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Topical Nanoemulgel for Treatment of Psorasis: Psoralea corylifolia (Bakuchi)

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ABSTRACT: India has a rich tradition of plant based knowledge of healthcare. Modern pharmaceutical technology is being combined with traditional health medicine to increase its efficacy. Psoriasis is a chronic inflammatory disease that affects 1–3% of the all-inclusive community with significant hindrance to the personal quality of life. These conditions may adversely affect the patient's quality of life and prompt psychosocial stretch. Psoriasis can be classified as mild, moderate, and severe conditions. Dermal treatment guaranteeing percutaneous penetration is presently very suggested in topical signs for psoriatic patients, which can be accomplished utilizing pharmaceutical Nanoparticles i.e., Nanoemulgel formulation. For topical drug delivery, poor permeability of drugs leads to a high cost of therapy and decreased patient compliance. This problem can be controlled by preparing lipid-based colloidal sub-micron drug delivery. Due to this technique concentration of drugs can be penetrated the skin as the lipophilic intracellular pathway of the skin allows penetration of materials of less than 20nm, hence drug repository is created in the stratum corneum and epidermis. This review aims to prepare Herbal Nanoemulgel containing psoraliya corylifolia.

KEYWORDS: Bakuchi (psoraliya corylifolia), Antipsoriatic activity, Topical Nanoemulgel.

I. INTRODUCTION:

Psoriasis is a hyper augmentation; an autoimmune skin disorder that influences 1–3% of the world's population. Psoriasis is a common skin circumstance that can be painful and itchy; between 1.5% and 3% of people in the world have psoriasis. The skin consists of millions of tiny skin cells. Normally, skin cells die and are replaced by new ones every 3 to 4 weeks. In psoriasis, your body begins producing new skin cells more quickly than normal leading to raised patches. This is related to your immune response, which is how your body fights disease and heals wounds. A reaction to psoriasis is triggered by your immune system even though there is no infection or wound to heal. The reasons why it does this are not completely understood but they are usually due to variations in your genes. Researchers around the world are pursuing new, effective & safer medicines from natural resources to treat psoriasis because synthetic drugs are associated with severe side effects. Psoriasis is a chronic condition, not contagious, but psoriasis can affect all areas of the skin, including the scalp, nails, and genital area. This condition can also affect folds in the skin, such as under your arms, the inside of elbows and knees, or under your breasts. These areas are called flexural areas. Psoriasis can range from being a very mild condition to being a very severe one. At the moment there is no cure for psoriasis, but it can be well managed with various treatments[1]

Mild to Moderate Psoriasis

Many patients with psoriasis have mild to moderate disease, affecting less than 5 percent of the skin surface area and sparing the genitals ,hands, feet, and face. These patients can often be treated successfully with topical therapies including corticosteroids, vitamin D, steroid creams, and tazarotene and calcineurin inhibitors. There are a few less common topical therapies, such as no medicated moisturizers, salicylic acid, cool tar, and anthralin. A vitamin D analogy is used as immunotherapy or in combination with phototherapy to treat psoriasis in patients with 5 to 20 percent body surface involvement. These agents have a slow onset of action but a longer disease-free interval than topical corticosteroids. Tazarotene is a teratogenic topical retinoid.[2] Tazarotene is as effective as topical corticosteroids in reducing psoriatic symptoms, but it is associated

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with a longer disease-free interval. In general, they improve symptoms with less skin atrophy than topical corticosteroids and are considered first-line treatments for facial and flexural psoriasis [2,3].

