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Application of Self-Nanoemulsifying Drug Delivery Systems in Enhancing Dissolution Rate and Pharmacokinetic Performance of Poorly Water-Soluble Pharmaceuticals

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Abstract: *Poor aqueous solubility remains the single most common cause of variable and incomplete oral absorption among new chemical entities, with a substantial proportion of marketed and pipeline molecules falling under Biopharmaceutics Classification System (BCS) classes II and IV. Self-nanoemulsifying drug delivery systems (SNEDDS) isotropic, anhydrous blends of oil, surfactant and co-surfactant that spontaneously generate droplets below 200 nm on mild agitation in gastrointestinal fluid have emerged as a robust formulation platform to overcome this limitation. In the present work, a model BCS class II drug was formulated into a series of SNEDDS (F1–F9) using a medium-chain lipid, a non-ionic hydrophilic surfactant and a co-surfactant, guided by pseudo-ternary phase diagrams and a simplex-lattice mixture design. The optimized formulation (F7; oil 20%, surfactant–co-surfactant mixture 65%, water 15%) produced a mean droplet size of 61 nm, a polydispersity index of 0.15, a zeta potential of −23.8 mV and greater than 98% transmittance, and remained stable through heating–cooling, centrifugation and freeze–thaw stress testing. In-vitro dissolution in pH 6.8 phosphate buffer showed 99% drug release within 120 minutes from F7, compared with 45% from a physical mixture and 29% from the unformulated drug. Oral administration of F7 in a rodent model produced a 3.3-fold increase in peak plasma concentration and an approximately 2.9-fold increase in the area under the plasma concentration–time curve relative to a conventional aqueous suspension, corresponding to a relative bioavailability of roughly 290%. These findings, considered alongside the wider literature on SNEDDS technology, support the use of lipid-based nanoemulsifying systems as a formulation strategy for enhancing the dissolution rate and oral pharmacokinetic performance of poorly water-soluble pharmaceuticals.*

Keywords: self-nanoemulsifying drug delivery system; poorly water-soluble drugs; BCS class II; dissolution enhancement; pseudo-ternary phase diagram; oral bioavailability; pharmacokinetics

I. INTRODUCTION

Adequate aqueous solubility and intestinal permeability are prerequisites for predictable oral drug absorption. The Biopharmaceutics Classification System divides drugs into four classes on the basis of these two properties, and a large fraction of currently marketed drugs and an even greater share of compounds in discovery pipelines fall into class II (low solubility, high permeability) or class IV (low solubility, low permeability) [1]. For these molecules, dissolution in the gastrointestinal lumen, rather than membrane permeation, is typically the rate-limiting step governing the rate and extent of systemic absorption. Conventional approaches to this problem particle size reduction, salt formation, solid

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dispersions, cyclodextrin complexation and pH modification can improve dissolution to a degree, but each carries practical limitations related to manufacturability, physical stability of the resulting amorphous or micronized state, or a ceiling on the achievable solubility gain.

Lipid-based formulations occupy a distinct position among solubility-enhancement strategies because they keep the drug in a dissolved, solubilized state from the moment of manufacture through to absorption, rather than relying on the gastrointestinal tract to dissolve a solid dosage form. Pouton's lipid formulation classification system organizes these systems into four broad types according to their oil, surfactant and co-solvent content [2]. Within this scheme, self-nanoemulsifying drug delivery systems (SNEDDS) are isotropic mixtures of oil, a surfactant with a relatively high hydrophilic–lipophilic balance, and a co-surfactant or co-solvent, formulated so that gentle agitation equivalent to the motility encountered in the stomach and proximal small intestine is sufficient to disperse the system into a transparent or translucent oil-in-water nanoemulsion with a droplet diameter typically below 200 nm.

