International Journal of Medical and Pharmaceutical Sciences
Open access peer-reviewed Journal
Volume 2, Issue 11, Page 36-46.
https://doi.org/10.5281/zenodo.24311199

Review Article

3D-Printed Self-Emulsifying Drug Delivery Systems (SEDDS) for Personalized Oral Drug Delivery: Manufacturing Challenges and Regulatory Perspectives

Priyadharshini R.*

Sir Issac Newton College of Pharmacy.

Self-Emulsifying Drug Delivery Systems (SEDDS) are widely used to enhance the oral bioavailability of poorly water-soluble Biopharmaceutics Classification System (BCS) Class II and IV drugs, but conventional liquid-filled capsule formats offer limited flexibility for individualized dosing. Three-dimensional (3D) printing has emerged as a promising technology for producing patient-specific dosage forms with precise control over dose, geometry, and release profile, and its convergence with SEDDS technology represents a novel and largely underexplored area of pharmaceutical research. This review examines the principal additive manufacturing platforms applied to SEDDS integration, including semi-solid extrusion, vat photopolymerization (stereolithography/digital light processing), fused deposition modeling, and inkjet/binder jetting, along with the strategies used to render inherently liquid or semi-solid SEDDS formulations printable. The personalization advantages of this approach, including precise dose titration, polypharmacy consolidation, and pediatric and geriatric dosing applications, are discussed alongside the significant manufacturing challenges that remain, including thermal and photochemical stability, rheological constraints, content uniformity, storage stability, and scale-up limitations. Particular attention is given to the regulatory landscape governing this emerging product class, where existing guidance remains centered on centralized, fixed-formulation manufacturing and has not yet established harmonized, product-specific standards for feedstock qualification, process validation, or decentralized point-of-care production. Continued progress in both formulation science and regulatory framework development will be necessary to translate 3D-printed SEDDS from proof-of-concept research toward clinical application in truly individualized oral drug therapy.

Keywords: 3D printing, additive manufacturing, self-emulsifying drug delivery systems, SEDDS, personalized medicine, oral drug delivery, regulatory perspectives

INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to its convenience, non-invasiveness, and high patient compliance. However, a significant proportion of newly discovered active pharmaceutical ingredients (APIs) suffer from poor aqueous solubility, resulting in low and variable oral bioavailability. This remains one of the most persistent challenges in modern pharmaceutical formulation science.

The Biopharmaceutics Classification System (BCS) categorizes drugs based on their aqueous solubility and intestinal permeability, dividing APIs into four classes: Class I (high solubility, high permeability), Class II (low solubility, high permeability), Class III (high solubility, low permeability), and Class IV (low solubility, low permeability). BCS Class II drugs (e.g., ibuprofen, carbamazepine, ketoconazole) dissolve slowly in gastrointestinal fluids, making dissolution the rate-limiting step for absorption, even though once dissolved, they cross intestinal membranes easily. BCS Class IV drugs (e.g., furosemide, hydrochlorothiazide) are the most formulation-challenging category, suffering from both poor dissolution and poor membrane permeability, often requiring combined solubilization and permeation-enhancement strategies. Together, these two classes represent

a large and growing share of the pharmaceutical development pipeline, making solubility enhancement a critical area of formulation research.

Self-Emulsifying Drug Delivery Systems (SEDDS) have emerged as a promising strategy to address this solubility challenge. They are isotropic mixtures, uniform, single-phase blends with consistent physical and chemical properties throughout, as opposed to heterogeneous mixtures with visibly separate phases, composed of an oil phase, a surfactant, and often a co-surfactant or co-solvent. When exposed to mild agitation in gastrointestinal fluids, these isotropic blends spontaneously self-emulsify, forming fine oil-in-water emulsion droplets, typically in the nanometer-to-micrometer range. This spontaneous emulsification presents the drug in a pre-dissolved, finely dispersed state, dramatically increasing the effective surface area available for absorption and improving both dissolution rate and intestinal permeability, directly addressing the core problems of BCS Class II and IV drugs. While effective, conventional SEDDS formulations are typically liquid-filled into soft or hard gelatin capsules, a format that offers little flexibility for dose individualization, particularly for pediatric, geriatric, or polypharmacy patients who require tailored dosing regimens.

