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Review: Characterization and Dissolution of Low Solubility Active Substances in S-SNEDDS Preparations with Various Manufacturing Methods

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Abstract
SNEDDS is composed of a drug, surfactants, co-surfactants, and oils. Developing and optimising the correct formulation is necessary to minimise time and expense, and ensure the correct formulation. This review aimed to determine the characteristics and solubility of S-SNEDDS preparations made employing various manufacturing methods and the most effective and efficient drying procedures for low-water-soluble active ingredients. The method utilised was a literature study technique, which involved searching for literature in the form of primary data in the form of national and international journals published in the last ten years, starting from 2011 to 2021. The methods of making S-SNEDDS examined were adsorption to the solid carrier, spray drying, and freeze-drying using various dryers. The method of producing S-SNEDDS, adsorption to a solid carrier, possessed better characteristics and dissolution of the drug than the other two methods. The recommended drier was Aerosil 200, which effectively binds moisture and produces powder characteristics that fulfill the requirements.

Keywords: Adsorbent; Characterization; Dissolution; Method; Review; S-SNEDDS

1. INTRODUCTION

A solid self-nanoemulsifying drug delivery system (S-SNEDDS) is a solidified form of a lipid-based drug delivery system, a novel delivery strategy for poorly soluble pharmaceuticals in water, as it combines the benefits of liquid SNEDDS and solid dosage forms (Syukri et al., 2025).

S-SNEDDS was selected for its efficacy in enhancing the bioavailability of poorly soluble oral medicines. The S-SNEDDS system combines the benefits of the liquid form of SNEDDS with a solid dosage form that can overcome limitations in liquid formulas, including high production costs, incompatibility with capsule shells, limited stability, irreversible drug deposition, and low drug loading (Buya et al., 2020; A. Nasr et al., 2016). S-SNEDDS possesses advantages, including high stability, and the dosage form is easy for patients to accept (A. Nasr et al., 2016).

The methods to convert liquid SNEDDS into S-SNEDDS include adsorption to the solid carrier, spray drying, and freeze-drying (Syukri et al., 2025). S-SNEDDS from various

variations of drug ingredients made using the above method will be tested for physical characteristics and drug release in vitro. It is necessary to develop an effective and efficient method of making S-SNEDDS.

This article aimed to discuss the method of making S-SNEDDS, which produced good physical characteristics and drug release by reviewing S-SNEDDS articles of various active substances with low solubility made using three distinct manufacturing methods: adsorption to the solid carrier, spray drying, and freeze-drying.

2. RESEARCH METHODS

This review article was compiled utilising a literature study technique with the assistance of search engines such as Google Scholar, PubMed, Biomed, NCBI, etc., to find supporting papers on the online journal provider's website. The literature search was carried out with the keywords "S-SNEDDS", "method", and "characteristic". Primary data were obtained from international journals and national journals. The inclusion criteria for the selected articles were research articles published in the last ten years (2011-2021). The exclusion criteria were articles with a systematic review type, meta-analysis, and articles that could not be downloaded in full text.

3. RESULTS AND DISCUSSION

The review was conducted on 20 (twenty) articles on physical characteristics and in vitro drug release of various drugs in S-SNEDDS by adsorption to the solid carrier, spray drying, and freeze-drying methods.

Each article on the manufacture of S-SNEDDS employed adsorption to the solid carrier, spray drying, freeze drying, physical properties testing, drug release, and the effect of utilising a dryer, which shared some similarities (Table 1).

