining popularity in contemporary society. The treatment of chronic skin conditions with innovative formulations developed in recent years is increasingly vital, as these conditions may be exacerbated by environmental hazards such as dust and pollution, excessive consumption of fatty foods, heightened sebum production by sebaceous glands, and poor dietary habits. Acne may present as inflammatory papules, pustules, nodules, cysts, and other characteristic lesions that can lead to pigmentary alterations and scarring. Hormonal fluctuations in the body may also lead to acne. Acne vulgaris is a common inflammatory skin condition. Acne impacts over 90% of adolescents, with 50% continuing to experience it in adulthood. At the age of forty, five per cent of women and one per cent of males continue to exhibit lesions. According to a study, acne in adolescents is increasingly prevalent, potentially due to the onset of puberty.^[3]

A liquid phase is encapsulated within a three-dimensional biodegradable gum matrix characterized by a significant degree of physical or chemical cross-linking. The intermediate characteristics of topical gels, situated between solid and liquid states, render them an excellent choice for diverse applications. In recent decades, topical gels have garnered significant attention from experts in industry, research and development, education, drug regulatory agencies, and various other areas. This article reviews the fundamental and recent advancements in topical gels, encompassing their classification and preparation methods. A distinct section addresses the utilization of hydrogel in medication delivery systems. Emphasis is placed on its classification, preparation methodology, and assessment criteria.^[4]

Topical drug delivery is the method of administering medications directly into the skin or mucosal surfaces to achieve a localized therapeutic effect. Frequently employed for the management of dermatological conditions, ocular infections, nasal and vaginal disorders, as well as analgesia.^[5] Among various clinical applications, topical drug delivery systems are among the most frequently applied because skin is one of the most accessible pathways for drug delivery.

On the other hand, topical medical treatments range from simple liquids and ointments to multiphase nanotechnology-based therapies. Advantage of topical administration system is bypass first pass metabolism. Topical preparations have other advantages as well: they allow one to bypass the risks and inconveniences of IV therapy and the variable absorption conditions such as alterations in pH, if enzymes are present or not, stomach emptying time.^[6]

Pharmaceutical dose forms, including semisolids, liquid preparations, sprays, and solid powders, are utilized as topically acting drugs. Semisolid formulations for topical medication administration primarily include gels, creams, and ointments.^[7] A gel formulation known as topical gel is applied directly to the skin or mucous membranes. Engineered to deliver active components to a targeted site for localized therapy, it offers benefits such as pain relief, inflammation reduction, and treatment of dermatological conditions. Typically transparent, smooth, and non-greasy, topical gels facilitate rapid absorption by the skin without leaving any trace.^[8] A gel is a two-component, crosslinked three-dimensional network of structural pieces interspersed with a substantial volume of fluid, creating an extensive rigid network that impedes the fluid's constant state within. A gel is a state of matter that is transitional between solid and liquid, exhibiting qualities of both, referred to as viscoelasticity. The structural elements constituting a gel network may

comprise inorganic particles or organic macromolecules, typically sized polymers.^[9] The topical distribution system is utilized when alternative medication administration routes are ineffective, or it is predominantly employed for pain treatment, contraception, and urinary incontinence. In recent decades, the treatment of diseases has predominantly involved administering antibiotics via oral, sublingual, rectal, parenteral, topical, and aerosol routes.^[10]