Three-dimensional (3D) printing, or additive manufacturing, has recently gained substantial attention in pharmaceutical sciences for its ability to produce patient-specific dosage forms with precise control over drug dose, release profile, and geometry. The convergence of 3D printing technology with SEDDS formulations represents a novel and largely underexplored area, offering the potential to combine the bioavailability-enhancing benefits of self-emulsification with the dose-personalization capabilities of additive manufacturing.

This review aims to consolidate current advances in 3D-printed SEDDS for personalized oral drug delivery, examine the key manufacturing challenges associated with integrating liquid/semi-solid lipid-based systems into solid printed dosage forms, and critically discuss the evolving regulatory landscape governing this emerging class of pharmaceutical products.

SEDDS Fundamentals

Types of Self-Emulsifying Systems

Self-emulsifying drug delivery systems are broadly classified based on the droplet size of the emulsion formed upon dispersion in aqueous media into three main subtypes: SEDDS, SMEDDS, and SNEDDS. However, it is important to note that the precise droplet size cutoffs distinguishing these subtypes are not standardized and vary considerably across the literature, with different authors proposing overlapping or even contradictory ranges.

SEDDS (Self-Emulsifying Drug Delivery Systems) generally refer to the broader parent category, producing coarser, opaque-to-translucent emulsions, commonly cited in the range of 100 nm to over 300 nm, and in some reports up to 1 μm.

SMEDDS (Self-Microemulsifying Drug Delivery Systems) are widely described as forming thermodynamically stable, optically clear or translucent microemulsions. Reported droplet size ranges vary substantially between sources, some define SMEDDS as below 100 nm, others place the range between 100 –250 nm, while still others describe it as below 50 nm.

SNEDDS (Self-Nanoemulsifying Drug Delivery Systems), a comparatively newer term, are typically described as producing transparent nanoemulsions. Similarly inconsistent ranges are reported, with some sources defining SNEDDS as less than 100 nm, others as 100–250 nm, and some as broadly as 20–200 nm.

Given these overlapping and sometimes reversed definitions across sources, several authors argue that droplet size alone is an unreliable classification criterion. A more mechanistically consistent distinction lies in thermodynamic behavior: microemulsions (associated with SMEDDS) are thermodynamically stable single-phase systems, whereas nanoemulsions (associated with SNEDDS) are only kinetically stable, despite frequently occupying similar or overlapping size ranges. The choice of terminology in a given study, therefore, often reflects the specific oil, surfactant, and co-surfactant composition used, along with the energy input required for emulsification, rather than droplet size in isolation.

Formulation Components

A typical SEDDS formulation consists of the following key components:

Oil phase: Serves as the primary solubilizing medium for lipophilic drugs and influences droplet size and self-emulsification efficiency. Commonly used oils include medium-chain triglycerides (e.g., Capmul MCM, Miglyol 812), long-chain triglycerides, and modified vegetable oils.

Surfactant: Reduces interfacial tension between the oil and aqueous phases, enabling spontaneous emulsification. Non-ionic surfactants with a high hydrophilic-lipophilic balance (HLB > 10) are preferred for their lower toxicity, such as Tween 80, Cremophor EL, and Labrasol.

Co-surfactant/Co-solvent: Enhances the fluidity of the interfacial film and improves drug solubilization capacity. Common examples include ethanol, propylene glycol, and polyethylene glycol (PEG 400).

Drug substance: The active pharmaceutical ingredient, typically a BCS Class II or IV compound with high lipid solubility (log P generally greater than 2).

