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NANO-LIPID CARRIERS: A PROMISING APPROACH TO ENHANCING SUNSCREEN EFFICACY AND SKIN PROTECTION

Anupriya Yadav[1], Iti Chauhan[1*] and Bhawna Sharma[2]

[1]Department of Pharmaceutics, I.T.S College of Pharmacy, Muradnagar, Ghaziabad, UP, India.

[2]Department of Pharmaceutics, Dr. K. N. MODI Institute of Pharmaceutical Education and Research, Modinagar, Ghaziabad, UP, India.

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***Corresponding Author**
Iti Chauhan
Department of Pharmaceutics, I.T.S College of Pharmacy, Muradnagar, Ghaziabad, UP, India.

ABSTRACT

Background: Sunscreens protect the skin from UV radiation, which can cause damage and skin cancer. However, typical sunscreen formulations have drawbacks such as low stability, uneven distribution, and poor skin retention. Nano-lipid carriers (NLCs) are a promising approach for increasing the transport and efficacy of sunscreen chemicals. NLCs, which are made up of solid lipid nanoparticles (SLNs) and nanostructured lipid carriers, can encapsulate both hydrophilic and lipophilic UV filters, resulting in improved skin penetration and longer-lasting protection. **Objective:** This study aims to assess how NLCs can enhance sunscreen efficacy, skin protection, and user comfort by improving UV filter stability, controlled release, and retention while minimizing irritation and photodegradation. **Methods:** A comprehensive literature search was conducted across several databases, including PubMed, Wikipedia, Academia, and Google Scholar. The search utilized a variety of key terms such as Nano-Lipid Carriers, UV, Sunscreen efficacy, skin protection, Nanocarriers, Nano-lipid carriers, Topical drug delivery, Solid-lipid nanoparticle, Liposomes, Nanoemulsions, Nanocarriers for sunscreen, Improved SPF, UVB protection, UVA protection, UV-blocking agents, absorber, UV reflectors and Photostability The focus of the search was specifically on Nano-Lipid Carriers as a promising approach to enhancing sunscreen efficacy and skin protection. Studies related to Nanostructured lipid carriers or sunscreen agents were excluded from the review. **Results:** NLC-based sunscreens demonstrated increased stability, controlled release of active

ingredients, and enhanced photoprotection. They improved skin penetration and retention while also providing antioxidant and anti-inflammatory properties. The formulations also caused minor skin irritation. **Conclusion:** In conclusion, NLCs improve sunscreen efficacy by enhancing stability, controlled release, and skin protection, paving the way for more effective and skin-friendly formulations.

KEYWORDS: Nano-lipid carriers, skin, UV rays, enhancing stability, SPF, solid lipid nanoparticle, skin protection, bioavailability.

1. INTRODUCTION

Nanostructured lipid carriers (NLCs) are poised to become a significant delivery system for both cosmetics and pharmaceuticals in the future. Since their introduction in 2005, they have garnered significant attention and sparked numerous studies exploring their potential applications. With ongoing advancements, the drug-loading capacity and storage stability of these carriers continue to improve. NLCs offer advantages over traditional liposomes by enhancing the percutaneous absorption of drugs or their active ingredients, thereby improving efficacy and reducing side effects. Recent studies have highlighted the progress made in the development of lipid-based drug delivery systems, including liposomes and oil-in-water (O/W) emulsions, underscoring their promise in medicine and skincare.[1] Sunscreens play a crucial role in safeguarding the skin from the damaging effects of ultraviolet (UV) radiation. With a wide variety of sunscreen formulations available, consumers often find it difficult to navigate their options. This article aims to clarify several common myths surrounding sunscreen, including the advantages of using higher SPF products, the application of sunscreen on darker skin tones, and the impact of sunscreen on vitamin D production.[2] For over 40 years, sunscreens have been the most popular method of protecting against UV radiation (UVR) in Western countries. There are both organic and inorganic filters with varying absorption spectra that either filter or scatter UVR. Protection against UVB is measured using the sun protection factor (SPF), which is based on the minimal erythema dose. In contrast, testing for UVA protection is less standardized; current methods include persistent pigment darkening and critical wavelength assessments.[3] Sunlight includes both ultraviolet **UVA** and UVB radiation. While UVB is crucial for vitamin D production, it is also the primary cause of sunburn and skin cancer. The use of sunscreen is recommended to mitigate the harmful effects of the sun, but it may potentially impact vitamin D levels.[4] Sunscreen creams can shield the skin against UV radiation's damaging effects, such as cancer,

aging, and reddening. The Mansur equation was used to determine the sun protection factor (SPF).[5]

It is commonly known that the primary cause of skin cancer is exposure to the sun. While periodic high-dose UV exposure is thought to contribute to the development of actinic keratosis, which is a precursor lesion of both basal cell carcinoma and squamous cell carcinoma, chronic continuous UV radiation is thought to cause malignant melanoma. The mechanisms of photoaging as well as photo carcinogenesis have lately come into focus. In this regard, it appears that using sunscreen has been increasingly significant and common during the past few decades. The effectiveness of sunscreens is still debatable, though. According to a number of studies, protection may be more compromised than previously thought due to improper use and insufficient UV spectrum efficacy. There are a lot of products on the sunscreen market. Zinc oxide and titanium dioxide provide broad-spectrum protection on their own, unlike many organic sunscreens, which often require a blend of multiple ingredients to achieve similar coverage. This makes inorganic sunscreens particularly beneficial for sensitive skin and long-lasting sun protection.[6]

The use of sunscreen products has long been recommended by healthcare professionals as a means of mitigating skin damage caused by ultraviolet radiation (UVR) from sunlight. However, there is a need for a more comprehensive understanding of the efficacy and safety of sunscreen products in light of the ongoing public health campaign promoting their use. The standard method for determining sunscreen efficacy, the sun protection factor (SPF), primarily measures protection against UVB radiation (290-320 nm). However, the SPF test does not adequately evaluate the full spectrum of photoprotection, particularly against long-wavelength UVA I radiation (340-400 nm). Furthermore, there is currently no universally accepted method for assessing UVA efficacy, despite the growing consumer demand for sunscreen products that provide broad-spectrum protection against both UVB and UVA radiation. Regarding the safety of UVB and UVA filters, commonly used organic and inorganic sunscreen ingredients generally exhibit favorable toxicological profiles, as demonstrated by acute, sub chronic, and chronic studies on animals and humans. In addition, most studies have shown that sunscreens are effective in preventing the harmful effects of UVR exposure. Based on this review of the available data, it is concluded that sunscreen ingredients and products do not pose a significant health risk to humans. Moreover, regular

use of appropriate broad-spectrum sunscreen products could have a substantial and positive impact on public health as part of a broader strategy to reduce UVR exposure.[7]

