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Review article°

RECENT NANO FORMS ON TOPICAL DELIVERY WITH ESSENTIAL OIL AND SYNTHETIC DRUGS: A COMPREHENSIVE REVIEW.

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Abstract:
Nanotechnology has revolutionized topical drug delivery by improving the penetration, stability, and controlled release of therapeutic retailers. Conventional topical formulations, which include gels and lotions, often have troubles with inconsistent drug release, low bioavailability, and bad skin penetration. These restrictions are addressed by the manner of nanodelivery systems, which encompass tailored shipping, expanded penetration, and higher drug encapsulation. Examples of these systems are nanoparticles, nanoemulsions, and nanogels. This evaluation examines current tendencies in topical nanodelivery systems with an emphasis on artificial and vital oils. Nanocarriers assist artificial oils that are regularly employed for their emollient qualities by improving balance and penetration. Nanotechnology enhances the healing overall performance of essential oils, which may be prized for antibacterial and anti-inflammatory houses. It also shields the oils from degradation and promotes deeper pores and skin absorption. The paper also emphasizes new tendencies in hybrid structures and smart nanocarriers that provide extra advantageous biocompatibility and on-call for drug release. These trends maintain terrific promise for better restoration effects and patient compliance in topical treatment delivery. The problems and ability paths for Nanodelivery device improvement are protected within the paper's end, with a focus on the need for further research and clinical translation.

Key words: Nanotechnology Nano emulsions, emulgel, stratum corneum,skin permeation ,anti-inflammatory, topical therapy, essential oils.

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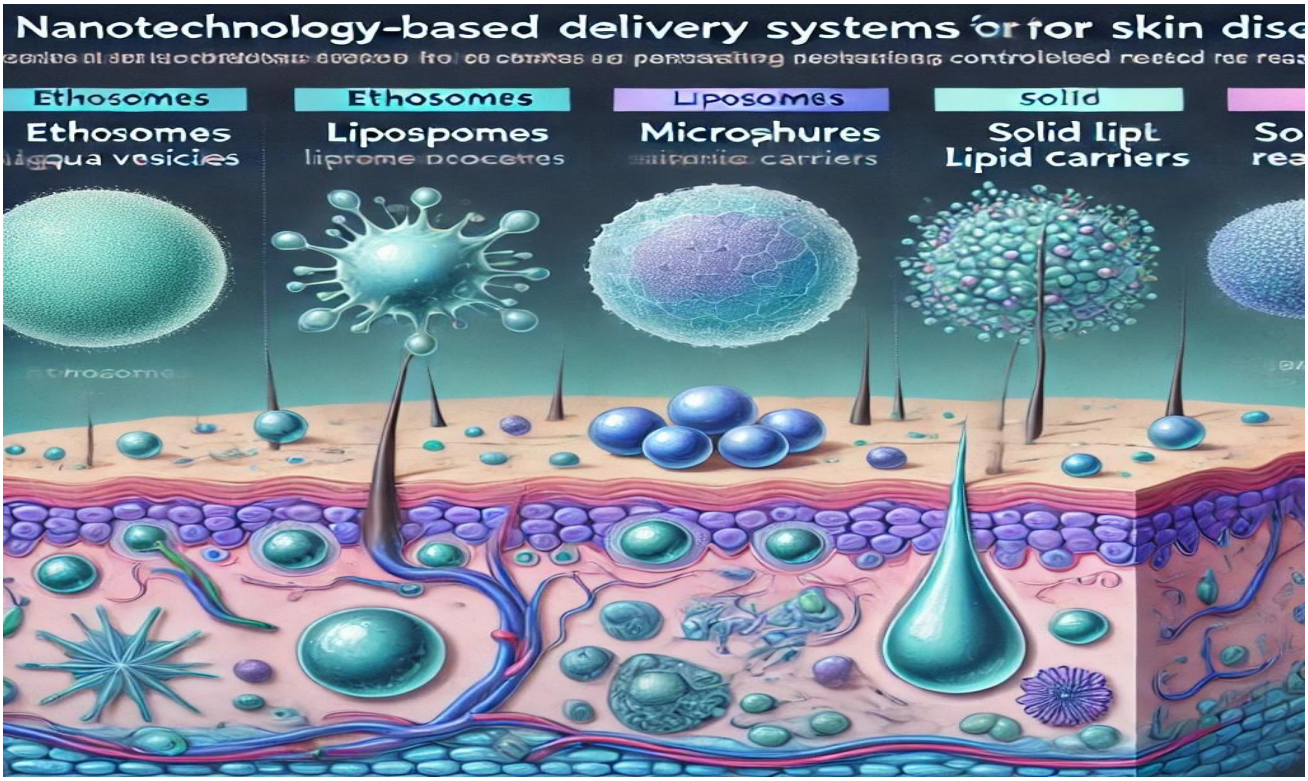


