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Formulation and Characterization Self-Nanoemulsifying Drug Delivery System (SNEDDS) Loaded Propolis Extract with Various Concentration of Tween 80 and PEG 400

Azica Kurnia Nirwana, Dewi Damayanti Abdul Karim, Untia Kartika Sari Ramadhani

Pharmacy Study Program, Faculty of Science, Sumatera Institute of Technology, Lampung, Indonesia

Background: Propolis is a natural resin produced by bees that contains various secondary metabolites with a range of activities, such as antioxidant, antibacterial, and anti-inflammatory. However, its low solubility and limited bioavailability may restrict its therapeutic potential. A Self-Nanoemulsifying Drug Delivery System (SNEDDS) formulation was developed and expected to overcome these limitations. **Aim:** This study was an attempt to develop a Propolis-loaded SNEDDS formulation as a modified drug development technology. **Methods:** Propolis-loaded SNEDDS were prepared using ultrasonication method with different ratios of Tween 80 : PEG 400 as a surfactant and cosurfactant. Propolis-loaded SNEDDS contained 750 mg of propolis extract. In the optimization process, the area of the nanoemulsion was determined by a ternary phase diagram construction method based on the transmittance values obtained from each formula. All the formulated propolis-loaded SNEDDS were evaluated through several parameters such as transmittance value, particle size distribution, zeta potential, and particle morphology. **Results:** The optimization results showed the nanoemulsion area formed at the concentration range of 8.3-12,5%, Tween 80 56.9-84.6% and PEG 400 7.7-23.1%. The results of SNEDDS propolis formula optimization with various concentration of Tween 80 : PEG 400 at F1 (11:1), F2 (10:2), and F3 (9:3) showed good characteristics with transmittance values of 89-98%, particle size 11-13 nm, polydispersity index of 0,1-0,3, and zeta potential -2 to -23 mV. **Conclusion:** Based on the characterization results, F3 with ratio of Tween 80: PEG 400 (9:3) is the best propolis-loaded SNEDDS formula seen from clarity, particle size and distribution, suitable zeta potential as well as spherical particle morphology.

Keywords: propolis, snedds, tween 80, PEG 400, drug delivery

Introduction

Propolis is a mixture of resins produced by bees from the shoots and skins of trees they consume. Propolis is an active substance with complex chemical components. The components contained in propolis include resin (45-55%), candles and fatty acids (25-35%), essential oils (10%), pollen (5%), and organic and mineral components (5%). The variation of the components contained in propolis is based on the region of origin and the plant source of the resin.[1] Propolis contains several compounds such as polyphenols and flavonoids, aromatic acids, diterpenoids, and triterpenoides. The biological activities of propolis include antibacterial, anti-inflammatory, antioxidant, and anti-cancer.[2] Flavonoids as the main constituent of propolis have aglycone components that cause propolis to be difficult to solve in water and have low bioavailability. One of the strategy to address the problem is with lipid carrier formulations such as the Self-Nanoemulsifying Drug Delivery System (SNEDDS).

Corresponding Author:
Untia Kartika Sari Ramadhani
Pharmacy Study Program, Faculty of Science
Sumatera Institute of Technology
Jl. Terusan Ryacudu, Lampung, 35365, Indonesia
e-mail: untia.sari@fa.itera.ac.id

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SNEDDS is the development of a nanoemulsion system where nanoemulsification is a thermodynamically more stable emulsion compared to macroemulsion and microemulsion. The main characteristic of nanoemulsion is the very small particle size (1-100 nm) that can prevent physical instability such as sedimentation and creaming.[6] The advantages of these SNEDDS are that they are easy to apply, economical, can increase the solubility of lipophilic compounds, can improve absorption, and are compatible for storage over a relatively long period of time because they have better physical and chemical stability than nanoemulsion system.[7] In this study, olive oil was chosen as an oil phase because it is an easy-to-obtain, economical and low-irritant vegetable oil. In the formulation, SNEDDS also used a mixture of Tween 80 and PEG 400 as surfactant and cosurfactant with various concentration ratio. Tween 80 has a HLB value of 15, whereas PEG 400 has a HLB of 13,1. One of the compatible surfactant and cosurfactant conditions for oil in water-type formulations is that they have HLB values above 10.[8]

