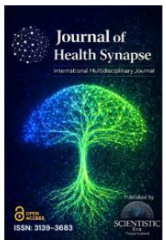
Research Article **ISSN: 3139-3683**

JOURNAL OF HEALTH SYNAPSE (JHS)
Peer Reviewed Refereed Open Access International Multidisciplinary Journal
Publisher: *Scientistic Era Private Limited*
Journal Hompage: *https://healthsynapse.org*



Development of Self-Emulsifying Drug Delivery Systems (SEDDS) for Enhanced Oral Bioavailability of Herbal Bioactives: A Comprehensive Review

Nainawat Hemant[a], **Rathore Abhimanyu Singh**[a*], **Chhajed Mahavir**[a]

[a]*Department of Pharmaceutics, Oxford International College, Indore, Madhya Pradesh, India*

***Corresponding author:** rathorejodha96@gmail.com

This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and the source are properly cited.

ARTICLE INFO

KEYWORDS:
Self-emulsifying drug delivery system (SEDDS); SMEDDS; SNEDDS; Herbal bioactives; Oral bioavailability; Pseudo-ternary phase diagram; Curcumin; Quercetin; Silymarin; Quality by Design (QbD).

ARTICLE HISTORY
Received Date: 30 September 2026
Revised Date: 15 October 2026
Accepted Date: 30 October 2026
Published Date: 15 November 2026

CITATION
Singh, R. A., Development of Self-Emulsifying Drug Delivery Systems (SEDDS) for Enhanced Oral Bioavailability of Herbal Bioactives: A Comprehensive Review, *Journal of Health Synapse (JHS), 1(4), 167-176.* https://doi.org/10.67529/jhs.v1i4.13

A B S T R A C T

Plant-derived bioactive compounds—including curcumin, quercetin, silymarin, resveratrol, and berberine—possess broad antioxidant, anti-inflammatory, hepatoprotective, antimicrobial, and metabolic therapeutic properties. Despite their promising pharmacological profiles, the oral clinical translation of many phytoconstituents is severely constrained by poor aqueous solubility, slow dissolution kinetics, chemical instability across gastrointestinal pH gradients, P-glycoprotein efflux, and extensive intestinal and hepatic first-pass metabolism. Self-emulsifying drug delivery systems (SEDDS), encompassing self-microemulsifying (SMEDDS) and self-nanoemulsifying (SNEDDS) formulations, represent isotropic mixtures of natural or synthetic lipids, surfactants, and co-surfactants or co-solvents that spontaneously generate fine oil-in-water emulsions upon gentle agitation in aqueous gastrointestinal media. By maintaining lipophilic herbal actives in a pre-dissolved submicron state, expanding interfacial surface area, and facilitating transcellular as well as chylomicron-mediated intestinal lymphatic transport, SEDDS significantly improve oral absorption and reduce pharmacokinetic variability. This review comprehensively examines the physicochemical principles and classification of self-emulsifying systems, lipid and surfactant screening, pseudo-ternary phase diagram construction, solidification into powders and pellets, dynamic light scattering (DLS) and electron microscopy characterization, Caco-2 permeability and in vivo pharmacokinetic case studies, Quality by Design (QbD) optimization, ICH stability guidelines, and Indian and international regulatory frameworks.

1. Introduction

Herbal medicines and purified plant secondary metabolites have served as cornerstones of preventive and therapeutic healthcare across centuries [5,52]. In modern pharmaceutical sciences, intense research has centered on structurally defined phytoconstituents—including curcumin, quercetin, silymarin, resveratrol, and berberine—owing to their well-documented antioxidant, anti-inflammatory, hepatoprotective, cardioprotective, antimicrobial, and metabolic regulatory activities [5–9,27–29]. Despite strong in vitro pharmacological potency, the clinical translation of these botanical compounds via the oral route is frequently hindered by poor aqueous solubility (characteristic of Biopharmaceutics Classification

System Class II and IV molecules), slow dissolution rates, chemical degradation in gastrointestinal fluids, intestinal efflux, and extensive pre-systemic metabolism [10–14].

Conventional oral solid and liquid dosage forms—such as compressed tablets, hard-shell capsules, and coarse aqueous suspensions—often fail to maintain lipophilic phytoconstituents in a solubilized state during gastrointestinal transit, resulting in erratic plasma profiles and subtherapeutic systemic exposure [14,18]. Lipid-based formulations, particularly self-emulsifying drug delivery systems (SEDDS), have emerged as highly versatile platforms to overcome dissolution-rate-limited oral absorption [1–4]. Comprising isotropic anhydrous blends of oils, surfactants, and co-surfactants or co-solvents, SEDDS spontaneously emulsify upon contact with aqueous gastrointestinal fluids under mild peristaltic agitation to generate fine oil-in-water (O/W) dispersions [1,2,13]. Depending on excipient composition and resultant droplet diameter, these formulations are subdivided into conventional SEDDS, self-microemulsifying drug delivery systems (SMEDDS), and self-nanoemulsifying drug delivery systems (SNEDDS) [2,4,42]. This review synthesizes the mechanistic principles, formulation design, pseudo-ternary phase screening, solidification approaches, analytical quality control, biopharmaceutical evaluation, Quality by Design (QbD) optimization, and regulatory considerations governing herbal SEDDS.

2. Fundamental Principles and Classification of Self-Emulsifying Systems

Self-emulsifying drug delivery systems are thermodynamically or kinetically stabilized anhydrous preconcentrates in which the lipophilic botanical active is molecularly dissolved within a lipid-surfactant vehicle [1,15]. Following oral administration and capsule shell rupture, gentle gastrointestinal motility provides the minimal mechanical energy required for spontaneous dispersion [3,17]. Surfactant molecules orient at the oil–water interface, lowering interfacial tension and facilitating the rapid formation of submicron lipid droplets that present a massive interfacial surface area for drug partitioning and pancreatic lipase digestion [11,12,36].