2. Importance of Sunscreen

The aim of this study was to assess how substrate roughness and product application techniques affect in vitro sun protection factor (SPF) measurements, as well as to identify the experimental conditions that provide the best correlation to in vivo SPF. In vitro SPF evaluations were conducted on 13 products, which included various formulation types with SPFs ranging from 20 to 75. Different in vitro SPF protocols were employed to compare their predictive accuracy in relation to in vivo SPF.[8] Nanostructured lipid carriers (NLC) represent a second-generation smart drug delivery system that features a solid matrix at room temperature. This carrier system is composed of physiological, biodegradable, and biocompatible lipid materials and surfactants, and it has been approved by regulatory authorities for various drug delivery applications. The rapid introduction of numerous products to the market highlights the success of this delivery system; since the launch of the first product, around 30 NLC formulations are now commercially available.[9] LNPs provide various advantages, including protecting drugs from degradation in the body, enhancing their solubility and effectiveness, facilitating targeted delivery to the site of disease, controlling drug release, and modifying the drug's distribution within the body.[10]

3. Classification of sunscreen

Sunscreen agents operate in a variety of ways, including by reflecting, dispersing, and blocking UV rays. Classification of Sunscreen agents is based on the composition and mechanism of action shown in Fig. 1.

3.1. Synthetic sunscreen: Both organic and inorganic filters are present in synthetic sunscreen. Chemical sunscreens are physical blockers that absorb high-energy UV radiation and reflect or scatter UV rays. Chemical sunscreen contains organic components that provide protection against a variety of UV rays. By dispersing the inorganic compound microparticles on the epidermis, the topmost layer of skin, the optical path of photons is increased, leading to a high absorption of photons. This, in turn, increases the compound's efficacy by raising the Sun Protection Factor (SPF).

3.2. Organic filters: Filters made of organic materials: Depending on their chemical makeup, organic materials will absorb particular UV light wavelengths. The filter changes from a low energy level to a high energy level.

3.3. Inorganic filters: UV rays are scattered and reflected back to the outside world by inorganic filters. It serves as a physical shield against ultraviolet light. Since these filters cover the whole UV spectrum, they are regarded as broad spectrum. Zinc oxide and titanium dioxide are common inorganic filters.[11]

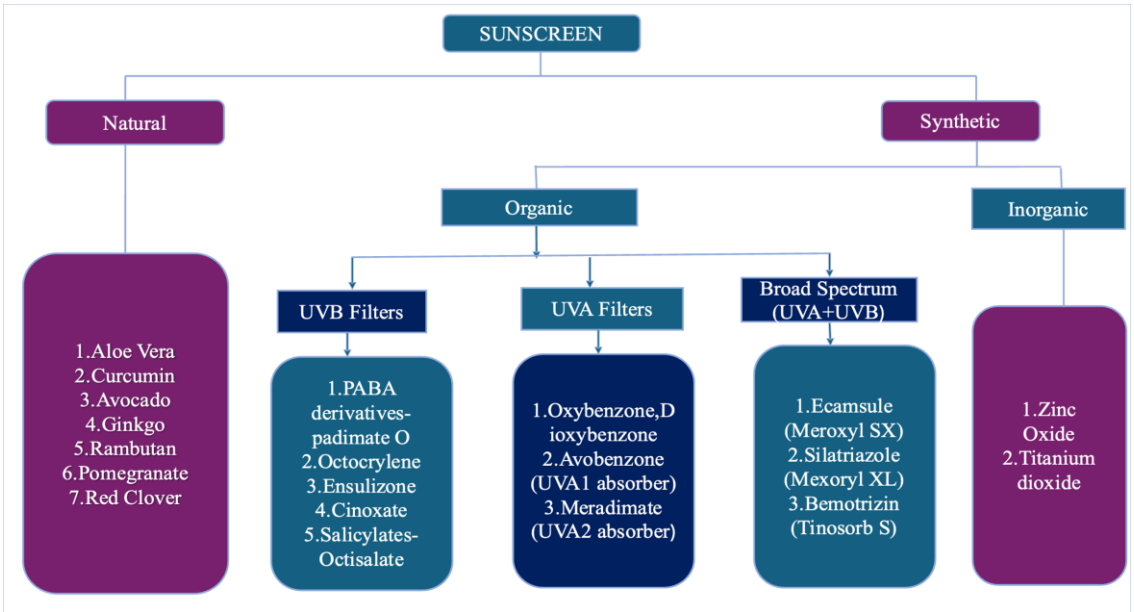

Fig. (1). Classification of Sunscreen agents.

4. Different formulation of natural sunscreen products

Because of their high entrapment efficiency and enhanced skin permeability, nano-formulations are employed. These are innovative dosage forms or technologies that integrate natural UV filters, botanical actives, and advanced delivery systems to enhance efficacy, safety, and user experience.

4.1. Solid lipid nanoparticle

Lipid that has been dispersed in water or an aqueous surfactant solution makes up solid lipid nanoparticles. It is between 50 and 100 nm in size and is a sub-micron colloidal carrier.

4.2. Nano emulsions

Submicron emulsions in the nano size range are called nano-emulsions. The interfacial tension is decreased by the stabilizing effects of surfactant and co-surfactant, which stabilize

two immiscible liquids, such as water and oil. These are kinetically and thermodynamically stable isotropic dispersions.

4.3. Phytosomes

The word "Phytosome" comes from the words "Phyto," which means "plant," and "some," which means "cell like." This plant extract creates lipid-compatible molecular complexes by loading it into phospholipid.

4.4. Niosomes

The aqueous solution of solutes and the lipophilic component of the bilayer will be enclosed by niosomes, a bilayer vesicular structure of non-ionic surfactant. Both unilamellar and multilamellar bilayer structures are possible.

4.5. Liposomes

Liposomes are tiny vesicles made of naturally occurring, non-toxic phospholipids and cholesterol. The size range is between 0.025 and 2.5 micrometres.[11]

5. SPF (Sun Protection Factor)

In recent years, research on Sun Protection Factor (SPF) has proven increasingly useful. Effective protection against UV radiation must be demonstrated by the various medicinal substances employed in the manufacturing of sunscreen creams and lotions. In this work, we evaluated various pharmaceutical excipients that have been licensed by the Indian Pharmacopeia in order to investigate the relationship between absorbance and SPF. Our results support the correlation between transmittance and absorbance, two important factors in determining a sunscreen's SPF and UV-blocking capacity. The SPF of the samples was analysed and computed using Mansur's equation, and changes in the label claims were ascribed to variances in the amounts of the constituents used in the formulations. Sunscreens having SPF values of 15, 20, 24, 30, 50, and 60 were included in the study.[12]

The most crucial metric for evaluating how well sunscreen protects the skin is the Sun Protection Factor (SPF). Since SPF values and UV radiation protection are strongly correlated, higher SPF values translate into better sunburn protection.[12]

In vitro methods for determining sun protection factor (SPF) values typically involve two processes.