Graphical abstract

1.**Introduction**

The field of healthcare is undergoing a dramatic transition driven by breakthroughs in science and technology never seen before this is simply called Innovation driven health care transformation. The diagnosis, treatment, and prevention of disease are being revolutionized by fields like artificial intelligence and nanotechnology[1]. This article examines novel findings that are revolutionizing healthcare delivery by improving patient outcomes and changing medical practices. Expecting even more dramatic developments that will completely transform how healthcare is used and accessed as research advances. Improving Topical Treatment Efficacy is more important than ever to increase the effectiveness of topical therapies[2] Conventional formulations—such as lotions, ointments, and gels—have long been used to treat a range of skin issues and enable the skin to absorb medication[3] But these traditional approaches frequently face major obstacles, such as poor drug release patterns, low bioavailability, and insufficient skin penetration. These restrictions may seriously impair these treatments therapeutic effects[4].

Nano delivery Systems Promise Novel approaches to address these issues include the use of nanoparticles, Nano emulsions, and nanogels in innovative nano delivery systems[5]. These cutting-edge technologies allow for regulated mechanisms in addition to improving medication encapsulation and stability. These delivery technologies greatly increase the capacity of active substances to reach deeper layers by taking advantage of their nanoscale features.layers of the skin, offering long-term medical advantages[6]. Researchers are actively looking into novel approaches to topical skin delivery, including the use of essential oils and other herbal remedies, with the goal of enhancing patient well-being[7].Nano-Based Formulations' Function Creating essential oil formulations based on nanotechnology, such as those with nigella seeds, avocado oil, tea tree, vetiver, ginger, and garlic oils, is one possible approach. These compositions are intended to improve stability, effectively permeate the skin, and work in conjunction with traditional treatments—particularly for patients that are resistant to them[8-10]. Choosing the right kind of nano-system is essential for the best possible contact with the skin. For example: Polymer .when smaller than 100 nm, these particles are useful in treating inflammatory skin conditions. Lipid Systems Drug penetration through the skin is improved by lipid Nano emulsions and nano-capsules ointments, and gels, include variable drug release, limited penetration, through the stratum corneum, and stability issues over time[11].Larger molecules and hydrophilic medications frequently cause these systems to malfunction, producing uneven treatment outcomes Contemporary

developments in nanotechnology augment medication delivery through targeted delivery, controlled release. improved penetration, and increased stability of formulations[12]. Topical medicines have a promising future to nanocarriers, which can efficiently deliver medications deeper into the skin while limiting side effects when compared to standard methods, traditional drug delivery has greatly evolved a way to nano delivery structures, which offer advanced efficacy, balance, and targeted delivery. By encapsulating lively materials in nanoparticles, Nano emulsions, and nanogels, these techniques allow more suitable penetration through the stratum corneum of the skin and controlled launch on the goal place[13] Fig 1