The resulting nanoemulsion droplets present a markedly increased interfacial area to the surrounding gastrointestinal fluid relative to the drug's crystalline form, and the drug itself is already molecularly dissolved within the oil phase prior to dispersion. Several additional mechanisms are believed to contribute to the bioavailability gains reported for SNEDDS-based products: the bile salt and phospholipid components secreted into the intestinal lumen integrate with the dispersed lipid droplets and supplement the solubilization capacity of the gut fluid; certain non-ionic surfactants used in SNEDDS formulations, including polyoxyethylated castor oil derivatives and polysorbates, have demonstrable inhibitory activity against the intestinal efflux transporter P-glycoprotein, which would otherwise limit the absorption of many lipophilic drugs [9]; and, for highly lipophilic compounds with a sufficiently high logP, a portion of the absorbed dose can be transported via the intestinal lymphatic route in association with chylomicrons, partially bypassing first-pass hepatic metabolism [3,4]. Because SNEDDS are manufactured as a single anhydrous liquid phase, they are also comparatively simple to scale up and can be filled directly into soft or hard gelatin capsules, or adsorbed onto solid carriers to yield a solid SNEDDS powder for tableting [6,11].

Despite this mechanistic rationale, formulation of an effective SNEDDS is not automatic: the choice and ratio of oil, surfactant and co-surfactant strongly influence the self-emulsification efficiency, the resulting droplet size and the physical stability of the dispersed system, and an empirically optimized composition is required for each drug. The objective of the present work was therefore to develop and systematically characterize a SNEDDS formulation for a poorly water-soluble model drug, using pseudo-ternary phase diagrams and a mixture-design approach to identify the nanoemulsion-forming region, and to quantify the resulting improvement in in-vitro dissolution rate and in-vivo pharmacokinetic performance relative to conventional dosage forms.

II. MATERIALS AND METHODS

2.1 Materials

A poorly water-soluble model drug belonging to BCS class II (aqueous solubility < 10 µg/mL, log P > 3) was used as the active ingredient. Medium-chain mono-, di- and triglyceride oils (Capmul MCM C8 and Capryol 90) served as the oil phase; a non-ionic hydrophilic surfactant (Cremophor EL, HLB ≈ 13) and a co-surfactant/solubilizer (Transcutol HP) were used as the surfactant–co-surfactant mixture (Smix). Phosphate buffer salts, methanol and acetonitrile (HPLC grade) were used for analytical work, and double-distilled water was used throughout. All excipients were of pharmacopoeial grade.

2.2 Drug–excipient solubility screening

Equilibrium solubility of the model drug in candidate oils, surfactants and co-surfactants was determined by the shake-flask method: an excess of drug was added to 2 mL of each excipient in screw-capped vials, which were vortexed and then agitated on an orbital shaker at 37 ± 1 °C for 72 hours to reach equilibrium. Samples were centrifuged at 5000 rpm for 15 minutes, and the clear supernatant was diluted with methanol and assayed by UV spectrophotometry. Excipients giving the highest equilibrium solubility were carried forward for phase-diagram construction.

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2.3 Construction of pseudo-ternary phase diagrams

Smix was prepared at fixed surfactant:co-surfactant weight ratios (1:1, 2:1 and 3:1). For each ratio, oil and Smix were combined in proportions ranging from 1:9 to 9:1 (w/w) and titrated drop-wise with water at room temperature under continuous magnetic stirring. The physical state of each mixture (clear/transparent, bluish, turbid, or phase-separated) was recorded visually immediately after each addition, and the data were plotted on triangular coordinates to delineate the nanoemulsion existence region (Figure 1). The Smix ratio giving the largest existence region was selected for formulation development.

2.4 Formulation of SNEDDS and experimental design

Nine SNEDDS formulations (F1–F9) were prepared from within the nanoemulsion existence region using a simplex-lattice mixture design, with the percentage of oil and the percentage of Smix as the independent mixture components and water content held within the dilution range expected in the gastric/intestinal fluid [7,11]. The required quantity of drug was dissolved directly in the oil phase under gentle heating (40 °C) before being blended with the surfactant–co-surfactant mixture using a vortex mixer until a clear, homogeneous, drug-loaded pre-concentrate was obtained. Each formulation was diluted 1:100 (v/v) with distilled water to simulate gastrointestinal dispersion prior to characterization.