As summarized in Table 1, self-emulsifying lipid formulations are classified according to their lipid-to-surfactant ratio, hydrophilic–lipophilic balance (HLB), optical clarity upon aqueous dilution, and characteristic droplet size distribution [2,4,42]. While these droplet-size thresholds serve as widely accepted pharmaceutical benchmarks, they represent indicative physicochemical classifications rather than rigid statutory definitions.

Table 1. Indicative Classification and Physicochemical Characteristics of Self-Emulsifying Drug Delivery Systems

Delivery System	Formulation Composition	Dispersion Appearance & Droplet Size	Key Biopharmaceutical Attributes
Conventional SEDDS	Isotropic blend of oil (40–80% w/w), nonionic surfactant (HLB <12), and optional co-solvent	Turbid to translucent O/W emulsion (typically >250–300 nm)	Requires mild GI agitation; improves dissolution of lipophilic actives over crystalline powders
Self-Microemulsifying (SMEDDS)	Reduced oil phase (<20–40% w/w), high-HLB surfactant (>12), and hydrophilic co-surfactant	Optically transparent or translucent microemulsion (<250 nm)	Rapid spontaneous dispersion (<1–2 min) with large interfacial area and minimal precipitation
Self-Nanoemulsifying (SNEDDS)	Optimized lipid, high-HLB surfactant, and co-surfactant/co-solvent mixture	Clear or bluish-translucent nanoemulsion (<200 nm)	Kinetically stable nanodroplets resistant to GI dilution; promotes rapid enterocyte uptake

As illustrated in Figure 1, the biopharmaceutical superiority of SEDDS stems from keeping the botanical active in a dissolved molecular state throughout gastric and intestinal transit, thereby bypassing the rate-limiting solid-state dissolution step [11,12]. Additionally, long-chain triglyceride excipients stimulate chylomicron assembly within enterocytes, routing lipophilic phytoconstituents into the intestinal lymphatic system and bypassing hepatic first-pass metabolism [31,32]. Nevertheless, formulators must carefully manage potential drawbacks, including drug precipitation upon aqueous dilution in the gastrointestinal lumen, surfactant-induced mucosal irritation at elevated concentrations, lipid auto-oxidation, and capsule shell incompatibility [19,35,37].

Figure 1. Spontaneous Self-Emulsification of Herbal SEDDS/SNEDDS and Gastrointestinal Absorption Pathways

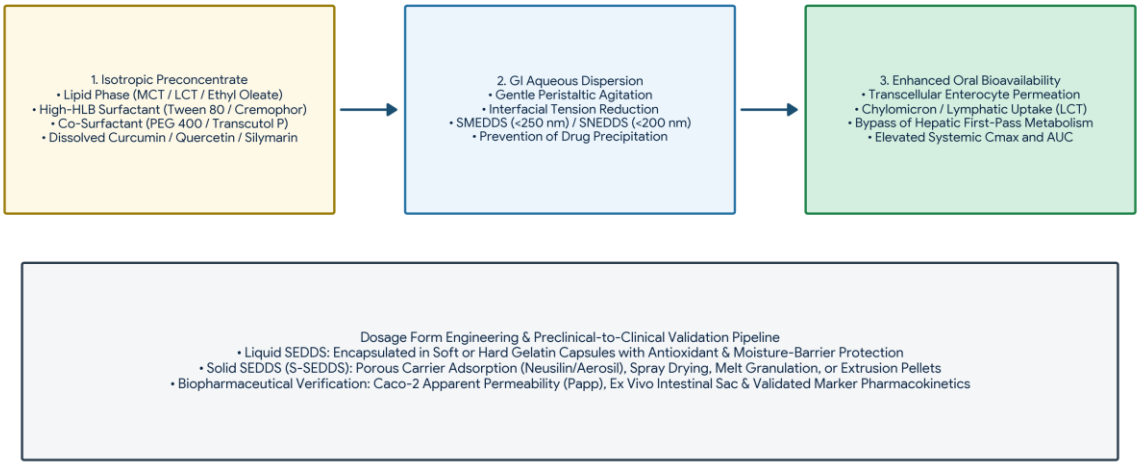


Figure 1. *Spontaneous self-emulsification of herbal SEDDS/SNEDDS in gastrointestinal fluids, transcellular and chylomicron-mediated lymphatic absorption pathways, and solidification technologies.*

3. Herbal Bioactives: Biopharmaceutical Challenges and Lipid Delivery Opportunities

3.1. Physicochemical and Metabolic Limitations of Phytoconstituents

Medicinal plant extracts encompass chemically diverse secondary metabolites—including flavonoids, diarylheptanoids, flavonolignans, stilbenoids, isoquinoline alkaloids, and triterpenoids—whose therapeutic exploitation is impeded by distinct biopharmaceutical constraints [5,53]:

- **Poor Aqueous Solubility:** High crystal lattice energy and lipophilicity restrict water solubility (e.g., curcumin <1 µg/mL; quercetin <10 µg/mL), preventing adequate dissolution in gastrointestinal fluids [7,8].
- **Extensive Pre-Systemic Metabolism:** Rapid phase-II glucuronidation, sulfation, and methylation in enterocytes and hepatocytes convert parent aglycones into less active conjugates, yielding low systemic bioavailability [27,28].
- **Chemical and Photolytic Instability:** Phenolic hydroxyls and conjugated double bonds undergo rapid hydrolytic cleavage at neutral-to-alkaline intestinal pH as well as light- and oxygen-mediated degradation [8,27].
- **P-Glycoprotein Efflux and Low Permeability:** Apical efflux transporters (such as P-gp and BCRP) and unfavorable molecular polarity restrict net transcellular flux across the intestinal epithelium [12,29].
- **Phytochemical Batch-to-Batch Variability:** Fluctuations in plant genotype, geographical origin, harvest season, and extraction solvent polarity alter marker ratios and excipient miscibility [5,51].
- **Limited Drug-Loading Capacity:** Maximum incorporation of crude or standardized botanical extracts into isotropic lipid preconcentrates is constrained by saturation solubility in the chosen oil–surfactant blend [10,14].

