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Phyto-Constituents of Capsicum Based Nanoparticles for the Treatment of Psoriasis

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Abstract: Psoriasis is a lifelong, immune-mediated inflammatory skin condition clinically defined by excessive keratinocyte hyperproliferation, profound extravascular dermal angiogenesis, and heavy leukocyte infiltration through the layers of cutaneous tissue [1]. Conventional topical and systemic medications often exhibit severe adverse effects, low drug bioavailability, and significant physical effects to enhance transdermal drug penetration [2]. Nowadays, herbal bioactive components from Capsicum species primarily focused on capsaicinoids, carotenoids, and flavonoids have attracted tremendous medical interest as potential healing agents due to their potent anti-inflammatory, antioxidant, and anti-proliferative activities [3]. Although, their medical translation is significantly limited by high lipophilicity, severe local skin infection, and speedy systemic clearance [4]. Higher nanotechnology-primarily based delivery methods including strong lipid nanoparticles, polymeric nanogels, nano emulsions, steel/metallic-oxide green-synthesized nanoparticles offer a remarkable opportunity to cross these pharmacological roadblocks [5]. This exhaustive review offers an in-intensity, multi-faceted evaluation of Capsicum phytochemistry, the pathophysiological rationale for focus on psoriasis, higher components techniques, mechanistic opinions, and translational clinical prospects documented number one medical literature [6].

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I. INTRODUCTION

➢ *Advent and Epidemiology of Psoriasis*

Psoriasis is a common persistent inflammatory dermatosis with approximate 2% to 3% of the worldwide human population across different geographic and ethnic populations afflicted by a massive socioeconomic and mental burden induced by this condition in affected individuals [7]. Clinically, the condition is characterized by demarcated erythematous plaques protected via silvery white scales predominantly localized on extensor surfaces including elbows, knees, scalp, and lumbosacral region at the same time that frequently progresses to debilitating psoriatic arthritis in a huge proportion of patients [8]. The condition immunopathogenesis involves complex crosstalk between the innate and adaptive immune structures centrally orchestrated by the interleukin-23/T helper 17 (IL-23/Th17) inflammatory axis, dendritic cell activation, and tumour necrosis component-alpha (TNF-alpha) signalling networks [9]. This persistent inflammatory cascade stimulates odd keratinocyte hyperproliferation and notably shortens the epidermal turnover times from nearly 28 days to a few to 4 days ensuing in defective barrier function, parakeratosis, and extreme pruritus [10]. conventional healing regimens–including topical corticosteroids, vitamin D analogues, and anthralin–regularly fail to obtain sustained remission together with inducing neighbourhood detrimental effects including skin atrophy, telangiectasia, and tachyphylaxis [11]. Systemic interventions including methotrexate, cyclosporine, and focused biologic remedies bring extensive dangers of hepatotoxicity, nephrotoxicity, and systemic immunosuppression thereby limiting their clinical application in the long-term [12]. therefore, there is an urgent clinical vital to broaden localized, secure, and affected patient-compliant healing options [13]. Botanical phytochemicals have gained tremendous attention in complementary dermatology including multitargeted pharmacological moves and favourable protection profiles [14]. inside this area, the genus Capsicum holds a vital pharmacological function due to its attention of pungent phenolic amides and antioxidant secondary metabolites [15]. Topical capsaicin in dermatology has been studied extensively for its mechanism of motion and medical application [16]. Medicinal plants still a cornerstone in the remedy of chronic hyperproliferative skin issues [17]. Oxidative stress and antioxidant remedy play important roles in regaining redox balance in psoriatic lesions [18]. Vanilloid receptors and neurogenic regulatory pathways govern those biological activities including nearby efferent activities of capsaicin-touchy sensory nerve endings that modulate the skin neurogenic inflammation and vascular responsiveness [19].

➢ *Phytochemical Profile of Capsicum Species*

The genus Capsicum belonging to the family Solanaceae own some cultivated species together with Capsicum annuum, Capsicum frutescens, and Capsicum Chinese that have been selected and cultivated for hundreds of years in tropical and temperate regions [20]. The fruits are