Mechanism of Self-Emulsification

Upon exposure to aqueous gastrointestinal fluids, combined with the mild mechanical agitation provided by gastric and intestinal motility, the SEDDS formulation spontaneously forms fine oil-in-water emulsion droplets. This process occurs due to the low free energy required for emulsification, driven by the surfactant's ability to lower interfacial tension to near-zero values. The resulting large interfacial surface area facilitates rapid drug partitioning into the aqueous phase, enhancing dissolution and subsequent absorption via intestinal lymphatic or portal pathways.

Advantages of SEDDS

- Enhanced solubility and bioavailability of poorly water-soluble drugs
- Reduced food effect on drug absorption
- Protection of drugs from gastrointestinal degradation
- Reduced inter- and intra-subject variability in absorption
- Potential for reduced dose requirements

Limitations of Conventional SEDDS

- Limited to liquid or semi-solid SEDDS formulations, which are typically filled into soft or hard gelatin capsules for oral administration, restricting formulation flexibility for dose individualization.
- Potential incompatibility between the liquid fill and capsule shell material over time
- Challenges in achieving precise, individualized dosing
- Physical instability concerns (precipitation, phase separation) during storage

3D Printing Technologies Applied to SEDDS

Integrating self-emulsifying systems into a 3D-printed dosage form requires reconciling two fundamentally different material states: SEDDS are liquid or semi-solid isotropic mixtures, while most additive manufacturing (AM) platforms are designed to process solid, semi-solid, or photocurable feedstocks into a mechanically stable, dimensionally defined structure. The choice of printing technology therefore dictates not only the achievable dose accuracy and geometry but also the extent to which the self-emulsifying properties of the formulation are preserved after processing. Five AM platforms have been most widely investigated for SEDDS integration: semi-solid extrusion (SSE), vat photopolymerization (stereolithography/digital light processing, SLA/DLP), fused deposition modeling (FDM), inkjet printing, and binder jetting.

Semi-Solid Extrusion (SSE) Printing

Semi-solid extrusion is generally regarded as the most compatible AM technique for SEDDS because it deposits material directly from a paste or gel state without requiring melting or photopolymerization, thereby avoiding thermal or photochemical stress on the oil-surfactant system. SEDDS can be thickened into an extrudable paste by blending with gelling agents (e.g., hydroxypropyl methylcellulose, Carbopol, colloidal silicon dioxide) or by adsorbing the liquid formulation onto porous solid carriers such as Neusilin US2, Aerosil, or magnesium aluminometasilicate prior to extrusion. The resulting semi-solid ink is deposited layer-by-layer through a nozzle under pneumatic or mechanical pressure, and the printed structure is typically dried or allowed to set to achieve adequate mechanical strength for handling. Because processing occurs near room temperature, SSE preserves the self-

emulsification behavior of the formulation more reliably than heat- or light-based methods, but print resolution and structural robustness are generally lower than with SLA/DLP.

Vat Photopolymerization (SLA/DLP)

SLA (Stereolithography Apparatus) and DLP (Digital Light Processing) printing offer high resolution and smooth surface finishes by selectively curing a liquid photopolymer resin with UV or visible light. Since SEDDS components are not inherently photocurable, incorporation typically involves dispersing the SEDDS within a photocurable resin matrix or encapsulating a pre-formed SEDDS core within a photopolymerized shell that subsequently releases the formulation upon dissolution or rupture. Key concerns for this approach include the biocompatibility and residual toxicity of photoinitiators and unreacted monomers, potential inhibition of the photopolymerization reaction by the oil and surfactant components, and drug or surfactant migration into the resin phase before curing is complete. These factors limit the pharmaceutical-grade resin options currently available and represent an active area of formulation research.

Unlike the nozzle-based deposition methods (SSE, FDM) or droplet-jetting methods (inkjet, binder jetting), vat photopolymerization relies on selective light-induced curing of a bulk liquid resin, representing a mechanistically distinct approach among AM platforms applied to SEDDS.

