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New Polyaphron Dispersion Technology for Topical Calcipotriene with Betamethasone Dipropionate Formulation in Psoriasis Treatment

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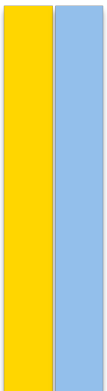

New Polyaphron Dispersion Technology for Topical Calcipotriene with Betamethasone Dipropionate Formulation in Psoriasis Treatment

Artigo de Revisão Bibliográfica

Dissertação de Mestrado Integrado em Medicina

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Dedication

To my family, whose unwavering support has been invaluable throughout my academic journey, playing a pivotal role in my pursuit of knowledge and personal growth.

Acknowledgments

To my mentor, Prof. Dr. Tiago Torres, whose extensive knowledge, and unwavering commitment to the field of Dermatology have inspired me throughout my academic journey.

Resumo

Introdução: A psoríase é uma doença inflamatória crónica da pele que afeta milhões de indivíduos em todo o mundo, sendo a psoríase em placas o subtipo mais comum. A etiologia da doença envolve a desregulação imunológica e a libertação anormal de citocinas. As opções de tratamento incluem fármacos tópicos, orais e biológicos, sendo a terapêutica de primeira linha a combinação de Calcipotrieno e Dipropionato de Betametasona. No entanto, a fraca adesão ao tratamento constitui um desafio. A tecnologia *Polyaphron Dispersion* oferece uma solução promissora ao melhorar as propriedades da formulação e a conveniência para o doente.

Objetivos: Esta revisão tem como objetivo avaliar a eficácia e segurança do creme de Calcipotrieno e Betametasona formulado com a tecnologia *Polyaphron Dispersion*. Avalia as potenciais vantagens deste sistema inovador de administração de fármacos em comparação com as opções de tratamento previamente existentes.

Métodos: Foi efetuada uma pesquisa bibliográfica para identificar artigos em inglês em várias bases de dados, nomeadamente Pubmed, Journal of the European Academy of Dermatology and Venereology, Journal of Drugs in Dermatology, Google Scholar, Science Direct, Cochrane Library, Scopus e ClinicalTrials.gov. A pesquisa abrangeu o período de 2009 a 2023, concentrando-se em publicações mais recentes. Para a pesquisa, utilizou-se uma combinação de termos e palavras-chave. A escolha dos artigos envolveu a análise do título, resumo e restante conteúdo de texto.

Discussão: A combinação de Calcipotrieno e Dipropionato de Betametasona em dose fixa é recomendada para o tratamento tópico da psoríase. O Calcipotrieno atua de forma semelhante à vitamina D3 e reduz a hiperproliferação dos queratinócitos, enquanto o Dipropionato de Betametasona apresenta efeitos anti-inflamatórios e imunossupressores. A combinação destas substâncias originou resultados significativamente melhores do que a utilização de qualquer uma delas isoladamente, alcançando a eficácia terapêutica em poucos dias. O desafio de as combinar num ambiente aquoso devido aos seus diferentes requisitos de pH foi resolvido recorrendo à tecnologia *Polyaphron Dispersion*, que permite a sua administração simultânea. Os ensaios clínicos demonstraram que o creme é eficaz na melhoria dos sintomas da psoríase em placas, sendo bem tolerado pelos doentes.

Conclusão: O creme Calcipotrieno e Betametasona demonstrou uma eficácia superior em vários parâmetros, oferecendo potenciais melhorias em termos de conveniência e resultados do tratamento. No entanto, é necessária investigação adicional para avaliar a segurança a longo prazo, a eficácia em grupos específicos de doentes e a aplicação em diferentes áreas do corpo.

Palavras-chave: Psoriasis, Calcipotriene and Betamethasone Dipropionate, Polyaphron Dispersion Technology.

Abstract

Introduction: Psoriasis is a chronic, inflammatory skin disease that affects millions worldwide, with plaque psoriasis being the most common subtype. The disease's etiology involves immune dysregulation and abnormal cytokine release. Treatment options include topical, oral, and biological drugs, with first-line therapy being the combination of Calcipotriene and Betamethasone Dipropionate. However, poor treatment adherence poses a challenge. The Polyaphron Dispersion technology offers a promising solution by improving formulation properties and patient convenience.