1. Measurement of UV radiation absorption or transmission through the sample.

2. Analysis of the absorption properties of the sample based on spectrophotometric analysis of dilute solutions.

Several factors can influence the determination of SPF values, including the type of solvents used, the viscosity of the sunscreen, the type of emulsion, the cuvette material, as well as the interactions between the vehicle and other components. The addition of other active ingredients can also impact the UV absorption of the sunscreen, either enhancing or reducing its effectiveness. In this study, the stability of emulsions was assessed by measuring their pH, conductivity, and viscosity. The objective of the proposed work is to determine the SPF values for different formulations using UV spectrophotometry.

Many attempts have been made to develop in vitro SPF testing methods. Everyone is exposed to sunlight, which includes electromagnetic radiation from the sun, particularly UV radiation. UV radiation carries the highest energy among the types of radiation that reach the Earth's surface. Generally, people are more exposed to sunlight and UV radiation during the summer season, especially in tropical regions.[12]

5.1. Tabular review of sunscreen agents incorporated in lipid nanoparticles

Sunscreen formulations play a crucial role in protecting the skin from harmful ultraviolet (UV) radiation, preventing sunburn, premature aging, and skin cancer. However, conventional sunscreen agents often face challenges such as poor photostability, skin irritation, and limited skin penetration. To overcome these limitations, lipid nanoparticles (LNPs), including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), have emerged as promising delivery systems for sunscreen agents. These nanocarriers enhance the stability, bioavailability, and controlled release of UV filters, thereby improving sunscreen efficacy and skin compatibility. This tabular review provides a comprehensive overview of various sunscreen agents incorporated into lipid nanoparticles, highlighting their formulation strategies, physicochemical characteristics, and photoprotective properties.

Sunscreen agent	Type of lipid nanoparticle	Lipids used/method of preparation	Key points	Reference
Safranal	SLN	Glyceryl monostearate, High shear homogenization and ultrasound.	1. SLN containing 4% safranal showed higher SPF values. 2. Enhanced skin hydration properties were observed.	[13]
Silymarin	SLN	Glyceryl	1.The developed	[14]

		monostearate, micro-emulsion method.	formulation exhibited excellent photoprotective efficacy. 2. SPF values determined through in vitro and in vivo methods were found to be 13.80 and 14.10, respectively.	
Oxybenzone	SLN	Glyceryl monostearate and Witepsol E85, Solvent diffusion method.	1.The formulation was evaluated for skin irritation potential, in vitro SPF and UVA protection efficacy. 2.A significant enhancement in both SPF and UVA protection factor was observed.	[15]
Alovera	SLN	Stearic acid, Micro emulsification technique.	1.Determine its photoprotective potential. 2. The in vitro SPF was determined to be 16.9 ± 2.44, while the in vivo SPF was approximately 14.81 ± 3.81.	[16]
Ethylhexyl triazone, bis-ethylhexyloxyphenol methoxyphenyl triazine, and ethylhexyl methoxycinnamate.	NLC	Miglyol 812, Hot high pressure homogenization technique.	1.Submicron dimensions and a similar capability to protect the in clouded actives from photo-instability phenomena. 2.Reduce the skin permeation abilities of the sun filters.	[17]
Lutein	NLC	Glycerol monostearate, melt emulsion ultrafiltration technique.	It has been reported that the chemical stability of lutein is enhanced when encapsulated in poly ε-caprolactone nano capsules.	[18]
Bemotrizinol	NLC	Miglyol 812, ultrasonication method.	It is a broad-spectrum UV filter with excellent photostability and efficacy against both UVA and UVB radiation. Its performance is further enhanced when delivered through submicron carriers. The small particle size improves skin penetration,	[19]

			ensuring better deposition in the upper skin layers.	
Bacuri butter	NLC	Polyglyceryl-3-dioleate, Ultrasonication Method.	The stability and skin penetration of SC-NLC were assessed to evaluate its integrity and safety.	[20]
Tocopherol acetate	SLN	Cetyl palmitate, In vitro techniques	1.Pure tocopherol exhibited the highest UV-blocking capacity. 2.Its stability decreased to the greatest extent under the tested conditions.	[21]
Fucoxanthin	SLN and NLC	Cetyl palmitate, High-pressure homogenizer.	SLN and NLC were used to increase the water content of the skin and showed an effective UV-blocking potential.	[22]
n-dodecyl-ferulate	SLN	Cetyl palmitate, Homogenization technique.	SLN investigated concerning particle size, surface electrical charge (zeta potential) and matrix crystallinity.	[23]
Rutin	NLC	Plurol® stearique, Photoprotective preparation.	Rutin provide a suitable cosmeceutical lipidic colloidal system of Rutin to be employed as a successful photoprotective preparation.	[24]
Safranal	SLN	Almond oil, Probe sonication technique.	Safranal effectively inhibits matrix metalloproteinases (MMPs) and demonstrates significant photoprotective properties, thereby enhancing the sun protection factor (SPF).	[25]
Diethyltoluamide ethylhexyl p-methoxy cinnamate	SLN	Stearic acid, ultrasonication technique.	The formulation was designed to minimize percutaneous absorption while sustaining the efficacy of the active compounds on the skin surface over an extended period.	[26]

5.2. UV protection and sunscreens

The primary environmental risk factor for nonmelanoma skin cancer and a possible risk factor for melanoma is ultraviolet (UV) exposure. Skin protection measures include wearing protective clothes, using sunscreen, and avoiding excessive exposure to direct sunlight during the hottest parts of the day. We cover the effects of UV radiation on the skin, how sunscreens block UV light, current sunscreen use guidelines, and new sunscreen labelling rules to give doctors the skills they need to counsel patients and respond to their questions, including which sunscreen to use.[27]

