IJBPAS, October, Special Issue, 2023, 12(10): 535-549
ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)
'A Bridge Between Laboratory and Reader'
www.ijbpas.com

DEVELOPMENT AND EVALUATION OF HERBAL ETHOSOMES OF *PASSIFLORA FOETIDA* LINN FOR THE TREATMENT OF PSORIASIS

UMESH JADHAO*[1] AND HARSHAL TARE[2]

1: Research Scholar, Faculty of Pharmacy, Oriental University, Indore, Madhya Pradesh, India

2: Research Guide, Faculty of Pharmacy, Oriental University, Indore, Madhya Pradesh, India

***Corresponding Author: Mr. Umesh Jadhao: EMail: umj81@rediffmail.com**

Received 7th July 2023; Revised 9th Aug. 2023; Accepted 30th Sept. 2023; Available online 15th Oct. 2023

https://doi.org/10.31032/IJBPAS/2023/12.10.1054

ABSTRACT

This study investigated how glycethosomes and Ethosomes promote intracellular and extracellular drug transport using imaging and cell line studies. This study prepares *Passiflora foetida* ethosomal gel and glycethosomal dispersion and evaluates their vesicle shape, size, PDI, ZP, EE, and *in vitro* permeation. Using modified heating methods, Ethosomes (10–40%) and soy phosphatidylcholine (1-3%) were synthesized. Next, *Passiflora foetida* was described and put on ethanolosomes. *Passiflora foetida*-loaded Ethosomes were 103±13-345±11 nm in size, with PDI ranging from 0.104 to 1.53 and glycethosomes from 1.53 to 0.293. ZP ranged from 16.6 to 40.1 mV and -18 to -43 mV. Optical and transmission electron microscopy showed unilamellar structure. Glycethosomes and Ethosomes had 42.5% to 90.01 % EE. The physicochemical features of *Passiflora foetida*-loaded Ethosomes dispersion after carbapol 934P was added to create a gel were studied. A *Passiflora foetida*-loaded ethosomal gel and Herbal drugs may be delivered through Ethosomes.

Keywords: Development, Evaluation, Herbal Ethosomes, *Passiflora foetida Linn*. And Psoriasis

1 INTRODUCTION

Herbal remedies date back to before the dawn of recorded civilization. As early as 3000 B.C.E., papyrus texts from China and Egypt describe plants used for therapeutic purposes. Traditional herbal medicine systems include Ayurveda, Siddha, Unani, and Traditional Chinese Medicine. Historically, many indigenous groups,

especially those of African and Native American descent, have used medicinal plants in rituals. The use of botanicals and other medicines derived from plants has increased dramatically in recent years in Western nations. The use of plant-based medicines was widespread in medical practice until around two centuries ago. The use of botanicals as medicine has decreased significantly in Western countries due to the easy availability of effective synthetic drugs. However, many third world nations kept reaping benefits from their extensive medicinal herbalism knowledge and practice **[1-2]**.

In Japan, Kampo Medicine is widely used, whereas in India, Siddha and Ayurvedic treatments are still used by a sizeable minority of the population. The Middle East and South Asia also make extensive use of traditional Chinese medicine (TCM) and Unani treatments. Many of the products marketed as "traditional herbal medicines" have been used for centuries, as suggested by the use of the term "traditional" when discussing herbal therapy. A large percentage of the population in many third-world nations relies on traditional healers and the plants they bring to treat illness. The use of herbal medicines has constantly maintained its appeal, mostly attributable to historical and cultural factors, despite the cohabitation of modern medicine and traditional ways. From a business perspective, these items are now more accessible, especially in industrialized nations. Drugs are sometimes promoted in modern society for uses that go beyond the bounds of the conventional therapeutic models from which they were originally developed **[3-4]**.

An example would be ephedra, which has been used to improve athletic performance and aid in weight loss. There are some tight regulations in place for the production of herbal medicines in a number of nations, but this is not the case everywhere. In Germany, herbal remedies are classified as "phytomedicines" and must meet the same rigorous criteria for quality and safety as pharmaceutical drugs. In contrast, the vast majority of herbal products sold in the United States are classified as dietary supplements, which do not need premarket clearance based on the aforementioned standards. The usage of therapeutic herbs may be dated back to almost 60,000 years ago, according to documents from ancient Babylon. Egyptian and Chinese records of plant medicine stretch back at least 5,000 years, but those from Asia Minor and Greece date back only around 2,500 years. There is a wide variety of herbal medicine systems, each with its own set of beliefs and practices that are shaped by its area of origin. TCM, or traditional Chinese medicine, is a kind of alternative medicine that has been practiced in China for thousands of years. A classic

herbal treatise, The Devine Farmer's Classic of Herbalism, was written in China around two thousand years ago. There is already a plethora of monographs and herbal Pharmacopeia's devoted to the study of certain plants. Hindu physicians and sages of antiquity founded Ayurveda, an ancient medical system that has been practiced in India for over five thousand years. More than 1500 plants and over 10,000 preparations are described in great detail in the Materia Medica. The government of India recognizes Ayurveda as a comprehensive medical system, unlike Western medicine. Kampo medicine is a Japanese traditional herbal treatment with a rich history dating back more than 1500 years and a wide variety of about 148 different formulae **[5-7]**.