The methods employed to create S-SNEDDS resulted in good drug release and Characterization, respectively. A standard and widely employed method based on the article is adsorption to a solid carrier, which has the advantages of being low cost, easy to perform, easy to optimise, can be employed on an industrial scale, produces good Characterization and drug release in vitro. Additionally, it may be utilised with materials that are sensitive to heat and moisture, making it superior to the other two methods, spray drying and freeze-drying (Syukri et al., 2025)

Research (Nasr et al., 2016) created 200 S-SNEDDS aerosil dryers utilising the spray drying method, which possessed good powder characteristics with drug release 2.12 times larger than the preparations on the market. Research (Manoharan & Subramanian, 2019)utilising a freeze-drying method with an Aerosil 200 dryer produced good characteristics with 1.5 times better drug release than commercially available pharmaceuticals. Research (Beg et al., 2012) created S-SNEDDS aerosil desiccant utilising the adsorption to solid carrier technique, which resulted in the release of 2.9 times the drug compared to the medicine already on the market, and had the characteristics of a powder that fulfilled the requirements.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods.

Article Title and Active Ingredients	Author, Year	Method	Research result
Design, Optimization, And Evaluation of Glipizide Solid Self-Nanoemulsifying Drug Delivery for Enhanced Solubility and Dissolution Active substance: Glipizide (BCS class II)	(Dash et al., 2015)	Method: Adsorption to a solid carrier Active substance: Glipizide Dryer: calcium carbonate and talc Characterization Test: a) Particle size, b) Micromeritic properties (Carr's index, Hausner's ratio, and angle of repose), c) Scanning electron microscopy (SEM) Dissolution Test: samples (S-SNEDDS, L-SNEDDS, Glucotrol) Tool: USP dissolution type-I apparatus	The findings of the S-SNEDDS Characterization test employing the adsorption to solid carrier method with calcium carbonate and talc desiccant: The size of the generated S-SNEDDS particles was 29,8 nm ($p>0,05$). A Carr's index value indicated good flow qualities between 18-20, a Hausner's ratio between 1,22-1,25, and an angle of repose between 25° and 30°. The SEM test findings revealed that glipizide was rectangular crystals with smooth surfaces; however, the S-SNEDDS SEM test results did not reveal any glipizide crystals. The S-SNEDDS SEM test results demonstrated that glipizide crystals were adsorbed and penetrated the pores of the S-SNEDDS drying agent/absorbent. As expected, the porous drying surface facilitates dispersion and forms nanoemulsions (Hu et al., 2012). The percentage of drug release within 15 minutes (DR15min) of S-SNEDDS, L-SNEDDS, and Glucotrol was 99,65%, 97,33% and 65,82%. The high DR15min values of S-SNEDDS and L-SNEDDS significantly differed from Glucotrol ($p<0,05$). The results indicated that S-SNEDDS enhanced in vitro dissolution.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Preparation And Statistical Optimization of Self-Nanoemulsifying Tablets of Efavirenz Using 23 Factorial Designs Active substance: Efavirenz (BCS class II)	(Selvam & Kulkarni, 2014)	Method: Adsorption to a solid carrier Active substance: Efavirenz Dryer: Aerosil, accurately MP 1000 and porous polystyrene spheres (PPB) Characterization test: a) Particle size b) Flow properties (Angle of repose) Dissolution Test: sample (S-SNEDDS and pure drug) Tool: USP dissolution type-II	The results of characterizing S-SNEDDS efavirenz by adsorption on the solid carrier were presented using three distinct dryers (Aerosil, accurately, and PPB). Aerosil dryers generated better particle size (12 nm) and angle of repose (18.7°) than accurately and PPB dryers. The dissolution test results revealed that S-SNEDDS had a higher in vitro drug dissolution rate than pure drugs.
