WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 17, 88-111. Review Article ISSN 2277–7105

NANOPARTICLE-ENABLED TRANSDERMAL DELIVERY OF CANNABIDIOL AND RELATED CANNABINOIDS: CARRIER CHEMISTRY, QUALITY-BY-DESIGN FORMULATION, AND THERAPEUTIC TRANSLATION

Pare Pankaj Rajendra*[1], Manish Kumar[2]

India.

Article Received on 27 July 2026,
Article Revised on 17 August 2026,
Article Published on 01 Sept. 2026,

https://doi.org/10.5281/zenodo.22156869

***Corresponding Author**
Pare Pankaj Rajendra
India.

How to cite this Article: Pare Pankaj Rajendra*[1], Manish Kumar[2]. (2026). Nanoparticle-Enabled Transdermal Delivery of Cannabidiol And Related Cannabinoids: Carrier Chemistry, Quality-By-Design Formulation, And Therapeutic Translation. World Journal of Pharmaceutical Research, 15(17), 88-111.

ABSTRACT

Cannabidiol (CBD) and related phytocannabinoids have attracted sustained pharmaceutical interest for their anti-inflammatory, analgesic and antioxidant properties, yet their clinical utility is persistently constrained by negligible aqueous solubility, extensive hepatic first-pass metabolism, and markedly variable oral bioavailability. Transdermal delivery offers a mechanistic route around these limitations by avoiding the gastrointestinal tract and hepatic first pass altogether. Realising this route in practice, however, requires overcoming the stratum corneum barrier, and a broad family of nanocarriers vesicular lipid systems (liposomes, ethosomes, transfersomes), solid lipid nanoparticles and nanostructured lipid carriers, and mesoporous inorganic carriers such as mesoporous silica nanoparticles (MSN) and magnesium aluminometasilicate (MAS) has been developed to that end. This review synthesises the published literature on nanoparticle-based transdermal delivery of cannabinoids and structurally comparable lipophilic actives, covering carrier chemistry and comparative performance, physical and chemical permeation-enhancement strategies, Quality-by-Design (QbD) approaches to nanoparticle and patch optimisation, general principles of transdermal patch evaluation, in-vitro release and permeation kinetics, stability considerations, preclinical and clinical anti-inflammatory evidence, carrier biosafety, the evolving regulatory landscape for cannabinoid-containing topical products, and the emerging role of artificial intelligence in formulation

design. Across this evidence base, mesoporous nanoparticle carriers combined with a Quality-by-Design-optimised transdermal patch represent a mechanistically well-supported and increasingly well-evidenced platform for cannabinoid delivery, though unresolved questions in chronic dermal nanotoxicology and an unsettled regulatory environment remain the principal barriers to clinical translation.

1. INTRODUCTION

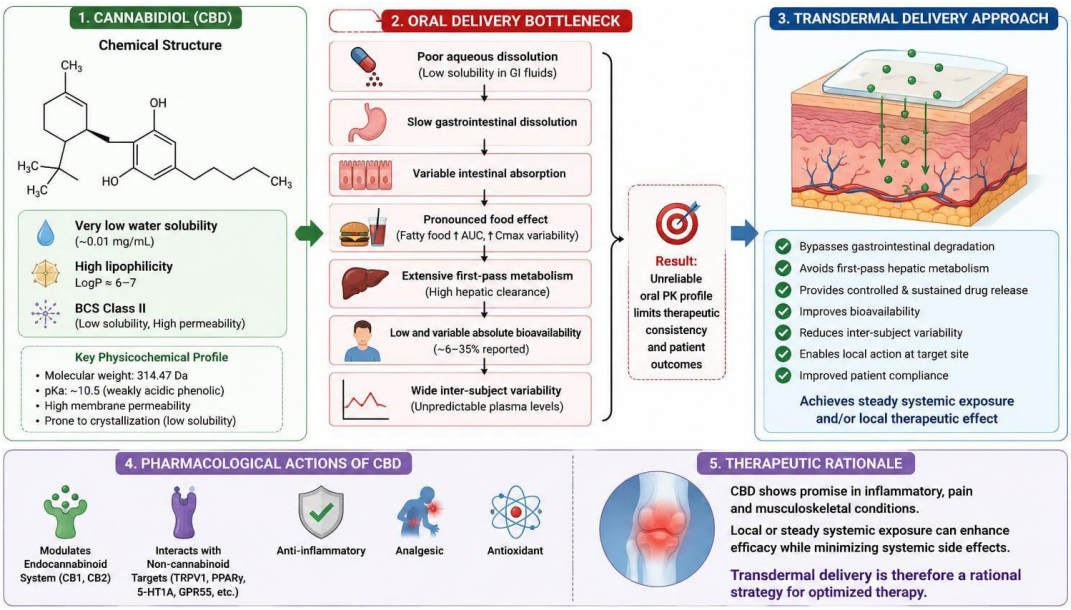
Cannabidiol (CBD), the principal non-psychoactive phytocannabinoid of Cannabis sativa, has moved from a niche botanical curiosity to a compound of substantial pharmaceutical and regulatory interest, driven by accumulating evidence of anti-inflammatory, analgesic, antioxidant and anticonvulsant activity.[1,2] Topical and transdermal application of CBD has attracted particular attention in dermatology and cosmetic science, where the compound's interaction with the cutaneous endocannabinoid system — modulating CB1, CB2, TRPV channels and PPAR receptors has been linked to benefit in inflammatory and proliferative skin conditions including acne, psoriasis, atopic and seborrheic dermatitis, and allergic contact dermatitis.[3,4]

Oral administration, by contrast, remains a poor match for CBD's physicochemical profile. The molecule is a Biopharmaceutics Classification System (BCS) class II compound with negligible aqueous solubility and high lipophilicity, and it undergoes extensive hepatic first-pass metabolism that leaves absolute oral bioavailability low and highly variable between subjects, an effect further complicated by a pronounced food-dependent absorption profile.[1,2] These pharmacokinetic limitations have motivated a wide range of bioavailability-enhancement strategies for the oral route, from lipid-based self-emulsifying drug delivery systems.[5] to the two cannabinoid products currently carrying formal marketing authorisation Epidiolex/Epidyolex (oral CBD solution, approved by the US FDA and subsequently the European Medicines Agency for seizures associated with Lennox-Gastaut and Dravet syndromes) and Sativex/nabiximols (an oromucosal THC-CBD spray approved for multiple sclerosis-related spasticity in numerous jurisdictions).[6,7,8] Both remain oral- or mucosal route products, and neither addresses the pharmacokinetic case for transdermal delivery of CBD specifically.