3.2. Candidate Botanical Bioactives for Self-Emulsifying Delivery

Incorporating poorly water-soluble phytoconstituents into optimized lipid vehicles protects labile functional groups from hydrolytic degradation, enhances mucosal wetting, and improves systemic exposure [5,14]. Table 2 outlines representative botanical bioactives investigated in self-emulsifying platforms, highlighting their botanical origins, primary pharmacological activities, and documented biopharmaceutical improvements.

Table 2. Representative Poorly Water-Soluble Herbal Bioactives Investigated in Self-Emulsifying Delivery Systems

Herbal Bioactive	Botanical Source	Major Pharmacological Activities	Formulation & Biopharmaceutical Rationale in SEDDS
Curcumin	Curcuma longa (rhizome)	Antioxidant, anti-inflammatory, neuroprotective, anticancer	Overcomes extreme hydrophobicity and alkaline GI hydrolysis;

			enhances plasma AUC [8,25]
Quercetin	Allium cepa, Malus domestica, berries	Antioxidant, anti-inflammatory, antidiabetic, cardioprotective	Improves dissolution, Caco-2 permeability, and systemic exposure over suspensions [7]
Silymarin	Silybum marianum (milk thistle seeds)	Hepatoprotective, antifibrotic, antioxidant	Enhances dissolution of flavonolignan complex and increases oral bioavailability [6,9,26]
Resveratrol	Vitis vinifera (grapes), Polygonum cuspidatum	Antioxidant, cardioprotective, anti-aging, metabolic modulator	Protects trans-isomer and mitigates rapid pre-systemic glucuronidation [27,28]
Berberine	Berberis aristata / Berberis vulgaris	Antimicrobial, antihyperglycemic, lipid-lowering	Improves intestinal membrane permeability and mitigates P-gp efflux [29]

4. Formulation Design, Excipient Screening, and Solidification Strategies

4.1. Lipid Phase Selection

The oil phase serves as the primary lipophilic solvent reservoir and governs drug loading, self-emulsification efficiency, and intestinal absorption pathways [1,10]. Commonly utilized lipid excipients include medium-chain triglycerides (MCTs, such as caprylic/capric triglycerides), long-chain triglycerides (LCTs, such as soybean, castor, sesame, and olive oils), mono- and diglycerides (Capmul MCM), and fatty acid esters (ethyl oleate, oleic acid, isopropyl myristate) [10,18]. MCTs generally exhibit superior solvent capacity and rapid emulsification, whereas LCTs promote chylomicron synthesis and lymphatic transport to circumvent hepatic first-pass clearance [31,32].

4.2. Surfactants, Co-Surfactants, and Precipitation Inhibitors

Nonionic surfactants with high hydrophilic–lipophilic balance (HLB >12)—including Tween 20, Tween 80, Cremophor RH 40 (polyoxyl 40 hydrogenated castor oil), Cremophor EL, and Labrasol—are preferred over ionic surfactants due to lower mucosal toxicity and pH-independent emulsification [14,19,45]. Co-surfactants and co-solvents—such as polyethylene glycol 400 (PEG 400), propylene glycol, Transcutol P (diethylene glycol monoethyl ether), ethanol, and glycerol—intercalate into the surfactant monolayer, reducing interfacial bending stress and expanding the self-emulsifying compositional domain [15,42]. However, total surfactant concentration must be minimized to prevent gastrointestinal irritation [19]. In supersaturable SEDDS (S-SEDDS), hydrophilic polymers such as HPMC or PVP are incorporated to inhibit drug nucleation and precipitation following aqueous dilution [23,24,37].

4.3. Solubility Screening, Pseudo-Ternary Phase Diagrams, and Solid SEDDS

Equilibrium saturation solubility is determined by adding excess herbal bioactive to individual oils, surfactants, and co-surfactants, equilibrating under isothermal shaking (25–37°C for 48–72 h), centrifuging, and quantifying dissolved solute via validated HPLC or UV-visible spectroscopy [4,14]. Using the top-performing excipients, pseudo-ternary phase diagrams are constructed via aqueous titration at fixed surfactant-to-co-surfactant weight ratios (Smix = 1:1, 2:1, 3:1) to map the isotropic O/W self-emulsifying region, as depicted in Figure 2A [2,15].

While liquid SEDDS preconcentrates are conventionally filled into soft or hard gelatin capsules, solidification into free-flowing powders, granules, or pellets enhances physical stability, prevents capsule leakage, and simplifies packaging [20,21]. Solid SEDDS (S-SEDDS) are produced via adsorption onto high-surface-area mesoporous carriers (e.g., Neusilin US2, Syloid, Aerosil), spray drying, melt granulation, or extrusion–spheronization, provided rapid re-emulsification upon contact with gastrointestinal fluid is preserved [20–22,38,39, 58-64].

Figure 2. Pseudo-Ternary Phase Diagram Screening, Analytical Characterization, and Quality by Design (QbD) Workflow