2. Anatomy of skin

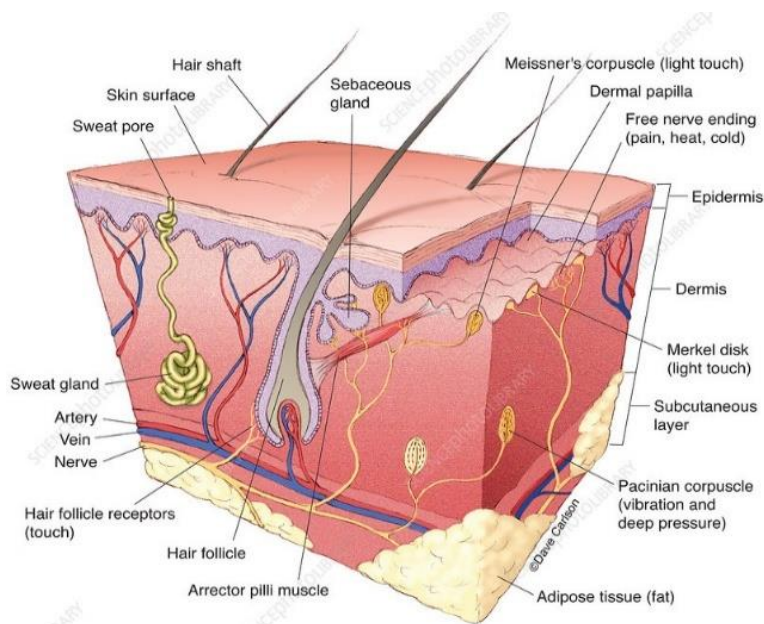


Fig. 1: Anatomy of skin.

The skin constitutes the largest organ of the human body. The skin serves as the primary line of defence. The skin comprises several cells and structures. The primary layers are the dermis, hypodermis, and epidermis. Each layer serves a distinct purpose in the overall operation of the skin. Each layer of the body exhibits varying thickness. The epidermis is most robust on the palms and soles, whereas it is weakest on the eyelids. The location of the skin influences the thickness of the dermis as well. Located beneath the dermis is the hypodermis, often known as subcutaneous connective tissue. The subcutaneous layer exhibits variability in thickness among individuals and throughout different regions of the body. The principal cutaneous appendages are sudoriferous glands, sebaceous glands, and hair follicles.

The skin envelops and safeguards the internal organs, bones, muscles, and ligaments. Hairy skin and glabrous skin are the two fundamental forms of skin. The skin can also be pale, sensitive, dry, sagging, and worn out.

Skin is essential for defending the body against infections and water loss.^[11,12] Additional functions encompass water resistance, insulation, temperature regulation, sensory perception, storage, and vitamin D production via ultraviolet (UV) radiation. It additionally safeguards vitamin B folates and facilitates the absorption of numerous drugs.^[13] Scar tissue production represents the skin's effort to recover from significant injuries. This is often discoloured and dull.^[14]

Natural items and conventional medications are advantageous for the treatment and prevention of several ailments.^[15]

They are gaining popularity as adjunctive therapy for common dermatological conditions.^[16]

Various traditional medical systems, such as Chinese Medicine, Ayurveda, Siddha, and the Unani System of Medicine, provide comprehensive documentation regarding the therapeutic application of plants. Approximately one-third of the most prevalent pharmaceuticals available today are derived from botanical or alternative natural sources.^[17,18]

3. Common skin problems

Dermatological diseases are a common affliction that can harm individuals in multiple ways and impact people of all ages. Although there are over one thousand conditions that can afflict the skin, the primary categories of skin diseases are outlined here.^[14]

3.1 Rashes



Fig. 2: Rashes on skin.

A rash is an aggregation of many patches or a designated region of inflamed skin surface. It may be triggered by infections, allergies, and hyperactive sebaceous glands, leading to psoriasis, dermatitis, eczema, and acne.^[19]

3.2. Viral Infections

A viral skin infection is any dermatological disorder or symptom caused by a viral pathogen. These vary from isolated lesions, such as warts, to extensive rashes, including measles or chickenpox. They manifest either by direct viral invasion of the skin or as a systemic viral infection that presents on the skin. Dermatological conditions impact individuals of all ages and vary from simple rashes to complex systemic diseases. Most viral exanthems are self-limiting. Warts, herpes simplex, and herpes zoster exemplify viral dermal infections.^[20]



Fig. 3: Viral infections on skin.

3.3 Bacterial Infections



Fig. 4: Bacterial infections on skin.

