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Proniosome-based smart delivery systems for Psoriasis-targeted bioactive therapy

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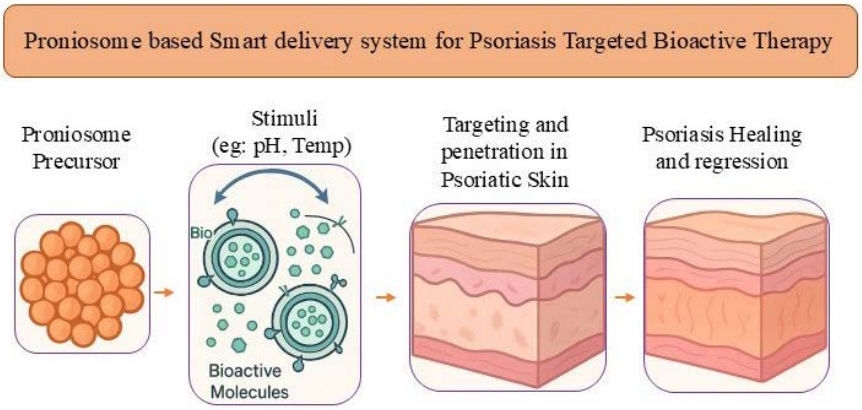
ABSTRACT



The growth in the field of nanotechnology has brought forth the growth of several breakthroughs that have prompted formulation of new solutions. Nanocarriers occur as minute encapsulating agents of the drug molecules thus stabilizing and improving the therapeutic effects of the encapsulated drugs. The self-assembly characteristic of proniosomes reduces the challenges that are normally encountered in liposomal and niosomal drug delivery systems. Due to their ability to self-assemble, proniosomes are the focus of constant investigating in the field of drug delivery systems. However, there is still great potential for future research concerning the development of new carrier materials for proniosomal formulation. Versatile proniosome-derived niosomes prove to be a reliable and relatively inexpensive system for drug delivery that possesses a number of significant advantages over conventional vesicular and traditional pharmaceutical formulations. Bioactive agents and recent advancements along with ethical considerations in the formation of proniosomes for psoriasis are further discussed in this review article. Novel hypotheses estimate repeated improvements in oral biopharmacokinetics, preferential drug targeting to the site of action, postponing the systemic biotransformation of the drug, which would lead to minimizing toxicity.

Keywords: Bioactive, Proniosomes, Psoriasis, Niosomes, Autoimmune disease

INTRODUCTION

Proniosomes represent a relatively newest approach in the context of drug delivery, which holds a great potential for optimizing the delivery of medications. It is new conventional niosomal systems that are dry formulations which can be easily reconstituted with water to get niosomal dispersions just before its application, which acts as remedy to numerous stability problems such as leakage or lumping noticed in the traditional niosomes. This makes proniosomes particularly advantageous for dosing, transportation, storage and distribution of drugs[1].

One of the main benefits of proniosomes is that they improve the solubility of drugs with lower aqueous solubility potentially increasing the bioavailability and thereby the therapeutic efficacy of the drug. It is most applicable for a large number of pharmaceuticals, these are both hydrophilic and lipophilic and applicable in as many routes as oral, topical, transdermal and vaginal administration. The structure of proniosomes is represented in Figure 1.

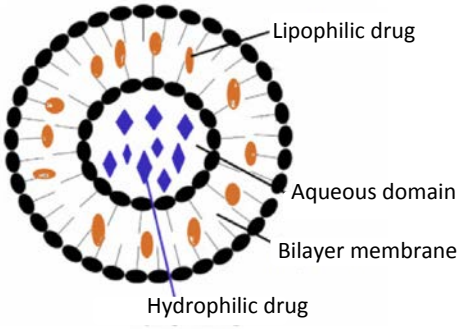


Figure 1. Structure of Proniosomes. Adapted from ref [2]

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Modern studies have demonstrated that the application of proniosomes can be successfully utilized for the treatment of such skin diseases as psoriasis – an autoimmune disease that causes the skin to become red and itchy. Psoriasis is among global skin disorders that shown in (Figure 2) have its impact on millions of people, and its severity differs from mild to severe ones[2]. Due to the ability to create a stable and multifunctional system for drug administration, the use of proniosomes can enhance psoriasis therapy. Their structure which is bilayer of nonionic surfactants and cholesterol make them more chemically stable as compared to liposomes whereas the liposome's can be costlier and inconsistent in quality. alsoproniosomes are dry in nature and have a good flowing nature; this facilitates handling, storage, and transportation. Proniosomes have other benefits which makes them suitable for treating psoriasis; these include increased drug permeation and controlled release[3]. This is particularly relevant to the topical preparations wherein the protracted action of the drug would prove therapeutic for the management of symptoms.

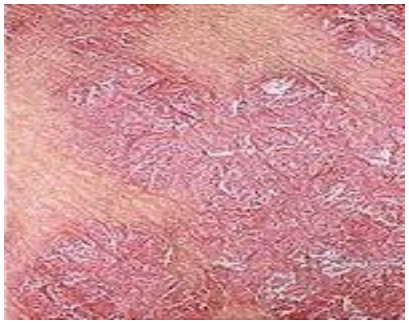

Figure 2. Psoriasis on dermis, adapted from ref [4]

Proniosomes are useful only as a carrier system for the drug where the drug is slowly released and helps in increasing the amount of drug that permeates the skin. It also makes the management of the diseases easy in that the effect of these drugs is not only prolonged but also the number of treatments given is also reduced, hence making it easier to make sure that the patients adhere to the schedule of the treatments given to them[4].

It is also a plus for proniosomal formulations that it offers new approaches to treat psoriasis with the use of bioactive compounds. There are many natural products that have been employed for centuries in traditional medicine for the treatment of various diseases; however, when it comes to obtaining pharmaceutical drugs from such compounds, several challenges come with the basal or poor solubility and bioavailability. Such compounds can be encapsulated in proniosomes and which enhances its stability as well as its therapeutic value. Curcumin, resveratrol and also the essential oils are reported to possess the attainable healing potency of psoriasis because of their possessing anti-inflammatory action, antioxidant and immunomodulatory activity[5]. When these compounds are incorporated into proniosomes, then they can directly be delivered to the skin regions that are affected. For instance, curcumin, which possesses very strong anti- inflammatory properties, can help decrease the redness and inflammation of psoriasis if delivered by proniosomal encapsulation. Consequently, through its antioxidant capacity, resveratrol could assist in diminishing the level of oxidative stress in psoriatic skin, hence, a healthier skin. Moreover, natural oils such as tea tree oil, lavender oil, neem oil, and many others have anti-microbial and soothing effects that can help patients with psoriasis. These oils can be increased into penetration of the skin through the use of proniosomes to ensure that the maximum benefits as regarded to treatment are achieved[4,6]. Such bioactives encapsulation in proniosomes also helps in preventing their degradation thus keeping the products effective from when they are produced to when they are used. Additionally, beneficial-based proniosomes can be developed to have selective action on the discontinued pathways contributing to the occurrence of psoriasis. Such a delivery extends the bioavailability of the bioactive compounds and, at the same time, reduces the risk of side effects, providing a safer therapeutic approach as compared to conventional treatments[7].

To sum up, proniosomes are a great achievement in the spheres of drug delivery systems which have great perspective for psoriasis' treatment. Because of these properties; stability, versatility and the efficiency in drug bioavailability, they are preferable to conventional systems. With further exploration of their potential, proniosomes could transform the psoriasis treatment landscape for patients, providing them with better solutions for their condition[7,8].