Several studies have explored SNEDDS for propolis to enhance its solubility and absorption. However, existing propolis-loaded SNEDDS formulations often rely on higher oil phase concentrations (>20%) or alternative surfactants (e.g., Labrasol or Cremophor EL), resulting in larger droplet sizes (>50 nm) and suboptimal stability under storage. A key research gap remains in developing low-oil SNEDDS with optimized non-ionic surfactant-cosurfactant ratios to achieve ultrasmall droplets (<20 nm) while maintaining thermodynamic stability and scalability. This study addresses these gaps by formulating propolis-loaded SNEDDS using olive oil as a low-irritant, economical oil phase (low concentration, ~10%) combined with Tween 80 (HLB 15) as surfactant and PEG 400 (HLB ~13) as cosurfactant. Optimizing their ratios is critical because it minimizes interfacial tension and ensures spontaneous emulsification upon aqueous dilution, directly influencing droplet size, polydispersity index (PDI), zeta potential, and long-term stability. This work systematically varies Tween 80:PEG 400 from for targeting superior physicochemical performance. By filling these formulation gaps, this research provides a refined SNEDDS strategy to improve propolis solubility and dispersion, potentially enhancing its utility in pharmaceutical development.

Propolis-loaded SNEDDS addresses the limitations of native propolis, particularly its poor aqueous solubility and low bioavailability, by enabling spontaneous formation of nanoemulsions with droplet sizes upon aqueous dilution. This lipid-based carrier system, optimized with low olive oil content (~10%) and Tween 80:PEG 400 ratios, achieves high transmittance (89-98%), low polydispersity index (0.1-0.3), and favorable zeta potential (-2 to -23 mV), indicating enhanced dispersion stability and potential for improved absorption compared to conventional extracts. Thus, increasing the solubility of propolis through drug delivery technology not only improves its therapeutic effectiveness, but also opens up wider opportunities in the development of modern drug formulations that are more efficient and safer. From a clinical perspective, these improvements offer tangible value by potentially enhancing the gastrointestinal absorption of propolis bioactives. This could support more consistent delivery of propolis's documented efficacy in targeted applications. Additionally, the stable nanoscale dispersion may enable lower dosing volumes while maintaining efficacy, improving formulation tolerability and ease of administration in pharmaceutical products.[3–5] Based on this, the research is aimed to develop a formulation that can improve the solubility and bioavailability of propolis so as to increase its usefulness.

Materials and methods

Propolis Sample Preparation

In this study, the propolis used comes from the kelulut bee, or the species Geniotrigona thoracica. Raw propolis was obtained from PT. Suhita Lebah Indonesia, located in Langkapura District, Bandar Lampung City, Lampung Province. The samples were first frozen at a temperature of <15°C. This was done to make the propolis raw material more brittle, thereby facilitating the grinding process to produce smaller propolis particles. Next, the frozen propolis was broken into small pieces and ground into a powder using a grinder. The propolis powder was then sieved using a 100-mesh sieve to separate the propolis from other materials still adhering to it. The sieved material was stored in an airtight jar to proceed immediately with the extraction process.

Extraction and Screening of Propolis Extract

10 grams of propolis simplisia powder was extracted using a 70% ethanol solvent with a simplisia and solvent ratio of 1:10. Extraction was done using the Ultrasound Assisted

Extraction (UAE) method with Ultrasonicator Elmasonic S180H instrument. The sonication results were filtered with a Buchner equipped with Whatman 1 filtering paper. The residue is re-sonicated with 100 mL of 70% ethanol at 30°C for 1 hour. The liquid extract obtained was compressed using a rotary evaporator at 40°C to obtain a thick propolis extract. Propolis extract continued with chemical content screening including Alkaloids, Phenolics, Flavonoids, Saponins, Steroids/Triterpenoids, and Tanins with screening methods referring to the guidelines in Farnsworth, 1996.[9]

