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Phytosomal Delivery of Quercetin via Hydrogel Systems: A Review of Emerging Strategies for Psoriasis Treatment

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ABSTRACT

Psoriasis is an inflammatory skin condition that is chronic and is characterized by hypergrowth of keratinocytes and oxidative stress as well as immune dys-response. Even though quercetin has a strong antioxidant and anti-inflammatory effect that predisposes it to the treatment of psoriasis, its therapeutic effect is limited due to low solubility, permeability and instability with topical use. A new quercetin-impregnated phytosomal hydrogel was created to address these shortcomings to improve the dermal bioavailability and therapeutic efficacy. The phytosome technology allows quercetin to become a stable complex with phospholipids, which is much more effective in penetrating the stratum corneum and preventing the oxidative degradation of quercetin. The phytosomal formulation was optimized with a nanoscale size of particles, appropriate zeta potential and high encapsulation ability that guaranteed good and long-term delivery of quercetin. Introduction into a hydrogel matrix also gave other advantages included release control, increased retention on the skin, and increased moisturizing of the skin, which facilitates drug permeation. In vitro and ex vivo analyses verified excellent antioxidant activity, release stability of quercetin, and increase in accumulation in layers of the skin. The formulation also displayed significant anti-inflammatory effects through the suppression of major cytokines and the change of the signal transduction pathways that play a central role in the pathogenesis of psoriasis, such as those that mediate the growth of keratinocytes and the oxidative imbalance. The therapeutic potential of the hydrogel was further confirmed by preclinical studies in which the epidermal thickness, inflammatory markers and oxidative stress indicators were significantly reduced without irritation or sensitization. All in all, quercetin-impregnated phytosomal hydrogel is a promising safe and advantageous topical intervention approach to the treatment of psoriasis, with better bioavailability and targeted delivery to deal with both inflammation and oxidative stress.

Keywords: Quercetin, Psoriasis therapy, Topical drug delivery, Nanoparticle drug delivery

1. INTRODUCTION

Psoriasis is a chronic, multifactorial, inflammatory skin condition which is identified by increased keratinocyte proliferation leading to thick, erythematous as well as scaly plaques. Having an estimated prevalence of 2-3 percent in the global population, psoriasis severely impairs the quality of life of the affected patients because they experience chronic discomfort, not to mention the overt lesions and psychological disorders.[1,2] Traditional treatment plans encompass a topical treatment that includes corticosteroids and vitamin D analogs, phototherapy, systemic immunosuppressants, and biologic drugs of particular immune mediators.[3,4] Despite the fact that these treatments offer some symptomatic relief, they are usually not without limitations such as adverse effects, non-uniform effectiveness, tachyphylaxis, and high cost. Besides, prolonged use of steroids can result in the atrophy of the skin, whereas the systemic therapies may lead to hepatotoxicity or severe immunosuppression. These difficulties create the demand of safer, effective, and more affordable options, particularly to the mild to moderate cases of psoriasis that still require the use of topical therapy as the first line of treatment.[5,6]

Quercetin, which is a naturally occurring flavonoid that is abundant in fruits, vegetables, and grains, has received a lot of attention because of its strong antioxidant, anti-inflammatory and immunomodulatory effects.[7,8] It has the ability to regulate some of the major molecular pathways in psoriasis such as the NF- 0 B, MAPK and JAK Stat pathways. Quercetin also inhibits the pro-inflammatory cytokine like TNF- alpha, IL-17 and IL-23 and through this mechanism disturbs the inflammatory cascade that forms psoriatic plaque.[9,10] Nevertheless, quercetin continues to have a high therapeutic potential despite being limited by low aqueous solubility, low chemical stability, and low penetration rates through the stratum corneum, which have prevented its use in clinical applications due to low bioavailability in topical delivery.[11,12]

Recent innovations in the system of drug delivery, especially phytosomes and hydrogels, provide some hopeful solutions to these shortcomings. Phytosomes increase the solubility, stability, and dermal absorption of quercetin by complexing the molecule with phospholipids, which resembles the natural components of cell membranes, and increases the level of penetration through the skin.[13,14] Adding quercetin-loaded phytosomes to a hydrogel backbone further enhances its therapeutic efficacy by offering a hydrated, calm, and biocompatible surrounding, which boosts retention on psoriatic skin, results in improved diffusion through the epidermis and provides the release of active ingredient over an extended period. Hydrogels also inhibit early degradation of drugs, hence enhancing stability of the formulation and topical performance.[15,16]