Transdermal delivery offers a mechanistically distinct alternative: it bypasses gastrointestinal absorption and hepatic first-pass metabolism entirely, in principle allowing more predictable systemic exposure or, for local musculoskeletal and dermatological indications, direct

delivery to the site of inflammation. Realising this in practice requires overcoming the skin's own barrier function, and a broad landscape of nanocarrier technologies spanning lipid vesicular systems and mesoporous inorganic particles has been developed for exactly this purpose across many lipophilic actives, cannabinoids included. This review synthesises that literature: it surveys nanocarrier chemistry and comparative performance, permeation-enhancement strategies, Quality-by-Design approaches to formulation optimisation, general principles of transdermal patch evaluation and release-kinetic characterisation, stability considerations, the preclinical and clinical anti-inflammatory evidence base, carrier biosafety, the regulatory landscape, and emerging computational approaches to formulation design.

The commercial and clinical context for this work has shifted considerably over the past decade. Consumer interest in CBD-containing topical and transdermal products has grown substantially faster than the regulatory and formulation-science evidence base underpinning them, producing a market in which product claims frequently outpace the pharmaceutical rigour with which those products have been characterised.[3,6] This asymmetry is itself part of the motivation for a formal review of the nanocarrier and Quality-by-Design literature underlying transdermal cannabinoid delivery: a mechanistically credible and increasingly well-evidenced formulation science exists, but it is scattered across the pharmaceutics, dermatology, materials-science and regulatory-affairs literatures rather than consolidated in one place, and it is frequently overshadowed in public discussion by less rigorously supported commercial claims. Bringing these strands together, as this review attempts to do, is intended to give both the formulation scientist and the clinical or regulatory reader a single, source-verified account of where the evidence for this delivery platform currently stands.



2. CBD and Cannabinoid Pharmacology: The Case Against Oral Delivery

CBD's low water solubility and high logP place it firmly among BCS class II actives, and its pharmacokinetic profile after oral dosing is characterised by wide inter-subject variability and a pronounced food effect on absorption.[1,2] Pharmacologically, CBD and related cannabinoids interact with the endocannabinoid system and a range of non-cannabinoid targets (TRPV channels, PPARγ, 5-HT1A, adenosine reuptake) to produce anti-inflammatory, analgesic, antioxidant and antimicrobial effects, with preclinical and early clinical evidence extending this activity to dermatological indications such as psoriasis, atopic dermatitis and wound healing.[3,4] Together, a difficult oral pharmacokinetic profile and a therapeutic indication that often benefits from local or steady systemic exposure form the central pharmacological argument for pursuing transdermal, rather than oral, delivery platforms for this class of molecule.

Because the only cannabinoid products with full marketing authorisation remain oral or oromucosal.[6,7,8] the transdermal route for CBD is still, at the level of approved medicines, an open therapeutic space rather than an established one. This is itself part of the rationale for the sustained formulation-science interest in the area: a mechanistically sound delivery route exists (transdermal application), but the nanocarrier and patch technologies needed to make it clinically and commercially viable are still being optimised and characterised across the literature reviewed in the sections that follow.

It is also worth distinguishing CBD from the wider cannabinoid class for the purposes of this review. Tetrahydrocannabinol (THC), the principal psychoactive cannabinoid, shares CBD's poor aqueous solubility and first-pass metabolic vulnerability but carries an additional layer of regulatory restriction tied specifically to its psychoactivity, meaning that nanocarrier and transdermal formulation strategies developed for THC cannot be directly repurposed for CBD without re-evaluating both the regulatory classification and, in mixed-cannabinoid extracts, the entrainment behaviour of multiple actives within the same carrier system. Minor cannabinoids (cannabigerol, cannabichromene, cannabinol and others) are increasingly co-formulated with CBD in both cosmetic and emerging pharmaceutical products, and while their physicochemical profiles are broadly similar to CBD's, the transdermal nanocarrier literature specific to these minor cannabinoids is, at present, minimal to non-existent, and the general principles reviewed in this article should be treated as a reasonable starting hypothesis for such actives rather than as directly established fact.

3. The Skin Barrier and the Rationale for Nanocarrier-Assisted Delivery

The stratum corneum's 'brick-and-mortar' architecture is the principal obstacle to transdermal absorption for most drug molecules. Permeation across it proceeds through three recognised pathways: the intercellular route through the continuous lipid matrix, the transcellular route directly through corneocytes, and the transappendageal route via hair follicles and sweat duct.[9] For a lipophilic, class II compound such as CBD, the intercellular lipid pathway is mechanistically the most relevant, but its tortuous, multiply-bilayered structure still imposes a substantial diffusional barrier even for well-partitioning molecules.[9]

Both chemical and technological strategies have been developed to overcome this barrier. Naturally derived and synthetic chemical permeation enhancers terpenes, fatty acids, alcohols such as ethanol and propylene glycol, and surfactants act by disordering the intercellular lipid packing or by increasing drug partitioning into the stratum corneum.[9,10] Physical enhancement technologies, including microneedle arrays, iontophoresis, sonophoresis and their combinations, mechanically or electrically create transient low-resistance pathways across the barrier and have been shown to substantially widen the range of molecules, including macromolecules and nanoparticles, that can be delivered transdermally.[10,11]

Nanoparticulate carriers add a complementary, largely passive mechanism: by concentrating drug at the skin surface, modifying local partitioning behaviour, and in some cases directly interacting with intercellular lipids, nanocarriers have repeatedly been shown to improve the

flux of otherwise poorly permeant lipophilic actives across excised and in-vivo skin.[9,10,11] For a BCS class II cannabinoid, combining a well-chosen nanocarrier with a permeation-enhancing patch matrix is generally what turns transdermal delivery from a theoretical proposition into a practically achievable one.

4. Nanocarrier Platforms for Transdermal Cannabinoid Delivery

4.1 Lipid Vesicular and Lipid Nanoparticle Systems

Lipid-based nanocarriers liposomes, ethosomes, transfersomes, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) form the most extensively characterised family of transdermal nanocarriers and provide an instructive comparative backdrop for mesoporous inorganic systems. Conventional liposomes, composed mainly of phospholipids, tend to remain in the upper skin layers with limited deep penetration.[12] Ethosomes, which incorporate a relatively high ethanol content, and transfersomes, which replace cholesterol with an 'edge activator' surfactant to confer ultra-deformability, have both been shown in head-to-head comparative studies to outperform conventional liposomes for transdermal delivery of lipophilic, poorly soluble anti-inflammatory actives such as celecoxib and diflunisal, achieving smaller vesicle sizes, favourable entrapment efficiencies, and measurably greater cutaneous flux.[13,14]