Optimization of SNEDDS Blank Formula

The subjects were healthy Indonesian males or females aged The optimization was done using 15 formulas with various ratio of in Tween 80 and PEG 400, while the Olive Oil ratios were left constant. The base formula was made by mixing Tween 80 and PEG 400 first using a magnetic stirrer at a speed of 500 rpm for 15 minutes after being homogeneous, adding olive oil into the mixture and re-mixing using the magnetical stirrer with the same speed and time. The mixture is then sonicated using ultrasonicator for 1 hour until nanoemulsion preconcentrate was produced. The entire formula was diluted with the aquadest (1:100) and the transmittance value was measured using the UV-Vis Spectrophotometer Thermo Scientific Genesys 150 with a wavelength of 650 nm. The formula that produces a clear visual with a transmittance value of >80% is taken as a terner phase diagram construction data using Chemix software.

Formulation of Propolis-loaded SNEDDS

Based on the optimization results, the three base formulas were selected which produced the widest emulsification area. 750 mg of propolis extract was incorporated into 5 mL (final concentration 150 mg/mL) of base formulas using a magnetic stirrer at a speed of 500 rpm for 15 minutes and continued with an ultrasonicator for 15 minutes at 30°C. Propolis-loaded SNEDDS was stored in a well-closed container at room temperature for further use.

Characterization of Propolis-Loaded SNEDDS

Propolis-loaded SNEDDS were characterized including transmittance values, particle size, polydispersity index, zeta potential, and particle morphology. Transmittance test was conducted by diluting propolis-loaded SNEDDS preconcentrate with distilled water (1:100). The diluted solution was then measured for transmittance using a UV-Vis Spectrophotometer Thermo Scientific Genesys 150 with a distilled water as a blank and measured at a maximum wavelength of 650 nm. Particle size, polydispersity index, and zeta potential were characterized using a Particle Size Analyzer (PSA) Horiba SZ-100. Samples were dispersed using distilled water and then put into cuvettes and stored in the sample holder. The measurement were replicated three times and the mean value along with SD was calculated.

Particle morphology were characterized using Transmission Electron Microscope (TEM) Hitachi H-9500. Prior to analysis, the prepared SNEDDS samples were diluted with distilled water to achieve a more uniform dispersion. A single drop of the sample was then placed on a copper grid coated with a carbon support film, and left to stand for several minutes to allow the particles to adsorb onto the grid surface. Excess sample was then absorbed using filter paper. The prepared grid was dried at room temperature before being observed using TEM.

Results

Extraction and Screening of Propolis Extract

In this study, 80 grams of propolis powder was used and produced 11,4783 grams of propolis extract. Based on the results, the percentage of extraction yields by the extraction process in this study was 14.34%. The magnitude of the yield obtained describes the effectiveness of the extraction method and the amount of active compounds on the strap that can be pulled. Screening results of propolis extract showed that propolis extract from the positive Trigona thoracica bee contains alkaloids, phenolics, saponins, and flavonoids.

Optimization of SNEDDS Blank Formula

The optimization of SNEDDS blank formula was carried out using 15 formulas with different component ratios with the transmittance value as the main indicator. Formulas with a qualifying transmittance value of >80% are taken as terner diagram construction data. The transmittance values are presented in **Table 1.**

The concentrations of each of SNEDDS components that qualify for transmittance values was entered into the diagram data and then the extrapolation point was determined based on the upper and lower limits of the Tween 80 and PEG 400 concentrations. Each point was connected to form a plot area and given color as a marker. From the optimization results of the fifteen

SNEDDS formula, a picture of the nanoemulsion area was obtained based on transmittance values as in **Figure 1.**

Out of 15 experimental formulas, 11 formulas with various ratio of the Tween 80: PEG 400 were obtained and calculated as the area of the nanoemulsion based on the transmittance value. From the results, the Olive Oil: Smix ratio with the most plot area is 1:12. Based on the ternary diagrams, the area of nanoemulsion formed in the concentration range of olive oil 8.3-12,5%, Tween 80 56.9-84.6% and PEG 400 7.7-23.1%. Based on these results, SNEDDS will form nanoemulsions with both of Tween 80 and PEG 400 concentrations which are in the concentration range based on the ternary diagrams. When one or both components have concentrations beyond the concentration limit range, the SNEDDS do not produce nanoemulsions based on the parameter of its transmittance value. Based on the optimization result, the optimal ratio of Olive Oil : Smix is 1:12 with each optimal ratio of olive oil : Tween 80 : PEG 400 was 1:11:1, 1:10:2, 1:9:3.