Fused Deposition Modeling (FDM) with Lipid-Loaded Filaments

FDM printing extrudes a thermoplastic filament through a heated nozzle, and its adaptation for SEDDS delivery generally relies on hot-melt extrusion (HME) to first embed the SEDDS within a polymeric matrix (e.g., polyvinyl alcohol, hydroxypropyl cellulose, or Kollidon-based carriers) to produce a printable filament. As with SSE, adsorption of the liquid SEDDS onto a solid porous carrier prior to HME is often used to reduce leakage and improve filament mechanical integrity. The principal challenge is thermal: HME and FDM printing nozzle temperatures commonly range from 120 to 200 degrees Celsius, which can promote surfactant degradation, oil oxidation, or volatilization of co-solvents, potentially compromising both drug stability and the self-emulsifying performance of the system. Formulators must therefore select thermally robust surfactants and oils and minimize residence time at elevated temperature.

Inkjet Printing

Inkjet printing deposits precise, small-volume droplets of a low-viscosity SEDDS formulation directly onto a substrate such as an orodispersible film or a pre-formed tablet core, using thermal or piezoelectric actuation of the printhead. Because processing occurs near room temperature without melting or curing, this approach preserves the self-emulsifying behavior and chemical stability of the formulation particularly well, and is attractive for personalized dosing of potent drugs at low doses. However, it is generally limited to formulations with viscosity and surface tension within a narrow printable range, restricting the technique to a comparatively small subset of low-viscosity SEDDS compositions.

Binder Jetting

Binder jetting differs fundamentally from inkjet printing: rather than depositing the drug-loaded formulation directly, a liquid binder is selectively jetted onto a powder bed to bind successive layers of powder into the final structure, with the SEDDS incorporated either within the powder bed or the binding liquid itself. This technique has been comparatively less explored for SEDDS delivery, as the interaction between the lipid-based liquid phase and the powder substrate can compromise binding efficiency and dimensional accuracy of the printed structure. Its principal advantage is that it requires no heat or light exposure during fabrication, making it a potentially viable low-stress alternative once formulation and process optimization challenges are addressed.

Figure 1: Additive Manufacturing Platforms Aplied to SEDDS-based Dosage Forms.

Strategies for Rendering SEDDS Printable

Across all five platforms, converting a liquid or semi-solid SEDDS into a printable feedstock generally relies on one or more of the following strategies:

- Adsorption onto solid porous carriers (e.g., colloidal silica, magnesium aluminometasilicate) to convert liquid SEDDS into a free-flowing or extrudable solid intermediate (SSE and FDM).

- Encapsulation of the liquid SEDDS core within a printed or pre-formed solid shell that releases the formulation upon dissolution, rupture, or disintegration (SLA/DLP).
- Blending with solidifying excipients such as waxes, gelling polymers, or self-emulsifying solid dispersions to raise viscosity into a printable paste. Used in: SSE (primarily) and FDM (via hot-melt extrusion polymer matrices).
- Direct low-volume deposition of the liquid SEDDS via inkjet printing onto a solid substrate, avoiding the need for solidification altogether (Inkjet Printing).
- Incorporation into the solid powder substrate, where SEDDS or SEDDS-loaded solid intermediates are pre-blended into the powder bed prior to selective binder deposition (binder jetting).

The optimal strategy depends on the physicochemical properties of the drug and SEDDS components, the required dose range, and the target release profile, and no single approach has yet emerged as universally superior; this remains one of the central formulation challenges discussed further in the following section.

Personalization Advantages of 3D-Printed SEDDS

The convergence of SEDDS technology with 3D printing directly addresses a core limitation of conventional lipid-based capsule formulations: their fixed-dose nature. Unlike standard manufacturing, which produces batches of identical fixed-strength units, additive manufacturing enables dose and geometry to be adjusted computationally, on a per-patient basis, without requiring a change in manufacturing line or tooling. This section outlines the specific clinical contexts in which this capability offers meaningful advantages.

