Marigold (*Tagetes* spp.) as a Hypoallergenic Botanical Resource

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Abstract

Marigold (*Tagetes* spp.) is widely cultivated as both an ornamental flower and a medicinal herb, with a long history of use in traditional healing systems, especially Ayurveda. It is appreciated for its cooling nature and its ability to ease inflammation, combat microbial growth, and calm irritated tissues. In Ayurvedic practice, marigold is believed to help restore equilibrium among Vata, Pitta, and Kapha by alleviating excess heat and inflammatory disturbances. Traditional remedies prepared from its flowers and leaves—such as decoctions, infused oils, poultices, and topical herbal formulations—have been applied for skin problems, mild eye discomfort, digestive complaints, and wound management. These longstanding applications suggest its possible usefulness in strengthening the skin barrier and reducing hypersensitivity responses, supporting its consideration as a plant-based hypoallergenic option. Scientific investigations, particularly on *Tagetes erecta* (African marigold), reveal a rich composition of biologically active compounds, including carotenoids like lutein, flavonoids, and other antioxidant molecules. These constituents exhibit antimicrobial, antifungal, anti-inflammatory, hepatoprotective, and anticoagulant properties. The antioxidant activity may help counteract oxidative stress and inflammatory pathways that are often linked to allergic reactions. Moreover, its gently bitter and astringent qualities are traditionally associated with soothing inflamed tissues and promoting balanced immune function. Although traditional knowledge and preliminary research indicate therapeutic promise, comprehensive clinical studies confirming its hypoallergenic benefits are still insufficient. Marigold is typically regarded as safe when used in appropriate amounts; however, people sensitive to plants in the Asteraceae family may experience allergic reactions, and special caution is advised for pregnant women and other sensitive groups. Overall, marigold remains a multifaceted botanical with notable ornamental and medicinal importance, deserving further scientific evaluation for its role in modern hypoallergenic therapy.

1. Introduction

Marigold (*Tagetes* spp.) has long been utilized in traditional medicine and contemporary herbal practice for its calming, antimicrobial, and anti-inflammatory actions. Within Ayurvedic literature, it is described as having a cooling potency that helps pacify imbalances of Vata, Pitta, and Kapha by alleviating excess heat, irritation, and inflammatory disturbances in the body[1]. Historically, various formulations such as decoctions, infused oils, poultices, and topical herbal applications have been employed to manage dermatological conditions, minor eye complaints, digestive discomfort, and wound care. These traditional applications indicate its possible value in moderating hypersensitivity reactions and strengthening the skin's protective barrier. While ornamental marigold varieties have shown promise in laboratory and traditional settings,

comprehensive clinical validation remains limited[2]. The plant is generally regarded as safe when used appropriately; however, individuals sensitive to members of the Asteraceae family may experience contact dermatitis or allergic reactions. Consequently, careful use is recommended for pregnant women and those with known plant sensitivities[2]. Among the different species, *Tagetes erecta* (African marigold) is especially recognized for its diverse phytochemical profile, including carotenoids, flavonoids, and other biologically active constituents[3]. Compounds such as lutein and related antioxidants are associated with antimicrobial, antifungal, hepatoprotective, and anticoagulant effects. The antioxidant capacity of these constituents may contribute to reduced oxidative stress and inflammatory responses, mechanisms that are relevant in allergic and hypersensitivity conditions. In traditional practice, its mildly bitter and astringent characteristics are considered beneficial for soothing inflamed tissues and supporting immune balance.Beyond its medicinal attributes, marigold is a hardy horticultural species that flourishes in temperate climates with relatively low maintenance requirements[4]. Its combined ornamental, nutritional, and therapeutic significance underscores its potential as a natural hypoallergenic agent. Nevertheless, further well-designed clinical investigations are required to confirm its safety profile and efficacy in allergy-related applications within modern healthcare systems.