Characterization of Propolis-Loaded SNEDDS

SNEDDS characterization parameters included transmittance value, particle size, polydispersity index, and zeta potential. The characterization results are presented in **Table 2**. From the characterization results, the two out of three propolis-loaded SNEDDS formulas had zeta potential values in the appropriate range of ±10 mv to ±30 mv. It indicated that formula 2 and formula 3 are moderately stable. Formula 1 was an unstable formula because of the lower zeta potential value. This formula can cause rapid coagulation or flocculation. Formula 3 was the formula with the best electrostatic stability because it has greater zeta potential value than the other two formulas. The result of the particle size characterization of the three formulas showed that propolis-loaded SNEDDS had the corresponding

Table 1. Optimization of propolis-loaded SNEDDS.

Ratio			Transmittance value (%)	Remarks
Olive Oil	**Tween 80**	**PEG 400**		
1	7	1	92.1	Qualified
	6	2	88	Qualified
	5	3	54.4	Not Qualified
	8	1	94	Qualified
	7	2	89.1	Qualified
	6	3	67.8	Not Qualified
	9	1	93.6	Qualified
	8	2	90	Qualified
	7	3	72.9	Not Qualified
	10	1	94.7	Qualified
	9	2	89	Qualified
	8	3	77.4	Not Qualified
	11	1	98.9	Qualified
	10	2	96.6	Qualified
	9	3	89.3	Qualified

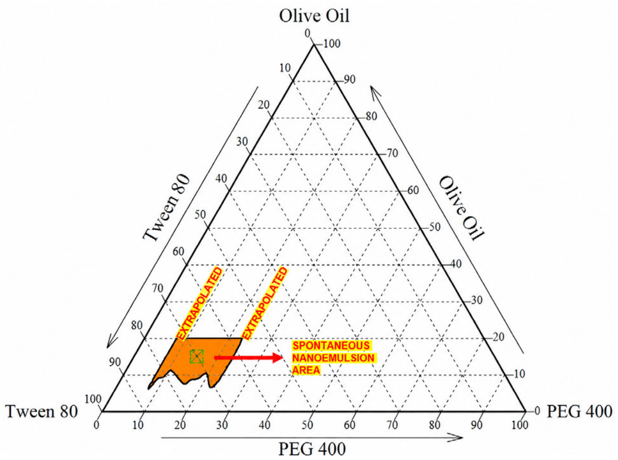

Figure 1. Ternary diagram of propolis-loaded SNEDDS.

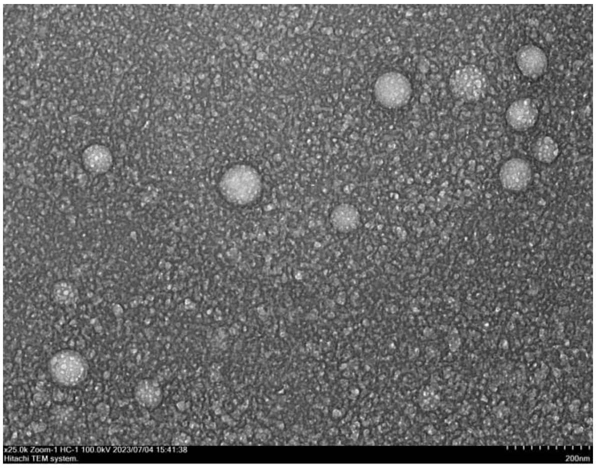

Figure 2. TEM image of propolis-loaded SNEDDS.

particle sizes because it was in the nanoemulsion range, i.e. 1 - 100 nm. The three formulas produced particle sizes in the range of 11-13 nm. The whole formula also had a polydispersity index <0.5 which indicates that the entire formula had good particle size distribution. Of the three formula, Formula 3, was the formula with the smallest particle size and polydispersity index.