SLNs, composed entirely of solid lipids, form an occlusive film on the skin surface that promotes hydration and a slow-release profile, whereas NLCs combine solid and liquid lipids into a less-ordered matrix that typically improves drug loading capacity and confers a more flexible release profile; across comparative reviews, NLCs and ethosomes are generally identified as the most effective choices where deeper stratum corneum penetration is the design goal.[15] These lipid-based platforms have also been explicitly integrated with Quality-by-Design methodology in recent reviews, reflecting the same statistical optimisation logic applied to mesoporous carriers later in this review.[15] Nanoparticle-based corticosteroid delivery systems provide a directly comparable anti-inflammatory precedent: comparative evaluation of lipid nanocapsules, polymeric nanoparticles and ethosomes for hydrocortisone and hydrocortisone butyrate delivery across ex-vivo human and porcine skin found ethosomes to be the most effective carrier for both transdermal and dermal targeting, albeit with a more pronounced effect on the underlying skin barrier.[16]

4.2 Mesoporous Inorganic Carriers: MSN and MAS

Mesoporous silica nanoparticles (MSN) and magnesium aluminometasilicate (MAS, widely known by the commercial name Neusilin®) represent a mechanistically distinct, inorganic alternative to lipid-based carriers. Both present a large internal surface area and a tunable, ordered pore network — 2 to 50 nm by the IUPAC definition of the mesoporous range into which a lipophilic drug can be adsorbed, substantially increasing the fraction of drug held in an amorphous, more readily desorbed state relative to the crystalline bulk material.[17,18,19,20] MSN synthesis typically proceeds via a sol-gel process with surfactant self-assembly under hydrothermal conditions, allowing fine control over pore diameter, particle morphology and surface functionalisation, which in turn governs both drug-loading capacity and release behaviour.[18,19,22] MAS, by contrast, is produced industrially by spray-drying to yield a fine, ultralight, chemically inert granule that has an extensive and long-standing precedent as a pharmaceutical excipient for solid oral dosage forms.

That precedent is directly relevant to transdermal cannabinoid formulation. MAS has been repeatedly shown to improve the handling, physical stability and, in several cases, the in-vivo pharmacokinetic performance of poorly soluble lipophilic actives adsorbed onto it, including ibuprofen, cyclosporine, aceclofenac and sorafenib.[23,24,25,26,27,28,29] The mechanism in each case is broadly consistent: adsorption onto the porous silicate surface stabilises the drug in an amorphous or complexed state, protects it against thermal or hydrolytic degradation, and, for self-emulsifying and lipid-based formulations specifically, allows a liquid or semi-solid drug-loaded phase to be converted into a free-flowing, more processable solid intermediate.[23,27] These same properties high adsorption capacity, chemical inertness, and a demonstrated ability to stabilise structurally comparable lipophilic small molecules are what make MAS (and MSN more broadly) a rational carrier choice for cannabinoid transdermal formulation, and they are the basis for a small but growing body of work applying mesoporous nanoparticles specifically to transdermal delivery.[18]

A directly relevant precedent for anti-inflammatory transdermal application comes from a colchicine-loaded mesoporous-silica-nanoparticle/hydrogel composite incorporated into a cotton-supported transdermal patch, developed specifically for osteoarthritis management; this system demonstrated that a mesoporous-carrier patch can be engineered to acceptable pharmaceutical-elegance standards while delivering an anti-inflammatory payload at a

therapeutically meaningful, controlled rate,[30] which is the same design target pursued for cannabinoids in the formulation literature discussed in the sections that follow.

4.3 Comparative Positioning of Carrier Platforms

Read across Sections 4.1 and 4.2, the nanocarrier literature does not point to a single universally superior platform for transdermal cannabinoid delivery; rather, each carrier family trades off a distinct set of properties. Lipid vesicular systems (liposomes, ethosomes, transfersomes) generally offer the most extensive existing safety and manufacturing precedent and, for ethosomes and transfersomes specifically, the strongest demonstrated deep-skin-penetration performance, but this penetration advantage is frequently coupled to a measurable, sometimes pronounced, disruptive effect on the stratum corneum barrier itself.[13,14,16] Solid lipid nanoparticles and nanostructured lipid carriers sit at an intermediate point, offering better physical and chemical stability of the loaded drug than conventional liposomes together with a more occlusive, sustained-release surface behaviour, at the cost of generally lower drug-loading capacity for a given particle size.[15] Mesoporous inorganic carriers (MSN, MAS) offer the highest reported drug-loading and entrapment-efficiency ceiling of the platforms reviewed here, a strong existing excipient-safety precedent from oral solid-dosage use, and comparatively simple, scalable manufacturing by adsorption rather than emulsification.[18,19,23,27] but they carry the least mature chronic dermal-toxicology evidence base of the carrier families discussed, a gap addressed directly in Section 10. For a specific development programme, the choice between these platforms is therefore a formulation-strategy decision that should be driven by which trade-off penetration depth versus barrier disruption, loading capacity versus toxicology maturity, manufacturing simplicity versus release-profile tunability — is most consequential for the intended indication and dosing route, rather than by any one platform's general reputation in the literature.

4.4 Analytical Characterisation of Mesoporous Nanoparticle Carriers

Confirming that a mesoporous carrier has performed as intended both before and after drug loading relies on a standard set of solid-state and surface-analytical techniques that recur throughout the MSN and MAS literature reviewed above. Nitrogen adsorption–desorption analysis (Brunauer–Emmett–Teller, BET) is the standard method for confirming specific surface area and pore-volume changes on drug loading, since a measurable reduction in both is the expected signature of successful pore occupation.[19,32] Particle size and surface charge are typically confirmed by dynamic light scattering and zeta-potential measurement, while

transmission or scanning electron microscopy provides direct morphological confirmation of particle shape and, where resolution allows, pore ordering. Differential scanning calorimetry and powder X-ray diffraction are used together to establish the solid-state form of the adsorbed drug the disappearance or marked attenuation of a crystalline melting endotherm or diffraction pattern after loading is the conventional evidence that the drug has been converted to, or is present predominantly in, an amorphous, carrier-associated state, which is mechanistically central to the dissolution- and stability-enhancing effect these carriers are used for in the first place.[23,29] Fourier-transform infrared spectroscopy is commonly used alongside these techniques to detect any chemical interaction (as distinct from purely physical adsorption) between drug and carrier surface, a distinction that matters both for release-mechanism interpretation and for regulatory characterisation of the drug product.