2 MATERIALS AND METHODOLOGY

2.1 Materials

Table 1: List of Equipment's/Instrument

Sr. No.	Equipment/Instrument	Manufacturer
1.	Magnetic stirrer	Remi Motors
2.	Electronic Balance	Remi Motors
3.	FT-IR Spectrophotometer	Shimadzu
4.	Zetasizer	Malvern Instruments
5.	SEM	Motic
6.	UV-Spectroscopy	Remi Motors
7.	Triple blade stirrer	Remi Motors,
8.	Sonicator	Bandelin RK 100H
9.	Digital Melting Point Apparatus	Remi Motors
10.	Research Centrifuge	Remi Motors

Table 2 List of chemicals

Sr No.	Material	Manufacturer
1.	*Passiflora foetida* Extract	Complimentary pack
2.	Lecithin ex. Soya, 30% Phospholipon® 90H	Sisco Research Laboratories Pvt. Ltd.
3.	Propylene glycol	Sisco Research Laboratories Pvt. Ltd.
4.	HPMC	S. D. Fine Chemicals
5.	Absolute Ethanol (99.9%)	Merck, India
6.	Cholesterol	Sisco Research Laboratories Pvt. Ltd
7.	Methanol (HPLC grade)	Merck, India
8.	Dipotassium Hydrogen Phosphate Dihydrate	S. D. Fine Chemicals
9.	Potassium Dihydrogen Phosphate	S. D. Fine Chemicals
10	Triethanolamine	Sisco Research Laboratories Pvt. Ltd

2.2 Selection, collection and authentication of herb

Passiflora foetida plants were collected from the flower garden. Selected plant was authenticated and utilised for further study. To begin, we dried the plant's seeds. They were then pulverized, passed through 40-mesh sieves, and stored in an airtight container **[8]**.

2.3 Extraction and Phytochemical Screening of selected herb

Then, various extraction techniques, including as liquid extraction, distillation, compression, and sublimation, are used to remove the beneficial compounds from the plant components. Solvent extraction is the standard method for harvesting useful compounds from plants **[9]**.

2.4 Preformulation Studies

2.4.1 Determination of Melting Point

The capillary technique was used in order to ascertain the drug's melting point.

2.4.2 Compatibility studies using FTIR spectroscopy

By comparing the infrared spectra peaks of pure substances with the physical combination of the medicine and excipients, FT-IR spectroscopy may be used to investigate and anticipate possible physicochemical interactions or incompatibilities between various components in a formulation **[10]**.

2.4.3 Organoleptic properties

The organoleptic qualities of *Passiflora foetida* stem were evaluated by color, smell, taste, shape, and size in accordance with WHO quality control protocols for herbal medicine **[11]**.

2.4.4 UV Spectral Analysis

The UV examination of the purified fractions was conducted within the wavelength range of 200-400nm. The baseline was appropriately set, with methanol serving as a blank. Prior to the examination, the bioactive fractions were carefully removed from the TLC plate and afterwards centrifuged in methanol **[12]**.

2.5 Development of Novel Carrier Systems containing Drugs (Ethosomes)

Here we used cold method for the preparation of Ethosomes.

2.6 Evaluation of Novel Carrier Systems (Ethosomes)

Any dosage form or delivery mechanism must be characterized to ensure its success in the production process and as a therapeutic intervention. It's also important to have a replicable product. Similarities exist between Ethosomes and other vesicular transport systems in terms of their properties. Vesicle surface and form may be studied using SEM and TEM, allowing for the visualization of vesicles that are unilamellar or multilamellar, as well as those that are almost spherical **[13]**.

2.6.1 Morphology by SEM, TEM

To quantify these Nano-vesicle features, we used transmission electron microscopy (Jeol® JEM 2100, USA). To make the nano-formulations visible under a microscope at 10- 30 kV voltage, they were diluted with 50 µl of solution **[14]**.

2.6.2 Microscopic Evaluation

Fluorescent microscopy was used to investigate the capacity of fluorescent

marker-loaded Ethosomes to pass through human skin **[15]**.

2.6.3 Particle size analysis

The Malvern Nano-Zetasizer (Nano-ZS, Malvern Instruments, Worcestershire, UK) was used to take the readings; it is equipped with an avalanche photodiode detector and a He-Ne laser that operates at 633 nm **[16]**.

2.6.4 Zeta potential

Using a Zeta sizer 3000HSA and the dynamic light scattering technique, we determined the average particle size of an ethosomal colloidal solution. Scattering at an angle of 90 degrees was used to take the reading from the sample in a quartz cuvette. Each formulation's observations were recorded three times **[17]**.

2.6.5 Entrapment efficiency

For one hour at 10 degrees Celsius, a millilitre of the formulation was centrifuged at a rate of 20,000 rpm. The amount of medicine in the supernatant was determined by ultraviolet spectroscopy at 282 nm **[18]**.

