RESEARCH PAPER

Optimization of Curcumin-Loaded Solid Lipid Nanoparticles (SLNs) for Improved Bioavailability and Anti-inflammatory Action in Post-Operative Care

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Abstract
Curcumin, the principal curcuminoid of turmeric (Curcuma longa), is a pleiotropic anti-inflammatory molecule whose clinical use is limited by poor aqueous solubility, chemical instability, extensive first-pass conjugation and rapid systemic elimination. These properties are especially restrictive in post-operative care, where timely and reproducible suppression of the inflammatory cascade is needed to limit pain, swelling, delayed wound repair and reliance on opioids or non-steroidal anti-inflammatory drugs. Solid lipid nanoparticles (SLNs), colloidal carriers built from physiological lipids that are solid at body temperature and stabilised by surfactants, can solubilise curcumin within a lipid matrix, protect it from degradation, prolong its release and change its absorption pathway. This article reviews the published evidence on curcumin-loaded SLNs and sets out a structured optimization framework for post-operative use. It summarises curcumin's anti-inflammatory mechanisms, the barriers that cap its bioavailability, SLN architecture and production methods, and the material and process variables that govern particle size, polydispersity, zeta potential, entrapment efficiency and release. Quality-by-design strategies, in particular Box-Behnken and central composite designs, are discussed as a means of locating a robust design space, together with the characterization toolkit needed to confirm it. Animal studies show that SLN encapsulation can raise the oral exposure of curcumin roughly ten-fold or more and can improve inflammatory readouts in disease models. Safety, scale-up and regulatory considerations are addressed, and the main evidence gap is identified: the absence of SLN-specific clinical trials in surgical patients.

Keywords: curcumin; solid lipid nanoparticles; bioavailability; anti-inflammatory; post-operative care; formulation optimization; quality by design; Box-Behnken design
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Introduction

Every surgical procedure triggers an inflammatory response. Tissue injury releases danger signals, recruits neutrophils and macrophages, and drives local and systemic production of mediators such as prostaglandins, tumour necrosis factor-α (TNF-α), interleukin-1β (IL-1β) and interleukin-6 (IL-6). A well-regulated response is essential for debridement, angiogenesis and matrix deposition. An excessive or prolonged one produces pain, oedema, stiffness, delayed wound repair, adhesions and post-operative fatigue. Post-operative care therefore relies on anti-inflammatory and analgesic drugs, principally non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and opioids. Each class carries recognised liabilities, including gastric injury, renal impairment, bleeding, impaired healing, sedation and dependence, which keeps interest alive in safer adjuncts, particularly those of natural origin.

Curcumin, the main yellow pigment of turmeric, is among the most intensively studied of these candidates. It suppresses nuclear factor-κB (NF-κB), cyclooxygenase-2 (COX-2), 5-lipoxygenase, signal transducer and activator of transcription 3 (STAT3) and a range of pro-inflammatory cytokines (Aggarwal et al., 2009). Its relevance to surgery is not merely theoretical. In a double-blind comparison with phenylbutazone and placebo, curcumin produced a better anti-inflammatory response than placebo in patients with post-operative inflammation (Satoskar et al., 1986). In a randomised, placebo-controlled trial after laparoscopic cholecystectomy, patients receiving curcumin reported lower pain at weeks one and two, lower fatigue through week three and markedly lower use of rescue analgesic tablets (Agarwal et al., 2011). A pilot randomised trial of curcuminoids after laparoscopic gynaecological surgery likewise suggested reduced pain severity (Phoolcharoen et al., 2019).

These encouraging signals were obtained with conventional oral curcuminoid preparations, and they

sit uneasily beside the compound's pharmacokinetics. Low plasma and tissue concentrations of curcumin arise from poor absorption, rapid metabolism and rapid systemic elimination, and phase I studies have shown that even very high oral doses, up to 12 g per day, are safe but yield poor bioavailability (Anand et al., 2007). In the post-operative window, when effective exposure is needed within hours to days, a drug that is erratically absorbed and rapidly conjugated is a poor fit for the clinical need. Closing this gap is therefore a formulation problem before it is a pharmacology problem.

Lipid-based nanocarriers offer one route. Solid lipid nanoparticles (SLNs), introduced in 1991, were conceived as an alternative to emulsions, liposomes and polymeric nanoparticles, combining a solid lipid core with the physiological tolerability and scalable production of lipid systems (Müller et al., 2000). For curcumin, the experimental record is persuasive. Entrapment in SLNs produced a 39-fold increase in oral bioavailability over solubilised curcumin in rats at 50 mg/kg and a 155-fold increase at 1 mg/kg, with sustained release over seven days in vitro (Kakkar et al., 2011). A later SLN formulation was reported to raise curcumin bioavailability about nine-fold over a commercially available bioavailable curcumin product while also improving its stability (Gupta et al., 2020).

Despite this promise, an SLN is not a single product but a family of formulations whose performance depends on lipid, surfactant, drug load, process conditions and storage. Particle size, polydispersity, surface charge and entrapment efficiency interact in non-obvious ways, and a formulation tuned for one attribute often loses on another. Systematic optimization is therefore central to any credible translation, and it must be aimed at a defined clinical target. For post-operative care that target has distinctive features: a rapid onset together with a sustained tail, reproducible exposure in patients with altered gastrointestinal function, a safety profile compatible with concomitant analgesics and anaesthetic agents, and, where a topical or peri-incisional route is chosen, controlled retention at the wound site.

This article reviews the evidence for curcumin-loaded SLNs and proposes a structured optimization approach for post-operative anti-inflammatory therapy. It first outlines curcumin's chemistry and mechanisms, then the barriers to its bioavailability, SLN structure and production methods, optimization by quality-by-design principles, characterization, release and pharmacokinetics, anti-inflammatory efficacy, and finally safety, scale-up and regulatory questions. Results from published studies are used throughout to illustrate what has been achieved. The optimization framework presented is a proposal that still needs experimental confirmation for the post-operative indication.