Acute bacterial infections and skin structure infections are two classifications of bacterial skin infections, alongside skin and soft tissue infections. Cellulitis and erythrasma are intricate bacterial infections influenced by adipose tissue. Additional intricate bacterial diseases encompass erysipelas, wound infections, and severe cutaneous abscesses.

3.4 Fungal Infection



Fig. 5: Fungal infection on skin.

Moisture and maceration in intertriginous areas foster an ideal environment for the proliferation of yeasts, including *Candida* species. This induces inflammation and erythema, along with satellite lesions in the inguinal region, beneath the mammary glands, and within the abdominal folds. Friction and maceration are significant factors in the proliferation of candidiasis. While less prevalent, individuals with obesity may also experience candidal folliculitis.

Although oral drugs such as fluconazole or itraconazole, as well as topical antifungals like ketoconazole and econazole creams, can effectively address the condition, they do not prevent recurrences.

3.5 Pigmentation Problems



Fig. 6: Pigmentation on skin.

Individuals with aberrant pigmentation, including those with vitiligo, melasma, and post-inflammatory hyperpigmentation (PIHP), may harbor significant worries. Loss of pigment, typically observed in the lips and fingertips, is referred to as vitiligo. Melasma, characterized by symmetrical areas of hyperpigmentation, can arise from various sources, including excessive UV radiation exposure, chemical agents, hormonal imbalances in females, or genetic anomalies.^[21] PIHP is frequently linked to cutaneous inflammation and may present during surgical procedures, laser ablation, dermatitis exacerbations, or in those receiving photosensitizing therapies.^[22,23]

4 Introduction to gels

Topical medication delivery is the method of administering pharmaceuticals directly into the skin or mucosal surfaces to achieve a localized therapeutic effect. Frequently utilized for the management of dermatological disorders, ocular infections, nasal and vaginal conditions, as well as analgesia.^[24] Topical drug delivery systems are among the most commonly utilized therapeutic applications due to the skin being one of the most accessible routes for medication administration. Conversely, topical medical treatments vary from basic liquids and ointments to complex nanotechnology-based remedies. The advantage of a topical delivery approach is the avoidance of first-pass metabolism. Topical preparations offer additional benefits: they circumvent the hazards and difficulties associated with intravenous therapy and the varied absorption conditions influenced by factors such as pH variations, the presence of enzymes, and gastric emptying time.^[25] Pharmaceutical dose forms, including semisolids, liquid preparations, sprays, and solid powders, are utilized as topically acting drugs. Semisolid formulations for topical medication administration primarily include gels, creams, and ointments.^[26] A gel formulation known as topical gel is applied directly to the skin or mucous membranes. Engineered to deliver active components to a targeted site for localized therapy, it offers benefits such as pain relief, inflammatory mitigation, and treatment of dermatological conditions. Typically transparent, smooth, and non-greasy, topical gels facilitate rapid absorption by the skin without leaving residue.^[27] A gel is a two-component, crosslinked three-dimensional network of structural pieces interspersed with a substantial volume of fluid, creating an unyielding network structure that 'traps' the fluid in a constant state. A gel is a state of matter that is transitional between solid and liquid, exhibiting qualities of both, referred to as viscoelasticity. The structural elements constituting a gel network may comprise inorganic particles or organic macromolecules, typically sized polymers.^[28]

The topical delivery system is occasionally used if other routes of drug administration fails or primarily it is used in pain relief, contraception and urine incontinence. In last decades the approach towards treating any sort of disease has been administration of anti-biotic drugs in human body by various routes such as oral, sublingual, rectal, parental, topical, aerosolise etc (29). Topical drug delivery refers to the application of a drug formulation directly onto the skin to treat cutaneous disorders, such as acne, or to address cutaneous lesions associated with systemic diseases, such as psoriasis, with the objective of confining the pharmacological effects of the drugs.