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chemically very diverse containing a rich assortment of secondary metabolites such as capsaicinoids, carotenoids, flavonoids, and volatile aroma compounds displaying synergistic biological activities [21]. Capsaicinoids are Almohad's like phenolic amides synthesized only in the placental tissues of the genus Capsicum through the condensation of vanillyl amine and branched chain fatty acids [22]. The first and most abundant capsaicinoids is capsaicin (trans-8-methyl-N-vanillyl-6-nonenamide) accountable for nearly sixty nine% of total capsaicin content material and drives most of the people of its pharmacological activities [23]. Dihydrocapsaics in incorporates more less 22% of total capsaicinoids and has similar pungency and physiological potency in biological assays [24]. Minor congeners (such as nordihydrocapsaicin, homocapsaicin, and homodihydrocapsaicin) also modulate the overall biological profile and receptor affinity [25]. Carotenoids are responsible for the typical pink, orange, and yellow coloration of mature chili culmination. They act as important pigments during photosynthesis and ripening process of chili fruits [26]. Primary carotenoid materials consist of capsanthin, caps Rubin, beta-carotene, zeaxanthin, lutein, and cryptoxanthin that accumulate in chromoplasts at some point during fruit maturation [27]. These lipophilic pigments feature as strong organic antioxidants scavenging the reactive oxygen species (ROS) generated at some stage during psoriatic inflammatory cascades and protect the mobile membranes from destructive oxidative stresses [28]. Biological activities of chili peppers and their active components had been significantly classified across dietary and pharmacological literature [29]. Capsicum tissues include high contents of bioactive flavonoids (including quercetin, luteolin, apigenin, and kaempferol) and phenolic acids (which include ferulic acid, caffeic acid, and p-coumaric acid) [30]. These components exert synergistic suppression of inflammatory transcription factors significantly nuclear aspect kappa B (NF-kappaB) and cyclooxygenase-2 (COX-2) and thereby interrupt the inflammatory loop [31]. Phytochemical components and biological activities of the domesticated Capsicum species validate their therapeutic use in traditional and modern medicine [32].

- *Pathophysiological Cause for Capsicum Phytoconstituents in Psoriasis*

Healing logic of Capsicum bioactive use for management of psoriasis control is through direct neuro-immuno-cutaneous modulation and multi-targeted molecular signalling [33]. Psoriasis pathogenesis is driven mostly through immune dysregulation where there is a mediating role of aberrant T-cellular activation and dendritic cell crosstalk to promote sustained cutaneous inflammation [34]. Psoriasis as a systemic disease is driven by complicated cytokine network that maintains sustained reworking of tissues and system comorbidities [35]. Pathogenesis and clinical manifestations of psoriasis define striking epidermal alterations such as prominent acanthosis and inflammatory microabscesses [36]. Capsaicin acts as a selective agonist for temporary receptor ability vanilloid 1 (TRPV1) ion channels expressed on cutaneous sensory C-fibers and keratinocytes [37]. initial receptor activation results in burning and stinging clinical sensations that is followed by practical desensitization and depletion of substance P, calcitonin gene associated peptide (CGRP) and other neuropeptides that mediate neurogenic infection, pruritus and keratinocyte proliferation in psoriatic plaques [38]. Psoriasis immunopathology and clinical manifestations continue to confer therapeutic targets for management of neurogenic pathways [39]. Moreover, capsaicin and accompanying flavonoid fractions can suppress the pathological release of pro-inflammatory cytokines such as TNF-alpha, IL-6, IL-17, IL-22 and vascular endothelial increase factor (VEGF) [40]. Psoriasis medical shows and healing principles to management confer combination strategies to manipulate refractory plaque formation [41]. Pathophysiology, clinical presentation and treatment strategies guide modern dermatological care and personalized patient care [42]. Psoriasis control strategies define common medical care frameworks across major dermatological societies worldwide [43]. Psoriasis epidemiology, clinical functions and system treatments set up basic clinical standards against which new therapies may be compared [44]. Antioxidant characteristics of Capsicum extracts use in dermatological cutaneous inflammation confer mechanisms to mitigate oxidative tissue injury and reduce lipid peroxidation [45]. Antioxidant capacity and phenolic content levels in peppers are affected by maturity and species version during agricultural harvesting [46]. Variations in carotenoid and capsaicin contents in chili peppers affect raw material selection for pharmaceutical extraction [47]. Capsicum species possess powerful antioxidant and anti-inflammatory activities that rival synthetic pharmaceutical vendors [48]. Anti-inflammatory effects of capsaicinoids use in cutaneous models are well documented through reductions in oedema and leukocyte infiltration [49]. Effects of capsaicin use in lipid metabolism and inflammation confer mechanisms to highlight systemic metabolic interaction and therapeutic pleiotropy [50].

- *Barriers of Traditional Capsicum Formulations*

Not with standing their wonderful pharmacological homes, unfastened capsaicin and traditional crude extracts confront serious formula limitations that critically limit their clinical translation and affected person attractiveness [51]. Direct topical software of unformulated capsaicin commonly results in extreme burning, stinging, erythema, and pruritus, leading to profound affected person non-compliance and early remedy cessation [52]. Moreover, capsaicinoids have excessive lipophilicity (octanol-water partition coefficient log P approximating three.0) that hinders effective green partitioning throughout the hydrophilic stratum corneum barrier and limits shallow subcutaneous penetration [53]. traditional lotions and ointments floor fast oxidative breakdown, terrible skin retention, and non-precise systemic absorption, requiring common re-application that further leads to extra intense nearby cutaneous contamination and infection [54]. Nanocarrier-primarily based herbal drug transport systems clear up those older formulation limitations via imparting managed unlock and localized accumulation [55]. Lipid-based nanocarriers for transdermal drug transport current popularity and way forward for overcoming the skin barrier impermeability [56]. Phytochemical-loaded nanoparticles in dermatology current cantered release profiles that limit systemic toxicity and neighbourhood infection [57].