Formulation and Development of CoQ10-Loaded s-SNEDDS for Enhancement of Oral Bioavailability Active substance: Coenzyme Q10 (CoQ10) (BCS class II)	(Akhter et al., 2014)	Method: Spray drying Active substance: Coenzyme Q10 (CoQ10) Dryer: Aerosil 300 Characterization Test: Particle size, PDI, and viscosity Dissolution Test: sample (S-SNEDDS CoQ10, generic drugs and CoQ10 powder) Tool: USP dissolution apparatus II	The particle size, PDI, and viscosity test results from the Characterization of S-SNEDDS CoQ10 fulfilled the requirements, 35,6 nm, 0,28, and 13±1,03. S-SNEDDS CoQ10 resulted in drug dissolution of 97,5±4,5 % at 1.2 hours, whereas CoQ10 generic drugs and CoQ10 powder resulted in 57,96±0,54 % and 0,3±0,06 %. Simultaneously, the drug release from S-SNEDDS was significantly higher ($p<0,05$) than that of generic drugs and CoQ10 powder.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Design, Formulation, and In-Vitro Characterization of Irbesartan Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) Prepared Using Spray Drying Technique Active substance: Irbesartan (IRB) (BCS class II)	(Nasr et al., 2016)	Method: Spray drying Active substance: Irbesartan (IRB) Dryer: Aerosil 200 Characterization Test: a) Flow properties (Angle of repose, bulk density, Tapped Density, Compressibility Index, and Hausner's ratio) Dissolution Test: sample (S-SNEDDS, pure drug, and generic drug) Device: USP dissolution apparatus type II	The S-SNEDDS irbesartan characterization test employing the spray drying method and the Aerosil 200 dryer revealed good flow properties, with the values of angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio were 26.01°±0.55, respectively; 26,01°±0,55; 0,53±0,01 g/mL; 0,58±0,01 g/mL; 9,74±1,61 9% and 1,11±0,02. In vitro drug dissolution results on S-SNEDDS IRB, pure drug, and generic drug were 92,08±0,93%, 9,73±0,54% and 43,34±1,49%, respectively. The low solubility rate of IRB (pure drug) could be increased by preparing S-SNEDDS.
Development And Investigation of Novel Solid Self-Nanoemulsifying System Loaded with Hydrochlorothiazide for The Treatment of Hypertension Active substance: Hydrochlorthiazide (HCZ) (BCS class II)	(Dubey et al., 2018)	Method: Adsorption to a solid carrier Active substance: Hydrochlorthiazide (HCZ) Dryer: microcrystalline cellulose (MCC) Characterization test: a) Particle size b) Flow properties (Angle of repose, bulk density, Tapped Density, Compressibility Index, and Hausner's ratio) Dissolution Test: sample (S-SNEDDS and pure drug) Tool: USP dissolution type-II (paddle)	The particle size of S-SNEDDS HCZ with MCC dryer is 69,2 nm with good flow properties as indicated by the values of angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio fulfilled the requirements, respectively, 26,52°; 0,53g/mL; 0,61 g/mL; 15,26% and 1,09. The S-SNEDDS dissolution test reached 100% at the 180th minute, whereas the pure drug reached 77,4% at the 240th minute. The results indicated that S-SNEDDS HCZ preparation with an MCC dryer had better dissolution than the pure drug.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Self-Nano Emulsifying Solid of Clopidogrel - Development, Characterization, Evaluation, and Effect on Bioavailability Active substance: Clopidogrel (BCS class II)	(Manoharan & Subramanian, 2019)	Method: Freeze drying Active substance: Clopidogrel Dryer: Aerosil 200 Characterization Test: a) Scanning electron microscopy (SEM) Dissolution Test: Samples (S-SNEDDS and generic drugs: Tool: USP-I dissolution test apparatus	Characterization of S-SNEDDS clopidogrel by the freeze-drying method and the Aerosil 200 dryer, which was analysed using SEM, revealed crystals with a smooth surface and irregular shape. The dissolution test results revealed that S-SNEDDS clopidogrel had a dissolution rate that was 1,5 times greater than generic drugs.
Preparation And Statistical Optimization of Self-Nanoemulsifying Tablets of Efavirenz Using 23 Factorial Designs Active substance: Efavirenz (BCS class II)	(Selvam & Kulkarni, 2014)	Method: Adsorption to a solid carrier Active substance: Efavirenz Dryer: Aerosil, accurately MP 1000 and porous polystyrene spheres (PPB) Characterization test: a) Particle size b) Flow properties (Angle of repose) Dissolution Test: sample (S-SNEDDS and pure drug) Tool: USP dissolution type-II	The results of characterizing S-SNEDDS efavirenz by adsorption on the solid carrier were presented using three distinct dryers (Aerosil, accurately, and PPB). Aerosil dryers generated better particle size (12 nm) and angle of repose (18.7°) than accurately and PPB dryers. The dissolution test results revealed that S-SNEDDS had a higher in vitro drug dissolution rate than pure drugs.