5. Classification of gels

5.1 Based on number of phases Colloidal phase

5.1.1 Inorganic (Two-phase) System:^[31]

This system consists of aggregates of small particles rather than larger molecules. The stability of the gel structure is compromised when the size of the dispersed phase is significantly large, resulting in a three-dimensional arrangement within the gel. Such gels are required to demonstrate thixotropic properties, changing from a semisolid state to a liquid upon agitation. Examples of this type include gels formulated with aluminium hydroxide and bentonite magma.

5.1.2 Organic (Single-phase) Systems

This technology features twisted threads that accommodate big organic molecules in a fully dissolved state. The majority of organic gels are categorized as single-phase solutions, encompassing organic liquids such as plastic bases and gelling agents like carbomer and tragacanth.

5.2 Based on the nature of gelling agent

5.2.1 Hydrogels (Water-based)

A hydrogel is a three-dimensional network composed of hydrophilic polymers, characterised by its exceptional capacity to interact with and retain significant amounts of water and biological fluids. This characteristic results from the existence of many functional groups, including amino ($-\text{NH}_2$), carboxylic acid ($-\text{COOH}$), hydroxyl ($-\text{OH}$), amide ($-\text{CONH}$), and sulfone ($-\text{SO}_3\text{H}$) within the polymer chains. The extent of polymer hydration varies with the properties of the aqueous environment and the polymer's composition.

Types of Hydrogels

- pH-Sensitive Hydrogel
- Temperature-Sensitive Hydrogel
- Nano Hydrogels
- Glucose-Sensitive Hydrogel

5.2.2 Organogold organ gels.

Frequently termed oleaginous gels, these substances are distinguished by the presence of both polar and non-polar groups, with a notable majority of the non-polar component. These gels can absorb up to 35% water because they tend to swell in wet conditions. Agents responsible for gelation, referred to as organogels, are generally low-molecular-weight chemicals that can increase viscosity in organic solvents. Organogels are known for their thermodynamic stability, transparency, viscoelastic properties, biocompatibility, and isotropic behaviour, typically consisting of phospholipids coupled with suitable organic and polar solvents.^[32]

5.2.3 Cergol.^[30]

A xerogel is a solid gel that has experienced dehydration, leading to continual contraction. It generally maintains a significant degree of porosity, between 15% and 50%, accompanied by a substantial surface area quantified in square meters per gram. Typical instances of xerogels comprise strips of gum tragacanth, beta-cyclodextrin, anhydrous cellulose, polystyrene, gelatin sheets, and acacia tears.

5.3 Based on rheological properties^[33]

Gels are recognized for their non-Newtonian flow properties and can be classified into the following categories:

5.3.1 Plastic Gels

Global Journal of Pharmaceutical Research An instance of this category encompasses Bingham bodies and flocculated suspensions of aluminum hydroxide, which exhibit plastic flow behavior. The renogram depicts a yield value, beyond which the elastic gel undergoes deformation and commences flow.

5.3.2 Pseudoplastic Gels

This category includes liquid dispersions including tragacanth, sodium alginate, and sodium carboxymethyl cellulose (Na CMC), which exhibit pseudoplastic flow properties. In these gels, viscosity decreases with an increase in shear rate, and they lack a yield value.

5.3.3 Thixotropic Gels

Thixotropic gels possess weak interparticle interactions that can be disturbed by agitation. Upon the cessation of agitation, the solution returns to a gel state as the particles re-establish their connections. Thixotropic gels include kaolin, bentonite, and agar.

5.4 Based on physical nature^[31]

5.4.1 Elastic gels

Gels including agar, pectin, guar gum, and alginates demonstrate elastic properties. The fibrous molecules are linked at junctions by relatively weak interactions, such as hydrogen bonds and dipole attractions. When a molecule possesses a free -COOH group, an extra link, termed a salt bridge (-COO-X-COO), may develop between two adjacent strand networks. Prominent instances of this gel category encompass alginate and Carbopol.