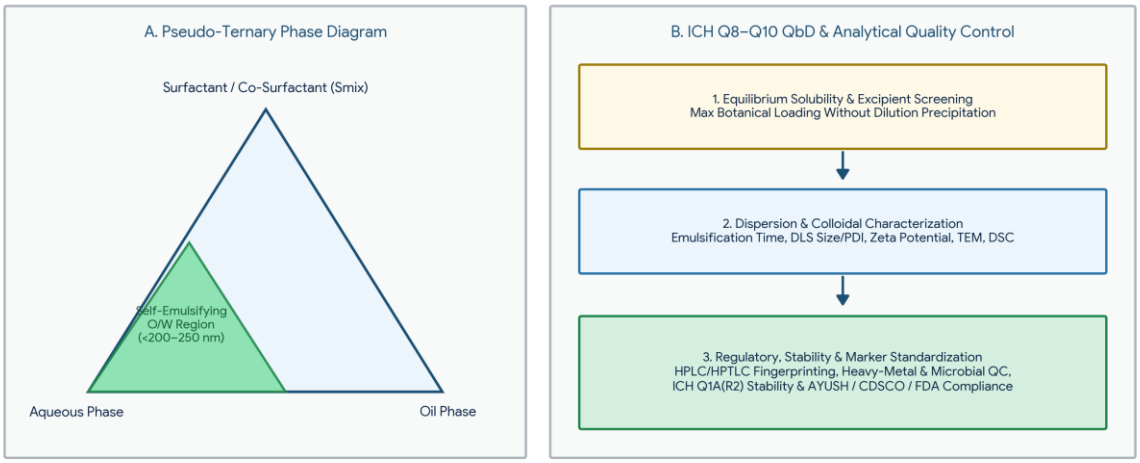


Figure 2. *Pseudo-ternary phase diagram construction for identifying the self-emulsifying domain (A) and ICH Q8–Q10 Quality by Design (QbD) and analytical quality control workflow (B).*

5. Physicochemical Characterization and Analytical Quality Control

Rigorous physicochemical evaluation ensures colloidal stability, rapid dispersion, and reproducible drug release [4,36]. Self-emulsification efficiency is assessed in USP Dissolution Apparatus II (50 rpm, 37 ± 0.5°C) across simulated gastric (pH 1.2) and intestinal (pH 6.8) fluids by recording emulsification time (<1–2 min), optical clarity, dispersibility grade (Grades A–E), and absence of phase separation or drug crystallization across 100- to 1000-fold dilutions [1,37]. Thermodynamic stability is verified via heating–cooling cycles (4°C and 45°C), centrifugation (3500–5000 rpm), and freeze–thaw stress testing (−20°C and +25°C) [14,42,57].

In vitro drug release is quantified under sink conditions using dialysis-bag or USP II methods, expressing cumulative percentage release as [4,25]:

Drug Release (%) = (Amount of Bioactive Released / Total Bioactive Content) × 100

As detailed in Table 3, complementary instrumental and chromatographic techniques are integrated to characterize colloidal droplet dimensions, thermal compatibility, lipid integrity, and phytochemical marker assay [4,5,54]. Notably, nonionic surfactant-stabilized SEDDS often exhibit modest absolute zeta potential values yet remain physically stable due to robust steric hindrance from polyoxyethylene chains [15,34].

Table 3. Analytical and Physicochemical Quality Control Techniques for Herbal SEDDS Formulations

Analytical Technique	Measured Property / Parameter	Pharmaceutical & Quality Control Application
Dynamic Light Scattering (DLS)	Mean hydrodynamic droplet size & polydispersity index (PDI)	Verifies sub-200/250 nm droplet size and unimodal distribution (PDI < 0.30) upon dilution
Zeta Potential Analyzer	Electrokinetic surface charge (mV)	Evaluates electrostatic repulsion alongside steric stabilization of dispersed droplets
Electron Microscopy (TEM / AFM)	Nanodroplet morphology and surface topography	Confirms spherical droplet geometry and absence of precipitated drug crystals
HPLC & HPTLC Fingerprinting	Quantitative marker assay & multi-component profile	Monitors drug loading, release kinetics, stability, and batch-to-batch extract consistency
UV-Visible Spectrophotometry	Rapid absorbance quantification	Supports preliminary equilibrium solubility screening where excipient

		interference is absent
FTIR & DSC / TGA	Vibrational spectra & thermal phase transitions	Detects drug–excipient compatibility, molecular dispersion, and thermal stability
Gas Chromatography (GC)	Fatty acid composition & residual solvents	Monitors lipid oxidative degradation and ICH Q3C residual solvent compliance

6. In Vitro Permeability, In Vivo Pharmacokinetics, and Case Studies

6.1. Biopharmaceutical Evaluation Models

Establishing biopharmaceutical superiority over conventional herbal powders or suspensions requires tiered permeability and pharmacokinetic testing [11,12]: (1) Caco-2 human colon adenocarcinoma cell monolayers cultured on Transwell inserts to determine the apparent permeability coefficient (Papp) and evaluate P-gp efflux modulation [7,19]; (2) ex vivo everted or non-everted rodent intestinal sac permeation studies quantifying mucosal-to-serosal flux [28]; and (3) in vivo animal pharmacokinetic studies (conducted under Institutional Animal Ethics Committee approval) measuring peak plasma concentration (Cmax), time to reach Cmax (Tmax), area under the plasma concentration–time curve (AUC0–t), elimination half-life (t½), and relative oral bioavailability [6–9]. Because botanical extracts contain multiple active constituents with distinct metabolic fates, validated LC-MS/MS or HPLC methods must monitor specific parent markers and conjugated metabolites [5,27].

6.2. Landmark Preclinical Case Studies

Experimental studies across major phytoconstituents illustrate the translational potential of self-emulsifying systems while underscoring the necessity of compound-specific optimization:

- **Silymarin SMEDDS:** Li et al. formulated a silymarin SMEDDS comprising 10% ethyl linoleate, 30% Cremophor EL, and 60% ethanol, achieving complete in vitro dissolution and a ~2.2-fold increase in relative oral bioavailability in fasted beagle dogs compared with commercial hard capsules [6].
- **Quercetin SNEDDS:** Tran et al. developed an isotropic quercetin SNEDDS composed of castor oil, Tween 80, Cremophor RH 40, and PEG 400 (mean droplet size ~208.8 nm), which significantly enhanced apical-to-basolateral transport across Caco-2 monolayers and increased plasma AUC and Cmax in rats by approximately 2-fold and 3-fold, respectively, versus aqueous suspension [7].
- **Curcumin SMEDDS:** Cui et al. demonstrated that incorporating curcumin into an optimized lipid-surfactant microemulsion concentrate markedly improved aqueous dispersion, chemical stability, and oral absorption in rats compared with unformulated curcumin suspension [8].
- **Solid Self-Emulsifying Silymarin Pellets:** Iosio et al. successfully converted liquid silymarin self-emulsifying systems into solid pellets via extrusion–spheronization using microcrystalline cellulose and lactose, preserving rapid emulsification and enhanced in vivo bioavailability while improving solid-dosage manufacturability [9].