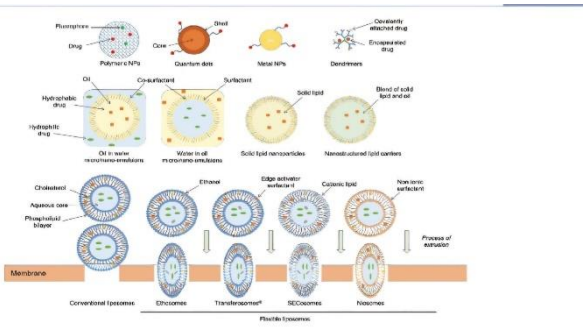


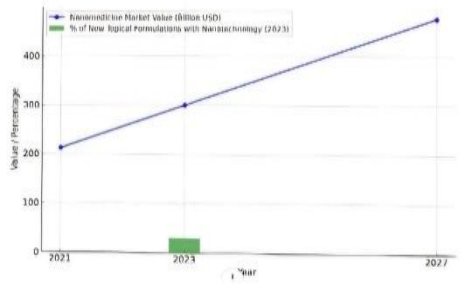
Figure 1: Nano delivery systems for topical and transdermal drug delivery

2.**Need of the study:**

According to a study in Advanced Drug Delivery Reviews, as compared to standard formulations, nanoparticle-based systems can beautify the amount of active chemicals that penetrate the skin by using up to ten instances. Solid lipid nanoparticles (SLNs), for example, had been tested to boost the bioavailability of poorly soluble medicines utilizing 50–80%. Furthermore, it has been found that the small droplet sizes of nanoemulsions (typically 20-200 nm) decorate the stableness and effectiveness of unstable vital oils. Data shows that the antimicrobial pastime of formulations using tea tree oil nanoemulsions became 60% better than that of widespread emulsions [14].

2.1:Future market

The growing use of nanodelivery systems in topical applications is highlighted using marketplace facts. With a compound annual boom rate (CAGR) of 12.5%, the worldwide market for nanomedicine is expected to attain $475 billion by 2027 from its anticipated $212 billion in 2021. The increasing call for revolutionary skin care products is riding the speedy growth of the marketplace quarter committed to dermatology and nanotechnology.



According to estimates, around 30% of all newly advanced topical formulations in 2023 included naotechnology of a few kind[15] Fig2.

Fig 2:Growth rate in the future market.

3.Mechanisms of Action

Drug administration via the skin is advanced via nanodelivery systems because they improve penetration and modify the release of lively components. Because of their small size, nanoparticles, and nanostructures can get beyond the stratum corneum, which is the principle impediment to remedy absorption. Moreover, medicinal drugs may be released from nanocarriers underneath controlled situations and guarded against degradation, ensuring lengthy-lasting healing benefits[16].

3.1Skin Penetration and Absorption: are several methods by which nanoparticles can enter the skin, such as follicular (via hair follicles), transcellular (through cells), and intercellular (between cells). Drug absorption is improved through their powerful interplay with skin cells, which is made viable with the aid of their small length and large floor vicinity.[17-19]

3.2 Physiology of skin: Skin is typically the first line of defense against internal imbalances and is a reflection of one's health and well-being[20]. Comprehending the diverse functions of skin and its constituent parts is crucial for acknowledging not just its physiological duties but also its consequences in domains like dermatology, cosmetics, and overall health. This investigation explores the complexities of the skin and its components, shedding light on the relationship between form and function in this essential organ.[21].

3.3.Skin and its layers: The epidermis,dermis and hypodermis are the three main layers that make up the entire structure of human skin. Epidermis

- Stratum Corneum:The outermost layer that acts as a shield against environmental damage, made up of dead keratinocytes.
- Stratum Lucidum:Only found in thick skin (soles and palms), providing extra defense.
- Stratum Granulosum:Consists of keratinocytes that start to aggregate keratin granules and lose their nuclei.
- Stratum Spinosum:Provides elasticity and strength; desmosome connections give cells their spiny appearance.
- Stratum Basale: The lowest layer, where mitosis produces new keratinocytes.
- Dermis the Papillary Layer:Blood vessels and sensory receptors are found in this superficial layer of loose connective tissue.
- Reticular Layer: Stronger and denser layer that contains sweat glands, bigger blood vessels, and hair follicles.
- Hypodermis: (Layer Subcutaneous) Made up of connective tissue and fat, it stores and insulates the body[22-24] .Fig 3