The overall characterization parameters indicated that of the three formulas, Forumla 3 was the best propolis-loaded SNEDDS formula. Furthermore, this result was validated by the morphological characterization of SNEDDS particles using the Transmission Electron Microscope (TEM). TEM characterization result showed that propolis-loaded SNEDDS particles have a spherical shape.

Discussion

This study used ultrasound-assisted extraction (UAE) because it has strong potential to produce propolis extracts with relatively high yields. Previous comparative work showed that among maceration, microwave-assisted extraction (MAE), and UAE, the UAE method gave the best extraction yield for propolis.[10] This supports the choice of UAE in the present work, since a higher yield is advantageous not only for improving process efficiency, but also for maximizing recovery of bioactive constituents available for formulation. In addition, the extraction yield obtained in this study provides an initial indication of how effectively the selected method was able to recover soluble components from the propolis raw material. The choice of 70% ethanol as the extraction solvent was also appropriate because solvent polarity must match the target compounds to be extracted. Ethanol 70% is widely used as a universal solvent because it can extract a broad range of compounds, from nonpolar and semipolar to polar fractions, while remaining relatively safe and less toxic than many alternative organic solvents.[11] This is particularly relevant for propolis, which contains a chemically diverse mixture of secondary metabolites. Consistent with previous findings, propolis extract in this study was positive for alkaloids, flavonoids, and polyphenols, confirming that the extraction conditions were suitable for recovering the main bioactive fractions expected in propolis.[12] In general, propolis is known to contain polyphenols, including flavonoids, phenolic acids, and esters, as well as phenolic aldehydes, ketones, acids and their derivatives, minerals, and enzymes. This compositional diversity explains why solvent selection plays such an important role in determining extract quality and downstream formulation performance.

The results showed that the formulation performance of propolis-loaded SNEDDS was strongly dependent on the balance between the oil phase, surfactant, and co-surfactant. Olive oil was suitable as the oil phase because it is practical for topical preparations and provides a skin-friendly lipid base. Tween 80, as a nonionic surfactant with a high HLB value, was effective in reducing interfacial tension, while PEG 400 improved interfacial flexibility and supported emulsification. The use of Tween 80 and PEG 400 together was important because surfactant alone is often insufficient to achieve optimal interfacial disruption in SNEDDS systems.[13] One of the most important steps in optimizing the SNEDDS formula was the use of a ternary phase diagram. The ternary phase diagram is used to identify the nanoemulsion region based on self-

Table 2. Characterization result of propolis-loaded SNEDDS.

Formula	Ratio (Olive Oil : Tween 80 : PEG 400)	Avg. Transmittance (%)	Avg. Particle Size (nm)	Avg. Polydispersity Index	Avg. Zeta Potential (Mv)
1	01.11.01	98.933 ± 0.05	11.933 ± 0.12	0.334 ± 0.01	-2.267 ± 1.65
2	01.10.02	96.633 ± 0.05	13.033 ± 0.12	0.244 ± 0.02	-10.567 ± 1.14
3	01.09.03	89.367 ± 0.19	11.067 ± 0.12	0.189 ± 0.02	-23.833 ± 2.88

emulsification behavior and to estimate the upper and lower limits of each SNEDDS component.[14] In other words, it provides a practical map of composition space, showing where spontaneous nanoemulsion formation is possible and where it is not. The principle behind this method is based on systematically increasing or decreasing component concentrations and then confirming the resulting physical characteristics.[15] In this study, the ternary phase diagram demonstrated that the formulation window was narrow and strongly composition dependent. This supports the need for systematic optimization rather than arbitrary selection of excipient ratios, because even small changes in formulation composition clearly influenced whether the system could form a nanoemulsion. The variation in Tween 80 and PEG 400 ratios was therefore essential, because the physical properties of SNEDDS depend heavily on the exact composition of the Smix. A suitable ratio can produce smaller droplets, better dispersion, and improved system stability, whereas an inappropriate ratio may lead to poor emulsification or reduced transparency.