5. Quality-by-Design Approaches to Nanoparticle and Patch Optimisation

Quality-by-Design, as codified in ICH Q8(R2), reframes formulation development around a predefined quality target product profile, systematic identification of critical quality attributes and critical process parameters, risk assessment under ICH Q9 principles, and a validated design space within which the process is understood to consistently deliver acceptable product quality.[31,35] This represents a deliberate move away from one-factor-at-a-time optimisation toward statistically designed experimentation, and recent methodological reviews trace this transition further toward machine-learning-assisted and Bayesian optimisation approaches, discussed separately in Section 13.[31]

Response surface methodology most commonly implemented through Box–Behnken or Central Composite experimental designs, with factorial and mixture designs used for screening or component-ratio problems is the statistical tool most frequently applied to nanoparticle and transdermal formulation optimisation in the pharmaceutical literature.[31,32]

These designs allow critical quality attributes such as entrapment efficiency, particle size, zeta potential and polydispersity to be modelled as continuous functions of formulation and process variables using a comparatively small, structured number of experimental runs, with the resulting response surfaces and contour or desirability plots used to identify an optimum formulation within the design space.[31,32] Applied specifically to transdermal nanoparticle systems, Box–Behnken-based optimisation has been used, for example, to develop nanostructured lipid carriers for transdermal delivery of gliclazide, and Neusilin-based surface solid dispersions have been optimised by an analogous QbD workflow to improve the

pharmacokinetic performance of a poorly soluble oncology drug delivered by a different route, illustrating that the same statistical logic transfers across both the carrier class and the delivery route.[17,24]

In practice, a QbD workflow for a mesoporous-nanoparticle transdermal cannabinoid formulation typically proceeds through definition of the target product profile (a stable, high-entrapment, controlled-release patch), identification of critical material attributes of the carrier (surface area, pore volume, particle size) and critical process parameters of the loading and patch-casting steps, risk-ranking of these variables against the target quality attributes, execution of a Box–Behnken or Central Composite design across the highest-risk variables, and generation of a validated design space from which an optimum formulation is selected and confirmed experimentally.[31,32] This general sequence, rather than any single formulation's specific numerical outputs, is the transferable methodological contribution of the QbD literature to transdermal cannabinoid delivery, and it is the framework within which the illustrative optimisation work referenced elsewhere in this manuscript's supporting materials should be read.

6. Transdermal Patch Design and General Evaluation Framework

Once a nanoparticle carrier is optimised, it must be incorporated into a patch architecture matrix, reservoir, or drug-in-adhesive each of which distributes the drug-loaded carrier differently within the device and imposes different release-rate-limiting behaviour.[33] Matrix-type patches, in which the nanoparticle-loaded drug is dispersed directly within a polymeric film (commonly based on HPMC, Eudragit grades, polyvinyl alcohol, or pressure-sensitive adhesive blends), are the most widely reported architecture in the nanoparticle-transdermal literature because they are comparatively straightforward to cast and characterise at laboratory scale, while reservoir and drug-in-adhesive designs offer more precise zero-order release control at the cost of greater manufacturing complexity.[33]

Regardless of architecture, patches carrying nanoparticulate cannabinoid formulations are evaluated against a standard pharmaceutical battery: physical appearance and flexibility; thickness uniformity; folding endurance as a proxy for mechanical durability under repeated wear; weight and drug-content uniformity, confirming homogeneous nanoparticle distribution within the casting solution; percentage moisture content and moisture uptake, which bear directly on both mechanical integrity and microbial stability; and tensile or elongation behaviour where the patch is intended for use on a mobile joint or flexible skin site. This

evaluation framework is applied consistently across the transdermal-patch literature irrespective of the active or carrier involved, and it is the same framework against which mesoporous-nanoparticle cannabinoid patches should be, and generally are, assessed before progression to release and permeation testing.[30,33]

The excipient palette used to build these matrices is itself fairly consistent across the nanoparticle-transdermal literature. Film-forming polymers such as hydroxypropyl methylcellulose (HPMC), various Eudragit® grades, ethyl cellulose, and polyvinyl alcohol/polyvinylpyrrolidone blends are used, alone or in combination, to control mechanical strength, flexibility and baseline permeability of the matrix itself.[33] Plasticizers (commonly propylene glycol, glycerin or low-molecular-weight polyethylene glycols) are added to prevent film brittleness and cracking on flexion, which is a particular concern for patches intended for joint application given the mechanical stress of repeated movement. Chemical penetration enhancers the same broad classes discussed in Section 3, including fatty acid esters, terpenes and short-chain alcohols are frequently incorporated directly into the matrix alongside the nanoparticle-loaded drug, and the choice and concentration of enhancer is itself commonly treated as a critical formulation variable within the QbD workflow described in Section 5, rather than fixed independently of it.[9,10,33] The nanoparticle carrier and the surrounding patch matrix are therefore best understood as a coupled formulation system: carrier-level variables (entrapment efficiency, particle size) and matrix-level variables (polymer ratio, plasticizer level, enhancer concentration) jointly determine the patch's overall release and permeation performance, and optimisation studies that treat only one of these two levels risk missing interactions between them.

7. In-Vitro Release and Permeation Kinetics: General Principles

Franz diffusion cell methodology remains the pharmaceutical standard for characterising both drug release from a transdermal patch and its permeation across excised skin or a synthetic membrane surrogate. Resulting cumulative-release or cumulative-permeation profiles are conventionally fitted to a family of mathematical models zero-order, first-order, Higuchi, and Korsmeyer–Peppas being the most widely applied in the pharmaceutical patch literature, with more recent methodological reviews also incorporating Peppas–Sahlin, Weibull, Gompertz, Hixson–Crowell, Baker–Lonsdale and Hopfenberg treatments, and, increasingly, physiologically based pharmacokinetic (PBPK) and in-vitro–in-vivo correlation (IVIVC) approaches that connect release kinetics to predicted systemic exposure.[33,34]

Across the matrix-type transdermal patch literature generally, zero-order and Korsmeyer–Peppas models most consistently provide the best statistical fit, indicating diffusion-controlled release that is frequently non-Fickian in character that is, governed by a combination of drug diffusion through the polymer matrix and polymer chain relaxation rather than by diffusion alone.[33] For nanoparticle-loaded patches specifically, the rate-limiting step can additionally include desorption of the drug from the carrier's mesopores or vesicular bilayer before it partitions into the patch matrix and then into the skin, a two-stage process that mechanistic modelling work on structurally analogous transdermal systems has begun to resolve using multiscale diffusion frameworks linking microscopic carrier-level transport to macroscopic patch-level flux.[34] The general expectation for a well-optimised mesoporous-nanoparticle cannabinoid patch, consistent with this broader literature, is therefore a release profile that approximates zero-order or near-zero-order kinetics with a Korsmeyer–Peppas release exponent indicative of anomalous, non-Fickian transport a qualitative benchmark against which any specific formulation's release data should be interpreted, rather than a fixed numerical target.