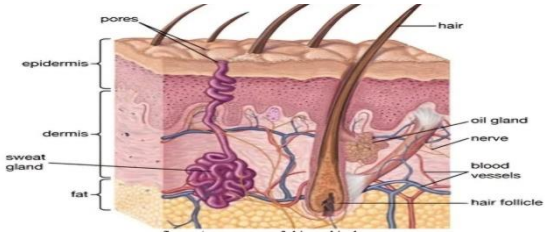


Fig3:Skin and its layers

4.Novel Advances and Emerging Trends: Topical drug delivery (TDD) is a technique that allows for the localized treatment of a variety of skin disorders, including acne, psoriasis, and eczema. It involves applying drugs directly to the skin. This path has historical roots in prehistoric times, when salves and ointments were widely Lipophilic compounds that are smaller have an easier time penetrating. A crucial development in the nanodelivery era is represented through clever delivery (TDD). These devices can deliver medications at a suitable time and place in response to environmental cues inclusive of pH, temperature, and light [25]. Fig 4

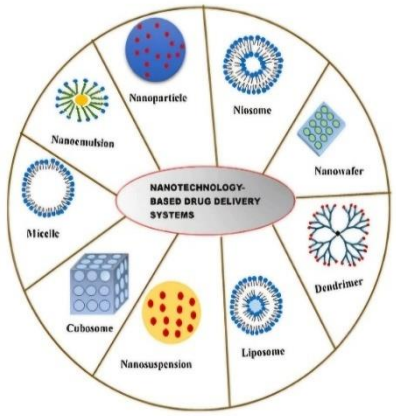


Figure 4:Nanotechnology and nano forms

4.1 Types of skin disorders for TDD:

A common skin condition that affects the face and back, acne is brought on by Propionibacterium acnes colonization, elevated testosterone levels, pro-inflammatory cytokines, and aberrant sebaceous gland keratinization that irritates the skin. The development of novel medication delivery systems to improve absorption and lessen adverse effects has been prompted by the fact that traditional topical Ftherapies frequently produce skin irritation and insufficient responses. Atopic dermatitis, often known as eczema, is a chronic skin illness characterized by extreme redness, swelling, itching, and weeping. It is believed to be caused by a confluence of immunological, environmental, and hereditary factors. The prognosis for melanoma, a dangerous skin cancer that starts in the melanocytes, varies according to the stage at which it develops, however newer forms of treatment like immunotherapy are improving it both vitiligo and psoriasis are complex skin conditions. Psoriasis is a long-term inflammatory disease that causes raised, scaly areas on the knees, elbows, trunk, and scalp. It is characterized by inflammation and rapid skin cell turnover. Although the precise origin is uncertain, immunological dysfunction and genetic factors are thought to be involved. On the other hand, vitiligo, which results from the loss of melanocytes, appears as smooth, chalky white areas on the skin. The depigmentation is caused by a complicated interaction between triggers like as stress or trauma and autoimmune disorders.

Although there are a number of therapies available for these illnesses, not everyone will benefit from them[26-29].

4.2 Nano forms for TDD

Nanostructures offer a promising approach for drug delivery, providing benefits such as enhanced bioavailability, targeted delivery, and reduced toxicity. Nano emulsions, dendrimers, liposomes, nanoemulgels, niosomes, ethosomes, solid lipid nanoparticles, and micellar nanoparticles are among the various nanostructures being explored for this purpose. Each has unique advantages, including improved stability, controlled release, and biocompatibility. By carefully selecting the appropriate nanostructure, researchers can optimize drug delivery and improve [30-33] Table :1