7. Quality by Design (QbD), Stability, and Regulatory Framework

Implementing Quality by Design (QbD) in accordance with ICH Q8(R2), Quality Risk Management under ICH Q9(R1), and Pharmaceutical Quality Systems under ICH Q10 (illustrated in Figure 2B) ensures scalable, reproducible manufacturing [46–49]. Critical Material Attributes (CMAs—oil chain length, Smix ratio, drug loading) and Critical Process Parameters (CPPs—mixing temperature, shear speed, spray-drying or encapsulation conditions) are systematically mapped onto Critical Quality Attributes (CQAs—emulsification time, droplet size, PDI, and dissolution) via D-optimal mixture or Box–Behnken Design of Experiments (DoE) [4,46-47].

Accelerated and long-term stability protocols aligned with ICH Q1A(R2) monitor physical appearance, post-dilution droplet size and PDI, emulsification time, lipid peroxide/acid values, gelatin capsule shell brittleness, and HPLC/HPTLC marker retention in light- and moisture-protective packaging [65-70]. From a regulatory standpoint, herbal SEDDS products in India are governed by the Ministry of AYUSH, the Central Drugs Standard Control Organisation (CDSCO phytopharmaceutical guidelines), or the Drugs and Cosmetics Act and Rules depending on therapeutic claims, requiring authenticated botanical sourcing, heavy-metal, pesticide, mycotoxin, and microbial limit compliance, and excipient safety justification [71-82].

8. Current Challenges and Future Perspectives

Despite compelling preclinical gains, broader clinical commercialization of herbal SEDDS requires resolving several scientific bottlenecks [35,43]: (i) preventing supersaturation collapse and drug precipitation upon gastrointestinal dilution and lipid lipolysis [36,37]; (ii) reducing high surfactant levels through synergistic natural phospholipids and biosurfactants [19,30]; (iii) standardizing multi-component botanical extracts via quantitative HPLC/LC-MS fingerprinting [5]; (iv) maintaining rapid

dispersion kinetics in solid-SEDDS tablets and pellets over extended shelf life [20,21]; and (v) conducting well-powered human pharmacokinetic and randomized clinical efficacy trials to substantiate therapeutic claims [33,35].

9. Conclusion

Self-emulsifying drug delivery systems (SEDDS, SMEDDS, and SNEDDS) represent a highly effective lipid-based pharmaceutical strategy for overcoming the poor aqueous solubility, slow dissolution, chemical instability, and pre-systemic metabolism of lipophilic herbal bioactives such as curcumin, quercetin, silymarin, resveratrol, and berberine. By combining equilibrium solubility screening, pseudo-ternary phase diagram optimization, solid-SEDDS engineering, validated HPLC/HPTLC analytical quality control, ICH Q8–Q10 QbD principles, and comparative pharmacokinetic validation, researchers can systematically translate promising botanical actives into stable, scalable, and clinically effective oral therapeutics.

References

1. Singh B, Bandopadhyay S, Kapil R, Singh R, Katare OP. Self-emulsifying drug delivery systems (SEDDS): formulation development, characterization, and applications. Crit Rev Ther Drug Carrier Syst. 2009;26(5):427-521. doi:10.1615/critrevtherdrugcarriersyst.v26.i5.10.
2. Chouhan N, Mittal V, Kaushik D, Khatkar A, Raina M. Self emulsifying drug delivery system (SEDDS) for phytoconstituents: a review. Curr Drug Deliv. 2015;12(2):244-53. doi:10.2174/1567201811666141021142606.
3. Li X, Yuan Q, Huang Y, Zhou Y, Liu Y. Development of silymarin self-microemulsifying drug delivery system with enhanced oral bioavailability. AAPS PharmSciTech. 2010;11(2):672-8. doi:10.1208/s12249-010-9432-x. PubMed
4. Tran TH, Guo Y, Song D, Bruno RS, Lu X. Quercetin-containing self-nanoemulsifying drug delivery system for improving oral bioavailability. J Pharm Sci. 2014;103(3):840-52. doi:10.1002/jps.23858. PubMed
5. Cui J, Yu B, Zhao Y, Zhu W, Li H, Lou H, et al. Enhancement of oral absorption of curcumin by self-microemulsifying drug delivery systems. Int J Pharm. 2009;371(1-2):148-55. doi:10.1016/j.ijpharm.2008.12.009. ScienceDirect
6. Iosio T, Voinovich D, Perissutti B, Serdoz F, Hasa D, Grabnar I, et al. Oral bioavailability of silymarin phytocomplex formulated as self-emulsifying pellets. Phytomedicine. 2011;18(6):505-12. doi:10.1016/j.phymed.2010.10.012. PubMed
7. Pouton CW, Porter CJH. Formulation of lipid-based delivery systems for oral administration: materials, methods and strategies. Adv Drug Deliv Rev. 2008;60(6):625-37. doi:10.1016/j.addr.2007.10.010. PubMed
8. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Pharmaceutical development Q8(R2). Geneva: ICH; 2009. FDA
9. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Stability testing of new drug substances and products Q1A(R2). Geneva: ICH; 2003. European Medicines Agency (EMA)
10. Chhajed M, Rathore AS, Chhajed AJ, Lodha RJ, Yadav J, Sinha P, Bukkawar A, Patil P, Wathore S, Dubey I. Impact of National Education Policy 2020 on Internationalization of Pharmacy Education in India: Progress, Opportunities and Challenges.
11. Yadav J, Gupta D, Chhajed M, Rathore AS. Artificial Intelligence-Driven Design and Optimization of Micro needle-Based Drug Delivery System: A Review. International Journal of Advanced Research in Science, Communication and Technology. 2025 Oct;5(1):920-
12. Chhajed M, Rathore AS, Dulkar D, Sharma G. Autonomus Incident Remediation: A Closed Analytical Methods Validation in Pharmaceutical Analysis From Assumption to Realistic Optimization : A Review. International Journal of Advanced Research in Science, Communication and Technology. 2025 June; 5(8):737
13. Chhajed M, Chhajed AJ, Lodha RJ, Rathore AS, Bukkawar A, Mandloi M. Chronobiology and its Relevance to Drug Administration : Advancing Chronotherapeutic for Precision Medicine. International Journal of Advanced Research in Science, Communication and Technology. 2025 Dec;5(1):850
14. Chhajed M, Chhajed AJ, Rathore AS, Dwivedi SK, Verma Swapnil. Phytochemical Investigation and Pharmacological Evaluation for Antimicrobial, Anthelmintic and Antioxidant Activity of Solanum xanthocarpum Sehrad & Wendl. International Journal of Advanced Research in Science, Communication and Technology. 2026 Jan;6(4):767
15. Chhajed M, Rathore AS, Chouhan S, Mandloi M, Waghela R. Potential Herbal Drugs for the Treatment of Epileptic Seizures:A Review. International Journal of Advanced Research in Science, Communication and Technology. 2025 March;5(8):620
16. Dulakar D, Sinha P, Yadav J, Ahirwar S, Rathore AS, Chhajed M. Phytochemical Study of Murraya Koenigii:A

