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REVIEW

Spray Drying for Pharmaceutical Raw Materials: A Systematic Review on Enhancing Bioavailability and Stability

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Abstract: Spray drying is extensively utilized in pharmaceutical development because of its scalability, cost-effectiveness, and capacity to customize solid-state characteristics. This systematic review (PubMed and Scopus, 2021–2025) assesses the impact of spray drying on the bioavailability and stability of active pharmaceutical ingredients (API) and natural products within solid dispersions (SD), solid self-nanoemulsifying drug delivery systems (S-SNEDDS), and microencapsulation. A total of 27 qualifying studies were identified and offered quantitative comparisons with untreated controls. SDs yielded AUC enhancements of 9–20-fold (eg, oxyberberine approximately 9-fold, quercetin approximately 20-fold) and dissolution improvements of 2–6-fold. S-SNEDDS produced AUC enhancements of 4–9.9-fold (sorafenib approximately 4.6-fold, enzalutamide approximately 7-fold, niclosamide approximately 9.9-fold). Microencapsulation enhanced oxidative stability (eg, approximately 3-fold reduction in peroxide value pepper seed oil and encapsulation efficiency of pomegranate seed oil reaching 90%). Benefits were contingent upon the carrier, especially with PVP/PVPVA, HPMC/HPMCAS, soluplus, and maltodextrin with protein systems. Spray drying provides superior scalability and particle engineering control compared to freeze or vacuum drying, while it still poses hazards of thermal and oxidative stress. Ongoing deficiencies encompass inadequate carrier comparisons, insufficient mechanistic comprehension of drying kinetics, and issues related to scale-up and regulation. This review offers mechanistic insights and a standardized approach to facilitate future formulation development.

Keywords: bioavailability, natural ingredient, pharmaceutical ingredient, spray drying, stability

Introduction

The pharmaceutical and cosmetic industries acknowledge the significance of pharmaceutical raw materials and natural goods owing to their robust market demand, resource accessibility, and proven safety profiles. Pharmaceutical compounds frequently exhibit inadequate solubility and restricted bioavailability, whereas natural goods are susceptible to chemical and physical deterioration.[1,2] Improving solubility, bioavailability, and stability is crucial to avert degradation induced by pH, humidity, and light. Spray-drying encapsulation provides an efficient method that enhances solubility and bioavailability, while ensuring prolonged stability and product quality.[3,4]

Spray drying is an economical method that generates homogeneous spherical powders while minimizing moisture content without sacrificing product quality. It provides adaptable, scalable, and entirely automated continuous processing, appropriate for both heat-stable and heat-sensitive chemicals.[3,5–9] Spray drying remains a pivotal technique for solid product development, processing solutions, suspensions, dispersions, or emulsions to produce powders or granules with generally low moisture content (<5%), hence improving storage stability.[6] The qualities of a product, including moisture content, particle density, and size, are significantly influenced by the drying temperature and the choice of carrier.[10,11] Employing polymer-based encapsulation, spray drying generates micro-sized particles between 5 and 5000 μm by the interaction of the active core, polymeric wall material, and solvent, culminating in a cohesive film that stabilizes and safeguards the active chemical.[6]

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Spray drying offers continuous operation, high throughput, narrow particle-size distributions,[12–14] spherical morphology, and tunability of the solid state (amorphization, porosity). Freeze and vacuum drying excel for labile biologics but face higher capital expenditure/operational expenditure, longer cycles, lower yields, and limited control over particle engineering for oral solids. Freeze drying poses difficulties in large-scale production owing to elevated equipment expenses, increased energy usage, and comparatively diminished yield.[15] Despite its numerous benefits, spray-dried products encounter various challenges, such as potential thermal and oxidative stress, carrier incompatibility, and recrystallization risks, necessitating judicious solvent selection, precise control of inlet and outlet temperatures, adherence to feed solids and viscosity targets, and the use of stabilizing polymers and surfactants.[15]

The selection of carriers is essential, as polymers, surfactants, proteins, and polysaccharides influence the stability, solubility enhancement, and overall efficacy of spray-dried formulations.[16] Maltodextrin, a biodegradable starch derivative with low viscosity, is extensively utilized in spray-drying microencapsulation due to its cost-effectiveness, neutral sensory characteristics, and robust oxidative protection.[17,18] Eudragit L100 offers pH-dependent dissolution and is recognized as a polymer for intestinal-targeted delivery and nanoparticulate systems.[19] Soluplus, an amphiphilic graft copolymer, improves aqueous solubility by stabilizing poorly soluble pharmaceuticals inside molecularly distributed amorphous matrices.[20] CMC, an anionic cellulose derivative, enhances colloidal stability via hydrogen bonding and electrostatic interactions,[21] serving as a thickening and film-forming agent.[22] PVP K30 stabilizes amorphous pharmaceuticals by inhibiting aggregation and recrystallization, thus enhancing solubility and storage stability.[22]

Regulatory frameworks additionally influence the advancement of spray-dried systems. Regulatory agencies generally accept spray-dried solid dispersion (SD), solid self-nanoemulsifying drug delivery systems (S-SNEDDS), and microencapsulation when manufacturers demonstrate sufficient control over polymorphism and amorphous content, residual solvent levels, and excipient safety including PVP, HPMC/HPMCAS, soluplus, maltodextrin, and protein-based carriers and provide dissolution and supersaturation data substantiated by relevant stability and bioperformance justifications.[23]

This review primarily examines pharmaceutical active ingredients, with a secondary discussion of natural products like oils, peptides, and antioxidant compounds to demonstrate how spray-drying-based microencapsulation can resolve stability and solubility issues in complex bioactive materials. This systematic review is essential for elucidating the long-term effects, stability, and potential interactions of diverse carriers and formulation strategies in the development of pharmaceutical products utilizing solid dispersion, microencapsulation, and solid-SNEDDS, while also identifying research gaps that necessitate further exploration.

Methods

This study employs a systematic literature review design following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The identification strategy was conducted by formulating research questions using the PICO (Population, Intervention, Comparison, and Outcome) framework, which was then adapted into keywords for database searches. The literature search was limited by predefined inclusion and exclusion criteria. Data sources were PubMed and Scopus, using the keywords ("spray" AND "drying") AND ("solid"), supplemented with Medical Subject Headings (MeSH) to ensure greater specificity.

The PICO framework included four key elements: Population (P): active pharmaceutical ingredients (API) and natural products in the pharmaceutical field; Intervention (I): the use of spray drying methods; Comparison (C): formulations processed with spray drying versus those without treatment; Outcome (O): improvement in bioavailability and stability.

The inclusion criteria for this review were as follows: (1) original research articles, (2) published between 2021 and 2025, (3) full-text accessible, (4) use of a spray dryer as the experimental instrument, (5) studies investigating API and/or natural products as the research objects, and (6) availability of data on bioavailability and/or stability outcomes, with comparative results between treated and untreated groups. Articles not meeting these criteria, including non-original articles and duplicates, were excluded.

Result

A total of 27 articles fulfilled the inclusion criteria based on the search conducted across the two selected databases. The preliminary search, employing the required keywords, produced 1,534 main articles. Out of them, 928 publications were

evaluated based on titles and abstracts, while 657 were subjected to full-text analysis. Subsequent to this evaluation, 27 articles were deemed eligible for inclusion, with no exclusions during the eligibility phase. Nevertheless, 630 articles were excluded for not satisfying the inclusion criteria.

The 27 research analyzed reported outcomes regarding bioavailability and stability, contrasting treated samples with untreated controls. The methodological attributes of these studies are encapsulated in Table 1, and the article selection procedure is depicted in the PRISMA flow diagram Figure 1.

Discussion

Spray drying converts liquid formulations into solid forms through rapid solvent removal[50] and is widely used in pharmaceuticals due to its suitability for heat-sensitive API, continuous operation, and consistent powder quality.[51] Among the studies examined, 6 assessed stability, while 23 indicated enhancements in bioavailability across various pharmaceutical source materials and natural products. Multiple individual and composite carriers were employed, with solid dispersions becoming the predominant method for improving solubility and bioavailability. This method can produce micron-sized particles in a short processing time.[52,53] Prior to spray drying, the active pharmaceutical ingredient (API) and carrier are first dissolved in a single solvent or a mixture of solvents. The subsequent removal of the solvent during spray drying produces a finely dispersed molecular mixture of the drug and the carrier[54] and it illustrates that spray drying safeguards encapsulated substances against oxidation and breakdown, hence prolonging shelf life.[6] It also improves bioavailability by augmenting solubility via amorphization and expanding the surface area of the encapsulated medication.[7–9] The components of a laboratory-scale spray dryer are depicted in Figure 2.

Solid Dispersion

Solid dispersions (SD) represent a potent formulation approach employed to enhance the solubility and bioavailability of poorly water-soluble pharmaceuticals. Solid dispersions entail the incorporation of the active pharmaceutical ingredient (API) into a solid matrix, often comprising a polymeric carrier, to improve the dissolving rate and stability of the medicine.[55] SDs are primarily classified into crystalline solid dispersions (CSD) and amorphous solid dispersions (ASD) according to polymer characteristics.[55]

Amorphous solid dispersions (ASD) are extensively employed to enhance the dissolution rate of poorly soluble pharmaceuticals, given that the amorphous state possesses elevated free energy and facilitates more rapid dissolution.[55] Crystalline solid dispersion (CSD) often employ semi-crystalline polymers to inhibit drug nucleation and crystal growth and reduce drug crystalline size, increasing the drug dissolution rate.[56] Enteric Solid Dispersion (ESD) is a solid dispersion formulated to safeguard the medicine from the stomach's acidic environment. This formulation employs polymers that breakdown at elevated pH values, typically in the small intestine, to liberate the medicine. ESD is particularly advantageous for medications that are unstable or cause gastric irritation.[24] Surface-Attached Solid Dispersion (SASD) entails the adsorption of the medication onto the surface of a carrier, usually a porous substance. This method is advantageous for pharmaceuticals that are challenging to distribute uniformly within a matrix. SASD facilitates the stabilization of the active ingredient on a carrier's surface, thereby improving the drug's solubility and bioavailability without requiring an amorphous matrix.[26] Ternary Solid Dispersion (TSD) comprises three components: the medication, a polymeric carrier, and an extra excipient, such as a surfactant or co-polymer. The incorporation of the third component further augments solubility and dissolution rate, typically by enhancing the drug's wettability or augmenting the carrier's ability to solvate the drug. The formulation of ternary drug solid dispersions by the amalgamation of polymers and surfactants has been documented to efficiently address challenges associated with insufficient drug solubility and poor resistance to recrystallization, while simultaneously facilitating a decrease in polymer concentration.[57,58]

Spray drying enables rapid vitrification and high apparent solubility, but stability hinges on polymer choice and drug loading. More hydrophilic polymers (eg, PVP/PVPVA) often boost dissolution yet increase moisture uptake and recrystallization risk; enteric or amphiphilic polymers (eg, HPMCAS, eudragit types, soluplus) improve physical stability and supersaturation maintenance but may slow release or require higher polymer fractions. pH-modifiers and surfactants can accelerate dissolution but may lower glass transition temperatures (Tg), narrowing stability margins in humid/tropical climates.[59–63] Schematic representation of solid dispersion system by spray drying is illustrated in Figure 3.

Table 1 Evaluation of Bioavailability and Stability Improvements Achieved via Spray Drying

Author	Compound	Carrier Composition	System	Spray Drying Condition	Experimental Method	Quantitative Outcomes	Key Limitation
Active Pharmaceutical Ingredients							
[24]	Stiripentol	Eduragit L100 The drug-to-polymer ratio employed was 1:5 (w/w), Stripentol:Eudragit L100	Enteric Solid Dispersion	Inlet temperature: 45°C	In vitro: Solubility and dissolution assessments were conducted utilizing a USP Type II dissolution equipment with 0.1N HCl (simulated gastric fluid) and pH 6.8 PBS (simulated intestinal fluid). Ultraviolet spectrophotometry was employed to determine the concentration of Stiripentol. In vivo: Male Sprague-Dawley rats were utilized for pharmacokinetic investigations. The oral bioavailability of STP-SDG-ETs was evaluated in comparison to STP suspensions: Rats received a dosage of 40 mg/kg of either STP suspensions or STP-SDG. Plasma samples were obtained at various time intervals (0.25 to 24 hours) and analyzed using HPLC. In vivo intestinal permeability was evaluated via a single pass intestinal perfusion research in rats to elucidate the absorption properties of STP-SDG	$AUC_{0\text{-}t}$ (μg h/mL) increase 1.4-fold The STP content under acidic conditions after 24 hours increase 1.4-fold	Carrier Efficacy: While Eudragit L100 offered substantial protection against gastric degradation, the solubility rate in intestinal fluid (SIF) warrants enhancement. Effervescent System: Although the bioavailability is improved, the effervescent tablet formulation may encounter stability concerns with prolonged storage. Scale-Up: The dry granulation technique employed for effervescent tablets necessitates meticulous scaling up to guarantee homogeneity in tablet compression, flow characteristics, and consistent medication release. Bioavailability versus Release Profile: Although STP-SDG enhanced bioavailability, the attainment of constant and controlled release, together the preservation of acid protection in vivo, continued to pose a difficulty.
[25]	Terbinafine	Soluplus 10% w/v	Amorphous Solid Dispersion (ASD)	Inlet 130 °C, Outlet 80 ±1 °C, feed ~3 mL/min, air flow 500 L/h, aspiration 100%; samples stored in a desiccator at room temperature.	In vitro Supersaturation study of ASD at pH 6,5, 37°C, UPLC quantification. tests conducted in triplicate (n = 3)	$AUC_{5\text{-}120\ minute}$ increase 11.7-fold	In vitro performance exclusively (lacking in vivo/ex vivo pharmacokinetics); Stability restricted to approximately 90 days at room temperature in a desiccator (absent ICH relative humidity/chemical stability data); Single-carrier amorphous solid dispersion (soluplus) utilized in the final formulation (no corresponding amorphous solid dispersion comparators); Absence of pediatric palatability/acceptability data; Laboratory-scale spray-drying parameters provided (B-290) without scale-up assessment.

[26]	Methotrexate	Na-CMC with SLS MTX/Na-CMC/SLS = 3/0.5/0.5 (w/w/w)	Surface-Attached Solid Dispersion (SASD)	Inlet air temperature: 130 °C. Outlet air temperature: 75–85 °C. Feed rate: 5 mL/min. Aspirator: 100% (−45 mbar). Atomizing air pressure: 4 kg/cm²	In vitro investigations: Aqueous solubility assessment The solubility of MTX was assessed in the presence of various polymers and surfactants. Na-CMC and SLS were determined to be optimum. Solubility values are shown as mean ± standard deviation (n = 3). In vitro dissolution was conducted using USP II methodology at 100 rpm, with 900 mL of water maintained at 37 ± 0.5 °C. Each capsule contained a powder quantity equivalent to 50 mg of MTX. In vivo study: (pharmacokinetics in rats) Male Sprague–Dawley rats (n = 6 per group) were administered orally at a dosage of 20 mg/kg MTX, utilizing either raw MTX powder or the optimized F6 SASD. Plasma methotrexate was measured using high-performance liquid chromatography.	AUC (h.ng/mL) increase 2.8-fold. Cmax (ng/mL) increase 3.4-fold. Methotrexate Photostability concentration on day 20 increase 1.5-fold.	The stabilization process is inadequately clarified, and there has been no evaluation of long-term effects, scalability, or safety.
[27]	Olaparib (OLA)	PVPK 30 with Aerosol 200	Solid Self-Nanoemulsifying Drug Delivery system (S-SNEDDS)	Inlet air temperature: 100 °C. Outlet air temperature: 50 °C. Drying air blower rate: 0.4 m³/min. Spray pressure: 100 kPa.	Dissolution was evaluated in vitro using a USP paddle at 37 °C and 100 rpm in simulated gastric fluid (0.2 M HCl, pH 1.2) and simulated intestinal buffer (phosphate buffer, pH 6.8).In vitro cytotoxicity and apoptosis: The optimized SNEDDS (OLS-352) diminished viability in a concentration-dependent way and triggered caspase-3/7 activation in SK-OV-3 (ovarian cancer) and MCF-7 (breast cancer) cells. A Caco-2 transport assay (ex vivo-like barrier model) employed a Caco-2 monolayer model (TEER > 200 Ω cm² to verify integrity) to simulate intestinal absorption.	Dissolution profile 0–120 min: -pH 1.2 increase 5.2-fold -pH 6.8 increase 3.7-fold	The study lacked in vivo pharmacokinetic evaluation, could not define the optimal drug loading relative to carrier load, and failed to offer long-term stability evidence beyond four weeks, hence constraining direct applicability to clinical dosing and shelf-life assertions.
[28]	Rifaximin	1:1 w/w (50% drug loading) Rifaximin: Whey Protein Beta-Lactoglobulin	Amorphous Solid Dispersion (ASD)	Inlet temperature: 100 °C. Atomization air: 473 L/h. Drying air: 35 m³/h. Outlet < 65 °C.	In vitro: non-sink powder dissolution in pH 1.2, pH 4.5, and FaSSIF-V2 (pH 6.5) at room temp, sampling to 120 min, HPLC quantification. triplicate for each formulation/media	Cmax at: -pH 1.2: increase 11-fold -pH 4.5: increase 10.9-fold -pH 6.5: increase 16.3-fold	No in vivo or ex vivo data—only in vitro dissolution; Limited stability period (5 weeks; physical stability exclusively); No chronic ICH conditions or monitoring of chemical stability/degradants; Certain characterizations are conducted with a single replication (n=1) (eg, DSC/TGA), hence constraining precision.
[29]	Coenzym Q10	CoQ10:Soluplus = 1:7 w/w	Amorphous Solid Dispersion (ASD)	Feed rate: 2.0 g/min (100 g batch processed). Inlet temperature: 75 °C. Air flow rate: 0.27–0.30 m³/min.	In vitro: Solubility assessment at 25 °C in aqueous solution. The dissolution of crystalline CoQ10 and SD 1:7 was evaluated in simulated stomach juice (pH 1.2) and intestinal buffer (pH 6.8) under the following conditions: USP paddle, 900 mL medium, 100 rpm, 37 ± 0.5 °C, with sampling conducted up to 60 minutes; each sample represented 30 mg of CoQ10. In vivo pharmacokinetic investigation: Male Sprague Dawley rats were allocated into two groups (n = 6 per group) and administered crystalline CoQ10 (60 mg/kg) and CoQ10: Soluplus® SD 1:7 (60 mg/kg) orally. Plasma CoQ10 levels were taken over a 24-hour period and evaluated via HPLC.	$AUC_{0\text{-}24}$ (μg h/mL) increase 7.4-fold Cmax increase 6.1-fold	Absence of long-term stability evaluation and the deficiency of mechanistic investigations to clarify absorption and storage stability under physiological settings.

(*Continued*)

Table 1 (Continued).