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Spray Dried Self-Nanoemulsifying Drug Delivery Systems for Sertraline Hcl: Pharmacokinetic Study in Healthy Volunteers Active substance: Sertraline (BCS class II)	(Ammar et al., 2018)	Method: Spray drying Active substance: sertraline Dryer: hydrophilic solid carrier, PVP, and lactose Characterization Test: Particle size and zeta potential Dissolution Test: Sample (S-SNEDDS sertraline and generic drug (Lustral® tablet))	Comparison of the particle size of S-SNEDDS sertraline between PVP and lactose dryers resulted in S-SNEDDS with PVP dryer having a significantly smaller particle size ($p<0.05$) than S-SNEDDS with lactose dryer. The zeta potential value of S-SNEDDS with PVP and lactose dryer fulfilled the requirements between 30 and +30 mV. Generic drug (Lustral® tablet) dissolution yielded a lower dissolution value (89.23%) ($p<0.05$) than S-SNEDDS with PVP dryer (96.96%) and lactose (93.80%). S-SNEDDS treated with PVP dryer revealed a greater dissolution rate ($p<0.05$) than S-SNEDDS treated with lactose dryer, which might be attributed to an increase in effective surface area.
Formulation And Evaluation of Novel Lipid-Based Solid Self-Nanoemulsifying Drug Delivery System of Repaglinide Active substance: Repaglinide (BCS class II)	(Reddy et al., 2014)	Method: Adsorption to a solid carrier Active substance: Repaglinide Dryer: Neusillin Characterization Test: a) Flow properties (angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio) Dissolution Test: sample (S-SNEDDS and pure drug) Device: USP dissolution apparatus type II	The S-SNEDDS repaglinide Characterization test results include an angle of repose with a value of 24.2°, which indicates good flow properties. The results of bulk density, tapped density, compressibility index, and Hausner's ratio were 1.25 g/ml, 1.53 g/ml, 18.3% and 1.22. The value of the Hausner ratio was a parameter to determine the flow properties of the powder. The Hausner ratio of S-SNEDDS powder was <1.25, which revealed good flow properties. The results of the release of S-SNEDDS preparations were 95.4%, whereas the pure drug had a drug release of 61.9% at 60 minutes. The results indicated that S-SNEDDS preparations were better than the pure drug's release.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Solidification Of Meloxicam Self-Nano Emulsifying Drug Delivery System Formulation Incorporated into Soluble and Insoluble Carriers Using Freeze Drying Method Active substance: Meloxicam (BCS class II)	(Kuncahyo et al., 2019)	Method: Freeze drying Active substance: meloxicam Dryer: mannitol (M) and fumed silica (FS) Characterization Test: a) emulsification time, b) % transmittance (% T), and c) particle size Dissolution Test: S-SNEDDS M, S-SNEDDS FS, and pure drug meloxicam Device: USP dissolution apparatus type II	The emulsification time of S-SNEDDS with an FS dryer was greater than that of S-SNEDDS with a mannitol (M) dryer ($P<0.05$). The acceptable transmittance percentage is close to 100%. The % T results of the two S-SNEDDS preparations were significantly different ($p<0.05$), i.e., % T S-SNEDDS M was greater than S-SNEDDS FS. The result of the S-SNEDDS M particle size test is 122.2 nm, whereas the S-SNEDDS FS is 478.7 nm. The drug dissolution in both S-SNEDDS preparations was 3-4 times greater than that of pure drug meloxicam. These results evidenced that a significant increase in drug release could enhance the likelihood of better drug bioavailability.
Formulation and in-vitro Characterization of Solid Self Nanoemulsifying Drug Delivery System (s-SNEDDS) of Simvastatin Active substance: Simvastatin (BCS class II)	(Reddy & Sowjanya, 2015)	Method: Adsorption to a solid carrier Active substance: simvastatin Dryer: crospovidone Characterization Test: a) particle size, b) PDI, and c) flow properties (angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio) Dissolution Test: sample (S-SNEDDS, pure drug, and generic drug) Tool: USP-Type II dissolution test apparatus	The average particle size and PDI results were 16.27nm and 0.276, respectively. The result of PDI <0.3 indicated that the particle size of S-SNEDDS was uniformly distributed. The results of the flow properties test carried out revealed good powder flow properties, as revealed by the value of angle of repose (27.998 ± 1.302)°, bulk density (0.367 ± 0.015)g/mL, Tapped density (0.41 ± 0.015) g/mL, compressibility Index (9.85 ± 0.38)% and Hausner's ratio (1.11 ± 0.006). The percentage of drug release of S-SNEDDS was found to be greater than that of pure drug and the simvastatin generic drug. The percentage of the release of S-SNEDDS drug was 84.86 ± 2.08% at the 60th minute, whereas pure drugs and generic drug were 14.53 ± 2.88% and 48.42 ± 2.32%..