Review. International Journal of Advanced Research in Science, Communication and Technology. 2026 Feb;6(3):758
17. Rathore AS, Chhajed M, Rathore M, Yadav J, Patidar M, Jain A. Antioxidants in Indian Culture: A Comprehensive Study. International Journal of Advanced Research in Science, Communication and Technology. 2025 May;5(10):543
18. Chhajed M, Rathore AS, Jain A, Tanwar A, Patidar M. Formulation and Evaluation of Nanosuspension for Solubility and Dissolution Enhancement of Poorly Water soluble drugs. International Journal of Advanced Research in Science, Communication and Technology. 2025 July;5(1):794
19. Rathore AS, Chhajed M, Sinha P, Tanwar A, Awasthy A, Patidar Rajnandni. Anti- Aging: the way You Manage The Age. International Journal of Advanced Research in Science, Communication and Technology. 2025 Jan;5(2):807
20. Chhajed M, Rathore AS, Patil S, Patel AL, Kushwah N. Formulation and Evaluation of Rutin Phytosomes. International Journal of Advanced Research in Science, Communication and Technology. 2026 March;6(1):761
21. Rathore AS, Panwar AS. Formulation Optimization and Biological Evalution of Spinach based Glutathione Mouth Dissolving Granules for Anti Aging Potential. Journal of Health Synape. 2026 Oct;1(4):33- 48
22. Panwar AS, Rathore AS, Kaithwar K, Dhokpande A. Nanoengineered Drug Delivery Systems to Overcome Multidrug Resistance in Cancer. Journal of Health Synape. 2026 June;1(2):65-74
23. Rathore AS, Panwar AS, Dongre N. International Journal of Taxicological and Pharmacological Research. 2021 April;11(2):37-45
24. Baghel JS, Maheshwari RK. Novel application of mixed solvency concept in the development of fast dissolving solid dispersion of poorly water-soluble drug, torsemide and its evaluations. World J Pharm Res. 2020;9(1):1820-1839. doi:10.20959/wjpr20201-16587.
25. Gandhi MY, Prasad SB, Kumar V, Soni H, Rawat H, Mishra SK, et al. Quantification of phytochemicals and metal ions as well as the determination of volatile compounds, antioxidant, antimicrobial and antacid activities of the *Mimosa pudica* L. leaf: Exploration of neglected and under-utilized part. Chem Biodivers. 2023;20(10):e202301049.
26. Shamim, Ali S, Ali T, Sharma H, Kishor BN, Jha SK. Recent advances in monodisperse gold nanoparticle delivery, synthesis, and emerging applications in cancer therapy. Plasmonics. 2025;20(9):7121–41.
27. Jha SK, Singh N, Shanker OR, Antil I, Baghel JS, Huddar V, et al. A review on integrative approaches in oncology: Bridging Ayurvedic medicine and modern cancer therapeutics. Front Nat Prod. 2025;4:1635197.
28. Sharma S, Kumar C, Kushwaha H, Jha SK, Chawla S, Sharma A, et al. Advancing anticancer drug development: Overcoming challenges and exploring new therapeutic strategies. Ayush J Integr Oncol. 2025;2(1):8–27.
29. Gandhi Y, Kumar V, Singh G, Prasad SB, Mishra SK, Soni H, et al. Chemoprofiling and medicinal potential of underutilized leaves of *Cyperus scariosus*. Sci Rep. 2024;14(1):7263.
30. Singh A, Jha SK, Dwivedi PC, Srivastava U, Pal A. Revolutionizing healthcare: Integrating electronics, AI, traditional, and conventional methods. World J Adv Res Rev. 2024;23:2426–34.
31. Jha SK, Islam M, Kumar R, Rana L, Saifi MA, Ali S, et al. Evaluation of *Vernonia amygdalina* Del. containing phytoconstituents as potential inhibitors of monkeypox virus using molecular docking analysis. World J Adv Res Rev. 2023;17(1):1112–22.
32. Jha SK, Mishra AK, Kumar V, Dane G, Kumari S, Charde V, et al. Ecological and behavioral impacts of COVID-19 on human existence and potential preventive measures through traditional and alternative medicine: A narrative review. Pharmacol Res Nat Prod. 2024;3:100042.
33. Sonawane SM, Lohiya GV, Rao AK, Beniwal M, Chavan SU, Aparadh VM, et al. Conjunctivitis in unusual populations: A review of rare cases and challenges in diagnosis and management. World J Adv Res Rev. 2023;19(3):1326–36.
34. Khan R, Maheshwari D, Chauhan S, Lohiya GV, Kumar C, Antil I, et al. Exploring the potential therapeutic value of *Solanum lycopersicum* L. phytoconstituents for Parkinson's disease through molecular docking analysis. World J Adv Res Rev. 2023;20:488–501.
35. Sonkar V, Jha SK, Tiwari S, Akarsh A, Priya S, Sharan P, et al. Characterization and explanation of the soil fertility state of Sakaldiha block in the Chandauli District of Uttar Pradesh's industrial area. World J Adv Res Rev. 2023;18:63–72.
36. Singh NK, Sengar AS, Jha SK. A review of Ayurvedic measures for preventing COVID-19 and promoting health during pregnancy. J Indian Syst Med. 2024;12(2):61–5.
37. Trivedi LM, Saxena S, Sharma S, Beniwal M, Jha SK, Rao AK, et al. Characterization, profiling, and molecular docking analysis of phytochemicals derived from *Daucus carota* for evaluating their potential role in cardiovascular disease assessment. World J Adv Res Rev. 2023;20:159–75.
38. Mehta V, Zargar AA, Attri P, Jha SK. Bagging the role of herbal drugs in the management of cervical cancer. Ayush J Integr Oncol. 2025;2(1):35–43.

