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TOPICAL PROBIOTIC GEL: AN OVERVIEW

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Abstract: Topical drug delivery system is a painless route of drug administration. There are different skin diseases and infections caused by fungus and microorganisms. which are treated with the probiotics or living microorganism which are used as active pharmaceutical agent. The purpose of writing this review article was to compile the recent literature with a special focus on a rational approaches of topical probiotic gel formulation and basic components of topical drug delivery systems. Topical applications of drugs have advantages of delivering the drug directly at the site of action and acting for a prolong period of time. Skin is one of the most widespread and important accessible organs on the human body for topical incorporation. it is the main route of topical drug delivery system. Many widely used topical probiotic products like ointments, creams and lotions have number of disadvantages as they are usually very sticky causing un-comfort to the patient after application. Moreover, they also have less spreading coefficient and need to apply with rubbing and also have the problem of stability , due to all these factors, within the major group of semisolid preparations; the use of gels has increased both in cosmetics and in pharmaceutical preparations because, A probiotic gel is colloid and it is typically 99% by weight formed by liquid material, which is immobilized by surface tension between it and a macromolecular network of fibers built from a small amount of a gelatinous ingredient present in the formation. In this revive we discus about the general Prepration and evaluation of probiotic gel

Index Terms - Skin, Probiotic, gel, Topical, Novel,

I.INTRODUCTION

The important need of microorganisms in human health dates back to the era when Louis Pasteur first discovered the importance of fermentation and also brought attention to the fact that the consumption of fermented food is be beneficial for human body. Oral and topical probiotics are used for treatment of several skin infections. Microorganisms present inside our body, in both the gut and on our skin. The skin microbiome has several species of microorganisms. Any imbalance in these microorganisms results in skin disorders. Acne, atopic dermatitis, psoriasis, and rosacea are some common skin conditions that arise due to an imbalance in the existing skin microbiome.

Probiotics are well known clinical applications in many skin disorders and probiotic bacterial therapy may have a great potential in preventing and treating several skin infections. Research studies have established a interlink between the disturbed gut microbiome and inflammatory skin infection, thereby increasing the potential of oral probiotics as a treatment option for skin disorders. However, there is very tiny information and clinical studies that have studied the efficacy of topically administered probiotic products. The topical application of probiotic bacteria may help to increase the skin's natural barrier by having a direct effect at the site of action. Some cosmetic preparations may help in selection in the normal skin microbiome by being selective in their activity.

Topical probiotics have been used to maintain a health of skin microbiome since the starting of the 20th century, the last decade is a dramatic rise in commercially available topical probiotic products. With the increasing need of these topical products and the dearth of clinical trials or efficacy studies to establish their