Precise Dose Titration

Conventional SEDDS capsules are manufactured in discrete fixed strengths (e.g., 50 mg, 100 mg), forcing clinicians to either accept an imprecise dose or resort to unsafe practices such as opening capsules and attempting to divide a liquid or semi-solid fill by eye. 3D printing removes this constraint by allowing the printed volume, infill density, or number of deposited layers to be directly correlated with drug dose. A prescriber can therefore specify an exact milligram dose, and the printer produces a dosage form calibrated to that value, which is particularly valuable for drugs with a narrow therapeutic index, where small deviations in dose can meaningfully affect efficacy or toxicity.

Polypharmacy and Fixed-Dose Combinations

Patients on multi-drug regimens, common among elderly and chronically ill populations, often face reduced adherence simply due to the number of individual tablets or capsules they must take. 3D printing enables the fabrication of "polypills": single printed dosage forms containing multiple SEDDS-loaded drugs, each potentially with an independently tailored release profile, within discrete printed compartments or layers. This consolidates a complex regimen into a single administration event, an approach that has already been demonstrated conceptually with non-SEDDS polypills and is a natural extension for lipid-based combination therapies.

Pediatric Dosing

Children require doses that scale with body weight, age, or body surface area, a requirement poorly served by adult-oriented, fixed-strength capsule formats. Extemporaneous manipulation of liquid SEDDS capsules for pediatric use, such as puncturing a capsule to extract a partial dose, introduces dosing inaccuracy and formulation instability once the capsule shell is breached. Printed SEDDS dosage forms allow a pharmacy or manufacturer to generate a precise, age-appropriate dose in a format designed for pediatric administration (e.g., a smaller, more palatable printed shape or an orodispersible substrate loaded via inkjet deposition), without depending on capsule manipulation at the point of care.

Geriatric Dosing

Elderly patients frequently present with polypharmacy, swallowing difficulties (dysphagia), and altered pharmacokinetics due to age-related physiological changes, all factors that benefit from individualized dosing and administration formats. 3D printing allows dosage forms to be tailored not only in strength but also in size, shape, and disintegration characteristics, for example, producing smaller, softer, or faster-dissolving printed structures optimized for patients with swallowing impairment, while still delivering the bioavailability benefits of the underlying SEDDS formulation.

Point-of-Care and Decentralized Manufacturing

Perhaps the most transformative long-term implication of 3D-printed SEDDS is the potential for decentralized, on-demand production at the hospital pharmacy or point-of-care level, rather than centralized mass manufacturing of fixed-strength batches. Under this model, a prescription could be printed to an individual patient's exact dose specification at the time of dispensing, using pre-qualified SEDDS "ink" cartridges loaded into a compact printer. While this model remains largely at the research and pilot stage, given the extemporaneous compounding infrastructure already present in hospital pharmacies, it represents a plausible near-term pathway for clinical translation, one that intersects directly with the regulatory questions addressed later in this review.

Manufacturing Challenges

While the previous sections outlined the platforms available for printing SEDDS-based dosage forms, translating this concept from laboratory proof-of-concept to a reliable, reproducible pharmaceutical product requires overcoming a distinct set of formulation, process, and quality-related obstacles. These challenges are summarized below.

Thermal and Photochemical Stability

SEDDS components, particularly non-ionic surfactants and co-solvents, are susceptible to degradation under the processing conditions required by several AM platforms. In FDM-based approaches, hot-melt extrusion and nozzle temperatures in the range of 120 –200°C can promote surfactant oxidation, volatilization of co-solvents such as ethanol or propylene glycol, and, in some cases, chemical degradation of thermolabile drugs. In SLA/DLP printing, ultraviolet or visible light exposure required for photopolymerization raises separate concerns: potential photodegradation of light-sensitive APIs, generation of reactive species from photoinitiators that may interact with oil or surfactant components, and inhibition of the curing reaction itself by lipidic material. Even SSE, generally considered the mildest option, is not entirely free of concern, as prolonged processing or drying steps can still promote oxidation of unsaturated oils.