Severe Psoriasis

Patients with more severe psoriasis necessities more than 5 % of the body surface area or contain the hands, feet, face, or genitals are generally treated with phototherapy in consonance with systemic therapies.[3] Systemic therapies involve methotrexate, cyclosporine, acitretin, and biologic therapies.[3,4]

TYPES OF PSORIASIS

Psoriasis is considered to be an immune-mediated infection with a genealogical premise including an aggregate between hyperplastic epidermal keratinocytes and a small number of immune cells compose of T-cells, neutrophils, dendrites cells, and macrophages. Psoriasis does not expand starting with one individual, then onto the next by contact, however, can be transmitted hereditarily. [5,6] From a clinical perspective, psoriasis can be viewed as a broad range of different skin signs. The great part of the abrasion has normal characteristics involving erythema, thickening. Although the size of abrasion can change from a pinhead up to a distance of 22 cm, fringes of abrasion are normally round, oval, or polycyclic. Even though it can impact any region, knees, elbows, lumbo-sacral district, scalp, and genital zone are a long time of interval involved.[7] Psoriasis is examined based on clinical history (skin rash, changes to nails, and joint association) and is normally clear. Sometimes, patients have atypical skin abrasion that should be separated from tinea, mycosis fungoides, discoid lupus, seborrheic dermatitis, or non-particular skin signs, for example, insignificant scaling of the scalp, segregated flexural erythema, or genital abrasion. perceptive evaluation of all body surfaces may reveal undeclared, diagnostically helpful highlights, and a skin biopsy may periodically be shown. A different class of psoriasis is as follows and depicted in Figure 1.

Plaque psoriasis (psoriasis Vulgaris):

It is also known as severe stationary psoriasis and involves 85–90% of people with psoriasis. It's pitched up as raised red-colored patches with silvery-white scales. This abrasion can be very itchy and painful, and in severe conditions, it may even crack and bleed.

Inverse psoriasis (flexural psoriasis):

It is characterized by bright red, shiny abrasion which emerges in skin folds such as armpits, groin area, and under the breast. The condition deteriorates as a result of fraction and sweat, and it is susceptible to fungal infection.

Nail psoriasis:

35–40% of people can get psoriasis. It is distinguished by pinhead-sized depression in the nail, whitening of the nail, blood clots in capillaries under the nail, yellow-red discoloration called oil spot or salmon spot, subungual hyperkeratosis, and onycholysis.

Erythrodermic psoriasis:

It is a rare type of psoriasis that affectsonly3% of people with psoriasis. It can come in two varieties: First, progressive chronic plaque psoriasis which grows in scope and confluent, and second, erythroderma which as a result, the body's thermoregulatory capacity is impaired, resulting in hypothermia widespread inflammation of the body's surface severe itching, pain, and swelling. This type of psoriasis is potentially fatal.

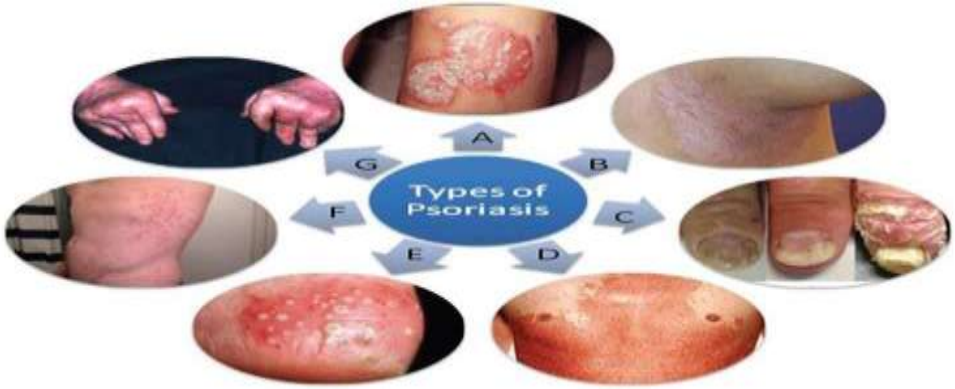

Figure 1: Types of psoriasis.(a) Plaque psoriasis, (b) inverse psoriasis, (c) nail psoriasis, (d) erythrodermic psoriasis, (e) pustular psoriasis, (f) guttate psoriasis, (g) psoriasis arthritis)

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Pustular psoriasis:

It is distinguished by raised bumps filled with noninfectious pus or pustules. These pustules are commonly found on the hands and feet, but they can also be generalized with random widespread patches on any part of the body.