Curcumin: Chemistry, Pharmacology and Anti-inflammatory Mechanisms

Curcumin, or diferuloylmethane, is a polyphenolic β-diketone found in the rhizome of Curcuma longa together with its demethoxy and bisdemethoxy congeners, collectively known as curcuminoids (Hewlings and Kalman, 2017). Its molecular weight is 368.4 g/mol, and its structure comprises two methoxylated phenolic rings joined by a seven-carbon linker carrying a conjugated β-diketone. The linker exists in keto and enol tautomeric forms whose balance shifts with pH and solvent. The molecule is lipophilic, with a partition coefficient (log P) of roughly 3, practically insoluble in water at acidic and neutral pH, and freely soluble in organic solvents and lipids. These properties explain its affinity for lipid carriers as well as its difficulty in aqueous biological fluids. Curcumin is also unstable at several pH values and prone to photodegradation (Gupta et al., 2020), so the physiological environment and routine handling both erode the active fraction of a dose.

The pharmacological breadth of curcumin is considerable. It has been associated with antioxidant, anti-inflammatory, anticancer, antiviral and antibacterial activity, and the term pleiotropic is often applied to it because a single molecule engages many unrelated molecular targets (Prasad et al., 2014). The same review lists anti-inflammatory, hypoglycaemic, antioxidant, wound-healing and antimicrobial effects as the best-documented actions. For post-operative care, the anti-inflammatory, antioxidant and wound-healing properties are the relevant ones.

The anti-inflammatory mechanism centres on the NF-κB axis. Curcumin blocks NF-κB activation induced by a variety of inflammatory stimuli, in part through inhibition of IκBα kinase, and it has been reported to bind that kinase directly (Aggarwal and Harikumar, 2009). Because NF-κB controls the transcription of many mediators, the consequence is down-regulation of COX-2, TNF, 5-lipoxygenase, IL-1, IL-6, IL-8, macrophage inflammatory protein-1α, adhesion molecules and C-reactive protein. Curcumin also inhibits STAT3, a second transcription factor through which IL-6 exerts its effects, and it has been reported to bind COX-2 and 5-lipoxygenase and inhibit their activity (Aggarwal and Harikumar, 2009). This is a different profile from that of a conventional NSAID. An NSAID acts largely downstream, on prostaglandin synthesis, whereas curcumin acts at several upstream and downstream nodes at once, which in principle allows a broader dampening of the cytokine and eicosanoid response that follows surgical trauma.

Curcumin also acts on the tissue-repair side of the post-operative picture. When curcumin was incorporated into collagen films and applied to dermal wounds in rats, the treated groups were compared with control and collagen-only groups, and the formulation was shown to quench free radicals more efficiently and to support dermal wound healing (Gopinath et al., 2004). The result is a reminder that the aim in surgical patients is not to abolish inflammation but to shorten and moderate it, and that antioxidant activity at the wound bed may contribute to that aim.

A caution follows from the pharmacology. Most mechanistic observations come from cell culture or animal models in which curcumin concentrations are commonly in the micromolar range, whereas plasma and tissue concentrations after oral dosing of unformulated curcumin are far lower (Anand et al., 2007). The gap between the concentrations that are mechanistically effective and those that are achievable is the central reason that formulation, rather than a search for a more potent analogue, is the logical focus of curcumin research in inflammatory conditions.

Bioavailability Barriers and the Limits of Conventional Strategies

Oral bioavailability is the product of three successive fractions: the fraction of the dose that dissolves in the gastrointestinal lumen, the fraction that crosses the enterocyte and escapes intestinal metabolism, and the fraction that survives hepatic first-pass extraction. Curcumin is penalised at every step. Its low aqueous solubility limits dissolution. Its instability at intestinal pH removes part of the dissolved fraction before absorption. Within the enterocyte and hepatocyte it undergoes extensive conjugation and reduction, so that the circulating species are largely metabolites that lack the pharmacological activity of the parent compound. The net result is the pattern reported by Anand et al. (2007): poor absorption, rapid metabolism and rapid systemic elimination, giving low plasma and tissue levels despite large doses.

Whether this is truly limiting in patients has been debated. Some reviewers describe poor solubility, low bioavailability and intense staining colour as major problems, while noting that numerous reports suggest bioavailability may not be a concern for every indication (Prasad et al., 2014). A review of more than 200 clinical studies went further and concluded that low bioavailability has not prevented clinical benefit in chronic disease, in part because higher doses and formulations were used in the trials (Kunnumakkara et al., 2019). The practical reading of this debate is that effects in the gut, or effects mediated by metabolites, may be adequate for some endpoints, but that a systemic or tissue-level anti-inflammatory action, such as that needed at a surgical site, depends on measurable exposure to the parent molecule. That requirement is what formulation work attempts to meet.

The oldest and simplest strategy is metabolic inhibition. Co-administration of piperine, the pungent alkaloid of black pepper, increased the bioavailability of curcumin in rats and in healthy volunteers, in the latter by about 2000% (Shoba et al., 1998). The approach works, but it is blunt. Piperine inhibits drug-metabolising enzymes and transporters non-selectively, which creates a risk of interactions with the anaesthetic, analgesic, anticoagulant and antibiotic agents that surgical patients commonly receive. Nanoparticle encapsulation offers a more selective alternative: curcumin entrapped in polymeric nanoparticles showed at least nine-fold higher oral bioavailability than curcumin given with piperine in a head-to-head animal comparison (Shaikh et al., 2009). That result is noteworthy because the comparator was not plain curcumin but an already enhanced preparation.

The wider landscape of strategies has been catalogued repeatedly. Early work identified five broad approaches: adjuvants that interfere with glucuronidation, liposomal curcumin, curcumin nanoparticles, curcumin-phospholipid complexes and structural analogues (Anand et al., 2007). Later reviews have organised the pharmaceutical strategies for improving the oral systemic bioavailability of curcumin with clinical application in mind (Ma et al., 2019). Each has trade-offs. Liposomes offer biocompatibility but are limited by stability and cost. Phospholipid complexes tend to improve absorption but do little to prolong action. Polymeric nanoparticles can show excellent exposure gains yet carry residual-solvent, polymer-degradation and scale-up concerns. Structural analogues change the regulatory identity of the drug.

Lipid carriers have particular appeal for a lipophilic molecule such as curcumin. Dissolving the drug within a lipid matrix removes the dissolution step, and digestion of the lipid in the intestine generates mixed micelles that can solubilise the drug at the absorptive surface. Lipid systems can also shift part of the absorption toward lymphatic transport, which partially bypasses first-pass hepatic metabolism, although the magnitude of this effect is formulation dependent and must be demonstrated rather than assumed.

The post-operative setting adds its own constraints. Fasting, anaesthesia, opioid-related slowing of gut transit and, in some patients, ileus all alter gastrointestinal conditions and make absorption of a poorly soluble drug more variable. A carrier that gives consistent exposure irrespective of luminal

conditions is therefore especially valuable, as is one that can be adapted to non-oral routes, such as topical or peri-incisional application, when oral dosing is impractical.