Structure & Components of Proniosomes

Specifically, proniosomes are dry, friable powders that change into niosomes when exposed to moisture. These structures are generally formed of non-ionic surfactants and cholesterol; these two combine to form a bilayer in a manner similar to the cell membranes. This bilayer structure can enable proniosomes to carry water soluble as well as fat soluble drugs, which makes proniosomes very useful. Thus, the content of proniosomes is based on a bilayer characterized by the presence of non-ionic surfactants[9,10]. These surfactants align in a manner whereby their heads, which are attracted to water, are on the outer side of the vesicle while their tails, which have a repulsion to water, are contained within the liquid. This formation allows the bilayer to accumulate the drugs that have different solubility characteristics[11]. It is a hydrated-matrix structure in prion disease and usually has a semi-transparent, gel-like appearance under the microscope. Anhydrates in their dry form have a hexagonal, blackish color. After hydration, they constitute noisome suspensions that can be used for several approaches to giving medicine[12].

Components involved in the proniosomes include

- Surfactant-
  Surfactant helps in increasing the rate of solubility and permeability of drugs due to wettability and emulsification properties. Surfactants used for the preparation of proniosomes are chosen from the series with regard to their HLB value. Lower HLB value of a substantially nonionic surfactant within the range of 4–8 provides stable proniosomal structure along with good drug solubilization. Results were revealed showing that the HLB value increases with the size of vesicles of proniosomes. Surfactants are used for numerous purposes; they are used as solubilizers, wetting

agents, as emulsifiers among other roles they can play the role of permeability enhancers. The non-ionic amphiphiles applied mainly for epoxy-ether formulations are alkyl ethers, esters, amides and esters of fatty acids[13,14].

- Carrier - There is great variation in the quantity of the surfactant and other constituents possible in the formulation. Further, the loading capacity is higher because of the greater surface area, which in turn makes it easier to use. It should not be toxic or hazardous, and should have the ability to flow freely with low solubility in the loaded combination solution but should be soluble in water in order to facilitate hydration of the loaded mixture. Carrier materials used are sorbitol, mannitol, maltodextrin, glucose, lactose and sucrose stearate where sucrose stearate is obtained in solid compacts[15].
- Solvent- The major effect on vesicle size and the rate of permeation depends on the type of alcohol: Specifically, they are ethanol > propanol > butanol > isopropanol arranged in the ascending order of polarity. Since the branched chains are formed, isopropanol forms smaller vesicles as compared to ethanol. Phosphate buffer (pH 7.4) glycerol 0.1% was prepared with distilled hot water used as an aqueous phase of the proniosomes. Some examples are chloroform, ethyl/methyl alcohol[16].
- Drug - The choice of drugs to be incorporated into the proniosomes compositions are characterized by low aqueous solubility, short plasma half life, high dose, controlled release system and adverse drug effects[17].
- Lecithin - based on their origin they are usually referred to by names like; egg lecithin that is extracted from egg yolks & soya lecithin that is derived from soya beans. The component of lecithin is known as phosphatidylcholine. In the vesicular system it plays number of important role such as: In the vesicular system it plays number of important role such as[18]:
  i] This was because its high Tc augmented the percent drug entrapment.
  ii] It avoids leakage of drugs.
  [iii] It plays the role of the permeation promoters
- Cholesterol- As the membrane additive, the used cholesterol is naturally occurring steroid. The steroids are the part of the cell membrane & the occurrence of these molecules in the membrane defines all the main changes concerning the bilayer stability, permeability & fluidity. It prevents the aggregation by the addition of the molecules that stabilize the system against the formation of the aggregate by the repulsive steric or the electrostatic effects[19].

Mechanism of action

Psoriasis is a long-term disease characterized by rebuilding of skin cells and inflammation of the skin. Proniosomes are advantageous for the delivery of drugs in treating this condition,[20] in the following ways.

- Enhanced Penetration: It is due to the structure of the proniosomes that drugs have a better chance of percolating into the stratum corneum of the skin. The surfactants in proniosomes are capable of destabilizing the lipid matrix of this barrier so that the drug gets into deeper layers of the epidermis[21].
- Sustained Release: Hence, it can be seen that proniosomes can give a sustaining and sustained release of the drug which is very essential in the case of psoriasis. Adhering to the recommended dosage of the medicine also keeps one's symptoms in check and prevents periodic outbreaks[22].
- Targeted Delivery: Due to their dual lipophilic-hydrophilic character, proniosomes are capable of encapsulating hydrophilic as well as hydrophobic active agents and delivering them to individual layers of the skin[23]. Thus, the localized delivery reduces the chances of having systemic side effects while at the same time increasing the efficacy of the treatment.
- Anti-inflammatory and Immunomodulatory Effects: Drugs prescribed for treatment of psoriasis like corticosteroids and immunosuppressives have enhanced prospects when administered through proniosomal formulations. Morphological changes of these drugs into proniosomes increase their bioavailability and efficacy, thus offering improved inflammation and immune response,[24] in psoriasis.
- Improved Stability and Bioavailability: Cholesterol and other stabilizers that are incorporated in the proniosomal system helps in increasing the stability of the encapsulated drug, thus improving its bio availability and prompt desired therapeutic response[25].The transformation of proniosomes into niosomes and then fusion with the skin surface shown in Figure 3.

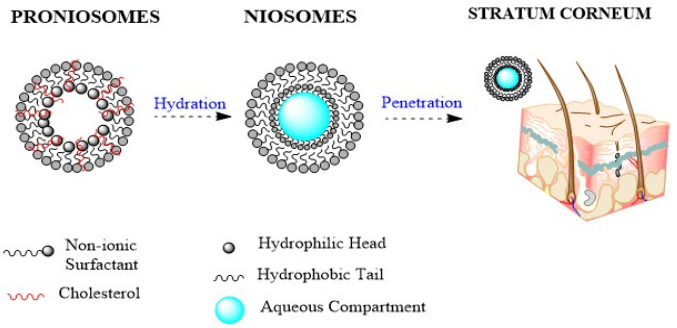

Figure 3. Illustration of the transformation of proniosomes into niosomes and then fusion with the skin surface.

TYPES OF PRONIOSOMES FOR PSORIASIS TREATMENT

Proniosomes represent a new approach in the concept of drug delivery system which is supposed to enhance the bioavailability of the various therapeutic agents along with their controlled release mechanism. They hold the following benefits in the management of chronic instances such as psoriasis, where topical and extended delivery is imperative[26]. The main categories of proniosomes utilized in psoriasis therapy are dry granules and liquid crystalline structures.

1. Dry Granular Proniosomes

Dry granules for formulation of psoriasis treatment contain proniosomes and they are more effective to be used with the carrier like sorbitol and maltodextrin[15,27].

Sorbitol-Based Proniosomes: These are obtained by adding non-ionic surfactants on vesicles and sorbitol as a carrier. The preparation includes the use of a surfactant and solvent to spray the solid sorbitol, this leads to the evaporation of the solvent. It

provides a dry, powder like product which when moistened spontaneously forms a vesicular structure. The use of sorbitol based proniosomes is beneficial because the formulation is stable and does not require the use of more thought provoking aqueous vehicles, although the solid surfactant cake that may occur on rehydration,[28] can be a hindrance.

Maltodextrin-Based Proniosomes: Proniosomes prepared from maltodextrin are developed via fast slurry method and it is not affiliated with the ratio of surfactant and carrier[29]. This leads to the formulation with higher percentage of surfactant which will give the thinner layer of the surface as compared to the sorbitol based proniosomes. Therefore, the process of rehydration is much easier as well as effective. This is advantageous in the therapy of psoriasis due to the fact that the thin layer provides better control of the release of the active ingredients[30].