Rheological Constraints

Each AM platform imposes a narrow, technology-specific viscosity and flow-behavior window that the SEDDS-derived feedstock must satisfy. Native liquid SEDDS formulations are typically far too low in viscosity to be printed directly by SSE or extruded as a filament in FDM, necessitating the addition of thickening or solidifying excipients, which in turn can alter the self-emulsification kinetics of the original formulation. Conversely, formulations thickened excessively to meet printability requirements may fail to achieve adequate nozzle flow or layer adhesion. For inkjet approaches, the acceptable viscosity and surface tension range is considerably narrower still, limiting the technique to a subset of low-viscosity SEDDS compositions and constraining formulation flexibility.

Drug Loading and Content Uniformity

Achieving consistent, accurate drug distribution throughout a printed structure, and consistent dose from one printed unit to the next, is complicated by the heterogeneous nature of SEDDS-loaded feedstocks. When a liquid SEDDS is adsorbed onto a porous solid carrier or blended into a polymer matrix, incomplete or uneven mixing can create localized variation in drug concentration. This risk is compounded in multi-material or multi-layer printed structures intended for polypharmacy applications, where cross-contamination between adjacent drug-loaded regions or diffusion during processing can compromise both dose accuracy and, in fixed-dose combination products, drug-drug segregation requirements.

Physical and Chemical Stability During Storage

Once printed, the solid or semi-solid SEDDS-loaded dosage form must remain physically and chemically stable over its intended shelf life. Key concerns include precipitation of the drug from a supersaturated state within the matrix, phase separation between the oil and solid carrier components, and gradual migration or leaching of surfactant or oil to the surface of the printed structure over time. These instability mechanisms are generally less well characterized for printed SEDDS systems than for conventional liquid-filled capsules, given the comparatively limited long-term stability data currently available in the published literature.

Scale-Up Limitations

The majority of published work on 3D-printed SEDDS remains at bench or pilot scale, typically producing single units or small batches under tightly controlled laboratory conditions. Translating this to commercial-scale, Good Manufacturing Practice (GMP)-compliant production introduces substantial unresolved questions: achievable print speed per unit, consistency across multiple printheads or printers operating in parallel, and the feasibility of continuous versus batch printing workflows. Unlike conventional tablet compression or capsule filling, which benefit from decades of established high-throughput manufacturing infrastructure, pharmaceutical-grade AM equipment capable of validated, high-volume production remains largely underdeveloped.

Excipient Toxicity and Biocompatibility

Several materials required to render SEDDS printable, including photoinitiators and photocurable resins for SLA/DLP, or novel polymer carriers for FDM filament production, are not universally established as pharmaceutical-grade excipients with documented oral safety profiles. The pool of resins and polymers with regulatory precedent for oral human use remains considerably smaller than the broader catalog of materials used in industrial or dental 3D printing, restricting formulators to a narrow subset of qualified options and slowing formulation development.

Quality Control and In-Process Monitoring

Conventional pharmaceutical manufacturing relies on well-established, standardized analytical methods for in-process and final product quality control, including dissolution testing, content uniformity assays, and weight variation testing. Equivalent standardized methods for 3D-printed dosage forms, and particularly for SEDDS-loaded printed structures, are still under development. Real-time, in-line monitoring capable of verifying dose accuracy and formulation integrity during the printing process itself, analogous to process analytical technology (PAT) used in conventional manufacturing, remains an active area of research rather than an established capability.

Regulatory Perspectives

The regulatory framework governing pharmaceutical products has historically been built around fixed-formulation, mass-manufactured dosage forms produced under centralized Good Manufacturing Practice (GMP) conditions. The emergence of 3D-printed, patient-personalized SEDDS dosage forms challenges several foundational assumptions of this framework, and regulatory guidance specific to this product class remains in an early, evolving stage.