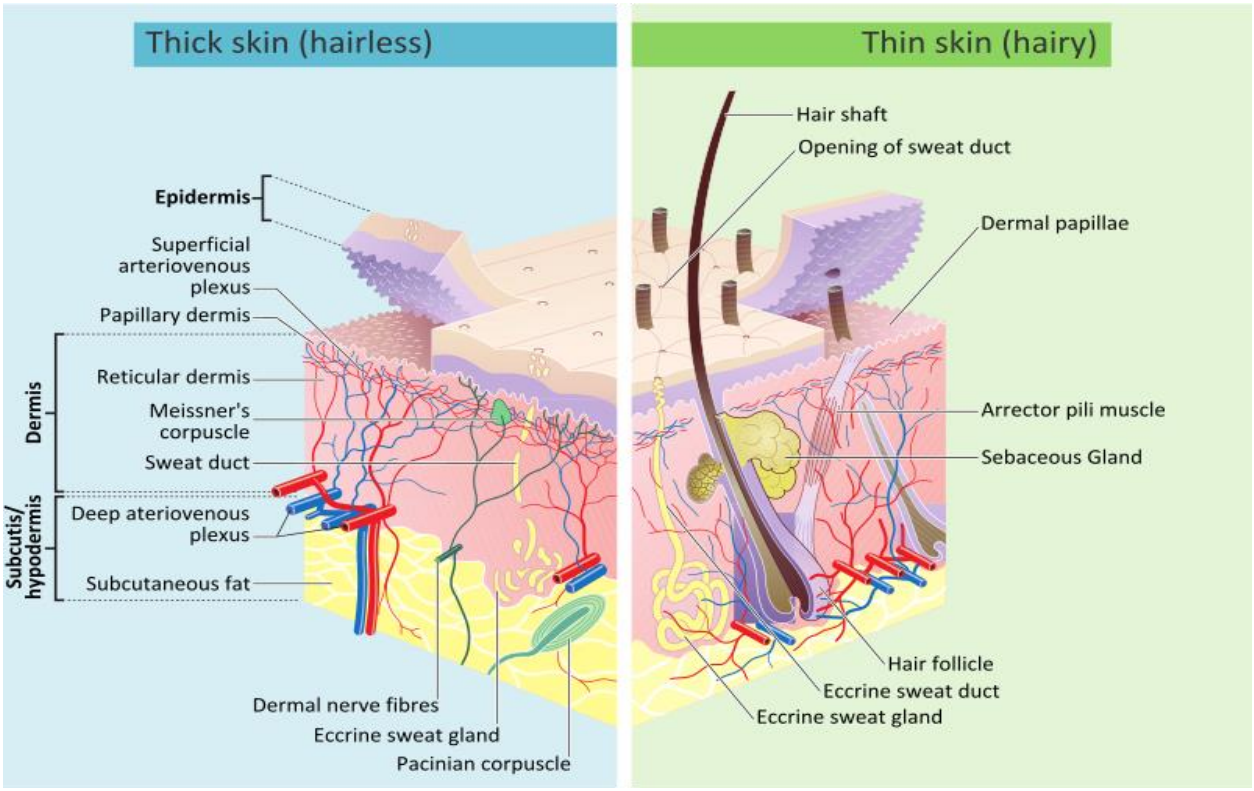
clinical strength, we aimed to write a detailed review article on the use of topical probiotics in treating skin disorders.

RECENT NOVEL APPROACH IN TOPICAL PROBIOTICS:

Probiotic Coate Apparels, probiotic coated clothing Hospital clothing, aprons, Microbial contamination of trousers and other clothing worn by hospital workers and hospital Diseases that cause infections. Although antibiotics are added to laundry detergents to kill bacteria on clothing, using probiotics on hospital clothing is a new way to use topical probiotics to treat skin diseases and conditions. In one of these studies, researchers

II. ANATOMY OF SKIN

Human skin comprises of three layers but mutually dependent with other tissues tissues.



Epidermis:

Epidermis consists of multilayered epithelium and has 5 layers:

1.Stratum corneum.
2. Transparent layer
3. Granular layer
4. Spiny layer and
5. Germinal layer

Dermis:

The layer beneath the dermis is a thick tissue and elastic layer composed mainly of collagen, elastin and fibrils, giving it flexibility and strength. The dermis contains blood vessels, sweat glands, sebaceous glands, hair follicles and blood vessels. The dermis is a vascular, collagen-rich connective tissue containing mucopolysaccharides, collectively referred to as the matrix.

Hypodermis:

Hypodermis is the inner layer of the dermis. Skin is the connection between the skin and tissues in the body, such as muscles and bones. Sweat glands, sebaceous glands and hair follicles enfold in epidermis but they stem from dermis. Sweat glands release a dilute salt solution into the surface of skin. The evaporation of this dilute salt solution makes skin cool and this is important for temperature regulation of both body and skin