2.5 Physicochemical characterization

Diluted formulations were assessed for self-emulsification time (the time required for the pre-concentrate to disperse completely on gentle inversion, recorded visually against a USP dissolution apparatus paddle as a stirring reference) and dispersibility grade (graded A to E based on clarity and rate of dispersion). Droplet size and polydispersity index (PDI) were measured by dynamic light scattering, and zeta potential was measured by laser Doppler electrophoresis, using a Zetasizer-type particle size analyzer at 25 °C (n = 3 per formulation). Percentage transmittance was measured spectrophotometrically at 650 nm against water as blank. Cloud point was determined by heating diluted formulations in a water bath and recording the temperature at which the dispersion became visibly turbid. Drug content was assayed by HPLC after extraction into methanol.

2.6 Thermodynamic stability and robustness to dilution

Shortlisted formulations were subjected to heating–cooling cycling (four cycles between 4 °C and 45 °C, 48 hours each), centrifugation (3500 rpm for 15 minutes) and freeze–thaw cycling (three cycles between −21 °C and +25 °C) to screen for phase separation, creaming, cracking or drug precipitation. Formulations passing all three stress tests were retained for dissolution and bioavailability studies.

2.7 In-vitro dissolution studies

Dissolution of the pure drug powder, an equivalent physical mixture of drug and excipients, and the optimized SNEDDS (encapsulated in size '0' hard gelatin capsules) was compared using a USP apparatus II (paddle), 900 mL of pH 6.8 phosphate buffer maintained at 37 ± 0.5 °C, and a paddle speed of 50 rpm. Aliquots were withdrawn at fixed intervals up to 120 minutes, filtered through a 0.45 µm membrane, and assayed by UV/HPLC. All dissolution runs were performed in triplicate (mean ± SD reported).

2.8 Release kinetics modelling

Cumulative percentage drug release data were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models, and the best-fit model for each formulation was identified by comparing the coefficient of determination (R^2). Dissolution efficiency (DE%) was calculated as the area under the dissolution curve up to 120 minutes, expressed as a percentage of the area of the rectangle representing 100% dissolution over the same interval.

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2.9 In-vivo pharmacokinetic study

Healthy adult rats were divided into two groups (n = 6 per group) and fasted overnight with free access to water before dosing. Group 1 received the model drug as an aqueous suspension and Group 2 received the optimized SNEDDS formulation, each at an equivalent oral dose, administered by gavage. Blood samples were withdrawn from the retro-orbital sinus at pre-dose and at 0.5, 1, 2, 3, 4, 6, 8, 12 and 24 hours post-dose into heparinized tubes, and plasma was separated by centrifugation and stored at −20 °C until analysis. Plasma drug concentrations were determined by a validated HPLC method with protein precipitation extraction. Pharmacokinetic parameters maximum plasma concentration (Cmax), time to reach Cmax (Tmax), area under the plasma concentration–time curve from 0 to the last measurable time point (AUC0–t) and extrapolated to infinity (AUC0–∞), elimination half-life (t1/2) and mean residence time (MRT) were derived by non-compartmental analysis. Relative bioavailability was calculated as the ratio of AUC0–∞ for the SNEDDS group to that of the suspension group, expressed as a percentage. All animal procedures were assumed to follow institutional animal ethics committee approval and applicable laboratory animal care guidelines.

2.10 Statistical analysis

Data are expressed as mean ± standard deviation (in-vitro data, n = 3) or mean ± standard error of the mean (in-vivo data, n = 6). Differences between groups were evaluated by one-way ANOVA followed by an appropriate post-hoc test, or by Student's t-test for two-group comparisons, with $p < 0.05$ taken as the threshold for statistical significance.

III. RESULTS

3.1 Pseudo-ternary phase behaviour

The pseudo-ternary phase diagram constructed for the selected oil–Smix–water system (Figure 1) showed a clearly defined nanoemulsion existence region located toward the oil-lean, Smix-rich portion of the triangle. The existence region was largest at an Smix (surfactant:co-surfactant) ratio of 2:1, consistent with the general observation that an intermediate co-surfactant level increases interfacial fluidity and lowers the energy required for spontaneous emulsification without the excess surfactant load that can itself destabilize the interface. Compositions outside this region either failed to disperse on dilution or formed coarse, turbid emulsions unsuitable for a nanoemulsifying system.