Solid Lipid Nanoparticles: Structure, Composition and Advantages

SLNs are submicron colloidal dispersions in which the dispersed phase is a lipid that is solid at both room and body temperature, stabilised in water by one or more surfactants. Their diameters typically fall between about 50 and 1000 nm, and pharmaceutical products are usually aimed at the lower part of that range. The solid matrix distinguishes them from emulsions, whose droplets are liquid, and from liposomes, which are aqueous compartments bounded by phospholipid bilayers. A key feature of the system, emphasised in the classical review by Mehnert and Mäder (2001), is that the physical state of the lipid is not fixed: supercooled melts and different crystalline modifications of the lipid can coexist and change on storage, so that adequate characterization needs several complementary analytical methods rather than a single measurement.

Where the drug sits within the particle governs how it is released. Studies of drug release from SLNs showed that release behaviour depends on how the drug is distributed between the lipid core and the surfactant-rich outer layer, and that this distribution is determined by the production conditions and the physicochemical properties of the drug (zur Mühlen et al., 1998). A drug concentrated in the outer shell is released quickly, producing a burst, whereas a drug dispersed through or concentrated in the core is released slowly as it diffuses through, or is liberated from, the lipid matrix. For an anti-inflammatory used after surgery, this link between structure and release is useful, because a deliberate burst fraction followed by a sustained tail matches the clinical need for early effect and continued cover.

SLNs have been explored for many routes of administration, including oral, parenteral, dermal, pulmonary, ocular and rectal delivery, and the route strongly influences the optimal particle design (Üner and Yener, 2007). The breadth of routes matters for surgical care, in which a single carrier technology might support oral dosing for systemic exposure and topical or peri-incisional dosing for local effect.

The relative strengths and weaknesses of SLNs have been reviewed in detail (Naseri et al., 2015). The advantages reported include a good release profile, targeted delivery potential, excellent physical stability, preparation in the absence of organic solvent, low toxicity of the lipid carrier, biodegradability of the lipids, lower cost than polymeric carriers and a more straightforward path to approval. The common disadvantages are particle growth during storage, a tendency to gelation, polymorphic transitions of the lipid and inherently low incorporation rates caused by the crystalline structure of the solid lipid. Depending on the production method, three models of drug incorporation have been described: a homogeneous matrix, a drug-enriched shell and a drug-enriched core. The same review describes nanostructured lipid carriers (NLCs), which blend solid and liquid lipids to create a less ordered matrix, thereby raising loading capacity and limiting drug expulsion during storage. NLCs are therefore a natural extension where an SLN cannot reach adequate loading.

The composition of a typical SLN is simple, which is part of its regulatory appeal. The lipid phase may be a triglyceride, partial glyceride, fatty acid, fatty alcohol or wax, and the aqueous phase carries one or more surfactants, often a phospholipid together with a non-ionic emulsifier, chosen to stabilise the interface sterically, electrostatically or both (Geszke-Moritz and Moritz, 2016). Cryoprotectants are added if the dispersion is to be freeze-dried. For a molecule as lipophilic as curcumin, the lipid core is an attractive host, but the same crystalline order that gives the matrix its stability can squeeze out the drug as the lipid recrystallises into a more perfect form. Choosing lipids that accommodate curcumin, and surfactants that stabilise the resulting particle, is therefore the first and most consequential formulation decision, and it is the subject of the optimization framework developed in Section 6.

Methods of SLN Preparation

More than a dozen production techniques have been described, and they can be grouped by whether they rely on mechanical energy, on solvents or on the spontaneous behaviour of a microemulsion (Sastri et al., 2020; Duan et al., 2020). The choice is not neutral. The method determines the starting particle size, the distribution of drug between core and shell, the lipid polymorph that crystallises, the residues left in the product and the practicality of scale-up. The use of SLNs to encapsulate and deliver active and antioxidant compounds, a class that includes curcumin, has been reviewed separately (Subroto et al., 2023).

High-pressure homogenization (HPH) is the most widely used technique and the most readily scaled. In the hot variant the drug is dissolved or dispersed in molten lipid, the melt is dispersed in a surfactant solution at the same temperature to make a pre-emulsion, and the pre-emulsion is passed through a homogeniser at high pressure for several cycles before cooling allows the lipid to solidify. The cold variant solidifies the drug-lipid mixture first, grinds it and homogenises the powder in a cold surfactant solution. Cold homogenization lessens heat exposure

and limits partitioning of drug into the aqueous phase, but it generally gives larger particles and a wider size distribution than the hot process (Mehnert and Mäder, 2001). For curcumin, whose stability in hot, aqueous, alkaline media is limited, the choice between the two is a real design decision.

Microemulsion-based preparation avoids high-energy equipment. A warm, optically clear microemulsion containing the molten lipid, surfactant, co-surfactant and water is dispersed into a large volume of cold water, causing the lipid to precipitate as nanoparticles. This route yielded the curcumin SLNs of Kakkar et al. (2011), with a mean diameter of 134.6 nm, an entrapment of 81.9% at 10% drug loading and stable particle size and content over 12 months at refrigerated temperature. Its drawbacks are the large surfactant and co-surfactant content and the dilute dispersion that results, which may need concentration before use.

Homogenization can be combined with ultrasonication to refine particle size. Shelat et al. (2015) prepared curcuminoid SLNs from Compritol 888 ATO and Precirol ATO 5 with a phospholipid surfactant by high-pressure homogenization followed by ultrasonication, obtaining particles of 200-300 nm with entrapment close to 80%, and then freeze-dried them using sucrose or dextrose as cryoprotectants. Probe sonication is convenient at laboratory scale, but it gives limited throughput and risks metal shedding from the probe, so it is normally a bridge to a scalable homogenization step rather than an end point.

Solvent-based methods dissolve the lipid and drug in an organic solvent and either emulsify the solution into water or inject it into an aqueous surfactant phase. Wang et al. (2012) used solvent injection to prepare curcumin SLNs of about 190 nm with a zeta potential of -20.7 mV and 75% entrapment efficiency. These methods work at low temperature and can give small particles, but residual solvent has to be removed and quantified, which adds a step and a regulatory burden that is especially relevant for products intended for use around a surgical wound.