2. What is hypo allergen?

Allergen-specific immunotherapy (AIT) is the only established treatment that can modify the natural course of allergic disease and provide prolonged symptom relief by administering gradually increasing amounts of allergen extracts. Despite its effectiveness, traditional AIT carries the possibility of immunoglobulin E (IgE)-mediated side effects. To improve its safety and therapeutic efficiency, researchers have focused on developing hypoallergens—engineered allergen variants that display reduced IgE-binding ability while maintaining T-lymphocyte (T-cell) stimulatory capacity. However, designing such modified allergens is difficult because predicting structural alterations that lower allergenicity without diminishing immune activation remains complex. Directed molecular evolution offers a powerful alternative strategy. Techniques such as deoxyribonucleic acid (DNA) shuffling allow the creation of diverse protein variants with enhanced or modified biological characteristics, even in the absence of detailed knowledge about their structure–function relationships. In this study, multigene DNA shuffling was carried out using three genes encoding dust mite allergens, generating a broad library of recombinant shuffled variants. These proteins were expressed and systematically evaluated for their ability to bind IgE antibodies. Screening identified nine variants with substantially decreased IgE-binding activity compared to the original allergens. Notably, two selected candidates preserved their capacity to activate allergen-specific T-cell responses and successfully stimulated the production of protective immunoglobulin G (IgG) antibodies in immunized mice. Overall, these findings demonstrate that directed molecular evolution is a promising and innovative approach for producing hypoallergenic allergen derivatives, potentially enhancing the safety and effectiveness of allergen-specific immunotherapy. The increase in allergic diseases has prompted the need for effective treatments, particularly targeting IgE-mediated allergies. The only long-lasting solution currently available is allergen-specific immunotherapy (ASIT), which

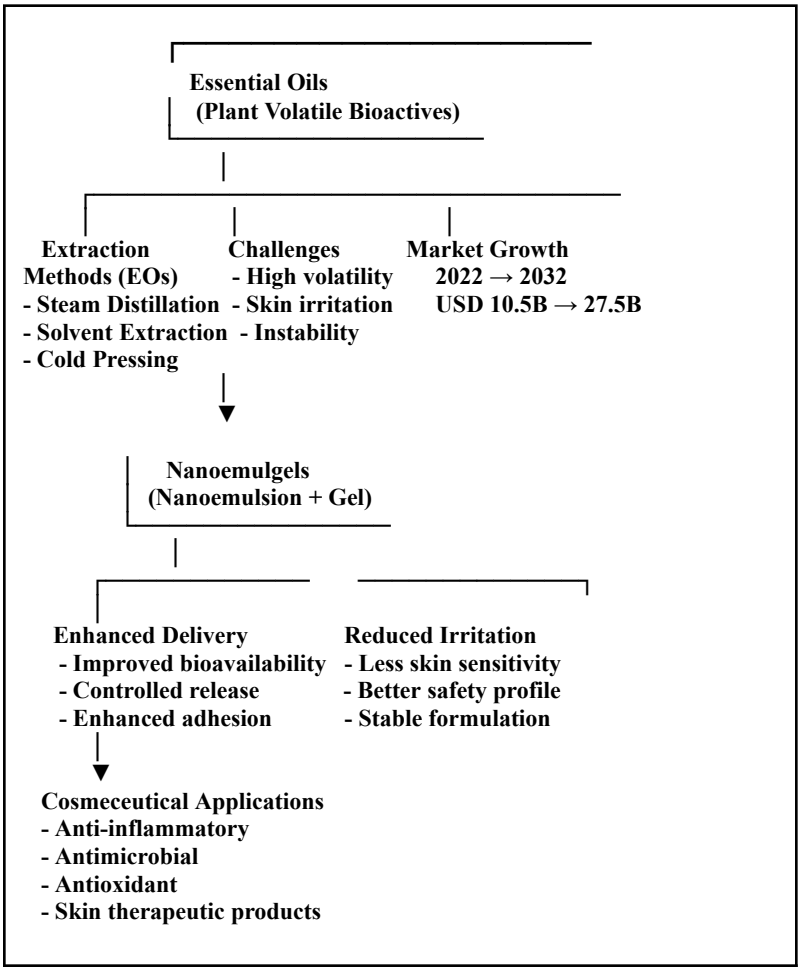
involves repeated allergen extract administration. However, this method poses risks of local and systemic side effects. To overcome these issues, hypoallergenic variants of allergens are being developed using recombinant techniques. Approaches include site-directed mutagenesis to disrupt IgE-binding sites, though challenges exist as mutations do not always guarantee reduced reactivity. Directed molecular evolution through DNA shuffling helps create hypoallergens without in-depth structural knowledge, allowing for the selection of proteins with desired properties from large libraries. The study involved the application of multigene recombination to allergens from dust mites, utilizing patient samples for genetic and immunological analysis, ultimately aiming to enhance the safety and efficacy of ASIT through hypoallergenic constructs.

