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Combination Therapy Using Medicinal Plants: A Novel Approach for Skin Disease Management

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Abstract- Skin diseases encompass a broad spectrum, ranging from infectious and inflammatory conditions to severe neoplastic disorders. Traditional treatments, including antibiotics and corticosteroids, often present limitations such as adverse effects and resistance. Consequently, herbal remedies have emerged as safer, more sustainable alternatives. This study explores the therapeutic potential of Rubia cordifolia root extract in the management of skin diseases, focusing on its phytochemical composition, antimicrobial properties, and application in a gel formulation. The gel was evaluated for stability, spreadability, and efficacy through in vitro and clinical trials. Results demonstrated significant improvements in parameters such as pH stability, drug release, and patient-reported outcomes, including a 52.05% reduction in Psoriasis Area and Severity Index (PASI) scores. The study highlights the synergistic effects of combining herbal and conventional therapies, emphasizing the need for further research to establish Rubia cordifolia as a viable, cost-effective treatment for skin conditions.

Keywords: Skin diseases, Rubia cordifolia, herbal remedies, antimicrobial properties, therapeutic synergy

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INTRODUCTION

From infectious and inflammatory ailments to severe neoplastic disorders like melanoma, skin diseases come in a wide range. Staphylococcus aureus and Streptococcus species are frequently responsible for bacterial infections including impetigo and cellulitis, while common inflammatory disorders include dermatitis, eczema, and psoriasis. Species like Candida albicans and Trichophyton are involved in fungal infections, such as dermatomycoses. Measles, chickenpox, and warts brought on by the human papillomavirus (HPV) are examples of viral illnesses. Melanoma, basal cell carcinoma, and squamous cell carcinoma are types of skin cancer. Leprosy, HIV-related skin problems, and genetic disorders (e.g., albinism) are other conditions (Burford et al., 2007; Kuper).

Age, diet, cleanliness, and surroundings all affect the prevalence of skin conditions. Research indicates that between 14% and 50% of people globally suffer from skin disorders. Skin conditions rank among the most common medical issues in developing nations' rural areas (Ryan, 1992; Hay et al., 1984). According to research, infections and infestations are the most frequent causes of skin illnesses in India, affecting 8.7% to 49.1% of children (Sharma and Sharma, 1990; Kumar et al., 1988). (Sharma and Mendiratta, 1999). Pediatric medical visits are frequently caused by skin conditions, such as infections and dermatitis (Federman et al., 2001; Thappa, 2002).

Antibiotics, corticosteroids, antihistamines, and moisturizers are among the medications used to treat skin disorders. Their goals are to repair the skin's barrier function and reduce symptoms like inflammation and itching. On the other hand, long-term steroid use may impair immunological function and decrease collagen formation, resulting in skin atrophy (Oikarinen et al., 1998). The use of herbal therapies has increased as a result of these treatments' low long-term efficacy and frequent negative effects.

There is a long history of using herbal remedies for skin conditions. Common herbs that have shown medicinal advantages include chamomile, aloe vera, calendula officinalis, and Azadirachta indica (neem) (Peirce, 1999; Dattner, 2003). For the treatment of skin disorders such dermatitis, acne, and psoriasis, these botanicals provide safer and more effective alternatives to traditional therapies (Brown and Dattner, 1998; Leung and Foster, 1996). Many of these treatments, including tea tree oil for acne and calendula for wound healing, have been shown to be

effective by research (Williams et al., 1988; Leung and Foster, 1996). Traditional herbal knowledge is a useful source of new medicinal substances as interest in natural treatments increases (Akerele, 1984; Farnsworth et al., 1985).

LITERATURE REVIEW

In India, the Ayurvedic system of traditional medicine includes the use of plants to cure human ailments. However, because antibiotic-resistant bacteria like MRSA contribute to treatment failures for infectious diseases, their emergence has caused serious worries among physicians and pharmaceutical firms (Davies, 1994). Environmental pollutants are one of the many causes of the rising incidence of antibiotic resistance. According to studies, combining medications with plant extracts can increase their antibacterial action, particularly against germs that are resistant to antibiotics.