5.3. Sunscreen Photoprotection

Photoprotection is a vital health strategy to mitigate the harmful effects of ultraviolet radiation (UVR) and visible light (VL). This paper reviews various methods of photoprotection, with a particular focus on sunscreen. The most suitable sunscreen formulation for individual use depends on several factors, including the specific active ingredients, which vary in their effectiveness against different wavelengths of UVR and VL. Certain dermatologic conditions can either cause photosensitivity or be exacerbated by exposure to specific parts of the light spectrum. In such cases, tailored sunscreen recommendations can address these concerns. Sunscreen is not a one-size-fits-all product. Personalizing sunscreen selection is crucial to enhancing patient compliance and achieving better clinical outcomes. Health care providers can help guide informed product choices by staying up to date on evolving sunscreen formulations and counselling patients on their proper application. This review aims to summarize various forms of photoprotection, discuss the absorption of sunscreen ingredients, highlight potential adverse effects, and explore disease-specific preferences for chemical, physical, or oral agents that can reduce the harmful effects of UVR and VL.[28]

Sunscreens The Sun Protection Factor (SPF) is a widely recognized metric used in the marketing of. However, many consumers and patients lack a clear understanding of how sunscreens work and the limitations of SPF. Various aspects of SPF can be confusing, such as the race for higher numbers, the impact of insufficient sunscreen application on SPF, and concerns about whether sunscreens should be used at all due to their potential interference with Vitamin D synthesis. These misunderstandings negatively affect consumer compliance, which is a key factor in effective sun protection. also, how SPF is determined, and where the limitations of current methods exist. It introduces a dynamic perspective, examining both the

'UV radiation applied' and the 'UV dose transmitted' through sunscreen onto the skin or onto a substrate in vitro. This approach helps to deepen understanding and presents promising new methods for in vitro assessment. An advanced variation of in vitro testing involves in silico calculations based on the absorption spectrum of UV filters and assumptions about the irregular film of sunscreen on the skin. Using a sunscreen simulator program, it is possible to determine how SPF is affected by the application of smaller amounts of sunscreen. Beyond SPF, the paper also discusses UVA protection. The degree of UVA protection is crucial for evaluating the overall quality of sun protection, while SPF primarily reflects the quantity of protection. Additionally, the paper examines other protection factors, including IPF, iSPF, RSF, and p53, and explores how sunscreens might inhibit Vitamin D3 synthesis. In conclusion, it is argued that the accuracy and reliability of SPF and other protection factors will improve significantly with the development of true broad-spectrum sunscreens, as opposed to the current UVB-biased formulations. Uniform protection profiles in broad-spectrum sunscreens ensure more consistent protection, regardless of the action spectrum of the endpoint or the UV radiation source.[29]

5.4. Sun Spectrum (UVA, UVB, UVC)

The skin, being the largest organ of the human body, plays a crucial role in maintaining homeostasis and protecting the body from harmful ultraviolet radiation (UVR). Disruptions in this balance can lead to various issues such as wrinkles, hair loss, blisters, rashes, life-threatening cancers, and immune system disorders. UV radiation is categorized into three types: UVA, UVB, and UVC. UVC is less of a concern since its rays are absorbed by the ozone layer and do not reach the Earth's surface. Therefore, photoprotection against both UVA and UVB radiation is essential for safeguarding skin health. UVA radiation (320–400nm) has a longer wavelength, allowing its rays to penetrate deeper into the skin, reaching both the epidermis and dermis. UVA can be further divided into UVA I (320–400nm or "far UVA") and UVA II (320–340nm or "near UVA"). UVA rays are present throughout the day, including during the morning and late afternoon. Because UVA rays can penetrate window glass, individuals with heightened photosensitivity may experience effects even indoors. Studies have shown that multiple low-dose exposures to UVA are linked to significant histological changes in both the dermis and epidermis. UVB radiation (290–320nm), often referred to as the "burning rays," are primarily associated with the need for sunscreen protection. Most automobile glass and windows effectively block these rays.[30] In fig. [2]. the ultraviolet component of the electromagnetic spectrum source is shown.

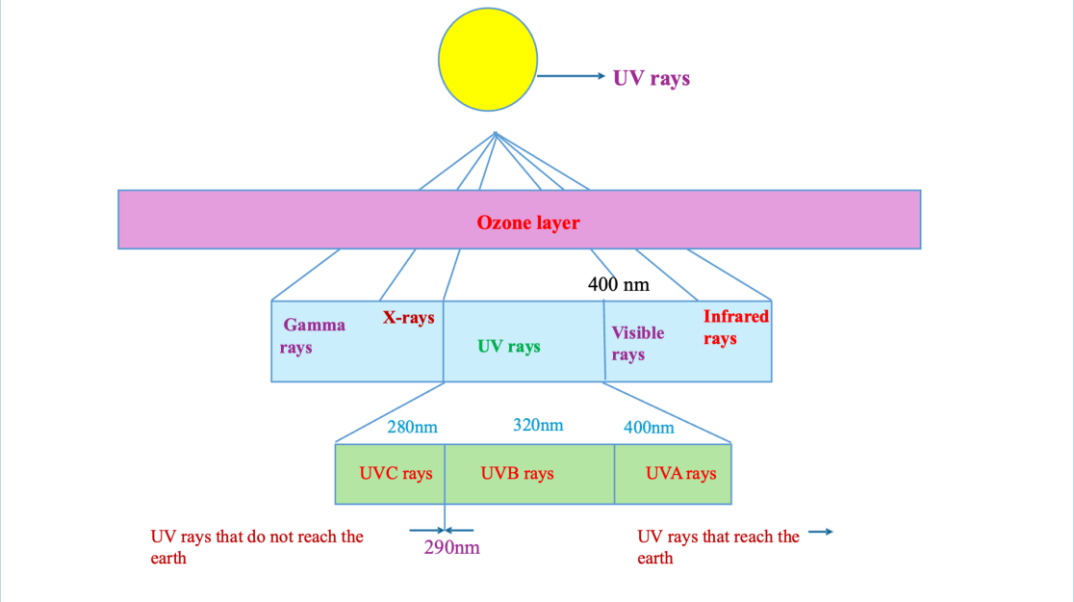

Fig. (2). The ultraviolet component of the electromagnetic spectrum source.