8. Stability Considerations

ICH Q1A(R2)-aligned accelerated and long-term stability testing is the standard means of establishing a shelf-life claim for any transdermal patch, typically assessing drug content, in-vitro release performance, physical integrity and microbial quality after storage at defined elevated-temperature and elevated-humidity conditions over one, three and six months, with real-time storage data collected in parallel.[36] For nanoparticle-loaded patches specifically, stability assessment must also consider whether the carrier itself remains intact and whether the adsorbed or encapsulated drug remains associated with the carrier rather than migrating into the surrounding matrix or crystallising out over time a failure mode documented for several MAS-adsorbed lipophilic drugs under prolonged storage, and one that formulation strategies such as polymer-blocking of the mesopore surface have been specifically developed to mitigate.[26] Reported experience with MAS-adsorbed actives generally indicates that the drug-stabilising role of the carrier, evident in improved thermal and hydrolytic stability during initial formulation, extends into accelerated storage as well, supporting the broader rationale for mesoporous-carrier use in cannabinoid transdermal systems where oxidative and photolytic degradation of the parent molecule is an additional concern.[23,29]

9. Preclinical and Clinical Evidence for Transdermal Cannabinoid Anti-Inflammatory Delivery

The pharmacological rationale for transdermal CBD delivery in inflammatory conditions rests on a body of in-vivo evidence that predates, and now sits alongside, the mesoporous-nanoparticle formulation literature. An early and frequently cited proof of concept demonstrated that a transdermal CBD gel produced measurable anti-inflammatory and analgesic effects in a murine model.[37] This was substantially extended by work in a rat complete Freund's adjuvant monoarthritic knee model, in which transdermal CBD gel dose-dependently reduced joint swelling, spontaneous pain-related limb posture, immune cell infiltration and synovial membrane thickening, alongside dose-dependent reductions in pro-inflammatory biomarkers measured in spinal cord and dorsal root ganglia tissue, without evident adverse effects on exploratory behaviour.[38]

This cannabinoid-specific evidence sits within a considerably larger literature on nanoparticle-mediated transdermal and topical delivery for inflammatory indications more broadly. A recent in-vivo-focused review of nanoparticle-based transdermal and topical anti-inflammatory delivery, surveying a decade of rodent inflammation models, found that most published nanocarrier studies still concentrate on formulation characterisation rather than therapeutic outcome, with organic (lipid-based) nanoparticles more frequently carried through to in-vivo efficacy testing than inorganic carriers to date a gap that is directly relevant to mesoporous-carrier cannabinoid systems, where in-vivo evidence remains comparatively sparse relative to formulation-characterisation work.[39] Complementary reviews of nanoparticle-based anti-inflammatory drug delivery and of advanced topical nanocarrier systems for psoriasis reinforce the same broad conclusion: nanocarrier technology for inflammatory skin and joint conditions is mechanistically mature but preclinical-outcome data, and clinical data in particular, still lag the pace of formulation innovation.[40,41] Microneedle-mediated delivery of nanoparticle-carried actives, including anti-inflammatory agents, has been proposed as a complementary strategy for extending the depth and consistency of nanocarrier delivery in exactly this evidence gap.[42]

Taken together, this literature supports a general expectation rather than a guaranteed outcome that a well-optimised mesoporous-nanoparticle CBD transdermal patch, evaluated in a standard acute inflammation model such as carrageenan-induced paw oedema or a chronic model such as adjuvant-induced arthritis, would be anticipated to produce a measurable

reduction in inflammatory endpoints relative to disease control, consistent with both the cannabinoid-specific precedent.[37,38] and the mesoporous-carrier anti-inflammatory precedent from colchicine delivery.[30] Confirming this for any individual formulation, however, remains an empirical question for the specific in-vivo study in question rather than something the general literature can establish on its own.

The clinical evidence landscape for topical and transdermal CBD in humans, as distinct from the preclinical rodent literature summarised above, remains comparatively thin and is dominated by small, often open-label or industry-sponsored studies rather than large randomised controlled trials. Recent dermatology-focused reviews of CBD's topical applications catalogue preliminary clinical support across acne, psoriasis, atopic and seborrheic dermatitis, pruritus and selected wound-healing indications, while consistently flagging that the underlying trials are frequently small, heterogeneous in formulation and dosing, and rarely designed with the rigour of a registration-track pharmaceutical trial.[3,4] This is an important qualifier on the anti-inflammatory rationale developed in this section: the mechanistic and preclinical case for transdermal cannabinoid delivery is considerably stronger than the confirmatory human clinical-trial evidence currently available for nanocarrier-based formulations of it specifically, and this gap should be stated plainly rather than implied.

Table 1: Comparative preclinical anti-inflammatory outcomes across nanocarrier-based transdermal systems.

Nanocarrier system	Active	In-Vivo model	Reported anti inflammatory outcome
Ethosomes / transfersomes (vs conventional liposomes)	Diflunisal	Carrageenan-induced rat paw oedema	Both nanovesicular carriers showed significantly higher inhibition of paw oedema and reduced writhing versus conventional liposomes, alongside superior skin flux and entrapment efficiencies of 46.7–66.0%.
Mesoporous silica nanoparticle/hydrogel-loaded cotton patch	Colchicine	Transdermal management model of osteoarthritis-associated inflammation	The MSN/hydrogel composite patch was reported as an effective transdermal encapsulator system for

			anti-inflammatory colchicine delivery in an osteoarthritis management context
Radially mesoporous silica nanoparticles	Dexamethasone	Rheumatoid arthritis model	Sustained anti-inflammatory effect was achieved through controlled dexamethasone release from the radial mesopore architecture.
Ethosomal gel	Mometasone furoate	Carrageenan-induced rat joint arthritis	The optimised ethosomal gel was reported as a potential arthritis treatment, outperforming non-vesicular controls in the same model.
Dissolving microneedle patch + ethosomes	Iguratimod + colchicine	Recurrent gout (transdermal combination delivery)	Combining a dissolving microneedle patch with ethosomal carriers enabled transdermal co-delivery of both actives for gout management.
Mesoporous silica nanoparticles (dermal delivery)	Methotrexate	Skin-delivery/permeation evaluation (ex vivo)	MSNs were established as a promising skin-delivery system, improving cutaneous retention of methotrexate relevant to inflammatory dermatoses.
Transdermal gel (non-nanoparticulate benchmark)	Cannabidiol	Rat complete Freund's adjuvant monoarthritic knee model	Dose-dependent reduction of joint swelling, immune cell infiltration and synovial thickening, with lowered pro-inflammatory biomarkers in spinal cord/DRG and no evident adverse effects — the reference pharmacodynamic precedent for transdermal CBD.