Oxidative stress and chronic immune-mediated inflammation have a close association with psoriasis pathogenesis. Having high concentrations of reactive oxygen species (ROS) will increase lipid peroxidation, damage to DNA, and dysfunction of the keratinocytes, in addition to up-regulating such inflammatory cytokines as TNF-a, IL-17, and IL-23.[17,18] This is a self-reinforcing cycle that enhances hyperproliferation of the keratinocytes and inflammatory cell invasion. Inflammatory signaling magnitude can be reduced by antioxidants such as quercetin, which neutralizes the effects of oxidative stress and provides a synergistic treatment effect. Thus, incorporating quercetin into novel topical vehicles (phytosomal hydrogels) is one of the viable solutions to interrupt this pathology and enhance the clinical results in the psoriasis treatment.[19,20]

1.1 Quercetin

Quercetin is a natural flavonoid and it is very abundant in fruits, vegetables, and various medicinal plants. Its antioxidant, anti-inflammatory, antiviral, and immunomodulatory properties are very strong and it is one of the most commonly investigated phytochemicals in the therapeutic context.[21,22] Quercetin, being an antioxidant, has sufficient ability to scavenging harmful free radicals and oxidative damages to cellular components as an antioxidant. It is also an anti-inflammatory agent due to its capacity to cause inhibition of major enzymes and intermediates of inflammation, which include cyclooxygenase, lipoxygenase and nitric oxide synthase.[23,24] Also, quercetin alters immune signaling and decreases the generation of pro-inflammatory cytokines, such as TNF- 0, IL- 6, IL- 1 7, and IL- 23, which are fundamental in the pathogenesis of psoriasis. The extensive pharmacological effects of quercetin have indicated that this natural therapeutic agent could be useful in the treatment of chronic inflammatory disorders that provides a safer option to a number of synthetic medicines that may lead to side effects in the body after extended use.[25,26]

Although quercetin has potential uses as a therapy, the clinical utilization of the compound, particularly as a topical agent, is severely limited by a low aqueous solubility, limited permeability across the stratum corneum, and limited stability in nearly all physiological environments.[27,28] Quercetin is readily oxidized, photodegraded, and hydrolyzed leading to decreased drug activity prior to reaching the target tissue. Also, its solubility in water is low, which causes ineffective loading of the drug in standard topical preparations, high skin penetration, and low therapy responses. The stratum corneum is the main barrier to permeation of the drug and therefore the low lipophilicity and instability of quercetin is yet another obstacle to its ability to have any significant therapeutic effect in psoriatic lesions.[29,30]

To overcome these problems, there is need to develop more improved drug delivery systems to increase the aqueous solubility, stability and dermal bioavailability of quercetin. A possible way forward is developing quercetin into a phytosome complex, in which case it becomes associated with phospholipids in form of a molecular complex. This molecule increases the lipophilicity of quercetin, its resistance against degradation, and its diffusion into deep layers of the skin.[31,32] These quercetin-based phytosomes are further embedded as hydrogel to enhance drug retention, dermal hydration, and release to provide a prolonged therapeutic effect. Combinations of phytosomal encapsulation and hydrogel formulation provide a promising measurement to address the biopharmaceutical drawbacks of quercetin and derive the best out of this ingredient in the treatment of psoriasis.[33,34]

1.2 Phytosomes

Phytosomes represent improved oral delivery systems of the herbal drugs whereby bioactive plant components are conjugated with phospholipids to promote their solubility, stability and bioavailability significantly. This special structural arrangement enables the phytosomes to rise above the most prevalent biopharmaceutical challenges encountered by natural molecules, like low aqueous solubility, low membrane permeability, and metabolism shortcomings and degradation.[35,36]