Author	Compound	Carrier Composition	System	Spray Drying Condition	Experimental Method	Quantitative Outcomes	Key Limitation
[30]	Apremilast (APST)	D-α-tocopherol polyethylene glycol 1000 succinate (TPGS) with Poly(1-vinylpyrrolidone-co-vinyl acetate) (PVPVA). APST:TPGS:PVPVA = 0.35:1.50:2.50 (w/w/w)	Amorphous Solid Dispersion (ASD)	Inlet temperature: 30 °C. Aspirator: 100%. Pump rate: 25%. Airflow: 400 L/h.	In vitro: Dissolution was conducted in phosphate buffer (pH 6.8) at 37 °C, 100 rpm. In vivo (pharmacokinetics in rats): Subjects: Male Sprague Dawley rats (n = 3 per group). Dosage: 2 mg/kg orally APST. Those experiment was performed in triplicate.	$AUC_{0-\infty}$ (h.ng/mL) increase 12.9-fold. Cmax (ng/mL) increase 22-fold	Utilization of volatile organic solvent (dichloromethane), limited reproducibility on a small scale, and absence of long-term physical stability and human pharmacokinetic validation, which must be resolved prior to clinical translation.
[31]	Sorafenib	93 wt% Combination of PVP K 30 and Aerosol 200 with lipid/surfactant matrix (1:2:1 = Capmul MCM:Tween80:Tetraglycol) w/w and 6.6 wt% drug loading	Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS)	Inlet temperature: 100 °C Outlet temperature: 50 °C Airflow rate: 0.40 m^3/min Spray pressure: 100 kPa	In vitro cytotoxicity assays on Hep3B (liver) and KB (oral cancer) cells demonstrated verified anticancer activity. In vitro dissolving in simulated stomach and intestinal fluids using USP apparatus II. The ex vivo transport investigation on Caco-2 cell monolayers indicated that solid SNEDDS had significant transepithelial transport, but the raw drug shown no transport. In vivo pharmacokinetic investigation in rats (n = 3) Oral dosage of S-SNEDDS (F22, 50 mg/kg).	AUC (h.ng/mL) increase 4.6-fold	The limited in vivo sample size, absence of long-term stability, and insufficient large-scale process validation are constraints that necessitate additional research prior to clinical application
[32]	Bavdegalutamide (ARV-110)	Polyvinyl alcohol (PVA) 70%/ARV-110 30% w/w	Amorphous Solid Dispersion (ASD)	Inlet temperature; 80 °C Outlet; 45 °C Nitrogen (flow rate); 35 m^3/h Aspirator: 100% Atomizing air flow: 670 L/min (N_2, 55 mm nozzle) Feed rate: 4 mL/min	In vitro: Dissolution investigations were conducted in phosphate buffer (pH 6.8) and biorelevant media (SGF to FaSSIF transition) utilizing magnetic stirring (100 rpm) and HPLC measurement The Western blot assay assessed FKBP51 degradation in HEK293T cells following a 24-hour exposure. All experiments were performed in triplicate	Cmax increase 3.5 fold	Stability was evaluated solely for four weeks at 5 °C; there is an absence of long-term and accelerated stability data. Despite the execution of in vitro dissolution and activity experiments, no in vivo pharmacokinetic validation was undertaken. The enhancement of solubility is contingent upon the polymer grade and the miscibility between the drug and polymer; scalability for industrial application has not been assessed.
[33]	Gefitinib	PVP with Eudragit S 100, 4:1 w/w	Solid Dispersion	Inlet Temperature: 90°C. Feeding Rate: 3 mL/min. Atomising Air Pressure: 3000 psi. Nitrogen Gas Flow Rate: 600 L/h.	In vitro: The dissolution and release of Gefitinib from solid dispersions were evaluated at several pH values mimicking the gastrointestinal tract (pH 1.2, 6.5, and 7.2).Ex Vivo: Mucoadhesion tests were conducted utilizing excised sheep intestinal tissue to assess the interaction and retention of the solid dispersion formulations. Triplicate for in vitro experiments	The % drug release at pH 7.2 over 12 hours: SDZDPS increase 3.4-fold.	Although the formulations shown no increased toxicity relative to pure Gefitinib, it is advisable to perform additional in vivo experiments to evaluate the efficacy of the formulations.The ex vivo mucoadhesion investigation revealed that formulations with HPMC exhibited prolonged retention, which may influence the characteristics of excised tissues during evaluation.The breakdown of Gefitinib was protracted at elevated pH levels (pH 7.2), necessitating extended testing durations (up to 15 hours).

[34]	Candesartan Cilexetil (CC)	The Combination of PVP K30 with Na_2CO_3 CC/PVPK30/ Na_2CO_3, which at the ratio of 1:0.5:1 (w/w/w)	Amorphous Solid Dispersion (ASD)	Air Inlet Temperature: 120°C. Air Outlet Temperature: 65–70°C. Atomization Pressure: 0.15 MPa. Flow Rate: 3.5 mL/min.	The solubility of the CC formulations (pure drug, physical mixture, and solid dispersion) was evaluated under different pH settings (pH 1.2, 4.0, 6.8, and water) to ascertain the dissolution profiles. In vitro dissolution tests were performed utilizing a USP Type II dissolution device. This studies were performed in triplicate.In vivo: Pharmacokinetic investigations were performed on Sprague-Dawley rats. The bioavailability of the improved formulation with treatment was assessed against that of the pure CC medication. The rats received either CC suspension or formulation with treatment, and blood samples were collected at designated time intervals for plasma concentration assessment via UHPLC.	AUC (h.ng/mL) increase 4.5-fold	The pH-modulated amorphous solid dispersion markedly enhanced solubility, nevertheless, the incorporation of pH modifiers such as sodium carbonate presents issues concerning hygroscopicity and formulation stability. Stability under real-time settings exhibited no notable deterioration over 12 weeks; nevertheless, extended experiments beyond this duration are required for more definitive stability data. The use of organic solvents in the formulation process may result in toxicity concerns, necessitating the optimization of solvent removal during spray drying to prevent residual solvent in the final product.
[35]	Griseofulvin	(Soluplus + Neusilin + sodium dodecyl sulfate (SDS)) GF:Soluplus:Neusilin® US2 = 3:6:3 w/w, plus a small SDS fraction. 25 wt % GF and 75 wt % carrier	Amorphous Solid Dispersion (ASD)	Inlet temperature: 75 °C. Air flow rate: 0.3 m^3/min downward through a column ~1.59 m tall, 0.15 m diameter. Feed rate: 1.6 g/min using a peristaltic pump (~200 g batch total). Atomizing air pressure: 2 bar, bi-fluid nozzle with 0.2 mm tip. Atomizing air flow rate: 202.7 L/min. Cyclone pressure: 55–60 mbar to collect particles	Dissolution/supersaturation assessments (USP II paddle), Medium: 1000 mL of deionized water at 37 °C (supersaturated conditions for griseofulvin, with a crystalline solubility of approximately 14.2 mg/L at 37 °C). Dose: 50 mg GF per 1000 mL, paddle speed 50 rpm. Sampling intervals: 1–30 minutes, UV measurement at 291 nm following filtering (0.1 µm PVDF). The results were conducted in triplicate and reported as mean ± relative standard deviation	Concentration AC with Neusilin® US2 after 30 minute increase 3.7-fold	Absence of in vivo validation for bioavailability improvement, and the necessity to assess long-term stability under fluctuating humidity and extensive spray-drying conditions
[36]	Olaparib (OLA)	OLA:HPMC P645 polymeric carriers at a 1:2 (w/w) ratio.	Amorphous Solid Dispersions (ASD)	Inlet temperature: 85 °C Outlet temperature: 55 °C Feed flow rate: 1.5 mL/min Atomizing air pressure: 0.1 MPa	In vitro: dissolution and solubility investigations at pH 1.2 and 6.8 utilizing USP Apparatus II In vivo: pharmacokinetic assessment in Sprague Dawley rats (20 mg/kg oral administration)	AUC_{0-24} (ng.h/mL) increase 4.2-fold. Cmax (ng/mL) Increase 10.7-fold	Potential recrystallization in specific polymer systems, lack of human pharmacokinetic validation, and restricted scalability owing to small-scale spray-drying conditions.
[37]	Dexibuprofen	Hydroxypropyl-β-cyclodextrin (HP-β-CD) is used at 1 g per formulation	Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS)	Inlet Temperature: 120°C. Outlet Temperature: 70 ± 5°C. Spray-Air Pressure: 4 kg/cm^2. Flow Rate: 5.4 mL/min.	In Vitro:Solubility Assessments: The solubility of the unprocessed medication was compared with that of the formulated Solid SNEDDS preparations.dissolving Studies: Dissolution profiles were analyzed utilizing a USP Type II dissolving device in 900 mL of distilled water at 37°C, with paddle rotation set at 100 rpm. This studies were performed in triplicate.In Vivo:Pharmacokinetic Study: Male Sprague-Dawley rats (9 weeks old) were administered the raw medication and the formulated preparations orally at a dosage of 10 mg/kg. Blood samples were obtained at many time intervals, and plasma concentrations were assessed via HPLC.	AUC (h.µg/mL) increase 1.9-fold. Cmax (µg/mL) increase 5.8-fold	The investigation revealed that whereas both Ca-silicate and HP-β-CD improved drug solubility, the hydrophilicity of the carrier did not substantially influence the dissolution rate or bioavailability. The variations in carrier type mostly influenced medication solubility and the formulation morphology (eg, spherical versus aggregated particles). Solubility versus Dissolution: The HP-β-CD-based systems exhibited superior solubility yet demonstrated a slower initial dissolution rate in comparison to Ca-silicate-based systems, likely attributable to the characteristics of the carrier and the microencapsulation method.

(*Continued*)

Table 1 (Continued).

Author	Compound	Carrier Composition	System	Spray Drying Condition	Experimental Method	Quantitative Outcomes	Key Limitation
[38]	Niclosamide	Calcium silicate 1g 1% (w/t)	Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS)	Inlet temperature: 140°C. Outlet temperature: 70°C. Feed rate: 15 mL/min. Airflow: 600 L/h.	In vitro: Dissolution Testing: The dissolution rates of the formulations were compared with niclosamide alone utilizing the USP dissolution equipment II. Solubility Investigation: The solubility of Niclosamide was assessed in several excipient formulations to determine the most efficacious options for SNEDDS. In vivo: Pharmacokinetic Study: Sprague-Dawley rats received the formulations (niclosamide alone and solid SNEDDS). Blood samples were obtained at predetermined intervals for plasma concentration measurement via HPLC.	AUC (h.μg/mL) increase 9.8-fold. Cmax (μg/mL) increase 18.7-fold	SNEDDS formulations exhibited increased instability at elevated oil ratios, indicating the necessity for optimization to ensure long-term stability.
[39]	Enzalutamide	Kollidon VA64 70% (w/w)	Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS)	Inlet temperature: 80 °C Outlet temperature: 60 °C Feed (pumping) flow rate: 3 mL/min Atomizing air pressure: 0.1 MPa	In vitro assessment of the solubility of ENZ from various S-SNEDDS formulations in aqueous solutions and buffer systems. Dissolution tests conducted using USP Apparatus II in media at pH levels of 1.2, 4.0, 6.8, and distilled water, with sampling extending to 120 minutes In vivo pharmacokinetic investigation in male Sprague-Dawley rats with oral dose of 50 mg/kg. Plasma ENZ concentrations were measured by HPLC, and non-compartmental pharmacokinetic characteristics (Cmax, AUC_{0-72}) were determined	AUC_{0-72} (μg.h/mL) increase 7.3-fold. Cmax (μg/mL) increase 6.4-fold	Bioavailability findings are restricted to rats; the long-term stability and scalability of the acetone-based spray-dried solid SNEDDS remain unverified, and the formulation's efficacy is significantly contingent upon the preservation of the amorphous state through polymeric recrystallization inhibitors
[40]	Ezetimibe (EZT)	91 wt% Kollidon® VA64 (PVP/VA) and 9 wt% ezetimibe	Amorphous Solid Dispersion (ASD)	Inlet temperature: 76 °C Outlet temperature: 58 °C Aspirator flow: 100% Drying gas flow rate: ~600 L/min Liquid feed rate: 3.4 mL/min Nozzle diameter: 0.7 mm	Dissolution assessment (in vitro) the USP/Pharmacopeial paddle apparatus (Vision Elite 8) utilizes 500 mL of 0.5% sodium lauryl sulfate (SLS) at 75 rpm at a temperature of 37 ± 0.5 °C, which is the FDA-recommended medium for ezetimibe. Sink conditions were verified, with a measured solubility of approximately 66.2 mg/L in 0.5% SLS. Quantification using UV at 248 nm. Experiments were conducted in triplicate and shown as mean ± standard deviation.	Concentration after dissolution at 1h increase 3.5-fold	The study lacks pharmacokinetic and bioavailability data for these specific spray-dried dispersions in both animals and humans. Amorphization transpired at low polymer content (20 wt%), although optimal dissolution (> 85–95%) necessitated elevated polymer fractions (≥ 66 wt%), perhaps constraining dose viability. Systems including < 20 wt% Kollidon® VA64 exhibited partial amorphous characteristics and demonstrated recrystallization, signifying restricted stability.
[1]	Aceclofenac	Na-CMC with aceclofenac 1/1 w/w	Solid-Self-nanoemulsifying drug delivery systems (S-SNEDDS)	Inlet temperature: Ranging from 110°C to 140° C depending on the formulation. Outlet temperature: Typically between 70°C and 75°C. Spray-air pressure: 4 kg/cm². Aspiration: 100% (−50 mbar). Flow rate: Varies from 5.4 to 10.8 mL/mi	In vitro techniques were utilized to assess the dissolution and drug release of the formulations. Caco-2 cell lines were employed to evaluate the cytotoxicity and bioadhesion characteristics of the formulations. Preclinical (in vivo) evaluations were performed on rats to compare the bioavailability of the formulations, demonstrating considerable enhancements in drug plasma concentration following oral administration of the nanoparticles. Triplicate for in vitro experiments	AUC (h.μg/mL) increase 2.9-fold Cmax (μg/mL) increase 3.9-fold	The mucoadhesive characteristics, while improved in certain formulations (particularly those based on HPMC), may not completely correlate with in vivo efficacy, as indicated by the cell culture experiments. Additional in vivo investigations are required to evaluate the true therapeutic efficacy of these formulations. The cytotoxicity results demonstrated that the drug-loaded formulations did not significantly limit cell growth relative to the pure drug, indicating that the mucoadhesive capabilities of the system may require additional examination under more intricate biological conditions.

[41]	Lacidipine	Combonation Gelucire and soluplus with ratio (6:1)	Ternary Solid Dispersion	Inlet temperature: 240°C. Outlet temperature: 183°C. Spray nozzle: Pneumatic atomizer with a 12.5 Kg/cm² air pressure.	In vitro: Dissolving Testing: Conducted with the USP Type II dissolving device. Dissolution tests were conducted in pH 4.50 acetate buffer, pH 6.8 phosphate buffer, and 1% Tween 20 solutions. Samples were obtained at specified intervals (5, 10, 15, 30, 60, 90, 120, 180, and 240 minutes) and analyzed via HPLC to ascertain the drug release profiles. HPLC Analysis: The quantitative analysis of Lacidipine was conducted utilizing a Gemini C18 column with an isocratic mobile phase comprising water and acetonitrile in a ratio of 11:89 (v/v). The experiments were conducted in triplicate In vivo: Pharmacokinetic Study: Male Sprague-Dawley rats were administered either raw Lacidipine solution or the formulated solid dispersions (LS and LSG). Blood samples were obtained at 0.25, 1, 2, 4, 6, 8, 12, and 24 hours following injection to assess plasma concentrations of Lacidipine using HPLC.	AUC 0–∞ (h.μg/mL) increase 3.6-fold. Cmax (μg/mL) increase 1.6-fold	Soluplus and Gelucire enhanced the solubility of Lacidipine; nevertheless, sustaining supersaturation over an extended duration remained problematic. The spring-parachute effect could not be consistently regulated in every instance, resulting in possible crystallization over time. The stability of the ternary solid dispersion under elevated humidity and light exposure was problematic. Photodegradation of Lacidipine occurred upon light exposure, resulting in a substantial decrease in drug content. The hygroscopic characteristics of the formulations resulted in diminished stability under elevated humidity, impacting the drug's dissolving rate and bioavailability over extended storage periods. Optimal storage conditions (dry and cool) were necessary to maintain the formulation's efficacy.
Natural Materials							
[42]	Pomegranate seed oil	The combination of Whey Protein Isolate (WPI) 25% WPI + 10% MD	Microencapsulation	Inlet air temperature: 125 °C Outlet air temperature: 60–67 °C. Air flow rate: 40–42 m³/min. Feed rate: 5.2 g/min. Pump rate: 40%.	In vitro: Oxidative stability assessment (accelerated storage) Microcapsules and bulk (unencapsulated) oil were subjected to storage at 60 °C for 15 days, with an exposure duration of 8 hours each day, to induce oxidation. On days 1, 5, 10, and 15, they assessed peroxide value (PV) indicative of primary oxidation products and p-Anisidine value (p-AV) representative of secondary oxidation products (aldehydes, ketones).	On day 15: Peroksidase Value decrease 1.2-fold p-AV decrease 1.1-fold. Totox value decrease 1.1-fold.	Only accelerated oxidative and physical stability were evaluated; there was no assessment of real-time shelf life, no biological evaluation, and restricted formulation capacity.
[43]	Oxyberberine	45.9 ± 3.31% (w/w%) of HPMCAS (Hydroxypropyl methylcellulose acetate succinate), together with oxyberberine (OBB)	Amorphous Solid Dispersion (ASD)	Outlet temperature: 101 °C, flow rate: 3.15 mL/min	In vitro dissolution USP-II paddles, 0.3% SDS, 250 mL, 100 rpm, 37 ± 0.5 °C; HPLC analysis. triplicate for each formulation In vivo pharmacokinetics in male Sprague-Dawley rats, n = 6 per group, comparing OBB-HPMCAS to OBB suspension (single oral dose of 100 mg/kg); analyzed by LC–MS/MS	$AUC_{0\text{-}24}$ (μg/mL.h) increase 9-fold	Inlet temperature was not documented; only exit and flow parameters were tuned; scale-up aspects such as humidity control and nozzle energy were not investigated. Dissolution medium (0.3% SDS) is non-biorelevant; FaSSIF/FeSSIF comparison absent, which may affect in-vitro/in-vivo translation
[44]	Trans-resveratol	Eudragit E/HCl, Eudragit 100 (dimethylaminoethyl methacrylate:butyl methacrylate:methyl methacrylate = 2:1:1) trans-resveratrol: Eudragit E/HCl ratio of 10: 90 (w/w)	Amorphous Solid Dispersion (ASD)	Solvent for feed: ethanol (3% w/v solids; 70% ethanol for HPMC). Feed rate: 4 to 6 mL per minute. Atomization pressure: 5 kPa (two-fluid nozzle, co-current flow). Inlet temperature: 80–100 °C. Outlet temperature: 55–70 °C.	In vitro investigationsDissolution testing: USP paddle method, 100 rpm, 37 ± 0.5 °C, utilizing 500 mL of pH 1.2 or 6.8 medium (non-sink conditions). The 10:90 Eudragit E/HCl dispersion attained complete dissolution in 30 minutes and sustained supersaturation for 48 hours.In vivo pharmacokinetic research (rats) Male Sprague Dawley rats (n = 5 per group) were administered oral dosages of 20 mg kg^{-1} resveratrol in the following forms: (1) raw drug, (2) Eudragit E/HCl SD 10/90. Plasma concentrations were measured by $HPLC_{0\text{–}8\ h}$	$AUC_{0\text{-}8h}$ (ng.h/mL) increase 4.2-fold. Cmax (ng/mL) increase 5.5-fold.	Absence of long-term stability assessment beyond 48 hours, and deficiency of mechanistic data regarding intestine absorption or large-scale manufacturability.

(*Continued*)

Table 1 (Continued).