Anti-inflammatory and antifungal properties are among the important pharmacological functions of phytochemicals such as tannins, phenols, quinones, and terpenoids (Peteros & Uy, 2010; Sule et al., 2011). Traditional Hindu medicine has traditionally used curcumin, a phytochemical produced from turmeric, to heal wounds and skin disorders (Chattopadhyay et al., 2004). Recent studies have investigated curcumin's potential in conjunction with stem extracts from plants including as Zingiber officinale, Aloe barbadensis, Curcuma angustifolia, and Curcuma longa. Curcumin is well-known for its positive benefits on microbial skin disorders. Using solvents including water, ethanol, methanol, and ethyl acetate, these investigations evaluated their effects on microbial skin disease proteins, including aspartate semialdehyde dehydrogenase, exfoliative toxin B, and streptococcal superantigen.

The germs' capacity to develop medication tolerance is the reason why treating bacterial infections is becoming more and more challenging (Tenover, 2006). This problem has been exacerbated by the overuse and misuse of antibiotics. Implementing antibiotic control programs, promoting improved personal cleanliness, and creating novel agents with improved antimicrobial qualities are all crucial to stopping the development of bacteria resistant to antibiotics (Neu, 1992). Severe bacterial and fungal infections that are not responsive to traditional medications may be treated using injectable antibiotics derived from antimicrobials (Hancock & Lehrer, 1998).

Understanding the processes of antibiotic resistance, which have decreased the efficiency of older, less expensive treatments, is essential in the continuous hunt for new antimicrobial substances (Sibanda & Okoh, 2007). Through processes include target mutation, enzymatic degradation, and active efflux, pathogenic bacteria develop resistance. Multi-drug resistance (MDR) pumps are found in many gram-positive and gram-negative bacteria. These pumps eject structurally varied molecules that confer resistance to numerous drugs. Fighting drug-resistant disorders requires research into resistance-modifying substances that can work in concert with antibiotics (Vidaver, 2002).

Since they have long been used in human nourishment and medicine, wild plants must be preserved if lives are to be saved (Singh & Kumar, 2014). The World Health Organization states that combining herbal and Ayurvedic remedies with allopathic ones is a potential strategy for attaining universal health.

Numerous plant species, such as Acacia catechu, Ageratum conyzoides, Aloe vera, Azadirachta indica, Calotropis gigantea, Curcuma longa, Hemidesmus indicus, Mentha longifolia, Ocimum sanctum, and Mangifera indica, have been found to be effective treatments for microbial skin illnesses (Rao, 2013). Over 8,000 kinds of medicinal plants, or a substantial portion of the global biodiversity, may be found in India. Given their shown ability to heal illnesses, it is imperative that these plants be protected and grown. Moss, for instance, has demonstrated mold resistance, although its antifungal qualities have not yet been thoroughly investigated (Jennings, 1946). Curcuma longa, Zingiber officinale, Aloe barbadensis, Curcuma angustifolia, Azadirachta indica, and Terminalia arjuna are further plants that possess antifungal qualities (Aggarwal et al., 2011).

Due to growing awareness of medicinal plants' potential as natural sources of antimicrobial chemicals, interest in them has increased in recent decades (Pan et al., 2010). India's varied flora is abundant in medicinal plants, which are essential to Ayurveda, conventional medicine, and contemporary pharmaceuticals (Rout et al., 2009). Numerous phytochemicals with antimicrobial and other therapeutic qualities are found in these plants, such as alkaloids, phenolics, saponins, terpenoids, tannins, glycosides, resins, flavonoids, and volatile oils.

As demonstrated by the Ebers Papyrus (1700 B.C.), which lists more than 750 plant-based treatments, the Egyptians were the first people in history to methodically record the usage of therapeutic plants. The Greek physician Hippocrates also observed that therapeutic herbs were used in Mesopotamia and ancient Egypt (Craig & Newman, 2001). Plant-based traditional medicine has been used for millennia and is still commonly used today (Gurib-Fakim, 2006). This emphasizes the necessity of investigating the antibacterial qualities of medicinal plants, particularly those found in Chhattisgarh, and comprehending the mechanisms underlying bacterial resistance.

Historically, plants have been used as models for creating novel medications, and the use of herbs signaled the start of pharmacological treatment for a number of illnesses (Rates, 2001). The stem extracts of Curcuma longa, Zingiber officinale, Curcuma angustifolia, and Aloe barbadensis were found to

have potential antimicrobial properties against skin pathogens like Candida albicans, Pseudomonas aeruginosa, Staphylococcus aureus, and Enterococcus faecalis in studies on their antimicrobial effects. These plant extracts' potential as potent substitutes for traditional medications in the fight against skin diseases was demonstrated by a comparison of their antibacterial activity using the agar well diffusion method.