2. Liquid Crystalline Proniosomes

Liquid crystalline proniosomes or proniosomal gels are the advanced formulation concept specially utilized in transdermal drug delivery systems in the management of psoriasis. These proniosomes are further described as possessing a lyotropic liquid crystalline phase, which stems from the operations between the surfactants and water. This state can be obtained by utilizing methods such as temperature changes, addition of solvent, or both[31,32]. The lamellar phase in liquid crystalline proniosomes is an alternating arrangement of lipid bilayer with aqueous phases. The given organization offers remarkable stability and a high degree of entrapment efficiency to the therapeutic agents. The gel form of these proniosomes serves as a drug reservoir and is incorporated into transdermal patches. These patches include; an aluminum foil support material, a plastic sheet and nylon mesh to ensure homogeneity[33]. Benefits associated with liquid crystalline proniosomes include; marked stability, high drug entrapment efficiency, improvement in penetration and ease in scaling up the process. That is why they are able to overcome the necessity of using some pharmaceutical excipients[34]. Their effectiveness became clear while treating topically psoriasis.

PREPARATION OF PRONIOSOMES

Proniosomes can be considered a peculiar innovative approach to the development of drug delivery systems that have marked differences in comparison with niosomes, mainly concerning the treatment of psoriasis. These carriers which are made up of nonionic surfactants, cholesterol or lecithin and other constituents are produced by several stated techniques. Both methods affect the characteristics of the final proniosomal gel and its ability to deliver therapeutic agents to the skin of the affected area[35,36]. The following section summaries the preparative methodologies for treatment procedures using proniosomes particularly in the case of psoriasis.

1. Coacervation Phase Separation Method

Coacervation phase separation has been reported as one of the fundamental methods of creating proniosomes because of its ease and effectiveness[37]. This method entails the incorporation of the surfactants and all the other constituents in an organic solvent which is accompanied by heating hence promoting the dissolution of surfactants. The obtained mixture is subjected to hydration resulting in formation of gel[38].

Procedure:

Dissolution and Heating: The nonionic surfactants, cholesterol or lecithin, and the active drug are dissolved in an organic solvent that is chloroform or ethanol, inside a glass vial. The vial is sealed and placed in a water bath and kept at a temperature ranging from 60°C to 70°C for about 5 minutes. This remark helps to enhance effective dissolution of the surfactant and other components[39].

Hydration: When the complete dissolution occurs, an aqueous phase is introduced into the organic mixture. This step causes the formation of a gel phase rather than a dispersion to be formed in this step. Next, the products are cooled at the RT temperature; where a proniosomal gel is formed in the mixture[40].

Advantages and Limitations:

Advantages: This procedure is quite simple and does not involve any complex apparatus; it is convenient to prepare samples in the laboratory scale.

Limitations: It is more appropriate for small scale preparations and may not be very appropriate for large scale production since it does the operations in batches[41,42].

2. Slurry Method

The slurry method makes use of maltodextrin as a carrier and is regarded as having a high yield with regard to proniosomes. In this technique maltodextrin powder is added to the surfactant solutions and after some time evaporated to derive the maltodextrin/surfactant powders[43].

Procedure:

1. Mixing: Consequently, the surfactant solution is mixed with maltodextrin powder in the rotary evaporator. The quantity of the surfactants and maltodextrin used is adjusted in such a way that facilitates the correct formation of the proniosomes[44].
2. Evaporation: The mixture is then placed in a rotary evaporator in order that it may take vacuum there by acquiring the state of a free flowing dry powder. This step helps in confirming that all the solvent has been eliminated; what remains is the proniosomal powder.
3. Drug Incorporation: Drugs can either be adsorbed on to the surfactant coated carrier or dissolved in the aqueous phase used to hydrate the proniosomes[45,46].

Advantages and Limitations:

- Advantages: It is soluble in water and has surfactants and drugs; thus, it serves as a carrier because it shields them from oxidation and hydrolysis. This method also yielded to production of a dry powder form of spice which can be easily managed and stored[47].
- Limitations: This method is time consuming and the equipment used such as the rotary evaporator is complex to use. It is also connected with the possibility of losing some materials during the particular batch treatment[48].

3. Spray Coated Method

Spray-coated is the method in which a solution containing a surfactant is sprayed on a carrier and is followed by the process of solvent elimination. This method is especially useful for lipophilic drugs and guarantees the formation of multilamellar vesicles[49].

Procedure:

1. Spraying: Spraying of a solution of one or more surfactants in an organic solvent over the carrier material.

Depending on the choice of the carrier, which can be maltodextrin or other appropriate substances[50], the coating with the surfactant is uniform.

2. Solvent Removal: The solvent is evaporated under vacuum at a temperature of 65°C to 70°C for 15 to 20 minutes. This step is continued until the carrier is adequately loaded with the surfactant[51].
3. Hydration: The carrier is then hydrated with the said surfactant to form multilamellar vesicles. This hydration process is important in the process of achieving final proniosomal structure[52].

Advantages and Limitations:

- Advantages: The choice of using the spray-coated is that it offers a uniform deposition of the surfactant on the carrier which is suitable for lipophilic drugs. It also has fairly good reproducibility as well as acceptable stability of the proniosomal system.
- Limitations: The method can cause meaningful degradation of carrier particles during the high-speed coating processes and is sensitive to the spraying conditions[53,54].

The methods of preparation of different types of proniosomes with advantages and disadvantages discussed in Table 1.

Table 1. The preparation of different types of proniosomes methods with advantages and disadvantages

S. No	Method	Materials Required	Advantages	Disadvantages
1	Coacervation phase separation Method	Surfactant, Cholesterol, Organic solvent, Aqueous Phase	High encapsulation efficiency	Requires precise control on process conditions
2	Slurry Method	Surfactant, cholesterol, carrier, organic solvent, aqueous phase	Easily scalable for industrial preparation	Involves use of hazardous organic solvent
3	Spray Coated Method	Surfactant, cholesterol, organic solvent, carrier	Fast and efficient process	Requires specialized equipment

BIOACTIVE AGENTS FOR PRONIOSOMES IN PSORIASIS

The use of natural bioactive agents is now considered as suitable to treat psoriasis due to their alleviating and curative values. On the same note, curcumin, which is derived from turmeric, has outstanding features that include anti-inflammatory and antioxidant to facilitate relief of psoriasis symptoms[55]. Another interesting product as a potential agent is resveratrol which can be found in grapes and berries; its effects include anti-inflammation and immune regulation. Quercetin is a member of the flavonoid family and has been known to have a positive impact in reducing skin inflammation and oxidative stress which in turn become a solution to individuals affected by psoriasis[56].

Tea tree oil, lavender oil, and eucalyptus oil to mention but a few are good for skin disorders such as psoriasis. It is used for anti-inflammatory, antimicrobial, and various skin conditions that need some relief from the inflammation affecting their skin. The plant called ‘’aloe ‘’is soothing and healing to the skin and it is reputed to diminish swelling and also encourage the formation of skin tissue. The polyphenols especially EGCG found in green tea extract have an anti-inflammatory and antioxidant effect[57,58]. Called boswellic acid it helps to reduce inflammation and modulates the immune system and is derived from the Boswellia serrata tree. Another natural remedy is silymarin from milk thistle characterized by anti-inflammatory and antioxidant activity[59]. Capsaicin derived from chili peppers also has analgesic and anti-inflammatory potency as well as enhances the immune system just like glycyrrhizin from licorice root. Fish oil and flaxseed oil containing the omega-3 Fatty acids have received a lot of attention because of their potent anti-inflammatory properties[60].