2.7 Development of Topical formulation of Optimized Novel Carrier System

An appropriate amount of the formulation from the optimized batch (EF3) was mixed with a previously prepared aqueous solution of HPMC (1g in 100ml) to produce ethosomal cream (1%). The HPMC aqueous solution was stirred with a magnetic stirrer until a clear solution was achieved. Next, some triethanolamine was added in very little amounts. After the gel had thickened to the right point, it was mixed in a consistent manner for an extended amount of time **[19]**.

2.8 Evaluation of Topical formulations of Optimized Novel Carrier System

2.8.1 Visualization of vesicles by transmission electron microscope (TEM) and optical microscope

A little amount of the material was deposited on a carbon-coated copper grid and examined using a transmission electron microscope (TEM). A 1 percent phosphotungustic acid water solution was used to produce a negative stain after 15 minutes. A transmission electron microscope was used to analyse the samples after the grid had been let to air dry for an adequate amount of time. Optical microscopy is another method for studying vesicles **[20]**.

2.8.2 Physical Examination and homogeneity

The visual examination of the ethosomal gel formulations and the generated Ethosomes was conducted to assess potential variations in color intensity. Once the gels that were produced had solidified inside the designated container, a visual examination was conducted in order to assess their uniformity. Furthermore, a thorough examination was conducted to assess their visual characteristics and determine the presence of any conglomerates **[21]**.

2.8.3 Drug content determination

Five hundred milligrams of the gel were extracted and mixed into fifty milliliters of 7.4-pH phosphate buffer solution (PBS). After filtering the solution via paper, 50 µL were collected as the resultant filtrate. Three and a half milliliters of distilled water were added to the filter for the purpose of diluting the solution. The gel's concentration was then compared to the known amount of medication in the sample using spectrophotometric analysis performed at a wavelength of 203 nanometers **[22]**.

2.8.4 Wash ability:

Rinsing the skin with water after applying a little amount of gel to check whether it could be totally removed was tested.

2.8.5 pH determination

The ethosomal gel formulation's viscosity was tested with a Brookfield viscometer (Model No DV-III ULTRA) at 100 rpm with spindle no. 06, and the pH was determined with a digital pH meter (RI-152-R) **[23]**.

2.9 Biological Evaluation of Topical formulations

2.9.1 Histopathological Study

After 24 hours of therapy, animals were put under general anaesthetic, and biopsies of the damaged epidermis were taken and stored in 10% formalin for further analysis in tissue sections. Samples will be cross-sectioned and paraffin-embedded for light microscopic examination. Then, we looked at the hyperkeratosis, orthokeratosis, and parakeratosis that occurred in these tissues under the microscope.

2.9.2 Skin irritation test:

Male Wister rats were groomed by having their belly hair shaved. For 24 hours, spread 0.5 grams of the same ingredient over an area of 4 square centimetres before applying the created product to the shaved skin. The magnitude of the decreases in inflammation was seen after 24, 48, and 72 hours following administration of the formulation. The average ratings for erythema were calculated after taking into account the severity of the condition **[24]**.

3 RESULT AND DISCUSION

3.1 Selection, collection and authentication of herb (Figure 1).

3.2 Standardization of Plant extract and Excipient

From powdered dry seeds, researchers discovered that they could extract between 25 and 30 percent oil. **Table 3** Determination of Phytochemical Characteristics of Plant Extract.

3.3 Extraction and Phytochemical Screening of selected herb

P. foetida L. plant was utilised for the study. The identity of the plant was confirmed by referring to both the records of the herbarium and the standard flora. The remaining chemicals and solvents that were used in this investigation were acquired from HiMedia Laboratories, which is located in India. In the course of our

investigation, we made use of a Soxhlet extractor **(Figure 2)**, a UV Trans illuminator, and a UV spectrophotometer-1800. The leaf powder weighed fifty grams before the extraction procedure, and the final weight of the unprocessed, pure extracts was one point eleven grams. During the extraction process, tannins, saponins, and any other compounds that may have caused interference were effectively eliminated.

3.4 Preformulation Studies

3.4.1 Melting point Determination

The medication's melting point was discovered to be 195^0C using the capillary technique, which involves introducing the substance into a digital melting point instrument.

3.4.2 Compatibility studies using Fourier-transform infrared spectroscopy.

Passiflora foetida L. ethanol extract was used in the experiment to practice Fourier-transform infrared spectroscopy. Data from the Fourier Transform Infrared (FTIR) spectrometer show that the drug and excipients get along swimmingly, with no negative interactions between them. Therefore, it was decided to go on with the formulation development process. The infrared spectra collected by observing light having a wavelength between 4000$cm^{-1}$to 400cm^{-}1.

3.4.3 Analytical method development (Table 5, Figure 3)

3.4.4 Organoleptic properties

The Organoleptic features of stem demonstrated in **Table 6**.