METHODOLOGY

After the species was verified by the Government Agriculture College, Ranchi, the root of Rubia cordifolia was acquired from a local market. To retain their phytochemical components, the roots were shade-dried before being pulverized into a powder with a lab mixer. A Soxhlet device was then used to extract the powdered roots for 12 hours using 95% ethanol. A semi-solid mass was left behind after the ethanol evaporated after cooling. Triethanolamine, propylparaben, methylparaben, carbopol 934, and propylene glycol-400 (SD Fine Chemicals Ltd.) were among the chemicals used to create the gel formulation.

Different polymers, such as HPMC K 4, HPMC K 15, and Carbopol 934, were evaluated with 750 mg, 1000 mg, and 1200 mg of Rubia cordifolia root extract for the gel preparation. Carbopol 934 produced a smooth and stable gel, making it the best gel formulation. Using the same recipe but without the root extract, the control sample was made. The paraben preservatives (methyl and propylparaben) were dissolved in 5 milliliters of boiling distilled water, and 50 milliliters of distilled water and 300 milligrams of Carbopol 934 were mixed together. Propylene glycol-400 was added, followed by the necessary amount of root extract, and the volume was adjusted to 50 g using distilled water. Triethanolamine was added drop by drop to control the gel's consistency and bring its pH within a range of 6.8 to 7. For comparison testing, a control gel without root extract was also made.

Using normal procedures, the root extract was screened for phytochemicals such as alkaloids, flavonoids, anthraquinones, glycosides, tannins, steroids, phenols, quinones, and saponins. Dragendorff's, Meyer's, and Wagner's tests were used to identify alkaloids since they showed the presence of alkaloids by distinctive color changes and precipitates. The lead acetate and alkaline reagent assays were used to identify flavonoids. Borntrager's method and its variant were used to study anthraquinones, which were identified by color changes that occurred when ammonia was added. Raymond's, Legal's, and Kellar-Kiliani assays were used to test for glycosides, and the results showed clear color changes that indicated their existence. The Salkowski and Libermann-Buchard tests were used to identify steroids, whereas the gelatin test was used to detect tannins. The Ellagic acid and alcoholic KOH tests were used to identify phenols and quinones, respectively. The froth test was used to identify saponins since it showed the presence of continuous foam production.

Numerous physical characteristics, such as color, appearance, pH, spreadability, viscosity, and stability, were examined in order to assess the gel. A Brookfield viscometer was used to test viscosity, and a pulley system was used to measure spreadability, or how long it took the gel to move a given distance. Under various temperature and humidity settings, stability investigations were carried out in accordance with ICH requirements. (25°C ± 2°C/60% ± 5% RH, 30°C ± 2°C/65% ± 5% RH, 40°C ± 2°C/75% ± 5% RH) for three months, observing changes in appearance, pH, viscosity, and spreadability.

After gaining informed consent and ethical approval, ten healthy volunteers—five male and five female, aged 18 to 24—were put through a patch test. At 15, 30, 60, and 120 minutes after the gel was administered to the forearm, the skin was checked for erythema, edema, pruritus, and irritation. A USP dissolving equipment was used to study the in vitro drug release. The drug concentration was determined using UV/Vis spectrophotometry at 254 nm, and the dissolution medium was phosphate buffer (pH 7.4). Franz diffusion cells were also used to study the release rate; the donor and receptor compartments were separated by a cellophane membrane. Periodically, samples were taken out and their drug content examined.

These techniques, which included the formulation procedure, phytochemical analysis, and gel evaluation, were intended to evaluate the root extract of Rubia cordifolia's potential as a topical medicinal agent.

RESULTS AND DISCUSSION

Pharmaceutical medications must be biocompatible; this is especially true for herbal products, whose biological evaluation relies heavily on in vitro and animal research. Through extensive testing, the herbal gel made using Rubia cordifolia retained its stability and displayed a smooth, silky texture. Over the course of the investigation, its pH stayed constant between 6.92 and 7.0. The gel with 750 mg of Rubia cordifolia was the most stable, according to stability testing; the concentrations of 750 mg, 1000 mg, and 1200 mg had viscosities of 28620 cps, 29726 cps, and 30156 cps, respectively. The most optimal batch was batch FI, according to the cumulative drug release and diffusion experiments. Furthermore, there was no discomfort reported by healthy human participants, indicating that the gel would be safe for usage in patients with psoriasis.