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Inexperienced nanotechnology in pharmaceutical drug transport revolutionizes sustainable manufacturing and biocompatible service layout [58].

II. NANOTECHNOLOGY-PRIMARILY BASED SHIPPING SYSTEMS FOR CAPSICUM

Phytoconstituents to overcome the shipping bottlenecks linked formerly seen in conventional formulations, sophisticated nano-carrier platforms were engineered to optimize drug encapsulation efficacy, manipulate release kinetics, enhance localized pores and skin accumulation, and decrease unfavourable close to side effects [59]. Guidance and characterization of stealth lipid nanoparticles act as most elementary drug providers in state-of-the-art pharmaceutical generation [60]. Liposomes act as selective drug shipping structures for topical control, enhance skin penetration and active compound balance [61].

➢ *Lipid-Based Totally Nanoparticles (SLNs and NLCs)*

Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid vendors (NLCs) use physiological biocompatible lipids stabilized with the help of surfactants to acquire high entrainment capacities of lipophilic capsaicinoids [62]. The solid lipid matrix of these nanoparticles forms an occlusive hydrophobic layer on top of the stratum corneum, reducing Trans epidermal water loss and promoting deep follicular and intercellular penetration into psoriatic lesions [63]. Released release profiles prevent any burst release behaviour and efficiently subdue initial test-site online stinging, improving patient tolerance [64].

Nanostructured lipid vendors (NLC) function as new drug delivery systems for topical application which can hold higher drug loads due to imperfect lipid crystal matrices [65]. System of lipid-primarily based delivery platforms for oral and topical regulate guarantees highest drug loading and bodily balance [66]. Novel mechanisms and units enable a successful transdermal drug shipping by means of altering skin permeation kinetics [67]. Transdermal drug supply shipping enhancement techniques optimize medicinal drug's therapy index and bioavailability [68]. Passive enhancement techniques in topical and transdermal drug shipping suggest service layout and thermodynamic activity [69]. Pores and skin barrier principles of perceptual absorption steer mathematical modelling and components optimization [70].

➢ *Polymeric Nanoparticles and Nano gels*

Biodegradable polymers such as poly (lactic-co-glycolic acid) (PLGA), chitosan, and silk fibroin are greatly applied to synthesize strong nanoparticles with tunable degradation costs [71]. Polymer mediated dermal delivery system controls the rate of drug release and protect labile botanical extract from proteolytic degradation [72]. Handbook of pharmaceutical controlled release technology current chapter provides simple basic polymer technology and diffusion mechanics [73]. Nanoparticles and microparticles act as a good drug vendor in contemporary pharmacy [74]. Colloidal drug delivery systems provide a structural balance and protect you aggregation in top ointment formulations [75]. Pharmacokinetics of Topical Nanocarriers in psoriasis fashions confirmed focused healing localization and prolonged pores and skin residency [76]. Membrane fusion dynamics enable the intracellular delivery of bioactive enclosed inside encapsulating nanoparticles into excessive-proliferative keratinocytes [77]. Chitosan-primarily based nanocarriers have inherent antimicrobial and wound-recovery properties, moreover chitosan-based nanocarriers with capsaicinoids systems combated secondary pores and skin infections in psoriatic plaques [78]. Recent advances on chitosan-based micro- and nanoparticles in drug delivery covers various aspects of cross-linking and mucoadhesive traits [79]. Chitosan-based totally microspheres have prolonged launch kinetics and ideal biocompatibility responses [80]. Silk fibroin biomaterials for tissue engineering and drug delivery have good biocompatibility and mechanical houses [81]. Organic silk fibroin proteins in drug delivery have strong mechanical properties and managed pores and skin digestion [82]. Incorporating nano-formulations in Carbopol or hydrogel bases has achieved ideal spread ability and prolonged house time on psoriatic lesions [83].

➢ *Green-Synthesized Steel and Metallic-Oxide*

Nanoparticles In past times innovative area, bio-stimulated inexperienced synthesis has been conducted by using Capsicum fruit or leafy extracts as herbal decreasing and stabilizing dealers to synthesize silver (AgNPs), gold (AuNPs), and copper oxide (CuO) nanoparticles without toxic chemicals [84]. Inexperienced synthesis of silver nanoparticles using plant extracts has many biomedical applications, synthesised AgNPs combines steel antimicrobial application with phytochemical anti-inflammatory coronas [85].

III. CONCLUSION

In conclusion, novelistic blend of phytoconstituents of Capsicum in cutting-edge nanotechnology is amazingly promising and highly inspiring and multitargeted approach for treatment of psoriasis. Basic and stringent pharmaceutical constraints of limiting conventional psoriasis therapy with heaped-up systemic toxicity, skin atrophy, and noncompliance of patients are bypassed by sequestration of capsaicinoids and carotenoids and flavonoids in lipid/polymer nanocarrier system. Targeted cutaneous localization, sustained release, and minimized local adverse effects (burning, stinging) are achieved by these sophisticated nanocarrier system. Finally, conjugation of botanical phytochemistry and green nanotechnology has made way for safe, patients compliant, and clinically relevant dermatological therapeutics.

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