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
A novel solid self-nanoemulsifying drug delivery system (S-SNEDDS) for improved stability and oral bioavailability of an oily drug, 1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol Active substance: 1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol (PLAG)	(Kim et al., 2017)	Method: Spray drying Active substance: 1-palmitoyl-2- linoleoyl-3-acetyl-rac-glycerol (PLAG) Dryer: calcium silicate Characterization Test: a) particle size and PDI Dissolution Test: sample (S-SNEDDS, pure drug, and soft capsule generic drug) Tool: USP dissolution testing apparatus II (paddle)	The particle yield and PDI from S-SNEDDS with calcium silicate dryer fulfilled the requirements with a value of 270 nm and PDI 0.252. The results of the dissolution test revealed that the release of S-SNEDDS drugs, pure drugs, and generic drugs were 80%, 20% and 20%, respectively. These results indicated that the S-formula S-SNEDDS could increase PLAG's solubility and drug release in vitro.
Formulation And Optimization of Solid Self-Nanoemulsifying System Using Porous Carriers for Oral Delivery of Cinnarizine Active substance: Cinnarizine (CNZ) (BCS class II)	(Aboutaleb et al., 2016)	Method: Adsorption to a solid carrier Active substance: Cinarizin (CNZ) Dryers: Aeroperl 300, Aerosil 200, hydrophilic nanosilica, and Neusilin US2 Characterization Test: a) Flow properties (angle of repose, Carr's index, and Hausner ratio) Dissolution Test: Sample (S-SNEDDS and commercial drug (Stugeron®))	The results of the Characterization of flow properties of all formulations of S-SNEDDS CNZ revealed good flow properties with a range of values of angle of repose less than 31°, Carr's index (14.77 - 17.93)%, and Hausner's ratio less than 1.2. The percentage of drug dissolution of all formulations of S-SNEDDS was significantly ($p<0.05$), which had a higher value than the generic drug at 5 minutes. This increase in S-SNEDDS dissolution could be caused by the small particle size of the preparation (nm). S-SNEDDS formulation with hydrophilic nanosilica dryer resulted in the highest dissolution rate compared to other dryers.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Design And Evaluation of Solid Self-Nanoemulsifying Drug Delivery Systems (S-Snedds) For Nebivolol Hydrochloride Active substance: Nebivolol (NEB) (BCS class II)	(Narkhede et al., 2014)	Method: Freeze drying Active substance: Nebivolol (NEB) Dryer: D-mannitol (S1), trehalose (S2), lactose (S3) Characterization Test: a) Percent transmittance, b) particle size Dissolution Test: samples (S-SNEDDS S1, S2 and S3; generic drug and pure drug) Tool: USP dissolution type-I apparatus	The per cent transmittance and particle size results on S-SNEDDS with a d-mannitol dryer produced the best value compared to S-SNEDDS with trehalose and lactose dryers. The dissolution results of all S-SNEDDS formulations were greater than those of generic and pure drugs. Drug release from S-SNEDDS formulation with mannitol dryer had the highest dissolution rate among other dryers, more than 85% within 120 minutes.
Development, Optimization, and Characterization of Solid Self-Nanoemulsifying Drug Delivery Systems of Valsartan Using Porous Carriers Active substance: Valsartan (BCS class II)	(Beg et al., 2012)	Method: Adsorption to a solid carrier Active substance: Valsartan Dryers: Aerosil 200, Sylysia 350, and Neusilin US2 Characterization Test: Flow properties (angle of repose, Carr's index, and Hausner ratio) Dissolution Test: sample (S-SNEDDS, pure drug, and generic drug (Valzaar®)) Tool: USP type-II dissolution apparatus	All S-SNEDDS formulations that were tested for their flow characteristics yielded positive results. The angle of repose of all formulations was less than 31°, Carr's index was less than <25% and Hausner's ratio was less than <1.2. The findings of the dissolution indicated that 90 percent of the S-SNEDDS drug was released in 30 minutes, but the release rates of pure drug and Valzaar were 29.2% percent and 31%, respectively. Due to the improved solubility of the active ingredient, the S-SNEDDS formulation boosts the dissolution of valsartan by 3-3.5 times.