3.5 Evaluation of Novel Carrier Systems (Ethosomes)

3.5.1 Morphology by SEM, TEM

Surface-enhanced microscopy (SEM) makes surface markings on solid materials using a concentrated stream of high-energy electrons. What's in a sample may be seen thanks to secondary electrons and backscattered electrons. Secondary electrons reveal the samples' 3D form and layered structure, whereas backscattered electrons reveal the diversity of a multiphase system's constituent parts **(Figure 4, 5)**.

3.5.2 Particle size, PDI, zeta potential and entrapment efficiency

The maximum entrapment efficiency was found in the third iteration (EF3) of the enhanced formulation, guaranteeing a significant therapeutic benefit from the presence of an adequate dosage inside the system. The formulation has an advantageous negative zeta potential, which reduces the likelihood of aggregation and guarantees the formulation's long-term survival **(Table 7)**.

3.6 Evaluation of Topical formulations of Optimized Novel Carrier System

3.6.1 Physical examination and homogeneity

The color, uniformity, consistency, and phase separation of the final ethosomal cream mixture were all looked at. The makeup of the cream was found to be uniform and free of both small particles and changes in color strength.

3.6.2 Spreading coefficient

The cream with the improved formulation has a spredability of 8.50–9.50 Sec/g **(Table 8)**.

3.7 Biological Evaluation of Topical formulations

3.7.1 Ex-vivo Permeation Study

Table 9 and Figure 6 show that after 24 hours of testing, the cumulative percentage release of the basic drug solution was 6.97%, whereas the release of ethosomal gel with salicylic acid was 36.13 percent and without salicylic acid was 17.5 percent. The release profile of the ethosomal gel was found to be more favourable than that of the plain *Passiflora foetida Linn* solution. However, the amount of salicylic acid that was penetrating the ethosomal gel increased. They pointed to salicylic acid's pH-lowering properties and the increased solvent penetration as causes. It was previously thought that ethanol was an efficient permeability booster. Therefore, ethosomal gel is superior to basic medicinal solutions in terms of epidermal penetration. The pH is raised by the absence of salicylic acid, preventing the extract of *Passiflora foetida* from combining with the gel system. Therefore, the combination of salicylic acid and the standard ethosomal gel formulation of *Passiflora foetida Linn* results in more epidermal penetration than either component alone.

3.7.2 Skin Retention Study

The percentage of skin retention for ethosomal cream in drug solution was 13.66% (permeation: 6.97%), ethosomal cream with *Passiflora foetida* was 43.01% (permeation: 26.13%), and ethosomal cream without Salicylic acid was 24.47% (permeation: 17.5%) after 24 *in vitro* tests. *Passiflora foetida*-containing ethosomal cream had 19% greater penetration than ethosomal cream without *Passiflora foetida*. Due to the larger particle size (376nm), this was the case. In contrast, penetration and retention decreased without salicylic inclusion. The cumulative drug release (retention plus permeability) of the enhanced formulation was 69.14% **(Figure 7, 8)**.

3.7.3 Histopathological Study (Figure 9)

Figure 1: Seeds and plant of *Passiflora foetida*

Table 3: Standardization of *Passiflora foetida* extract

Physicochemical parameter	Results
Colour	Pale yellow
Specific gravity	6.8968
Saponification value (mg KOH/g of oil)	167.8
Acid Value (mg KOH/g of oil)	2.68
Iodine value (g of ICI/100 g of oil)	95.7
Peroxide value (meq/kg)	6.10

Table 4: Standardization of excipients

Sr. No.	Test	Specification	Observation
1.	Appearance	Flakes	Compliance
2.	Color	Pale yellow color	Compliance
3.	Odor	Typical	Compliance
4.	Solubility	Insoluble in water, slightly soluble in hot acetone, alcohol, benzene and petroleum ether	Compliance
5.	Melting point	66-72^{0}C	66.50C
6.	Saponification value	43-65 mg KOH/g	58 mg KOH/g
7.	Acid value	12-22 mg KOH/g	18 mg KOH/g
8.	Ester value	31-43 mg KOH/g	37 mg KOH/g

Figure 2: Soxhlet extraction used for study

Table 5: Standard Calibration curve of *Passiflora foetida* L extract

Concentration (µg / ml)	Absorbance
0	0
10	0.244
20	0.489
30	0.740
40	1.001
50	1.250