III. FACTORS AFFECTING TOPICAL ABSORPTION OF DRUG

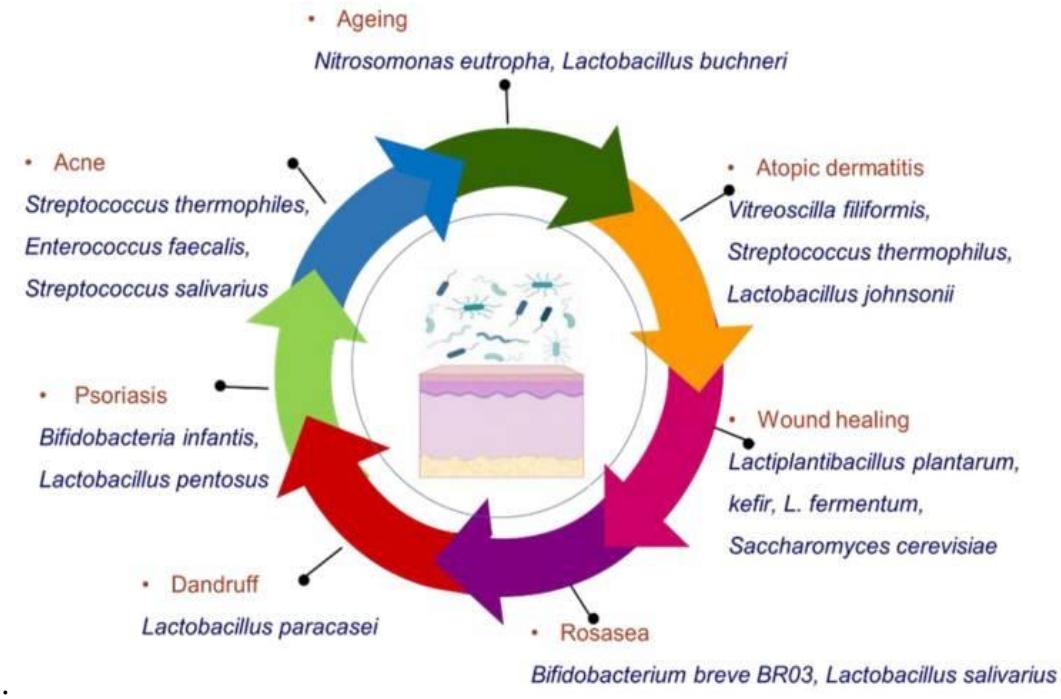
The factors that affect the topical absorption of drug are as follows:

1)Physiological factors.
Skin thickness.
Lipid content.
Density of hair follicles.
Density of sweat glands.
Skin pH.
Blood flow.
Hydration of skin.
Inflammation of skin.

2)Physiochemical factors.
Molecular weight
Partition coefficient.

IV. TOPICAL PROBIOTICS FOR THE MANAGEMENT OF SKIN DIFFRENT SKIN CONDITIONS.

Some researches on animals and in humans have been conducted in order to define the exact role of topical probiotics in maintaining microbial balance in skin disorders and their role in dermatology as a whole. shows the various probiotic microorganisms that have shown beneficial effects in the management of some common disorders.



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V. ROLE OF TOPICAL PROBIOTICS IN THE SKIN MICROBIOME

Researchers continue to explore the connection between the gut-skin axis in various skin diseases. As our understanding of the role of the microbiome in various skin diseases continues to deepen, it has become possible to modulate the immune system by restoring microbiome balance. It emerged as a new research method. This simple approach to treatment involves the use of oral and topical probiotics. Probiotics are beneficial bacteria that contribute to body health. Over the years there has been an increase in oral and topical use in cosmetics and in the treatment of skin diseases. When a new product is introduced to the market, many researchers conduct studies to determine the product's effectiveness, performance, safety and training. Topical probiotics are considered a safe treatment without side effects, especially when compared to traditional treatments for skin conditions. However, the number of clinical studies and effectiveness studies conducted in this field is limited. Most cosmetics are still used as personal beauty products and clinical trials are ongoing. Although the exact mechanism by which probiotics improve skin health is unknown, many documents and

patents document their beneficial effects on skin health, and the data continues to grow. Many patent applications have been filed regarding the use of topical probiotics in skin care.

VI. PROBIOTIC SELECTION:

1. Identification of bacteria: Safe probiotic products must identify the bacteria used and state the actual bacteria on the label. This is important because some recent reports indicate that the identity of the recalled virus does not match the data on the product. Molecular methods such as 16r DNA sequencing or DNA/DNA hybridization are now available and correct taxonomic nomenclature needs to be used.