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Impact of Solid Carriers and Spray Drying on Pre/and Post-Compression Properties, Dissolution Rate, And Bioavailability of Solid Self-Nanoemulsifying Drug Delivery System Loaded With Simvastatin Active substance: Simvastatin (BCS class II)	(Sharma et al., 2018)	Method: Spray drying Active substance: simvastatin Dryer: Aerosil 200 (A-200), Sodium Carboxy Methyl Cellulose (Na-CMC), and lactose Characterization Test: a) Particle size b) Flow properties (angle of repose, bulk and Tapped density, Carr's index) Dissolution Test: sample (S-SNEDDS A-200, generic drug and pure drug) Tool: USP dissolution type-I apparatus	Particle size testing revealed that S-SNEDDS with Na-CMC and lactose dryers produced large particle sizes (418.16 ± 1.34) nm and (566.18 ± 9.69) nm, whereas S-SNEDDS A-200 produced small particle sizes of 75.26 ± 2.38. nm. The results of flow properties revealed that S-SNEDDS A-200 produced powders with the best flow properties, namely with an angle of repose value <31° and a Carr's index <25%. These results indicate that the dryer A-200 produces the best S-SNEDDS powder. The results of the S-SNEDDS A-200 dissolution test resulted in >90% drug release in 10 minutes, whereas generic drugs and pure drugs only released <45% in 60 minutes. The results of drug release in the formulation of S-SNEDDS A-200 were 2 times greater than those of pure drugs and generic drugs.
Development And Pharmacokinetic Evaluation of Spray-Dried Self-Nanoemulsifying Drug Delivery System of Sertraline Active substance: Sertraline (BCS class II)	(Rahman et al., 2016)	Method: Spray drying Active substance: sertraline Dryer: Dextran 40 Characterization Test: a) particle size and b) PDI Dissolution Test: sample (S-SNEDDS and pure drug) Tool: USP type-II dissolution apparatus	The particle size and PDI tests on S-SNEDDS revealed 68.8 ± 1.08 nm and 0.184 ± 0.024. These results were not significantly different ($p>0.05$) from SNEDDS liquid preparations. The dissolution test results revealed that the release of S-SNEDDS drug had the highest value of 95% in 45 minutes, and was 6 times higher than the pure drug. The release of the S-SNEDDS formulation was significantly ($p<0.01$) higher than that of the pure drug. This high drug release could lead to an increase in the absorption and bioavailability of the drug.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) of Darunavir for Improved Dissolution and Oral Bioavailability: In-Vitro And In Vivo Evaluation Active substance: Darunavir (BCS class II)	(Inugala et al., 2015)	Method: Adsorption to a solid carrier Active substance: darunavir Dryer: Neucilin US2 Characterization Test: Flow properties (Carr's index and Hausner ratio) Dissolution Test: sample (S-SNEDDS darunavir and pure drug) Equipment: USP type II apparatus	SNEDDS formulated with US2 neucillin dryer produced a powder with good flow properties as indicated by the value of Carr's index (18.6 ± 0.1) % and Hausner ratio 1.18 ± 0.15. The powder produced by the S-SNEDDS neucillin drier has a small particle size and a large surface area, which could enhance medication absorption. The dissolution profile demonstrated that S-SNEDDS had a rapid drug release of 61.7 ± 2.5% in 5 minutes compared to 35.6% in 60 minutes for the pure drug.
Self-Nanoemulsifying Drug Delivery System for Embelin: Design, Characterization and In-Vitro Studies Active substance: Embelin	(Parmar et al., 2015)	Method: Adsorption to a solid carrier Active substance: Embelin Dryer: Combination of Neusilin US2 and Aerosil 200 Characterization Test: a) Micromeritic properties (Carr's index, Hausner's ratio, and angle of repose) Dissolution Test: sample (L-SNEDDS, S-SNEDDS, Embelin tablet (pure drug)) Tool: USP dissolution type-II	Characterization of S-SNEDDS Embelin by adsorption to solid carrier method and combination dryer of Neusilin US2 and Aerosil 200 resulted in good flow properties with an angle of repose value of 25,5; Carr's index of 20,5 and Hausner's ratio of 1,15. The dissolution test for drug release was measured at 15 minutes with L-SNEDDS, S-SNEDDS, and pure drug samples. The resulting drug release was 99,60 ± 0,85%, 97,80 ± 1,27% and 5,7 ± 0,30%, respectively. The drug release of S-SNEDDS was slightly lower than that of L-SNEDDS; this could be owing to the presence of excipients, since S-SNEDDS was in tablet form, causing an extra dissolving process, namely the breakdown of tablets into granules, which resulted in less drug release.