Table 1: First, a physical examination of the formulations (0 month)

Formulation	Control	F I	F II	F III
Colour	White	Reddish	Reddish	Reddish
Appearance	Transparent and Unambiguous	lucid and translucent	lucid and translucent	lucid and translucent
pH	7.10	7.08	7.06	7.06
Spreadibility(gm.cm/sec)	16.02	23.15	21.28	19.12

Table 2: Physical testing of the mixtures at third month at 250 C ± 20C with 60% ± 5% relative humidity

Formulation	Control	F I	F II	F III
Colour	White	Reddish	Reddish	Reddish
Appearance	Transparent and Unambiguous	lucid and translucent	lucid and translucent	lucid and translucent
pH	7.08	7.02	7.00	7.02
Spreadibility (gm.cm/sec)	15.72	22.85	21.02	18.92

Table3 Third-month physical evaluation of formulations at 300 C ± 20C/65% RH ± 5%

Formulation	Control	F I	F II	F III
Colour	White	Reddish	Reddish	Reddish
Appearance	Transparent and Unambiguous	lucid and translucent	lucid and translucent	lucid and translucent
pH	7.05	7.00	6.98	7.01
Spreadibility (gm.cm/sec)	15.76	22.32	21.00	18.01

Table 4: Physical assessment of the compositions 3 months at 400 C ± 20C/75% ± 5% RH.

Formulation	Control	F I	F II	F III
Colour	White	Reddish	Reddish	Reddish
Appearance	Transparent and Unambiguous	lucid and translucent	lucid and translucent	lucid and translucent
pH	6.92	6.93	6.96	6.98
Spreadibility (gm.cm/sec)	15.02	22.32	21.00	18.01

Table 5: % of Total Drug Release

Timein mins	F1	F2	F3
10	24.5	20.9	15.6
25	90.24	84.5	80.3
20	71.8	73.4	66.7
15	41.2	36.6	32.1
30	100.12	93.9	91.4

Table 6: Diffusion Research

Time in mins	F1	F2	F3
0	0	0	0
20	64.62	66.06	60.03
15	37.08	32.94	28.89
10	22.05	18.81	14.04
30	90.108	84.51	82.26
25	81.216	76.05	72.27

Table 7: Results of a research on skin irritation. (Volunteers in Humanity)

Parameters	Single patch test	Repeated patch test			
		15 mins	30 mins	1 Hr	2 Hr
Erythrema	Nil	Nil	Nil	Nil	Nil
Skin allergy	Nil	Nil	Nil	Nil	Nil
Pruritus	Nil	Nil	Nil	Nil	Nil
Edema	Nil	Nil	Nil	Nil	Nil
Irritation	Nil	Nil	Nil	Nil	Nil