Guttate psoriasis:

In Latin, guttate means "drops." Guttate psoriasis is characterized by small, red, and scaly tear-shaped drops with silvery scales which appear on arms, legs, and the middle of the body. It is usually seen in persons younger than 30 It mostly occurs after an acute B hemolytic streptococcal infection of the pharynx or tonsil. The abrasion can vary from 10 to 100.

Psoriatic arthritis:

It is a chronic inflammatory arthritis that frequently occurs in association with nails and skin psoriasis. It is characterized by painful inflammation of the joints and the surrounding connective tissues. It can occur in any joint but mostly affects the joints of the toe and fingers which lead to dactylitis or sausage-shaped swelling on the fingers and toe. It can also affect the hips, knees, and sacral.

There are two theories fundamentals concerning the manners physiology of psoriasis. The primary hypothesis clarifies the advancement of psoriasis because of the growth that is and proliferation of the skin cells which is because of hyper proliferation of the epidermal cells and keratinocytes. In the second theory, T-cell- the mediated immune system is the primary driver of irritation which encourages overabundance of cell development. Excessive production of the skin cell is a secondary reaction to the factor generated by the immune system. Langerhans cell in the dermis goes as an example, an antigen-presenting cell that relocates to the lymph node (site of T-cell). White blood cell actuation is caused by the presence of Langerhans cell as an unrecognized antigen and because of co stimulatory signals. A co stimulatory signal is caused by lymphocytes' function-related antigen -3 and intracellular adhesive particles. Cytokines are discharged by T-cells in the dermis and epidermis because of the release of (tumor necrosis factor) protesting aggregation and epidermal hyper expansion. Immunosuppressant clear out psoriasis and proof of support for the immune-mediated model of psoriasis pathophysiology.

PATHOPHYSIOLOGY OF PSORIASIS

S.NO.	BOTANICAL NAME	FAMILY NAME	COMMON NAME	PLANTS PART USED
1.	Aloe Vera	Liliaceae	Aloes,kathalai	Leaf
2.	Alpinia galanga	Zingiberoside	Thai ginger	Rhizome
3.	Angelica Sinesis	Apiaceae	Chinese angelica	Root
4.	Psoralea corylifolia	Fabaceae	Psoralea	Seeds
5.	Annona squamosa	Annonacea	Sugar apple	Rhizome and leaf
6.	Argemone Mexicana L.	Papaveraceae	Prickly poppy	Root
7.	Azadirachata indica A. Juss.	Meliaceae	Neem,veppam	Leaves,bark,stem
8.	Caesalpinia bonducella	Caesalpiniaceae	Fever nut	Leaves
9.	Calendula officinalis	Compositae	Marigold	Flowers
10.	Capsicum annum	Solanceae	Milagai	Leaves
11.	Cassia fistula L	Caesalpiniaceae	Amaltas	Fruit Pulp
12.	Cassia tora L	Caesalpiniaceae	Sickle senna	Leaves
13.	Centella Asiatica L	Apiaceae	In*pennywort	Whole plant
14.	Crotalaria juncea	Leguminosae	Sunn hemp	Seeds

Table 1: Showing Plant Name, Family, Local Name, and Plant Parts Used

Potent Herbal drug: Psoralea corylifolia

Psoralea corylifolia Linn (Fabaceae) is an erect annual herb with broadly elliptic leaves, yellowish or bluish-purple flowers, and compressed, mucronate, dark chocolate to almost black colored seeds.[8] The most trusted Ayurvedic