Precedent: Spritam and the Current Regulatory Landscape

The most significant regulatory milestone in pharmaceutical 3D printing to date remains the 2015 FDA approval of Spritam (levetiracetam), the first 3D-printed drug product to reach market, manufactured using a binder jetting process to produce a rapidly disintegrating tablet. While this approval demonstrated that additive manufacturing can meet existing regulatory standards for a conventional, centrally-manufactured, fixed-dose product, it did not establish a pathway for personalized, point-of-care, or on-demand printed dosage forms, the use case most relevant to 3D-printed SEDDS. The FDA has since acknowledged 3D printing's growing role in drug development and healthcare more broadly, and has published discussion papers examining associated considerations, though comprehensive, product-specific guidance for personalized 3D-printed pharmaceuticals has not yet been finalized.

The Gap Between Device and Drug Product Regulation

A substantial portion of existing regulatory thinking on additive manufacturing originates from the medical device sector, where the FDA has issued technical

guidance addressing considerations such as design, testing, and characterization specific to devices produced via additive manufacturing. However, SEDDS-loaded dosage forms are drug products, not devices, and are therefore subject to a fundamentally different regulatory pathway, one centered on chemistry, manufacturing, and controls (CMC) requirements, bioequivalence, and GMP compliance rather than device-specific design controls. The absence of a drug-product-specific analog to existing device guidance represents a clear gap directly relevant to 3D-printed SEDDS, a lipid-based, self-emulsifying formulation with characteristics not addressed by device-oriented frameworks.

Feedstock and Process Parameter Standardization

Recent regulatory science literature has specifically highlighted the role of critical feedstock materials and process parameters as a prerequisite for establishing a harmonized regulatory framework for 3D-printed pharmaceutical products. For SEDDS-based feedstocks, this includes the need for standardized characterization of the oil-surfactant-carrier system prior to and after printing, validated critical process parameters for each AM platform (e.g., nozzle temperature ranges for FDM, light intensity and exposure time for SLA/DLP), and clearly defined acceptance criteria for content uniformity and dose accuracy in printed units. Without harmonized standards in these areas, both regulatory review and cross-study comparison of published SEDDS-AM research remain difficult.

Point-of-Care and Decentralized Manufacturing: An Unresolved Regulatory Model

Perhaps the most significant regulatory uncertainty concerns the decentralized, point-of-care printing model discussed in the personalization section of this review. Current pharmaceutical regulation is built around centralized manufacturing sites subject to periodic GMP inspection, batch release testing, and centralized quality oversight, a model poorly suited to a hospital pharmacy or clinical setting printing individualized doses on demand. Questions that remain largely unaddressed include: which party bears regulatory responsibility for a dosage form printed at the point of care (the device manufacturer, the feedstock supplier, or the printing pharmacy); how batch release and quality assurance testing should be adapted for single-unit or small-batch, on-demand production; and whether existing pharmacy compounding regulations, generally designed for simpler manipulations, are an appropriate regulatory analog for AM-based personalized dosage forms, or whether an entirely new regulatory category is required.

Public and Stakeholder Perspectives

Beyond formal regulatory guidance, patient and public acceptance is itself an emerging consideration relevant to eventual regulatory and clinical adoption. Survey-based research has found that personalized dosing and regulatory approval were the benefits most anticipated by the public regarding 3D-printed medicines, while regulatory approval and scientific validation were identified as the strongest predictors of public acceptance of the technology. This suggests that establishing clear, transparent regulatory pathways is not only a compliance necessity but also a meaningful factor in eventual clinical and market acceptance of 3D-printed SEDDS products.

SUMMARY

Taken together, the regulatory landscape for 3D-printed SEDDS remains characterized by a small number of favorable precedents (notably Spritam), device-oriented guidance of limited direct applicability, and an absence of harmonized, product-specific standards for feedstock qualification, process validation, and decentralized manufacturing oversight. Addressing these gaps will likely require coordinated effort between regulatory agencies, academic researchers, and industry stakeholders, a theme that connects directly to the future directions discussed in the following section.