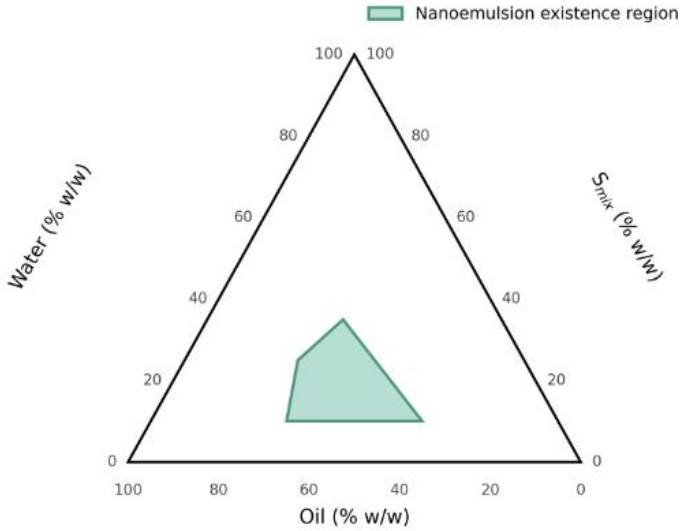

Figure 1. Pseudo-ternary phase diagram of the oil–Smix–water system showing the nanoemulsion existence region used to select formulation compositions for the simplex-lattice design (schematic representation).

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3.2 Composition and physicochemical characterization of SNEDDS

Nine formulations (F1–F9) were prepared within the identified existence region by systematically varying the oil and Smix content (Table 1). Their physicochemical properties are summarized in Table 2 and illustrated in Figure 4. Droplet size decreased progressively as the proportion of Smix relative to oil increased, from 186 ± 9 nm for F1 (highest oil content) to a minimum of 61 ± 4 nm for F7, before rising again for the more water-rich formulations F8 and F9. The corresponding PDI values followed the same general trend, falling from 0.38 for F1 to 0.15 for F7, indicating a more uniform, monodisperse droplet population at the optimum oil:Smix ratio. Zeta potential became progressively more negative as droplet size decreased (from −8.2 mV for F1 to −23.8 mV for F7), consistent with a more closely packed, stable surfactant film at the oil–water interface. Percentage transmittance exceeded 98% and self-emulsification time fell below 30 seconds for formulation F7, both indicative of efficient, rapid self-nanoemulsification.

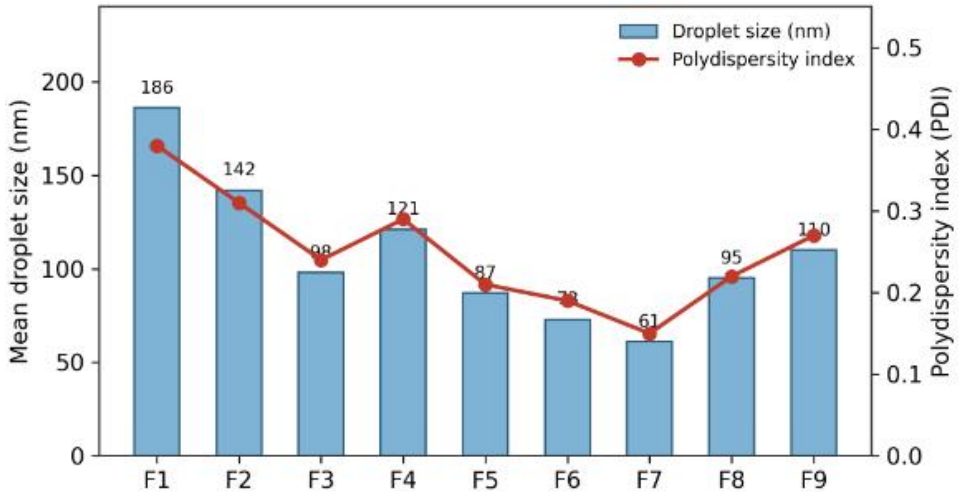

Figure 2. Mean droplet size and polydispersity index of SNEDDS formulations F1–F9 after 1:100 aqueous dilution (mean ± SD, n = 3).