Objectives: This review aims to evaluate the effectiveness and safety of Calcipotriene and Betamethasone cream formulated with Polyaphron Dispersion technology. It assesses the potential advantages of this unique drug delivery system compared to existing treatment options.

Methods: A bibliographic search was executed to identify English articles from multiple databases, namely Pubmed, Journal of the European Academy of Dermatology and Venereology, Journal of Drugs in Dermatology, Google Scholar, Science Direct, Cochrane Library, Scopus database, and ClinicalTrials.gov. The search spanned from 2009 to 2023, focusing on recent publications. A combination of MeSH terms and keywords was used for the search strategy. The screening of the articles involved analysing titles, abstracts, and full-text articles.

Discussion: The combination of Calcipotriene and Betamethasone Dipropionate at a fixed dose is recommended for the topical treatment of psoriasis vulgaris. Calcipotriene acts similarly to vitamin D3 and reduces the hyperproliferation of keratinocytes, while Betamethasone Dipropionate exhibits anti-inflammatory and immunosuppressive effects. Combining these two substances has resulted in significantly better outcomes than using either substance alone, achieving therapeutic efficacy within days. However, the challenge of combining them in an aqueous environment due to their different pH requirements was addressed using Polyaphron Dispersion technology, which allows simultaneous administration. Clinical trials have shown that Calcipotriene and Betamethasone Dipropionate PAD cream is effective in improving the symptoms of plaque psoriasis and is well-tolerated by patients.

Conclusion: Calcipotriene and Betamethasone PAD cream has shown superior efficacy in multiple parameters, offering potential improvements in convenience and treatment outcomes. Further research is needed to evaluate long-term safety, efficacy in specific patient groups, and application in different body areas.

Keywords: Psoriasis, Calcipotriene and Betamethasone Dipropionate, Polyaphron Dispersion Technology.

List of Abbreviations

BDP	Betamethasone Dipropionate
BSA	Body Surface Area
CAL	Calcipotriene
CCR6	Chemokine Receptor 6
DLQI	Dermatology Life Quality Index
HIV	Human Immunodeficiency Virus
IFN	Interferon
IL	Interleukin
mPASI	Modified Psoriasis Area and Severity Index
mPASI 75	75% or greater reduction from baseline in mPASI score
mRNA	Messenger Ribonucleic Acid
NF-kB	Nuclear Factor kappa-light-chain-enhancer of activated B cells
PAD	Polyaphron Dispersion
PASI 75	75% or greater reduction from baseline in PASI score
PGA	Physician Global Assessment
PTCS	Psoriasis Treatment Convenience Score
TNF-α	Tumor Necrosis Factor α
TS	Topical Suspension

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Introduction

Psoriasis is a chronic, immune-mediated, inflammatory disease that primarily affects the skin, underlying on a polygenic basis. It is estimated to impact 125 million people worldwide, making it a significant public health concern. [1,2]

Psoriasis is a heterogeneous disease that can be categorized into various subtypes based on its morphologic features. The most prevalent form is plaque psoriasis, accounting for 80% of cases. There are other subtypes, such as guttate psoriasis, erythrodermic psoriasis, and pustular psoriasis. [1] Plaque psoriasis is characterized by the presence of symmetric, well-defined, pink-to-erythematous, scaly plaques that can appear on any part of the body, with the trunk, scalp, gluteal fold, and extensor surfaces being the most affected areas. [1,2] Psoriasis often exhibits a cyclic evolution, with patients experiencing periods of flares and periods with fewer manifestations or remission. [2]

This condition affects both women and men equally and can develop at any age, although it commonly has two peaks of incidence, the first between ages 18 and 39 and the second between ages 50 and 69. This variability appears to be linked to a combination of genetic, environmental, and behavioural factors, with some associated triggers, including skin trauma, infections (such as HIV and streptococcal), smoking, medications (such as b-blockers, IFN-α, lithium), and stress. [1,2] These factors can impact the development and progression of psoriasis, contributing to the heterogeneous presentation of the disease.