In this study, 15 experimental formulas were prepared with different Tween 80:PEG 400 ratios, and only 11 formulas were found to fall within the nanoemulsion area based on transmittance values. This means that approximately 73.3% of the tested formulas were capable of spontaneous nanoemulsion formation under the selected conditions, while the remaining formulas fell outside the effective formulation window. The olive oil:Smix ratio with the broadest plot area was 1:12, indicating that a relatively high proportion of Smix was needed to adequately reduce interfacial tension and stabilize the oil phase. The nanoemulsion region was located within the concentration ranges of olive oil 8.3–12.5%, Tween 80 56.9–84.6%, and PEG 400 7.7–23.1%, which gives a clear quantitative boundary for acceptable formulation space.

The propolis-loaded SNEDDS was produced by incorporating 750 mg of propolis extract into the SNEDDS base using magnetic stirring followed by ultrasonication. The use of ultrasonication after magnetic stirring further improved the formulation quality. This additional high-energy step likely contributed to more uniform droplet formation and enhanced nanoemulsion clarity. The need to control temperature and stirring conditions also reflects the sensitivity of SNEDDS to processing parameters. In other words, not only the composition but also the manufacturing process determined whether a stable nanoemulsion could be obtained.[16] The principle of the ultrasonication method in the formation of SNEDDS is through the use of cavitational styles, i.e. vibrations and sound waves in breaking up the aggregation of particles to form particles with smaller size.[17] This helps explain why the final formulations were able to reach the nanoscale range. The need to control temperature and mixing conditions also reflects the sensitivity of SNEDDS to processing parameters. During manufacturing, factors such as temperature, stirring speed, and mixing intensity can significantly alter the final formulation characteristics.

Temperature is a particularly important variable because an increase in temperature can produce metastable conditions in SNEDDS by lowering mixture viscosity, increasing droplet collision frequency, and amplifying density differences between components.[18] A lower interfacial film viscosity can increase thermal agitation of dispersed particles, which refers to the continuous random motion induced by temperature changes and can contribute to instability.[19] Likewise, the mixing process must be carefully controlled: excessively rapid mixing may generate turbulence and non-uniform droplet dispersion, whereas overly slow mixing may prevent homogeneous blending of the system components.[20] These observations reinforce the idea that SNEDDS quality depends not only on composition, but also on processing conditions.

The characterization results confirmed that the developed propolis-loaded SNEDDS had favorable colloidal properties. Transmittance was used as the main screening parameter because it reflects the clarity and optical transparency of the formulation.[21] High transmittance values indicate low light scattering, which is typically associated with small droplet size and successful nanoemulsion formation. Since 11 of the 15 formulas satisfied the transmittance criterion, the study demonstrates that the propolis-loaded SNEDDS had a reasonably broad yet composition-sensitive nanoemulsion region. The formulation associated with the widest nanoemulsion area, at an olive oil:Smix ratio of 1:12, suggests that the selected excipient combination was well suited for stabilizing the system. This result is important because it links the diagrammatic formulation space directly to the measured physical behavior of the system.

Particle size analysis further supported these findings. All three selected formulas produced particle sizes in the range of 11–13 nm, which is clearly within the accepted nanoemulsion domain of 1–100 nm. Such small droplet sizes are desirable because they increase the surface area available for dispersion and can improve the efficiency of drug release and interaction with biological membranes. The formation of small droplets is also favored by increased surfactant and co-surfactant concentrations, which reduce interfacial tension by adsorbing around the droplet interface.[22] In this study, the size results were consistent with the high transmittance values, confirming that the formulations successfully formed nanoscale dispersions rather than coarse emulsions. Furthermore, to prove the absence of aggregation potential of the SNEDDS, a zeta potential test was carried out to determine the resistance rate between particles, a particle size test as well as a polydispersity index was carried to find out the size range and the uniformity of the particles.