10. Nanotoxicology and Carrier Biosafety

Mesoporous silica's biosafety profile is reasonably well characterised for oral and parenteral use but considerably less so for chronic dermal application. Systematic literature analysis combined with dedicated experimental toxicology indicates that acute toxicity of mesoporous silica particles is dose- and route-dependent, arising mainly after intravenous or intraperitoneal administration and only rarely after subcutaneous exposure, with no consistent relationship yet established between specific physicochemical carrier properties (particle size, pore architecture, surface functionalisation) and toxicological outcome.[43,44] Broader reviews of MSN-based transdermal delivery specifically conclude that biodistribution, chronic dermal toxicity, and regulatory-grade safety data remain comparatively sparse relative to the pace of formulation innovation in this space, identifying this evidence gap as the principal scientific obstacle to clinical translation of mesoporous-carrier transdermal systems generally, independent of the active ingredient under consideration.[18]

For lipid-based nanocarriers the safety picture is comparatively more mature, given decades of liposomal and lipid-nanoparticle use in approved parenteral and, more recently, mRNA-vaccine products, though dermal-specific chronic-exposure data for the more aggressive permeation-enhancing systems (concentrated ethosomes and highly deformable transfersomes in particular) remain an active area of investigation given their documented, sometimes pronounced, effect on stratum corneum barrier integrity itself.[16] A generalisable conclusion across both carrier families is that permeation-enhancing efficacy and dermal biocompatibility are not independent variables: carriers optimised aggressively for flux may do so partly by disrupting the very barrier being studied, and biosafety assessment for any cannabinoid transdermal nanocarrier should therefore evaluate both endpoints together rather than optimising flux in isolation.

11. Regulatory Landscape for Cannabinoid-Containing Transdermal and Topical Products

Regulatory treatment of CBD-containing products, transdermal and topical formulations included, remains unsettled and jurisdiction-dependent. In the United States, CBD products are subject to FDA oversight under the Federal Food, Drug, and Cosmetic Act, with the applicable regulatory framework depending on whether a given product is marketed and formulated as a cosmetic, a dietary supplement, or a drug; only Epidiolex carries a full drug approval, and the FDA has explicitly stated that no other CBD product currently on the

market has received such approval.[6,8] The permissible cannabinoid content of hemp-derived consumer products has itself been the subject of recent federal legislative revision, adding a further layer of regulatory fluidity that any transdermal cannabinoid product intended for the US market must track closely.[6]

Internationally, the pattern is broadly similar in structure though not in detail: the European Medicines Agency has approved cannabinoid-based medicines through its centralised procedure for specific, narrow indications (as with Epidyolex for treatment-resistant childhood epilepsy syndromes and, earlier, nabiximols for multiple sclerosis spasticity), while non-medicinal CBD products are regulated at the national or EU-cosmetics-framework level, and other jurisdictions such as Australia operate their own distinct access pathways for unapproved cannabis-based medicinal products.[7] For a mesoporous-nanoparticle transdermal CBD patch specifically, this means the regulatory pathway pursued medicinal product, cosmetic, or a hybrid 'cosmeceutical' positioning will materially determine both the safety and efficacy evidence required and the permissible cannabinoid dose per unit product, independent of the formulation science reviewed elsewhere in this article. This regulatory fluidity is a material barrier to commercial translation in its own right, separate from and additional to the technical formulation challenges discussed above.

There is, at present, no dedicated international harmonisation guideline specifically addressing nanoparticle-based transdermal cannabinoid products, meaning that developers must currently assemble a regulatory strategy from adjacent frameworks: general transdermal-patch guidance from bodies such as the FDA and EMA, nanomedicine-specific quality and safety guidance where the carrier itself is classified as a nanomaterial, and jurisdiction-specific cannabinoid-control legislation layered on top of both. This absence of a purpose-built framework is itself a translational barrier distinct from the underlying formulation science, and it is one that a coordinated regulatory-science effort rather than further formulation optimisation alone would be needed to resolve.

12. Artificial Intelligence and Next-Generation Optimisation Approaches

Beyond classical Box–Behnken and Central Composite response surface methodology, the pharmaceutical formulation literature has begun to incorporate machine-learning and artificial-intelligence-guided optimisation as a complementary, and in some applications a successor, approach. Artificial neural networks have been applied to predict, characterise and optimise pharmaceutical formulations across dosage forms, learning nonlinear relationships

between formulation variables and critical quality attributes that classical polynomial response-surface models can struggle to capture.[45] More broadly, AI and machine-learning-guided optimisation workflows including surrogate modelling, Bayesian optimisation and active learning have been applied across lipid nanoparticle, biologic and long-acting injectable formulation development, with reported reductions in the number of experimental runs required to reach an optimal formulation relative to conventional factorial or response-surface designs.[31]

For mesoporous-nanoparticle transdermal cannabinoid systems specifically, these methods remain at an early, largely exploratory stage relative to their application in oral solid-dosage and biologics formulation, but the same general logic applies: given a sufficiently large historical or generated dataset linking carrier and patch formulation variables to entrapment efficiency, particle size, release rate and permeation flux, machine-learning models could in principle narrow the experimental design space explored by classical QbD studies, complementing rather than replacing the risk-based QbD framework described in Section.[31,45] This is identified across the broader nanomedicine formulation literature as one of the more promising near-term methodological developments for accelerating translation of nanocarrier-based transdermal systems generally.[31]

A practical obstacle to wider adoption of these computational approaches in transdermal cannabinoid formulation specifically is data availability: machine-learning and Bayesian optimisation methods generally perform best with large, structured historical datasets connecting formulation inputs to measured outputs, and the cannabinoid-specific nanocarrier literature reviewed in this article, while growing, remains too small and methodologically heterogeneous to directly support such models without substantial data-harmonisation work first. Regulatory acceptance of AI-guided formulation development is itself still evolving; process-analytical-technology and QbD frameworks under ICH Q8–Q10 were designed around statistically interpretable, risk-based experimental design, and while regulators have shown general openness to model-informed development, the specific evidentiary bar for an AI-optimised nanoparticle transdermal formulation has not yet been settled in the way it has for classical response-surface-optimised formulations.[31,35] In the near term, therefore, AI-guided methods are more realistically positioned as a hypothesis-generation and design-space-narrowing tool that feeds into, rather than replaces, a conventional QbD confirmatory study of the kind described in Section 5.

13. Future Perspectives

Several directions stand out for this field going forward. First, standardised reporting of in-vitro–in-vivo correlation for mesoporous-carrier transdermal patches would allow the cross-study comparisons this review has had to make cautiously given wide variation in membrane type, enhancer use, patch surface area and animal model across the literature to be made with substantially more confidence.[33,34] Second, chronic rather than acute dermal biosafety data for MAS and MSN carriers, ideally generated under conditions that mirror realistic patch-wear regimens rather than single-dose exposure, would directly address the principal safety evidence gap identified in Section 10.[18,43] Third, given the regulatory volatility around cannabinoid content limits documented in Section 11, formulation strategies that are readily adaptable to shifting permissible-dose thresholds for example, patch designs in which drug loading can be adjusted without re-optimising the entire nanoparticle system would carry direct practical translational valu.[6] Fourth, combining mesoporous nanoparticle carriers with physical enhancement technologies such as microneedle arrays, an approach already explored for other nanoparticle-carried actives, represents a largely untested but mechanistically promising direction for cannabinoid delivery specifically, given the depth-of-penetration limitations noted for passive nanocarrier-only systems.[11,42] Finally, continued integration of AI-guided formulation optimisation with the risk-based QbD framework, rather than as a separate methodology, is likely to be where the most efficient near-term formulation gains for this class of delivery system are realised.[31,45]