The pathophysiology of the disease is characterized by abnormal activation of the immune system, leading to an increased release of proinflammatory cytokines from immune cells. This ongoing immune activation results in long-term damage to multiple tissues and organs, contributing to the systemic nature of the disease. [2] Several pathways have been implicated in the pathogenesis of psoriasis, including dysregulated antigen presentation, activation of NF-kB signalling pathways, abnormal differentiation of T helper cells, and enhanced IL-17 response. These pathways can interact with each other, resulting in a complex network of immune dysregulation that underlies the pathophysiology of psoriasis. [2]

Topical, oral, and biological drugs are among the treatment options available for psoriasis, along with phototherapy. [3] One of the most used treatments for mild to moderate psoriasis is the combination of vitamin D analogs and topical corticosteroids. The European, Canadian, and American Psoriatic Societies recommend the fixed dose combination of Calcipotriene and Betamethasone Dipropionate as a first-line treatment. [4]

Topical corticosteroids possess anti-inflammatory and antiproliferative properties that down-regulate the genes responsible for proinflammatory cytokines. [1] Vitamin D analogs inhibit keratinocyte proliferation and enhance its differentiation. [1,2] Although adverse effects such as burning and irritation can occur, they are uncommon. [1,3]

The combination of vitamin D and corticosteroids demonstrated significantly better efficacy than vitamin D alone or corticosteroids alone. [1,5] Combining Calcipotriene and Betamethasone in a single formulation has been shown to have a synergistic effect, reducing the number of corticosteroids used and minimizing potential adverse effects. [6,7] Calcipotriene can help reduce the atrophy and decreased epidermal barrier integrity caused by Betamethasone, while Betamethasone can counteract the potential irritant effects of Calcipotriene. In the past, these two medications were used separately, twice a day, or sequentially, but Calcipotriene's ability to penetrate through the stratum corneum into the epidermis was low. Therefore, developing better strategies to enhance its penetration was necessary. [6]

Over the years, poor adherence to psoriasis treatment has been observed, being a significant barrier to achieving treatment success. [8] The effectiveness of topical treatments is strongly linked to patient adherence, which is, in turn, affected by the physical and rheological properties of the vehicle. [9] This highlights the need to strike a balance between patient preferences and the treatment's safety and effectiveness.

In this context, the implementation of Polyaphron Dispersion technology has facilitated the development of topical formulations that offer enhanced properties, superior chemical stability, improved penetration, increased efficacy, and enhanced safety while also providing a more convenient application method for patients. [10]

Polyaphron droplets consist of an inner core of nonpolar solvent enclosed in an outer shell comprising a multilayer structure of surfactants, oil, and water. This technology stabilizes and separates the inner core from the continuous dispersal phase. [10] Compared to conventional formulations, using PAD technology reduces the amount of surfactant required, which decreases the risk of hydrolytic degradation of oil-soluble drugs solubilized in the aqueous phase. Additionally, PAD reduces the washout of epidermal lipids, which is crucial for maintaining the skin barrier function. [10]

Objectives

This review aims to assess the efficacy and safety of administering Calcipotriene and Betamethasone cream formulated with Polyaphron Dispersion technology for treating Psoriasis. Additionally, it will analyse the potential benefits of this new drug delivery system in terms of effectiveness, tolerability, and patient satisfaction, compared to other available treatment options for psoriasis.

Methods

This review aimed to identify relevant articles written in English from several databases, including Pubmed, Journal of the European Academy of Dermatology and Venereology, Journal of Drugs in Dermatology, Google Scholar, Science Direct, Cochrane Library, Scopus database, and ClinicalTrials.gov. The search was conducted from 2009 to 2023, with a preference for the most recent articles. Additional studies were identified through the reference lists of the included articles.

The search strategy employed a combination of Medical Subject Headings (MeSH) terms and keywords, such as ‘’Psoriasis’’, ‘’Calcipotriene and Betamethasone Dipropionate’’, ‘’Polyaphron Dispersion Technology’’, ‘’Topical Formulation’’, ‘’Topical Treatment’’, ‘’Adherence’’.

The screening process involved analysing the title and abstract to identify potentially relevant studies. Then, full-text articles were assessed, considering the relevance of the abstract.

This search yielded a total of 27 articles.