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herb for blood purification and skin health. Traditionally in India and China, Psoralea corylifolia has been used for the treatment of stomachic, deobstruent, anthelmintic, diuretic, vitiligo, and also certain skin diseases, such as leukoderma, psoriasis, and leprosy.[9] Psoralea corylifolia has been traditionally used as an Antipsoriatic agent because its chief constituent is psoralen which is a photoactive furocoumarin that binds to DNA, and forms photoproducts with pyrimidine base when exposed to UV light. This action inhibits DNA synthesis and decreases the keratinocyte hyper proliferation. [15] Psoralea corylifolia contains psoralen which are capable of absorbing radiant energy. In the UV range Photoactivation by Psoralen with (200– 320nm) is known to ameliorate various skin disorders such as psoriasis, vitiligo, and mycosis fungicides in humans. [10] Psoralea corylifolia has been traditionally used as an Antipsoriatic agent. Used for treatment of skin diseases like leukoderma etc. A compound ointment of the powdered seeds of Psoralea corylifolia and Cassia Tora with lime juice was tried in cases of ringworm with marked beneficial results. [11,12,13,14]

NOVEL AND ADVANCED APPROACHES FOR PSORIASIS

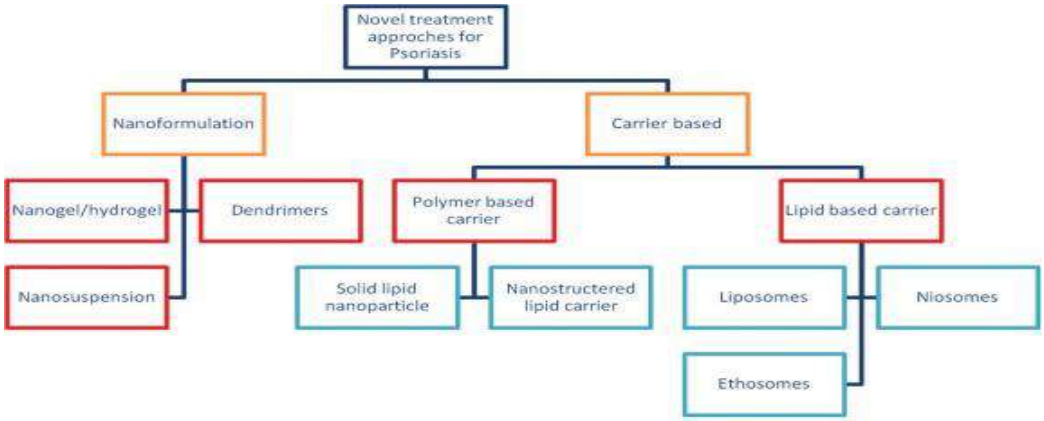

Figure 2: Novel treatment approaches for psoriasis

Nanoemulgel are having droplet size on the order of 100 nm. A typical Nanoemulsion with oil, water, and emulsifier. Nanoemulgel can be transferred into several dosages, topical, 0ral, intravenous, intranasal, ocular & pulmonary. They are endowed with higher solubilization capacity than simple micellar dispersion, greater kinetic stability than coarse Emulsion, and are used in cosmetic industries.[21]

Important Component of Nanoemulgel

Oils: Oils used in Nanoemulsion are usually mineral oils used as the vehicle for drugs E.g., castor oil & various fixed oils (cottonseed oil, maize oils, Arachis oil), eucalyptus oil, rose oil, clove oil, etc. [23]

Aqueous Phase: Commonly distilled water is used as an aqueous phase for the preparation of Nanoemulsion and hydrogel.

Surfactant and Co-Surfactant: surfactants are used to give emulsification at the time of formulation and control day-to-day stability during the shelf life of prepared Nanoemulsion. The general selection of surfactant depends on the type of emulsion [15].

Gelling Agent: Polymers essentially give the structural network for the preparation of gels and are known as gelling agents E.g., Natural - Agar, Tragacanth, Guar gum, Xanthan Gum, Semi-synthetic and Synthetic Carbopol, HPMC (cellulose derivatives) & poloxamers.

Permeation Enhancers: They interact with skin constituents to produce a reversible temporary increase in permeability.