Numerous useful phytochemicals, such as flavonoids, terpenoids and polyphenols, have strong therapeutic properties but have poor absorption by the oral route or topical application. Phytosome technology finds a solution to this problem by creating a molecular association between the phytoconstituent and a phospholipid like phosphatidylcholine.[37,38] This hydrogen bonding-polar-nonpolar affinity mediated interaction generates an amphiphilic complex that models the biological membrane and fits easily into lipid bilayers. Consequently, phytosomes improve the delivery of phytochemicals to cells and tissues in a much more efficient manner than plain simple mixtures or traditional carriers.[39,40]

The ability of a phytochemical to be encapsulated in the phospholipid matrix has a number of benefits, such as an increase in absorption, gastrointestinal and dermal stability, and enzymatic or oxidant degradation. Phytosomes have also controlled release properties and better pharmacokinetic profiles, which guarantee the extended duration of the active compound presence in the target position.[41,42] This results in a better therapeutic efficacy with a lower dosage. Phytosomal delivery systems have been popularly used in oral, topical applications, and transdermal instances. They have shown significant advantages in antioxidant therapy, anti-inflammatory therapy, hepatoprotection, cardiovascular therapy, neuroprotection and dermatological therapy. There is a significant improvement in the efficacy of the natural compounds of quercetin, curcumin, silymamarin, and catechins and resveratrol when presented as phytosomal.[43,44]

Technology is most useful in the dermal delivery of drugs. Phytosomes enhance greater penetration of the skin, deposition in the epidermal and dermal layers and release of active ingredients- properties that are important in controlling long term skin conditions such as psoriasis. Their natural biocompatibility, safety and use of GRAS status ingredients make them very appropriate in making pharmaceutical, nutraceutical and cosmeceutical formulations.

Altogether, phytosomes are a disruptive platform to fully harness the therapeutic potential of natural compounds by adequately overcoming solubility, stability, as well as permeability-related issues.[45,46]

The following methods are commonly used to prepare phytosomes:

1.2.1 Solvent evaporation technique

In this phytosome preparation technique, the active compound and phosphatidylcholine are dissolved in a specific stoichiometric proportion in a given solvent. The mixture is then heated at the most appropriate temperature, usually approximately 40 o C during 1 hour, to promote efficient formation of complex and ensure maximum entrapment of drugs. After heating, the rotary vacuum evaporation is used to extract the solvent to prevent the phytosomal complex. Diverse solvents can be employed though the recent trend has been towards more environmentally and health-friendly protic solvents like ethanol as opposed to the conventional aprotic solvents, like chloroform and dichloromethane, which are environmentally and health hazards. The approach provides stable and effective phytosomes.[47,48]

1.2.2 Lyophilization method

In this method, the phospholipids and phytoconstituents are dissolved individually using appropriate solvents and thereafter, they are mixed under controlled conditions. The mixed solutions then are stirreded with the help of the magnetic stirrer to facilitate the effective interaction and complexing of the constituents. Constant stirring is used to get a homogenous distribution of the mixture and to allow the formation of the stable phytosomal structures. After completion of the complex formation, solvent is removed followed by the isolation of the complex by using lyophilization to produce a dry stable phytosome powder. The simplicity, efficiency, and preservation of the integrity of heat-sensitive phytoconstituents throughout its processing are the strengths of this method.

1.2.3 Salting-out method

In this method, a standard plant extract or a phytoconstituent that is purified is dissolved in an aprotic solvent like acetone or dichloromethane with phosphatidylcholine. A magnetic stirrer is used to mix with the mixture overnight to achieve total interaction and to form phytosome complex. Having mixed adequately a non-solvent like n-hexane is added slowly to the solution resulting in the precipitation of the phytosomal complex because of reduced solubility. Filtration or centrifugation is then used to harvest the precipitated complex before it is dried to get the final phytosema product. This is a technique that yields a uniform and well-formed phytosomal complex with a high entrapment capacity.[49,50]

1.2.4 Co-solvency method

The phospholipids and dried plant extracts are dissolved separately in their respective flasks using an appropriate solvent like methanol in this technique. When the two components are completely dissolved, dropwise addition of the extract solution to the phospholipid solution under constant magnetic stirring is done. This is a regulated addition, which enhances consistent contacting of the molecules, which lead to the establishment of the phytosome complex. The stirring period is generally kept at a period of approximately one hour so as to ascertain total connection of the extract to the phospholipids. Upon complexation, the solvent can be removed and the resulting phytosome product harvested and dried. The method is easy, effective and applicable to heat labile phytoconstituents.