Author	Compound	Carrier Composition	System	Spray Drying Condition	Experimental Method	Quantitative Outcomes	Key Limitation
[45]	Quercetin (QUR)	Flavonoid (QUR)/PEG 8000	Crystalline Solid Dispersions (CSD)	Inlet air temperature: 55 °C Outlet air temperature: 32 °C Feed/input speed: 4 mL min^{-1} Atomizing nitrogen pressure: 0.1 MPa	In vitro dissolution of pure drug powder, physical mixes, and CSDs in various mediums (pH 1.2, pH 6.8, and PBS pH 7.4) at 37 °C and 75 rpm, with time-point sampling extending to 4 hours In vivo pharmacokinetic study conducted on Wistar rats. Rats were administered quercetin either alone or in combination with quercetin/PEG CSDs (PEG8000 at a 30:70 w/w ratio). Plasma samples were obtained over a 24-hour period and analyzed using HPLC	$AUC_{(0-\infty)}$ ($\mu g.mL^{-1}.h$) increase 20.7-fold AUC_{0-24} ($\mu g.mL^{-1}.h$) increase 16.8-fold C_{max} ($\mu g.mL^{-1}$) increase 10.8-fold	Insufficient assessment of long-term stability, coupled with the utilization of dichloromethane and limited-scale spray-drying conditions that restrict industrial applicability
[46]	Prickly Ash peel oleoresin	Gum Arabic (GA) = 1.5% (w/w) Maltodextrin (MD) = 3.5% (w/w) PPO (core) to encapsulating agent = 1:4 (w/w)	Microencapsulation	Inlet air temperature: 130 °C Outlet temperature: 60 ± 2 °C Feed flow rate: 8 mL/min Feed temperature: 25 ± 0.5 °C	In vitro antioxidant assays DPPH, hydroxyl radical scavenging, and lipid hydroperoxide inhibition to assess oxidative stability. All experiments were conducted in triplicate	DPPH on day 15 increase ± 1.5-fold Hydroxil Radical on day 15 increase ± 1.5-fold Inhibiton Lipid Peroxidation on day 15 increase ± 1.2-fold	The study is constrained by its only reliance on in vitro tests, brief storage assessment, and absence of industrial-scale validation for long-term stability
[47]	Pepper seed oil	Gum Arabic/Maltodextrin ratio: 1:5 (w/w); oil/total solids 20% (w/w)	Microencapsulation	Inlet air temperature on 184 °C Feed rate on 8 mL/min Pump rotation noted as 600 L/h	in vitro antimicrobial experiment comprising agar well diffusion, MIC, and MBC measurements. The state analyses were conducted in duplicate at a minimum	Peroxide value on day 4 decrease 3-fold	Outlet temperature and atomization specifics were unreported; storage duration was confined to one month (4/25 °C) and four-day accelerated assessments; antimicrobial evaluation was restricted (tetracycline demonstrated superiority); replication was conducted at a minimum of duplicate; excipient range was limited to GA/MD despite recognized coating-dependent influences; yield variability suggests the necessity for additional process optimization
[48]	Pea peptides	Maltodextrin with Gum tragacanth, MD:GT polysaccharide ratio of 9:1 and a glycopeptide ratio (wall:core) of 10:1	Microencapsulation	Inlet temperature on 180 °C	The study performed in vitro antioxidant assays, including hydroxyl, superoxide, and ABTS radical scavenging tests, to assess the antioxidant activity. All experiments were performed in duplicate	Hydroxyl Radical Scavenging Ability (%) at 40 °C on day 60 increase 1.5-fold Superoxide Anion Radical Scavenging Ability (%) at 40 °C on day 60 increase 25.2-fold ABTS Radical Scavenging Activity (%) at 40 °C on day 60 increase 1.6-fold	The findings are confined to in vitro experiments, without in vivo validation or mechanistic understanding of peptide-carrier interactions. Furthermore, the limited-scale spray-drying apparatus, brief storage duration (60 days), and lack of industrial or sensory assessment constrain the generalizability and practical applicability of the findings
[49]	Resveratrol	The combination of soluplus (50% w/w) with Cremophor EL (10% w/w) and PVPVA (30% w/w) with Labrasol (10% w/w)	Amorphous Solid Dispersions (ASD)	Inlet temperature: 110°C. Atomizing air flow: 667 L/h. Atomization pressure: 40 m3/h. Feed flow rate: 20 mL/min.	In vitro: dissolving tests were performed utilizing a USP Type II dissolving device. The solubility profile of resveratrol formulations was assessed at pH 1.2 (mimicking stomach conditions) and pH 6.8 (mimicking intestinal conditions). tests were performed in triplicate In vivo: Pharmacokinetic investigations were conducted utilizing male Sprague Dawley rats, with the formulation delivered via oral route. were conducted utilizing groups of rats, generally comprising six rats per group.	$AUC_{(0-\infty)}$ (ng/mL.h) on Sol+EL increase 3.5-fold. $AUC_{(0-\infty)}$ (ng/mL.h) on PVPVA+Lab increase 3.6-fold.	Despite the formulations exhibiting enhanced dissolution and solubility, the long-term stability and efficacy in practical applications (eg, absorption augmentation in human research) continue to be a problem. The surfactant's impact on enhancing bioavailability exhibited a dose-dependent response, indicating flexibility in the influence of various surfactant and polymer combinations on bioavailability across different formulations. Spray drying and secondary drying are intricate procedures that can result in variability in the end product, especially regarding the uniformity of the dispersion.

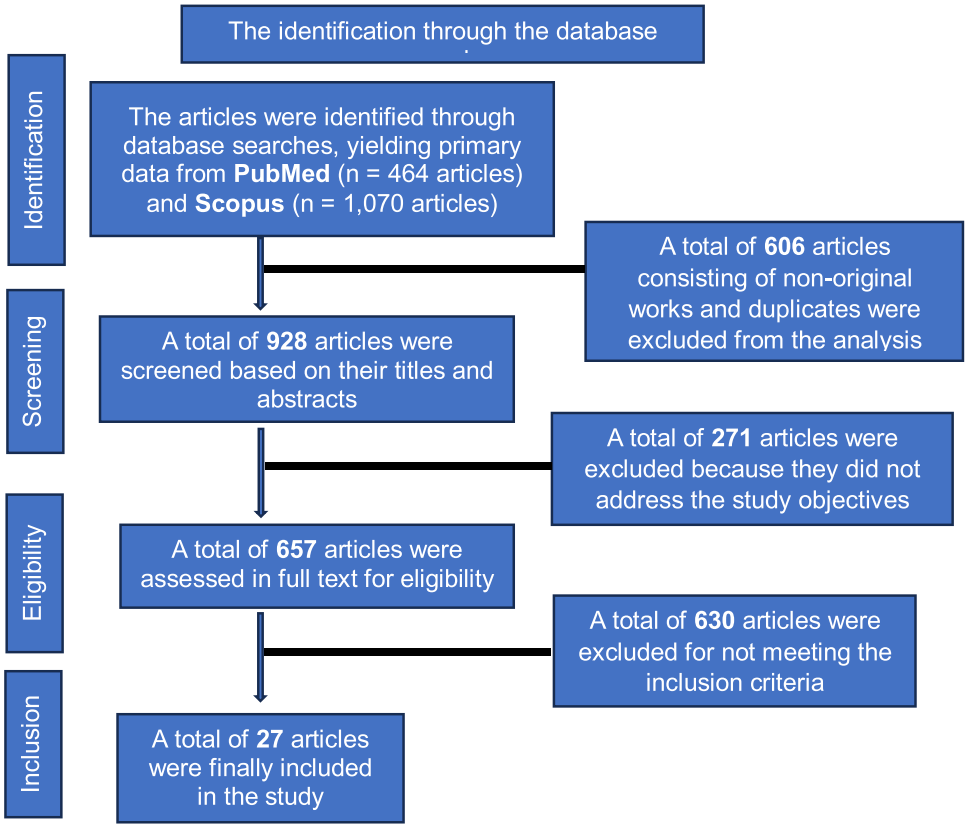

Figure 1 PRISMA flow diagram of study selection.

The various types of solid dispersion systems used to enhance bioavailability and stability have been discussed in this literature review, the following are the components that utilize the solid dispersion system are:

Terbinafine

Terbinafine (TER), a BCS Class II compound characterized by low solubility, 21, exhibited an 11.7-fold enhancement in $AUC_{5–120\ minutes}$ (mg/mL) (3500 vs 300) when synthesized as an amorphous solid dispersion with Soluplus.[64,65] The carrier boosted solubility by generating tiny, high-surface-area particles, and stabilizing terbinafine inside an amorphous, evenly dispersed polymer matrix, leading to significantly enhanced bioavailability relative to the untreated medication.[66] Simplified schematic amorphous solid dispersion is illustrated in Figure 3a.

Rifaximin

Rifaximin, a BCS Class IV medication characterized by inadequate solubility and permeability, shown significant bioavailability improvement when synthesized as an amorphous solid dispersion with β-lactoglobulin.[67] The ASD elevated Cmax (g/mL) by roughly 11-, 10.9-, and 16.3-fold at pH levels of 1.2 (13.7 vs 151.3), 4.5 (24.0 vs 260.6), and 6.5 (30.3 vs 492.7), respectively, in comparison to untreated rifaximin. The enhancement stemmed from the protein carrier transforming rifaximin into a stable amorphous form and diminishing particle size, therefore augmenting surface area, solubility, and overall bioavailability.[68,69]

Oxyberberine

Oxyberberine (OBB), a highly hydrophobic compound with extremely poor water solubility,[70] showed markedly improved absorption when formulated as an amorphous solid dispersion.[71] Using HPMCAS as the stabilizing polymer,[72,73] the ASD achieved 9-fold increase (1.26 ± 0.13 vs 11.34 ± 1.12) in $AUC_{0–24}$ (μg/mL.h) compared with untreated OBB. HPMCAS enhanced solubility by forming strong hydrophilic interactions with OBB,[70] reducing molecular mobility,[74] inhibiting

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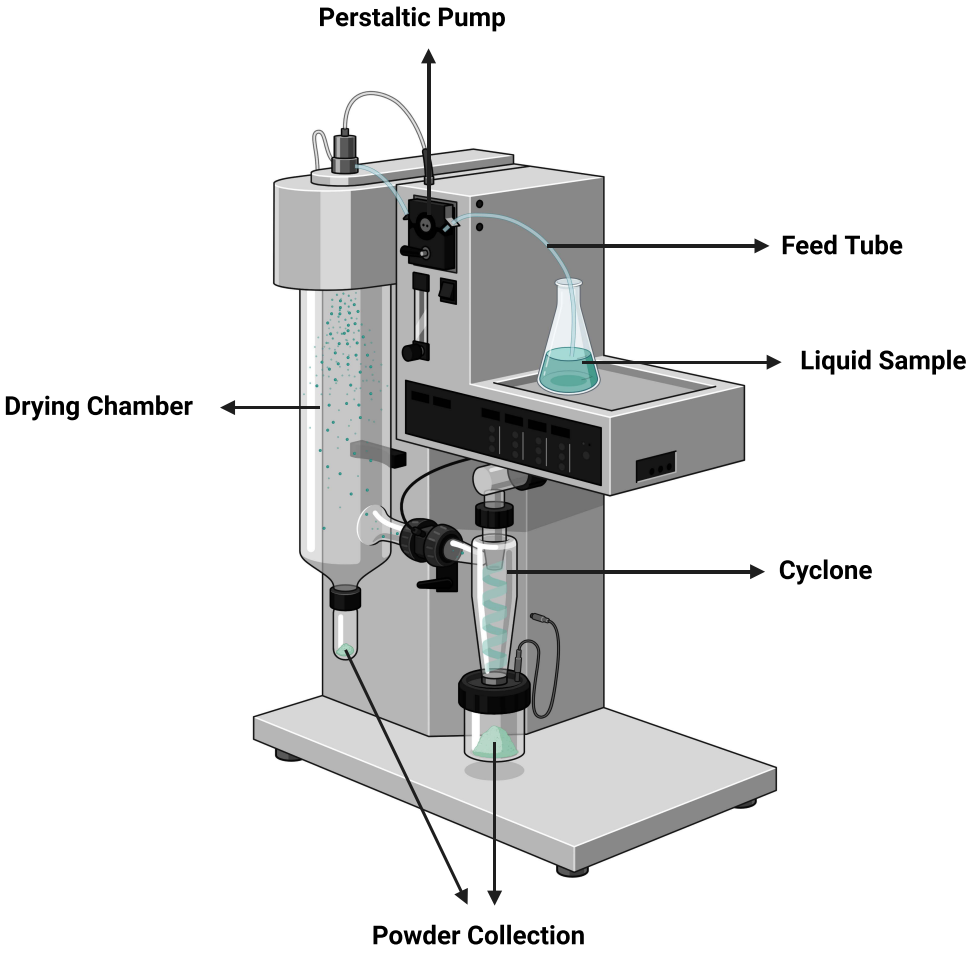

Figure 2 Laboratory spray dryer.

recrystallization,[75] and maintaining supersaturation during dissolution,[76] thereby preserving the amorphous state and significantly improving bioavailability.[77]

Quercetin

Quercetin, a BCS Class II compound with poor water solubility, demonstrated markedly improved bioavailability when formulated as a solid dispersion.[78,79] Using PEG 8000 as the carrier, the SD system produced a 20.7-fold increase in $AUC_{0-\infty}$ ($\mu g \cdot mL^{-1} \cdot h$) (304.820 ± 61.094 vs 14.753 ± 4.199), 16.8-fold in AUC_{0-24} ($\mu g \cdot mL^{-1} \cdot h$) (182.981 ± 13.770 vs 10.860 ± 1.351), and 10.8-fold in Cmax ($\mu g \cdot mL^{-1}$) (22.203 ± 2.147 vs 2.048 ± 0.334) compared with untreated quercetin. These improvements were attributed to PEG 8000 reducing quercetin crystallinity and enhancing solubility, resulting in a substantial increase in oral bioavailability.[80] Simplified schematic crystalline solid dispersion is illustrated in Figure 3b.

Olaparib

Olaparib (OLA), a BCS Class IV anticancer drug with extremely poor aqueous solubility (~0.1 mg/mL),[81] exhibits low oral absorption and requires high dosing.[82] Formulating olaparib as a solid dispersion effectively improves its solubility and bioavailability by molecularly dispersing the drug within a polymer matrix.[83] Amorphous OLA SDs produced a 4-fold increase in AUC_{0-24} (ng.h/mL) (1551.47 ± 484.09 vs 370.11 ± 63.75) and 10.7-fold in Cmax (ng/mL) (2001.25 ± 734.43 vs (187.31 ± 82.55) compared with crystalline OLA, supported by SEM[84] and PXRD data confirming amorphization without recrystallization.[85] Polymers such as HPMC,[86] particularly HPMC P645 with strong hydrogen-bonding capacity and a high glass transition temperature,[87] were shown to stabilize the amorphous state[88] and significantly enhance oral absorption.[89,90]

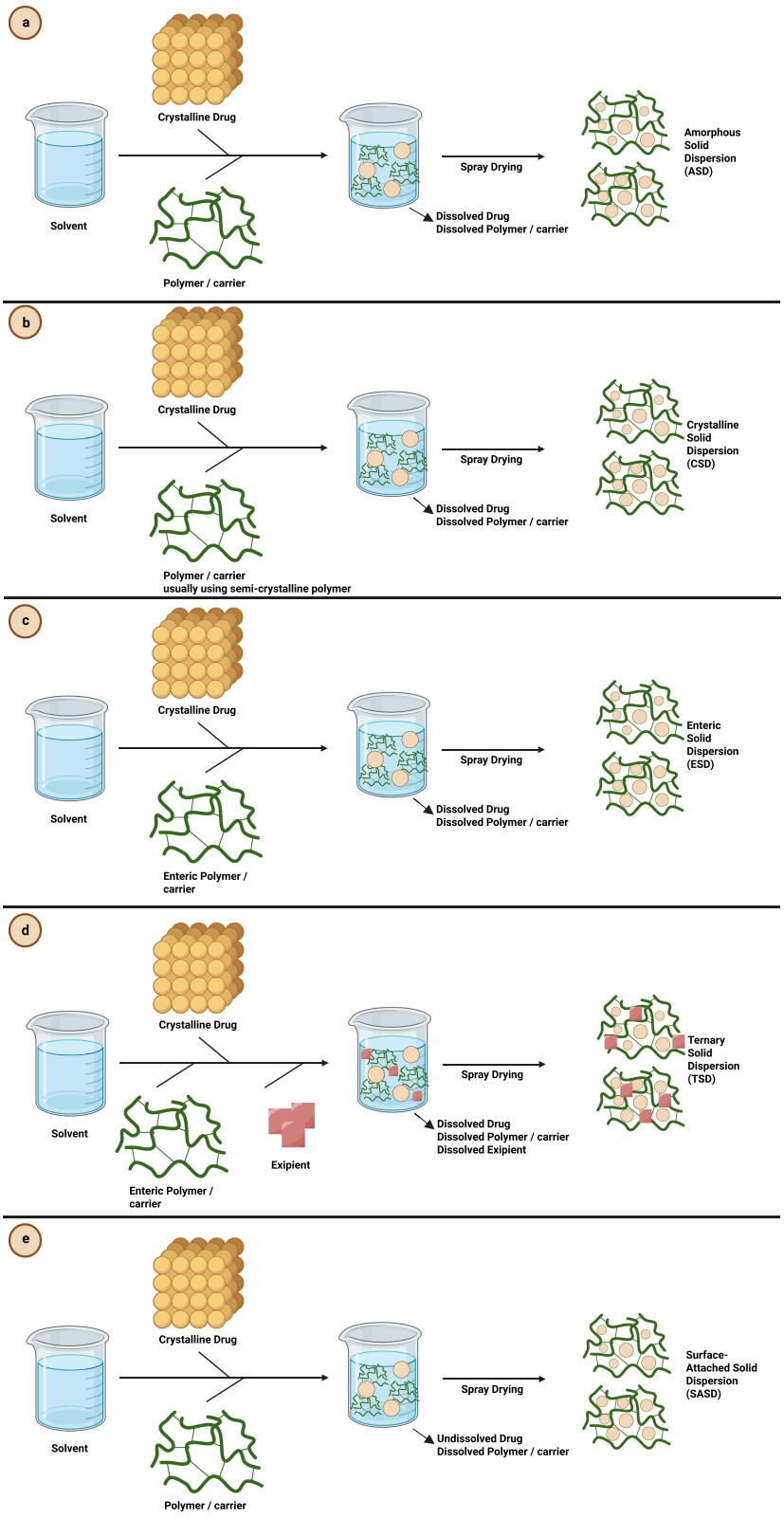

Figure 3 Simplified scheme of solid dispersion systems, amorphous solid dispersion (**a**), crystalline solid dispersion (**b**), enteric solid dispersion (**c**), ternary dispersion (**d**), surface-attached solid dispersion (**e**).

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Bavdegalutamide

Bavdegalutamide (ARV-110) is a PROTAC that specifically targets cereblon-containing E3 ubiquitin ligases, resulting in polyubiquitination and subsequent proteasomal destruction of target proteins.[91,92] The inadequate water solubility of ARV-110 necessitates strategies to improve its bioavailability, with spray-drying solid dispersion utilizing polyvinyl alcohol (PVA) as a carrier polymer recognized as an efficacious approach. This method markedly enhanced solubility in phosphate buffer (pH 6.8), leading to fast drug release within 5 minutes and sustained dissolution for 120 minutes.[93] The spray dried dispersion enhanced solubility by 3.5-fold relative to the untreated group (Cmax 34.0 μg/mL against 9.7 μg/mL). The spray dried dispersion preserved a stable temperature of 5°C for four weeks and inhibited recrystallization, maintaining elevated-free drug concentrations compared to the crystalline form for up to 6 hours.[94]

Ezetimibe

Solid dispersion (SD) methodologies have been utilized for ezetimibe (EZT),[95] Notwithstanding the presence of ionizable groups, its solubility remains unaltered by conventional stomach pH levels.[96] EZT categorizes as a BCS Class II compound. The issue of low solubility was mitigated by employing poly(vinylpyrrolidone-co-vinyl acetate) (PVP/VA) as a carrier in a spray-dried solid dispersion, leading to a substantial enhancement in solubility (3.5-fold) from 27.2 ± 3.5% in crystalline form to 95% in the dispersion. PVP/VA stabilizes the amorphous form of EZT by diminishing molecular mobility, hence inhibiting crystal formation and preserving the amorphous state over time.[97,98] Even minimal quantities of polymeric crystallization inhibitors, such as PVP/VA, can efficiently stabilize amorphous active pharmaceutical ingredients like felodipine and carbamazepine due to robust intermolecular interactions.[99–101]

Coenzyme Q10

Coenzyme Q10 (CoQ10), a lipophilic benzoquinone categorized as a BCS Class II compound, exhibits increased solubility through solid dispersion (SD) systems.[102] Lamichhane et al demonstrated that amorphous CoQ10, utilizing Soluplus as a carrier, exhibited 6.1-fold increase in Cmax (μg/mL) (2.276 ± 0.014 vs 0.374 ± 0.094) and 7.4-fold in AUC_{0-24} (μg·h/mL) (19.763 ± 0.005 vs 2.656 ± 0.005), in contrast to crystalline CoQ10.[29,103] These findings underscore the substantial improvement in solubility attributed to soluplus, which inhibits recrystallization and preserves CoQ10 in its amorphous state. Elevated soluplus concentration enhances wettability and diminishes crystallinity, hence augmenting solubility.[104] Soluplus can also self-assemble into micelles, hence improving solubility beyond its critical micelle concentration.[29,103]

Stiripentol

Stiripentol (STP) serves as an adjuvant therapy for Dravet syndrome, functioning as an antiepileptic by augmenting the action of the GABA neurotransmitter.[105,106] STP exhibits low water solubility (0.405 mg/mL) yet possesses strong permeability (log P = 3.01), with its absorption rate constrained by inadequate degradation in the intestines.[107] The amorphous variant of STP combined with eudragit L 100 improved drug release in SIF, exhibited delayedvrelease properties, and boosted bioavailability, as indicated 1.4-fold increase in AUC_{0-t} (29.99 ± 3.35 vs 21.62 ± 4.32).[24] This illustrates that STP in amorphous or solid dispersion form augments resistance to acid hydrolysis and boosts chemical stability after 24 hour (83.06% vs 59.92%).[107] Simplified schematic enteric solid dispersion is illustrated in Figure 3c.