Beta glucan, for example, extracted from oats and some types of mushrooms, builds up immunity levels[61], while caffeine has elements that have ‘anti-inflammatory and anti-shine’ benefits[62]. The oats’ avenanthramides mitigate inflammation and discomfort in the skin, making them suitable for calming inflammation[63]. Calendula and propolis extracts are also useful additives because they possess anti-inflammation, antimicrobial, and skin repairing properties[64]. Gotu kola, under Centella asiatica, is well known for its ability to heal wounds and pacify the skin; Echinacea and Arnica extracts have anti-inflammatory and immune boosters[65].

In the area of synthetic treatments, several are available for the specific management of psoriasis. It has been seen that encapsulation of Methotrexate in proniosomes decreases side effects and also provides targeted delivery[66]. Calcipotriol is a vitamin D related compound which has an effect on the skin cells and their growth and differentiation. Tacrolimus is used topically for anti-inflammatory actions and immunosuppressive purposes[67]. Tazarotene, once applied topically, regulates the uncontrolled growth of skin cells and decreases inflammation while Dithranol also controls excessive growth of skin cells[68].

The previous study also found that salicylic acid loosens the scales and improves the penetration of other topical agents. Betamethasone and Clobetasol Propionate are very powerful corticosteroids employed for reducing inflammation and suppressing immunity, particularly if the case is critical[69]. Coal tar works by hampering the activities of skin cells as well as reducing scaling and itching. Pimecrolimus may be used in treatment of mild to moderate psoriasis with inflammation[70]; Retinoic acid and Acitretin contain derivatives that assist in the normalization of skin cell division. For severe cases, Cyclosporine which tends to weaken the immune system of the body is administered[71].

Etanercept and Infliximab are examples of biologics and they bind to the tumor necrosis factor (TNF) due to its notorious anti-inflammatory properties[72]. Another biologic is ustekinumab which

acts on interleukin-12 and interleukin-23 and is useful where moderate to severe psoriasis is evident in a patient. These synthetic agents seem to offer a holistic view of the treatment of different parameters of psoriasis[73].

Many natural remedies are also available depending on plants and herbs to administrate psoriasis disease. Neem extract has shown to possess anti-inflammatory, antimicrobial and immunomodulatory activities[74]. The reported extracts of chamomile and witch hazel both have anti-inflammatory effects and help to heal. Turmeric and ginger extracts are added to knead out inflammation and scourge of quicksand antioxidants. Licorice extract also has glycyrrhizin which helps in controlling inflammation and modulation of the immune system[75,76]. The various types of bioactive agents used for the treatment of Psoriasis shown in Figure 4.

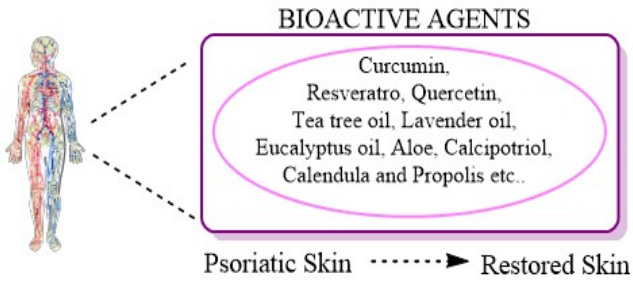

Figure 4. Types of Bioactive agents used for the treatment of Psoriasis.

RECENT TRENDS IN DELIVERY OF DRUG THROUGH PRONIOSOMES

Proniosomes have been previously employed in delivering several drugs through improvement of the carrier system.

- **Tazarotene**- Tazarotene is a retinoid which is used topically to treat psoriasis. Tazarotene has selectivity for the receptors involved in the synthesis of retinoic acid in the layers of the skin. In this study, the major side effects shown by the patient after using tazarotene were itching, erythema and burning sensation on the skin surface. Tazarotene is not able to penetrate through the skin and therefore do not cause systemic effects. Proniosomes in the topical management of psoriasis[77], therefore, require a residence time of the drug in the stratum corneum and the epidermis without the drug being systemically absorbed. Longer stay in the layers of the skin enhances the therapeutic index of the drug at the sites of action while preventing the absorption of the drug in systemic circulation removes the side effects of the drug for topical application[13,78].
- **Methotrexate**- Methotrexate (MTX) is an antifolate, antimetabolite, cytotoxic drug, which has selective immune-modulating and anti-inflammatory properties referring to the treatment of inflammatory diseases such as psoriasis. Though, low solubility and side effects by passing through the GI tract limited its systemic use[79].
- **Tacrolimus**- Tacrolimus is a macrolide immunosuppressive agent with a specific effect on T-lymphocytes. It is lipophilic in nature and hence tacrolimus has low solubility in water with increased degradation at the same time[80]. It also has a small factor of safety and therefore it becomes relevant to monitor the toxicity of providing floating drug dosage forms. The impact of the novel nanocarrier was assessed through skin permeation and retention study in vitro[81].
- **Betamethasone**- This is a corticosteroid that helps in treating psoriasis' Thus, the small amount of betamethasone dipropionate that is able to penetrate the skin barrier impairs the drug's effectiveness after it is applied topically. There are many forms of betamethasone in the market, some of which are in the form of lotions, ointments and creams and so on. All these failed to increase the permeability of this drug[20,82].

ETHICAL AND ENVIRONMENTAL CONSIDERATIONS

Through the creation and use of bioactive-based proniosomes in treating psoriasis, several ethical concerns arise and are as follows;

1. Informed Consent and Patient Safety: While focusing on the positive way that the targeted people can benefit from clinical trials or proniosome-based treatments, extreme care must also be taken to make sure that such people understood the associated risks. This entails transparency of information for the patient regarding the fact that no new treatment is fully tested and any adverse effects involved[83].
2. Equity in Access: Regarding the open issues of proniosome-based therapies, the concerned areas include mainly the commercialization aspects and issues pertaining to how affordable they are. Another downside of dramatic technological advancements could be that they may reach people selectively which could exacerbate health inequalities. Steps have to be taken to manage the availability of these new treatment methods rather than to be equally distributed among the different classes of the society[84,85].
3. Transparency in Research: Based on the topic, researchers and developers are subject to ethical requirements that should be followed when relaying their work's results. This feature involves reporting the conflicts of interest, releasing positive and negative outcomes and ensuring that research techniques and procedures used are credible and impartial[86].
4. Long-Term Effects and Data Privacy: Further, the effect and safety of the proniosome-based treatment must be evaluated to the fullest in long-term studies. Also, the protection of patient information and patients' anonymity during clinical research are vital to trust and credibility in the conducted studies[87].

The environmental impact of proniosome production and disposal is another important aspect to consider: The environmental impact of proniosome production and disposal is another important aspect to consider:

1. Sustainable Manufacturing Practices: Manufacturing of these proniosomes should be made in a way that has fewer effects on the environment. This means that production processes should adopt the principles of reduce, reuse, recycle, conserve energy and use environmentally friendly materials. Finding ways to reduce environmental effects in the preparation of proniosomes entailing green chemistry methods are achievable[88,89].

2. Biodegradability and Disposal: Reducing pollution in the environment requires that proniosome formulations and their components are biodegradable or recyclable. More research about the environmental occurrences of these materials and the formulation of proper disposal techniques that will not be damaging to the environment is crucial[90].
3. Resource Utilization: Minimizing wastage and optimal utilization of resources in synthesizing and manufacturing of the proniosomes would go a long way to reducing the impact of the products on the environment. These are in regard to resource efficiency which involves the enhancement of the utilization of raw materials and the minimization of the use of the non-renewable resource[91].
4. Impact of manufacturing by-products: Concerning the effects manifested through possible by-products introduced during the synthesis of proniosomes, one should consider the environmental issue. Measures so as to control or minimize them may alleviate their effects on the environment [92].