2.Availability of probiotic products: It is generally accepted that probiotic bacteria in food must remain active throughout storage and the digestive tract in order to have a positive effect on health. Live bacteria have been reported to reduce symptoms in people with eczema, while upregulation of inflammatory cells has been associated with gastrointestinal symptoms; This reveals the importance of survival. The minimum number of probiotics shown in different probiotic products; However, these levels will depend on the type of bacteria used. Dosage studies should be performed when testing probiotic strains to determine the quality of bacteria in a particular product. Traditionally, plate counting has been used to identify living organisms.

3. Gut Microbiota: The gut microbiome has been recognized as an important factor affecting our health and well-being. The human gut has a unique microbiota, creating an individual microbiota for each person. This unique microbiota depends on the environment and genetics. The total number of bacteria in the intestine can be estimated at 1012 bacteria per gram of intestine. The interaction between the microbiota and the host plays an important role in the human body, for example in establishing oral tolerance or maintaining intestinal homeostasis.

4. Probiotic Mechanism of Action: Many mechanisms of action have been proposed to explain the beneficial effects of probiotics. However, our understanding of the mechanism of action of probiotics is only preliminary and it should be noted that this mechanism may be different and all bacterial probiotics may have specific activities that affect the host. In general, probiotics do not permanently colonize the human intestine, but some types of bacteria can colonize the environment and alter the native microbiota. Specific probiotics have been reported to modulate local and systemic immune responses.

5. Benefits of Probiotics: Live microorganism species have long been used as medicine to treat stomach disorders. However, because different probiotics can interact with the host in different ways, more information is available about the most common probiotics and their health benefits, which are considered a type of infectious disease before health-related products are approved. It is important to understand that each probiotic strain is unique and different, and their properties and characteristics must be clearly defined. It is important that all kinds of diseases are known using modern methods and that these diseases are made available to all research groups involved in health assessment and systems.

6. Safety of Probiotics: Safety assessment is an important step in the selection and evaluation of probiotics. Very few probiotic strains have been specifically tested for safety, but the long-term safety history of some probiotics may be considered the best evidence of their safety. Although some Lactobacilli and Bifidobacterial have been associated with rare diseases, especially in patients with severe disease, the safety of members of the genus is generally accepted due to their history of safe and non-toxic use due to their origin.

CLASSIFICATION OF GELS

Gels are classified mainly by two methods based on:

1) Nature of colloid phase

a. Inorganic gels (Two phase system)

b. Organic gels (single phase system)

2) Based on nature of solvent

a. Hydrogel (Aqueous gels)

VII. PREPARATORY PRECAUTIONS FOR GELS

1) Selection of carriers/solvents including buffers and preservatives Pure water is usually used as the solvent. Ethanol, glycerol, PG, PEG 400, etc. can be used to increase the solubility of the therapeutic substance in the dosage form and/or to increase the penetration of the drug into the skin. Chemical compounds such as are used.

2) Buffers Buffers can be added to hydrogels and hydroalcoholic gels to control the pH value of the samples. The solubility of buffer salts decreases in hydroalcoholic carriers. For example, phosphate, citrate, etc. Certain

3) preservatives act synergistically with the hydrophilic polymers used to prepare the gel, thereby reducing the concentration of free (antimicrobials active) preservatives in the formulation. Therefore, the initial concentration of the reaction needs to be increased to compensate for this. For example, parabens, phenols, etc.

4) Antioxidants Can be included in the formulation to improve the chemical stability of medicinal drugs affected by oxidative degradation. Its choice depends on the nature of the carrier used in the preparation of the gel. Since most gels are water-based, water-soluble antioxidants are often used. For example, sodium metabisulfite, sodium formaldehyde sulfurylase, etc.