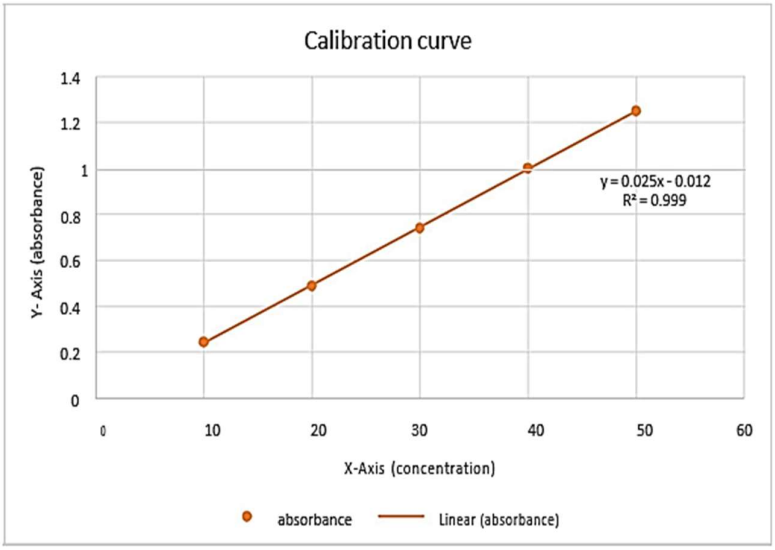

Figure 3: Standard Calibration graph of *Passiflora foetida* L extract

Table 6: Organoleptic characteristics of *Passiflora foetida* stem

Organoleptic characters	Observation
Colour	Green
Odour	Characteristic
Taste	Characteristic
Texture	Smooth

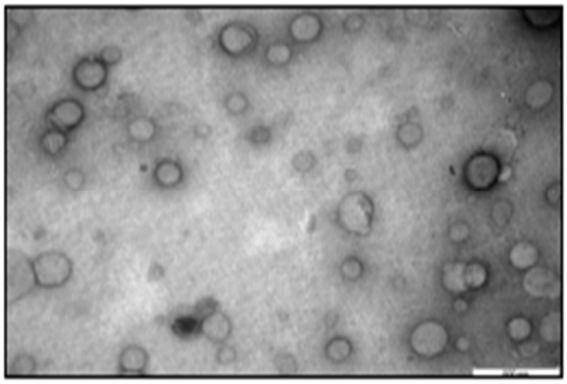

Figure 4: TEM image of optimized Ethosome formulation

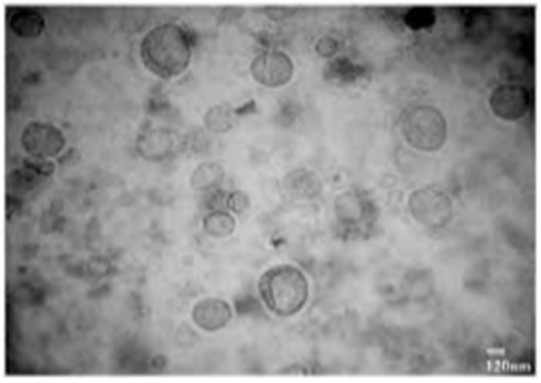

Figure 5: SEM image of optimized Ethosomes formulation

Table 7: Particle size, PDI, zeta potential and entrapment efficiency of prepared Ethosomes

Formula code	Particle size (nm)	PDI	Zeta Potential	Entrapment efficiency
EF1	185.7 ±4.32	0.08 ± 0.02	-6.85 ± 0.72	79.2 ± 1.23
EF2	138.9 ± 3.40	0.30 ± 0.11	-6.85 ± 1.01	82.6 ± 2.25
EF3	84.57 ± 2.50	0.34 ± 0.16	-13.2 ± 1.23	86.0 ± 3.26
EF4	192.2 ± 6.92	0.30 ± 0.09	-4.10 ± 0.84	64.8 ± 2.15
EF5	172.8 ± 2.67	0.310±0.09	-5.94 ± 0.35	68.8 ± 3.49
EF6	94.02 ± 4.06	0.261 ± 0.1	-6.50 ± 1.38	72.5 ± 1.36

Table 8: Spread ability of optimized cream enriched with Ethosomes of *Passiflora foetida* Linn.

Formulations	Spread ability (Sec/g)
Plain gel base (Carbopol 974P)	6.50-7.50
cream enriched with Ethosomes	8.50-9.50

Table 9: Percent cumulative release of Ethosomal gel with or without *Passiflora foetida* Linn extract and drug solution

Time (Hr)	%Cumulative Release (24 Hr)		
	Drug Solution	Ethosomal Gel with *Passiflora foetida* Linn extract	Ethosomal Gel Without *Passiflora foetida* Linn extract
1	1.63 ± 0.02	1.58 ± 0.01	1.44 ± 0.00
2	1.88 ± 0.01	2.06 ± 0.01	1.86 ± 0.09
3	2.15 ± 0.01	2.78 ± 0.01	2.34 ± 0.15
4	2.42 ± 0.01	3.18 ± 0.01	2.64 ± 0.14
5	2.64 ± 0.01	3.55 ± 0.01	3.06 ± 0.02
6	2.99 ± 0.01	5.24 ± 0.10	3.33 ± 0.02
7	3.54 ± 0.00	6.68 ± 0.10	3.78 ± 0.02
8	3.91 ± 0.00	10.40 ± 0.28	5.58 ± 0.06
24	6.97 ± 0.06	26.13 ± 1.61	17.15 ± 0.03

(EGWP*F*L= Ethosomal Gel with *Passiflora foetida* Linn extract; EGWOPF= Ethosomal Gel Without *Passiflora foetida* Linn extract)