Advantage Of Nanoemulgel [22]

i. Nanoemulgel also helps in the controlled release of drugs having a shorter half-life.
ii. Provide higher Spread-ability of the formulation than creams.
iii. Nanoemulgel are Nontoxic and non-irritant. Better load of drug compares to other formulation.
iv. Increase skin permeability and drug deposition. The stability of Nanoemulsion is enhanced due to the distribution of oil

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droplets in the Gel base; where the affinity of the drug toward oil determines stability.

v. Also, good adhesion on the skin with high solubilizing power leads to a high concentration gradient that increases penetration of the drug as it moves down.

vi. Moreover, these types of formulations give support to the delivery of lipophilic and poorly water-soluble drugs and also improve patient compliance.

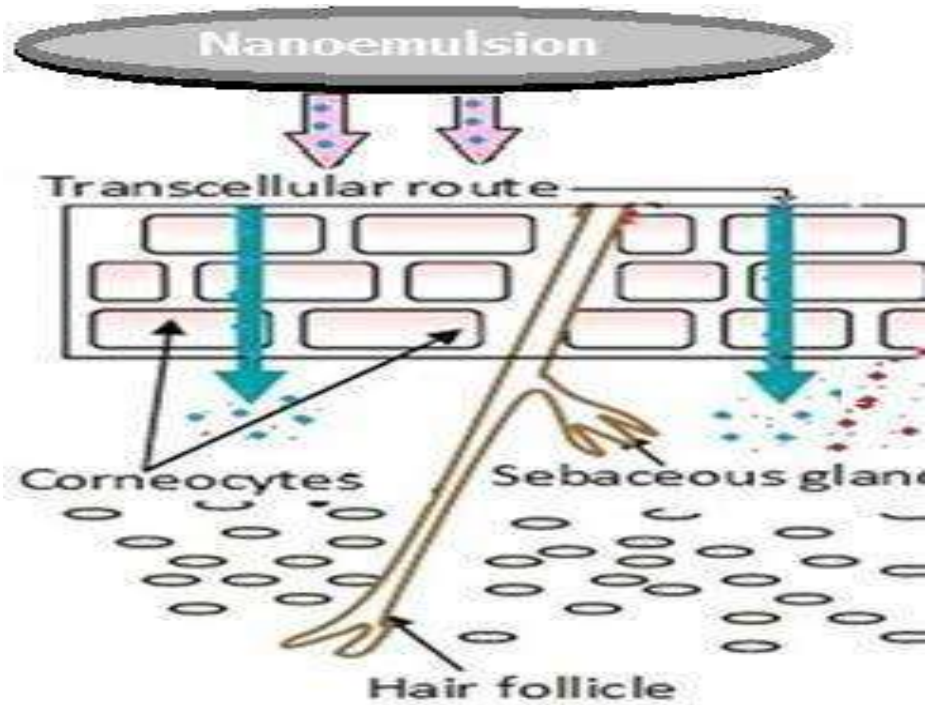

Figure 3: Mechanism of Nanoemulsion

Methods Of Formulation

Formulation of Nanoemulsion-gel can be summarized in the following steps,

1. Screening of components
2. Preparation of Nanoemulsion
3. Preparation of Nanoemulgel

Screening of components

Drug Solubility was determined in different oils by excess addition of drug into different components followed by continuously stirred 72 hours to achieve equilibrium. After that sample centrifugation and the supernatant was taken and solubility was determined by the appropriate analytical method.

Preparation of Nanoemulsion:

The drug is then solubilized in oil and oil is added to N mix, this mixture is diluted with water to form of Nanoemulsion of the given drug.

Preparation of Nanoemulgel:

Gel base is prepared using 1g of the Carbopol in a required quantity of water. After complete swelling and dispersion of Carbopol solution during 24 hours period, prepared Nanoemulsion is slowly added under continuous stirring. The addition of Triethanolamine gives homogeneous gel dispersion. Finally required remaining part is adjusted with distilled water.