By focusing on these ethical and environmental concerns, the advancement of bioactive-based proniosomes for the treatment of psoriasis can be achieved in an ethical and sustainable manner. That is why it is crucial to ensure that these aspects are to be further discussed and included into research and development as intensively as possible as their further evaluation and incorporation into the information on the use of proniosome base therapies will lead to the overall success and easy acceptance of the needed therapies[4,93].

TOXICITY CAUSED BY PRONIOSOMES

The major components of proniosomes are usually surfactants and cholesterol. Chemical structure of the surfactants is especially significant in the sense of toxicity of these compounds. Studies show that the ester types of surfactants are seen to be more toxic than the ether types of surfactants. This can be attributed to the hydrolysis of ester bonds by enzymes mostly as they produce some toxic byproducts[94].

Notably, the form of the proniosome formulation either as dry powders and/or gels hardly influences the general toxicity of the formulation. Findings about proniosome toxicity are scarce and, nonetheless, some findings can be discussed. For example, lomefloxacin incorporated proniosomes exhibit good ocular compatibility and it has been reported that there is less irritation in terms of redness, puffiness or inflammation to the eyes[95]. This means that, perhaps, in some cases, the use of proniosomes is well permissible in sensitive areas.

Non-ionic surfactants on the other hand, have been known to cause ocular irritation by affecting the cornea and conjunctival epithelial tissue resulting in reddening and swelling. This suggests a threat of ocular toxicity the more when using other surfactants that can cause eye irritation[96].

Cholesterol is generally chosen for proniosome formulations due to the low toxicity when applied to the eye area. Some analytic works have shown that, when cholesterol is mixed with the Span 60 surfactant, it is not likely to cause problems to the ocular tissues. Hence, when selecting the surfactants for the proniosome formulations targeted at psoriasis or other diseases, it is necessary to consider toxicity to a minimum[97].

In view of all the above discussed, it can be concluded that, in general, proniosomes have many advantages from the standpoint of developing them as the delivery form of the treatment for psoriasis, but certain issues, for instance, toxicity of some of the components, such as surfactants, must still be addressed. Non-ionic surfactant encapsulated in proniosomes should be used to minimize the ciliotoxicity in intranasal delivery and cytotoxicity in skin delivery. Consequently, appropriate choice of surfactants and cholesterol can minimize several side effects and thus improve the safety profile of the proniosomal formulations[98,99].

FUTURE PERSPECTIVES

The possibility of application of proniosomes does not limit itself to the basic concept of drug delivery system and adds a new dimension as far as delivery of nutraceuticals and cosmeceuticals are concerned including products derived from herbs. Due to versatility that encompasses almost all therapeutic agents including antibodies, peptides, vaccines, genes and sera, they have been regarded as one of the greatest achievements in the field of drug delivery systems[100]. Often, this kind of flexibility is especially useful in the creation of treatments for multiple diseases such as psoriasis, when the deepest layers of the skin require proper therapeutic agent deposition[101].

However, the current research towards proniosomes is promising, yet most of the advancements still lie in the experimental stage[102]. In order to come from the laboratory research to therapeutic applications more studies at a larger level including the pilot plant experiments are required. It is also important to scale up the formulations for real life application in order to establish their efficiency and safety based on proniosomes systems[103-105].

In addition, it is noted that there is a scientific and technology foundation process for vesicular systems that needs to be supported for the application of proniosomes. This infrastructure shall play a very important role in the process of turning promising scientific discoveries into marketable drugs.

CONCLUSION

Essentially, proniosomes are relatively new drug delivery systems and compared to other vesicular systems they serve a lot of benefits. Due to their structure and the capacity to incorporate and deliver a broad range of bioactive substances, nanoparticles can be regarded as a potentially effective system for the therapy of psoriasis. Besides increasing the stability and effectiveness of a therapeutic agent, the peculiarities of proniosomes' construction can serve as the starting point for the new trends in the creation of nutraceuticals, pharmaceuticals, and herbal formulations, and cosmetics.

The latest study emphasizes that the application of proniosomes can enhance drug delivery especially for skin diseases such as psoriasis which requires frequent and long-term treatment. Proniosome formulations that incorporate drugs that target the multiple facets of psoriasis could make a significant contribution to the existing treatment armamentarium and improve the quality of treatment outcomes for patients. Nevertheless, the shift from the

experimental phase to the practical one is not without difficulty, as it is shown below. The major development stages toward enhancing the efficacy of the proniosome-based treatment are the industrial-scale up of the current production, proving the safety of these treatments, and the formation of sound industrial facilities. Further studies on such areas will be crucial in translating proniosomes from the research facilities to consumers' use.

In conclusion, it is possible to state that the application of proniosomes has a positive potential in the treatment of psoriasis and similar skin diseases; however, there are certain issues that have to be resolved by using new achievements of science. Thus, with the development of the field, proniosomes may greatly influence the existing delivery systems and therapeutic modalities for psoriasis, thus offering better management for the disease.

AUTHOR CONTRIBUTIONS

All authors have contributed in the composition of this article, all read entire content of this manuscript and approved final version for publication.

COMPETING INTERESTS

Authors state no conflict of interest.