VIII. PREPARATION OF PROBIOTIC GEL

Example 1
Preparation of lactic acid gel
In this example, Lactobacillus acidophilus sample and plan are used. Description of the gel of the present invention
1. Classification of bacteria: Lactobacillus acidophilus CGMCC 1084 (China Microbial Culture Collection Committee) is cultured with MRS culture medium from 37° to 24 hours, centrifuged to collect the cells, and then
2. Gel Base: Whey concentrate as base (whey protein content is 3%), add appropriate amount of WPI until whey protein content is 12%, heat at 80°C for 20 minutes, cool to 45°C and leave;
3. Mixing: After centrifugation, mix and stop the bacteria and gel base in a limited ratio until the cell concentration reaches 1.5 × 10 11Cfu/ml;
4. Let stand and cool: Mix mixed bacteria and gel base and leave in a gel file at 6°C. The bacteria that can be counted on the probiotic gel can reach 10 11 Cfu/ml. Lactic acid bacteria microcapsules can be stored at 4°C for 9 months and live bacteria can still reach 10 10Cfu/ml

IX. EVALUATION OF PROBIOTIC-GELS:

The following criteria were used to assess gels:
• Homogeneity
• Grittiness
• Extrudability study
• pH Determination
• Viscosity
• Skin irritation study
• Drug content
• Spread ability
• In-vitro release
• Stability studies

Uniformity: Check the resulting gels for uniformity after placing them in the box. They examined the collected items and evaluated their appearance. 104 Roughness: If there is no obvious problem in the light, infinite analysis of four points is performed to determine the presence of the object. The gel preparation clearly meets the need to be free of specific properties and texture necessary for any successful preparation.

Extrudability: A good gel extrusion should be better if done using a small amount of gel. The gas bottle filling machine process is used to solve the extrusion problem of aluminum folding gas bottle content. Two clamps secure a folding cylinder containing 10 g of gel. Extrudability is not completely predetermined in terms of the weight (in grams) required to release a 0.5 cm strip of gel from a filled cylinder in 10 seconds.

pH Guarantee: Use a computer pH meter to adjust the pH of the gel. Dissolve 100 cc of refining liquid in 1 g of gel and refrigerate for 2 hours. Each pH value was estimated three times and the average was calculated. 105

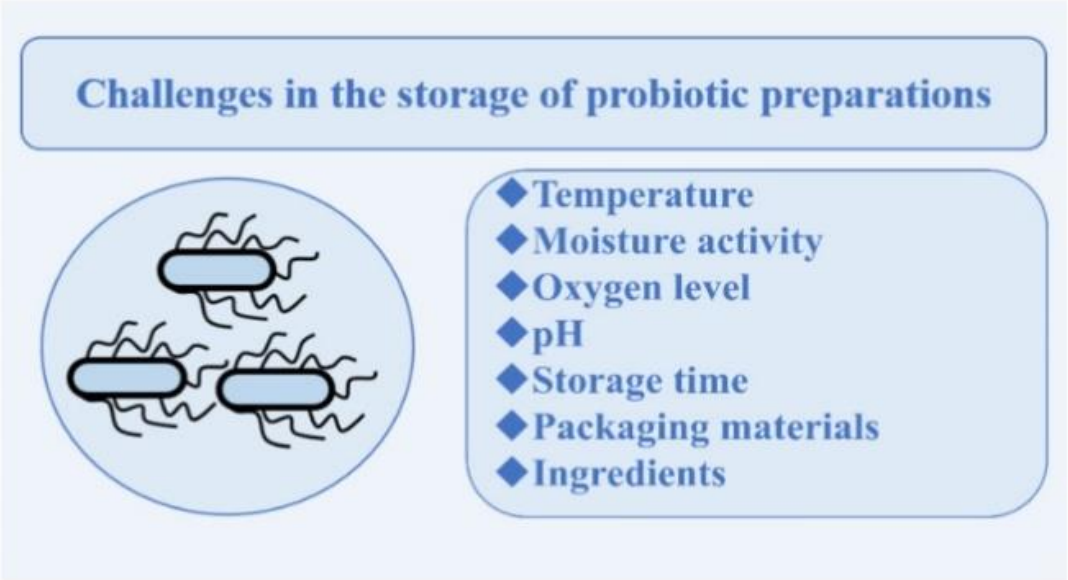
Viscosity: Estimate the consistency of the pre-assembled gel using a Brookfield viscometer. Using spindle number 64, hold the gel at speeds 20 and 30 and write down the relevant numbers. Investigation of infection: Two gels were used on guinea pigs of both genders (weighing between 400 and 500 grams) for skin irritation testing. These animals are fed regularly and have limited access to water. Animals are raised as usual. The hair on the back of the guinea pig is removed, leaving an area of 4cm2 on both sides, and one side is used for control and the other side is used for measurement. Use the gel (500 mg/guinea pig) twice daily for 7 days and record the vaccine and the vaccine (if any) at the site.