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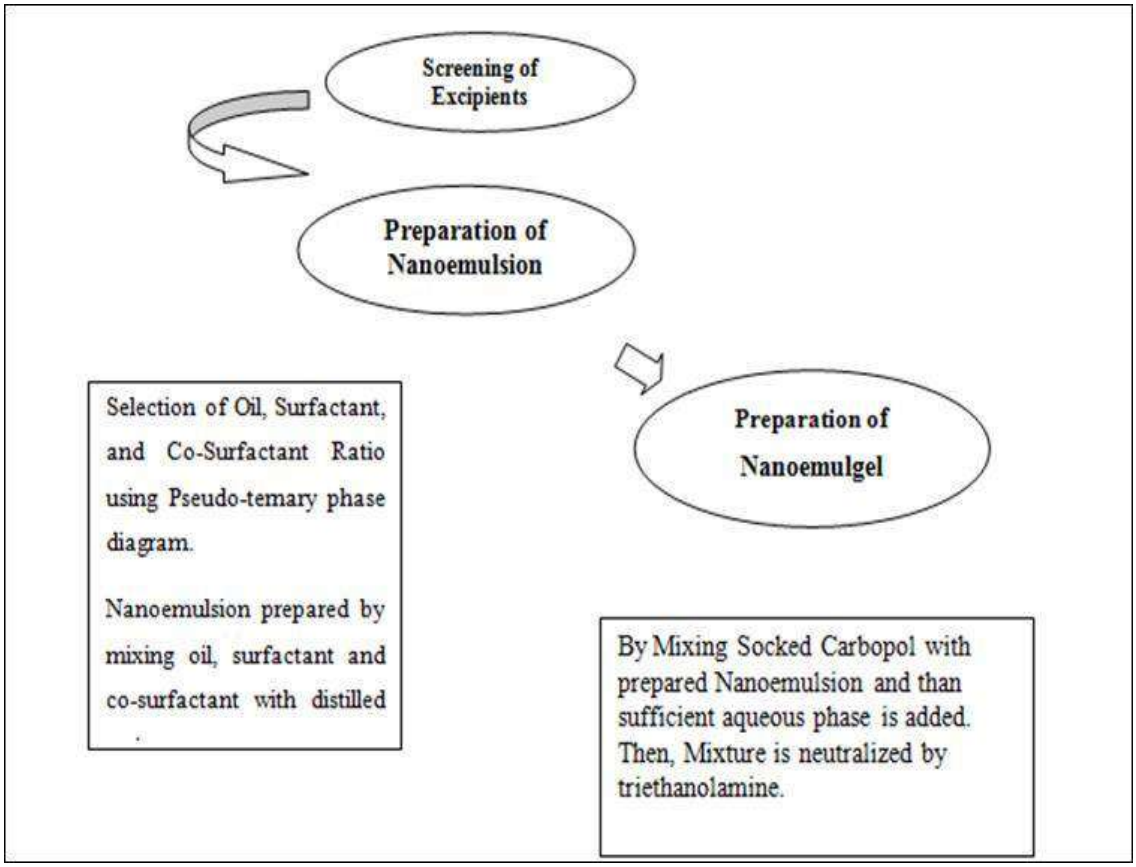

Optimization And Evaluation

Measurement of pH:

Various Topical formulations have pH between a range of 5-6 measured with a pH meter. For testing, 1g of gel is dissolved in 10ml of water. PH of each formulation is done in triplicate to avoid the error.[23]

Size of goblets:

For determination of this parameter 1 gm of gel was dissolved in water and stirred to get dispersion and then the sample was injected into the photocell of the Malvern zeta sizer.

Determination of Rheological properties:

20gm of Nanoemulsion-gel filled in a 25 ml beaker was used to measure viscosity by using spindle number S64 by Brookfield viscometer [23].

Accelerated stability studies:

As given in ICH guidelines, the formulation is stored in an oven at 37±2°C, 45±2°C, and 60±2°C differently for 3 months. Drug content is analyzed every two weeks by a suitable analytical method. Stability measurement depends on changes in pH of gel or drug degradation [23].

Determination of % drug content:

1 g of Nanoemulgel is blended with 25 ml of methanol. This arrangement is sonicated for 30 min, calculate. utilizing the appropriate explanatory strategy from this arrangement.