Table- 1 Nano forms with synthetic drugs

Acne	Utilizing reverse phase evaporation methods and incorporating Cryptotanshinone (CPT), the liposomal hydrogel (3DP-NH) was created for zit	Liposome
	a hydrogel using an isotretinoin- and erythromycin-encapsulated micro emulsion.(alam etal)	Nano model of Micro emulsion
	topical liposomes of encapsulated doxycycline Kashani-Asadi-Jafari etal	Form of nano (Liposomes.)
	Ethosomal gel using Carbopol and karanjin was entrapped as ethosomes with carbapol (Ansari et al)	Nano model ethosomes.
	hexyl-aminolevulinate (HA) loaded using photo dynamic technique potential.	Ethosomes the nano form.
atopic dermatitis	Topically delivered as nano capsule Cephalosporin A is Example	nano capsule
	(Almawash et al) combo of and fluticasone propionate in micro emulsion with levocetirizine di hydrochloride	microemulsion
	anol and phosphatidylcholine to form ethosomes.	ethosomes
	film-hydration technique used to prepare nano forms with cyanocobalamine.	Ethosomes, liposomes, transferosomes
	formulations loaded with anthralin, ethosomal and liposomal are prepared.	Ethosomes and liposomes
	(repalliet et al) SLN Is loaded with apremilast using hydro gel, hot emulsification and size reduction techniques	SLN
	clobetasol propion+ (CP) embedded Nano sponges were fabricated using hydrogels.	Nano sponge
	metformin were prepared by thin-film hydration technology. (jinabi kordi)	Liposomes
Wound repair and infection	liposomal formulation with pentoxifylline (PXT)	Niosomes.
Psoriasis	Carbopol liposomal gel, enloaded with cyclosporin suspension carbopol form (pandey et al)	NLC
	Arbutin loaded niosomes by ultra sonicated technique (radmark and coworkers)	
Psoriasis	nicotinamide (NIC) and methotrexate (MTX)by , ethano injection method coencapsulated	NLC
	NLCs loaded with dithranolin gel base(Priya darsini sathe et al)	NLC
	F Butenafine HCl(sp gondhkaret et al) fabricated into NLCs	NLC
Skincancer cell	Topical gel ethosomes filled with brucine based on HPMC. (ismailet al)	Ethosomes
Psoriasis	Thymoquinone loaded as ethosomes Psoriasis lesion and increases ortho keratosis.	Ethosomes
	Curcumin longa Nano particles RRR tocopheryl succinate grafted poly lysine conjugate (maoet al)	Nanoparticles

4.3 .Nature and its importance in TDD:

Many therapeutic plants that are used in the pharmaceutical business and as medicines are gifts from nature. Plants have been utilized by humans to treat common illnesses since ancient times, and some of these traditional remedies have persisted throughout history. Nowadays, folk medicine—which is mostly based on plants enjoys a respectable standing, particularly in developing nations..People have utilized plants for hundreds of years. Furthermore, the chemical diversity that arises from the evolution of secondary plant metabolites may match or even surpass that of commonly used pharmaceuticals. In addition to the health advantages derived from vitamins and minerals, naturally occurring substances referred to as phytochemicals are well recognized for their benefits[34-36].

Ayurveda, an age-old medical profession currently enjoying a revival, is arguably the most advanced and all-encompassing approach to treatment that humanity has ever seen. The fact that even in developing nations, over 35% of prescribed medications come from plants and 50% from natural sources highlights the significance of medicinal plants. Essential oils derived from numerous fragrant plants have been utilized for medical, religious, and aesthetic purposes. Essential oils are part of medicinal plants that become important in agricultural products volatile properties. . These herbal products are often used as additives in food, beverages, perfumes and cosmetic and medical conditions[37,38].

Tea tree oil, is derived from the leaves of the Australian Melaleuca alternifolia It contains various compounds, notably terpinen-4-ol, which provide antibacterial, antifungal, and antioxidant properties, aiding in inflammation reduction and healing. However, it may cause skin irritation or allergic reactions in some individuals[39].Nigella sativa, known as black cumin, contains bioactive compounds like thymoquinone and is used traditionally for various ailments, including inflammation and skin conditions. Bergamot oil, extracted from Citrus bergamia offers anti-inflammatory benefits and is used in aromatherapy. Curcuma longa, containing curcumin, is benefits in skin and heart too[40-42] **Table – 2**

Table - 2: Novel Drug Delivery With Essential Oils.