Content of medication verified: Establish concentration of medication by accurately measuring the gel (approximately 100 mg). mg) is melted and dissolved in 100 ml of phosphate carrier 7.4, then the mixture is stirred continuously on an attractive stirrer for 24 hours. All arrangements are voiced. The solution in the array was analyzed spectrophotometrically with appropriate dilutions after sonication and visualization.
Spread ability: Refers to the surface area over which the gel spreads rapidly when applied to the skin or affected area. The benefits of expansion also depend on its visibility. Spread ability is expressed as the number of seconds it takes for two slides to separate from the gel trapped between them when subjected to a given load. Better spread ability can be achieved by splitting two slides in less time. 106 It is calculated using the following formula: S = M. L / T where, M = weight. Tie at the top L = length of the slide T = time required to remove the slide.

In vitro permeation studies: To focus on the separation of the gel from the cellophane layer, diffusion studies of the gels were first carried out in the Keshary-Chien dispersion cell. Dispersion controls were performed at 37° using 25 ml of phosphate cradle (pH 7.4) as lysis medium and gel test (0.5 g) on cellophane membrane. At regular intervals of 1, 2, 3, 4, 5, 6, 7, and 8 h, 5 ml of each sample was removed and replaced with an equal amount of fresh lysis medium. The sample was then tested at 362 nm using a phosphate support to ensure the concentration of interest. The study performed with optimization of the stability study (F5) found no significant changes in transparency, pH and consistency compared to the first-time results. After a 12-day stability study, the gel formulation showed clear transparency, pH 5.2, and stable inconsistency. These observations indicate that the probiotic gel formulation is inherently stable and can be stored at room temperature.

X. STORAGE CONDITIONS

Storage is an important aspect of probiotic preparation before use because conditions directly affect the effectiveness of probiotic preparation. Biological activity and effectiveness of the preparation. Factors such as temperature, water activity, oxygen content, composition of probiotic preparations, storage time and pH are important factors during storage. Since probiotics are not very sensitive to temperature, they are usually stored at 4°C because storing them at room temperature will prolong their life. Studies have shown that probiotics, especially anaerobic bacteria such as Bifidobacterium bifidum, are stronger and more potent in the body in patients who are deprived of oxygen and water. To reduce the oxidative stress of probiotics in production, different oxygen groups such as cysteine and ascorbic acid were created and oxygen contamination of the packaging was reduced



XI. DIFFERENT MARKETED TOPICAL PROBIOTIC PRODUCT

product	***probiotic***	**efficacy**
Okana	*Bacillus* bacterial ferment extract	Helps skin retain its firmness and elasticity and keeps it feeling smooth and plump.
Amperna	*Unique probiotic complex*	Soothes irritated skin and calms redness. Tested on eczema, dermatitis, perioral dermatitis, rosacea, and acne-prone skin.
Cream	*1. Lactobacillus acidophilus 2. Lactobacillus rhamnosus*	Anti-photoaging
Probiotic Skin Cream Melvory	*lactobacilli probiotic (Lactobacillus ferment filtrate)*	Cleans away the bad bacteria on the skin. For acne-prone or teenage skin.
Andalou Brightening Probiotic + C Renewal Cream	*Bacillus coagulans*	Skin-friendly vegan probiotic microflora enzymatically supports dermal vitality, targeting over-exposed surface cells for a lighter, tighter, brighter looking appearance, and a luminous complexion.
Biossance Squalane + Probiotic Gel	*Lactococcus ferment lysate*	Helps restore the skin's balance and renew the skin barrier
Neogen Dermalogy Probiotics Double Action	*The patented complex of Bifida ferment lysate, Lactobacillus, and Streptococcus thermophilus ferment*	Protects the skin barrier
LaFlore Probiotic Serum Concentrate	*Lactococcus ferment lysate and live kefir Probiotics (Hansenula/Kloeckera/ Lactobacillus/Lactococcus/ Leuconostoc/Pediococcus/ Saccharomyces)*	Helps calm and smooth fine lines and wrinkles and boosts the skin's natural defense system.