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REFERENCES AND NOTES

1. R.P. Jangam, A.N. Thombre, N.P. Gaikwad. A review: Proniosomes as a novel drug delivery system. *Asian J. Pharmacy Technol.* **2017**, 7, 166-74.
2. M. Ajrin, F. Anjum. Proniosome: A promising approach for vesicular drug delivery. *Turkish J. Pharm. Sci.* **2022**, 31;19(4), 462.
3. K. Pandey. An overview on promising nanotechnological approaches for the treatment of psoriasis. *Recent Patents on Nanotechnology*. **2020**, 1, 14, 102-18.
4. Raharja, S.K. Mahil, J.N. Barker. Psoriasis: a brief overview. *Clinical Medicine*. **2021**, 1;21(3), 170-3.
5. K.D. Moudgil, S.H. Venkatesha. The anti-inflammatory and immunomodulatory activities of natural products to control autoimmune inflammation. *Int. J. Mol. Sci.* **2022**, 21,24, 95.
6. A. Mancuso, M.C. Cristiano, M. Fresta, D. Paolino. The challenge of nanovesicles for selective topical delivery for acne treatment: enhancing absorption whilst avoiding toxicity. *Int. J. Nanomed.* **2020**, 19, 9197-210.
7. M. Martínez-Ballesta, A. Gil-Izquierdo, C. García-Viguera, R. Domínguez-Perles. Nanoparticles and controlled delivery for bioactive compounds: Outlining challenges for new "smart-foods" for health. *Foods*. **2018**, 7; 7, 72.
8. K. Yadav, K.K. Sahu, R. Yadav, W. Raza, S. Minz, M.R. Singh. A complex molecular landscape to drug delivery concept for achieving precise therapy in psoriasis. *Medicine in Drug Discovery*. **2024**, 8, 100183.
9. S.M. Mawazi, T.J. Ann, R.T. Widodo. Exploring the Evolution of Niosomes: from Past Techniques to Future Advances in Preparation Methods - a Comprehensive Review. *BioNanoScience*. **2024**, 17, 1-22.
10. S. Chen, S. Hanning, J. Falconer, M. Locke, J. Wen. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications. *Eur. J. Pharmaceutics and Biopharmaceutics.* **2019**, 1; 144, 18-39.
11. L. Benedini, P. Messina. Proniosomes and niosomes for enhanced drug delivery. In Systems of Nanovesicular Drug Delivery. Academic Press. **2022**, 1, 15-128.
12. S.K. Ray, N. Bano, T. Shukla, N. Upmanyu , S.P. Pandey, G. Parkhe. Noisomes: as novel vesicular drug delivery system. *J. Drug Del. Therapeutics.* **2018**, 15; 8, 335-41.
13. S. Mittal, A. Chaudhary, A. Chaudhary, A. Kumar. Proniosomes: the effective and efficient drug-carrier system. *Therapeutic delivery*. **2020**, 1; 11, 125-37.
14. M.Y. de Freitas Araújo Reis, R.I. de Araújo Rêgo, B.P. Rocha, G.G Guedes, I.M. de Medeiros Ramalho, A.I. de Medeiros Cavalcanti. A general approach on surfactants use and properties in drug delivery systems. *Current Pharmaceutical Design.* **2021**, 1; 27, 4300-14.
15. K.T. Reddy, K. Gandla. Novel Vesicular Drug Delivery Systems Proniosomes. *Pharm Res*. **2022**, 6, 000272.
16. I. Pereira, S. Antunes, A.C. Santos, F.J. Veiga, A.M. Silva, P. Boonme. Microemulsions: Principles, Scope, Methods, and Applications in Transdermal Drug Delivery. In Nanotechnology and Nanomaterial Applications in Food, Health, and Biomedical Sciences. Apple Academic Press. **2019**, 23, 91-118.
17. C Soujanya, B. L. Satya, Y. Navya. A Review on Novel Vesicular Drug Delivery System: Proniosomes. *Manipal J. Pharmaceutical Sci.* **2020**, 1-6.
18. M. Schneider. Phospholipids. In Lipid technologies and applications. Routledge. **2018**, 2, 51-78.
19. S. Upadhye, I.N. Rafik. Proniosomes: A novel vesicular drug delivery system. *Am. j. PharmTech res*. **2020**, 10, 260-73.
20. S.L. Jyothi, K.L. Krishna, V.A. Shirin, R. Sankar, K. Pramod, H.V. Gangadharappa. Drug delivery systems for the treatment of psoriasis: Current status and prospects. *J. Drug Del. Sci. Technol.* **2021**, 1; 62, 102364.
21. M. Shabbir, U. Nagra, M. Zaman, A. Mahmood, K. Barkat. Lipid vesicles and nanoparticles for non-invasive topical and transdermal drug delivery. *Current Pharmaceutical Design.* **2020**, 1; 26, 2149-66.
22. P. Rios, A. Radhakrishnan, S.M. Thomas, N. Darvesh, S.E. Traus, A.C. Tricco. Guidelines for preventing respiratory illness in older adults aged 60 years and above living in long-term care: A rapid review of clinical practice guidelines. *medRxiv*. **2020,** 26, 2020-03.
23. F. Zakaria, S.E. Ashari, I.D. Azmi, M.B. Rahman. Recent advances in encapsulation of drug delivery (active substance) in cubosomes for skin diseases. *J. Drug Del. Sci. Technol.* **2022**, 1; 68, 103097.
24. T. Mulla. Proniosomes: A Comprehensive Review of Formulation, Characterization, and Applications (Doctoral dissertation, Xidian University).
25. S.J. Purohit, M. Tharmavaram , D. Rawtani, P. Prajapati, H. Pandya, A. Dey. Niosomes as cutting edge nanocarrier for controlled and targeted delivery of essential oils and biomolecules. *J. Drug Del. Sci. Technol.* **2022**, 1; 73, 103438.
26. T.L. Timis, I.A. Florian, S.C. Vesa, D.R. Mitrea, R.I. Orasan. An updated guide in the management of psoriasis for every practitioner. *Int. J. Clinical Practice.* **2021**, 75, 14290.
27. A. Saxena, P. Apurvi, R. Aslam. A Review on Proniosomes: A Propitious Outlook to the Provesicular Drug Delivery System. *Current drug delivery*. **2023**, 1; 20, 1115-26.
28. J.P. de Araújo. *Unveiling Novel Anticancer Drugs Activity Through Biophysical Studies: Applications in Drug Delivery Systems* (Doctoral dissertation, Universidade do Porto (Portugal)).
29. S. Deepika, K. Rizwana, B. Sharma. A review on proniosomes drug delivery: An innovative approach. *World J Pharm Res.* **2020**, 19; 9, 1322-33.
30. S. Kumar, H. Maurya. An Overview on Advance Vesicles Formulation as a Drug Carrier for NDDS. *Eur. J. Biomedical.* **2018**, 5, 292-303.
31. M. Chountoulesi, S. Pispas, I.K. Tseti, C. Demetzos. Lyotropic liquid crystalline nanostructures as drug delivery systems and vaccine platforms. *Pharmaceuticals*. **2022**, 31; 15, 429.
32. P. Trucillo. Drug carriers: Classification, administration, release profiles, and industrial approach. *Processes.* **2021**, 6; 9, 470.