Discussion

1. Calcipotriene and Betamethasone Dipropionate

A combination of Calcipotriene and Betamethasone Dipropionate at a fixed dose (concentration of 0.005%/0.064%) is recommended for topical treatment of psoriasis vulgaris of the trunk, limbs, and scalp in adults. [11]

Calcipotriene is an analog of vitamin D3 that acts similarly to natural 1,25(OH)2D3 [12]. It binds to a retinoid receptor on T cells and keratinocytes, regulating cell differentiation, growth, and immune functions. Its anti-inflammatory and immunomodulatory effects are due to its ability to reduce the hyperproliferation process of the keratinocytes, stabilize their differentiation, and lower the level of proinflammatory cytokines. [1,13]

Betamethasone Dipropionate is a potent synthetic glucocorticoid that exhibits anti-inflammatory and immunosuppressive effects by binding to cytosolic receptors and translocating to the nucleus. Once there, it regulates the transcription of various genes involved in the immune response. This action helps to reduce inflammation, erythema, and edema, suppresses excessive cell growth, and enhances the maturation of skin cells. [13]

According to an analysis of 131 randomized controlled trials, the use of a combination of vitamin D analog and corticosteroid had been found to result in significantly better outcomes than either substance used alone. [5] While topical vitamin D analogs may take several weeks to achieve their full effects, the combination can ensure therapeutic efficacy within days. Moreover, this combination reduces the required dose of corticosteroids, thereby mitigating the potential adverse effects. [7]

These two substances act synergistically in treating psoriasis, as Calcipotriene normalizes keratinocyte differentiation and Betamethasone reduces inflammation. [13] Research has shown that combining Calcipotriene and Betamethasone dipropionate in a topical formulation produces a synergistic effect by inhibiting the expression of cytokines linked to the IL-23/T17 pathogenic axis, including the expression of IL-17a, IL-23a, IL-22 and TNF-α mRNA in skin lesions. Moreover, the formulation leads to an expansion of CCR6+ γδ T17 cells in the draining lymph nodes. Notably, CAL/BDP also promotes the generation of regulatory CD8+ T cells and enhances the balance between regulatory CD8+ or CD4+ T cells and proinflammatory CCR6+ γδ T17 cells in the draining lymph nodes. [14] This demonstrates that the combination of these two substances positively affects psoriasis treatment.

Although these two substances act together, Calcipotriene is stable in alkaline environments, with a pH of around 8. At the same time, Betamethasone Dipropionate requires an acidic environment, with pH levels ranging from 4 to 6. As a result, combining them in an aqueous environment was considered unstable and led to their decomposition. [4,13] To address this challenge, initially, these substances were applied separately. However, considering that patients prefer a once-daily application regimen [15], there was a need to develop a formulation that could allow the simultaneous administration of both drugs.

Before the advent of PAD technology, commercially available Calcipotriene and Betamethasone dipropionate formulations in a fixed dose were limited to ointments, oleogels, and foams. [4,6,13,16] These are non-aqueous oil-to-paraffin-based formulations, often perceived as greasy and sticky, resulting in poor patient tolerance. [4] Understanding these formulations' mechanical properties is essential for establishing a comparison, as these properties significantly impact patient preferences and treatment adherence. [16]

Calcipotriene and Betamethasone ointments comprise a blend of liquid and solid oils combined with a potent solvent. Ointments offer several benefits, including penetrating the skin barrier effectively and providing hydration by reducing water loss through the epidermis. [6,10] These properties make ointments highly effective in glabrous areas, such as soles and palms, and in treating nail psoriasis affecting the nail matrix. [6] However, ointments also have certain drawbacks, including greasiness, a tendency to adhere to clothing, and challenges with application and rubbing. These factors can make them less visually appealing and less convenient for patients. [6,10]

The development of a new formulation was motivated by the necessity to treat scalp psoriasis, a condition characterized by thick, scaly lesions in areas with limited accessibility. The Calcipotriene and Betamethasone oleogel formulation was created to deliver the active ingredients to those affected areas effectively. [6,17] This formulation is a colloidal dispersion, where the solid dispersed phase is gelatinized using appropriate gelling agents. [16]

After researching to compare the effectiveness of ointment versus oleogel, it was observed that the latter exhibited a faster spread rate, requiring less than 5 minutes for daily application. Furthermore, patients who used oleogel reported higher levels of satisfaction. [18]

Calcipotriene and Betamethasone foam formulations are other options available. These substances can be classified into lipid anhydrous bases for Calcipotriene and Betamethasone, and volatile solvents that act as propellants. The foam formulations utilize a propellant to transform a liquid formulation into foam. This process enables the creation of a supersaturated drug layer on the skin, elevating its chemical potential and enhancing its capacity to penetrate the skin barrier. [6,13] Research has demonstrated that foam formulations exhibit superior efficacy than gels and

ointments, primarily attributed to their faster penetration and ability to achieve higher concentrations. [19] Moreover, a comparative analysis of these formulations revealed that the Calcipotriene Betamethasone foam outperformed the gel formulation containing the same components. [20]