5.4.2 Rigid Gels

These gels are composed of macromolecules interconnected by primary valence bonds, forming a stable framework. In silica gel, silicic acid molecules are interconnected via Si-O-Si-O linkages, resulting in a polymeric structure defined by a network of pores.

6. Advantages^[34,35]

- Avoid key metabolic processes.
- straightforward to utilize and uncomplicated to implement.
- Simple to discontinue medication.
- Pharmaceuticals are distributed carefully to specific regions. Avoid stomach discomfort.
- Permit the administration of medications characterized by brief biological half-lives and limited therapeutic ranges.
- enhanced patient adherence.

7. Disadvantages of Gels

- Skin irritation or dermatitis may arise as a result of the medicine or its excipients.
- Inadequate permeability of some pharmaceuticals via the dermis.
- Drugs with bigger particle sizes are not readily absorbed through the skin.
- Potential for allergic responses.
- Applicable solely to those medications that require minimal plasma concentrations for efficacy.
- The method is inappropriate for medications that cause skin irritation or sensitization (34,35).
- Brief shelf life - Herbal components may deteriorate more rapidly than synthetic constituents.
- bacteria contamination - Insufficient preservatives in natural extracts may promote bacteria proliferation.
- Batch-to-batch variability — The concentration of active chemicals may vary based on the origin of the herbs.

- Potential for allergic reactions — Certain individuals may experience skin irritation or allergy to specific herbal components.
- Delayed onset of action — Herbal gels may have a slower therapeutic effect compared to standard medicated gels.
- Stability concerns - Variations in colour, pH, or consistency may arise during storage.
- Inadequate clinical evidence - Certain herbal gels possess diminished scientific validation about their efficacy in comparison to conventional medications.

8. Ideal properties of topical gel^[36]

- The gel must demonstrate uniformity and clarity.
- It should readily fracture when exposed to shear or stress during container agitation.
- The gel must possess an inert composition.
- The gel must not possess sticky properties.
- It must not interact with any other element in the formulation.
- The gel must exhibit dependability.
- Application of the gel should not cause irritation to the skin or any area it is applied to.

9. Herbal drugs for skin disease

9.1 Curcumin in acne

The cutaneous and long-term disease of skin is acne which occurs when oil and dead cells of the skin clog the follicles of hair which results in abnormal production of sebum. There are several factors that play a prominent role in the generation and pathophysiology of acne, but the major factors are genetics, inflammation, hyperproliferation of follicles, infection by *Propionibacterium acnes* and sebaceous glands producing sebum in excess amount.^[37,38]

Curcumin's antibacterial and anti-inflammatory properties make it a plausible candidate for acne therapy. A microemulsion of curcumin with myristic acid was formulated in a study, enabling rapid administration of curcumin and efficiently suppressing the bacteria (*S. epidermidis*) linked to acne.^[39]

9.2 Protection against skin cancer

Skin cancer is a condition defined by the existence of malignant cells in the epidermal layers of the skin. Skin cancer is classified into two categories: melanoma and non-melanoma. Melanoma cancer pertains to melanocytes, whereas non-melanoma cancer pertains to squamous or basal cells. The majority of cutaneous neoplasms are categorized as non-melanoma.^[40]

9.3 Potential activity in iatrogenic dermatitis

Iatrogenic dermatitis encompasses various inflammatory skin conditions directly associated with medical interventions and pharmacological treatments. Examples include radiation-induced dermatitis and allergic contact dermatitis.

Numerous studies indicate the effectiveness of curcumin in preventing iatrogenic dermatitis. In experimental models, topical application of curcumin significantly enhances the recovery of epithelial cells and irradiated skin, attributable to its anti-inflammatory properties.^[41]

Curcumin's antioxidant and anti-inflammatory properties assist in preventing premature skin aging. It can partially shield the skin from UV damage, hence diminishing the likelihood of skin tumor growth and preventing premature aging.^[42]

9.4 Chamomile

The chamomile plant, part of the Asteraceae family, is indigenous to the Mediterranean and southern Europe. This species possesses a diverse array of secondary metabolites, such as flavonoids, coumarins, sesquiterpenes, and polyacetylenes, with its phytochemical composition varying according to the cultivation site. The ethnobotanical understanding of this plant has resulted in the extensive utilization of chamomile for numerous health concerns globally.^[43]

Chamomile influences the skin via chemicals such as apigenin and chamazulene, which offer anti-inflammatory, antioxidant, and calming properties. These components mitigate redness, alleviate irritation, and promote skin repair and regeneration.