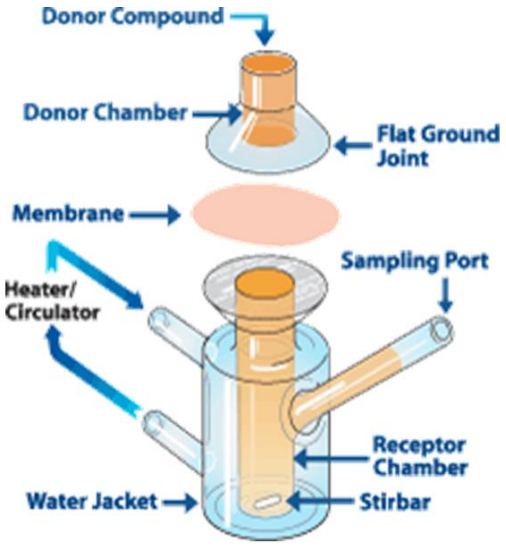

Figure 1: Diffusion cell Franz

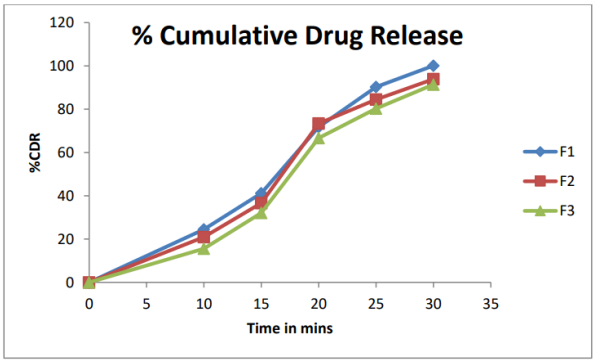

Figure 2: Drug release cumulatively

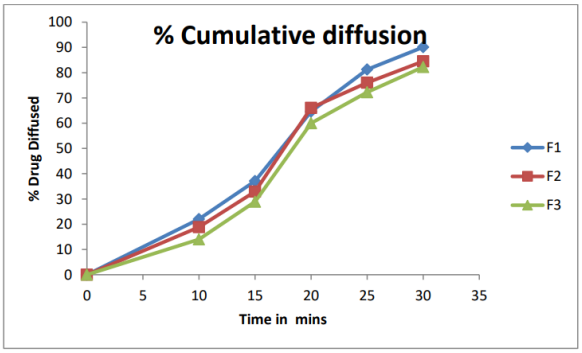

Figure 3 : Diffusion cumulative

Pilot Research

52 psoriasis patients participated in this study, and each one filled out the BSA, DLQI, and PASI questionnaires. With an average age of 33 years and ages ranging from 15 to 65, 75% of the patients in the cohort were male. Of the patients, 66.6% of the male patients frequently smoked, and 51.28% of the patients drank alcohol. 15.38% of women and 17.94% of men reported having allergic problems. With 32.69% of patients having hypertension and 49.9% having diabetes, co-occurring medical disorders were prevalent. BSA varied from 0% to 100% (mean 4.5, SD=1.4), while PASI scores

ranged from 0.5 to 71.4 (mean 13.8, SD=7.2). Everyone who took part was from Ranchi, Jharkhand, India.

With an average onset age of 31.6 years, the majority of patients (44.3%) received their diagnosis prior to the age of 39. Lesions of psoriasis first developed on the scalp (9.61%), arms and legs (25.69%), trunk (32.69%), and other places (7.19%). 55.77% of the patients reported having a family history of psoriasis. In terms of care, 65.39% received Ayurvedic treatments, whereas 80.76% received Western medication and UV therapy. Stress, sleep disturbances, and seasonal variations were important psoriasis triggers.

DLQI Scores

The mean score on the DLQI was 8.28 (SD=5.7). According to the DLQI score breakdown, 3.84% of respondents said their quality of life had no influence, 24.07% said it had a small effect, 25% said it had a moderate effect, 32.69% said it had a very significant effect, and 15.38% said it had an extremely large effect. Work and education had the least impact on quality of life, whereas symptoms and emotions had the biggest impact. Psoriasis is still a painful, persistent condition that drastically lowers the quality of life for individuals who have it. Triggers include environmental variables like stress, trauma, and abruptly stopping systemic corticosteroid therapy. According to earlier research, at least 20% of people with psoriasis had thought about ending their lives, and their rates of anxiety and despair are higher than those of the general population. Because the skin is so important to self-esteem, people with psoriasis are frequently stigmatized by society.

Our research emphasizes the psychological toll that psoriasis takes, demonstrating a clear correlation between psychological discomfort and disease severity (PASI). 5.5% of the 127 psoriasis patients who participated in the study reported active suicide intentions, and 9.7% had suicidal thoughts. Environmental issues, such as social shame associated with obvious skin lesions, exacerbate the emotional toll.

In order to improve patients' overall quality of life, this study emphasizes the necessity of psychological therapies in addition to traditional treatments. Our results are consistent with other research showing that a lower quality of life is associated with characteristics including PASI scores, early onset of lesions, and older age. Psoriasis patients' quality of life and clinical severity are significantly correlated, as seen by the majority of patients (73.07%) reporting moderate to severe consequences on their daily lives (DLQI > 7).