Conventional creams are formulated to prioritize aesthetics, making them convenient to apply and ensuring quick absorption into the skin without leaving residue on the clothing. [9,10] However, their lower capacity to deliver active ingredients through the skin barrier, makes them less effective than ointments. [10] Creams are emulsion-based formulations that typically contain higher concentrations of surfactants, ranging from 2 to 5%. Nevertheless, this aspect can cause skin irritation and compromise the integrity of the skin barrier function. [10]

Poor adherence in dermatology is often linked to limited cosmetic acceptability. It is crucial to consider organoleptic and application characteristics, such as spreadability and stickiness. Ointments, oleogels, and foams, known to cause discomfort due to their sticky or greasy texture, can be inconvenient for many patients. [21]

Research has consistently shown low adherence rates, ranging from 39% to 73%. [9,22] Over the years, several strategies have been developed to enhance adherence and optimize treatment outcomes in psoriasis management. These approaches encompass improving patient-physician communication, simplifying treatment instructions while retaining essential information, providing written instructions, and encouraging regular contact with healthcare providers. In topical therapy, factors such as effectiveness, application frequency, and patient satisfaction with the formulation's physical properties, particularly the vehicle's rheological and textural properties, play a pivotal role in promoting adherence. [9,22,23]

Studies have demonstrated that a topical product with high skin absorption, minimal residue on the skin, effective moisturizing properties, excellent tolerance, and a once-daily application regimen is suitable for at least 90% of patients. [15]

In this context, topical formulations should facilitate the rapid and even distribution of the active ingredients, specifically Calcipotriene and Betamethasone, over the affected area. Patients are generally reluctant to use products that are unpleasant, difficult, or time-consuming to apply. [22] Consequently, the need to develop a new technology that could reformulate the existing drugs, addressing the issues perceived as barriers to treatment adherence by the patients arose.

2. Polyaphron Dispersion Technology

The PAD technology has previously been employed in various industries. However, recent research has unveiled its potential importance in the formulation and topical administration of pharmaceutical agents. [10]

Polyaphrons, or colloidal liquid aphrons or liquid foams, comprise an inner core containing a nonpolar solvent enclosed by multiple layers of surfactants, oil, and water. This distinctive composition allows the creation of stable droplets, effectively isolating the inner core from the surrounding dispersed dynamic phase. [10]

The PAD formulations are constructed through a two-step process. In the first step, an oil-in-water PAD is created with a high oil content (80 to 90% w/w) to ensure the stability of the droplets persists even after dilution in the subsequent step. In the second step, one or more pre-stabilized PADs with high oil content are dispersed in an aqueous environment containing a polymeric gellant, forming a physically stable oil-in-water dispersion. [10]

PAD technology can be customized to fulfil different requirements, including creating visually appealing formulations and targeting specific body areas. These parameters are achieved through their unique ability to demonstrate thixotropic behaviour in the gel phase, allowing the formulations to be perceived as light lotions or heavy creams, despite having the same oil phase and similar penetration properties. Furthermore, this technology exhibits fewer temperature-induced phase changes, making it more reliable and consistent in different environmental conditions. [10]

The utilization of PAD technology in the formulation of Calcipotriene Betamethasone cream marks a significant milestone, as it is the first topical treatment to incorporate this technology. [7] By employing PAD technology, this well-established drug combination achieves unprecedented levels of drug penetration, ensuring enhanced efficacy, safety, and convenience. [10]

The rheological characteristics of PAD formulations are regulated by the polymeric gel present in the aqueous phase, distinguishing them from other emulsion creams that rely on larger quantities of surfactants and less suitable solid waxes for physical stability. [10] The droplet capsule technology allows for significantly lower amounts of surfactants, up to 30 times less than conventional creams and lotions with comparable oil levels. The decreased usage of surfactants aids in mitigating the risk of drug solubilization in the aqueous phase and subsequent hydrolytic degradation, which could cause skin damage and irritation. [10]

Furthermore, the physical-chemical stability enables complete solubilization of Calcipotriene and Betamethasone, even in water, which would otherwise take to significant degradation of both active ingredients. [4]