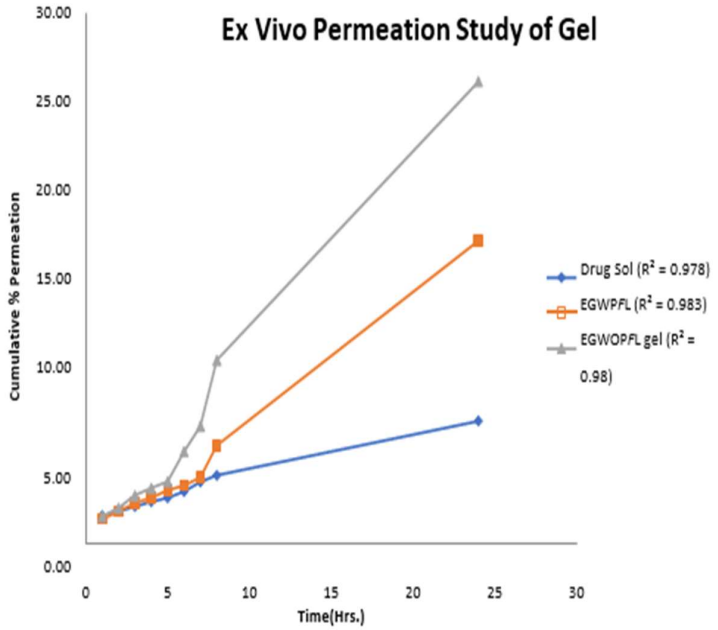

Figure 6: Comparison of % cumulative permeation of the ethosomal gel with the drug solution

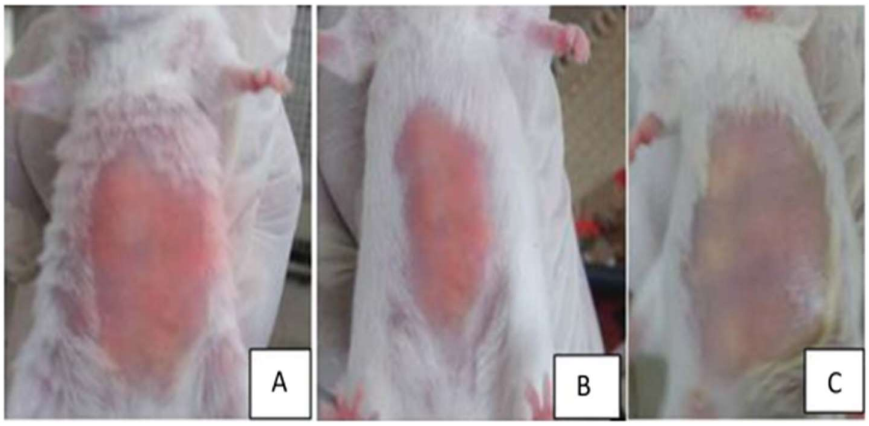

Figure 7: Psoriasis animal model A) Positive control animal B) Vaseline treated animal C) Ethosome of *Passiflora foetida* Linn optimized cream treated animal

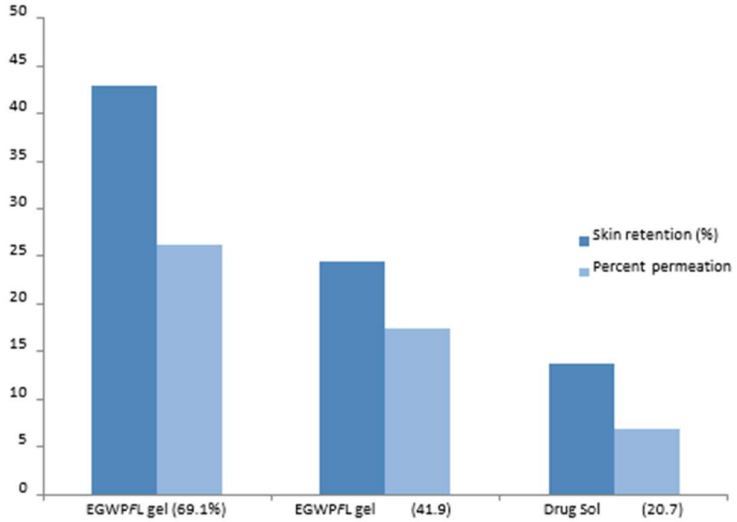

Figure 8: Comparison of % skin retention and % permeation of Ethosome of *Passiflora foetida* Linn extract with drug solution