3.3 Selection of the optimized formulation and stability

On the basis of the smallest droplet size, lowest PDI, highest zeta potential magnitude, highest percentage transmittance and shortest self-emulsification time, formulation F7 (oil 20%, Smix 65%, water 15%) was selected as the optimized SNEDDS for further study. F7, together with formulations F5–F9, passed heating–cooling cycling, centrifugation and freeze–thaw stress testing without visible phase separation, creaming, cracking or drug precipitation (Table 3), confirming adequate thermodynamic stability for downstream dissolution and pharmacokinetic evaluation. Formulations F1–F4, which contained a higher proportion of oil relative to Smix, showed partial phase separation on centrifugation and were excluded from further testing.

3.4 In-vitro dissolution and release kinetics

The dissolution profile of the optimized SNEDDS (F7) was compared with the pure drug powder and an equivalent physical mixture in pH 6.8 phosphate buffer (Figure 2). The pure drug released only 29 ± 3% of the labelled dose after 120 minutes, and the physical mixture performed only marginally better, releasing 45 ± 3%, confirming that simple physical blending with the excipients used in the SNEDDS does not by itself overcome the intrinsic dissolution-rate limitation of the drug. In contrast, the optimized SNEDDS released 28 ± 3% of the drug within the first 5 minutes and reached 99 ± 2% cumulative release by 120 minutes, with more than 90% release already achieved by 45 minutes. Dissolution efficiency, kinetic model fitting and the time to 50% release for each test article are summarized in Table 4; the SNEDDS dissolution data were best described by a first-order model, while the pure drug and physical mixture

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profiles were better fitted by the Higuchi model, consistent with diffusion-controlled release from a slowly wetting solid matrix.

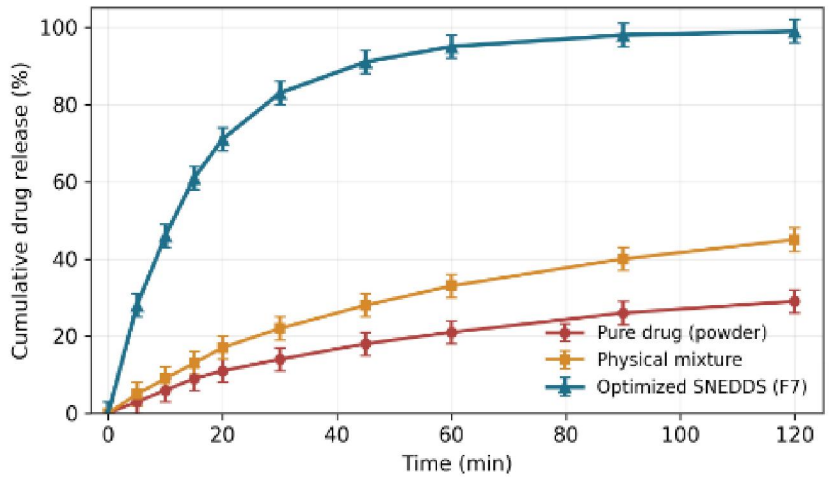

Figure 3. In-vitro dissolution profiles of the pure drug, physical mixture and optimized SNEDDS (F7) in pH 6.8 phosphate buffer (mean ± SD, n = 3).

3.5 In-vivo pharmacokinetic performance

Plasma concentration–time profiles after oral administration of the conventional suspension and the optimized SNEDDS are presented in Figure 3, and the derived pharmacokinetic parameters are summarized in Table 5. Cmax increased from 362 ± 28 ng/mL for the suspension to 1180 ± 95 ng/mL for the SNEDDS, a 3.3-fold increase, and Tmax was reduced from 3.0 to 2.0 hours, consistent with faster absorption from the pre-dissolved, nanoemulsified state. AUC0–∞ increased from 2450 ± 190 ng·h/mL for the suspension to 7120 ± 430 ng·h/mL for the SNEDDS, corresponding to a relative bioavailability of approximately 291%. Elimination half-life and mean residence time were not statistically different between the two groups, indicating that the SNEDDS altered the rate and extent of absorption without materially changing the drug's disposition once it reached the systemic circulation.