Resveratrol

Resveratrol (RES), a natural antioxidant present in fruits and nuts is classified as a BDDCS class II compound characterized by inadequate oral bioavailability (F < 2.6%)[108,109] and low solubility (20–30 μg/mL).[110] To enhance its bioavailability, solid dispersion (SD) approaches utilize polymers such as PVPVA and Soluplus, which establish robust hydrogen bonds with RES. The amphiphilic characteristics of cremophor EL (EL) and labrasol (Lab) improve wettability and solubility.[111] RES formulations using soluplus-EL (3232.49 ± 680.88) increase 3.5-fold and PVPVA-Lab (3275.26 ± 923.46) increase 3.6-fold exhibited markedly superior dissolving profiles, with $AUC_{0-\infty}$ (ng/mL.h) values exceeding thrice those of untreated RES (920.00 ± 229.24), signifying better solubility and bioavailability.[61]

Trans-Resveratrol

Trans-resveratrol (TRES) is biological form resveratrol often used in dietary supplements and classified as a BDDCS class II.[112,113] The limited water solubility of TRES (<60 μg/mL) restricts its oral absorption.[110] Prior methods to augment absorption concentrated on the utilization of surfactants, hence enhancing bioavailability relative to pure TRES.[114,115] Solid dispersion systems, especially those employing neutralized eudragit E/HCl, have demonstrated enhanced TRES solubility and oral bioavailability.[116] Eudragit E, which solubilizes under both acidic and gut pH conditions, stabilizes TRES in its amorphous state, inhibiting crystallization.[117] Spray-dried amorphous TRES combined with Eudragit E markedly elevated $AUC_{0–8\ h}$ (ng.h/mL) values increase 4.2-fold (583.9 ± 92.1) compared for untreated TRES (138.9 ± 22.0), also in Cmax (ng/mL) increase 5.5-fold (204.4 ± 25.5 vs 37.0 ± 7.7) hence affirming improved solubility and bioavailability.[118]

Lacidipine

Lacidipine (LCDP) is a BCS Class II chemical characterized by restricted water solubility.[119] Solid dispersion (SD) approaches have been employed to augment solubility, using Gelucire, a surfactant, facilitating solubility in aqueous conditions.[120] Gelucire enhanced solid-state medicine concentration when utilized in conjunction with spray drying.[121] The amalgamation of diminished particle size, augmented surface area, and Gelucire's hydrophilic characteristics improved hygroscopicity while concurrently diminishing drug-loading efficiency upon extended exposure to humidity. Following 10 days of exposure to extreme temperatures, LCDP amorphous properties and polymer linkages preserved robust dispersion, enhancing supersaturation stability and dissolution. The $AUC_{0-\infty}$ (h.μg/mL) values for LCDP SD were markedly elevated 3.6-fold compared to untreated LCDP (5.41 ± 1.81 vs 1.51 ± 0.92), also in Cmax (μg/mL) increase 1.6-fold (0.85 ± 0.30 vs 0.52 ± 0.25).[121] Simplified schematic ternary solid dispersion is illustrated in Figure 3d.

Methotrexate

Methotrexate (MTX) is a powerful chemotherapeutic agent characterized by low water solubility (0.01 mg/mL at 20°C) and restricted permeability, categorizing it as a BCS class IV medication.[122] MTX also unstable degrading in the presence of light, elevated pH, and high temperatures. This complicates the formulation of efficient oral formulations.[123,124] The limited solubility of BCS class II and IV medications results in sluggish dissolution, inadequate gastrointestinal absorption, and diminished oral bioavailability, hence impacting therapeutic efficacy.[60] To mitigate MTX's inadequate photostability, a surface-attached solid dispersion (SASD) approach that preserves crystallinity was employed to improve its solubility, bioavailability, and photostability.[125] Sodium carboxymethyl cellulose (Na-CMC) and sodium lauryl sulfate (SLS) enhanced solubility, yielding a 2.8-fold rise in AUC relative to untreated MTX (4890.45 ± 1447.53 vs 1738.71 ± 294.65). The improved solubility is ascribed to the hydrophilic carriers promoting accelerated water absorption and medication release. The MTX in the SASD formulation exhibited negligible degradation (about 5%) under UV radiation, whereas 65% of the pure medication degraded, demonstrating improved photostability. SASD enhances MTX's solubility, dissolution, bioavailability, and photostability while preserving its crystallinity.[126] Simplified schematic surface-attached solid dispersion is illustrated in Figure 3e.

Apremilast

Apremilast (APST) is classified as a BCS class IV medication, characterized by low solubility, dissolution rate, and bioavailability (20–33%), which constrains its therapeutic effectiveness.[127,128] D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) and poly(1-vinylpyrrolidone-co-vinyl acetate) (PVPVA) were employed to improve solubility and bioavailability. TPGS, a P-glycoprotein (P-gp) inhibitor, enhances intestinal absorption and intracellular accumulation, whereas PVPVA facilitates molecular dispersion.[129,130] TPGS additionally generates micelles that solubilize hydrophobic pharmaceuticals and lowers interfacial tension.[131] The hydrogen connection between carriers and APST inhibits recrystallization.[132] The AUC (h.ng/mL) for the solid dispersion is approximately 12.9-fold greater than that of crystalline APST (65.50 ± 5 vs 5.09 ± 5.2), also the Cmax (ng/mL) increase 22-fold (47.50 ± 29 vs 2.16 ± 1.5), signifying improved absorption and bioavailability attributable to the effects of TPGS and PVPVA on intestinal permeability.[126,133]

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Candesartan Cilexetil

Candesartan cilexetil (CC) is an effective antihypertensive prodrug with low solubility (BCS class II) and limited absorption.[76] To enhance its bioavailability, an amorphous solid dispersion (ASD) was formulated using a hydrophilic carrier, PVP K30, and a pH modulator, sodium carbonate, produced by spray drying.[134] The PVP K30 carrier improves water solubility and aids in water absorption, while spray drying reduces particle size and stabilizes the amorphous form of CC. This method enhances solubility and dissolution. Additionally, the incorporation of sodium caseinate further improves solubility and dissolution across physiological pH ranges. The AUC of the ASD formulation increased nearly 12-fold compared to untreated CC, demonstrating a significant improvement in bioavailability, increase 4.5-fold AUC (h.ng/mL) (65.50 ± 5 vs 5.09 ± 5.2).[135]

Gefitinib

Gefitinib (ZD), a weak base with pKa values of 5.4 and 7.2, is insoluble in water and categorized as a BCS class II medication, signifying low solubility and high permeability. Polyvinylpyrrolidone (PVP) were employed as carriers in spray-dried solid dispersions to improve solubility.[136,137] PVP boost the solubility and dissolution rate of ZD, also Eudragit S100 serves as a pH-sensitive polymer for the colon-targeted delivery of Gefitinib (ZD).[138] At a low pH, untreated ZD exhibits high solubility, with 94% dissolving within 30 minutes at pH 1.2. Nonetheless, solid dispersions containing PVP exhibited merely 16% and 15.5% release at pH 1.2 after a duration of 3 hours.[139,140] At pH 7.2, the drug release from PVP dispersions was approximately 3.4-fold more than that of untreated ZD, respectively (96.7% vs 28.7%).[141]

Griseofulvin

Griseofulvin is an antifungal medication with poor water solubility (BCS class II) but good permeability.[137] To enhance its solubility, two main methods are employed: reducing particle size to increase surface area and amorphizing the drug to achieve supersaturation.[142,143] Particle size reduction accelerates dissolution but is less effective for achieving supersaturation, which is crucial for drugs with solubility below 50 mg/mL. Neusilin, a high-performance stabilizer and flow enhancer, was used as a carrier with high porosity and adsorption capacity,[144,145] prevents recrystallization of amorphous drugs,[146] such as acid–base interactions and hydrogen bonding.[147] In formulations with Neusilin, the concentration of griseofulvin increased by 3.7-fold after 30 minutes (36 vs 10 (mg/L)), demonstrating enhanced solubility, sustained supersaturation, and improved drug release.[148]

Solid Self Nanoemulsifying Drug Delivery System

Solid self-nanoemulsifying drug delivery system (SNEDDS) is a system designed to enhance the solubility and bioavailability of poorly water-soluble pharmaceuticals. The process entails developing a robust formulation comprising lipophilic medicines, surfactants, and other excipients that, upon interaction with gastrointestinal fluids, generate a nanoemulsion. This nanoemulsion improves the solubility and bioavailability of the medicine in the body. Solid SNEDDS offer the advantages of a nanoemulsion technology while ensuring stability and facilitating handling typical of solid forms.[149]

This technique is particularly advantageous for lipophilic pharmaceuticals, necessitating emulsification to improve absorption. Additionally, solid SNEDDS can be effortlessly produced through techniques such as spray drying or hot-melt extrusion, guaranteeing a stable formulation that enhances drug bioavailability. Spray drying converts liquid SNEDDS into free-flowing powders using carriers such as silica (eg, aerosil), PVP, or cyclodextrins. Advantages include rapid dispersion, high apparent solubility, and improved handling. Limitations include payload caps set by carrier porosity/affinity, susceptibility to lipid oxidation, and humidity-driven phase changes. Carrier selection mediates a trade-off between flowability, redispersibility, and long-term physical stability.[27,38,39] Schematic representation of solid nanoemulsifying drug delivery system by spray drying is illustrated in Figure 4.

The components utilizing the S-SNEDDS system are as follows are:

Aceclofenac

Aceclofenac, characterized by low water solubility, exhibits diminished oral bioavailability, hence constraining its therapeutic effectiveness.[150] Solid self nanoemulsifying drug delivery system (SNEDDS) utilizing appropriate carriers, such as sodium carboxymethylcellulose (Na-CMC), effectively enhance solubility and bioavailability.[151] Na-CMC, a

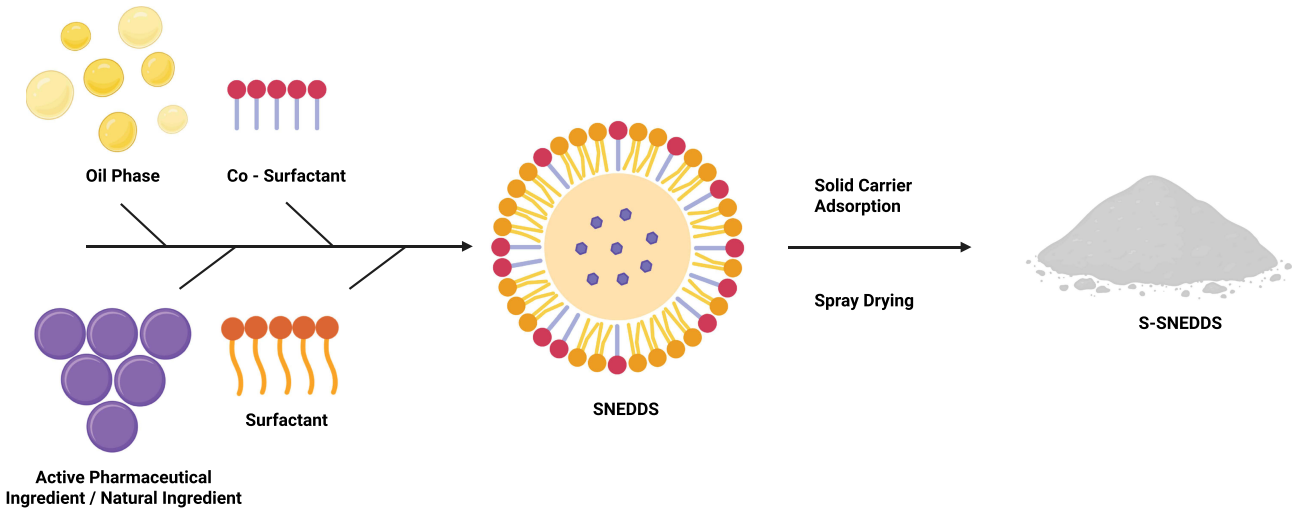

Figure 4 Simplified scheme of solid self nanoemulsifying drug delivery system (S-SNEDDS).

cellulose derivative characterized by its hydrophilic, nontoxic, biocompatible, and biodegradable attributes,[152] has been utilized in numerous therapeutic applications.[153] This study utilized Na-CMC as a carrier to formulate a solid SNEDDS, leading to 2.9-fold augmentation in AUC (h·µg/mL) (12.92 ± 2.88 vs 4.46 ± 0.45), also leading to 3.9-fold in Cmax (µg/mL) (5.81 ± 0.82 vs 1.49 ± 0.49) relative to the untreated group,[154] hence improving the bioavailability of aceclofenac.[155]

Olaparib

Olaparib (OLA) is classified as a BCS class IV medication, characterized by low water solubility, which leads to inadequate oral absorption and bioavailability.[86] To resolve this, solid self-nanoemulsifying drug delivery systems (S-SNEDDS) are employed, which generate nanoemulsions upon interaction with physiological fluids without requiring external energy.[87] Aerosil 200, characterized by its extensive surface area, functions as an adsorbent, whilst polyvinyl-pyrrolidone K30 (PVP K30) works as a precipitation inhibitor, improving solubility in gastrointestinal fluids.[156,157] Converting OLA from a crystalline to an amorphous state enhances its solubility and dissolution rates.[158] In the S-SNEDDS matrix, OLA is solubilized, enhancing the available surface area and dissolution rate.[159] This led to substantial dissolution profile until 120 minute increases 5.2-fold at pH 1.2 (89.9 ± 3.1% vs 17.2 ± 3.9%) and 3.7-fold at pH 6.8 (89.7 ± 0.4% vs 24.3 ± 3.7%) relative to untreated OLA, indicating improved bioavailability and consistent drug release despite variations in pH.[27]

Sorafenib

Sorafenib, a medication with low solubility, rapid hepatic metabolism, and P-glycoprotein substrate action, exhibits reduced oral bioavailability.[160] Comparable to olaparib, its solubility can be markedly improved through the utilization of solid self-nanoemulsifying drug delivery systems (S-SNEDDS).[161] Aerosil 200 functions as the solid carrier, whereas PVP K30 operates as a precipitation inhibitor in this formulation. Aerosil 200 offers an extensive surface area for adsorption, whereas PVP K30 enhances solubility in gastrointestinal fluids. Collectively, these elements inhibit recrystallization and markedly enhance the solubility of sorafenib. The AUC (h.µg/mL) value of sorafenib in S-SNEDDS was 4.6-fold greater than free sorafenib (136.1 ± 25.9 vs 29.8 ± 1.8), underscoring the enhancement in bioavailability attributed to improved dissolution and drug absorption.[9]

Enzalutamide

Enzalutamide (ENZ), an androgen receptor signaling inhibitor employed in prostate cancer therapy, exhibits low aqueous solubility (BCS class II) attributable to its lipophilic characteristics.[162] Amorphous solid dispersions enhance solubility and mitigate recrystallization in supersaturated conditions.[72] Kollidon VA64 served as a recrystallization inhibitor, and the drug release from S-SNEDDS was affected by its concentration. The improved oral bioavailability of ENZ in S-SNEDDS is due

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to the spontaneous generation of nanoemulsions in the gastrointestinal system and the polymer's capacity to preserve ENZ in an amorphous, supersaturated condition. This dual process enhances solubility and prolongs supersaturation, leading increase 7.3-fold at AUC_{0-72} (μg.h/mL) (274.4 ± 47.6 vs 37.5 ± 6.4) and 6.4-fold at Cmax (μg/mL) (8.9 ± 2.0 vs 1.4 ± 0.8) in bioavailability relative to untreated ENZ.[94]

Niclosamide

Niclosamide, a crystalline compound with limited solubility in water, however, soluble in ethanol, chloroform, and ether, has garnered interest for its potential repurposing in the treatment of Parkinson's disease, diabetes, and cancer.[163] Calcium silicate was employed as a porous polymeric carrier to enhance the solubility and stability of liquid SNEDDS by transforming it into a solid state.[164] Sodium alginate (Na-alginate) and poloxamer 407 were utilized to solubilize niclosamide.[165] Solid SNEDDS formulations markedly improved solubility by 158-fold relative to the pure medication (0.8 ± 0.3 vs 127.0 ± 18.4 μg/mL). These formulations enhanced solubility, dissolution rates, and plasma concentrations in rats, with AUC (h.μg/ mL) and Cmax (μg/mL) values increasing by 9.9-fold (7.37 ± 1.84 vs 0.75 ± 0.23) and 18.7-fold (1.68 ± 0.86 vs 0.09 ± 0.04), respectively, compared to untreated niclosamide, signifying a significant enhancement in bioavailability.[165]

Dexibuprofen

Dexibuprofen, the S-isomer of ibuprofen, is categorized as a BCS class II medication, characterized by low water solubility and high permeability.[166] This attribute impacts absorption and may affect bioavailability.[167] Hydroxypropyl-β-cyclodextrin (HP-β-CD) is hydrophilic, biocompatible, and frequently employed to solubilize poorly water-soluble pharmaceuticals owing to its truncated cone-shaped architecture, characterized by a hydrophobic cavity and a hydrophilic exterior.[168] The integration of HP-β-CD into solid SNEDDS significantly improved the solubility, dissolving, and oral bioavailability of dexibuprofen, thereby hastening its therapeutic start. AUC (h.μg/mL) and Cmax (μg/mL) increase 1.9-fold (48.15 ± 7.42 vs 24.81 ± 5.06) and 5.8-fold (51.00 ± 8.82 vs 8.85 ± 1.36) respectively, in comparison to untreated dexibuprofen.[169,170]

Microencapsulation

Microencapsulation entails encasing a medication or active chemical within a protective shell, typically composed of polymers or other materials. This method regulates medication release, safeguards it from environmental influences (including oxygen, light, and heat), and enhances the stability of the active component. The shell or matrix can facilitate sustained, delayed, or targeted drug release, contingent upon the microcapsule's architecture.[171]

Microencapsulation extends beyond enhancing solubility; it also serves to safeguard delicate substances (eg, vitamins, probiotics, tastes) and to guarantee the targeted or sustained release of the active ingredient. In contrast to Solid SNEDDS, which generates a nanoemulsion within the gastrointestinal tract, microencapsulation facilitates regulated release without the requirement of an emulsion system. Spray drying provides oxidation and light protection with carbohydrate/gum walls (eg, maltodextrin, gum arabic, WPI). It is typically superior to bulk evaporation for controlling droplet size and drying history, but may be inferior to FD when maximal bioactivity retention is paramount or when wall materials are highly hygroscopic, reducing shelf-life under high RH.[172] Schematic representation of microencapsulation system by spray drying is illustrated in Figure 5.