Spreadability of Gellifed Nanoemulgel:

It can be measured by using a Slip and Drag basis, as suggested by Multimer, here 2 gm of Nanoemulgel is kept on a lower ground slide which is fixed with a wooden block and sandwiched is prepared by other glass slide having a similar size which is attached with a hook having 500mg weight placed. After 5 min extra weight was placed on the pan connected with the second slide.

Skin irritation test:

0.25 gm Nanoemulgel is applied on each different site (two sites/rabbit). After 24 hr of application, rabbit skin sites are wiped and cleaned, and change in color of skin or unwanted change in external appearance is noted and checked**.**

In-vitro Diffusion studies:

Franz diffusion cell is used for performing diffusion study of prepared Nanoemulgel. A cellophane membrane is used for the study and 0.5 gm of sample is applied to the membrane and diffusion is carried out for 8 hr at 37±1°C using phosphate buffer (pH 7.4). At interval of 1 hr, 1 ml

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pg. the sample is collected and replaced with a new buffer solution. Collected sample analyses by using a suitable analytical method [24].

Assessment of skin permeation test:

The changes like chemical and structural in the epidermal layer are determined by using differential scanning calorimetry (DSC). To assess the mechanism of permeation, thermal transition in desiccated SC membrane of rats is investigated using DSC. Both treated and untreated skin samples are previously hydrated on 27% Sodium-Br solution for at least 48 hr to ensure lowering of hydration to 20%. The skin samples are stored over silica gel, for 3 days in desiccators before examining. The skin sheets are cut into pieces and 4mg weighted pieces are sealed in 10µL aluminum pans and kept in a differential scanning calorimetry unit along with an empty pan as reference. The flow of Nitrogen is adjusted to 20ml/min which is used as a pure gas. Samples are heated continuously at a 10°C/ min rate for the range of 30-400°C and fluctuations in DSC Graperies were noted and studied [24].

II. CONCLUSION:

Topical Nanoemulgel has proven a better option for an effective and convenient drug delivery system. Gel and non-greasy-like properties are giving more patient compliance and the lack of oily as a base provides better drug release compared to other formulations. Incorporation of Nanoemulsion into gel matrix makes formulation dually control released system, Problems like creaming and phase separation which is associated with classical emulsion gets resolved with improved Spreadability. The Nanoemulsion-loaded gel gives higher effectiveness in some topical disorders. The future of Nanoemulsion-Gel-based formulations may provide a better and more reliable solution for the delivery of hydrophobic drugs. A considerable lot of medications utilized as a part of the treatment of skin infection are hydrophobic natured and such medications can be conveyed successfully as Nanoemulgel where the drug is incorporated into the oil phase of Nanoemulsion and then merged with a gel base. Despite having a couple of impediments, Nanoemulgel has the likelihood to possess the focal place for topical conveyance for lipophilic drugs in the future.

REFERENCES:

[1]. http://www.sign.ac.uk/pdf/pat121. **PD**

[2]. Menter A, Korman NJ, Elmets CA, et al. (2009) American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol. 60(4):643-659.

[3]. Menter A, Korman NJ, Elmets CA, et al. (2010) Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. J Am Acad Dermatol.; 62(1):114-135

[4]. Chalmers RJ, O'Sullivan T, Owen CM, Griffiths CE. (2001) A systematic review of treatments for guttate psoriasis. Br J Dermatol; 145(6):891-4.

[5]. Ellis CN, Gorsulowsky DC, Hamilton TA, Billings JK, Brown MD, Heading ton JT, et al. Cyclosporine improves psoriasis double-blind study. JAMA 1986; 256:3110-6

[6]. Toichi E, Torres G, McCormick TS, Chang T, Mascelli MA, Kauffman, CL, et al. An anti-IL- 12p40 antibody down-regulates Type 1 cytokines, chemokines, and IL-12/IL-23 in psoriasis. J Immunol 2006; 177:4917-26

[7]. Sarac G, Kocal TT, Baglan T. A summary of clinical types of psoriasis. North Clin Istanbul 2016; 3:79-82.

[8]. Kirtikar KR, Basu BD, Indian Medicinal Plants, 2 nded (Internationa publishers, Dehradun), 717-721. 1987.