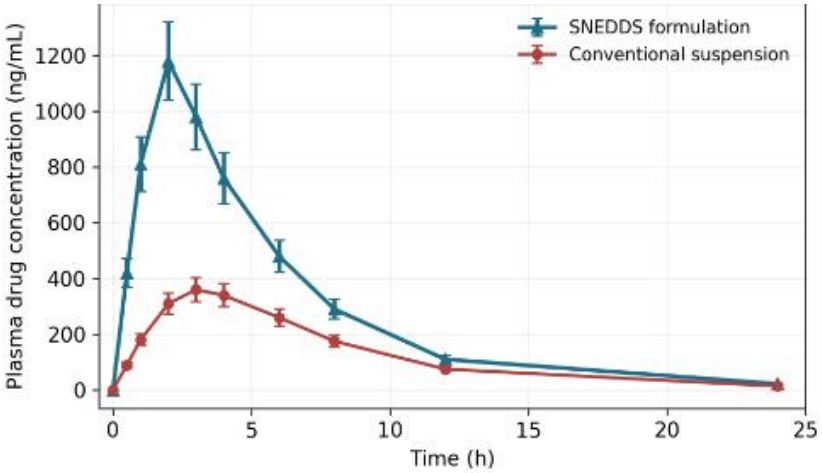

Figure 4. Mean plasma drug concentration–time profile after a single oral dose of the conventional suspension and the optimized SNEDDS formulation in rats (mean ± SD, n = 6).

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Table 1. Composition of SNEDDS formulations F1–F9

Formulation	Oil (% w/w)	Smix† (% w/w)	Water (% w/w)	Drug loading (mg/g)
F1	50	40	10	20
F2	45	45	10	20
F3	35	55	10	20
F4	40	45	15	20
F5	30	60	10	20
F6	25	60	15	20
F7*	20	65	15	20
F8	25	55	20	20
F9	30	50	20	20

†Smix = Cremophor EL : Transcutol HP at a fixed surfactant:co-surfactant ratio of 2:1 (w/w). *F7 = optimized formulation selected for dissolution and pharmacokinetic studies.

Table 2. Physicochemical characterization of SNEDDS formulations F1–F9 (mean ± SD, n = 3)

Formulation	Droplet size (nm)	PDI	Zeta potential (mV)	Transmittance (%)	Self-emulsification time (s)
F1	186 ± 9	0.38	−8.2 ± 0.7	78.4 ± 1.1	145 ± 6
F2	142 ± 7	0.31	−10.5 ± 0.6	84.1 ± 0.9	110 ± 5
F3	98 ± 5	0.24	−14.7 ± 0.8	89.6 ± 0.8	78 ± 4
F4	121 ± 6	0.29	−12.9 ± 0.5	86.2 ± 1.0	95 ± 5
F5	87 ± 4	0.21	−17.3 ± 0.6	92.8 ± 0.7	58 ± 3
F6	73 ± 4	0.19	−19.6 ± 0.5	95.4 ± 0.6	42 ± 3
F7*	61 ± 4	0.15	−23.8 ± 0.7	98.7 ± 0.4	28 ± 2
F8	95 ± 5	0.22	−15.1 ± 0.6	90.3 ± 0.7	66 ± 4
F9	110 ± 6	0.27	−11.8 ± 0.5	85.0 ± 0.9	102 ± 5

*F7 = optimized formulation. PDI = polydispersity index.