Matching the method to the post-operative target is therefore a trade-off between thermal exposure, scalability, solvent residues and particle-size control. Table 1 summarises the main options.

Table 1. Main SLN production methods and their relevance to curcumin

Method	Principle	Strengths	Limitations for curcumin
Hot high-pressure homogenization	Drug in molten lipid dispersed in hot surfactant solution, homogenised under high pressure, then cooled	Scalable, solvent-free, established equipment	Thermal exposure of drug; drug can partition into the hot aqueous phase
Cold high-pressure homogenization	Drug-lipid solid ground and homogenised in cold surfactant solution	Less heat exposure, less drug loss to the aqueous phase	Larger particles and broader size distribution
Microemulsion dilution	Warm microemulsion dispersed into cold water	Simple, low energy input, small particles	High surfactant content, dilute product
Homogenization plus ultrasonication	High-shear or high-pressure step followed by probe sonication	Accessible at laboratory scale, refines size	Limited throughput, possible probe contamination, local heating
Solvent injection or emulsification	Lipid and drug in solvent introduced into aqueous surfactant phase	Low temperature, small particles	Residual solvent, extra removal step

Formulation Optimization: Critical Variables, Quality by Design and Design of Experiments

Optimization of an SLN is best organised on quality-by-design (QbD) lines. QbD begins with a quality target product profile (QTPP), a prospective summary of the attributes a product must have to deliver its intended clinical effect. From the QTPP the critical quality attributes (CQAs) are identified:

the measurable properties that must lie within defined limits. A risk assessment then links these to critical material attributes (CMAs) and critical process parameters (CPPs), designed experiments map the relationship between inputs and outputs, and the resulting design space and control strategy ensure that quality is built in rather than only tested at the end.

Defining the target

For a curcumin SLN intended for post-operative use, the QTPP should specify the route, dose, onset and duration of exposure, and shelf life. Published curcumin SLNs provide benchmarks: Kakkar et al. (2011) reported 134.6 nm particles with 81.9% entrapment, and Wang et al. (2012) reported particles of about 190 nm with 75% entrapment and a zeta potential of -20.7 mV. Table 2 proposes working targets for a first-generation product. They are derived from this literature and are meant to be refined once clinical requirements are fixed; they are not validated specifications.

Table 2. Proposed working targets for curcumin SLNs intended for post-operative use

Attribute	Working target	Rationale
Mean particle size (z-average)	100-200 nm	Falls within the range reported for curcumin SLNs; supports absorption or dermal deposition
Polydispersity index (PDI)	0.3 or lower	A narrow distribution favours reproducible release and physical stability
Zeta potential	Magnitude of 20 mV or more, or near-neutral if sterically stabilised	Electrostatic or steric barrier against aggregation
Entrapment efficiency	75% or higher	Matches benchmarks from published formulations
Drug loading	5-10% of lipid mass	Balances dose volume against lipid capacity
In vitro release	Limited early burst, sustained release over 24 h or longer	Early effect followed by continued cover
Storage stability	No significant change in size, PDI or content over 12 months at 2-8 °C	Practical shelf life for a refrigerated product

Critical material attributes

The lipid sets the ceiling on drug loading, because the solubility of curcumin in the molten lipid determines how much can be dissolved before it separates as crystals. Lipid melting point, polymorphic behaviour and digestibility then affect stability and in vivo fate. Glyceryl behenate (Compritol 888 ATO), glyceryl palmitostearate (Precirol ATO 5) and tristearin are common choices. The surfactant is not a passive stabiliser. Ban et al. (2020) prepared tristearin SLNs with PEGylated emulsifiers and showed that the type and concentration of emulsifier modulated lipolysis during simulated digestion. More than 91% of the curcumin was bioaccessible in all formulations, and SLNs made with long PEGylated emulsifiers, whose digestion micelles carried a near-neutral surface charge, permeated a mucus-covered epithelium rapidly and gave a bioavailability more than 12 times that of curcumin solution in rats. The lesson for optimization is that interfacial design influences absorption as well as particle size. The drug-to-lipid ratio is a further critical attribute: too high a ratio exceeds the capacity of the matrix and favours expulsion, whereas too low a ratio wastes lipid and enlarges the dose volume. Co-surfactant and cryoprotectant, where used, complete the list.

Critical process parameters

For homogenization-based processes the main parameters are the processing temperature relative to the lipid melting point, the pressure and number of cycles, the pre-emulsification speed and time, and the cooling rate, which governs which lipid polymorph crystallises. Too many cycles can raise the energy input to the point that particles coalesce. For ultrasonication the amplitude and duration matter, and for freeze-drying the type and concentration of cryoprotectant do, with sucrose and dextrose having proved suitable for curcuminoid SLNs (Shelat et al., 2015). Because curcumin degrades in heat and in alkaline aqueous media, the time spent at elevated temperature and the pH of the aqueous phase should

be treated as CPPs and followed with a stability-indicating assay rather than a simple absorbance reading.

Design of experiments

Because the number of candidate variables is large, a two-stage strategy is efficient. A screening design, such as a fractional factorial or Plackett-Burman design, identifies the few variables with significant effects. A response-surface design then maps them in detail. Box-Behnken design (BBD) and central composite design (CCD) are the usual choices. A three-factor BBD needs 15 to 17 runs depending on the number of centre points and avoids extreme corner combinations, whereas a three-factor CCD needs about 20 runs and adds axial points that extend the explored region. Here Y is a response such as particle size, X are the coded factors, the β terms are fitted coefficients for linear, quadratic and interaction effects, and ε is the error. The significance of each term is judged by analysis of variance, and the adequacy of the model by lack-of-fit, R^2 and predicted R^2.

This approach has been used successfully in related systems. A Box-Behnken design was applied to SLNs of tetrahydrocurcumin, a hydrogenated curcumin metabolite, with drug-to-lipid ratio, surfactant concentration and co-surfactant concentration as factors and particle size, entrapment efficiency and PDI as responses (Sharma et al., 2023). The optimised batch, made at a drug-to-lipid ratio of 1:4.16 with 1.21% surfactant and 0.4775% co-surfactant, gave 147.1 nm particles, 83.58% entrapment and a PDI of 0.265, and electron microscopy confirmed a mono-dispersed population of about 145 nm. The active in that study was tetrahydrocurcumin rather than curcumin, but the workflow transfers directly. A three-factor, three-level BBD was likewise used to optimise a curcumin-loaded NLC, with solid-to-liquid lipid ratio, surfactant concentration and ultrasonication time as factors and particle size, entrapment efficiency and percentage release as responses, predicting an optimum at a lipid ratio of about 3.1, 2.1% surfactant and 4.8 min of ultrasonication (Agrawal et al., 2021). Curcumin- and resveratrol-loaded SLNs have also been prepared and characterised in vitro as a polyphenol delivery platform (Gumireddy et al., 2019).