1.2.5 Film formation technique

Under this technique, the required concentrations of the phytoconstituents and phospholipids are weighed accurately and put in a round-bottom flask and dissolved in methanol. This mixture is warmed up in a warm bath at a temperature of 4555 o C to enhance even dissolution and interaction. It is further subjected to rotary evaporation of about 45 C with a dry film formed of the phytosomal complex. The film is left to dry at ambient temperature overnight to make sure that all traces of organic solvents are eliminated. After complete drying, the phytosomal film gets put into a desiccator until subsequent use. The result of this technique is a phytosome formulation that is solvent free and stable and can be later rehydrated or incorporated.[51,52]

1.2.6 Quality by Design approach in the development of phytosomes

Quality by Design (QbD) methodology is being embraced more often than not in order to streamline the formulation and production procedure of phytosomes with a view to promoting stability, predictability, and compliance with regulations. QbD is backed by international regulatory authorities like the FDA and ICH and focuses on a profound knowledge of components of the formulation, parameters of the process and their effect on critical quality attributes (CQAs). QbD allows identifying and managing variables to affect phytoseme stability, particle size, entrapment efficiency and release profile, through systematic risk assessment tools, including Ishikawa charts, failure mode and effects analysis (FMEA), and design of experiments (DoE).[53,54]

Recent research demonstrates the usefulness of QbD in the simplified process of phytosome development to enable formulators to simulate the most preferable conditions and reduce the trial-and-error thinking. QbD implementation has also been reinforced by the development of analytical devices such as spectroscopic, chromatographic and thermal characterization techniques that allow close observance of a formulation behavior. Moreover, new AI and machine-learning algorithms are making data interpretation more advanced, real-time decisions, and process strength.

With the further development of research and technologies, the QbD principles integration is likely to become progressively more important in directing the establishment of innovative, safe and effective phytosome-based therapeutics, and finally enhancing their translation into the clinical and commercial practices.[55,56]

1.3 Topical and transdermal delivery of Quercetin-Loaded Phytosomal Hydrogel for Psoriasis Therapy

Psoriasis is a chronic inflammatory disease of the skin, which is characterized by the over-growth of the keratinocytes and the improper operation of the immune system, and is sometimes treated by unidrug or multimodal therapy. In spite of the documented strong antioxidant, anti-inflammatory and immunomodulatory properties of quercetin, which is a naturally occurring flavonoid, the potential of the product is limited by low aqueous solubility, low skin permeability, and poor bioavailability. Introduction of quercetin into phytosomal delivery system provides a viable solution to these constraints by increasing the physicochemical stability of the compound and the pharmacokinetic behavior. Due to complexation with phospholipids, phytosomes enhance lipophilicity, enhance membrane compatibility and enhance enhanced dermal absorption. This molecular structure enhances the penetration through stratum corneum, the resistance against oxidative degradation of quercetin, and a sustained release of the drug.[57,58]

Incorporation of quercetin-impregnated phytosomes into a hydrogel gel system also improves topical and transdermal delivery efficacy. The hydration, biocompatibility and spreadability of hydrogel provide a good softening of psoriatic plaques and better penetration of drugs. The phytosomal hydrogel provides an even distribution of drugs to the skin, deeper retention into the skin, and localized release at the site of action. Enhanced dermal localization enhances the effectiveness of therapeutic processes and the minimization of systemic absorption and other toxicities.[59,60]

The quercetin-phytosome hydrogel is a mechanistic regulator of the important inflammatory and oxidative pathways involved in the pathogenesis of psoriasis, including NF-kB, MAPK, and cytokines, including TNF-alpha, IL-6, and IL-17. It increases antioxidant defense to eliminate oxidative stress leading to hyperproliferation of keratinocytes and inflammatory exacerbation. The preclinical trials have shown excellent skin permeation, improved therapeutic effects, and observable clinical effects on erythema, scaling, and epidermal thickness in preclinical studies over the conventional formulations.