The Calcipotriene Betamethasone fixed dose combination is formulated using two sets of aphrons, where the active compounds are individually encapsulated within an aqueous phase with a pH of approximately 7.75. The cream comprises a high percentage of the dispersed oil phase (70-90%) and a minimum surfactant concentration (0.5-3% of the total weight). [6]

3. Clinical Trials

A pooled analysis of two phase-3, randomized, prospective, multicentre, parallel-group, investigator-blinded trials was conducted to investigate the efficacy and safety of a fixed dose combination of calcipotriene and betamethasone dipropionate cream for the topical treatment of plaque psoriasis. The trials were conducted in the United States of America (MC2-01-C2) and the European Union (MC2-01-C7). [4] Both studies had a similar design, consisting of an 8-week treatment period. The trials included subjects over 18 with mild-to-moderate psoriasis and 2 to 30% of the body area affected. Participants were instructed to apply CAL/BDP once daily. In addition, they were randomly assigned to one of three treatment groups: CAL/BDP PAD cream (551 patients), CAL/BDP gel (542 patients), and cream vehicle (178 patients). [4,24]

The efficacy was evaluated based on four parameters: Physician Global Assessment treatment success, change from baseline in modified Psoriasis Area and Severity Index, improvement in Dermatology Quality Life Index, and improvement in Psoriasis Treatment Convenience Score. [4,24]

The efficacy of CAL/BDP PAD cream in achieving PGA treatment success was significantly higher (43.2%) than CAL/BDP TS (31.9%) and the vehicle group (5.2%) at week 8. This difference was observed as early as week 4. Furthermore, the study demonstrated that the CAL/BDP PAD cream improved BSA outcomes with increasing severity of PGA. In contrast, the CAL/BDP TS did not exhibit the same level of improvement. Specifically, in individuals with BSA ≤ 10% and > 10%, the PGA treatment success for CAL/BDP PAD cream was 41.7% and 48.3%, respectively, while the corresponding rates for CAL/BDP TS were 33.0% and 28.7%, respectively. [4]

Throughout the study period, the change from baseline in mPASI was consistently more significant in the CAL/BDP PAD cream group compared to the CAL/BDP TS group. This difference was maintained until week 8, with a more remarkable improvement of 64.6% in the cream group compared to 56.4% in the TS group. Furthermore, a higher proportion of subjects in the CAL/BDP

PAD cream group (44.3%) achieved a more significant 75% or greater reduction in mPASI score than the CAL/BDP TS group (34.5%). [4]

At week 8, the CAL/BDP PAD cream demonstrated a more substantial impact on DLQI, with 43.8% of subjects achieving scores of 0 or 1, indicating the minimal impact of psoriasis on their quality of life. Moreover, the CAL/BDP PAD cream was reported to be more convenient in terms of PTCS, as it was perceived as less greasy than CAL/BDP TS. [4]

Safety was also assessed, and there were no statistically significant differences in adverse drug reactions between the treatment groups. The most frequently reported local site reactions in patients using CAL/BDP PAD cream included pain, irritation, and pruritus at the application site. [4,24] The results achieved in week 8 and other relevant outcomes are summarized in Table I.

Head-to-head clinical trials directly comparing the efficacy of CAL/BDP cream and CAL/BDP foam have not been conducted. However, an indirect comparison analysis was performed between these two formulations using CAL/BDP oleogel as a standard reference. Four outcomes were evaluated in this research: PGA treatment success, PASI75 response (individuals who achieved 75% or more outstanding improvement in PASI from baseline), improvement in DLQI, and treatment satisfaction. Although the duration of use varied between these formulations (four weeks for foam and eight weeks for cream), an indirect comparison was conducted. [25]

Two different studies were analysed for this purpose. The first study, PSO-ABLE, is a randomized, investigator-blinded, phase 3 clinical trial investigating the differences between CAL/BDP foam (185 patients) and CAL/BDP gel (188 patients) and their respective vehicles over 12 weeks. [25,26] On the other hand, the second study, PSO-INSIGHTFUL, is a phase 3, randomized, open-label study that assigned 212 patients to either CAL/BDP foam or CAL/BDP gel treatment for one week and then switched them to the other treatment for an additional week. [25,27]

The comparison revealed that both treatments were similarly effective in achieving PGA treatment success and PASI75 response at weeks 1, 4, and 6. However, at week 8, CAL/BDP foam demonstrated superior outcomes in these parameters compared to CAL/BDP cream. Nevertheless, in terms of improving DLQI, CAL/BDP cream was considered more effective. Patients also reported higher treatment satisfaction with CAL/BDP cream, which was easy to apply, non-greasy, and moisturizing. These striking results were evident from the first week of the treatment. [25]

In another study, a sensory evaluation of CAL/BDP cream vehicle was conducted by a panel of 16 experts. The panel assessed the sensory properties of the cream vehicle in four different aspects: appearance, pick up, rub out, and after-feel, using a scale ranging from 0 to 100%.