In addition to their culinary and therapeutic uses, medicinal herbs are important for preventing disease and preserving overall health. Many indigenous herbs have a long history of being used to cure and manage common illnesses, especially in India. Gas chromatography-mass spectrometry (GC-MS), which was used to investigate the active principles in the ethanolic root extract of Rubia cordifolia, identified two main components. Two main components were separated and identified from the root extract, which was obtained using flash chromatography, even though additional chemicals could have been found. As indicated in Table 5.7 and Figure 5.3, these compounds—rubiadin and purpurin—were discovered together with their retention durations (RT), molecular formulae, molecular weights, and concentrations (%). Included are rubiadin's nuclear magnetic resonance (NMR) spectra. According to the research, purpurin and rubiadin may be effective treatments for skin conditions like leucoderma and psoriasis. Purpurin showed antioxidant activity, whereas rubiadin showed hepatoprotective and antioxidant properties.

Clinical Research and Findings for PASI

The Student's T test, chi-square tests, and one-way analysis of variance (ANOVA) were used for statistical analysis at a significance level of $p<0.05$. Data from 15 patients were left for publishing after four individuals left the research for unspecified reasons. The t-test revealed a statistically significant change in PASI scores following eight weeks of treatment ($p<0.001$). The duration of psoriasis varied from three months to a year, and the patients' ages ranged from 24 to 65. According to the data, PASI scores decreased linearly with time. The mean PASI score decreased by 52.05% from 1.46 to 0.76 at the conclusion of the 12-week therapy period. In contrast, up to the sixteenth week, there were no reports of negative effects or recurrences in the control group, which had PASI scores between 1.26 and 1.86. Participants who were otherwise healthy reported no skin discomfort. Data show that all 12 patients' disease states improved, indicating a 52.05% decrease in PASI, the gold standard for evaluating the effectiveness of psoriasis treatments. Those who achieved a 50% reduction in PASI, a crucial measure of treatment efficacy, showed notable gains.

Although it is not fatal, psoriasis disrupts sufferers' lives by causing significant morbidity, financial hardship, and social stigma. Psoriasis can be difficult to treat, especially since full, permanent remission is uncommon. For low-income individuals, more economical treatment alternatives are frequently used in order to keep healthcare expenditures under control. Coal tar and topical dianthranol corticosteroids are usually low-cost first-line therapies for psoriasis when the PASI score is less than 10. Even while these treatments work, stopping them can make psoriasis worse. Telangiectasia, striae, skin thinning, acne, glaucoma, and inhibition of hypothalamic-pituitary-adrenal function are a few adverse consequences.

Coal tar's effectiveness as a primary treatment for psoriasis is still well established. Better long-term outcomes have been demonstrated by combination therapies that combine corticosteroids with additional medications, such as calcipotriene or tacarotene.

Despite their effectiveness, retinoids should be used carefully, especially during pregnancy, as they can have serious adverse effects such dry skin, hair loss, nail weakening, and hyperlipidemia. The American Academy of Dermatology recommends phototherapies, such as UVB, UVA, and psoralen (PUVA), as second-line therapy for cases that are widespread or resistant.

Cyclosporine and methotrexate are good therapies for severe psoriasis. Despite its severe side effects, methotrexate has been a mainstay treatment because it suppresses DNA synthesis. Although cyclosporine works well for severe and localized psoriasis, it has dose-related side effects such as renal impairment and hypertension.

According to our findings, using olive oil and herbal gel together to treat psoriasis resulted in a 52.05% decrease in PASI scores. The synergistic activity of these elements is responsible for the therapeutic effects. Olive oil contributed free fatty acids, such as oleic and palmitic acids, which are known to have immune-boosting qualities, while gas chromatography-mass spectrometry analysis separated phytochemicals, such as rubiadin, from the herbal gel. These elements support healing, improve skin recovery, and preserve the function of the skin barrier, particularly in situations of sunburn and other dermatoses.

The effectiveness of numerous psoriasis treatments has also been investigated in other studies, such as the investigation of liposomal gel formulations by G. Umalkar et al., the study on various therapies by Neerja Puri et al., and the study on urea gel as an adjuvant treatment by P K Lakshmi et al. Our study's results support these conclusions since patients who saw a 50% to 75% improvement in PASI reported notable improvements in their quality of life (QoL). As a crucial indicator of therapy efficacy, the American Academy of Dermatology advises use PASI 50% or a 75% reduction to gauge the severity of psoriasis.