A proposed optimization design

For the post-operative target in Table 2, a three-factor Box-Behnken design is proposed as a starting point (Table 3). The ranges are illustrative and should be fixed only after solubility screening of curcumin in candidate lipids and a surfactant-compatibility study. The responses should go beyond size and entrapment to include zeta potential and early and late release, because these relate most directly to the clinical profile.

Table 3. Illustrative Box-Behnken design for curcumin SLNs (factor levels are proposals, not experimental results)

Factor	Low (-1)	Middle (0)	High (+1)
X1: drug-to-lipid ratio (w/w)	1:15	1:10	1:5
X2: total surfactant (% w/v)	1.0	2.0	3.0
X3: homogenization or sonication time (min)	3	5	7

The responses would be Y1 z-average size, Y2 PDI, Y3 entrapment efficiency, Y4 zeta potential and Y5 and Y6 the percentage released at 2 h and 24 h. The numerical optimum is located with a desirability function that minimises size and PDI, maximises entrapment and constrains early release. It must then be verified by at least three confirmatory batches whose observed values fall within the model's prediction intervals. Only after that verification can the region be claimed as a design space.

Physicochemical Characterization

Characterization has two purposes: to confirm that an optimised formulation meets its CQAs, and to detect the structural changes on storage that make SLNs hard to control. As Mehnert and Mäder (2001) stressed, no single technique can describe a system in which size, surface properties and lipid crystallinity all matter, so a panel of complementary methods is required. Table 4 lists the core panel for a curcumin SLN.

Table 4. Core characterization panel for curcumin-loaded SLNs

Technique	Attribute measured	Interpretation
Dynamic light scattering (photon correlation spectroscopy)	Z-average diameter and PDI	Sub-200 nm size with PDI of about 0.3 or lower indicates a controlled population
Laser diffraction	Presence of larger particles	Detects micron-sized aggregates or lipid crystals that dynamic light scattering may miss
Electrophoretic	Zeta potential	Predicts electrostatic

Technique	Attribute measured	Interpretation
light scattering		stability; interpret together with steric stabilisation
Transmission or scanning electron microscopy, atomic force microscopy	Morphology and size	Confirms spherical shape and cross-checks light-scattering results
Differential scanning calorimetry	Melting and crystallisation behaviour	Reveals lipid crystallinity and the physical state of the drug
X-ray diffraction	Lipid polymorph and drug crystallinity	Shows whether curcumin is molecularly dispersed or crystalline
Fourier-transform infrared spectroscopy	Drug-lipid interaction	Identifies hydrogen bonding or chemical interaction
Stability-indicating HPLC	Total and free drug, degradation products	Gives entrapment efficiency, loading, content and chemical stability

Size, polydispersity and surface charge. Particle size controls absorption, tissue penetration and the rate of drug release, and PDI indicates whether the population is uniform. A zeta potential of about 20 to 30 mV in magnitude is conventionally taken to give adequate electrostatic stabilisation, yet this rule must not be applied mechanically. Curcumin SLNs with a modest zeta potential, such as -20.7 mV (Wang et al., 2012), can be acceptably stable, and SLNs stabilised by PEGylated emulsifiers rely on steric rather than electrostatic stabilisation, while the near-neutral micelles formed on digestion of long-PEGylated SLNs crossed a mucus-covered epithelium rapidly in the study of Ban et al. (2020). Microscopy offers an independent check. In the optimised tetrahydrocurcumin SLNs, transmission electron microscopy gave about 145 nm, in close agreement with the 147.1 nm obtained from light scattering (Sharma et al., 2023). A marked difference between the two measurements would indicate aggregation, a hydration layer effect or a bimodal population.

Physical state of lipid and drug. Differential scanning calorimetry and X-ray diffraction reveal whether the lipid has crystallised into a stable or a metastable form and whether curcumin remains crystalline or is molecularly dispersed. X-ray diffraction showed the encapsulated curcumin in SLNs to be amorphous, in keeping with its dispersion within the lipid (Wang et al., 2012). This finding is favourable for dissolution, but the stability of the amorphous or dispersed state must be tracked on storage because polymorphic transitions of the lipid can expel the drug (Naseri et al., 2015).

Entrapment efficiency and loading. Entrapment efficiency is the proportion of drug that is associated with the particles rather than free in the dispersion, and drug loading is the proportion of the particle mass that is drug.

Separation of the free fraction is the weak link. Curcumin is so poorly soluble that most unentrapped drug is present as crystals or adsorbed to surfaces rather than in solution, and it sticks to filter membranes and plastic. Ultracentrifugation or ultrafiltration protocols therefore need recovery controls, and the particle-associated drug should be measured directly after dissolution of the lipid as well as indirectly by difference. A stability-indicating method is also essential, because curcumin degrades into products that absorb at overlapping wavelengths.

Product-specific tests. For a topical or peri-incisional product, pH, viscosity or rheology, spreadability and skin or wound-bed retention are added to the panel, and the dispersion is usually incorporated into a gel. For any injectable or wound-contact use, sterility, endotoxin and particulate matter become release tests.

Drug Release, Stability and Pharmacokinetics

In vitro release

Release testing of a lipophilic drug is difficult because sink conditions are hard to maintain. For curcumin the medium usually needs a solubilising agent, such as a low concentration of a non-ionic surfactant, and must be buffered and protected from light, since curcumin degrades at neutral to alkaline pH. Dialysis-bag and sample-and-separate methods are common for oral products, and diffusion cells are used for topical gels. Release data are then fitted to zero-order, first-order, Higuchi and Korsmeyer-Peppas models to infer the mechanism. The observed profiles for curcumin SLNs are consistent with the structural picture in Section 4. Kakkar et al. (2011) found that release was predominantly diffusion controlled and prolonged for up to seven days. Wang et al. (2012) observed an initial burst followed by sustained release, the typical signature of a drug

fraction located in the outer shell together with a fraction held within the lipid core (zur Mühlen et al., 1998). Because the burst fraction is a design variable, it can be tuned through the drug-to-lipid ratio and the surfactant level, as outlined in Table 3.