The zeta potential data provided additional evidence of formulation stability. Zeta potential reflects the electrostatic repulsion between adjacent particles in a dispersed system and is therefore closely related to resistance against aggregation.[23] A higher magnitude of zeta potential generally indicates stronger interparticle repulsion and better stability during storage.[24] In this study, two of the three formulas showed zeta potential values within the approximate range of ±10 to ±30 mV, which suggests moderate electrostatic stability. Formula 2 and Formula 3 therefore appeared more stable than Formula 1, which showed a lower zeta potential and was considered less stable because weaker surface charge can promote coagulation or flocculation. This interpretation is directly supported by the data and is important because zeta potential is one of the key indicators of long-term physical stability in SNEDDS systems. Polydispersity index (PDI) results added another important layer of interpretation. PDI reflects the uniformity of particle size distribution, which is critical for predicting consistency and long-term stability. A PDI below 0.5 generally indicates a relatively uniform system, whereas broader size distribution can lead to aggregation or precipitation over time.[25] In this study, all three formulas had PDI values below 0.5, showing that the particles were reasonably uniform in size. Among them, Formula 3 had the smallest particle size and the lowest PDI, making it the most favorable formulation from the standpoint of both nanoscale dimension and homogeneity. This combination is particularly important because a small mean size alone is not sufficient if the size distribution is broad or unstable.

The superiority of Formula 3 was further reinforced by its morphology. Spherical shape is generally regarded as the ideal morphology for SNEDDS because it reflects thermodynamically favorable droplet organization.[26] Spherical droplets have the smallest surface-area-to-volume ratio, which helps minimize interfacial tension between oil and water phases and reduces the likelihood of coalescence. This contributes to physical stability and lowers the chance of droplet merging during storage. In addition, spherical morphology may facilitate interaction with biological membranes because smooth, symmetrical droplets tend to behave more consistently during dispersion and transport.[27,28] From a formulation standpoint, spherical particles also support more uniform quality control and more consistent drug release behavior. Therefore, the spherical morphology observed by TEM is fully aligned with the particle size, zeta potential, and PDI results, strengthening the overall conclusion that Formula 3 was the best SNEDDS formulation.

Taken together, the data show a clear progression from extraction to formulation and characterization. UAE with 70% ethanol produced a propolis extract containing the expected classes of bioactive compounds, providing a suitable starting material for nanoformulation. The SNEDDS optimization study then demonstrated that propolis could be successfully incorporated into an olive oil–Tween 80–PEG 400 system, but only within a defined compositional window. The ternary phase diagram, transmittance values, particle size distribution, zeta potential, PDI, and TEM morphology all converged to identify Formula 3 as the best formulation. Overall, these findings indicate that propolis-loaded SNEDDS can be successfully developed using this excipient system, although additional studies on storage stability, release behavior, and biological performance would still be needed to fully support product development.

Conclusion

The formulation of propolis-loaded SNEDDS with different Tween 80 and PEG 400 ratios significantly affected its physicochemical characteristics. Based on the optimization results, the nanoemulsion region was obtained at olive oil concentrations of 8.3-12.5%, Tween 80 concentrations of 56.9-84.6%, and PEG 400 concentrations of 7.7-23.1%. Among the tested formulas, Formula 3 with an olive oil:Tween 80:PEG 400 ratio of 1:9:3 showed the best overall performance, with a transmittance value of 89.367%, particle size of 11.067 nm, polydispersity index of 0.189, and zeta potential of -23.833 mV. These results indicate that Formula 3 produced a clear, nanosized, and relatively stable dispersion based on the measured physicochemical parameters. Overall, the study demonstrates that propolis can be successfully incorporated into a SNEDDS system, and that optimization of the surfactant and cosurfactant ratio is critical to obtaining favorable formulation characteristics. From a future clinical perspective, this optimized formulation may serve as a promising starting point for further development of propolis-based delivery systems, particularly for applications where improved dispersion and formulation stability are desirable. Nevertheless, any potential clinical relevance remains preliminary and should be confirmed through additional studies on storage stability, release behavior, permeation, pharmacokinetics, and biological efficacy before therapeutic claims can be made.

Authors' Contribution

AKN contributed to data curation, formal analysis, investigation, methodology, visualization, and preparation of the original draft manuscript. UKSR contributed to the conceptualization of the study, supervision, validation of the findings, funding acquisition, and critical review and editing of the manuscript. DDAK contributed to supervision, validation, and critical review and editing of the manuscript. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare no conflict of interest.

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