atopic dermatitis	using ultrasonic emulsification technique nano emulsions are encapsulated with (kildaci et al.) of linseed lso, evaluation by in vitro and in silico	nano form
	ethosomal cream was formulated by tea tree oil.(kumar and co workers)	Ethosomes
acne	azelaic acid + tea tree oil loaded as cosolvent using techniques of solvent injection .	ethosomes
Skin cancer	5-fluorouracil (5-FU) is fabricated into microsome	microsome
Fungal infection	Paclitaxel additional with camptothecin Skin cane	Dendrimers
	Miconazole and antimicrobial agent clotrimazole topicallyas dendrimer's	Dendrimers
Ocular, glaucoma	PAMAM enhance the ocular bioavailability of the medication.	dendrimers.
Melanoma with essential oil	B16F10 cell model THC tetra hydro curcumin is loaded.	Nano emulsion
Psoriasis	Optimized with ginger oikliposome formulation	Liposomes
	Curcumin and ibrutinib were encapsulated w(jain & team.)	Liposomes
Vitiligo	Berberine (BRB) oil loaded into hyalurosome (elhoulmoushy)	Ethosomes
	Photodynamic therapy With oleyl alcohol loaded with 8-MOP-3,8 methoxypsoralen	Ethosomes, hyalurosome
Fungal skin infections	Loaded with clove oil micro some is fabricated.	Microsome
	Essential ,+cinnamon +oregano essential oils and anti fungal l agent fluconazole e trapped	a
Psoriasis	A nano emulsion of nutmeg and coconut oil, along with carbochol1%. Cyclosporine.	Nanoemulsions
Chronic skin inflammation	Piperine (longumine)made from alginate and chitosan	Nanoemulsions

Anti ageing	embedded with melatonin in elastic mode	Liposomes
Rubrus fungus	Liposome are mixed with tea tree oil and olive oil.	liposome
Anti pigmentation and dark spots Whitening the skin and removing dark scars and blotches	essential oil selected specifically Lemon and grapefruit essential oil incorporated into nano forms .	Niosome
Anti pigmentation and dark spots Whitening the skin and removing dark scars and blotches.	Curcumin polyethylene glycol succincte, d-α-tocopherol acid and (etal) glycyrrhetinic acid	Ethosomes
Anti inflammatory, keratolytic, increases skin hydration.	Olive oil and calcipotriol.	NLC
10%herbal ointment 12 weeks reduce PASI	methotrexate +olive oil into nano emulsions	Nanoemulsions
24h applications decreases irritation	Propyl alcohol and isopropyl myristirate.	Nanoemulsions
Reduces inflammation, reduces erythema.	nanoform to incorporate propionate. clobesterol	Nanoemulsions
	berberine chloride dihydrate (BCD)& added into carbochol solution for ethosomes (srivatsava)	Ethosome
	palmarosa non encapsulated into NLC(Denise teimi Uchida)	
	INLC topical gel of curcumin along with ibrutinib(Harsha) (jainetal)	
Psoriasis	Nigella sativa(black cumin) :Black cumin	Ethosomes
Analgesic	Eucalyptus globulus essential oil is loaded as smaller micelle	micelles
Topical cream	solubilized aqueous pluronic P85 micellar systems Lavender oil	
Imiquimodinduced psoriasis,higherdrug permeation and accumulation in the skin	Capsicain encapsulated	NLC and SLN(nano structured lipd carrier and solid lipid nano particles)

5.Clinical Translation

A variety of limitations need to be triumph over to translate nanodelivery technology from the lab to medical settings, including medical validation, safety assessment, and regulatory approval.