Researchers blindly compared the CAL/BDP cream vehicle to a standard ointment based on petrolatum and a standard oleogel product to ensure impartial results. [21]

The appearance of the CAL/BDP PAD cream vehicle was assessed based on its shape integrity and gloss. The findings indicated that the cream vehicle had a lower shape integrity than the petrolatum, while their gloss levels were similar. On the other hand, the oleogel exhibited the highest gloss among the three formulations, but it had the lowest shape integrity. [21]

Regarding pick-up, petrolatum was deemed the least favourable option due to its high firmness, stickiness, and cohesiveness. However, CAL/BDP PAD cream vehicle and the oleogel showed comparable firmness, stickiness, cohesiveness, and peaking levels, with slightly better results observed for the oleogel. [21]

In terms of the rub-out properties on the skin, petrolatum was determined to be the greasiest and thickest product. In contrast, the CAL/BDP PAD cream vehicle was rated as the least greasy and the wettest, while the oleogel was observed to have the lowest absorbency among the three formulations. [21]

Concerning after-feel, petrolatum was found to be the glossiest and stickiest, leaving the highest residue on the skin. On the other hand, the oleogel had the lowest amount of residue. The oleogel and CAL/BDP PAD cream vehicle showed similar results regarding the other after-feel attributes. [21]

Conclusion

Psoriasis is a prevalent condition worldwide that markedly affects patients' quality of life. The combination of Calcipotriene and Betamethasone in a fixed dose has been extensively studied and shown to be effective for acute and maintenance therapy in psoriasis patients. However, most existing formulations are non-aqueous oil or paraffin-based, which can be perceived as greasy, sticky, and interfere with clothing, resulting in low treatment adherence.

Efforts are being made to enhance patient satisfaction and treatment outcomes by developing a more user-friendly formulation, specifically a cream. As a result, recent research has concentrated on innovative drug delivery systems, including Polyaphron Dispersion technology, to create a cream formulation that is more convenient and effective.

Polyaphron Dispersion technology stands out for its ability to produce cream formulations with significantly reduced amounts of surfactants while ensuring desirable stability marked by its physical-chemical robustness. This groundbreaking system creates a highly effective and stable cream with smaller droplet sizes, leading to enhanced skin penetration, improved drug solubility, and increased efficacy of topical treatments.

Numerous studies have consistently shown the superiority of CAL/BDP PAD cream, incorporating this technology, over other formulations across multiple parameters. These include PGA treatment success, BSA improvement, mPASI scores, DLQI, and patient satisfaction, all playing crucial roles in patient adherence and achieving favourable outcomes. These remarkable effects indicate a potential revolution in psoriasis treatment, offering enhanced convenience and efficacy and improving treatment outcomes.

Even though the initial results are promising, additional research is required to assess PAD cream's long-term safety and efficacy. Moreover, it is crucial to determine its suitability for younger patients and its effectiveness when applied to other body areas, including the scalp. By further exploring the clinical potential of this innovative drug delivery system, we can cater to a broader range of psoriasis patients, ultimately enhancing their quality of life.

Attachments

Table I

Phase 3 Clinical Trial: Efficacy at week 8.

Endpoint	CAL/BDP PAD Cream (551 patients)	CAL/BDP TS (542 patients)	Vehicle Cream (178 patients)
% PGA treatment success	43.2	31.9	5.2
mPASI, % change from baseline	-64.6	-56.4	-20
% mPASI 75	44.3	34.5	7.2
Change in DLQI from baseline	-6.5	-5.6	-2.5

Note: Proportion of patients obtaining PGA treatment success improvement, the percentage change in mPASI from baseline, the proportion of patients obtaining mPASI75, and change in DLQI from baseline.

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