33. A. Kharia, R. Gilhotra, A.K. Singhai. Overview of Transdermal Medicated Patches with its research updates in preceding years. *J. Drug Del. Therapeutics.* **2019**, 20; 9(3-s), 1094-102.
34. M.Z. Ahmad, A.A. Mohammed, M.M. Ibrahim. Technology overview and drug delivery application of proniosome. *Pharmaceutical Dev. Technol.* **2017**, 3; 22, 302-11.
35. M. Masjedi, T. Montahaei. An illustrated review on nonionic surfactant vesicles (niosomes) as an approach in modern drug delivery: Fabrication, characterization, pharmaceutical, and cosmetic applications. *J. Drug Del. Sci. Technol.* **2021**, 1; 61, 102234.
36. S. Chen, S. Hanning, J. Alconer, M. Locke, J. Wen. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications. *Eur. J. Pharmaceutics Biopharmaceutics.* **2019**, 1; 144, 18-39.
37. A. Morakul, V.B. Junyaprasert. Proniosomes: An effective carrier for dermal and transdermal delivery. *Songklanakarin J. Sci. Technol.* **2020**, 1; 42, 1171-86.
38. I.P. Fernández , R.G. Martín, F.A. Silva, M.G. Freire, V. Pino. Insights into coacervative and dispersive liquid-phase microextraction strategies with hydrophilic media–A review. *Analytica Chimica Acta.* **2021**, 25; 1143, 225-49.
39. S. Najafi, Y. Lin, A.P. Longhini, X. Zhang, K.T. Delaney, K.S. Kosik. Liquid–liquid phase separation of Tau by self and complex coacervation. *Protein Science*. **2021**, 30, 1393-407.
40. S. Park, R. Barnes, Y. Lin, B.J. Jeon, S. Najafi, K.T. Delaney. Dehydration entropy drives liquid-liquid phase separation by molecular crowding. *Communications Chemistry*. **2020**, 26; 3, 83.
41. M. Kutkut, A.K. Shakya, H. Nsairat, M. El-Tanani. Formulation, development, and in vitro evaluation of a nanoliposomal delivery system for mebendazole and gefitinib. *J. Appl. Pharm. Sci.* **2023**, 13 (6), 165–178.
42. J.A. Bakan. Microencapsulation using coacervation/phase separation techniques. In Controlled release technologies. CRC Press. **2019**, 16, 83-105.
43. M.H. Teaim, M. Yasser, M.A. El-Nabarawi, D.A. Helal. Proniosomal telmisartan tablets: formulation, in vitro evaluation and in vivo comparative pharmacokinetic study in rabbits. *Drug design, development and therapy*. **2020**, 31, 1319-31.
44. A. Madni, M.A. Rahim, M.A. Mahmood, A. Jabar, M. Rehman, H. Shah. Enhancement of dissolution and skin permeability of pentazocine by proniosomes and niosomalgel. *AAPS PharmSciTech*. **2018**, 19, 1544-53.
45. A. Saxena, P. Apurvi, R. Aslam. A review on proniosomes: a propitious outlook to the provesicular drug delivery system. *Current drug delivery*, **2023**, 20(8), 1115-1126.
46. R.M. Sammour, M. Taher, B. Chatterjee, A. Shahiwala, Mahmood S. Optimization of aceclofenacproniosomes by using different carriers, part 1: Development and characterization. *Pharmaceutics*. **2019**, 18; 11, 350.
47. R.A. Abd Elkarim, A.A. El-Shenawy, W.A. Abdelhafez, S.K. Osman. Novel nanosized Diacerein proliposomes for oral delivery: Development and in vitro/in vivo evaluation. *J. Appl. Pharm. Sci.* **2022**, 12 (7), 131–146.
48. A.A. Bachhav. Proniosome: A novel non-ionic provesicules as potential drug carrier. *Asian J. Pharmaceutics (AJP)*. **2016**, 10; 10(03).
49. N. Murugesan, C. Damodaran, S. Krishnamoorthy. Niosomal formulation of Quercetin and Resveratrol and in-vitro release studies. *J. Integr. Sci. Technol.* **2022**, 10 (2), 134–138.
50. R. Deshmukh, P. Wagh, J. Naik. Solvent evaporation and spray drying technique for micro-and nanospheres/particles preparation: A review. *Drying technology*. **2016**, 17; 34, 1758-72.
51. S. Khan, M. Shaharyar, M. Fazil, S. Baboota, J. Ali. Tacrolimus-loaded nanostructured lipid carriers for oral delivery–Optimization of production and characterization. *European Journal of Pharmaceutics and Biopharmaceutics.* **2016**, 1; 108, 277-88.
52. M. Ajrin, F. Anjum. Proniosome: A promising approach for vesicular drug delivery. *Turkish Journal of Pharmaceutical Sciences.* **2022**, 19(4), 462.
53. M.G. Nimbalwar, B.R. Gudalwar, W.A. Panchale, A.B. Wadekar, J.V. Manwar, R.L. Bakal. An overview of characterizations and applications of proniosomal drug delivery system. *GSC Advanced Research and Reviews.* **2021**, 30; 70, 25-34.
54. S.S. Suryawanshi, P.P. Patil, R.G. Gaikwad, S.S. Mali, S.L. Pol. Proniosomes: Modern drug delivery system. *Pharmaceutical Resonance*. **2021**, 41-56.
55. B.M. Razavi, M.G. Rahbardar, H. Hosseinzadeh. A review of therapeutic potentials of turmeric (Curcuma longa) and its active constituent, curcumin, on inflammatory disorders, pain, and their related patents. *Phytotherapy Research*. **2021**, 35, 6489-513.
56. Deepika, P.K. Maurya. Health benefits of quercetin in age-related diseases. *Molecules*. **2022**, 13; 27, 2498.
57. A.E. Dontje, C.C. Schuiling-Veninga, F.P. Hunsel, C. Ekhart, F. Demirci, H.J. Woerdenbag. The Therapeutic Potential of Essential Oils in Managing Inflammatory Skin Conditions: A Scoping Review. *Pharmaceuticals*. **2024**, 29; 17, 571.
58. A. Saleem, I. Naureen, M. Naeem, H.S. Murad, S. Maqsood, G. Tasleem. Aloe vera gel effect on skin and pharmacological properties. *Scholars Int. J. Anatomy Physiology*. **2022**, 5, 1-8.
59. H.M. Eltahir, M.A. Fawzy,E.M. Mohamed, M.A. Alrehany, A.M. Shehata, M.M. Abouzied. Antioxidant, anti-inflammatory and anti-fibrotic effects of Boswellia serrate gum resin in CCl4-induced hepatotoxicity. *Experimental Therapeutic Med.* **2020**, 1; 19, 1313-21.
60. A. Khanal, H.P. Devkota, S. Kaundinnyayana, P. Gyawali, R. Ananda, R. Adhikari. Culinary herbs and spices in Nepal: A review of their traditional uses, chemical constituents, and pharmacological activities. *Ethnobotany Res. Appl.*. **2021**, 14; 21, 1-8.
61. E.J. Murphy, E. Rezoagli, I. Major, N.J. Rowan, J.G. Laffey. β-glucan metabolic and immunomodulatory properties and potential for clinical application. *J. Fungi.* **2020**, 10; 6, 356.
62. A. Nehlig. Interindividual differences in caffeine metabolism and factors driving caffeine consumption. *Pharmacological Reviews*. **2018**, 1; 70, 384-411.
63. I.S. Kim, C.W. Hwang, W.S. Yang, C.H. Kim. Multiple antioxidative and bioactive molecules of oats (Avena sativa L.) in human health. *Antioxidants*. **2021**, 13; 10, 1454.
64. S.A. Mosaddad , A. Hussain, H. Tebyaniyan. Green alternatives as antimicrobial agents in mitigating periodontal diseases: a narrative review. *Microorganisms*. **2023**, 11; 11, 1269.
65. A. Whitlock. BotanicumMedicinale: A Modern Herbal of Medicinal Plants. MIT Press. **2020**, 20.
66. S. Gungor, M. Rezigue. Nanocarriers mediated topical drug delivery for psoriasis treatment. *Current Drug Metabolism*. **2017**, 1; 18, 454-68.
67. K.C. Kin, D. Hill, S.R. Feldman. Calcipotriene and betamethasone dipropionate for the topical treatment of plaque psoriasis. *Expert Review of Clinical Pharmacology*. **2016**, 2; 9, 789-97.
68. P. Biswasroy, D. Pradhan, B. Kar, G. Ghosh, G. Rath. Recent advancement in topical nanocarriers for the treatment of psoriasis. *Aaps Pharmscitech*. **2021**, 26; 22, 164.
69. M. Kraft, S. Soost, M. Worm. Topical and systemic corticosteroids. Kanerva's Occupational Dermatology. 2020, 1433-44.
70. G. Raut, S. Wairkar. Management of psoriasis with nutraceuticals: An update. Complementary therapies in clinical practice. **2018**, 1; 31, 25-30.
71. K. Sardana. Systemic Drugs in Dermatology. Jaypee Brothers Medical Publishers. **2021**, 30.
72. A. Campanati, M. Paolinelli, F. Diotallevi , E. Martina, E. Molinelli, A. Offidani. Pharmacodynamics of TNF α inhibitors for the treatment of psoriasis. *Expert Opin. Drug Metabolism & Toxicology*. **2019**, 2; 15, 913-25.
73. E.N. Ergen, N. Yusuf. Inhibition of interleukin-12 and/or interleukin-23 for the treatment of psoriasis: What is the evidence for an effect on malignancy? *Experimental Dermatology*. **2018**, 27, 737-47.
74. S. Uzzaman. Pharmacological activities of neem (Azadirachta indica): A review. *Int J Pharmacogn Life Sci.* **2020**, 1, 38-41.