Table 3. Thermodynamic stability and dispersibility of SNEDDS formulations F1–F9

Formulation	Heating–cooling cycling	Centrifugation (3500 rpm)	Freeze–thaw cycling	Dispersibility grade
F1	Fail (phase separation)	Fail	Fail	D
F2	Fail	Fail	Fail	D
F3	Pass	Fail (slight creaming)	Fail	C
F4	Pass	Fail	Pass	C
F5	Pass	Pass	Pass	B
F6	Pass	Pass	Pass	A
F7*	Pass	Pass	Pass	A
F8	Pass	Pass	Pass	A
F9	Pass	Pass	Pass	B

*F7 = optimized formulation. Dispersibility graded A (rapidly forming clear/bluish dispersion) to E (poor dispersion with oil droplets visible on the surface).

Table 4. In-vitro dissolution efficiency and release-kinetic parameters

Test article	CDR at 30 min (%)	CDR at 120 min (%)	Dissolution efficiency (%)	Best-fit model (R^2)
Pure drug (powder)	14 ± 2	29 ± 3	18.2	Higuchi (0.987)
Physical mixture	22 ± 2	45 ± 3	27.6	Higuchi (0.979)

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Optimized SNEDDS (F7)	83 ± 3	99 ± 2	86.9	First order (0.992)

CDR = cumulative drug release. Dissolution efficiency calculated up to 120 minutes by the area-under-curve method.

Table 5. Pharmacokinetic parameters following oral administration (mean ± SD/SEM, n = 6)

Parameter	Conventional suspension	Optimized SNEDDS (F7)	Fold change / % increase
Cmax (ng/mL)	362 ± 28	1180 ± 95	3.3-fold
Tmax (h)	3.0 ± 0.0	2.0 ± 0.0	−33%
AUC0–t (ng·h/mL)	2210 ± 180	6840 ± 410	3.1-fold
AUC0–∞ (ng·h/mL)	2450 ± 190	7120 ± 430	2.9-fold
t1/2 (h)	5.8 ± 0.6	5.4 ± 0.5	ns
MRT (h)	6.9 ± 0.7	6.1 ± 0.6	ns
Relative bioavailability (%)	100 (reference)	≈ 291	—

ns = not statistically significant ($p > 0.05$). Relative bioavailability = (AUC0–∞ SNEDDS / AUC0–∞ suspension) × 100.

IV. DISCUSSION

The progressive reduction in droplet size observed from F1 to F7 as the proportion of Smix relative to oil increased is consistent with the established understanding that surfactant availability at the oil–water interface, rather than oil content alone, governs the fineness of the dispersed system [2,4]. A higher surfactant load lowers the interfacial tension between the oil and aqueous phases more effectively and allows a greater interfacial area to be stabilized for a given amount of mechanical or osmotic energy input on dilution, producing the smaller, more uniform droplets reflected in the falling PDI values across F1–F7. The slight increase in droplet size seen for F8 and F9, despite their still-elevated Smix content, illustrates that this relationship is not strictly monotonic: once the water fraction of the pre-concentrate itself becomes large, the relative proportion of stabilizing surfactant per unit of newly created interface falls, and droplet size can rise again. This non-monotonic behaviour is a recurring feature of pseudo-ternary systems and underscores why empirical mapping of the existence region, rather than reliance on a single compositional rule, is necessary for each new drug–excipient combination [7,11].

The marked improvement in dissolution rate achieved with the optimized SNEDDS, relative to both the unformulated drug and a simple physical mixture of the same excipients, illustrates a point that is sometimes underappreciated in early formulation screening: dissolution enhancement from lipid-based systems is not primarily a function of which excipients are present, but of whether those excipients are organized, prior to dispersion, into a system that is already thermodynamically primed to self-emulsify. A physical mixture must first wet, then partition the drug between solid and liquid excipient domains, before any dissolution advantage can be realized, whereas a properly formulated SNEDDS presents the drug already molecularly dissolved in the oil phase, so that the rate-limiting step on dilution becomes the (rapid) self-emulsification process itself rather than solid-state dissolution. This distinction is broadly consistent with reports for other BCS class II drugs formulated as SNEDDS, including talinolol, where lipid-based systems releasing substantially more drug within two hours than the marketed tablet were attributed primarily to the maintenance of drug in a solubilized state through the dispersion and digestion process [5].