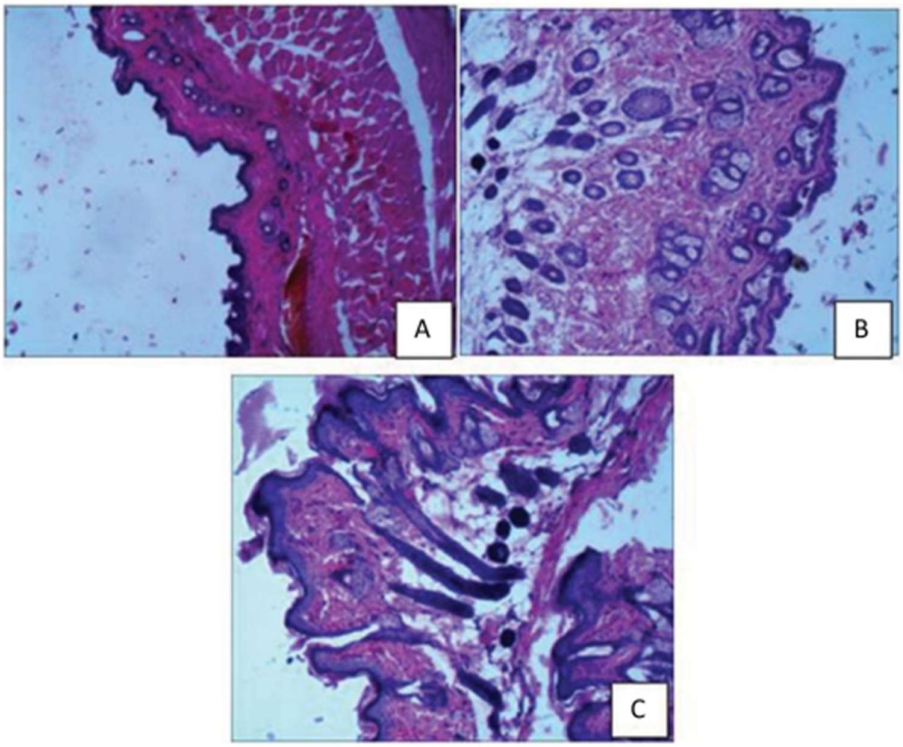

Figure 9: Histopathology of skin samples (100X)- (A) Negative control (Normal skin), (B) Positive Control, (C) Ethosome of *Passiflora foetida* cream

4 CONCLUSION

Psoriasis may be treated in a number of methods today, but finding an effective and safe drug remains difficult. Eighty percent or more of people with psoriasis regularly use topical therapies. Traditional topical formulations suffer from poor medicine absorption and penetration because of the skin barrier's features. Rigid and thick skin may also result from conditions including dehydration, hyperkeratosis, and epidermal hyperplasia. Psoriatic skin often cannot absorb medicine because of the aforementioned skin changes. Therefore, the

success of standard topical therapies in the clinic is still a major concern. Ethosomes' many benefits include better patient compliance, higher drug epidermal absorption, and practical use in industry. Hydrophilic, lipophilic, peptide, and other macromolecules may all be transported via Ethosomes. The substances utilized in their makeup have been deemed safe for use in pharmaceuticals and cosmetics. Psoriasis may be treated in a variety of ways. Unfortunately, none of these options can treat the ailment without negatively impacting the patient's willingness to cooperate. In addition, the focus of current therapies is on symptom relief rather than a complete recovery from the condition. To successfully treat psoriasis in a way that also increases patient adherence to therapy, finding a new medication component or delivery strategy is essential. New medication development, however, is arduous and time-consuming. Therefore, a novel and herbal-based medication delivery technique has been widely used for the distribution of anti-psoriatic pharmaceuticals. Herbal medicines for psoriasis have been shown to be safe and efficient in several scientific investigations, which are discussed in this article. Increased patient compliance is achieved with decreased adverse effects, dose, and administration frequency using a nano-based method. Nanoparticles, dendrimers, Nano capsules, NLC, SLN, liposomes, etc., have all been employed as drug delivery vehicles for psoriasis treatment. It has been reported that these carriers have increased in effectiveness, safety, and patient compliance. Psoriasis sufferers should expect Nanocarriers to play a significant part in the suggested therapy in the near future.

5 REFERENCES

[1] Clark RA. Gone but not forgotten: lesional memory in psoriatic skin. J Invest Dermatol 2011; 131(2): 283-5. http://dx.doi.org/10.1038/jid.2010.374 PMID: 21228808

[2] Globe D, Bayliss MS, Harrison DJ. The impact of itch symptoms in psoriasis: results from physician interviews and patient focus groups. Health Qual Life Outcomes 2009; 7(1): 62. http://dx.doi.org/10.1186/1477-7525-7-62

[3] Fernandes AR, Martins-Gomes C, Santini A, et al. Psoriasis vulgaris Pathophysiology of the disease and its classical treatment versus new drug delivery systems. Des Nanostructures Versatile Ther Appl 2018; pp. 379-406.

[4] Garg T, Rath G, Goyal AK. Ancient and advanced approaches for the treatment of an inflammatory autoimmune disease-psoriasis Critical Reviews™ in Therapeutic Drug Carrier Systems 2014; 31(4): 331-65.

[5] Mahović D, Mrsić F. Acupuncture as a Complementary Method of Traditional Psoriasis Treatment: Myth or Reality? Acta Dermatovenerol Croat 2016; 24(3): 221-2. PMID: 27663925

[6] Mehta CS, Dave AR, Shukla VD. A clinical study of some Ayurvedic compound drugs in the assessment quality of life of patients with Eka Kushtha (psoriasis). Ayu 2011; 32(3): 333-9. http://dx.doi.org/10.4103/0974-8520.93909 PMID: 22529646

[7] Riyaz N, Arakkal FR. Spa therapy in dermatology. Indian J Dermatol Venereol Leprol 2011; 77(2): 128-34. http://dx.doi.org/10.4103/0378-6323.77450

[8] Léauté-Labrèze Christine, Saillour Florence, Chêne Geneviève, et al. Saline Spa Water or Combined Water and UV-B for Psoriasis Vs Conventional UV-BLessons from the Salies de Béarn Randomized Study. Arch Dermatol 2001; 137(8): 1035-9.