Skin cancer is primarily caused by exposure to ultraviolet radiation (UV), with the sun being the main source of this radiation. Sunscreens were initially developed to prevent sunburn, and subsequent laboratory studies in rodents showed that they could reduce UV-induced skin cancer, which resembles human squamous cell carcinoma. Three randomized trials in older adults demonstrated that sunscreens could moderately reduce the occurrence of solar keratoses and squamous cell carcinoma, though no effect was observed for basal cell carcinoma. There is no suitable animal model for human melanoma, and observational studies often associate sunscreen use with a higher risk of nevi, melanoma, and basal cell carcinoma. These elevated risks tend to occur when sun exposure is intentional—such as when individuals aim to tan, achieve a "healthy" look, or simply spend extended periods in the sun with as much skin exposed as possible. Three randomized trials showed that sunscreen use by sun-sensitive individuals engaging in intentional sun exposure could increase the duration of sun exposure without reducing the risk of sunburn. This prolonged exposure may explain why sunscreen use has been linked to an increased risk of melanoma. Thus, improper use of sunscreen may extend sun exposure, enabling behaviours that would otherwise be unsustainable. Advertising for sunscreens and product labelling should inform consumers about the potential carcinogenic risks associated with sunscreen misuse. One potential solution is the use of a personal UV dosimeter, which can alert users when they are nearing their individual sunburn threshold without sunscreen. The combination of sunscreen

and a UV dosimeter could help reduce melanoma risk, particularly among individuals who engage in excessive sun exposure.[31]

6. Natural Compounds That Contribute to UV Protection

6.1. Niacinamide: Niacinamide is the active, water-soluble form of vitamin B3, known for its anti-inflammatory and antioxidant properties. These effects make it effective in treating various skin disorders. Additionally, when applied topically, niacinamide can help prevent immunosuppression induced by UVA and UVB radiation, thereby offering protection against photodamage. As a precursor to nicotinamide adenine dinucleotide (NAD+), niacinamide boosts ATP synthesis, which in turn enhances DNA repair. Given these benefits, niacinamide has emerged as a promising agent for skin cancer prevention.

6.2. Vitamin C: Vitamin C is a powerful antioxidant and water-soluble vitamin, widely popular in topical skincare products for its broad range of benefits, including anti-aging, anti-pigmentary, and photoprotective effects. Its photoprotective properties help reduce erythema, sunburn, and immunosuppression. Vitamin C acts as a free radical scavenger in the aqueous compartments of cells, protecting them from oxidative stress, especially from UV exposure, which is a primary source of free radicals. By neutralizing these radicals, vitamin C safeguards cellular structures and also regenerates vitamin E, another potent antioxidant. The antioxidant effects of vitamin C are driven by its ability to donate a hydrogen atom, forming a relatively stable ascorbyl-free radical. Additionally, vitamin C is effective in treating sunspots, as it inhibits the activity of tyrosinase, an enzyme involved in the production of melanin precursors.

6.3 Vitamin E: Vitamin C is a lipid-soluble vitamin known for its numerous beneficial effects on the skin. As a potent antioxidant, like vitamin C, it protects cell membranes from oxidative stress by scavenging free radicals. Vitamin E contains a chromane ring with a hydroxyl group that acts as a hydrogen donor, enabling it to neutralize free radicals. Furthermore, its hydrophobic side chain allows it to penetrate biological membranes. When applied topically, vitamin E helps reduce immunosuppression, photoaging, and the risk of skin cancer. Studies have shown that vitamin E and its derivatives can mitigate UV-induced erythema and edema. In fact, research indicates that a combination of 15% vitamin C and 1% vitamin E offers superior protection against sunburn and erythema after UV exposure compared to either vitamin alone, when applied topically to white Yorkshire pigs at the same

concentrations. This demonstrates that vitamins C and E work synergistically to protect against UV-induced photocarcinogenesis and photoaging.[32]

7. Protection Against Visible Light: The impact of visible light on the skin has received far less attention compared to UV radiation. While the role of visible light in skin damage is likely less significant than that of UV radiation, it is still an important factor in both physiological and pathological processes. Visible light sensitivity is particularly relevant in conditions such as porphyria, solar urticaria, and other idiopathic photodermatoses, including polymorphous light eruption. Additionally, patients undergoing photodynamic therapy can experience increased sensitivity to visible light, either temporarily (for a few days) due to topical treatments like aminolevulinic acid and methyl aminolevulinate, or for several weeks due to systemic agents such as porfimer sodium. Visible light exposure can increase pigmentation in individuals with skin types IV to VI. This suggests that protecting against visible light may be particularly important for individuals with darker skin tones who suffer from pigmentary disorders like post-inflammatory hyperpigmentation and melasma. Given these findings, further research into the effects of visible light on the skin is crucial.[33]

8. Brief Introduction to NLCs

Based on the lipid structure of prepared NLCs, they can be classified into three categories according to the composition of the lipid mixture and the method used for their preparation.[34] fig. [3] contain different types of NLC.

8.1. Imperfect type

In this type, the imperfection of the lipid matrix is achieved by using lipids with varying chemical characteristics, such as differences in carbon chain length and degree of saturation. The mixing of these lipids induces disorder in the crystal lattice and alters crystallization. As a result, the lipid matrix can accommodate a larger amount of drug and is less likely to expel it during storage, compared to using a single lipid.[34]

8.2. Amorphous type

In this type, the formation of a structureless, solid amorphous matrix results in a high drug payload, as the lipid matrix crystallizes into a less ordered, amorphous state. The use of medium-chain triglycerides, hydroxyoctacosanylhydroxystearate, or isopropylmyristate combined with solid lipids can create this pattern. Nuclear magnetic resonance (NMR) and

differential scanning calorimetry (DSC) are used to confirm the lipid's solid state and transition temperature, respectively.

8.3. Multiple type

In this type, the solid lipid matrix contains several nanosized liquid oil droplets, in which the drug is highly dissolved. As a result, drug encapsulation is enhanced. Additionally, the drug is released in a controlled manner, with reduced drug leakage (stability factor) since the tiny oil droplets are contained within the solid lipid matrix.[34]

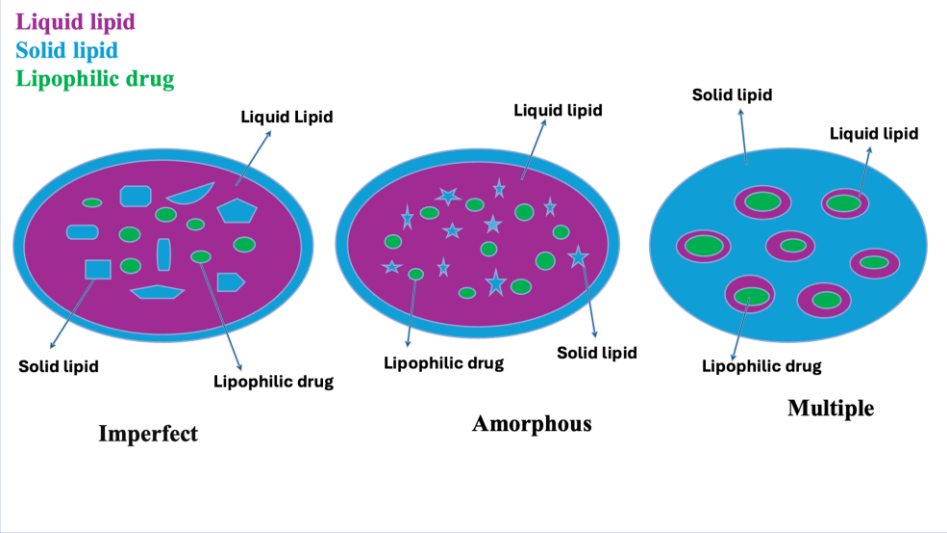

Fig. (3). Types of NLC.