In general, quercetin-loaded phytosomal hydrogel is a promising, targeted treatment option of psoriasis, which has better bioavailability, increased patient compliance, and the potential of topical and transdermal delivery.[61,62]

1.4 Characterization of Quercetin-Loaded Phytosomal Hydrogel

The formulation must be rigorously tested to ensure its quality and performance:

➢ **Drug content analysis**: To ensure that quercetin is well dispersed in the hydrogel matrix, the content analysis of drugs is necessary to ensure that the quercetin compound is evenly distributed in the phytosome complex and then evenly spread throughout the hydrogel matrix. The evaluation will guarantee precise dosaging, uniform therapeutic action and inter-lots reproducibility. The analysis determines the encapsulation efficiency by measuring the concentration of quercetin in the analyte and determines any loss of the drug in the formulation. Topical distribution of drugs Uniform distribution is paramount in ensuring credible topical delivery, sustained release and optimum therapeutic effects especially where treatment is detailed such as psoriasis which needs accurate therapeutic distribution.

➢ **Particle size and zeta potential** : The most important parameters in determining the stability of the phytosomes, the quality of dispersion and the general performance are particle size and zeta potential. Smooth, small particles increase skin penetration and bioavailability and homogenous particle size is an indicator of a well-developed system. A combination of these parameters guarantees the stability of the phytosomal formulation, quercetin delivery, and the therapeutic efficacy of quercetin in topical or transdermal hydrogel preparations.[63,64]

➢ **Viscosity and spreadability:** Tests on viscosity and spreadability are done to ascertain that the hydrogel has the right texture and consistency to be used by the patients. Ideal viscosity is easy to apply, results in even distribution of the drug, and retention of the drug on the skin is good without it being overly thick or thin. The spreadability defines the ease at which the hydrogel is dispersible on the affected regions and it affects the comfort of the user and the precision of dosing. Collectively, these assessments make it clear that the formulation is easy to use, has a positive effect on treatment outcomes, and can be used consistently, which are the main conditions of managing a disease like psoriasis in the long term.[65,66]

➢ **Skin penetration studies**: Skin penetration tests determine how the formulation can penetrate through the stratum corneum to reach deeper skin layers of the skin where quercetin needs to take place. These studies quantify how much drug permeated or is absorbed in the individual layers of the skin using ex vivo or in vitro models. Bioavailability and targeted delivery is important in treating psoriasis, which is gained by effective penetration. The effectiveness of these assays also assists in the comparison of the performance of phytosomal hydrogels with the conventional formulations such that the optimized system would lead to improved therapeutic results.[67]

➢ **Stability studies**: The long-term stability and integrity of the formulation are tested in different storage conditions (varying temperatures, humidity levels, light exposure, etc.). These tests will identify the stability of the phytosomal hydrogel in terms of physical appearance, drug content, viscosity, pH, and therapeutic performance in time. Stability assessment helps to be sure that quercetin is not subject to degradation and that the formulation keeps its quality throughout the shelf life. In general, stability tests prove the reliability, safety and the product can be stored and used in clinic in the long terms.[68,69]

1.5 Advantages of phytosomal formulations for psoriasis therapy Enhanced bioavailability:

The increased bioavailability is among the best benefits that phytosomal technology offers especially to flavonoids that are not normally soluble like quercetin. Despite its impressive antioxidant, anti-inflammatory, and anti-proliferative effects, quercetin has a very promising therapeutic potential in the management of chronic skin conditions such as psoriasis; however, it is hampered greatly in its therapeutic efficacy by low water solubility, low biological membrane permeability, and metabolism.[70,71] Phytosomes are useful in overcoming these constraints by the creation of a stable molecular complex between quercetin and phospholipids, mostly phosphatidylcholine. The interaction increases the lipophilicity of quercetin and allows it to be better absorbed by the skin lipids and enter further into the epidermal and dermal layers.

The phytosom phospholipid structure is closely related to the natural biological membranes, which enhances the phytosom compatibility with the skin tissue and the rapid absorption by stratum corneum. Therefore, compared to conventional topical formulations quercetin is more bioavailable and therapeutically active due to its delivery to target layers. Increased permeation guarantees the high levels of localization of drugs, better therapeutic activity, and less loss of drugs at the skin surface. The phytosomal complex is also useful in the release by a slow action of long term management of inflammatory diseases like psoriasis.[72,73]

Inclusiveness into a hydrogel base enhances further dispersion, stability, and delivery of quercetin in phytosomes. Hydrogels offer hydrated condition that increases skin permeability since it softens and loosens stratum corneum lipid matrix. This wet medium also shields quercetin against oxidative and photodegradation, meaning that the active ingredient will not degrade structurally during use. Phytosomes and hydrogels have a synergistic combination leading to better drug retention, controlled release, and better therapeutic performance.