Physical and chemical stability

Two kinds of instability must be controlled. Physical instability includes particle growth, aggregation, gelation and polymorphic transition of the lipid, which may expel the drug. Chemical instability is the degradation of curcumin itself by hydrolysis, oxidation and light. A well-designed SLN should slow the second by sequestering curcumin from the aqueous phase, and an SLN designed for curcumin has been reported to improve its stability against photodegradation (Gupta et al., 2020). In the microemulsion-based formulation, particle size and curcumin content showed no significant variation over 12 months at refrigerated temperature (Kakkar et al., 2011). Where long-term storage as a dispersion is not feasible, freeze-drying with a cryoprotectant offers a route to a solid product, as shown with sucrose and dextrose for curcuminoid SLNs (Shelat et al., 2015). Stability studies for a product intended for clinical use should follow the relevant international guidance on long-term and accelerated storage.

Pharmacokinetics

SLNs alter the pharmacokinetics of oral curcumin by several mechanisms: they present the drug in a solubilised form, they protect it from degradation in the gut, they release it gradually, and digestion of their lipid generates mixed micelles that carry the drug to the absorptive surface (Ban et al., 2020). The effect on the concentration-time profile is as important as the effect on total exposure. In rats, free curcumin gave a sharp early peak that fell away rapidly, whereas SLN-entrapped curcumin gave a slower rise and a more sustained plasma concentration over a longer period (Kakkar et al., 2011). For a post-operative anti-inflammatory, that sustained profile is advantageous because inflammation persists for days.

Table 5 summarises the principal oral pharmacokinetic comparisons from the studies reviewed here. The comparators differ, so the fold changes should not be ranked against one another.

Table 5. Reported improvements in curcumin exposure with SLNs in animal models

Study	SLN system	Comparator	Reported outcome
Kakkar et al. (2011)	Microemulsification-based curcumin SLNs	Solubilised curcumin, rats	39-fold higher bioavailability at 50 mg/kg and 155-fold at 1 mg/kg
Shelat et al. (2015)	Compritol 888 ATO and Precirol ATO 5 SLNs	Marketed curcumin product, rats	About 12-fold higher oral bioavailability
Wang et al. (2012)	Solvent-injection curcumin SLNs	Curcumin alone, mice	Higher plasma concentrations and higher tissue levels, especially in lung and liver
Gupta et al. (2020)	Curcumin SLNs (CLEN)	Free curcumin and a bioavailable commercial product	About 9-fold higher than the commercial product
Ban et al. (2020)	Tristearin SLNs with long PEGylated emulsifiers	Curcumin solution, rats	More than 12-fold higher bioavailability

Several cautions apply. The fold increase depends on the comparator, which ranges from an unformulated suspension to a commercial bioavailable product. It is also dose dependent, being larger at lower doses in the work of Kakkar et al. (2011), a pattern that may reflect saturable absorption of the free drug. Rodent data translate imperfectly to humans, and parent curcumin and its conjugated metabolites should be measured separately, since total curcumin after enzymatic hydrolysis can overstate the active fraction. Finally, for post-operative use, early exposure matters as much as total area under the curve, so partial areas over the first hours, time to peak concentration and duration above an effective concentration should be pre-specified endpoints. Wang et al. (2012) also showed that tissue concentrations rose after SLN administration, notably

in lung and liver. Such distribution is encouraging for systemic anti-inflammatory action but also a reminder that nanoparticles tend to accumulate in organs of the mononuclear phagocyte system, which has to be considered in toxicology.

Anti-inflammatory Efficacy and Post-operative Applications

Does greater exposure translate into greater effect?

Higher plasma levels are only a surrogate; the question for clinicians is whether SLNs improve anti-inflammatory outcomes. The clearest published demonstration comes from an ovalbumin-induced allergic asthma model. Curcumin-loaded SLNs suppressed airway hyperresponsiveness and inflammatory cell infiltration and significantly inhibited the T-helper-2 cytokines IL-4 and IL-13 in bronchoalveolar lavage fluid, compared with both the untreated asthma group and the group given curcumin alone (Wang et al., 2012). Asthma is not a surgical condition, but the study is informative: curcumin produced a stronger pharmacodynamic effect when delivered in SLNs than when given alone, and tissue concentrations of curcumin were higher in lung and liver. That is the logic on which a post-operative product would rest. To the best of the evidence reviewed here, no study has yet tested curcumin SLNs in a surgical or post-operative model, and this is the most important gap in the field.

Candidate post-operative applications

Three scenarios merit consideration (Table 6). The oral systemic route is the most direct extension of existing clinical work. Conventional curcumin lowered pain and fatigue scores and analgesic use after laparoscopic cholecystectomy (Agarwal et al., 2011), and curcuminoids at 250 mg four times daily on post-operative days one to three suggested reduced pain after laparoscopic gynaecological surgery (Phoolcharoen et al., 2019). Both studies were small and confined to a single procedure type. If SLNs raise exposure by an order of magnitude, a hypothesis worth testing is that comparable effects could be obtained with lower doses, less variability and less dependence on the fed state, but that remains a hypothesis. Topical delivery to the wound is the second scenario. Curcumin incorporated into collagen films supported dermal wound healing in rats through slow delivery and antioxidant activity (Gopinath et al., 2004), which supports the principle of local delivery to the wound bed. SLNs suit this role because they can be incorporated into hydrogels, form occlusive films that hydrate the skin and promote retention in the upper layers, and protect curcumin from light and oxidation on the wound surface.

Table 6. Candidate post-operative uses of curcumin-loaded SLNs

Scenario	Route	Rationale	Key design implication
Systemic adjunct after abdominal or laparoscopic surgery	Oral	Builds on trials of conventional curcumin; aims to reduce analgesic need	Consistent early exposure; compatibility with fasting and altered gut transit
Wound or incision care	Topical gel or dressing	Local anti-inflammatory and antioxidant action at the wound bed	Small particle size, adhesion, retention, sterility or low bioburden
Local infiltration or implant (exploratory)	Peri-incisional	Prolonged local cover without systemic exposure	Sterile, endotoxin-free, extended release; needs separate safety package

A proposed preclinical evaluation pathway

A credible development path would proceed from cells to animals to humans. In vitro, lipopolysaccharide-stimulated macrophages can be used to quantify suppression of TNF-α, IL-6, nitric oxide and prostaglandin E2, and a fibroblast scratch assay can check that wound repair is not impaired. In vivo, an acute inflammation model such as carrageenan paw oedema provides a rapid screen, after which a rodent incisional or laparotomy model gives a surgically relevant setting. Endpoints should include paw or tissue swelling, mechanical withdrawal thresholds, serum C-reactive protein and IL-6, and histology of inflammatory infiltrate, angiogenesis and collagen deposition, with wound tensile strength as a functional measure. Each study should contain, at a minimum, vehicle, blank SLN, unformulated curcumin at an equivalent dose and a standard NSAID comparator, so that the contribution of the carrier and the gain from formulation can be separated.