9. NLC FABRICATION

9.1. Ingredients Used for NLC: The Nanostructured Lipid Carrier (NLC) consists of key components, including solid lipid (SL), liquid lipid (LL), surfactants, and water. Typically, surfactants are first dispersed in water, then added to the lipid mixture, followed by homogenization. The ratio of solid lipid to liquid lipid ranges from 70:30 to 99.9:0.1. The concentration of surfactant varies from 0.5% to 5%.[35]

9.2. Lipids and Surfactants as Component of NLC: The lipid component is the primary ingredient in formulating Nanostructured Lipid Carriers (NLC), significantly influencing parameters such as drug encapsulation, stability, and prolonged release. The lipids used in NLC are biodegradable, non-toxic, and physiologically acceptable. While many lipids are available and possess GRAS (Generally Recognized As Safe) status, selecting the most suitable lipid for NLC remains a key concern. Key factors for lipid selection include the solubility of the drug in the lipid and the lipid’s partition coefficient. Studies show that the

solubility of the drug in the lipid directly impacts drug loading and encapsulation efficiency. Research also indicates that drug loading, particle charge, and size are influenced by the degree of lipid crystallization. Additionally, the melting point of the lipid plays a crucial role: a higher melting point increases the viscosity of the dispersed phase, which in turn raises the particle size. Other characteristics, such as lipid hydrophilicity and crystal shape, also affect NLC quality. Furthermore, increasing the lipid content by 5-10% tends to result in larger particle sizes. Therefore, selecting the appropriate lipid for NLC formulation is a critical consideration.[35]

10. Evaluation Parameter of NLC Formulation

10.1. Morphology: The effectiveness of an NLC formulation depends on factors such as particle size and shape. Studies show that the particle size of NLC formulations typically ranges from 10 to 1000 nm. However, for site-specific action, this range may be narrower (e.g., 50-300 nm for chemotherapeutic agents). The physical stability of an NLC formulation is influenced by both the particle size and its distribution within the formulation. Parameters such as entrapment efficiency, cellular uptake, and targeting potential can be affected by the shape of the particles present. Techniques such as Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) are essential for analysing particle shape. Generally, NLC formulations tend to exhibit spherical particles with a low surface area.

10.2. Surface charge: The surface charge of particles is influenced by the concentration of the lipid mixture and the surface-active agent. The term "zeta potential" is used to measure the surface charge of particles. Zeta potential (ZP) is determined based on electrophoretic mobility. A higher zeta potential value (> +30 mV) indicates reduced particle aggregation. Typically, the dispersion should have a zeta potential greater than +30 mV or less than -30 mV to ensure stability.

10.3. Entrapment Efficiency (EE): Entrapment efficiency (EE) refers to the percentage of the drug encapsulated within the particles, which determines the efficiency of the formulation. Lipophilic drugs generally exhibit higher entrapment efficiency compared to hydrophilic ones, as they are more readily solubilized in lipids. The drug release rate in an NLC formulation is significantly influenced by the EE, as a higher entrapment value alters the concentration gradient.

The Efficiency of Encapsulation (EE) is calculated using the formula.

$$Entrapment\ efficiency\ (\%) = \frac{w_a - w_s}{w_a}\ X\ 100$$

Where:

Where w_a= weight of drug added to the formulation

Ws =amount of drug determined in supernatant

10.4. In vitro drug diffusion study: A dialysis bag is used for in-vitro drug diffusion studies. To ensure optimal results, the dialysis membrane is first activated by soaking it in distilled water overnight. The prepared NLC formulation is then placed inside the bag, and both ends are sealed. The entire experiment is conducted under sink conditions. At specified time intervals, samples are withdrawn and replaced with fresh media. The samples are then analysed using a UV-visible spectrophotometer.[35]

11. Methods of Preparation of NLC

The preparation methods for NLCs include.[36]

11.1. Hot High-Pressure Homogenization Technique: High-pressure homogenization is an energy-intensive, scalable technique used to produce nano-sized colloidal systems, such as NLCs, SLNs, and nanoemulsions. It employs a top-down approach to reduce the size of microemulsion particles to the nanoscale through the application of high pressure. In this method, the solid lipid is first melted, and then the liquid lipid is added to form a heated lipid phase. Surfactants, with or without cosurfactants, are incorporated into water to form the aqueous phase. The preheated lipid phase is then mixed with the heated aqueous phase under constant stirring to create a microemulsion. This hot microemulsion is subsequently subjected to high-pressure homogenization for size reduction. The number of homogenization cycles can be adjusted to achieve the desired particle size. The resulting nanoemulsion is cooled, transforming it into NLCs. Using intermediate pressure (around 1000 bar) for extended periods results in smaller NLC particles, typically less than 100 nm. However, this process is not suitable for drugs or materials that are sensitive to high temperatures. Fig [4] depicts systematic steps to formulate NLC.

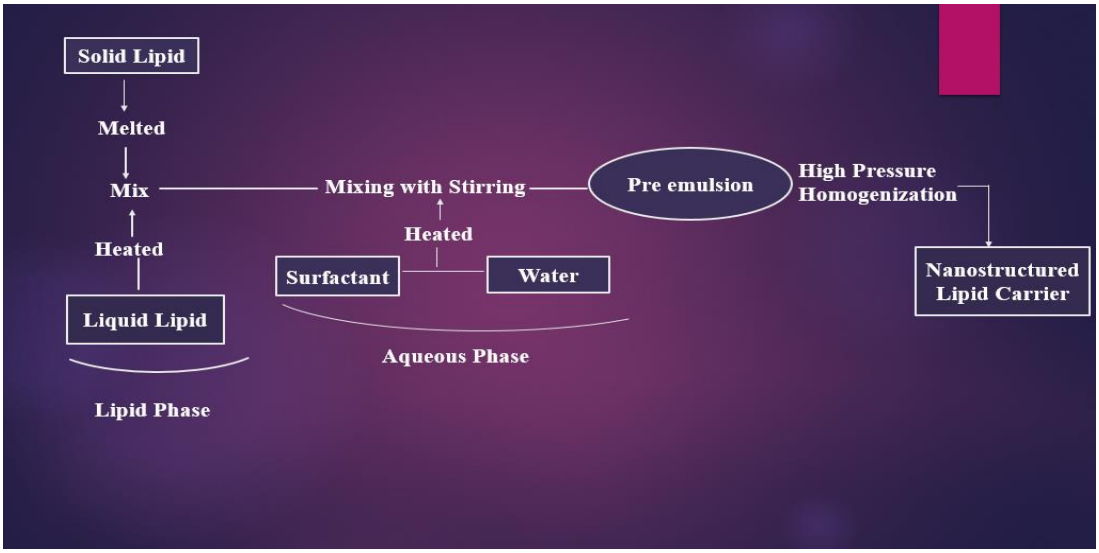

Fig. (4). Hot high-pressure homogenization.