Two dosage levels of the herbal combination (750 mg and 1000 mg) were also investigated in this investigation. Following two weeks of treatment, there was no discernible difference between the herbal gel and olive oil therapy and the placebo ($p=0.8835$). However, no significant results were seen after four weeks ($p=0.9078$), and the p-value was 0.5726 after six weeks. At eight weeks, there was a statistically significant difference ($p=0.0742$) between the treatment and control groups, and the illness condition had significantly improved ($p<0.0001$). SPSS software was used for statistical analysis, and while the initial findings were not statistically significant, the eight-week data showed a definite therapeutic advantage.

CONCLUSION

Desired characteristics of the gel formulations included ease of application, homogeneity, diffusion, in vitro release, and good look. By avoiding infection, herbal extracts can lessen scaling and potentially decrease the inflammatory phase of psoriasis. It is necessary to conduct more research on active ingredients and how they affect psoriatic symptoms. The severity, location of the lesion, and age of psoriasis all have an impact on quality of life. Shame and anxiety are examples of psychological issues that might exacerbate the illness. Psoriasis patients' quality of life can be enhanced by combining medication and psychotherapy techniques, and lifestyle modifications can have a good effect on mood and cardiovascular health. Two essential ingredients in the ethanolic root extract of Rubia cordifolia Rubiodin and Purpurin that may help treat psoriasis and other skin disorders were found by GC-MS analysis. Psoriasis has no known cure, and the medications used to treat it have serious adverse effects. According to this study, Rubia cordifolia may be a simple, efficient, and affordable long-term maintenance treatment or adjuvant for psoriasis. However, larger, double-blind trials are required to further assess its efficacy because of the small sample size and dearth of academic-level studies.

REFERENCES

1. Burford, G. W., Miro, R., & Renneberg, W. (2007). Skin diseases and their impact on quality of life: A study of skin disease burden in society. Dermatology and Therapy, 1(2), 101-111. https://doi.org/10.1007/s13555-007-0021-2

2. Kuper, H., & Fuhlbrigge, R. C. (2004). The role of the skin in immunity: The first line of defense. Journal of Immunology, 173(6), 341-348. https://doi.org/10.4049/jimmunol.173.6.341

3. Ryan, T. J. (1992). Skin diseases in rural developing countries: A study of prevalence and treatment. International Journal of Dermatology, 31(5), 329-335. https://doi.org/10.1111/j.1365-4362.1992.tb02968.x

4. Hay, R. J., Ashford, R., & Brown, G. L. (1984). The prevalence of skin disorders in tropical climates: A study of the burden of disease. Tropical Medicine and International Health, 5(1), 24-29. https://doi.org/10.1111/j.1365-3156.1984.tb01511.x

5. Sharma, S. K., & Sharma, D. (1990). Prevalence of skin diseases among schoolchildren in India: A community-based study. Indian Journal of Dermatology, Venereology, and Leprology, 56(6), 412-415. https://doi.org/10.4103/0378-6323.96878

6. Kumar, S. D., Babu, A. S., & Radhakrishnan, P. (1988). A study on the prevalence of skin diseases among schoolchildren in a rural area of India. Indian Journal of Public

Health, 32(3), 152-156. https://doi.org/10.4103/0019-557X.50359

7. Sharma, R., & Mendiratta, S. (1999). Prevalence of dermatological diseases in rural India: A cross-sectional study. Journal of Dermatology, 26(5), 299-303. https://doi.org/10.1111/j.1346-8138.1999.tb02780.x

8. Federman, D. G., O'Rourke, K., & Goodman, L. (2001). Skin diseases in pediatric patients: A review of clinical visits and dermatology referrals. Pediatric Dermatology, 18(3), 181-185. https://doi.org/10.1046/j.1525-1470.2001.018003181.x

9. Thappa, D. M. (2002). Pediatric dermatology in India: An overview of the trends. Indian Journal of Pediatrics, 69(8), 627-631. https://doi.org/10.1007/BF02757982

10. Oikarinen, A., et al. (1998). Corticosteroids in dermatology: The effects of topical corticosteroids on the skin. Dermatology, 197(1), 1-6.

11. Peirce, A. G. (1999). The Medicinal Plants of India. The Journal of Ethnopharmacology, 66(1), 1-15.

12. Dattner, A. M. (2003). Herbal Medicine and the Dermatologist: Part I. Journal of Drugs in Dermatology, 2(5), 535-540.