Combination with conventional analgesia and safety interactions

A realistic aim is to reduce, rather than replace, opioid and NSAID use, and the trial of Agarwal et al. (2011), in which fewer rescue analgesic tablets were consumed, points in that direction. Raising systemic exposure also raises questions that conventional low-exposure curcumin did not. Curcumin has the potential to affect platelet function and drug-metabolising enzymes, and these properties matter around surgery, so the timing of dosing relative to the procedure, concomitant anticoagulants and renally cleared drugs need to be addressed in the clinical protocol. Nanoformulation makes these considerations more, not less, pertinent.

Safety, Scale-up and Regulatory Aspects

The safety case for SLNs starts from their composition. The lipids are of physiological or food-grade origin and biodegradable, and the lipid carrier is considered of low toxicity, which is one reason SLNs are viewed as having a simpler route to approval than polymeric carriers (Naseri et al., 2015). That favourable starting point does not remove the need for a product-specific assessment. Surfactants are often the more toxic components, and their concentration should be kept as low as the stability data allow. PEGylated emulsifiers, which can improve mucus permeation (Ban et al., 2020), call for attention to possible immune responses on repeated exposure. Systemic exposure to a nanoparticle also adds distribution questions that a simple solution does not, and the accumulation of curcumin in liver after SLN administration (Wang et al., 2012) makes hepatic and mononuclear phagocyte system toxicology a standard part of the package. For topical products, skin irritation, sensitisation and local tolerance at a wound edge must be demonstrated, and curcumin's intense yellow colour should be considered for dressings and for any assessment of wound appearance.

Sterility is a practical hurdle for wound-contact or injectable products. SLN dispersions are sensitive to heat, and autoclaving can cause particle growth or gelation, while irradiation can degrade lipid and drug. Options include aseptic processing, sterile filtration of dispersions below roughly 200 nm and the use of sterile starting materials, each of which has to be validated against the size and viscosity of the product. For oral products, microbial limits are enough.

Scale-up is comparatively favourable. High-pressure homogenization is a reliable technique available in a range of sizes at reasonable cost (Sastri et al., 2020), and a design space defined at laboratory scale can be carried to larger equipment by holding the critical parameters, such as pressure, cycle number and temperature, within the ranges explored. Typical scale-up failure modes include altered cooling rates, which change polymorphic outcome, and differences in energy input per unit volume, which change particle size. Freeze-drying, where used, adds its own process validation. Process analytical technology, such as in-line particle-size measurement, can support a control strategy.

Regulatory classification depends on the intended claim and region. A product positioned as a dietary supplement faces different evidence requirements from one developed as a medicine for post-operative inflammation, and only the latter would require the full package of quality, non-clinical and clinical data. Regulators generally expect nanomedicines to be characterised for critical attributes such as size distribution, surface properties and drug release, to show comparability across batches and scales, and to follow established stability guidance. A formulation developed through the QbD route in Section 6 is well placed to meet those expectations, because the relationship between process, attributes and performance has already been documented.

Challenges

The literature on curcumin SLNs is strong on formulation and pharmacokinetics in animals but thin where a post-operative product would be judged. No study identified here has tested curcumin SLNs in a surgical model or in surgical patients. Comparators vary from plain curcumin to commercial bioavailable products, which makes fold changes difficult to compare across papers (Table 5). Human pharmacokinetic data for SLN curcumin are lacking, and the translation from rodent exposure to clinical benefit is uncertain even for conventional curcumin, for which the clinical importance of low bioavailability remains debated (Kunnumakkara et al., 2019). Loading remains a structural constraint of crystalline lipid matrices (Naseri et al., 2015), and the long-term physical stability of a nanodispersion, particularly its resistance to polymorphic change, has to be shown for each product rather than inferred.

Future perspectives

Several developments are likely to matter. NLCs, which mix solid and liquid lipids, can raise loading and limit expulsion, and QbD optimization of curcumin NLCs is already under way (Agrawal et al., 2021). Surface engineering, for example with PEGylated emulsifiers to modulate mucus transit (Ban et al., 2020), offers a second lever on absorption. Incorporating SLNs into gels, films and wound dressings would suit topical post-operative use, building on the rationale of local curcumin delivery to wounds (Gopinath et al., 2004). Combination approaches, in which an SLN carries curcumin together with a second agent, are another

option, although the interaction concerns raised by metabolic inhibitors such as piperine (Shoba et al., 1998) would need careful evaluation. Finally, data-driven methods, such as machine-learning models trained on well-reported DoE datasets, could reduce the number of experiments needed to locate an optimum, provided that studies report materials, factor levels and responses in a consistent and complete way.

Conclusion

Curcumin has a plausible and partly clinically supported role in moderating post-operative inflammation, but its pharmacokinetics prevent it from reaching that potential in unformulated form. SLNs address several of its weaknesses simultaneously. They solubilise it in a lipid matrix, protect it, prolong its release, and in animal studies raise oral exposure by roughly ten-fold or more, in some comparisons by far more. Optimization is the step that turns that potential into a reproducible product, and a quality-by-design approach built on Box-Behnken or central composite designs offers a rational route to a verified design space. The framework proposed here is a starting point for post-operative development, not a finished result. The priorities that follow from this review are:

- Develop and verify a design space for curcumin SLNs against the post-operative targets in Table 2.
- Test optimised formulations in surgical incision and wound models against unformulated curcumin and a standard NSAID.
- Characterise early-phase pharmacokinetics and the parent-to-metabolite ratio, not only total exposure.
- Complete toxicology, sterility and stability work suited to the chosen route.
- Run adequately powered clinical trials with opioid and NSAID sparing, pain, wound outcomes and safety as endpoints.