The following are the components that utilize the microencapsulation system are:

Pepper Seed Oil

Pepper seed oil (PSO), abundant in unsaturated fatty acids, is susceptible to oxidative deterioration, compromising its nutritional value and sensory attributes.[173] It encounters difficulties in achieving uniform distribution within water-based food matrices and experiences oxidation during thermal processing. The microencapsulation of PSO safeguards it against oxidative degradation and enhances the delivery of bioactive components.[63] This procedure entails emulsifying the oil with coating agents such as polymers and subsequently drying the emulsion.[174] Oxidative stability assessments revealed that free PSO exhibited a substantial rise in peroxide value (18 meq/kg) after four days at 60°C, but encapsulated PSO with gum arabic (GA) and maltodextrin (MD) displayed a considerably lower peroxide value (6 meq/kg), indicating

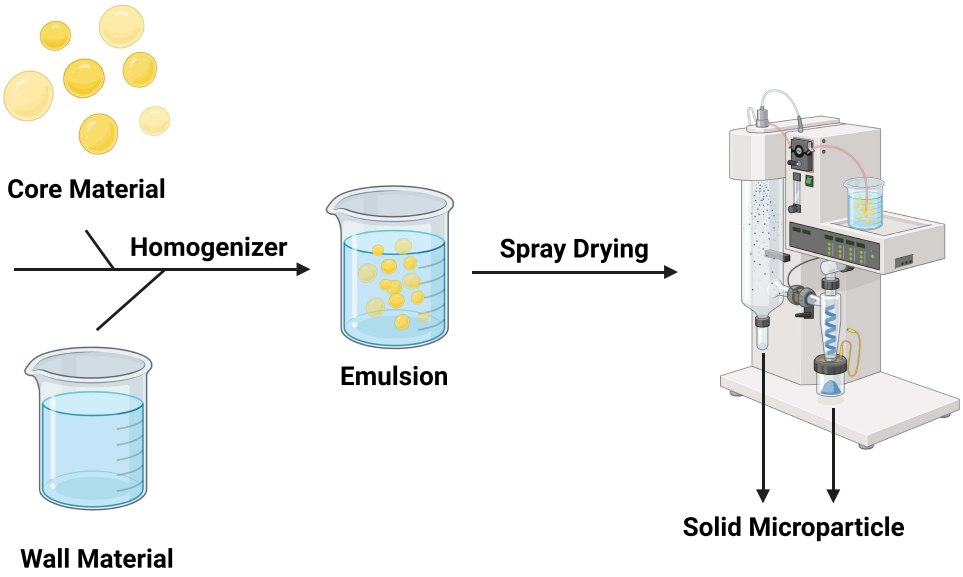

Figure 5 Simplified scheme of microencapsulation system.

enhanced stability. MD, obtained from maize starch, and GA, a prevalent coating agent,[175] improved the oxidative stability and shelf life of PSO by creating robust microcapsules with superior emulsifying characteristics.[176]

Pea Peptides

Pea peptides (PP), originating from peas, are water-soluble chains comprising 22 amino acids that possess antioxidant and anti-inflammatory effects; nevertheless,[177] they are susceptible to oxidation and hydrolysis.[178] Maltodextrin (MD) aids in stabilizing peptides and concealing bitterness, however it may independently induce microcapsule rupture.[179] Gum tragacanth (GT), a natural and biodegradable hydrocolloid, improves thermal stability and antioxidant activity, positioning it as a viable alternative to conventional carriers such as gum arabic (GA). The encapsulation of PP with MD and GT produced stable peptides that exhibited 25.2-fold enhancement in superoxide (25.2% vs 0%), 1.5-fold in hydroxyl (70.2% vs 47%) and ABTS (40.3% vs 24.46%) radical scavenging ability at 40°C on day 60, relative to untreated PP. This improvement is likely attributable to augmented surface area contact, rendering the peptides more vulnerable to breakdown under specific environmental circumstances. The stability of peptides is influenced by variables such as temperature, pH, and salinity, with certain amino acids, like threonine, serine, and cysteine, exhibiting notable instability in alkaline environments.[180]

Prickly Ash Peel Oleoresin (PPO)

Prickly ash peel oleoresin (PPO) is a concentrated essential oil derived from Sichuan pepper, characterized by its potent aroma, yet exhibiting low water solubility and high volatility, hence complicating its transit, storage, and stability.[181] PPO was encapsulated via spray-drying utilizing soy protein isolate (SPI) or gum arabic (GA) in conjunction with maltodextrin (MD) to resolve these difficulties.[182,183] Maltodextrin and GA serve as efficient encapsulating agents owing to their emulsifying and film-forming properties, enhancing PPO's stability by mitigating exposure to light, heat, and oxygen.[184] Encapsulation improved PPO's antioxidant efficacy by preserving flavor ingredients and safeguarding active oil constituents. The antioxidant activity, assessed through DPPH scavenging, hydroxyl radical scavenging, and lipid peroxidation inhibition, shown notable enhancements in encapsulated PPO, with increases of ± 20% (± 60% vs ± 40%) in DPPH scavenging, ± 20% (± 60% vs ± 40%) in hydroxyl radical scavenging, and ± 10% (± 60% vs ± 50%) in lipid peroxidation relative to free PPO.[185]

Pomegranate Seed Oil (PGSO)

Pomegranate seed oil (PGSO), abundant in polyunsaturated fatty acids such as punicic acid (65–80%), and bioactive constituents including phenols, flavonoids, ellagitannins, and anthocyanidins, provides numerous health advantages,

encompassing diminished diabetes risk, reduced blood pressure, obesity control, and skin improvement.[186,187] Nonetheless, PGSO is particularly vulnerable to oxidative deterioration caused by heat, light, oxygen, and humidity. To address this, carbohydrates such as maltodextrin (MD) and proteins like whey protein (WP) are employed as encapsulating agents.[188] Encapsulation using WP and MD markedly decreased peroxide concentrations, postponing oxidation. The maximum encapsulation efficiency (90%) was attained using 25% whey protein and 10% maltodextrin at a drying temperature of 150°C. This combination enhanced storage stability and safeguarded active components, but lipid oxidation was more evident in particles with diminished encapsulation efficiency, as indicated by the value of peroxide ($meqO_2$/kg) decrease 1.2-fold (12.5 vs 14.8), *p*-Anisidine ($meqO_2$/kg) decrease 1.1-fold (21.9 vs 24.6), and totox ($meqO_2$/kg) decrease 1.1-fold (34.4 vs 39.4) compare to free PSO during a 15-day period.[189]

Scale-up of Spray Drying Processes

Scale up Consideration

When transitioning from pilot to industrial scale, it is essential to ensure consistency in fluid dynamics and processing parameters.[190] The subsequent measures can facilitate effective scale-up while regulating viscosity:

Maintaining Fluid Dynamics

Fluid dynamic parameters, including feed flow rate and retentate pressure, must be evaluated and optimized according to the operational scale. Sustaining uniform fluid dynamics across scales is crucial for reliable scale-up. The selection of geometry, including channel length and height, influences fluid dynamics and must be considered in the scaling process.[191]

Model-Based Methodologies

Employing model-based methodologies facilitates the incorporation of predictive analysis into the scaling procedure. Models may replicate the behavior of droplet formation and drying kinetics across different scales, offering insights into how variations in viscosity and other parameters may influence the final result. The approach delineates a methodology for the effective development of the spray drying process, including essential engineering models.[192,193]

Use of Advanced Measurement Techniques

Utilizing inline process analytical technologies to monitor viscosity and other essential parameters in real time enables prompt modifications during the spray drying process, hence ensuring product quality and uniformity. Acoustic flowmeters have been employed to detect viscosity with precision, facilitating enhanced regulation of the spray drying environment.[194,195]

Understanding and Managing Viscosity

Dilution of Feed Solutions

Decreasing the concentration of the feed solution can effectively reduce viscosity. This method requires careful calibration, as excessive dilution may result in inadequate solid content in the final product. For products where viscosity is a concern, it is essential to maintain an ideal solid content to achieve a high-quality spray-dried powder.[196,197]

Use of Surfactants or Viscosity Modifiers

The inclusion of surfactants might diminish the effective viscosity of the feed solution, facilitating improved atomization during the spray drying process. The incorporation of hydroxypropyl cellulose (HPC) or polyvinyl alcohol (PVA) has demonstrated favorable outcomes in reducing viscosity problems while preserving the efficacy of the active ingredient.[198]

Temperature Control

Elevating the feed temperature helps reduce viscosity, as temperature significantly influences the rheological characteristics of polymeric solutions. Modifying the temperature of the feed solution before atomization enhances flow properties, resulting in more uniform droplet production.[199]

Practical Examples and Considerations

Air Temperature

The operating air temperature influences viscosity and evaporation rates. Modifications in air temperature can regulate the drying rate and influence particle shape. Elevated temperatures may decrease drying durations but could also result in the heat destruction of sensitive substances.[200]

Feed Flow Rate

The velocity of the feed entering the dryer affects droplet size and dispersion. An ideal flow rate guarantees consistent droplet generation while reducing viscosity-related issues.[201]

Atomization Technique

Selecting the appropriate atomization technology such as rotary atomizers or nozzle atomizers can profoundly influence the management of feed viscosity. Rotary atomizers are more appropriate for high-viscosity feed solutions compared to nozzle atomizers.[202]

Comparative Analysis and Future[188,189]

Comparative Analysis

Spray drying (SDG) is a versatile platform for engineering solid dispersion (ASD), solid SNEDDS (S-SNEDDS), and microencapsulation systems, with clear contexts where it is either advantageous or suboptimal. Versus hot melt extrusion (HME), SDG operates at lower thermal loads and accommodates thermolabile APIs and solvent-processable excipients, enables fine control of particle size/morphology, and readily scales from lab to commercial spray dryers. However, HME often achieves higher drug–polymer intimacy and robust amorphization without residual solvents; SDG can be inferior when feed solubility is limited, solvent handling is constrained, or long-term amorphous stability is marginal.[203–205]

Compared with freeze-drying (FD), SDG offers far greater throughput and tighter particle engineering but may yield lower encapsulation efficiency for highly volatile oils and can be more sensitive to feed composition and atomization conditions; FD can outperform SDG for extremely labile bioconstituents where sublimation preserves structure. Relative to solvent evaporation/co-precipitation in bulk, SDG provides superior control over drying kinetics and particle attributes, yet may suffer from nozzle fouling, cyclone losses (lower yield), and the need for flammable-solvent controls.[203–205]

Future Perspectives

Nano Spray Drying

Nanotechnology, specifically nano spray drying, has enhanced drug delivery methods by generating nanoparticles with superior attributes, including narrow size distributions, suitable for intricate drug compositions. A primary advantage of nano spray drying is its capacity to encapsulate active compounds within polymeric matrix, safeguarding delicate molecules and facilitating targeted distribution. This method transforms liquid feedstocks into dry powders, which is especially advantageous for safeguarding compositions from deterioration. Recent research have investigated nanoparticle synthesis for catalytic applications, highlighting the importance of precise control over particle morphology and dimensions.[117]

Nano spray drying has been utilized to produce sophisticated materials such as hierarchical zeolite microspheres to improve catalysis. Nano spray drying technology has potential for enhancing sophisticated medicine formulations and material production, hence improving therapy alternatives. Submicron particles with smaller size distributions improve solubility and absorption, especially for poorly soluble active pharmaceutical ingredients; yet, issues related to throughput, yield, and agglomeration control persist.[6,206]

Greener Processes

The incorporation of green solvents in the development of solid dispersions, self-nanoemulsifying drug delivery systems (SNEDDS), and microencapsulation through spray drying markedly improves the sustainability and safety of pharmaceutical manufacturing. These environmentally sustainable solvents diminish ecological impact while enhancing the effectiveness of medicine delivery systems. The selection of solvent influences polymer conformation and drug

interactions, hence affecting the dissolution rate and bioavailability of the active pharmaceutical ingredient (API). Ethanol mixed with water serves as a sustainable substitute for conventional organic solvents, enhancing the encapsulation efficiency and mechanical characteristics of solid dispersions. SNEDDS formulated with eco-friendly solvents exhibit comparable or superior drug content and release properties relative to liquid counterparts, hence improving the stability and bioavailability of lipophilic pharmaceuticals.[207,208]

The incorporation of non-toxic carriers and environmentally friendly solvents enhances the efficacy and safety of SNEDDS, rendering them more appropriate for medicinal applications. Furthermore, in microencapsulation, eco-friendly solvents can safeguard sensitive active pharmaceutical ingredients (APIs) and enhance their release characteristics, thereby mitigating the health hazards linked to hazardous solvents. The integration of green solvents in pharmaceutical formulations signifies a shift towards enhanced sustainability, in accordance with advancing regulatory criteria. Investigations in this domain are crucial for the progression of sustainable drug delivery methods, augmenting bioavailability, and bolstering patient safety.[209–211]

Process Analytical Technology (PAT) and Quality by Design (QbD)

Process Analytical Technology (PAT) offers real-time insights into production through the monitoring of critical quality attributes (CQAs) and critical process parameters (CPPs). Established by the FDA in 2004, PAT improves comprehension of production processes, facilitating continuous monitoring and control, which is essential in spray drying where factors like as temperature, pressure, and feed composition influence product quality.[23,212,213]

Quality by Design (QbD) enhances Process Analytical Technology (PAT) by establishing processes with predetermined quality objectives, emphasizing the correlation between product characteristics and process factors to mitigate risks. In spray drying, Quality by Design (QbD) necessitates meticulous selection of excipients, comprehension of their interactions with active pharmaceutical ingredients (APIs), and optimization of process parameters for stability and efficacy. While PAT and QbD provide substantial advantages, like enhanced product uniformity and expedited regulatory approval, they also pose problems, notably the intricacy of real-time monitoring systems. Upon implementation, these technologies enhance manufacturing reliability and product quality, exemplified by the utilization of online mass spectrometry to forecast endpoint clarity, illustrating how real-time data may inform process decisions and optimize production workflows.[23,212–215]

Current Controversies and Divergent Findings

The literature has a continuous discourse on many parameters influencing the generation and efficacy of amorphous solid dispersions (ASDs). These encompass: (i) the permissible degree of residual crystallinity prior to performance deterioration, (ii) the comparative efficacy of hydrophilic versus enteric polymers in sustaining supersaturation in biorelevant media, (iii) the influence of surfactants that enhance wetting yet may also plasticize the matrix, (iv) the stability implications of pH modifiers, and (v) the interplay between processing temperature and humidity with composition on stability outcomes. Discrepancies in findings frequently stem from variations in drug load, polymer ratio, media, and storage conditions; clearly addressing these variables may facilitate the reconciliation of divergent study conclusions. The selection of solvents for spray drying is a critical factor that influences the stability and bioavailability of ASDs. Some research indicates that organic solvents improve drug–polymer interactions and solubility, while other studies express concerns regarding the long-term stability of ASDs created using this method. Research indicates that spray drying with specific solvents can enhance immediate bioavailability, although it may jeopardize long-term stability due to the influence of evaporation kinetics on the physical stability of dispersions.[216–218]

The comparative effectiveness of spray drying and hot-melt extrusion (HME) is also contested. Spray drying is esteemed for its simplicity and scalability, whereas hot melt extrusion (HME) provides superior control over process parameters and stability for specific formulations. This indicates that integrating these strategies may enhance performance optimization. The selection of excipients profoundly influences ASD formulation. Hydroxypropyl methylcellulose acetate succinate (HPMCAS) enhances solubility; yet, altering its concentrations and formulations poses difficulties. Research demonstrates that a comprehensive understanding of drug–excipient interactions is crucial for optimizing formulations, necessitating customized techniques for particular formulation requirements.[216–218]

Safety, Toxicity, and Regulatory Considerations

Current regulatory frameworks from entities such as the FDA, EMA, and WHO underscore the necessity of diminishing dependence on conventional organic solvents due to their significant toxicity and environmental risks. Concerns about the safety and toxicological characteristics of solvents necessitate that producers adopt alternatives that adhere to changing regulatory standards. Regulatory trends in spray drying, especially with green solvents and safety considerations, indicate a notable transition towards enhancing sustainability and safety in pharmaceutical manufacture.[23,219]

Research indicates that employing less hazardous solvents in spray drying enhances the safety profiles of the produced items. The implementation of green solvents in spray drying processes is motivated by regulatory requirements and public desire for safer industrial methods. The concepts of green chemistry promote the utilization of solvents that provide less risks to human health and the environment. Conventional solvents present health and safety hazards owing to their toxicity and flammability, particularly in spray drying processes. Green solvents, such as ethanol and bio-based alternatives, exhibit lower toxicity and mitigate workplace health risks. Traditional solvents such as methanol and acetone frequently provide toxicity and flammability hazards. Utilizing water as a solvent reduces energy consumption and adheres to the principles of green chemistry. Water and ethanol are becoming acknowledged as more suitable options for the processing of medicinal compounds. Incorporating a minor proportion of water in spray drying enhances the solubility and microstructural properties of solid dispersions, concurrently reducing dependence on toxic solvents. Regulatory agencies require that items comply with defined safety and efficacy requirements. The use of nanoparticles in combination with spray-dried formulations presents considerable safety and toxicity concerns. Recent literature underscores the necessity of comprehensive toxicokinetic and risk assessment evaluations of nanomaterials to comply with safety recommendations for their handling and processing. Comprehending the mechanisms of spray drying that generate particle matter interacting with biological systems through suitable toxicity evaluations is essential.[211,220–223]

In addition to the solvent, another safety consideration is the carrier employed such as the safety profile of soluplus as an excipient in pediatric pharmaceutical formulations has been assessed. Preclinical research indicated that soluplus is non-toxic in animal models and shows little systemic exposure. Clinical findings from research involving adult populations further corroborate its safety in pediatric patients. Soluplus has been determined to be safe for oral formulations designed for pediatric populations and is regarded as a dependable carrier in the creation of pediatric pharmaceutical dosage forms.[66] PEG 8000 is a hydrophilic, biocompatible, and non-toxic homopolymer extensively utilized in pharmaceutical applications and also has received FDA approval for anti-inflammatory and antifungal purposes.[224]

Additionally, the safety of the formulation system must be evaluated, specifically regarding its potential hazardous effects or its safety in vivo such as oxyberberine amorphous solid dispersion (OBB-ASD) exhibited hepatoprotective effects in a mouse model of acute liver injury (ALI) induced by LPS/D-GalN. The findings indicated that the OBB-ASD formulation enhanced liver function by diminishing liver damage indicators, such as AST and ALT levels, in comparison to untreated controls. Histopathological analysis indicated that OBB-ASDs markedly mitigated liver damage, including bleeding, necrosis, and inflammatory cell infiltration, thereby restoring the liver's state to nearly normal levels. The protective benefits against oxidative stress and inflammatory reactions were ascribed to the regulation of the TLR4/NF-κB pathway.[43]

Conclusion

Spray drying has become a multifaceted method for improving the solubility, bioavailability, and stability of poorly water-soluble medicines and natural bioactive chemicals via systems like solid dispersions, solid SNEDDS, and microencapsulation. The efficacy of these formulations relies on the compatibility between the medicine and carrier, the physicochemical qualities of excipients, and the processing parameters that determine the final solid state. This review illustrates that spray-dried systems consistently enhance solubility and absorption of several APIs, while significantly improving the stability of natural oils and peptides. Future research must emphasize comparative carrier evaluations and mechanistic investigations that connect drying kinetics to drug-excipient interactions, facilitating more predictable, scalable, and logical design of spray-dried pharmaceutical formulations.

Abbreviations:

SD, Solid Dispersion; SDG, Spray Drying; FD, Freeze Drying; ASD, Amorphous Solid Dispersion; CSD, Crystalline Solid Dispersion; TSD, Ternary Solid Dispersion; MD, Maltodextrin; GT, Gum Tragacanth; SNEDDS, Self Nanoemulsifying Drug Delivery System; S-SNEDDS, Solid Self Nanoemulsifying Drug Delivery System; Tg, Glass transition; ESD, Enteric solid dispersion; SASD, Surface-attached solid dispersion; API, Active pharmaceutical ingredients; ARV-110, Bavdegalutamide; PVA, Polyvinyl alcohol; PVP, Polyvinylpyrrolidone; PVPVA, Poly(vinylpyrrolidone-co-vinyl acetate); HPMC, Hydroxypropyl methylcellulose; HPMCAS, Hydroxypropyl methylcellulose acetate succinate; CMC, Carboxymethyl cellulose; Na-CMC, Sodium carboxymethyl cellulose; BCS, Biopharmaceutical classification system; BDDCS, Biopharmaceutical drug disposition classification; AUC, Area under curve; Cmax, Maximum concentration; Tmax, Time to reach Cmax; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; P, Population; I, Intervention; C, Formulation; O, Outcome; TER, Terbinafine; OBB, Oxyberberine; OLA, Olaparib; EZT, Ezetimibe; CoQ10, Coenzyme Q10; STP, Stiripentol; RES, Resveratrol; LCDP, Lacidipine; MTX, Methotrexate; ABTS, 2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); APST, Apremilast; ZD, Gefitinib; ENZ, Enzalutamide; CC, Candesartan cilexetil; PSO, Pepper seed oil; PP, Pea peptides; PGSO, Pomegranate seed oil; PPO, Prickly ash peel oleoresin; SPI, Soy protein isolate; WP, whey protein; GA, Gum arabic; TLR4, Toll-Like Receptor 4; NF-κB, Nuclear Factor kappa-light-chain-enhancer of activated B cells; LPS, Lipopolysaccharide; D-GalN, D-galactosamine; PEG, Polyethylene glycol; FDA, Food and drug administration; ALI, Acute liver injury; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; PAT, Process analytical technology; QbD, Quality by design; CQAs, Critical quality attributes; CPPs, Critical process parameters; HME, Hot melt extrusion; HPC, Hydroxypropyl cellulose; HP-β-CD, Hydroxypropyl-β-cyclodextrin; PVP K30, povidone (polyvinylpyrrolidone) K30; TPGS, D-α-tocopheryl polyethylene glycol 1000 succinate; P-gp, P-glycoprotein; GABA, Gamma-aminobutyric acid; EL, Cremophor EL; Lab, Labrasol; SIF, Simulation intestinal fluid; SEM, Scanning electron microscopy; PXRD, Powder x-ray diffraction; SDZDPS, Spray dried gefitinib with PVP and eudragit S 100; Na_2CO_3, Sodium carbonate; USP, United States Pharmacopeia; HPLC, High-Performance Liquid Chromatography; UHPLC, Ultra High-Performance Liquid Chromatography; UV, spektrofotometri ultraviolet; PVDF, Polyvinylidene fluoride; DS, Differential Scanning Calorimetry; TGA, Thermogravimetric Analysis; SLS, Sodium lauryl sulfate; GF, Griseofulvin; SDS, Sodium dodecyl sulfate; QUR, Quercetin; p-AV, p-Anisidine Value; PV, Peroxide Value; LC-MS, Liquid chromatography-mass spectrometry; FeSSIF, Fed state simulated intestinal fluid; FaS, Minimum inhibitory concentration; MBC, Minimum bactericidal concentration.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could influence the work reported in this study.