39. Chauhan S, Jha SK, Tamta A, Sharma V, Kumar C, Lohiya G, et al. Descriptive analytical study based on profiling, morphological, pomological and pharmacological traits to identify the genotypes of the promising mango *Mangifera indica* L. World J Adv Res Rev. 2023;19:1544–53.
40. Tamta, Arnima, and Sudhanshu Kumar Jha. "Screening of Germplasms and Population Dynamics of Major Insect Pests of Spring Green Gram Vigna radiata (Linn.)." PhD diss., Doctoral Dissertation, Doctoral Dissertation, GB Pant University of Agriculture and Technology, Pantnagar-263145 (Uttarakhand).
41. Kumar R, Verma H, Ali M, Midha T, Kumar D, Jha SK. Review of mitigating cancer risk through Ayurvedic practices: A holistic approach to combating sedentarism. Ayush J Integr Oncol. 2025;2(2):86–90.
42. Patel S, Singh S, Gupta AK, Dalimbe AY, Muthoju SM, Pawar AR, et al. Ayurveda and common Indian spices: A natural alternative for cancer therapy. Ayush J Integr Oncol. 2025;2(2):91–102.
43. Jha KT. Stereoisomerism in chemistry and drug development: Optical, geometrical, and conformational isomers. 2025.
44. Jha SK, Gupta A, Huddar VG. Botanical breakthroughs: The growing impact of plant-derived compounds in cancer treatment. Ayush J Integr Oncol. 2025;2(2):62–7.
45. Sharma A, Jha SK, Huddar VG. Integrative role of Ayurvedic phytochemicals in cancer treatment: Targeting signaling pathways, boosting chemosensitivity, and utilizing traditional therapeutics. Ayush J Integr Oncol. 2025;2(2):77–85.
46. Jha SK, Charde V, Kumar V, Narasimhaji CV. Vitiligo treatment with natural bioactive: A narrative review. Nat Prod J. 2026;16(3):e22103155337960.
47. Zargar AA, Mehta V, Gupta R, Bhandari K, Sharma MC, Balaji P, et al. Incretin hormones: Mechanisms, therapeutic implications, and future directions in glucose regulation and diabetes management. Curr Proteom. 2025;22:100014.
48. Doshi R, Lohiya G. Synthesis, in-silico design and spectral characterization, elucidation of *Cannabis sativa* L. (Cannabaceae) containing phytoconstituents demonstrating novel therapeutic efficacy against epilepsy.
49. Shrivastav S, Tyagi R, Singh M, Jha S. The effectiveness of curcumin on dysmenorrhea. Int J Med Sci Pharma Res. 2022;8(4):8–12.
50. Sharma S, Yadav C, Chawla S, Jha SK. Beyond chemotherapy: Exploring the potential of phytomedicine in oncology. Ayush J Integr Oncol. 2025;2(3):133–45.
51. Badal R, Ranjan S, Jha SK, Kumar L, Patel AK, Yadav P, et al. GC-MS/MS and HR-LCMS-QTOF analysis of various extracts of Saraswata Ghrita: A comprehensive dataset on phytochemical compounds. Data Brief. 2025;61:111675.
52. Ahlawat A, Chauhan S, Antil I, Jha SK, Huddar VG. Examining the impact of the microbiome on cancer immunotherapy outcomes: A review. Ayush J Integr Oncol. 2025;2(3):118–24.
53. Gupta AJ, Huddar VG, Jha SK, Soni U. Traditional wisdom in modern oncology: Ayurvedic pain relief and supportive care. Ayush J Integr Oncol. 2025;2(3):178–87.
54. Sandrepogu J, Khandelwal P, Tiwari SK, Jha SK, Chauhan S, Sharma H, et al. A holistic paradigm for cancer care: Merging Ayurveda with contemporary oncology. Ayush J Integr Oncol. 2025;2(4):254–61.
55. Antil I, Bangarwa S, Jha SK, Gupta AJ, Soni U, Huddar VG, et al. Exploring the chemopreventive and anticancer effects of green tea. Ayush J Integr Oncol. 2025;2(3):158–68.
56. Attri P, Zargar AA, Mehta V, Mushtaq SU, Jha SK, Soni U. Genetic basis of cancer: Harnessing natural remedies for therapeutic potential. Ayush J Integr Oncol. 2025;2(3):188–94.
57. Chauhan S, Jha SK, Huddar VG, Ahlawat A, Sharma S, Tripathi A, et al. Targeting cancer at the molecular level: A biochemical and medicinal chemistry approach. Ayush J Integr Oncol. 2025;2(3):169–77.
58. Pandey JK, Verma SK, Kumar J, Perwej Y, Jha SK, Panchal BY, et al. Transformative role of advanced neural computation in clinical image diagnostics: A review of key concepts and applications. Semin Ultrasound CT MR. 2026;47(5):374–90.
59. Sharma H, Mahto RR, Jha SK, Chauhan S, Khandelwal P, Tiwari SK. Rasayana-based adjuvant strategies in cancer care: An Ayurvedic-oncologic perspective. Iran J Blood Cancer. 2025;17(4):35–68.
60. Raj H, Sharma S, Tripathi A, Huddar VG, Jha SK. Herbal medicine in cancer therapy: A comprehensive review of phytoconstituents, mechanisms, and clinical applications. Ayush J Integr Oncol. 2025;2(3):146–57.
61. Shamim PT, Khatri N, Yadav AK, Mishra B, Khan MR, Behera SK, et al. Role of human chorionic gonadotropin in frozen-thawed embryo transfer cycles for secretory transformation: A narrative review. Eur Chem Bull. 2023;12(8):5477–93.
62. Mandal P, Kumar J, Bora D, Hashmi SA, Tiwari M, Gupta R, et al. Literature review on forensic implications of illicit drug metabolism: A medicinal chemistry perspective. J Forensic Leg Med. 2026;103158.
63. Kumar C, Chauhan P, Chauhan S, Jha SK, Lohiya G. Phyto-pharmacognostic experimental study of *Epimedium sagittatum* and *Gloriosa superba* L. for the treatment of hypogonadism. Int J Innov Sci Res Technol. 2023;8(6):254–60.