Table 1. Characterization and dissolution of low-soluble active substances in S-SNEDDS preparations with various manufacturing methods (*Continued*).

Article Title and Active Ingredients	Author, Year	Method	Research result
Effects of Solid Carriers on The Crystalline Properties, Dissolution, And Bioavailability of Flurbiprofen in Solid Self-Nanoemulsifying Drug Delivery System (Solid SNEDDS) Active substance: Flurbiprofen (BCS class II)	(Kang et al., 2011)	Method: Spray drying Active substance: flurbiprofen Dryer: Aerosil 200 and magnesium stearate Characterization Test: a) particle size and b) SEM Dissolution Test: sample (S-SNEDDS Aerosil 200, S-SNEDDS mg stearate, and powder)	The results of the S-SNEDDS particle size test with the aerosil dryer were 98 ± 2 nm, and the S-SNEDDS with the mg stearate dryer were 1940 ± 140 nm. SEM test results of the powder revealed that the flurbiprofen S-SNEDDS and flurbiprofen powder produced rectangular crystals with a smooth surface. The results of the SEM test on S-SNEDDS aerosil produced a particle form with a rough surface, which indicated that the liquid preparation of SNEDDS was absorbed in the pores of the aerosol. In contrast, in S-SNEDDS, mg stearate agglomeration occurred since the liquid S-SNEDDS was not completely absorbed. In the dissolution test, the release of aerosolized S-SNEDDS preparations reached 80% in 5 minutes, which is evidence of the fastest emulsification time and the smallest particle size compared to S-SNEDDS preparations with other dryers.
Development And Evaluation Of Solid Self-Nano Emulsifying Drug Delivery System Of Poorly Soluble Olmesartan Medoxomil By Using Adsorption Onto Solid Carrier Technique Active substance: Olmesartan medoxomil (OLM) (BCS class II)	(B. S. Reddy et al., 2016)	Method: Adsorption to a solid carrier Active substance: Olmesartan medoxomil (OLM) Dryer: Neusilin US2 Characterization test: a) Particle size and zeta potential, b) Flow properties (Angle of repose, bulk density, Tapped Density, Compressibility Index, and Hausner's ratio) Dissolution Test: sample (S-SNEDDS, Olmesartan medoxomil tablet (plain drug)) Tool: USP dissolution type-II	The particle size and zeta potential of the S-SNEDDS OLM produced were 58,5 nm and -15,3 mV, respectively. The S-SNEDDS OLM flow properties test consists of an angle of repose, bulk density, tapped density, compressibility index, and Hausdorff's ratio. The values of each of these tests were 28,275 ± 1,021, respectively; 28,275 ± 1,021; 0,369 ± 0,014 g/mL; 0,42 ± 0,016 g/mL; 9,86 ± 0,039% and 1,139 ± 0,008. The results of the flow properties test show that the flow properties fulfilled the requirements of the S-SNEDDS dissolution test at 90 minutes with 0.1 N HCl media, revealing 86.89% drug release, whereas OLM tablets had 36,25% drug release. The results indicated that the S-SNEDDS formula could increase OLM drug solubility and drug release in vitro.