5.1Regulatory Hurdles: Since the sector of nanomedicine regulation continues to grow, clean policies must be created to address the precise problems provided through nanocarriers. Before approving a nanomedicine, regulatory bodies just like the FDA and EMA demand considerable data on its satisfaction, protection, and efficacy. Evaluating the possibility of toxicity, lengthy-term impacts, and interactions with biological systems are all included in this. Creating standardized strategies to assess those parameters is essential to ensuring that nanodelivery systems are successfully carried out in clinical settings [43,44]

5.2Safety Evaluation: Because of their small length and unique characteristics, nanoparticles may also interact abruptly with organic systems, which raises questions about their protection. Certain nanoparticles, for example, can cross the skin's protecting layer and input the bloodstream, which could have terrible effects. To verify the safety of these systems over a prolonged period is necessary, especially considering the possibility of pores and skin irritation, allergies, or other aspect effects. Safe usage of nanocarriers in healing settings calls for them to be non-toxic, biocompatible, and no longer gather in the body[45,46].

5.3Clinical Validation: Although preclinical studies have proven the promise of nanodelivery systems, human scientific validation is required to verify the structures' effectiveness and safety. This involves appearing in medical trials to gauge how properly nanocarriers work as topical medicinal drug delivery automobiles and to gauge how they affect patient outcomes. These studies should be planned to provide solid evidence that, in terms of patient compliance, safety, and efficacy, nano delivery strategies are superior to conventional formulations[47,48]

6.Technical challenges:

Despite the benefits of topical medication delivery using nanotechnology for treating skin illnesses, there are problems with clinical translation and commercialization of nanomedicine. Obstacles to the practical application of nanomedicine include the high cost, reproducibility problems, scale constraints, and stability of produced nanoparticles. It is challenging to comply with characterization and evaluation protocols, clinical efficacy testing, safety assessments, and regulatory requirements for topical drug manufacturing. Understanding the physicochemical characteristics of nanocarriers in the dermal distribution of medicinal medicines is contingent upon interdisciplinary collaborations[49,50].

Although nano delivery technologies display high-quality promise, some technical issues still want to be resolved earlier than their entire benefits in topical programs can be found.

6.1Manufacturing Complexities: Producing nanocarriers on a massive scale offers several issues, mainly in terms of consistency and pleasantness. The manufacturing of nanoparticles consists of complicated techniques that require careful control to gain consistency, such as ground trade and size control. One most important obstacles that must be addressed is scaling up these approaches without sacrificing the desired properties of the nanocarriers[51,52].

6.2 Stability and Scalability: Stability troubles can arise in nano delivery structures, especially in those that use complicated formulations and hybrid nanocarriers or Nano emulsions. These structures' lengthy-time period balance can be impacted by using factors such as aggregation, sedimentation, and section separation, which could bring about reduced efficacy. For nanocarriers to be successful, stability in the course of the garage and alertness has to be guaranteed. Commercial viability also relies upon developing scalable production methods that can yield reliable and consistent formulations [53].

7.Conclusions

In conclusion, the use of nanotechnology in dermatology has the potential to revolutionize the treatment of skin disorders. However, there is more to experiment regarding topical application of nanotechnologies as a treatment chosen for skin diseases. Future research should continue to transition from preclinical to trials of clinical research l to better understand the real impact of these nano-carriers. Finding the right nano-carrier for each skin disorder will be an exciting future challenge that will help enhance the benefits of nanotechnology. It is proven that based carriers offer a promising alternative to conventional therapy and can change safety and effectiveness in the treatment of disorders of skin[54].

The perfect choices of nano-system is very crucial and important for effective interaction with the skin. Polymeric nanoparticles, particularly those under 100 nm with a charge, are deemed suitable for skin disorders of inflammation due to their selective mediators in inflamed skin. On the other hand, lipid nano forms of emulsions and capsule aid in enhanced permeation trans dermally across different skin layers, in encapsulate making them a potential option for topical therapy.

The Nevertheless, further clinical and pre clinical trials are necessary to evaluate the potential activity and safety of these natural agents thoroughly and the new advancements in their formulations, such as Solid lipid , nano structured LCs, and Nano emulsions. More work on guide lines, regulatory conditions quality control must be established to standardize herbal medicine, ensuring its efficacy and safety for a large population. In total advancements of nanotechnology delivery systems of botanical agents and oils against psoriasis and other skin disorders. Hold considerable promise but require further investigation and regulatory support to achieve maximum benefit[55].

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