64. Raj H, Jha SK, Negi M, Khandelwal P, Chauhan S, Sharma H, et al. Integrative oncology: A comprehensive comparative analysis of herbal and allopathic medicine in cancer treatment. Curr Pharm Res. 2025;1:427–35.
65. Dhiman S, Thakur N, Dwivedi PC, Pande P, Jha SK, Lohiya GV. Phytochemicals: Investigating bioactive compounds for antifungal uses and quality issues in functional foods and therapeutics. 2024:258–68.
66. Singh V, Mandal P, Kaur N, Bora D, Gupta R, Kumar A, et al. Synthesis, characterization, and binding interactions of rhodanine-3-acetic acid-based compound for latent fingerprint development. J Forensic Sci. 2026;71(1):584–92.
67. Jha SK, Chaturvedi SK, Singh SK, Chauhan S, Chauhan P, Singh H, et al. Synthesis and in-silico design of a novel silver metal ciprofloxacin compound. World J Adv Res Rev. 2023;18(1):885–92.
68. Mahto RR, Bansal KS, Soni H, Tiwari SK, Sandrepogu J, Bhatted SK. Efficacy of Vidangadi Loha and Phalatrikadi Ghana Vati with and without the prior administration of Virechana Karma in Madhumeha (obese diabetic): A randomized controlled trial. Int J Drug Deliv Technol. 2026;16(41s):1275–81.
69. Shivani, Thakur N, Lohiya GV, Gupta R, Dhiman S, Bharadwaj S, et al. Natural origins, bioavailability and therapeutic potential of astaxanthin: A systematic review across diverse health applications. 2024:5929–39.
70. Tamta A, Jha SK. Implications of green technology for climate change mitigation minimizing waste and pollution. TIDEE. 2023;22(4):476.
71. Kaur AK, Venkatasubramanian H, Sarma S, Gupta R, Singh RG, Chaudhary B, et al. Targeting cancer pathways with phytochemicals: Molecular mechanisms and clinical potential. Curr Proteom. 2026;23(6):100182.
72. Patel S, Paliwal A, Jha SK, Singh R, Mishra AK. Environmental neurotoxicants as accelerators of brain ageing: Exposomic mechanisms linking pollution to amyloidogenesis and Alzheimer's disease. Int J Environ Health Res. 2026:1–21.
73. Dhiman S, Thakur N, Jha SK, Karkare P, Bora D, Sahu RK, et al. Pyrazole derivatives: A comprehensive review of synthesis, antimicrobial activity, structure-activity relationships, and therapeutic potential. Curr Proteom. 2026;23(5):100154.
74. Mundada AB, Mundada PA, Kathirvel S, Kumar PR, Krishnamoorthy P, Ezzaoui N, et al. Ion channels as emerging drug targets: Pharmacological insights and therapeutic advances. Curr Proteom. 2026;23(4):100141.
75. Midha T, Kumar D, Kumar A, Jha SK. Rasayana therapy in Ayurveda: A promising approach for cancer support and immunomodulation. [Publication details required].
76. Garg N, Sharma R, Bhojani MK, Rai S, More AB, Jha SK. Bridging traditional wisdom and modern science: An integrative approach to breast cancer care. Ayush J Integr Oncol. 2026;3(2):81–9.
77. Jha SK, Negi M, Singh K, Shukla D, Sharma H, Khandelwal P, et al. Harmonizing traditional Ayurvedic knowledge with modern science: A comprehensive review. Curr Pharm Res. 2026:393–410.
78. Antil I, Jha SK, Negi M, Sharma H, Tiwari SK. Baicalein from *Scutellaria baicalensis* as natural therapeutic agent for glioblastoma. Curr Pharm Res. 2025;1:411–26.
79. Mahto RR, Sharma H, Bhatted SK, Jha SK, Tiwari SK, Chauhan S, et al. Diabetes and erectile dysfunction: Exploring the Ayurvedic understanding of Madhumehaj Klaibya. Curr Pharm Res. 2026:446–57.
80. Gangurde RB, Goel P. Approach towards type 2 diabetes mellitus-induced erectile dysfunction (DMED): A case study.
81. Maheshwari RK, Jain S, Padria A, Mulani P, Baghel JS, Maheshwari N. Eco-friendly extraction using solids: a novel application of mixed solvency concept. J Drug Deliv Ther. 2019;9(2):244-249. doi:10.22270/jddt.v9i2.2409.
82. Kushwah P, Jain G, Patidar A, Baghel JS, Agarwal A. From ancient remedies to modern marvels: unveiling the medicinal secrets of Nyctanthes arbor-tristis and Piper betle Linn. leaves - a comprehensive review. Int J Pharm Sci Med. 2023;8(12):11-24. doi:10.47760/ijpsm.2023.v08i12.002.