The pharmacokinetic gains observed for the optimized SNEDDS a roughly 3-fold increase in Cmax and a 2.9-fold increase in AUC relative to the conventional suspension are of a magnitude broadly comparable with bioavailability improvements reported elsewhere in the SNEDDS literature for other poorly soluble actives, where fold-increases in Cmax and AUC ranging from approximately 1.5- to 3-fold have been documented for different BCS class II model drugs depending on the extent of first-pass metabolism, P-glycoprotein-mediated efflux and intestinal permeability of the specific compound [5,8]. Several mechanisms plausibly act in combination to produce this effect. First, the markedly faster and more complete in-vitro dissolution demonstrated in the present study indicates that, in vivo, a

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higher proportion of the administered dose is likely to be presented to the absorptive intestinal epithelium in dissolved form before transit through the absorption window is complete, rather than remaining as undissolved solid that passes through the small intestine largely unabsorbed. Second, the non-ionic surfactant used in the Smix is structurally related to excipients shown to inhibit P-glycoprotein-mediated efflux at the intestinal brush border, an action that would tend to increase the net absorptive flux for any drug that is itself an efflux-transporter substrate [9]. Third, for sufficiently lipophilic drugs, co-administration with digestible medium-chain lipids can promote a degree of intestinal lymphatic transport, which both increases the absorbed fraction and reduces first-pass hepatic extraction for drugs that are also high-clearance hepatic substrates [3,4]. The absence of a significant difference in elimination half-life and mean residence time between the two treatment groups in the present study suggests that the SNEDDS acted principally at the absorption phase rather than altering subsequent distribution or elimination, which is the pattern generally expected when an oral lipid-based delivery system enhances bioavailability through dissolution and absorption mechanisms rather than through systemic pharmacokinetic interactions.

From a practical formulation-science perspective, several considerations merit attention when translating SNEDDS technology from bench-scale optimization to a deliverable product. Liquid SNEDDS, while straightforward to manufacture, must usually be filled into soft gelatin capsules, which adds cost and introduces compatibility considerations between the fill and the capsule shell; conversion to a solid SNEDDS by adsorption onto a porous carrier or by spray-drying can mitigate this limitation and has been demonstrated to preserve, and in some cases improve, the dissolution advantage of the parent liquid system while enabling conventional tableting or encapsulation in hard-shell capsules [6,10,11]. Quality-by-design and design-of-experiment approaches, including the simplex-lattice and Box–Behnken designs used in formulation screening for several other BCS class II drugs, provide a systematic and statistically defensible route to identifying an optimum composition without the need for an exhaustive trial-and-error search of the full pseudo-ternary space [7,10,11]. Long-term physical and chemical stability of the optimized formulation, drug loading capacity relative to the intended clinical dose, and the cost and regulatory acceptability of the chosen excipients are additional factors that determine whether a laboratory-optimized SNEDDS can be developed into a viable commercial dosage form, and these considerations fall outside the scope of the present dissolution and pharmacokinetic evaluation but warrant attention in subsequent development work [10,12,13].

V. CONCLUSION

A self-nanoemulsifying drug delivery system was successfully developed and optimized for a poorly water-soluble model drug using pseudo-ternary phase diagrams and a simplex-lattice mixture design. The optimized formulation produced sub-100 nm, low-polydispersity droplets that were stable under thermodynamic stress testing, achieved markedly faster and more complete in-vitro dissolution than either the unformulated drug or a physical mixture of the same excipients, and delivered a roughly three-fold increase in both peak plasma concentration and overall systemic exposure relative to a conventional aqueous suspension following oral administration. These findings reinforce the broader body of evidence supporting SNEDDS as a versatile, scalable formulation platform for BCS class II and IV drugs, and indicate that careful, systematic optimization of the oil:surfactant:co-surfactant ratio is central to realizing the dissolution and bioavailability benefits that this technology can offer. Future work should extend this evaluation to solid SNEDDS formats, long-term stability under accelerated storage conditions, and confirmation of the pharmacokinetic advantage in a higher-order animal model or, ultimately, in human subjects.

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