11.2. Cold High-Pressure Homogenization Technique: Similar to hot high-pressure homogenization, this process involves mixing the lipid phase with a cold aqueous solution, typically maintained at a temperature range of 2°C to 6°C, with constant stirring. The resulting coarse NLC suspension is then homogenized using a high-pressure homogenizer at low temperatures. This method is particularly suitable for drugs and materials that are sensitive to high temperatures and cannot tolerate heat exposure.

11.3. High-Speed Homogenization: This method of NLC preparation closely resembles hot high-pressure homogenization, with the key difference being the replacement of high pressure with a high shear rate. The lipid phase is prepared by mixing liquid lipid with melted solid lipid, while the aqueous phase is made by dissolving surfactant in water. The heated lipid phase and aqueous phase are then homogenized using a high-speed homogenizer at high rotation speeds (RPM) for an extended period (10-30 minutes). The resulting mixture is cooled to room temperature to form NLCs. The speed of homogenization directly influences the particle size of the nanocarriers. Before cooling, the liquid nanoemulsion can also be sonicated for 5 minutes using an ultrasonic probe to further reduce the particle size of the NLC. In some cases, the melt emulsification method has been described, where the same process is employed but with low-speed homogenization and extended sonication time. Fig. [5] shows a flowchart of steps required to formulate NLC through High-speed homogenization.

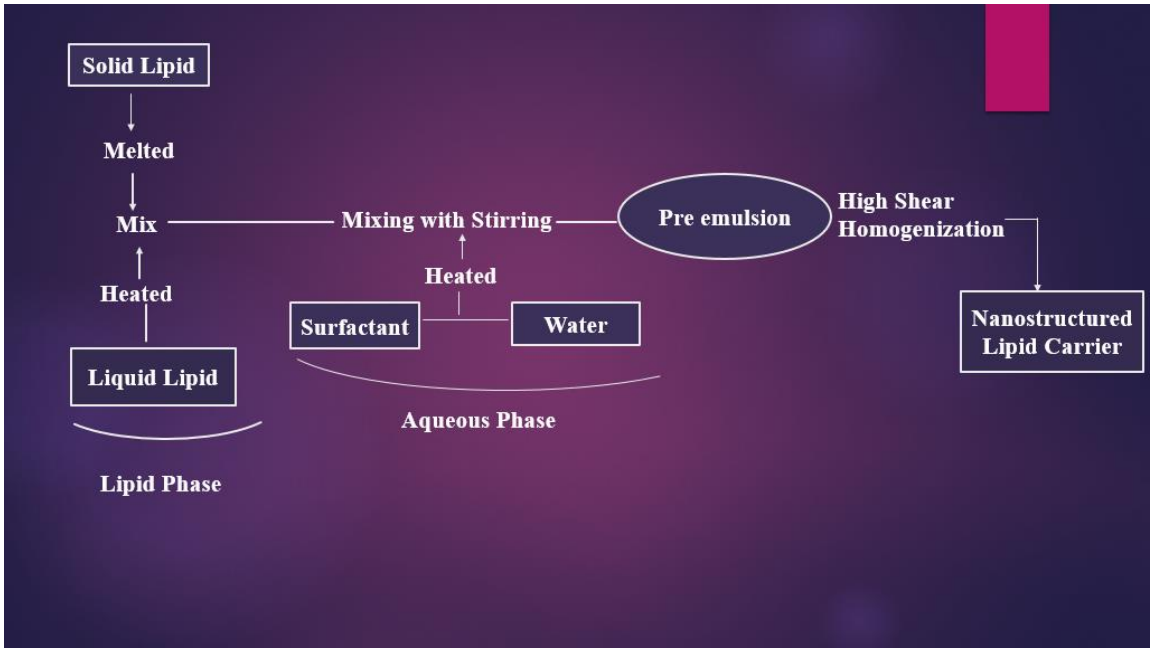

Fig. (5). High speed homogenization.

11.4. Microemulsion: In the microemulsion technique, the liquid lipid is added to the molten solid lipid, and the resulting mixture is combined with an aqueous phase to form a microemulsion. This microemulsion is then rapidly cooled using cold water to create the NLC dispersion system. The ratio of microemulsion to water influences the particle size of the NLCs. While this method is relatively simple, it requires a high amount of surfactant and cosurfactant**.**

11.5. Solvent diffusion and evaporation technique: In this technique, the liquid lipid is added to molten solid lipid, which is dissolved in either a single organic solvent or a combination of solvents at high temperature. This lipid solution is then mixed with an aqueous solution containing surfactant while stirring. The prepared dispersion is subsequently ultrasonicated to form an oil-in-water nanoemulsion, which is cooled with gentle stirring until the organic solvent is evaporated. This method is low in energy consumption and avoids the physical stress associated with high pressure or shear. However, due to the use of organic solvents, an additional step is required to remove any residual toxic solvent. Fig. [6] shows Solvent diffusion or solvent evaporation technique for the preparation of NLC.