References

1. Cheon S, Kim JS, Woo MR, et al. Establishment of nanoparticle screening technique: a pivotal role of sodium carboxymethylcellulose in enhancing oral bioavailability of poorly water-soluble aceclofenac. *Int J Biol Macromol*. 2024;277(P2):134246. doi:10.1016/j.ijbiomac.2024.134246
2. Michalak M. Plant extracts as skin care and therapeutic agents. *Int J Mol Sci*. 2023;24(20):15444. doi:10.3390/ijms242015444
3. Grassia M, Messia MC, Marconi E, et al. Microencapsulation of phenolic extracts from cocoa shells to enrich chocolate bars. *Plant Foods Human Nutr*. 2021;76(4):449–457. doi:10.1007/s11130-021-00917-4
4. Pratama R, Abdassah M, Chaerunisaa AY. Review: stabilitas Bahan Alam dalam Mikroenkapsulasi. *Majalah Farmasetika*. 2021;6(3):213. doi:10.24198/mfarmasetika.v6i3.33172
5. Turchiuli C, Gianfrancesco A, Palzer S, Dumoulin E. Evolution of particle properties during spray drying in relation with stickiness and agglomeration control. *Powder Technol*. 2011;208(2):433–440. doi:10.1016/j.powtec.2010.08.040
6. Santos D, Maurício AC, Sencadas V, Santos JD, Fernandes MH, Gomes PS. Spray drying: an overview. In: *Biomaterials - Physics and Chemistry - New Edition*. InTech; 2018. doi:10.5772/intechopen.72247

7. Wang M, Rosenberg Y, Rosenberg M. Microcapsules consisting of whey proteins-coated droplets of lipids embedded in wall matrices of spray-dried microcapsules consisting mainly of non-fat milk solids. *Foods*. 2021;10(9):2105. doi:10.3390/foods10092105
8. Al-Zoubi N, Odeh F, Partheniadis I, Gharaibeh S, Nikolakakis I. Spray drying of naproxen and naproxen sodium for improved tableting and dissolution – physicochemical characterization and compression performance. *Pharm Dev Technol*. 2021;26(2):193–208. doi:10.1080/10837450.2020.1853769
9. Chen ZQ, Liu Y, Zhao JH, Wang L, Feng NP. Improved oral bioavailability of poorly water-soluble indirubin by a supersaturatable self-microemulsifying drug delivery system. *Int J Nanomed*. 2012;7:1115–1125. doi:10.2147/IJN.S28761
10. Tonon RV, Brabet C, Hubinger MD. Influence of process conditions on the physicochemical properties of açai (Euterpe oleraceae Mart.) powder produced by spray drying. *J Food Eng*. 2008;88(3):411–418. doi:10.1016/j.jfoodeng.2008.02.029
11. Igual M, Ramires S, Mosquera LH, Martínez-Navarrete N. Optimization of spray drying conditions for lulo (Solanum quitoense L.) pulp. *Powder Technol*. 2014;256:233–238. doi:10.1016/j.powtec.2014.02.003
12. Kha TC, Nguyen MH, Roach PD. Effects of spray drying conditions on the physicochemical and antioxidant properties of the Gac (Momordica cochinchinensis) fruit aril powder. *J Food Eng*. 2010;98(3):385–392. doi:10.1016/j.jfoodeng.2010.01.016
13. Goula AM, Adamopoulos KG, Kazakis NA. Influence of spray drying conditions on tomato powder properties. *Drying Technol*. 2004;22(5):1129–1151. doi:10.1081/DRT-120038584
14. Fazaeli M, Emam-Djomeh Z, Kalbasi Ashtari A, Omid M. Effect of spray drying conditions and feed composition on the physical properties of black mulberry juice powder. *Food Bioprod Process*. 2012;90(4):667–675. doi:10.1016/j.fbp.2012.04.006
15. Hsu C. Chemical composition, physical properties, and antioxidant activities of yam flours as affected by different drying methods. *Food Chem*. 2003;83(1):85–92. doi:10.1016/S0308-8146(03)00053-0
16. Bejenaru C, Radu A, Segneanu AE, et al. Pharmaceutical applications of biomass polymers: review of current research and perspectives. *Polymers*. 2024;16(9):1182. doi:10.3390/polym16091182
17. Laureanti EJG, Paiva TS, de Matos Jorge LM, Jorge RMM. Microencapsulation of bioactive compound extracts using maltodextrin and gum arabic by spray and freeze-drying techniques. *Int J Biol Macromol*. 2023;253:126969. doi:10.1016/j.ijbiomac.2023.126969
18. Xu Y, Yan X, Zheng H, et al. The application of encapsulation technology in the food industry: classifications, recent advances, and perspectives. *Food Chem X*. 2024;21:101240. doi:10.1016/j.fochx.2024.101240
19. Elmowafy M, Alhakamy NA, Shalaby K, et al. Hybrid polylactic acid/Eudragit L100 nanoparticles: a promising system for enhancement of bioavailability and pharmacodynamic efficacy of luteolin. *J Drug Deliv Sci Technol*. 2021;65:102727. doi:10.1016/j.jddst.2021.102727
20. Attia MS, Elshahat A, Hamdy A, et al. Soluplus® as a solubilizing excipient for poorly water-soluble drugs: recent advances in formulation strategies and pharmaceutical product features. *J Drug Deliv Sci Technol*. 2023;84:104519. doi:10.1016/j.jddst.2023.104519
21. Chalah K, Benmounah A, Mahdad M, Kheribet R. Rheological study of sodium carboxymethylcellulose: effect of concentration and molecular weight. *Mater Today Proc*. 2022;53:185–190. doi:10.1016/j.matpr.2021.12.502
22. Kim MS, Ha ES, Choo GH, Baek IH. Preparation and in vivo evaluation of a dutasteride-loaded solid-supersaturatable self-microemulsifying drug delivery system. *Int J Mol Sci*. 2015;16(5):10821–10833. doi:10.3390/ijms160510821
23. McAuliffe MAP, O'Mahony GE, Blackshields CA, et al. The use of PAT and off-line methods for monitoring of roller compacted ribbon and granule properties with a view to continuous processing. *Org Process Res Dev*. 2015;19(1):158–166. doi:10.1021/op5000013
24. Wang Y, Xu S, Xiao Z, et al. Stiripentol enteric solid dispersion-loaded effervescent tablets: enhanced dissolution, stability, and absorption. *AAPS Pharm Sci Tech*. 2022;23(5). doi:10.1208/s12249-022-02261-5
25. Boza IAF, da Silva SL, Guedes NB, Bazzo GC, Stulzer HK. Pediatric formulation optimization using a rational design: exploring amorphous solid dispersion technology with terbinafine hydrochloride as a case study. *AAPS Pharm Sci Tech*. 2025;26(1):40. doi:10.1208/s12249-024-03012-4
26. Raj Giri B, Suk Kim J, Hyuck Park J, et al. Improved bioavailability and high photostability of methotrexate by spray-dried surface-attached solid dispersion with an aqueous medium. *Pharmaceutics*. 2021;13(1):111. doi:10.3390/pharmaceutics13010111
27. Shin Y, Kim M, Kim C, et al. Development and characterization of olaparib-loaded solid self-nanoemulsifying drug delivery system (S-SNEDDS) for pharmaceutical applications. *AAPS Pharm Sci Tech*. 2024;25(7):1–14. doi:10.1208/s12249-024-02927-2
28. Zhuo X, Margrethe Brekstad Kjellin M, Schaal Z, Zhang T, Löbmann K, Leng D. A comparative study between a protein based amorphous formulation and other dissolution rate enhancing approaches: a case study with rifaximin. *Pharmaceutics*. 2023;15(1). doi:10.3390/pharmaceutics15010126
29. Lamichhane S, Seo JE, Keum T, et al. Enhancing solubility and bioavailability of coenzyme Q10: formulation of solid dispersions using Soluplus® as a carrier. *Arch Pharm Res*. 2022;45(1):29–37. doi:10.1007/s12272-022-01368-4
30. Yang L, Wu P, Xu J, et al. Development of apremilast solid dispersion using TPGS and PVPVA with enhanced solubility and bioavailability. *AAPS Pharm Sci Tech*. 2021;22(4). doi:10.1208/s12249-021-02005-x
31. Lim C, Lee D, Kim M, et al. Development of a sorafenib-loaded solid self-nanoemulsifying drug delivery system: formulation optimization and characterization of enhanced properties. *J Drug Deliv Sci Technol*. 2023;82:1–25. doi:10.1016/j.jddst.2023.104374
32. Mareczek L, Mueller LK, Halstenberg L, et al. Use of poly(vinyl alcohol) in spray-dried dispersions: enhancing solubility and stability of proteolysis targeting chimeras. *Pharmaceutics*. 2024;16(7). doi:10.3390/pharmaceutics16070924
33. Mustafa WW, Fletcher J, Khoder M, Alany RG. Solid dispersions of gefitinib prepared by spray drying with improved mucoadhesive and drug dissolution properties. *AAPS Pharm Sci Tech*. 2022;23(1). doi:10.1208/s12249-021-02187-4
34. Poudel S, Kim DW. Developing ph-modulated spray dried amorphous solid dispersion of candesartan cilexetil with enhanced in vitro and in vivo performance. *Pharmaceutics*. 2021;13(4). doi:10.3390/pharmaceutics13040497
35. Lin Z, Zheng K, Azad MA, Davé RN. Preparation of free-flowing spray-dried amorphous composites using neusilin®. *AAPS Pharm Sci Tech*. 2023;24(1):1–11. doi:10.1208/s12249-023-02511-0
36. Yun T, Lee S, Yun S, Cho D, Bang K, Kim K. Investigation of stabilized amorphous solid dispersions to improve oral olaparib absorption. *Pharmaceutics*. 2024;16(7). doi:10.3390/pharmaceutics16070958
37. Kim JS, Din F, Cho HJ, et al. Impact of carrier hydrophilicity on solid self nano-emulsifying drug delivery system and self nano-emulsifying granule system. *Int J Pharm*. 2023:648(August):123578. doi:10.1016/j.ijpharm.2023.123578
38. Baek K, Woo MR, Din FU, et al. Comparison of solid self-nanoemulsifying systems and surface-coated microspheres: improving oral bioavailability of niclosamide. *Int J Nanomed*. 2024;19:13857–13874. doi:10.2147/IJN.S494083

39. Lee SM, Lee JG, Yun TH, Kim CH, Cho JH, Kim KS. The impact of polymers on enzalutamide solid self-nanoemulsifying drug delivery system and improved bioavailability. *Pharmaceutics*. 2024;16(4). doi:10.3390/pharmaceutics16040457
40. Szafraniec-Szczęsny J, Antosik-Rogóż A, Kurek M, et al. How does the addition of kollidon®va64 inhibit the recrystallization and improve ezetimibe dissolution from amorphous solid dispersions?. *Pharmaceutics*. 2021;13(2):1–15. doi:10.3390/pharmaceutics13020147
41. Shen J, Hu A, Yang Y, et al. Ternary solid dispersions of lacidipine: enhancing dissolution and supersaturation maintenance through strategic formulation optimization. *Int J Pharm*. 2024:654(March):123989. doi:10.1016/j.ijpharm.2024.123989
42. Kori AH, Mahesar SA, Khaskheli AR, et al. Effect of wall material and inlet drying temperature on microencapsulation and oxidative stability of pomegranate seed oil using spray drying. *J Oleo Sci*. 2022;71(1):31–41. doi:10.5650/JOS.ESS21105
43. Chen T, Li Q, Ai G, et al. Enhancing hepatoprotective action: oxyberberine amorphous solid dispersion system targeting TLR4. *Sci Rep*. 2024;14(1):1–18. doi:10.1038/s41598-024-65190-2
44. Ha ES, Choi DH, Baek IH, Park H, Kim MS. Enhanced oral bioavailability of resveratrol by using neutralized eudragit e solid dispersion prepared via spray drying. *Antioxidants*. 2021;10(1):1–12. doi:10.3390/antiox10010090
45. Huang H, Zhang Y, Hu C. Study on the crystallinity of PEG on the crystalline size of flavonoids in a crystalline dispersion system. *Eur J Pharm Biopharm*. 2024;205(July). doi:10.1016/j.ejpb.2024.114536
46. Zhang Z, Zhang Z, Li X, et al. Preparation and characterization of prickly ash peel oleoresin microcapsules and flavor retention analysis. *Foods*. 2024;13(11):1–18. doi:10.3390/foods13111726
47. Karaaslan M, Şengün F, Cansu Ü, Başyiğit B, Sağlam H, Karaaslan A. Gum arabic/maltodextrin microencapsulation confers peroxidation stability and antimicrobial ability to pepper seed oil. *Food Chem*. 2021;337(July 2020). doi:10.1016/j.foodchem.2020.127748
48. Liu KK, Liu HR, Wen L, et al. Enhancing storage stability of pea peptides through encapsulation in maltodextrin and gum tragacanth via monitoring scavenge ability to free radicals. *Int J Biol Macromol*. 2024;276(P1):133736. doi:10.1016/j.ijbiomac.2024.133736
49. Jia X, Chen J, Cheng H, et al. Use of surfactant-based amorphous solid dispersions for BDDCS class II drugs to enhance oral bioavailability: a case report of resveratrol. *Int J Pharm*. 2023;641(January):123059. doi:10.1016/j.ijpharm.2023.123059
50. Bejan A. Fundamentals of exergy analysis, entropy generation minimization, and the generation of flow architecture. *Int J Energy Res*. 2002;26 (7):0–43. doi:10.1002/er.804
51. Ziaee A, Albadarin AB, Padrela L, Femmer T, O'Reilly E, Walker G. Spray drying of pharmaceuticals and biopharmaceuticals: critical parameters and experimental process optimization approaches. *Eur J Pharm Sci*. 2019;127:300–318. doi:10.1016/j.ejps.2018.10.026
52. Li X, Anton N, Arpagaus C, Belleteix F, Vandamme TF. Nanoparticles by spray drying using innovative new technology: the Büchi nano spray dryer B-90. *J Control Release*. 2010;147(2):304–310. doi:10.1016/j.jconrel.2010.07.113
53. Lee SH, Heng D, Ng WK, Chan HK, Tan RBH. Nano spray drying: a novel method for preparing protein nanoparticles for protein therapy. *Int J Pharm*. 2011;403(1–2):192–200. doi:10.1016/j.ijpharm.2010.10.012
54. Vehring R, Foss WR, Lechuga-Ballesteros D. Particle formation in spray drying. *J Aerosol Sci*. 2007;38(7):728–746. doi:10.1016/j.jaerosci.2007.04.005
55. França MT, Martins Marcos T, Costa PFA, et al. Eutectic mixture and amorphous solid dispersion: two different supersaturating drug delivery system strategies to improve griseofulvin release using saccharin. *Int J Pharm*. 2022;615:121498. doi:10.1016/j.ijpharm.2022.121498
56. Wang X, Zhang L, Ma D, et al. Characterizing and exploring the differences in dissolution and stability between crystalline solid dispersion and amorphous solid dispersion. *AAPS Pharm Sci Tech*. 2020;21(7):262. doi:10.1208/s12249-020-01802-0
57. Borde S, Hegde P, Prathipati P, North J, Kumari D, Chauhan H. Formulation and characterization of ternary amorphous solid dispersions of a highly potent anti-tubercular agent and curcumin. *J Drug Deliv Sci Technol*. 2021;64:102564. doi:10.1016/j.jddst.2021.102564
58. Budiman A, Lailasari E, Nurani NV, et al. Ternary solid dispersions: a review of the preparation, characterization, mechanism of drug release, and physical stability. *Pharmaceutics*. 2023;15(8):2116. doi:10.3390/pharmaceutics15082116
59. Gharsallaoui A, Roudaut G, Chambin O, Voilley A, Saurel R. Applications of spray-drying in microencapsulation of food ingredients: an overview. *Food Res Int*. 2007;40(9):1107–1121. doi:10.1016/j.foodres.2007.07.004
60. Tran TH, Poudel BK, Marasini N, et al. Preparation and evaluation of raloxifene-loaded solid dispersion nanoparticle by spray-drying technique without an organic solvent. *Int J Pharm*. 2013;443(1–2):50–57. doi:10.1016/j.ijpharm.2013.01.013
61. Deshpande TM, Shi H, Pietryka J, Hoag SW, Medek A. Investigation of polymer/surfactant interactions and their impact on itraconazole solubility and precipitation kinetics for developing spray-dried amorphous solid dispersions. *Mol Pharm*. 2018;15(3):962–974. doi:10.1021/acs.molpharmaceut.7b00902
62. Valková V, Ďúranová H, Falcimaigne-Cordin A, et al. Impact of freeze- and spray-drying microencapsulation techniques on β-glucan powder biological activity: a comparative study. *Foods*. 2022;11(15):2267. doi:10.3390/foods11152267
63. Rodríguez-Hernández GR, González-García R, Grajales-Lagunes A, Ruiz-Cabrera* MA, Abud-Archila M. Spray-drying of cactus pear juice (opuntia streptacantha): effect on the physicochemical properties of powder and reconstituted product. *Drying Technol*. 2005;23(4):955–973. doi:10.1080/DRT-200054251
64. Tubic-Grozdanis M, Bolger MB, Langguth P. Application of gastrointestinal simulation for extensions for biowaivers of highly permeable compounds. *AAPS J*. 2008;10(1):213–226. doi:10.1208/s12248-008-9023-x
65. Kondoros BA, Laczkovich O, Berkesi O, Aigner Z Analytical investigation of cyclodextrin complexation using the co-grinding technique in the case of terbinafine hydrochloride. In: *The 1st International Electronic Conference on Pharmaceutics*. MDPI; 2020:19. doi:10.3390/IECP2020-08714
66. Schmitt G. Safety of soluplus® in pediatrics. *Appl Drug Res Clin Trials and Regulatory Affairs*. 2022;9(1):30–32. doi:10.2174/2667337109666221116092457
67. Beig A, Fine-Shamir N, Lindley D, Miller JM, Dahan A. Advantageous solubility-permeability interplay when using amorphous solid dispersion (ASD) formulation for the BCS class IV P-gp substrate rifaximin: simultaneous increase of both the solubility and the permeability. *AAPS J*. 2017;19(3):806–813. doi:10.1208/s12248-017-0052-1
68. Caraceni P, Vargas V, Solà E, et al. The use of rifaximin in patients with cirrhosis. *Hepatology*. 2021;74(3):1660–1673. doi:10.1002/hep.31708
69. Mishra J, Bohr A, Rades T, Grohganz H, Löbmann K. Whey proteins as stabilizers in amorphous solid dispersions. *Eur J Pharm Sci*. 2019;128:144–151. doi:10.1016/j.ejps.2018.12.002
70. Choi JS, Kwon SH, Lee SE, et al. Use of acidifier and solubilizer in tadalafil solid dispersion to enhance the in vitro dissolution and oral bioavailability in rats. *Int J Pharm*. 2017;526(1–2):77–87. doi:10.1016/j.ijpharm.2017.04.056