Although the word "hypoallergenic" suggests that a product is less prone to trigger allergy reactions, it is not defined by any scientific or regulatory standards. Customers may be at danger as a result of businesses claiming hypoallergenicity without providing regulatory bodies with supporting evidence. Numerous products branded as hypoallergenic still contain allergens, according to studies. It is recommended that people be aware of their individual allergies, carefully review ingredient lists, and ask manufacturers for clarification on hypoallergenic claims. In the end, hypoallergenic products are not always safe for users, even though they may lessen the chance of allergies.[6]

3. Essential Oil Nanoemulgels

Essential oils (EOs) are highly concentrated, volatile, and hydrophobic substances obtained from different plant parts such as leaves, flowers, bark, and roots. They are widely utilized across industries including food processing, cosmetics, aromatherapy, and pharmaceutical formulations due to their aromatic and therapeutic properties. A significant proportion—nearly 90%—of essential oils are administered via topical or transdermal routes. However, their practical application is often limited by high volatility, chemical instability, and the possibility of skin sensitivity or irritation. To overcome these challenges, advanced delivery systems have been developed, particularly nanoemulgels. Nanoemulgels integrate nanoemulsion technology with a suitable gelling matrix, resulting in improved stability, enhanced skin adhesion, controlled release of active compounds, and reduced irritation potential. This formulation approach enhances the bioavailability of essential oil constituents while preserving their therapeutic effectiveness. Recent research highlights various extraction techniques for essential oils, such as steam distillation and solvent extraction, along with key formulation parameters that influence nanoemulgel preparation, including droplet size, surfactant concentration, and gel composition. These systems have demonstrated promising applications in cosmeceuticals, particularly for their anti-inflammatory, antimicrobial, and antioxidant effects. The global demand for essential oils continues to expand rapidly, reflecting a growing consumer shift toward natural and environmentally friendly products. Market projections estimate an increase from approximately USD 10.5 billion in 2022 to nearly USD 27.5 billion by 2032, underscoring their rising popularity and commercial significance across diverse sectors.[7]

Table No.3.1. Essentials oils and Nanoemulgel



4. Nanoemulgels for Enhanced Topical Drug Delivery

A comprehensive literature of nanoemulgels underscores its action as advanced topical delivery systems for lipophilic drugs with low solubility and reduced oral bioavailability. They enhance drug retention and control release by integrating oil-in-water nanoemulsions into a gel matrix, overcoming challenges of conventional dosage forms like variable absorption and first-pass metabolism. Additionally, nanoemulgels increases direct dermal administration, improving skin permeation and reducing gastrointestinal side effects. Their non-greasy application and low irritation also boost patient acceptance and adherence. The literature elaborates on formulation, preparation techniques, and evaluation parameters, highlighting their advantages in improving drug penetration and treatment process.[8]

5. Nanoemulgels as Advanced Drug Delivery System:

This discussion about nanoemulgels as an advanced delivery system for hydrophobic and poorly soluble drugs. By combining a nanoscale emulsion with a gel base, nanoemulgels improve drug stability, solubility, and bioavailability. It highlights key advantages such as controlled release, targeted delivery, and enhanced therapeutic effectiveness. Applications in dermatology, cosmetics, and pharmaceuticals are also addressed, along with future prospects for this promising technology. Oils such as flaxseed oil (FSO), papaya seed oil (PSO), and grape seed oil (GSO) have antioxidant effects and act as a barrier to stop water loss in the skin, which is a protective organ. This study uses a designed nanoemulgel to assess their antioxidant and skin-whitening properties. PSO was found to have the greatest oleic acid content (54.04%) when the oils' phenolic and flavonoid contents were examined. Every oil showed high antioxidant qualities and tyrosinase enzyme inhibition. The globule size and PDI of the optimized nanoemulsion were determined to be 181 nm and 0.292, respectively. For formulation optimization and efficacy assessment, more study is advised.[9] The epidermis, dermis, and hypodermis are the three layers that make up the skin, the biggest organ in the body. Each layer has a unique structure and function. The outermost layer of the epidermis is made up of several strata, including the stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum. Keratinocytes and melanocytes, which are necessary for pigmentation and protection, are found in these strata. Adipose tissue is found in the hypodermis, the lowest layer, whereas sweat glands, hair follicles, and blood vessels are found in the dermis, which supports the epidermis. The skin performs a variety of tasks, including as protecting the body from infections, controlling body temperature and water outflow, and boosting immunity. Its extensive functions highlight how important it is for preserving health and addressing environmental risks.[10]

6. Preparation of Nanoemulgel:

A nanoemulgel with 4% carrot seed oil was created in this work as a natural anti-aging and sunscreen. The physical stability, pH, globule size, and Sun Protection Factor (SPF) of three formulations made with Tween 80 and sorbitol as surfactants were assessed. For 12 weeks at room temperature, the nanoemulgel remained stable and showed a mean droplet size of 338.34 nm, staying in the nano size without phase separation. With an SPF of 20.28, it outperformed the emulgel, which had an SPF of 13.94. Skin study following treatment revealed decreases in wrinkles, spots, and pore size. According to the findings, the nanoemulgel formulation is superior to conventional emulgel preparations for sunscreen and skin anti-aging.[11] Work focused on the physical characterisation and in vivo evaluation of a feboxostat (FXT) loaded nanoemulgel (NEG) for transdermal distribution. High sheared homogenization was used to synthesize the NEG, which met USP criteria for optimal drug content, suitable pH, and outstanding thermodynamic stability. Important results include droplet diameters ranging from 148.6 nm to 498.3 nm across several formulations and a viscosity of 4587 cp. FXT showed strong anti-inflammatory action in rat models, and its in vitro drug release and ex-vivo

penetration rates were encouraging. The limited bioavailability and adverse effects of oral FXT therapy were addressed by the NEG formulation, which showed promise as a viable effective substitute.[12]