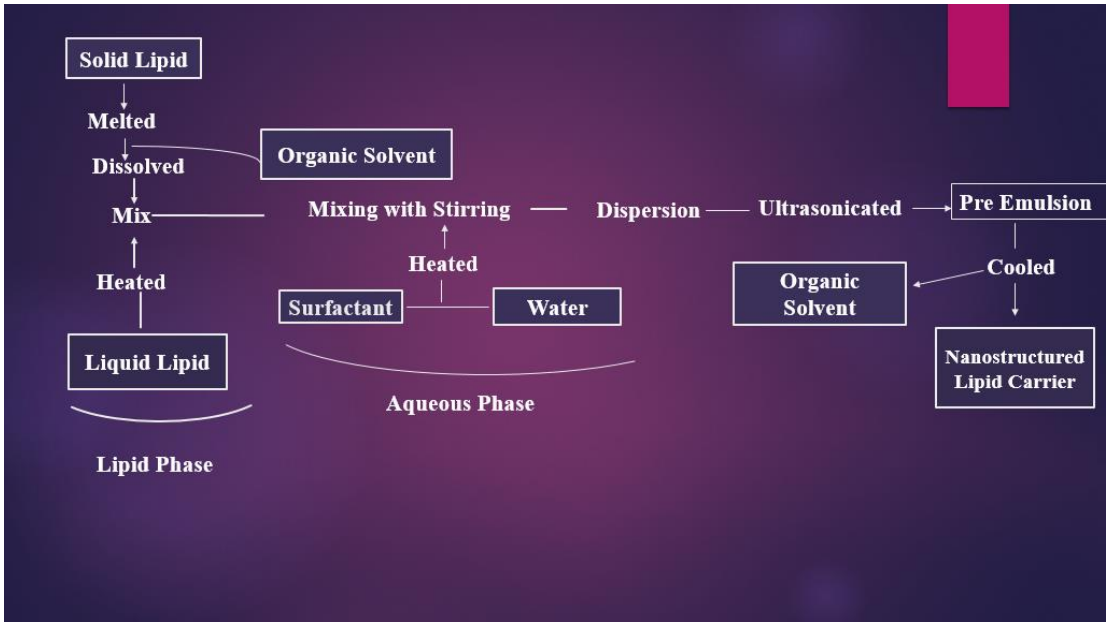

Fig. (6). Solvent diffusion and evaporation technique.

11.**6. Hot melt extrusion technique:** The hot melt extrusion technique involves feeding raw materials into a barrel, followed by sonication to obtain NLCs. In this process, a mixture of the drug and solid lipid is introduced into the extruder barrel using a volumetric feeder. Liquid lipid and aqueous solutions are then added through a peristaltic pump at the extrusion temperature. The mixture is extruded at the component's melt temperature to form a pre-emulsion. The resulting hot pre-emulsion is further sonicated to reduce the NLC particle size. Fig. [7] shows the steps to prepare NLC by hot melt extrusion technique.

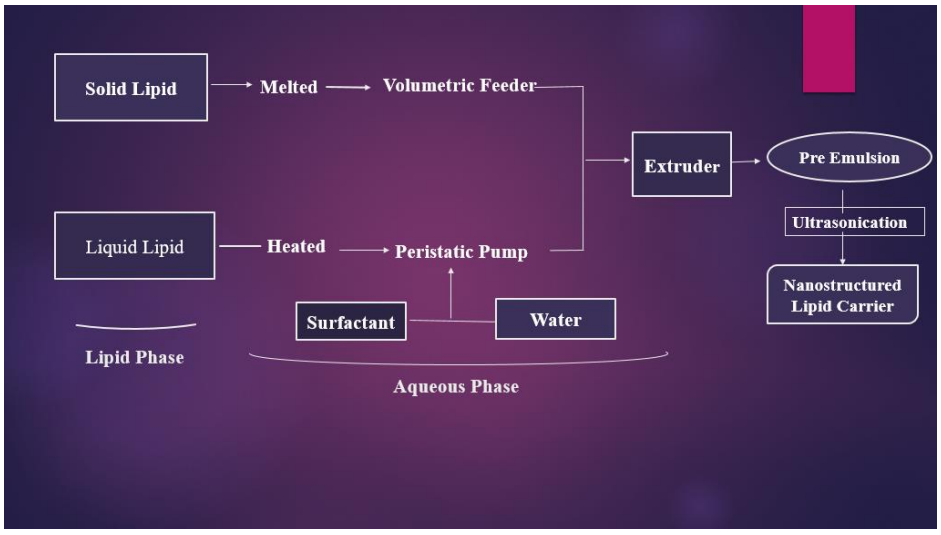

Fig. (7). Hot melt extrusion technique.

11.7. Solvent injection technique: In this technique, the lipid phase is dissolved in a water-miscible solvent or a mixture of solvents with the help of heat to melt the solid lipid. The resulting organic phase is then rapidly injected into an aqueous phase containing a surfactant or buffer solution while stirring continuously. As the solvent diffuses, lipid precipitation occurs, leading to the formation of lipid nanocarriers. The particle size is influenced by the rate of solvent diffusion and the content of the emulsifier. Fig. [8] shows steps to prepare NLC by hot melt extrusion technique.

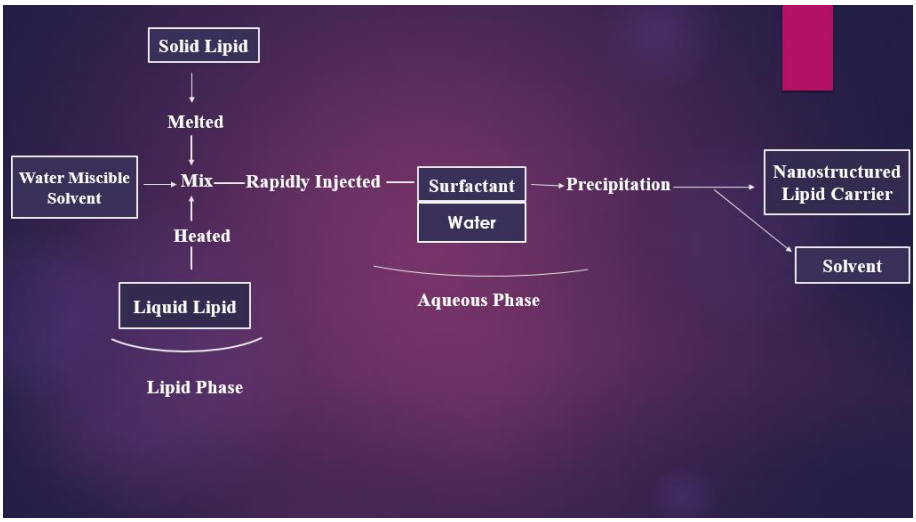

Fig. (8). Solvent injection technique.

Development of Sunscreen: The development of sunscreens demands a comprehensive understanding of both the skin's anatomy and physiology, as well as the physical and chemical properties of the ingredients intended for the formulation. The stability of organic compounds and excipients must be carefully evaluated, as some may become unstable when exposed to UV radiation. In contrast, inorganic sunscreens typically pose fewer stability challenges and exhibit lower toxicity. Additionally, the product's aesthetic appeal is crucial in ensuring consumer satisfaction and encouraging consistent usage.[37]

CONCLUSION

In this study we embarked on NLCs considerably improve sunscreen efficacy by improving stability, controlled release, and skin penetration, resulting in improved UV protection. These carriers represent a viable way to creating more effective, stable, and skin-friendly sunscreen compositions with minimum discomfort.

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