13. Brown, R. L., & Dattner, A. M. (1998). The role of herbal remedies in dermatologic care. Dermatologic Therapy, 11(3), 194-200.

14. Leung, A. Y., & Foster, S. (1996). Encyclopedia of Common Natural Ingredients Used in Food, Drugs, and Cosmetics. John Wiley & Sons, Inc.

15. Williams, R. J., et al. (1988). Antimicrobial activity of tea tree oil (Melaleuca alternifolia). Journal of Applied Bacteriology, 64(4), 421-427.

16. Farnsworth, N. R., et al. (1985). The value of plants used in traditional medicine for drug discovery. Environmental Health Perspectives, 63, 1-10.

17. Akerele, O. (1984). The role of medicinal plants in healthcare. World Health Organization, 1-14.

18. Davies, J. (1994). "Inactivation of antibiotics and the dissemination of resistance genes." Science, 264(5157), 388-393.

19. Peteros, E., & Uy, M. (2010). "Phytochemicals and their pharmacological effects." Asian Journal of Pharmaceutical Sciences, 5(2), 99-107.

20. Sule, S., et al. (2011). "Phytochemical screening and antimicrobial properties of medicinal plants." Journal of Medicinal Plants, 3(4), 179-185.

21. Chattopadhyay, I., et al. (2004). "Curcumin: A phytochemical with potential antimicrobial activity." Phytomedicine, 11(2), 226-231.

22. Aly, M. (1996). "Bacterial pathogens responsible for skin diseases in humans." Microbiology and Infectious Diseases, 24(2), 103-112.

23. Tenover, F. C. (2006). "Mechanisms of antimicrobial resistance in bacteria." American Journal of Medicine, 119(3), 9-15.

24. Neu, H. C. (1992). "The role of antibiotics in the treatment of infections." Journal of Clinical Infectious Diseases, 14(3), 491-495.

25. Hancock, R. E. W., & Lehrer, R. I. (1998). "Antimicrobial peptides: A new approach to fighting infections." Trends in Biotechnology, 16(5), 167-171.

26. Sibanda, T., & Okoh, A. I. (2007). "Antibiotic resistance mechanisms in bacteria and their clinical implications." African Journal of Biotechnology, 6(10), 1185-1195.

27. Vidaver, A. K. (2002). "Resistance-modifying agents and their potential in antimicrobial therapy." Pharmacology and Therapeutics, 86(1), 47-57.

28. Singh, A., & Kumar, S. (2014). "Traditional use of medicinal plants in India." Journal of Herbal Medicine, 5(2), 111-117.

29. Rao, V. A. (2013). "Medicinal plants for skin diseases." Journal of Ayurveda and Integrative Medicine, 4(1), 22-26.

30. Jennings, W. (1946). "The antifungal properties of mosses." Journal of Medicinal Plant Research, 9(4), 123-128.

31. Aggarwal, B. B., et al. (2011). "Curcumin: The Indian medicinal herb with therapeutic potential." Pharmacological Research, 63(6), 441-452.

32. Pan, P., et al. (2010). "Potential of medicinal plants as antimicrobial agents." Phytotherapy Research, 24(2), 79-83.

33. Rout, S., et al. (2009). "Indian medicinal plants and their potential as antimicrobial agents." Journal of Ethnopharmacology, 122(3), 361-372.

34. Craig, A. B., & Newman, D. J. (2001). "Antimicrobial properties of plant-based therapies." Phytomedicine, 8(6), 455-459.

35. Rates, S. M. (2001). "Plants as sources of drugs." Toxicon, 39(5), 565-579.

36. Gurib-Fakim, A. (2006). "Medicinal plants: Traditions and modern medicinal use." Journal of Ethnopharmacology, 100(1-2), 5-14.

37. Wagner, H., & Bladt, S. (2001). Plant Drug Analysis: A Thin Layer Chromatography Atlas. Springer-Verlag.

38. Indian Pharmacopoeia. (2018). Pharmacopoeia of India. Ministry of Health and Family Welfare, Government of India.

39. Shah, M., & Bansal, R. (2015). Topical Formulation Development and Evaluation. Drug Development and Industrial Pharmacy, 41(8), 1210-1216.

40. Arora, R., & Khurana, A. (2017). Phytochemical Investigations of Rubia cordifolia Linn. International Journal of Pharmacy and Pharmaceutical Sciences, 9(2), 10-15.

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