All in all, phytosomal incorporation enhances the bioavailability, clinical action, and dermal absorption of quercetin considerably. This enhanced performance enables low doses to give significant therapeutic benefit with minimal systemic exposures and the possible side effects, which make phytosomal hydrogels a very viable approach to topical psoriasis treatment. [74,75]

Stability:

A very important factor influencing the therapeutic performance of quercetin is stability as this bioactive flavonoid is very sensitive to the environmental influences like oxygen, light, and heat. These conditions cause quick oxidation, photodegradation, and thermal degradation, resulting in the severe morphological change and a significant decrease of its antioxidant and anti-inflammatory activity. The addition of quercetin to a phytosomal system significantly increases its stability because the phospholipid bilayer provides a protective effect. In phytosomes, quercetin presents a strong molecular complex with phosphatidylcholine which encircles the molecule and covers its active sites to external stressors.[76,77]

The lipid bi-layer serves to hold back quercetin to the outer world, reducing the exposure of quercetin to the oxidative environment and inhibiting the degradation pathways (hydrolysis, photolysis, and free radical reaction). This encapsulation shield protects the chemical breakdown, and thus increases the therapeutic levels of quercetin in the long term. Its retained bioactivity increases its clinical lifespan, thus phytosomal quercetin is more confident to be utilized in long term topical therapy like in psoriasis treatment.

The phospholipid matrix also provides the amphiphilic property of quercetin which is stable in both aqueous and lipid environments and does not precipitate as it remains evenly dispersed in topical or transdermal formulations. Phytosomal quercetin introduced into hydrogels exhibits enhanced oxidative stability and eliminates crystal formation of the drug reducing to controlled release and predictable treatment effect. These attributes are required to ensure quality of the products and this is more so in formulations that are to be used repeatedly or on a long term basis.[78,79]

Phytosomes increase the shelf life of quercetin-based preparations by enhancing chemical and physical stability and increasing their efficacy in the storage and use. This increased stability is directly proportional to an increase in bioavailability in that a higher percentage of intact quercetin gets to the target tissues. In general, phytosomes have a strong stabilization system, which is the lipid bilayer that enables quercetin to maintain its activity, which increases its reliability and utility in therapy, and which allows it to be delivered to the skin at long durations.[80,81]

Targeted delivery:

The most critical benefits of phytosomal technology are targeted delivery, particularly in topical and transdermal use, involving the treatment of chronic inflammatory inflammation of the skin, e.g. psoriasis. Phytosomes enable quercetin to be administered in a controlled and sustained form where therapeutically effective concentrations of quercetin are required deep into the skin layers especially viable epidermis and dermis where the pathways of inflammatory and oxidative activity are most necessary to be modulated. In comparison to the traditional topical preparations in which the drug is usually released quickly and concentrated on the skin surface, phytosomal encapsulation controls the diffusion of quercetin through the stratum corneum, to ensure steady and long lasting concentration at the target site.

Since phospholipids are structurally similar to the natural lipids found in the skin cell membranes they readily enter lipid-rich layers of the skin, and increase both permeation and retention. This biomimetic interaction enhances greater dermal uptake of quercetin which enhances therapeutic efficiency and reduces systemic absorption. Less systemic exposure can reduce the adverse effects thus phytosomal formulations are safer in long term management of psoriasis. In addition, the phytosome structure has the natural property to delay the release of quercetin, which has resulted in prolonged therapeutic effect, which functions against the chronic nature of the disease.[82,83]

It is also enhanced when used in hydrogel-based delivery. Hydrogels are known to keep the skin skin hydrated which makes the stratum corneum soft and easier to penetrate. The phytosome structure of quercetin is lipid-rich and is used in conjunction with the hydrophilic gel matrix to facilitate slow, controlled delivery of quercetin. This complex helps increase prolonged antioxidant and anti-inflammatory effects which is important in inhibiting erythema, scaling, and epidermal hyperproliferation of psoriasis.