14. Limitations of the Current Evidence Base

Several general limitations qualify the synthesis presented in this review and are worth stating explicitly rather than leaving implicit. First, direct head-to-head comparison across the studies cited throughout Sections 4 through 9 is complicated by substantial methodological heterogeneity different membrane types and species of origin for permeation testing, different patch surface areas and application durations, and different inflammation models and endpoints for pharmacodynamic evaluation such that apparent differences in reported performance between carrier systems may partly reflect methodological variation rather than genuine differences in carrier performance. Second, the cannabinoid-specific transdermal literature remains considerably smaller than the general nanoparticle-transdermal literature for other lipophilic actives, meaning that a portion of the case built in this review necessarily rests on extrapolation from structurally or mechanistically analogous systems (colchicine, corticosteroids, other NSAIDs) rather than head-to-head cannabinoid data. Third, as noted in

Section 9, the human clinical evidence base for nanocarrier-formulated transdermal CBD specifically is minimal, and the preclinical rodent evidence reviewed here should not be read as a substitute for that missing clinical data. Finally, because cannabinoid regulatory status is genuinely in flux across major markets, some of the regulatory detail summarised in Section 11 should be treated as a snapshot rather than a stable reference, and readers using this review to inform an active development programme should verify current regulatory status directly with the relevant national authority rather than relying solely on the account given here.

15. CONCLUSION

Nanoparticle carriers both lipid-based vesicular systems and mesoporous inorganic carriers such as magnesium aluminometasilicate offer a mechanistically well-supported route to overcoming CBD's oral bioavailability limitations by enabling a Quality-by-Design-optimised transdermal patch with high entrapment efficiency, controlled release, and preclinical anti-inflammatory precedent from both cannabinoid-specific and structurally analogous mesoporous-carrier studies. The evidence reviewed here spanning carrier chemistry, permeation-enhancement strategy, QbD-based formulation optimisation, general patch evaluation and release-kinetic principles, stability, preclinical and clinical pharmacodynamics, carrier biosafety, and the regulatory landscape supports this platform's therapeutic rationale. Regulatory ambiguity around cannabinoid-containing topical products and incomplete chronic dermal biosafety data for mesoporous carriers remain the principal barriers to clinical translation, and are the two areas where further evidence generation would most directly advance the field.

REFERENCES

1. Perucca E, Bialer M. Critical aspects affecting cannabidiol oral bioavailability and metabolic elimination, and related clinical implications. CNS Drugs, 2020; 34(8): 795–800.
2. Millar SA, Stone NL, Yates AS, O'Sullivan SE. A systematic review on the pharmacokinetics of cannabidiol in humans. Front Pharmacol., 2018; 9: 1365.
3. Rusu A, Farcaș AM, Oancea OL, Tanase C. Cannabidiol in skin health: a comprehensive review of topical applications in dermatology and cosmetic science. Biomolecules, 2025; 15: 1219.

4. Martins AM, Gomes AL, Boas IV, Marto J, Ribeiro HM. Cannabis-based products for the treatment of skin inflammatory diseases: a timely review. Pharmaceuticals, 2022; 15: 210.
5. Knaub K, Sartorius T, Dharsono T, Wacker R, Wilhelm M, Schön C. A novel self-emulsifying drug delivery system (SEDDS) based on VESIsorb® formulation technology improving the oral bioavailability of cannabidiol in healthy subjects. Molecules, 2019; 24(16): 2967.
6. U.S. Food and Drug Administration. FDA regulation of cannabis and cannabis-derived products, including cannabidiol (CBD) [Internet]. Silver Spring (MD): FDA., 2025; [cited 2026 Aug 1].
7. GW Pharmaceuticals plc. GW Pharmaceuticals receives European Commission approval for EPIDYOLEX® (cannabidiol) for the treatment of seizures in patients with two rare, severe forms of childhood-onset epilepsy [press release]. London: GW Pharmaceuticals, 2019 Sep 23.
8. U.S. Food and Drug Administration. FDA and cannabis: research and drug approval process [Internet]. Silver Spring (MD): FDA., 2024; [cited 2026 Aug 1].
9. Schafer N, Balwierz R, Biernat P, Ochędzan-Siodłak W, Lipok J. Natural ingredients of transdermal drug delivery systems as permeation enhancers of active substances through the stratum corneum. Mol Pharm., 2023; 20(7): 3278–97.
10. Ramadon D, McCrudden MTC, Courtenay AJ, Donnelly RF. Enhancement strategies for transdermal drug delivery systems: current trends and applications. Drug Deliv Transl Res., 2022; 12(4): 758–91.
11. Tapfumaneyi P, Imran M, Mohammed Y, Roberts MS. Recent advances and future prospective of topical and transdermal delivery systems. Front Drug Deliv., 2022; 2: 957732.
12. Elsayed MMA, Abdallah OY, Naggar VF, Khalafallah NM. Lipid vesicles for skin delivery of drugs: reviewing three decades of research. Int J Pharm., 2007; 332(1–2): 1–16.
13. Bragagni M, Mennini N, Maestrelli F, Cirri M, Mura P. Comparative study of liposomes, transfersomes and ethosomes as carriers for improving topical delivery of celecoxib. Drug Deliv., 2012; 19(7): 354–61.
14. Abd El-Alim SH, Kassem AA, Basha M, Salama A. Comparative study of liposomes, ethosomes and transfersomes as carriers for enhancing the transdermal delivery of diflunisal: in vitro and in vivo evaluation. Int J Pharm., 2019; 563: 293–303.