Dot and Key 72 h hydrating gel and Probiotics	*Saccharomyces black tea ferment, Lactobacillus*	Provides hours long moisturization and restores microbiome balance

XII. ADVANTAGES OF GEL FORMULATIONS:
1. Compared to other probiotic formulations, probiotic gels are simple to manufacture.
2. probiotic Gel is a sophisticated, non-greasy composition.
3. probiotic Gels offer fantastic adhesion to the application region.
4. probiotic Gels are eco-friendly and biocompatible.
5. Be incredibly resilient to stressful situations

XIII. DISADVANTAGES OF GEL FORMULATION:
1. probiotic Gels have a more gradual and persistent effect.
2. The additives or gelators could irritate people.
3. The risk of microbial or fungal assault on gel is increased by the presence of water.
4. The formulation's solvent loss dries to gel.
5. In some gels, flocculation results in an unstable gel

XIV. APPLICATION OF GELS:
1. For topical applications, probiotic gel is applied directly to the skin, mucous membranes or eyes.
2. They are available as implants or intramuscular injections of long-acting medications.
3. Gel products are useful as suppository bases, colloidal agents in suspensions, thickeners in oral solutions, and binders in granulation solutions.
4. Beauty gels are widely used in many products, skin and hair products.
5. Since the scalp is one of the parts of the body where it is so oily that patients cannot avoid cosmetics and lotions, topical steroids in gel form can be used to treat the scalp.
6. Compared with creams, probiotic gels have better potential as dispensing agents in cosmetic applications because they are strong, non-sticky, need less electricity during operation, and have beauty.

XV. REGULATORY ASPECTS OF PROBIOTICS IN TOPICAL SKIN CARE AND THE CHALLENGES

Since probiotics have many uses in skin treatment, it is important to regulate the label and business models correctly. Almost all cosmetics containing probiotics have not yet gone beyond personal care products. Additionally, these cosmetic products are sterile and may contain antibiotics, which can affect the ability of probiotics and further alter the microbiota of recipients with pre-existing disease conditions. Therefore, safety should be the primary focus when regulating probiotics. There are currently no specific guidelines for the commercialization of probiotics, and products are regulated based on their end use, whether as a medicine, medical device, food, drug or make-up. Probiotic products with health claims may be advertised as medicinal or medicinal. If the product contains a disease that cannot be used, it will be considered a medical device.

Probiotic skin care products are a recent innovation, and there is currently no scientific evidence on the effectiveness and safety of topical probiotics. In addition, the clear boundaries between food, medicine and cosmetics make it difficult to develop and promote probiotic cosmetics. Cosmetics are not produced under sterile conditions and therefore do not require sterility testing. These products often contain preservatives to control the growth of bacteria.

These antibiotics may affect the viability of probiotic bacteria and may also alter the microbiota of the recipient. Pharmaceutical preparations containing probiotics have not yet progressed beyond personal care products; Due to their high colony-forming unit load, it is difficult for such preparations to pass US FDA regulations regarding microbial load. Performance testing is an important issue in testing these products. Probiotic topical preparations used to treat acne have been tested for microbial counts according to the United States Pharmacopoeia (USP). Cosmetic products were found to not contain "unacceptable" live bacteria and therefore need not contain less than 1,000 CFU per USP. Competitive disease testing is difficult for samples containing live bacteria. In one particular study, a free sample was tested for 14 and 28 days. After days 14 and 28 of the challenge tests, the blank preparation showed a decrease in the number of inoculated bacteria and no increase in yeast or mold. In this particular formulation, it turns out that one of the reasons why milk preserves itself and does not need other preservatives besides cosmetic products is the lack of water activity:

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