Future Perspectives

The convergence of SEDDS technology and 3D printing remains at an early stage, but several developing trends suggest promising directions for advancing this field from proof-of-concept research toward clinical and commercial translation.

Artificial Intelligence and Computational Formulation Design

The integration of AI and machine learning tools into pharmaceutical formulation is increasingly being used to predict optimal SEDDS compositions, oil-surfactant-cosurfactant ratios, and printability parameters

based on a target drug's physicochemical properties, potentially reducing the extensive trial-and-error formulation screening currently required. Applied to 3D-printed SEDDS specifically, such tools could accelerate the identification of thermally stable, printable formulations for a given drug, and support real-time process parameter adjustment during printing itself.

Advanced and Hybrid Printing Techniques

Emerging AM approaches, including multi-material and multi-nozzle printing, may allow SEDDS-loaded regions to be combined within a single dosage form alongside immediate- or modified-release components, enabling more sophisticated combination products than currently achievable with single-platform printing. Similarly, continued refinement of low-temperature and photoinitiator-free curing methods may help address the thermal and photochemical stability concerns that currently limit FDM and SLA/DLP applicability to sensitive SEDDS formulations.

Point-of-Care Manufacturing Infrastructure

As discussed in the regulatory section, decentralized printing at the hospital or community pharmacy level remains largely conceptual at present. Continued development of compact, pharmacy-suitable printers, pre-qualified SEDDS "ink" cartridge systems, and standardized quality-control protocols suitable for small-batch or single-unit production will likely be necessary before this model can move from pilot studies to routine clinical use.

Expanded Application to Biologics and Novel Modalities

While this review has focused on small-molecule BCS Class II/IV drugs, similar lipid-based self-emulsifying strategies are beginning to be explored for the oral delivery of biologics and other high-molecular-weight or fragile therapeutic agents, which face their own significant bioavailability barriers. Should 3D-printed SEDDS platforms prove adaptable to these more complex payloads, the clinical relevance of this technology could extend considerably beyond its current small-molecule focus.

Regulatory Science Development

Finally, continued collaboration between regulatory agencies, academic researchers, and industry will be necessary to establish the harmonized feedstock characterization standards, process validation frameworks, and decentralized manufacturing oversight models identified as current gaps in this review. Pilot regulatory frameworks already being explored for other personalized 3D-printed products may serve as useful templates for SEDDS-specific guidance as the evidence base matures.

CONCLUSION

The integration of 3D printing with self-emulsifying drug delivery systems (SEDDS) represents a novel convergence in pharmaceutical formulation science, combining the bioavailability-enhancing capacity of SEDDS for poorly water-soluble BCS Class II and IV drugs with the dose-personalization and geometric flexibility of additive manufacturing; among the five AM platforms reviewed, semi-solid extrusion currently offers the most favorable balance of process mildness and SEDDS compatibility, though substantial manufacturing challenges, including thermal and photochemical stability, rheological constraints, content uniformity, long-term stability, and the absence of validated GMP-compliant infrastructure, remain unresolved and are compounded by a parallel regulatory gap in harmonized, product-specific standards for feedstock qualification, process validation, and decentralized point-of-care production. Realizing the clinical potential of 3D-printed SEDDS will require coordinated progress in both formulation/process engineering and regulatory science, with near-term priorities including expanded stability and bioequivalence data, standardized feedstock characterization methods, and continued dialogue between industry, academia, and health authorities.

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Cite: Priyadharshini R., 3D-Printed Self-Emulsifying Drug Delivery Systems (SEDDS) for Personalized Oral Drug Delivery: Manufacturing Challenges and Regulatory Perspectives, Int. J. Med. Pharm. Sci., 2026, 2 (11), 36-46. https://doi.org/10.5281/zenodo.24311199