75. K. Sun, A. Mears, B. Hailemeskel. Dark Circles and Puffy Eyes–The Use of Cucumber Slices, Chamomile Tea Bags, Witch Hazel, Arnica, and Students Survey. *Pharmacophore*. **2024**, 15, 41-7.
76. R. Tiwari, S.K. Latheef, I. Ahmed, H. Iqbal, M.H. Bule, K. Dhama. Herbal immunomodulators-a remedial panacea for designing and developing effective drugs and medicines: current scenario and future prospects. *Current Drug Metabolism.* **2018**, 1; 19, 264-301.
77. M. Zasada, E. Budzisz. Retinoids: active molecules influencing skin structure formation in cosmetic and dermatological treatments. *Advances in Dermatology and Allergology/PostępyDermatologiiiAlergologii*. **2019**, 4; 36, 392-7.
78. L.C. Guenther. Topical therapy II: Retinoids, immunomodulators, and others. Advances in Psoriasis: A Multisystemic Guide. **2021**, 51-69.
79. X. Yang, Y. Tang, M. Wang, Y. Wang, W. Wang, M. Pang. Co-delivery of methotrexate and nicotinamide by cerosomes for topical psoriasis treatment with enhanced efficacy. *International Journal of Pharmaceutics.* **2021**, 10; 605, 120826.
80. B. Dheer, P.N. Gupta, R. Shankar. Tacrolimus: an updated review on delivering strategies for multifarious diseases. *European Journal of Pharmaceutical Sciences.* **2018**, 1; 114, 217-27.
81. G. Singhvi, S. Hejmad, V.K. Rapalli, S.K. Dubey, S. Dube. Nanocarriers for topical delivery in psoriasis. In *Delivery of drugs* **2020**, 75-96.
82. R. Yan, S. Jiang, Y. Wu, X.H. Gao, H.D. Chen. Topical calcipotriol/betamethasone dipropionate for psoriasis vulgaris: A systematic review. *Indian journal of dermatology, venereology and leprology.* **2016**, 1; 82, 135.
83. M, Sharma, R. Rathi, S. Kaur, I. Singh, E. Abd Kadir, A.M. Chahardehi. Antiinflammatory activity of herbal bioactive-based formulations for topical administration. In Recent Developments in Anti-Inflammatory Therapy. Academic Press. 2023, 1, 245-277.
84. P. Kumar, A. Verma, S. Ashique, M. Bhowmick, S. Mohanto, A. Singh. Unlocking the role of Herbal Cosmeceutical in Anti-ageing and Skin Ageing Associated Diseases. *Cutaneous and Ocular Toxicology*. **2024**, 17, 1-30.
85. M.R Singh, D. Singh, J. Kanwar, N.S. Chauhan, editors. Advances and avenues in the development of novel carriers for bioactives and biological agents. Academic Press, **2020**, 7.
86. R. Unissa, P.M. Kumar, M. Pasha, S. Begum, B. Maheswari. Psoriasis: a comprehensive review. *Asian J. Res. Pharmaceutical Sci.* **2019**, 9, 29-38.
87. J. Rajkumar, G.V. Radha. Topical drug delivery of 5-fluorouracil proniosomal gel for the treatment of skin cancer: in vitro and in vivo evaluation. *Pharmaceutical Sciences Asia*. **2021**, 1;48(2).
88. H.M. Dawaba, E.H. Elsaied, E.A. Ibrahim, M.I. Afouna. Investigation of proniosomes gel as a promising carrier for transdermal delivery of Glimepiride. *Universal J. Pharm. Res.* **2016**, 1.
89. B.A. Witika, K.E. Bassey, P.H. Demana, X. Siwe-Noundou, M.S. Poka. Current advances in specialisedniosomal drug delivery: Manufacture, characterization and drug delivery applications. *Int. J. Mol. Sci.* **2022**, 26; 23, 9668.
90. M.I. Khan, A. Madni, J. Hirvonen, L. Peltonen. Ultrasonic processing technique as a green preparation approach for diacerein-loaded niosomes. *AAPS PharmSciTech*. **2017**, 18, 1554-63.
91. M. Madani, S. Hosny, D.M. Alshangiti, N. Nady, S.A. Alkhursani, H. Alkhaldi. Green synthesis of nanoparticles for varied applications: Green renewable resources and energy-efficient synthetic routes. *Nanotechnology Reviews*. **2022**, 4; 11, 731-59.
92. P. Ramburrun, R.A. Khan, Y.E. Choonara. Design, preparation, and functionalization of nanobiomaterials for enhanced efficacy in current and future biomedical applications. Nanotechnology Reviews. **2022**, 3; 11, 1802-26.
93. T. Limongi, F. Susa, M. Marini, M. Allione , B. Torre, R. Pisano. Lipid-based nanovesicular drug delivery systems. *Nanomaterials*. **2021**, 14; 11, 3391.
94. G.S. Myneni, G. Radha, G.V Soujanya. Novel vesicular drug delivery systems: a review. *J Pharm Res.* **2021**, 11, 1650-64.
95. B. Das, A.K. Nayak, S. Mallick. Lipid-based nanocarriers for ocular drug delivery: An updated review. *Journal of Drug Delivery Science and Technology.* **2022**, 1; 76, 103780.
96. B. Kapoor, R. Gupta, S.K. Singh, M. Gulati, S. Singh. Prodrugs, phospholipids and vesicular delivery-An effective triumvirate of pharmacosomes. *Advances in colloid and interface science*. **2018**, 1; 253, 35-65.
97. S. Yasamineh, P. Yasamineh, H.G. Kalajahi, O. Gholizadeh, Z. Yekanipour, H. Afkhami. A state-of-the-art review on the recent advances of niosomes as a targeted drug delivery system. *International J. Pharmaceutics.* **2022**, 25; 624, 121878.
98. R. Muzzalupo. Niosomes and proniosomes for enhanced skin delivery. Percutaneous Penetration Enhancers Chemical Methods in Penetration Enhancement: *Nanocarriers*. **2016**,147-60.
99. A.E. Eldeeb, S. Salah, M. Ghorab. Proniosomal gel-derived niosomes: an approach to sustain and improve the ocular delivery of brimonidine tartrate; formulation, in-vitro characterization, and in-vivo pharmacodynamic study. *Drug delivery*. **2019**, 1; 26, 509-21.
100. A.A. Yetisgin, S. Cetinel, M. Zuvin, A. Kosar, O. Kutlu. Therapeutic nanoparticles and their targeted delivery applications. *Molecules*. **2020**, 8; 25, 2193.
101. A. Pandey, N. Srivastava, R.C. Dubey, S. Dhaneshwar, A.K. Shukla. Anti-psoriatic evaluation of aloe emodin-loaded topical hydrogel in an imiquimod-induced human plaque-type psoriasis in BALB/c mice. *J. Appl. Pharm. Sci.* **2024**, 14 (9), 279–291.
102. S. Bale, A. Khurana, A.S. Reddy, M. Singh, C. Godugu. Overview on therapeutic applications of microparticulate drug delivery systems. *Critical Reviews™ in Therapeutic Drug Carrier Systems*. **2016**, 33(4).
103. C.A. Dehelean, I. Marcovici, C. Soica, M. Mioc, D. Coricovac, S. Iurciuc. Plant-derived anticancer compounds as new perspectives in drug discovery and alternative therapy. *Molecules*. **2021** 19; 26, 1109.
104. Y.T.H. Tran, G.N. Tran, A.L. Hoang, G.T.T. Vu. Niosomes loaded with diclofenac for transdermal administration: Physico-chemical characterization, ex vivo and in vivo skin permeation studies. *J. Appl. Pharm. Sci.* **2020**, 10 (12), 53–61.
105. M. Khatoon, K.U. Shah, F.U. Din, S.U. Shah, A.U. Rehman, N. Dilawar. Proniosomes derived niosomes: recent advancements in drug delivery and targeting. *Drug delivery*. **2017**, 1, 24, 56-69