9.4 Rosemary

The medicinal herb rosemary, scientifically classified as *Rosmarinus officinalis* L., originates from the Mediterranean region and is cultivated globally. Besides its therapeutic applications, it is commonly utilized as a condiment and food preservative. The bioactive molecules, or phytochemicals, in *R. officinalis* L. exhibit a range of pharmacological actions, including anti-inflammatory, antioxidant, antibacterial, antiproliferative, anticancer, as well as protective, inhibitory, and attenuating properties. Therefore, this Review included both in vitro and in vivo research that address the therapeutic and preventative effects of *R. officinalis* L. on certain physiological illnesses produced by chemical, biological, or biochemical agents. Thus, the methods, processes, findings, and conclusions were explained. The primary goal of this study was to demonstrate that plant-based products may be used in place of currently available medications.^[44]

Rosemary benefits the skin through compounds like rosmarinic acid, carnosic acid, and ursolic acid, which exhibit antioxidant, anti-inflammatory, and antimicrobial properties. These bioactives help protect against oxidative damage, reduce acne, and improve skin tone and elasticity.^[45]

CONCLUSION

This review has highlighted the fundamental aspects of skin anatomy, common skin diseases, and the significance of herbal medicine in dermatological therapy. It also discussed the formulation and classification of gels, including hydrogels, colloidal systems, and rheological characteristics, which influence the stability, spreadability, and therapeutic performance of topical preparations. Furthermore, the review summarised commonly used medicinal plants and commercially available polyherbal gel formulations that demonstrate the growing acceptance of herbal products in both pharmaceutical research and the healthcare market.

Despite their considerable therapeutic potential, herbal gels require rigorous standardisation of raw materials, optimisation of formulation parameters, quality control, stability assessment, and clinical validation to ensure consistent efficacy and safety. Advances in pharmaceutical technologies, phytochemical characterisation, nanotechnology, and evidence-based research are expected to further improve the effectiveness of herbal topical formulations. Overall,

herbal gel-based drug delivery systems represent a sustainable and patient-friendly approach to managing skin diseases, offering significant opportunities for future research, product development, and commercialisation in modern dermatological care while supporting the integration of traditional herbal medicine with contemporary pharmaceutical sciences.

10. Marketed polyherbal gels

Table 1: Marketed Polyherbal Gels

S. No.	Product (Brand)	Polyherbal Drug	Manufacturer	Indications
1	Rumalaya Gel	Indian Wintergreen, Shallaki, Nirgundi,	The Himalaya Drug Company	Relief of joint pain ^[46]
2	Tentex Royal Performance Gel	Tridax, Betel, Aloe vera	The Himalaya Drug Company	Moisturising intimate gel ^[47]
3	Pilefine Herbal Gel	Kasisadi Oil, Jatyadi Oil, Punarnava, Raktachandan	Healing Pharma India Pvt. Ltd.	Relief from piles ^[48]
4	Pilestrust Herbal Gel	Punarnava Extract, Raktachandan Extract	Biomech Healthcare Pvt. Ltd.	Piles, anal fissures ^[49]
5	Ayur Mastilep Topical Herbal Gel	Turmeric, Licorice, Paederia, Eucalyptus	Royal Herbal Land Pvt. Ltd.	Management of mastitis, ^[50]
6	Hiora-GA Gel	Triphala, Yashtimadhu, Khadira, Nimba, Babbula	The Himalaya Drug Company	Gingivitis, gum inflammation ^[51]

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