S-SNEDDS preparations using the adsorption to solid carrier method, which operate as adsorbents, are produced using several dryers. The dryer must have a large particle surface area to absorb moisture and oil from the liquid formulation of SNEDDS (Kuruvila et al., 2017). According to research, the best used drier is Aerosil 200 (Selvam & Kulkarni, 2014). Preparation of S-SNEDDS with adsorption to solid carrier method using Aerosil dryer, accurately MP 1000, and porous polystyrene spheres (PPB). This study resulted in S-SNEDDS with an aerosol dryer producing the smallest particle size (12 nm), the best angle of repose (18.7°), and the most significant drug dissolution compared to the other two dryers. Research (Kang et al., 2011) made S-SNEDDS by spray drying using an Aerosil 200 dryer and magnesium stearate to produce particle sizes of 98 ± 2 nm for the Aerosil dryer and 1940 ± 140 nm for the magnesium stearate dryer. The dissolution test results revealed that the S-SNEDDS aerosol dryer reached 80% in 5 minutes, indicating the quickest emulsification time and smallest particle size compared to S-SNEDDS preparations with other dryers. Sodium Carboxy Methyl Cellulose (Na-CMC) and lactose were utilised to produce S-SNEDDS by spray drying (Sharma et al., 2018). The findings indicated that S-SNEDDS powder dried with an aerosil dryer generated the smallest particle size and excellent flow characteristics; however, S-SNEDDS powder dried with other dryers did not fulfill the requirements. The dissolution results demonstrated that S-SNEDDD aerosil desiccant had >90% drug release in 10 minutes.

4. CONCLUSION

This review article demonstrated the development of various methods of S-SNEDDS formulations of water-soluble active ingredients. The methods of making S-SNEDDS that have been studied include adsorption to a solid carrier, spray drying, and freeze-drying with different dryers. The method recommended in this review was adsorption to the solid carrier with an aerosil dryer, which produced S-SNEDDS with better characteristics.

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CONFLICT OF INTEREST

All authors declared that there was no conflict of interest.

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