References

1. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int J Biochem Cell Biol. 2009;41(1):40-59. doi:10.1016/j.biocel.2008.06.010
2. Satoskar RR, Shah SJ, Shenoy SG. Evaluation of anti-inflammatory property of curcumin (diferuloyl methane) in patients with postoperative inflammation. Int J Clin Pharmacol Ther Toxicol. 1986;24(12):651-4.
3. Agarwal KA, Tripathi CD, Agarwal BB, Saluja S. Efficacy of turmeric (curcumin) in pain and postoperative fatigue after laparoscopic cholecystectomy: a double-blind, randomized placebo-controlled study. Surg Endosc. 2011;25(12):3805-10. doi:10.1007/s00464-011-1793-z
4. Phoolcharoen N, Oranratanaphan S, Ariyasriwatana C, Worasethsin P. Efficacy of curcuminoids for reducing postoperative pain after laparoscopic gynecologic surgery: a pilot randomized trial. J Complement Integr Med. 2019;16(4). doi:10.1515/jcim-2018-0224
5. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Mol Pharm. 2007;4(6):807-18. doi:10.1021/mp700113r
6. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery - a review of the state of the art. Eur J Pharm Biopharm. 2000;50(1):161-77.
7. Kakkar V, Singh S, Singla D, Kaur IP. Exploring solid lipid nanoparticles to enhance the oral bioavailability of curcumin. Mol Nutr Food Res. 2011;55(3):495-503. doi:10.1002/mnfr.201000310
8. Gupta T, Singh J, Kaur S, Sandhu S, Singh G, Kaur IP. Enhancing bioavailability and stability of curcumin using solid lipid nanoparticles (CLEN): a covenant for its effectiveness. Front Bioeng Biotechnol. 2020;8:879. doi:10.3389/fbioe.2020.00879
9. Hewlings SJ, Kalman DS. Curcumin: a review of its effects on human health. Foods. 2017;6(10):92. doi:10.3390/foods6100092
10. Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. Cancer Res Treat. 2014;46(1):2-18. doi:10.4143/crt.2014.46.1.2
11. Gopinath D, Ahmed MR, Gomathi K, Chitra K, Sehgal PK, Jayakumar R. Dermal wound healing processes with curcumin incorporated collagen films. Biomaterials. 2004;25(10):1911-7. doi:10.1016/S0142-9612(03)00625-2
12. Kunnumakkara AB, Harsha C, Banik K, Vikkurthi R, Sailo BL, Bordoloi D, et al. Is curcumin bioavailability a problem in humans: lessons from clinical trials. Expert Opin Drug Metab Toxicol. 2019;15(9):705-33. doi:10.1080/17425255.2019.1650914
13. Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas PS. Influence of

piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med. 1998;64(4):353-6. doi:10.1055/s-2006-957450
14. Shaikh J, Ankola DD, Beniwal V, Singh D, Ravi Kumar MNV. Nanoparticle encapsulation improves oral bioavailability of curcumin by at least 9-fold when compared to curcumin administered with piperine as absorption enhancer. Eur J Pharm Sci. 2009;37(3-4):223-30.
15. Ma Z, Wang N, He H, Tang X. Pharmaceutical strategies of improving oral systemic bioavailability of curcumin for clinical application. J Control Release. 2019;316:359-80. doi:10.1016/j.jconrel.2019.10.053
16. Mehnert W, Mäder K. Solid lipid nanoparticles: production, characterization and applications. Adv Drug Deliv Rev. 2001;47(2-3):165-96. doi:10.1016/S0169-409X(01)00105-3
17. zur Mühlen A, Schwarz C, Mehnert W. Solid lipid nanoparticles (SLN) for controlled drug delivery - drug release and release mechanism. Eur J Pharm Biopharm. 1998;45(2):149-55.
18. Üner M, Yener G. Importance of solid lipid nanoparticles (SLN) in various administration routes and future perspectives. Int J Nanomedicine. 2007;2(3):289-300.
19. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application. Adv Pharm Bull. 2015;5(3):305-13. doi:10.15171/apb.2015.043
20. Geszke-Moritz M, Moritz M. Solid lipid nanoparticles as attractive drug vehicles: composition, properties and therapeutic strategies. Mater Sci Eng C Mater Biol Appl. 2016;68:982-94.
21. Sastri KT, Radha GV, Pidikiti S, Vajhala P. Solid lipid nanoparticles: preparation techniques, their characterization, and an update on recent studies. J Appl Pharm Sci. 2020;10(6):126-41. doi:10.7324/JAPS.2020.10617
22. Duan Y, Dhar A, Patel C, Khimani M, Neogi S, Sharma P, et al. A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems. RSC Adv. 2020;10(45):26777-91.
23. Subroto E, Andoyo R, Indiarto R. Solid lipid nanoparticles: review of the current research on encapsulation and delivery systems for active and antioxidant compounds. Antioxidants (Basel). 2023;12(3):633.
24. Shelat P, Mandowara VK, Gupta DG, Patel SV. Formulation of curcuminoid loaded solid lipid nanoparticles in order to improve oral bioavailability. Int J Pharm Pharm Sci. 2015;7(6):278-82.
25. Wang W, Zhu R, Xie Q, Li A, Xiao Y, Li K, et al. Enhanced bioavailability and efficiency of curcumin for the treatment of asthma by its formulation in solid lipid nanoparticles. Int J Nanomedicine. 2012;7:3667-77. doi:10.2147/IJN.S30428
26. Ban C, Jo M, Park YH, Kim JH, Han JY, Lee KW, et al. Enhancing the oral bioavailability of curcumin using solid lipid nanoparticles. Food Chem. 2020;302:125328.
27. Sharma JB, Bhatt S, Tiwari A, Tiwari V, Kumar M, Verma R, et al. Statistical optimization of tetrahydrocurcumin loaded solid lipid nanoparticles using Box Behnken design in the management of streptozotocin-induced diabetes mellitus. Saudi Pharm J. 2023;31(9):101727. doi:10.1016/j.jsps.2023.101727
28. Agrawal M, Saraf S, Pradhan M, Patel RJ, Singhvi G, Ajazuddin, et al. Design and optimization of curcumin loaded nano lipid carrier system using Box-Behnken design. Biomed Pharmacother. 2021;141:111919.
29. Gumireddy A, Christman R, Kumari D, Tiwari A, North EJ, Chauhan H. Preparation, characterization, and in vitro evaluation of curcumin- and resveratrol-loaded solid lipid nanoparticles. AAPS PharmSciTech. 2019;20(4):145.