15. Antonara L, Triantafyllopoulou E, Chountoulesi M, Pippa N, Dallas PP, Rekkas DM. Lipid-based drug delivery systems: concepts and recent advances in transdermal applications. Nanomaterials, 2025; 15(17): 1326.
16. Kalvodová A, Dvořáková K, Petrová E, Michniak-Kohn BB, Zbytovská J. The contest of nanoparticles: searching for the most effective topical delivery of corticosteroids. Pharmaceutics, 2023; 15(2): 513.
17. Jahan S, Aqil M, Ahad A, Imam SS, Waheed A, Qadir A, Ali A. Nanostructured lipid carrier for transdermal gliclazide delivery: development and optimization by Box-Behnken design. Inorg Nano-Met Chem., 2024; 54(5): 474–87.
18. Kolimi P, Narala S, Youssef AAA, Nyavanandi D, Dudhipala N. A systemic review on development of mesoporous nanoparticles as a vehicle for transdermal drug delivery. Nanotheranostics, 2023; 7(1): 70–89.
19. Kazemzadeh P, Sayadi K, Toolabi A, Sayadi J, Zeraati M, Chauhan NPS, Sargazi G. Structure-property relationship for different mesoporous silica nanoparticles and its drug delivery applications: a review. Front Chem., 2022; 10: 823785.
20. Oh JY, Yang G, Choi E, Ryu J. Mesoporous silica nanoparticle-supported nanocarriers with enhanced drug loading, encapsulation stability, and targeting efficiency. Biomater Sci., 2022; 10: 1448–55.
21. Zhang W, Liu H, Qiu X, Zuo F, Wang B. Mesoporous silica nanoparticles as a drug delivery mechanism. Open Life Sci., 2024; 19(1): 20220867.
22. Vallet-Regí M, Colilla M, Izquierdo-Barba I, Manzano M. Mesoporous silica nanoparticles for drug delivery: current insights. Molecules, 2017; 23: 47.
23. Krupa A, Szlęk J, Jany BR, Jachowicz R. Preformulation studies on solid self-emulsifying systems in powder form containing magnesium aluminometasilicate as porous carrier. AAPS PharmSciTech., 2014.
24. Panda BK, Chellampillai B, Ghodake S, Mali AJ, Kamble R. Investigation of magnesium aluminometasilicate (Neusilin US2) based surface solid dispersion of sorafenib tosylate using QbD approach: in vitro and in vivo pharmacokinetic study. ADMET DMPK., 2024; 12(4): 687–702.
25. Sander C, Holm P. Porous magnesium aluminometasilicate tablets as carrier of a cyclosporine self-emulsifying formulation. AAPS PharmSciTech., 2009; 10: 1388–95.
26. Vadher AH, Parikh JR, Parikh RH, Solanki AB. Preparation and characterization of co-grinded mixtures of aceclofenac and Neusilin US2 for dissolution enhancement of aceclofenac. AAPS PharmSciTech., 2009; 10: 606–14.

27. Beg S, Swain S, Singh HP, Patra CN, Rao MEB. Development, optimization, and characterization of solid self-nanoemulsifying drug delivery systems of valsartan using porous carriers. AAPS PharmSciTech., 2012; 13: 1416–27.
28. Chakraborty S, Shukla D, Vuddanda PR, Mishra B, Singh S. Utilization of adsorption technique in the development of oral delivery system of lipid based nanoparticles. Colloids Surf B Biointerfaces, 2010; 81: 563–9.
29. Krupa A, Majda D, Jachowicz R, Mozgawa W. Solid-state interaction of ibuprofen and Neusilin US2. Thermochim Acta., 2010; 509: 12–7.
30. Mohamed AL, Elmotasem H, Salama AAA. Colchicine mesoporous silica nanoparticles/hydrogel composite loaded cotton patches as a new encapsulator system for transdermal osteoarthritis management. Int J Biol Macromol., 2020; 164: 1149–63.
31. Türkdoğan A, Alloush T, Demiralp B. Experimental design in pharmaceutical formulation development: achievements, limitations and the transition toward intelligent optimization. Sci Pharm., 2026; 94(2): 38.
32. Kayesh R, et al. Quality-by-design approach and optimization of risk factors by Box-Behnken design in orally disintegrating tablet formulation. J Sci Res., 2021; 13(3): 935–50.
33. Garg I, Verma M, Chaurasia U, Negi T, Rawat S, et al. Understanding drug diffusion and permeation in transdermal patches: a kinetic perspective. Eur J Pharm Biopharm., 2026 Jun 18. doi: 10.1016/j.ejpb.2026.115152.
34. Defraeye T, Bahrami F, Ding L, Malini RI, Terrier A, Rossi RM. Predicting transdermal fentanyl delivery using mechanistic simulations for tailored therapy. Front Pharmacol., 2020; 11: 585393.
35. International Council for Harmonisation. ICH Q8(R2): Pharmaceutical Development. Geneva: ICH., 2009.
36. International Council for Harmonisation. ICH Q1A(R2): Stability Testing of New Drug Substances and Products. Geneva: ICH., 2003.
37. Lodzki M, Godin B, Rakou L, Mechoulam R, Gallily R, Touitou E. Cannabidiol-transdermal delivery and anti-inflammatory effect in a murine model. J Control Release, 2003; 93: 377–87.
38. Hammell DC, Zhang LP, Ma F, Abshire SM, McIlwrath SL, Stinchcomb AL, Westlund KN. Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis. Eur J Pain., 2016; 20(6): 936–48.

39. Athinodorou AM, Papanikolaou E, Zygouri P, Spyrou K, Athinodorou IP, Vezyraki P, Stamatis H, Tsamis KI, Lakkas L, Markopoulos GS, Peschos D, Simos YV. Nanoparticle-based drug carriers in transdermal and topical delivery: an in vivo review of anti-inflammatory efficacy. Biochem Pharmacol., 2025.
40. Wang H, Zhou Y, Sun Q, Zhou C, Hu S, Lenahan C, Xu W, Deng Y, Li G, Tao S. Update on nanoparticle-based drug delivery system for anti-inflammatory treatment. Front Bioeng Biotechnol., 2021; 9: 630352.
41. Zhang M, Hong S, Sun X, Zhou Y, Luo Y, Liu L, Wang J, Wang C, Lin N, Li X. Exploration of and insights into advanced topical nanocarrier systems for the treatment of psoriasis. Front Med., 2022; 9: 1017126.
42. Jiang X, Zhao H, Li W. Microneedle-mediated transdermal delivery of drug-carrying nanoparticles. Front Bioeng Biotechnol., 2022; 10: 840395.
43. Sun L, Sogo Y, Wang X, Ito A. Biosafety of mesoporous silica nanoparticles: a combined experimental and literature study. J Mater Sci Mater Med. 2021; 32(9): 102.
44. Rascol E, Pisani C, Dorandeu C, Nyalosaso J, Charnay C, et al. Biosafety of mesoporous silica nanoparticles. Biomimetics, 2018; 3(3): 22.
45. Wang S, Di J, Wang D, Dai X, Hua Y, Gao X, Zheng A, Gao J. State-of-the-art review of artificial neural networks to predict, characterize and optimize pharmaceutical formulation. Pharmaceutics, 2022; 14: 183.
46. Kuskov AN, Kukovyakina EV, Krasnoselskaya EN. Nanotechnology-based drug delivery systems. Pharmaceutics, 2025; 17(7): 817.
47. Hailu SA, Bogner RH. Complex effects of drug/silicate ratio, solid-state equivalent pH, and moisture on chemical stability of amorphous quinapril hydrochloride coground with silicates. J Pharm Sci., 2010.
48. Heikkilä T, Salonen J, Tuura J, Hamdy MS, Mul G, Kumar N, et al. Mesoporous silica material TUD-1 as a drug delivery system. Int J Pharm., 2007; 331: 133–8.