In general, phytosomal hydrogels can deliver quercetin locally, sustained and effectively, maximizing the effect of treatment, enhancing compliance with therapy in patients, and reducing systemic adverse effects, so they represent one of the most promising approaches to targeted treatment of psoriasis.[84,85]

2. CONCLUSION

Pytosomal hydrogel loaded with quercetin is a novel promising formulation in the management of psoriasis. Psoriasis is a long-lasting, immunologically regulated disease of the skin, which is caused by inflammatory changes, oxidative stress, and disturbed proliferation of keratinocytes. Quercetin is a natural flavonoid that has potent antioxidant, anti-inflammatory and immunomodulatory effects, which directly attack these pathogenic processes. Poor solubility, instability and insufficient skin penetration has however traditionally constrained its use as a therapeutic agent. Phytosomal encapsulation can break these barriers because forming a complex with phospholipid gives quercetin to the phytosomal encapsulation better solubility, chemical stability, and dermal bioavailability. Phytosome formulation enhances its absorption with the lipid of the skin and its deeper and efficient absorption across the stratum corneum and provides sustained pharmaceutical release.

Introduction of quercetin-phytosomes into a hydrogel base is an additional way to improve therapeutic performance. Hydrogels are not only highly hydrated, biocompatible and spreadable, but also assist in softening psoriatic plaques and enhancing drug permeation. This association leads to increased retention of the drug at the point of action, decreased exposure at the systemic level and lower adverse effects than the traditional topical agents. Phytosomal and delivery of quercetin by hydrogel combined with the bioactivity results in the increased control of inflammation, oxidative stress decrease, and the regulation of cytokines that mediate the development of psoriasis.

Regardless of these benefits, additional efforts are required to determine the clinical potential of the formulation completely. Formulation parameters such as particle size, encapsulation efficiency, stability and release behavior need to be optimized so that repeated therapeutic results can be obtained. Furthermore, there should be substantial preclinical research and clinical research done to confirm its safety, efficacy and tolerability over the long term. Through further studies, quercetin-impregnated phytosomal hydrogel can become a safe, effective, and available topical treatment of psoriasis.

FUTURE ASPECT

Subsequent studies to be conducted to quercetin-loaded phytosomal hydrogel ought to focus on the design of clinical trials that determine the therapeutic effects of phytosomal hydrogel in human psoriasis patients. Whereas preclinical evidence suggests a good anti-inflammatory and antioxidant effect, clinical trials are required to establish the effective results in the real world, appropriate dose frequency, tolerability, and long-term outcomes in patients. These trials would also be useful to compare the performance of the formulation against other standard treatments of corticosteroids, vitamin D analogs and biologics, thus determining its clinical relevance and possible use in the management of psoriasis.

The other direction that is of significance is to research on the synergistic nature of quercetin when used with other anti-psoriatic agents. The capability of quercetin to regulate a variety of different inflammatory pathways can be interpreted as implying that it can either support the activity of other available the treatment or even enable a reduction in the dosage of more efficient drugs, therefore, reducing the number of adverse effects. When mixed with the quercetin, salicylic acid, coal tar, vitamin D analogs, or herbal actives could have complimentary effects, resulting in a better plaque-reduction effect, erythema reduction, and faster healing. It can be of use to assess these synergistic interactions so that more multi-functional topical formulations can be created.

It is also important that safety studies be carried out over long term in order to ascertain that there is no repeat effect or long-term effect such as dermatological or systematic effects. Despite the fact that phytosomal hydrogels are usually biocompatible, chronic diseases such as psoriasis usually demand lifelong therapy. It is important to determine whether the skin can be sensitized, irritated, cumulatively poisoned, or skin barrier modified when evaluating any potential problem to establish safety. Periodic systemic absorption monitoring will also assist in establishing whether phytosomal delivery can significantly decrease systemic exposure as compared to the traditional preparations.

On the whole, detailed clinical testing, synergy testing, and prospective safety evaluation constitute necessary steps to successful translation of quercetin-loaded phytosomal hydrogels into credible treatment opportunities of psoriasis.

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