[9] Sathyanarayana Rao TS, Basavaraj KH, Das K. Psychosomatic paradigms in psoriasis: Psoriasis, stress and mental health. Indian J Psychiatry 2013; 55(4): 313-5. http://dx.doi.org/10.4103/0019-5545.120531 PMID: 24459298

[10] Lesiak A, Narbutt J, Pawlaczyk M, Sysa-Jedrzejowska A, Krzyścin J. Vitamin D serum level changes in psoriatic patients treated with narrowband ultraviolet B phototherapy are related to the season of the irradiation. Photodermatol Photoimmunol Photomed 2011; 27(6): 304-10.

[11] Dogra S, Mahajan R. Psoriasis: Epidemiology, clinical features, co-morbidities, and clinical scoring. Indian Dermatol Online J 2016; 7(6): 471-80. http://dx.doi.org/10.4103/2229-5178.193906 PMID: 27990381

[12] Lebwohl M, Freeman AK, Chapman MS, Feldman SR, Hartle JE, Henning A. Tacrolimus Ointment Study Group. Tacrolimus ointment is effective for facial and intertriginous psoriasis. J Am Acad Dermatol 2004; 51(5): 723-30. http://dx.doi.org/10.1016/j.jaad.2004.07.011 PMID: 15523350

[13] Berger TG, Duvic M, Van Voorhees AS, VanBeek MJ, Frieden IJ. American Academy of Dermatology Association Task Force. The use of topical calcineurin inhibitors in dermatology: safety concerns. Report of the American Academy of Dermatology Association Task Force. J Am Acad Dermatol 2006; 54(5): 818-23. http://dx.doi.org/10.1016/j.jaad.2006.01.054 PMID: 16635663

[14] Wang C, Lin A. Efficacy of topical calcineurin inhibitors in psoriasis. J Cutan Med Surg 2014; 18(1): 8-14.

http://dx.doi.org/10.2310/7750.2013.13059

[15] Bruner CR, Feldman SR, Ventrapragada M, Fleischer AB Jr. A systematic review of adverse effects associated with topical treatments for psoriasis. Dermatol Online J 2003; 9(1): 2. PMID: 12639460

[16] Ashcroft DM, Po AL, Williams HC, Griffiths CE. Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis. BMJ 2000; 320(7240): 963-7.

[17] Hannuksela-Svahn A, Pukkala E, Läärä E, Poikolainen K, Karvonen J. Psoriasis, its treatment, and cancer in a cohort of Finnish patients. J Invest Dermatol 2000; 114(3): 587-90.

[18] Singh D, Pradhan M, Shrivastava S, Murthy SN, Singh MR. Chapter 11 – skin autoimmune disorders: lipid biopolymers and colloidal delivery systems for topical delivery A2 - Grumezescu, Alexandru Mihai Nano biomaterials in Galenic Formulations and Cosmetics. William Andrew Publishing 2016; pp. 257-96.

[19] Pischon H, Radbruch M, Ostrowski A, et al. Stratum corneum targeting by dendritic core-multishell-Nanocarriers in a mouse model of psoriasis. Nanomedicine (Lond) 2017; 13(1): 317-27. http://dx.doi.org/10.1016/j.nano.2016.09.004

[20] Matsumura Y, Ananthaswamy HN. Toxic effects of ultraviolet radiation on the skin. Toxicol Appl Pharmacol 2004; 195(3): 298-308.

[21] Hoffman MB, Hill D, Feldman SR. Current challenges and emerging drug delivery strategies for the treatment of psoriasis. Expert Opin Drug Deliv 2016; 13(10): 1461-73. http://dx.doi.org/10.1080/17425247.2016.1188801 PMID: 27164301

[22] Pradhan M, Singh D, Singh MR. Novel colloidal carriers for psoriasis: current issues, mechanistic insight and novel delivery approaches. J Control Release 2013; 170(3): 380-95. http://dx.doi.org/10.1016/j.jconrel.2013.05.020 PMID: 23770117

[23] Rawat M, Singh D, Saraf S, Saraf S. Nanocarriers: promising vehicle for bioactive drugs. Biol Pharm Bull 2006; 29(9): 1790-8. http://dx.doi.org/10.1248/bpb.29.1790 PMID: 16946487

[24] Singh D, Pradhan M, Nag M, Singh MR. Vesicular system: Versatile carrier for transdermal delivery of bioactive. Artif Cells Nanomed Biotechnol 2015; 43(4): 282-90. http://dx.doi.org/10.3109/21691401.2014.883401 PMID: 24564350.