[9]. Kotiyal JP, Sharma D (1992) Phytochemical studies of Psoralea species, Bulletin of Medico- Ethnobotanical Research, 13, 209–223.

[10]. Conner JK, Neumeier R, (2002) The effects of ultraviolet B radiation and intra-specific competition on growth, pollination success and lifetime female fitness in Phacelia campanularia and P. purshii (Hydrophyllaceae), Am J Bot, 89, 103-110

[11]. Anusha S, Haja Sherief S, Sindhura S, Jaya Preethi P, Siva Kumar T (2013) Synergistic effect of indigenous medicinal plant extracts on psoriasis International Journal of Phyto pharmacy Vol. 3 (1), pp. Jan- Feb; 23-29.

[12]. Tejinder Kaur Marwaha (2013) Formulation Design and Evaluation of Herbal Antipsoriatic Emulgel Journal of Pharmaceutical and Scientific Innovation JPSI 2 (3), May-Jun, 30-42.

[13]. Raghuvaran Jhansi Laxmi, R. Karthikeyan, P. Srinivasa Babu, R.V.V. Narendra Babu (2013) Formulation and evaluation of Antipsoriatic gel using natural excipients Journal of Acute Disease 115-121.

[14]. Ruhl S, Wang Z, Lou Y, Totzke F, Kubbutat MH, Chovolou Y, et al. Babchi Oil 2018. Available from: http://www.ayurvedicoils.com/tag/b Takeuchi-oil. [Last accessed on 2018 Apr 12]

[15]. R Sigh (2014) Emulgel: A Recent Approach for Topical Drug Delivery System. Asian Journal of Pharmaceutical Research and Development 2(2): 13-15.

[16]. S Pant, A Badola, S Baluni, W Pant (2015) A Review on Emulgel Novel Approach for Topical Drug Delivery System. World Journal of Pharmacy and Pharmaceutical Sciences 4(10): 1728-1743

[17]. F Shakeel, S Baboota, An Ahuja, J Ali, Shafiq S, et al. (2008) Skin Permeation Mechanism of Aceclofenac Using Novel Nanoemulsion Formulation. Pharmacies 63: 580-584.

[18]. Maibach, R Feldmann, T Milby, seat WF (1971) Regional Variation in Percutaneous Penetration in Man. Archives of Environmental Health, An International Journal 23(3): 208- 211.

[19]. Y Kalia, R Guy (2001) Modelling Transdermal Drug Release. Advanced Drug Delivery Reviews 48: 159-172. Delivery of Fluconazole In-Vitro Skin Penetration and Permeation using Emulsions as Dosage Forms. Drug Development and Industrial Pharmacy 33: 273-280.

[20]. Y Tanwar, A Jain (2012) Formulation and Evaluation of Topical Diclofenac Sodium Gel Using Different Gelling Agent. Asian Journal of Pharmaceutical Research and Health Care 4(1): 1-6.

[21]. Montenegro L, C Carbone, G Condorelli, R Drago, G Puglisi, et al. (2006) Effect of Oil Phase Lipophilicity on In Vitro Drug Release from O/W Microemulsions with Low Surfactant Content. Drug Development and Industrial Pharmacy 32: 539-548.

[22]. R Shankar, V Tiwari, C Mishra, C Singh, D Sharma, et al. (2015) Formulation and Evaluation of Ketoconazole Nanoemulsion Gel for Topical Delivery. American Journal of Pharma tech Research 5(5): 446- 462.

[23]. J Modi, J Patel (2011) Nanoemulsion-Based Gel Formulation of Aceclofenac for Topical Delivery. International Journal Pharmacy and Pharmaceutical Science Research 1(1): 6-12.

[24]. H Masmoudi, P Piccerelle, Yvelines Le D, Jacky Kister (2006) A Rheological Method to Evaluate The Physical Stability of Highly Viscous Pharmaceutical Oil-In-Water Emulsions. Pharmaceutical Research 23(8): 1937-1947