The study focuses on developing a nanoemulgel formulation for mupirocin (MUP), an effective topical antibiotic with limited skin permeability. By incorporating a pre-prepared MUP nanoemulsion into a Carbopol gel at a 1:1 ratio, the research aims to enhance MUP's rheological and physicochemical properties. The nanoemulgel formulations were characterized and evaluated for stability, viscosity, spreadability, skin permeation, and antibacterial effectiveness. Results indicated that while both formulations had lower skin permeability than a marketed control, they significantly improved local accumulation efficiency after 8 hours. Additionally, micro-CT imaging confirmed the deeper penetration of MUP into skin layers. Despite no substantial difference in antibacterial activity compared to the control, the nanoemulgels displayed advantages due to reduced mupirocin content, positioning them as promising carriers for targeting skin lesions requiring high drug deposition with lower permeability.[13] Numerous therapeutic molecules targeted at resolving health care issues have been developed in recent years as a result of notable advances in drug discovery. Nevertheless, more than half of these medications are classified as BSC class II/IV and have limited therapeutic use. Topical medication delivery has found success with nanotechnological methods, especially with nanoemulsion-based gels (nanoemulgels). By incorporating lipophilic medications into a gel base with finely dispersed oil droplets, this formulation improves drug absorption, particularly for lipophilic pharmaceuticals. This boosts skin absorption coefficients and targets particular areas while reducing systemic problems. Despite several disadvantages, nanoemulgel formulations are a potential option for the topical delivery of lipophilic medications due to their strong therapeutic safety, non-greasy texture, high patient tolerance, and ease of application.[14] Preparing and assessing the physical stability and in vitro SPF value of a sunscreen nanoemulgel with 4% grape seed oil and anisotriazine was the goal of the study. 2% Carbopol 940 gel was used to construct the formulations, which were then tested for stability over a 12-week period in a variety of settings. According to the results, the emulgel showed phase separation, but the nanoemulgel containing 3.2% anisotriazine was physically stable. The SPF values for the nanoemulgel (19.325), the emulgel (11.913), and the nanoemulgel without anisotriazine (11.169) showed that the nanoemulgel had better protective qualities. The nanoemulgel formulation's spherical droplet shape was shown using transmission electron microscopy. In comparison to the other formulations, the one containing grape seed oil and anisotriazine was generally more stable and had a higher SPF.[15] Hydrogels serve as an effective drug delivery system for topical wound healing applications, notable for their non-adhesiveness and moisture retention. This study focuses on developing a curcumin-loaded nanogel pharmaceutical product aimed at enhancing curcumin’s therapeutic efficacy for wound healing despite its limited solubility and skin penetration. A high-energy ultrasonic emulsification technique was used to create a nanoemulsion with a droplet size of 56.25 nm and low polydispersity, optimized through varying surfactant ratios. The final curcumin nanoemulgel, incorporated into a Carbopol® 940 hydrogel,

exhibited improved skin penetrability and thixotropic behavior compared to conventional formulations. In vivo studies confirmed significant wound healing efficacy, highlighting the potential of nanomedicine in improving biopharmaceutical properties of curcumin.[16]

7. Discussion

Research paper examines nanoemulgels as a drug delivery method, emphasizing how well they work to get around problems with hydrophobic or poorly soluble medications. While contrasting them with traditional emulgels, it talks about the benefits of nanoemulgels, including increased stability, controlled release, and enhanced solubility. The research looks at patent trends, preparation techniques, formulation strategies, and potential uses in dermatology, cosmetics, and medicines. To gather and evaluate pertinent data about nanoemulgels and their potential to enhance patient acceptability and target delivery, a thorough review of the literature was undertaken.[17]

8. Conclusion

Gelled emulsions that promote skin penetration and bioavailability make up Nanoemulgel, an efficient delivery strategy for lipophilic drugs. These systems are effective in treating diseases like psoriasis and rheumatoid arthritis because of their high medication loading and controllable drug release. Nanoemulgels are a promising way to administer hydrophobic drugs topically because of their composition, which permits improved permeability and extended drug release. Their formulation, component screening, and developments in pharmacokinetic and pharmacodynamic research .[18]

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