71. Ueda K, Higashi K, Yamamoto K, Moribe K. The effect of HPMCAS functional groups on drug crystallization from the supersaturated state and dissolution improvement. *Int J Pharm*. 2014;464(1–2):205–213. doi:10.1016/j.ijpharm.2014.01.005
72. Wilson V, Lou X, Osterling DJ, et al. Relationship between amorphous solid dispersion in vivo absorption and in vitro dissolution: phase behavior during dissolution, speciation, and membrane mass transport. *J Control Release*. 2018;292:172–182. doi:10.1016/j.jconrel.2018.11.003
73. Butreddy A. Hydroxypropyl methylcellulose acetate succinate as an exceptional polymer for amorphous solid dispersion formulations: a review from bench to clinic. *Eur J Pharm Biopharm*. 2022;177:289–307. doi:10.1016/j.ejpb.2022.07.010
74. Chen X, McClements DJ, Zhu Y, et al. Enhancement of the solubility, stability and bioaccessibility of quercetin using protein-based excipient emulsions. *Food Res Int*. 2018;114:30–37. doi:10.1016/j.foodres.2018.07.062
75. Kim CH, Lee SG, Kang MJ, Lee S, Choi YW. Surface modification of lipid-based nanocarriers for cancer cell-specific drug targeting. *J Pharm Investig*. 2017;47(3):203–227. doi:10.1007/s40005-017-0329-5
76. Singh A, Van den Mooter G. Spray drying formulation of amorphous solid dispersions. *Adv Drug Deliv Rev*. 2016;100:27–50. doi:10.1016/j.addr.2015.12.010
77. Yu DG, Li JJ, Williams GR, Zhao M. Electrospun amorphous solid dispersions of poorly water-soluble drugs: a review. *J Control Release*. 2018;292:91–110. doi:10.1016/j.jconrel.2018.08.016
78. Petrussa E, Braidot E, Zancani M, et al. Plant flavonoids—biosynthesis, transport and involvement in stress responses. *Int J Mol Sci*. 2013;14(7):14950–14973. doi:10.3390/ijms140714950
79. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. Lu KP, Sastre J, eds. *Sci World J*. 2013;2013(1). doi:10.1155/2013/162750
80. Alshehri S, Imam SS, Altamimi MA, et al. Enhanced dissolution of luteolin by solid dispersion prepared by different methods: physicochemical characterization and antioxidant activity. *ACS Omega*. 2020;5(12):6461–6471. doi:10.1021/acsomega.9b04075
81. Freire Boullosa L, Van Loenhout J, Flieswasser T, et al. Auranofin synergizes with the PARP inhibitor olaparib to Induce ROS-mediated cell death in mutant p53 cancers. *Antioxidants*. 2023;12(3):667. doi:10.3390/antiox12030667
82. Hirlekar BU, Nuthi A, Singh KD, Murty US, Dixit VA. An overview of compound properties, multiparameter optimization, and computational drug design methods for PARP-1 inhibitor drugs. *Eur J Med Chem*. 2023;252:115300. doi:10.1016/j.ejmech.2023.115300
83. Orleni M, Canil G, Posocco B, Gagno S, Toffoli G. Bioanalytical methods for poly(ADP-ribose) polymerase inhibitor quantification: a review for therapeutic drug monitoring. *Ther Drug Monit*. 2023;45(3):306–317. doi:10.1097/FTD.0000000000001081
84. Sun Z, Zhang H, He H, et al. Cooperative effect of polyvinylpyrrolidone and HPMC E5 on dissolution and bioavailability of nimodipine solid dispersions and tablets. *Asian J Pharm Sci*. 2019;14(6):668–676. doi:10.1016/j.ajps.2018.08.005
85. Saha SK, Joshi A, Singh R, Jana S, Dubey K. An investigation into solubility and dissolution improvement of alectinib hydrochloride as a third-generation amorphous solid dispersion. *J Drug Deliv Sci Technol*. 2023;81:104259. doi:10.1016/j.jddst.2023.104259
86. Rocha B, de Morais LA, Viana MC, Carneiro G. Promising strategies for improving oral bioavailability of poor water-soluble drugs. *Expert Opin Drug Discov*. 2023;18(6):615–627. doi:10.1080/17460441.2023.2211801
87. Tran P, Pyo YC, Kim DH, Lee SE, Kim JK, Park JS. Overview of the manufacturing methods of solid dispersion technology for improving the solubility of poorly water-soluble drugs and application to anticancer drugs. *Pharmaceutics*. 2019;11(3):132. doi:10.3390/pharmaceutics11030132
88. Marsac PJ, Konno H, Rumondor ACF, Taylor LS. Recrystallization of nifedipine and felodipine from amorphous molecular level solid dispersions containing poly(vinylpyrrolidone) and sorbed water. *Pharm Res*. 2008;25(3):647–656. doi:10.1007/s11095-007-9420-3
89. Panizzon GP, Giacomini Bueno F, Ueda-Nakamura T, Nakamura CV, Dias Filho BP. Manufacturing different types of solid dispersions of BCS class IV polyphenol (daidzein) by spray drying: formulation and bioavailability. *Pharmaceutics*. 2019;11(10):492. doi:10.3390/pharmaceutics11100492
90. Huang R, Han J, Wang R, et al. Surfactant-free solid dispersion of BCS class IV drug in an amorphous chitosan oligosaccharide matrix for concomitant dissolution in vitro - permeability increase. *Eur J Pharm Sci*. 2019;130:147–155. doi:10.1016/j.ejps.2019.01.031
91. Yang W, Saboo S, Zhou L, Askin S, Bak A. Early evaluation of opportunities in oral delivery of PROTACs to overcome their molecular challenges. *Drug Discov Today*. 2024;29(2):103865. doi:10.1016/j.drudis.2023.103865
92. Yang W, Gadgil P, Krishnamurthy VR, et al. The evolving druggability and developability space: chemically modified new modalities and emerging small molecules. *AAPS J*. 2020;22(2):21. doi:10.1208/s12248-019-0402-2
93. Yedla P, Babalghith AO, Andra VV, Syed R. PROTACs in the management of prostate cancer. *Molecules*. 2023;28(9):3698. doi:10.3390/molecules28093698
94. Bhujbal SV, Mitra B, Jain U, et al. Pharmaceutical amorphous solid dispersion: a review of manufacturing strategies. *Acta Pharm Sin B*. 2021;11(8):2505–2536. doi:10.1016/j.apsb.2021.05.014
95. Nutescu EA, Shapiro NL. Ezetimibe: a selective cholesterol absorption inhibitor. *Pharmacother J Human Pharmacol Drug Ther*. 2003;23(11):1463–1474. doi:10.1592/phco.23.14.1463.31942
96. Shimpi MR, Childs SL, Boström D, Velaga SP. New cocrystals of ezetimibe with l -proline and imidazole. *CrystEngComm*. 2014;16(38):8984–8993. doi:10.1039/C4CE01127A
97. Marsac PJ, Shamblin SL, Taylor LS. Theoretical and practical approaches for prediction of drug–polymer miscibility and solubility. *Pharm Res*. 2006;23(10):2417–2426. doi:10.1007/s11095-006-9063-9
98. Rumondor ACF, Marsac PJ, Stanford LA, Taylor LS. Phase behavior of poly(vinylpyrrolidone) containing amorphous solid dispersions in the presence of moisture. *Mol Pharm*. 2009;6(5):1492–1505. doi:10.1021/mp900050c
99. Trasi NS, Taylor LS. Effect of polymers on nucleation and crystal growth of amorphous Acetaminophen. *CrystEngComm*. 2012;14(16):5188. doi:10.1039/c2ce25374g
100. Vojinović T, Medarević D, Vranić E, et al. Development of ternary solid dispersions with hydrophilic polymer and surface adsorbent for improving dissolution rate of carbamazepine. *Saudi Pharm J*. 2018;26(5):725–732. doi:10.1016/j.jsps.2018.02.017
101. Konno H, Taylor LS. Influence of different polymers on the crystallization tendency of molecularly dispersed amorphous felodipine. *J Pharm Sci*. 2006;95(12):2692–2705. doi:10.1002/jps.20697
102. Shamma RN, Basha M. Soluplus®: a novel polymeric solubilizer for optimization of Carvedilol solid dispersions: formulation design and effect of method of preparation. *Powder Technol*. 2013;237:406–414. doi:10.1016/j.powtec.2012.12.038
103. Chun ZY, Li S, Liu C, et al. Soluplus micelles for improving the oral bioavailability of scopoletin and their hypouricemic effect in vivo. *Acta Pharmacol Sin*. 2017;38(3):424–433. doi:10.1038/aps.2016.126

104. Mantle D, Dybring A. Bioavailability of coenzyme Q10: an overview of the absorption process and subsequent metabolism. *Antioxidants*. 2020;9(5):386. doi:10.3390/antiox9050386
105. Frampton JE. Stiripentol: a review in dravet syndrome. *Drugs*. 2019;79(16):1785–1796. doi:10.1007/s40265-019-01204-y
106. Buck ML, Goodkin HP. Stiripentol: a novel antiseizure medication for the management of dravet syndrome. *Ann Pharmacother*. 2019;53 (11):1136–1144. doi:10.1177/1060028019856008
107. Trabs N, Trabs M, Stodieck S, House PM. Influence of stiripentol on perampanel serum levels. *Epilepsy Res*. 2020;164:106367. doi:10.1016/j.eplepsyres.2020.106367
108. Li Y, Zhang R, Zhang Q, et al. Dual strategy for improving the oral bioavailability of resveratrol: enhancing water solubility and inhibiting glucuronidation. *J Agric Food Chem*. 2021;69(32):9249–9258. doi:10.1021/acs.jafc.1c02602
109. Peñalva R, Morales J, González-Navarro CJ, et al. Increased oral bioavailability of resveratrol by its encapsulation in casein nanoparticles. *Int J Mol Sci*. 2018;19(9):2816. doi:10.3390/ijms19092816
110. Amri A, Chaumeil JC, Sfar S, Charrueau C. Administration of resveratrol: what formulation solutions to bioavailability limitations?. *J Control Release*. 2012;158(2):182–193. doi:10.1016/j.jconrel.2011.09.083
111. Nowak M, Gajda M, Baranowski P, Szymczyk P, Karolewicz B, Nartowski KP. Stabilisation and growth of metastable form ii of fluconazole in amorphous solid dispersions. *Pharmaceutics*. 2019;12(1):12. doi:10.3390/pharmaceutics12010012
112. Rodríguez-Varela C, Labarta E. Clinical application of antioxidants to improve human oocyte mitochondrial function: a review. *Antioxidants*. 2020;9(12):1197. doi:10.3390/antiox9121197
113. Esparza I, Cimminelli MJ, Moler JA, Jiménez-Moreno N, Ancín-Azpilicueta C. Stability of phenolic compounds in grape stem extracts. *Antioxidants*. 2020;9(8):720. doi:10.3390/antiox9080720
114. Calvo-Castro LA, Schiborr C, David F, et al. The oral bioavailability of trans resveratrol from a grapevine shoot extract in healthy humans is significantly increased by micellar solubilization. *Mol Nutr Food Res*. 2018;62(9). doi:10.1002/mnfr.201701057
115. Amiot MJ, Romier B, Anh Dao TM, et al. Optimization of trans-resveratrol bioavailability for human therapy. *Biochimie*. 2013;95(6):1233–1238. doi:10.1016/j.biochi.2013.01.008
116. Yoshida T, Kurimoto I, Yoshihara K, et al. Aminoalkyl methacrylate copolymers for improving the solubility of tacrolimus. I: evaluation of solid dispersion formulations. *Int J Pharm*. 2012;428(1–2):18–24. doi:10.1016/j.ijpharm.2012.02.041
117. Arpagaus C. PLA/PLGA nanoparticles prepared by nano spray drying. *J Pharm Investig*. 2019;49(4):405–426. doi:10.1007/s40005-019-00441-3
118. Ha ES, Baek IH, Cho W, Hwang SJ, Kim MS. Preparation and evaluation of solid dispersion of atorvastatin calcium with soluplus® by spray drying technique. *Chem Pharm Bull*. 2014;62(6):545–551. doi:10.1248/cpb.c14-00030
119. Akram A, Irfan M, Abualsunun WA, Bukhary DM, Alissa M. How to improve solubility and dissolution of irbesartan by fabricating ternary solid dispersions: optimization and in-vitro characterization. *Pharmaceutics*. 2022;14(11):2264. doi:10.3390/pharmaceutics14112264
120. Al-Obaidi H, Lawrence MJ, Buckton G. Atypical effects of incorporated surfactants on stability and dissolution properties of amorphous polymeric dispersions. *J Pharm Pharmacol*. 2016;68(11):1373–1383. doi:10.1111/jphp.12645
121. Chaudhari SP, Dugar RP. Application of surfactants in solid dispersion technology for improving solubility of poorly water soluble drugs. *J Drug Deliv Sci Technol*. 2017;41:68–77. doi:10.1016/j.jddst.2017.06.010
122. Abolmaali SS, Tamaddon AM, Dinarvand R. A review of therapeutic challenges and achievements of methotrexate delivery systems for treatment of cancer and rheumatoid arthritis. *Cancer Chemother Pharmacol*. 2013;71(5):1115–1130. doi:10.1007/s00280-012-2062-0
123. Chen J, Huang L, Lai H, et al. Methotrexate-loaded pegylated chitosan nanoparticles: synthesis, characterization, and in vitro and in vivo antitumoral activity. *Mol Pharm*. 2014;11(7):2213–2223. doi:10.1021/mp400269z
124. Khan ZA, Tripathi R, Mishra B. Methotrexate: a detailed review on drug delivery and clinical aspects. *Expert Opin Drug Deliv*. 2012;9(2):151–169. doi:10.1517/17425247.2012.642362
125. Kim DS, Cho JH, Park JH, et al. Self-microemulsifying drug delivery system (SMEDDS) for improved oral delivery and photostability of methotrexate. *Int J Nanomed*. 2019;14:4949–4960. doi:10.2147/IJN.S211014
126. Kim DS, Choi JS, Kim DW, et al. Comparison of solvent wetted and kneaded l -sulpiride loaded solid dispersions: powder characterization and in vivo evaluation. *Int J Pharm*. 2016;511(1):351–358. doi:10.1016/j.ijpharm.2016.07.006
127. Schett G, Sloan VS, Stevens RM, Schafer P. Apremilast: a novel PDE4 inhibitor in the treatment of autoimmune and inflammatory diseases. *Ther Adv Musculoskelet Dis*. 2010;2(5):271–278. doi:10.1177/1759720X10381432
128. Schafer P. Apremilast mechanism of action and application to psoriasis and psoriatic arthritis. *Biochem Pharmacol*. 2012;83(12):1583–1590. doi:10.1016/j.bcp.2012.01.001
129. Janssens S, Nagels S, de Armas HN, D'Autry W, Van Schepdael A, Van den Mooter G. Formulation and characterization of ternary solid dispersions made up of Itraconazole and two excipients, TPGS 1000 and PVPVA 64, that were selected based on a supersaturation screening study. *Eur J Pharm Biopharm*. 2008;69(1):158–166. doi:10.1016/j.ejpb.2007.11.004
130. Liu Y, Sun C, Li W, et al. Preparation and characterization of syringic acid–loaded TPGS liposome with enhanced oral bioavailability and in vivo antioxidant efficiency. *AAPS Pharm Sci Tech*. 2019;20(3):98. doi:10.1208/s12249-019-1290-6
131. Hurley D, Potter CB, Walker GM, Higginbotham CL. Investigation of ethylene oxide-co-propylene oxide for dissolution enhancement of hot-melt extruded solid dispersions. *J Pharm Sci*. 2018;107(5):1372–1382. doi:10.1016/j.xphs.2018.01.016
132. Song IS, Cha JS, Choi MK. Characterization, in vivo and in vitro evaluation of solid dispersion of curcumin containing d-α-tocopheryl polyethylene glycol 1000 succinate and mannitol. *Molecules*. 2016;21(10):1386. doi:10.3390/molecules21101386
133. Andey T, Sudhakar G, Marepally S, Patel A, Banerjee R, Singh M. Lipid nanocarriers of a lipid-conjugated estrogenic derivative inhibit tumor growth and enhance cisplatin activity against triple-negative breast cancer: pharmacokinetic and efficacy evaluation. *Mol Pharm*. 2015;12 (4):1105–1120. doi:10.1021/mp5008629
134. Vasconcelos T, Marques S, Das Neves J, Sarmento B. Amorphous solid dispersions: rational selection of a manufacturing process. *Adv Drug Deliv Rev*. 2016;100:85–101. doi:10.1016/j.addr.2016.01.012
135. Surampalli G, Nanjwade BK, Patil PA, Chilla R. Novel tablet formulation of amorphous candesartan cilexetil solid dispersions involving P-gp inhibition for optimal drug delivery: in vitro and in vivo evaluation. *Drug Deliv*. 2016;23(7):2124–2138. doi:10.3109/10717544.2014.945017
136. Bergman E, Forsell P, Persson EM, et al. Pharmacokinetics of gefitinib in humans: the influence of gastrointestinal factors. *Int J Pharm*. 2007;341(1–2):134–142. doi:10.1016/j.ijpharm.2007.04.002

137. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. *Pharm Res*. 1995;12(3):413–420. doi:10.1023/A:1016212804288
138. Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non–small-cell lung cancer to gefitinib. *N Engl J Med*. 2004;350(21):2129–2139. doi:10.1056/NEJMoa040938
139. Motallae S, Taheri A, Homayouni A. Preparation and characterization of solid dispersions of celecoxib obtained by spray-drying ethanolic suspensions containing PVP-K30 or isomalt. *J Drug Deliv Sci Technol*. 2018;46:188–196. doi:10.1016/j.jddst.2018.05.020
140. Smeets A, Koekoekx R, Clasen C, Van den Mooter G. Amorphous solid dispersions of darunavir: comparison between spray drying and electrospraying. *Eur J Pharm Biopharm*. 2018;130:96–107. doi:10.1016/j.ejpb.2018.06.021
141. Gu JM, Robinson JR, Leung SH. Binding of acrylic polymers to mucin/epithelial surfaces: structure-property relationships. *Crit Rev Ther Drug Carrier Syst*. 1988;5(1):21–67.
142. Sai Gouthami K, Kumar D, Thipparaboina R, Chavan RB, Shastri NR. Can crystal engineering be as beneficial as micronisation and overcome its pitfalls?: a case study with cilostazol. *Int J Pharm*. 2015;491(1–2):26–34. doi:10.1016/j.ijpharm.2015.06.009
143. Salunke S, O'Brien F, Cheng Thiam Tan D, et al. Oral drug delivery strategies for development of poorly water soluble drugs in paediatric patient population. *Adv Drug Deliv Rev*. 2022;190:114507. doi:10.1016/j.addr.2022.114507
144. Gupta MK, Goldman D, Bogner RH, Tseng YC. Enhanced drug dissolution and bulk properties of solid dispersions granulated with a surface adsorbent. *Pharm Dev Technol*. 2001;6(4):563–572. doi:10.1081/PDT-120000294
145. Augustijns P, Brewster ME. Supersaturating drug delivery systems: fast is not necessarily good enough. *J Pharm Sci*. 2012;101(1):7–9. doi:10.1002/jps.22750
146. Allgeier MC, Piper JL, Hinds J, et al. Isolation and physical property optimization of an amorphous drug substance utilizing a high surface area magnesium aluminometasilicate (neusilin ® US2). *J Pharm Sci*. 2016;105(10):3105–3114. doi:10.1016/j.xphs.2016.06.019
147. Azad M, Moreno J, Bilgili E, Davé R. Fast dissolution of poorly water soluble drugs from fluidized bed coated nanocomposites: impact of carrier size. *Int J Pharm*. 2016;513(1–2):319–331. doi:10.1016/j.ijpharm.2016.09.046
148. Surwase SA, Itkonen L, Aaltonen J, et al. Polymer incorporation method affects the physical stability of amorphous indomethacin in aqueous suspension. *Eur J Pharm Biopharm*. 2015;96:32–43. doi:10.1016/j.ejpb.2015.06.005
149. Choi SA, Park EJ, Lee JH, et al. Preparation and characterization of pazopanib hydrochloride-loaded four-component self-nanoemulsifying drug delivery systems preconcentrate for enhanced solubility and dissolution. *Pharmaceutics*. 2022;14(9):1875. doi:10.3390/pharmaceutics14091875
150. Khan KU, Minhas MU, Badshah SF, Suhail M, Ahmad A, Ijaz S. Overview of nanoparticulate strategies for solubility enhancement of poorly soluble drugs. *Life Sci*. 2022;291:120301. doi:10.1016/j.lfs.2022.120301
151. Sheng Y, Gao J, Yin ZZ, Kang J, Kong Y. Dual-drug delivery system based on the hydrogels of alginate and sodium carboxymethyl cellulose for colorectal cancer treatment. *Carbohydr Polym*. 2021;269:118325. doi:10.1016/j.carbpol.2021.118325
152. Yan M, Chen T, Zhang S, Lu T, Sun X. A core-shell structured alginate hydrogel beads with tunable thickness of carboxymethyl cellulose coating for pH responsive drug delivery. *J Biomater Sci Polym Ed*. 2021;32(6):763–778. doi:10.1080/09205063.2020.1866350
153. Kim JS, Kim J, Lee SM, et al. Development of guar gum-based dual-layer wound dressing containing Lactobacillus plantarum: rapid recovery and mechanically flexibility. *Int J Biol Macromol*. 2022;221:1572–1579. doi:10.1016/j.ijbiomac.2022.09.049
154. Mann G, Gurave PM, Kaul A, et al. Polymeric and electrospun patches for drug delivery through buccal route: formulation and biointerface evaluation. *J Drug Deliv Sci Technol*. 2022;68:103030. doi:10.1016/j.jddst.2021.103030
155. Sarimsakov A, Shukurov A, Yunusov K, Rashidova S, Letfullin R. Drug delivery polymer systems for ophthalmic administration of anti- viral agents. *Curr Drug Deliv*. 2020;17(5):406–413. doi:10.2174/1567201817666200427215848
156. Van Eerdenbrugh B, Van Speybroeck M, Mols R, et al. Itraconazole/TPGS/Aerosil®200 solid dispersions. *Eur J Pharm Sci*. 2009;38(3):270–278. doi:10.1016/j.ejps.2009.08.002
157. Lee DR, Ho MJ, Choi YW, Kang MJ. A polyvinylpyrrolidone-based supersaturable self-emulsifying drug delivery system for enhanced dissolution of cyclosporine a. *Polymers*. 2017;9(4):124. doi:10.3390/polym9040124
158. Sweed NM, Fayez AM, El-Emam SZ, Dawoud MHS. Response surface optimization of self nano-emulsifying drug delivery system of rosuvastatin calcium for hepatocellular carcinoma. *J Pharm Investig*. 2021;51(1):85–101. doi:10.1007/s40005-020-00497-6
159. Seo YG, Kim DW, Yousaf AM, et al. Solid self-nanoemulsifying drug delivery system (SNEDDS) for enhanced oral bioavailability of poorly water-soluble tacrolimus: physicochemical characterisation and pharmacokinetics. *J Microencapsul*. 2015;32(5):503–510. doi:10.3109/02652048.2015.1057252
160. Zhu YJ, Zheng B, Wang HY, Chen L. New knowledge of the mechanisms of sorafenib resistance in liver cancer. *Acta Pharmacol Sin*. 2017;38(5):614–622. doi:10.1038/aps.2017.5
161. Hussain A, Shakeel F, Singh SK, et al. Solidified SNEDDS for the oral delivery of rifampicin: evaluation, proof of concept, in vivo kinetics, and in silico GastroPlusTM simulation. *Int J Pharm*. 2019;566:203–217. doi:10.1016/j.ijpharm.2019.05.061
162. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med*. 2014;371(5):424–433. doi:10.1056/NEJMoa1405095
163. Barbosa EJ, Löbenberg R, de Araujo GLB, Bou-Chacra NA. Niclosamide repositioning for treating cancer: challenges and nano-based drug delivery opportunities. *Eur J Pharm Biopharm*. 2019;141:58–69. doi:10.1016/j.ejpb.2019.05.004
164. Mattheolabakis G, Rigas B, Constantinides PP. Nanodelivery strategies in cancer chemotherapy: biological rationale and pharmaceutical perspectives. *Nanomedicine*. 2012;7(10):1577–1590. doi:10.2217/nnm.12.128
165. Xu J, Shi PY, Li H, Zhou J. Broad spectrum antiviral agent niclosamide and its therapeutic potential. *ACS Infect Dis*. 2020;6(5):909–915. doi:10.1021/acsinfecdis.0c00052
166. Tran P, Park JS. Formulation of solid dispersion to improve dissolution and oral bioavailability of poorly soluble dexibuprofen. *Pharm Dev Technol*. 2021;26(4):422–430. doi:10.1080/10837450.2021.1884259
167. Gratieri T, Pinho LAG, Oliveira MA, et al. Hydroxypropyl-β-cyclodextrin-complexed naringenin by solvent change precipitation for improving anti-inflammatory effect in vivo. *Carbohydr Polym*. 2020;231:115769. doi:10.1016/j.carbpol.2019.115769
168. Haddad E, Pagès M, Violleau F, et al. Ozonized 2-hydroxypropyl-β-cyclodextrins as novel materials with oxidative and bactericidal properties. *Carbohydr Polym*. 2022;291:119516. doi:10.1016/j.carbpol.2022.119516

169. Gao S, Liu Y, Jiang J, et al. Physicochemical properties and fungicidal activity of inclusion complexes of fungicide chlorothalonil with β-cyclodextrin and hydroxypropyl-β-cyclodextrin. *J Mol Liq*. 2019;293:111513. doi:10.1016/j.molliq.2019.111513
170. Celebioglu A, Uyar T. Metronidazole/Hydroxypropyl-β-Cyclodextrin inclusion complex nanofibrous webs as fast-dissolving oral drug delivery system. *Int J Pharm*. 2019;572:118828. doi:10.1016/j.ijpharm.2019.118828
171. Zhang H, Song G, Ma W, et al. Microencapsulation protects the biological activity of sea buckthorn seed oil. *Front Nutr*. 2023:9. doi:10.3389/fnut.2022.1043879
172. Cui T, Chen C, Jia A, et al. Characterization and human microfold cell assay of fish oil microcapsules: effect of spray drying and freeze-drying using konjac glucomannan (KGM)-soybean protein isolate (SPI) as wall materials. *J Funct Foods*. 2021;83:104542. doi:10.1016/j.jff.2021.104542
173. Jarret RL, Levy IJ, Potter TL, Cermak SC. Seed oil and fatty acid composition in Capsicum spp. *J Food Comp Analysis*. 2013;30(2):102–108. doi:10.1016/j.jfca.2013.02.005
174. Tonon RV, Grosso CRF, Hubinger MD. Influence of emulsion composition and inlet air temperature on the microencapsulation of flaxseed oil by spray drying. *Food Res Int*. 2011;44(1):282–289. doi:10.1016/j.foodres.2010.10.018
175. Balasubramani P, Palaniswamy PT, Visvanathan R, Thirupathi V, Subbarayan A, Prakash Maran J. Microencapsulation of garlic oleoresin using maltodextrin as wall material by spray drying technology. *Int J Biol Macromol*. 2015;72:210–217. doi:10.1016/j.ijbiomac.2014.08.011
176. de Barros Fernandes RV, Borges SV, Botrel DA. Gum arabic/starch/maltodextrin/inulin as wall materials on the microencapsulation of rosemary essential oil. *Carbohydr Polym*. 2014;101:524–532. doi:10.1016/j.carbpol.2013.09.083
177. Cosson A, Oliveira Correia L, Descamps N, Saint-Eve A, Souchon I. Identification and characterization of the main peptides in pea protein isolates using ultra high-performance liquid chromatography coupled with mass spectrometry and bioinformatics tools. *Food Chem*. 2022;367:130747. doi:10.1016/j.foodchem.2021.130747
178. Castro-López C, Espinoza-González C, Ramos-González R, et al. Spray-drying encapsulation of microwave-assisted extracted polyphenols from Moringa oleifera: influence of tragacanth, locust bean, and carboxymethyl-cellulose formulations. *Food Res Int*. 2021;144:110291. doi:10.1016/j.foodres.2021.110291
179. Carpentier J, Conforto E, Chaigneau C, Vendeville JE, Maugard T. Microencapsulation and controlled release of α-tocopherol by complex coacervation between pea protein and tragacanth gum: a comparative study with arabic and tara gums. *Innovative Food Sci Emerg Technol*. 2022;77:102951. doi:10.1016/j.ifset.2022.102951
180. Pei J, Gao X, Pan D, et al. Advances in the stability challenges of bioactive peptides and improvement strategies. *Curr Res Food Sci*. 2022;5:2162–2170. doi:10.1016/j.crfs.2022.10.031
181. Luo J, Ke J, Hou X, et al. Composition, structure and flavor mechanism of numbing substances in Chinese prickly ash in the genus Zanthoxylum: a review. *Food Chem*. 2022;373:131454. doi:10.1016/j.foodchem.2021.131454
182. Li J, Hou X, Jiang L, et al. Optimization and characterization of Sichuan pepper (Zanthoxylum bungeanum maxim) resin microcapsule encapsulated with β-cyclodextrin. *LWT*. 2022;171:114120. doi:10.1016/j.lwt.2022.114120
183. Wangkulangkool M, Ketthaisong D, Tangwongchai R, Boonmars T, Lomthaisong K. Microencapsulation of chia oil using whey protein and gum arabic for oxidation prevention: a comparative study of spray-drying and freeze-drying methods. *Processes*. 2023;11(5):1462. doi:10.3390/pr11051462
184. Lin Y, Xu J, Gao X. Development of antioxidant sodium alginate gel beads encapsulating curcumin/gum Arabic/gelatin microcapsules. *Food Hydrocoll*. 2024;152:109901. doi:10.1016/j.foodhyd.2024.109901
185. Zhou D, Pan Y, Ye J, Jia J, Ma J, Ge F. Preparation of walnut oil microcapsules employing soybean protein isolate and maltodextrin with enhanced oxidation stability of walnut oil. *LWT Food Sci Technol*. 2017;83:292–297. doi:10.1016/j.lwt.2017.05.029
186. Al Juhaimi F, Özcan MM, Ghafoor K. Characterization of pomegranate (Punica granatum L.) seed and oils. *Eur J Lipid Sci Technol*. 2017;119(10). doi:10.1002/ejlt.201700074
187. Lee CJ, Chen LG, Liang WL, Wang CC. Anti-inflammatory effects of Punica granatum Linne in vitro and in vivo. *Food Chem*. 2010;118(2):315–322. doi:10.1016/j.foodchem.2009.04.123
188. KZY X, Zhu C, Kim MS, Yamahara J, Li Y. Pomegranate flower ameliorates fatty liver in an animal model of type 2 diabetes and obesity. *J Ethnopharmacol*. 2009;123(2):280–287. doi:10.1016/j.jep.2009.03.035
189. Aghbashlo M, Mobli H, Madadlou A, Rafiee S. Influence of wall material and inlet drying air temperature on the microencapsulation of fish oil by spray drying. *Food Bioproc Tech*. 2013;6(6):1561–1569. doi:10.1007/s11947-012-0796-7
190. Eijkelboom NM, van Boven AP, Siemons I, et al. Particle structure development during spray drying from a single droplet to pilot-scale perspective. *J Food Eng*. 2023;337:111222. doi:10.1016/j.jfoodeng.2022.111222
191. Milanesi A, Rizzuto F, Rinaldi M, Foglio Bonda A, Segale L, Giovannelli L. Thermodynamic balance vs. computational fluid dynamics approach for the outlet temperature estimation of a benchtop spray dryer. *Pharmaceutics*. 2022;14(2):296. doi:10.3390/pharmaceutics14020296
192. Jang EH, Park YS, Kim MS, Choi DH. Model-based scale-up methodologies for pharmaceutical granulation. *Pharmaceutics*. 2020;12(5):453. doi:10.3390/pharmaceutics12050453
193. Muñoz López CA, Peeters K, Van Impe J. Data-driven modeling of the spray drying process. process monitoring and prediction of the particle size in pharmaceutical production. *ACS Omega*. 2024;9(24):25678–25693. doi:10.1021/acsomega.3c08032
194. Bista A, Tobin JT, Kennedy D, O'Donnell CP, O'Shea N. Effect of composition and total solids content of dairy samples on acoustic transmission and impedance signals. *Measurement*. 2023;214:112757. doi:10.1016/j.measurement.2023.112757
195. Ralbovsky NM, Dixit G, Lomont JP, et al. Process analytical technology for real-time monitoring of pharmaceutical bioconjugation reactions. *Org Process Res Dev*. 2025;29(2):353–362. doi:10.1021/acs.oprd.4c00399
196. Gawałek J. Effect of spray dryer scale size on the properties of dried beetroot juice. *Molecules*. 2021;26(21):6700. doi:10.3390/molecules26216700
197. Linke T, Happe J, Kohlus R. Laboratory-scale superheated steam spray drying of food and dairy products. *Drying Technol*. 2022;40(8):1703–1714. doi:10.1080/07373937.2020.1870127
198. Xin X, Essien S, Dell K, Woo MW, Baroutian S. Effects of spray-drying and freeze-drying on bioactive and volatile compounds of smoke powder food flavouring. *Food Bioproc Tech*. 2022;15(4):785–794. doi:10.1007/s11947-022-02779-3
199. Bista A, Tobin JT, O'Donnell CP, O'Shea N. Monitoring viscosity and total solids content of milk protein concentrate using an inline acoustic flowmeter at laboratory scale. *Foods*. 2020;9(9):1310. doi:10.3390/foods9091310

200. Cortés-Rojas DF, Souza CRF, Oliveira WP. Optimization of spray drying conditions for production of Bidens pilosa L. dried extract. *Chem Eng Res Des*. 2015;93:366–376. doi:10.1016/j.cherd.2014.06.010
201. Behboudi-Jobbehdar S, Soukoulis C, Yonekura L, Fisk I. Optimization of spray-drying process conditions for the production of maximally viable microencapsulated *L. acidophilus* NCIMB 701748. *Drying Technol*. 2013;31(11):1274–1283. doi:10.1080/07373937.2013.788509
202. Gouaou I, Shamaei S, Koutchoukali MS, Bouhelassa M, Tsotsas E, Kharaghani A. Impact of operating conditions on a single droplet and spray drying of hydroxypropylated pea starch: process performance and final powder properties. *Asia-Pac J Chem Eng*. 2019;14(1). doi:10.1002/apj.2268
203. Niu J, Zhao B, Guo X, Yin T. Effects of vacuum freeze-drying and vacuum spray-drying on biochemical properties and functionalities of myofibrillar proteins from silver carp. *J Food Qual*. 2019;2019:1–8. doi:10.1155/2019/9457835
204. HARIADI H, AMIEN S, KARUNIAWAN A, et al. Effect of three drying methods on physicochemical properties of powdered butterfly pea flower extract (Clitoria ternatea L.). *Food Sci Technol*. 2024:44. doi:10.5327/fst.00119
205. Papoutsis K, Golding JB, Vuong Q, et al. Encapsulation of citrus by-product extracts by spray-drying and freeze-drying using combinations of maltodextrin with soybean protein and ι-carrageenan. *Foods*. 2018;7(7):115. doi:10.3390/foods7070115
206. Kaval B, Şen FD, Batmaz KK, Ekinci M, Öztürk AA. Latest research about active pharmaceutical ingredient loaded poly lactic acid-co-glycolic acid (PLGA) based drug delivery system in Türkiye. *Euro J Life Sci*. 2023;1(3):127–139. doi:10.55971/EJLS.1197082
207. Dalsin MC, Tale S, Reineke TM. Solution-state polymer assemblies influence BCS class II drug dissolution and supersaturation maintenance. *Biomacromolecules*. 2014;15(2):500–511. doi:10.1021/bm401431t
208. Alwadei M, Kazi M, Alanazi FK. Novel oral dosage regimen based on self-nanoemulsifying drug delivery systems for codelivery of phytochemicals – curcumin and thymoquinone. *Saudi Pharm J*. 2019;27(6):866–876. doi:10.1016/j.jsps.2019.05.008
209. Al-Obaidi H, Brocchini S, Buckton G. Anomalous properties of spray dried solid dispersions. *J Pharm Sci*. 2009;98(12):4724–4737. doi:10.1002/jps.21782
210. Nasr A, Gardouh A, Ghorab M. Novel solid self-nanoemulsifying drug delivery system (S-SNEDDS) for oral delivery of olmesartan medoxomil: design, formulation, pharmacokinetic and bioavailability evaluation. *Pharmaceutics*. 2016;8(3):20. doi:10.3390/pharmaceutics8030020
211. Rizi K, Green RJ, Donaldson M, Williams AC. Production of pH-responsive microparticles by spray drying: investigation of experimental parameter effects on morphological and release properties. *J Pharm Sci*. 2011;100(2):566–579. doi:10.1002/jps.22291
212. Visser JC, Dohmen WMC, Hinrichs WLJ, Breitkreutz J, Frijlink HW, Woerdenbag HJ. Quality by design approach for optimizing the formulation and physical properties of extemporaneously prepared orodispersible films. *Int J Pharm*. 2015;485(1–2):70–76. doi:10.1016/j.ijpharm.2015.03.005
213. Riley BS, Li X. Quality by design and process analytical technology for sterile products—where are we now?. *AAPS Pharm Sci Tech*. 2011;12(1):114–118. doi:10.1208/s12249-010-9566-x
214. Dodda AG, Saranteas K, Henson MA. Using online mass spectrometry to predict the end point during drying of pharmaceutical products. *Org Process Res Dev*. 2015;19(1):122–131. doi:10.1021/op400272t
215. De Leersnyder F, Peeters E, Djalabi H, et al. Development and validation of an in-line NIR spectroscopic method for continuous blend potency determination in the feed frame of a tablet press. *J Pharm Biomed Anal*. 2018;151:274–283. doi:10.1016/j.jpba.2018.01.032
216. Dedroog S, Adriaensens P, Van den Mooter G. Gaining insight into the role of the solvent during spray drying of amorphous solid dispersions by studying evaporation kinetics. *Mol Pharm*. 2022;19(5):1604–1618. doi:10.1021/acs.molpharmaceut.2c00095
217. Parupathi P, Dhoppalapudi S. The role of surfactants in preserving the stability of amorphous solid dispersions: a review. *GSC Bio Pharmaceutical Sciences*. 2022;21(3):039–047. doi:10.30574/gscbps.2022.21.3.0454
218. Schönfeld BV, Westedt U, Wagner KG. Compression of amorphous solid dispersions prepared by hot-melt extrusion, spray drying and vacuum drum drying. *Int J Pharm X*. 2021;3:100102. doi:10.1016/j.ijpx.2021.100102
219. Rajora A, Chhabra G. Quality by design approach: regulatory need, current, and future perspective. *Asian J Pharm Clin Res*. 2021;29–35. doi:10.22159/ajpcr.2021.v14i6.33733
220. Chen Q, Riviere JE, Lin Z. Toxicokinetics, dose–response, and risk assessment of nanomaterials: methodology, challenges, and future perspectives. *WIREs Nanomed Nanobiotechnol*. 2022;14(6). doi:10.1002/wnan.1808
221. Dheyab AS, Abu Bakar MF, AlOmar M, Sabran SF, Muhamad Hanafi AF, Mohamad A. Deep eutectic solvents (DESs) as green extraction media of beneficial bioactive phytochemicals. *Separations*. 2021;8(10):176. doi:10.3390/separations8100176
222. Yabré M, Ferey L, Somé IT, Gaudin K. Greening reversed-phase liquid chromatography methods using alternative solvents for pharmaceutical analysis. *Molecules*. 2018;23(5):1065. doi:10.3390/molecules23051065
223. Simone E, Zhang W, Nagy ZK. Analysis of the crystallization process of a biopharmaceutical compound in the presence of impurities using process analytical technology (PAT) tools. *J Chem Technol Biotechnol*. 2016;91(5):1461–1470. doi:10.1002/jctb.4743
224. Berger M, Toussaint F, Ben DS, et al. Poly(vinyl pyrrolidone) derivatives as PEG alternatives for stealth, non-toxic and less immunogenic siRNA-containing lipoplex delivery. *J Control Release*. 2023;361:87–101. doi:10.1016/j.jconrel.2023.07.031