Pharmacy Education (2024) 24(3) 304 - 309
https://doi.org/10.46542/pe.2024.243.304309

IGSCPS SPECIAL EDITION

RESEARCH ARTICLE

Formulation of self-nanoemulsifying drug delivery system (SNEDDS) of combined 70% ethanolic of *Begonia medicinalis* herbs and *Moringa oleifera* leaves

Nur Asita[1], Muhammad Sulaiman Zubair[2], Yandi Syukri[1], Evi Sulastri[2]

[1] Departement of Pharmacy, Faculty of Mathematics and Natural Sciences, Indonesia Islamic University, Yogyakarta, Indonesia
[2] Departement of Pharmacy, Faculty of Mathematics and Natural Sciences, Tadulako University, Palu, Central Sulawesi, Indonesia

Keywords
B. medicinalis
Characterisation
Combination
M. oleifera
SNEDDS
Stability

Correspondence
Muhammad Sulaiman Zubair
Department of Pharmacy
Faculty of Mathematics and Natural Sciences
Tadulako University
Central Sulawesi
Indonesia *sulaimanzubair@untad.ac.id*

Abstract

Background: Benalu batu (*Begonia medicinalis*) and kelor leaves (*Moringa oleifera*) are empirically used as alternative therapies by people in Central Sulawesi to maintain their health. Our previous research showed that the combination of these two plant extracts possessed an immunomodulatory activity. Self-Nanoemulsifying Drug Delivery System (SNEDDS) formulation was performed to improve the extract's bioavailability, solubility and stability. **Objective**: This study aims to formulate and characterise SNEDDS preparations of combined ethanolic extract of *B. medicinalis* herbs and *M. oleifera* leaves and further test its stability. **Method**: SNEDDS formulation was started by screening for proper oil, surfactant, and co-surfactant. The formula was then optimised using a ternary phase diagram and characterisation. The stability test was performed using centrifugation, heating-cooling, and freeze-thaw cycles. **Results**: The optimal SNEDDS formula consists of isopropyl myristate (10%), tween 80 (50%) and propylene glycol (40%). The characterisation values obtained were: Transmittance value 83.785 ± 0.275%, particle size 18.666 ± 0.208 nm, polydispersity index 0.664 ± 0.0085, and zeta potential -39.20 ± 0.2 mV. The formula was stable during three stability evaluation tests. **Conclusion**: The optimal formula met the SNEDDS characteristics requirements and showed good stability.

Introduction

Medicinal plants are abundant in Indonesia and have long been used as herbal medicine to treat various diseases. According to the National Basic Health Survey, herbal medicine is used by between 40% and 59% of the population in Indonesia (Harvey *et al.*, 2015; WHO, 2019). These plants include benalu batu (*Begonia medicinalis*) and kelor (*Moringa oleifera*).

The efficacy of Benalu batu (*B. medicinalis*) has been proven in several studies. This plant reportedly showed cytotoxic activity against cancer cell lines of HCT-116 and MCF-7 (Zubair *et al.*, 2020). Meanwhile, Kelor (*M. oleifera*) leaf extract was reported to improve the immune system, increase the activity and capacity of macrophages, the percentage of eosinophil cells, banded neutrophils, lymphocytes, as well as reduce the percentage of neutrophil segments and monocytes from male white rats (Husni *et al.*, 2021). Previous studies showed that the combination of 70% ethanol extract of *B. medicinalis* and *M. oleifera* leaves with a dose of 100: 100 mg/Kg BW exhibited an immunostimulant property by increasing macrophage phagocytosis activity and TNF-α/IFN-γ levels in Wistar rat infected with *Staphylococcus aureus* (Zubair *et al.*, 2022).

The oral route of administration is more widely preferred and convenient, but poor aqueous solubility

is the cause of low therapeutic efficacy. This is due to poor oral bioavailability, dose proportionality, and high intra- and inter-subject variability (Kassem *et al.*, 2016). A Self-Nanoemulsifying Drug Delivery System (SNEDDS) formulation can be used to address these limitations. SNEDDS formulations have gained widespread recognition within the herbal product development sphere due to their capacity to augment solubility and bioavailability. Previous investigations concerning propolis extract showed the stability of SNEDDS formulations, as evidenced by the absence of precipitation or phase separation during assessments (Fitria *et al.*, 2021).

The literature review explains that using medicinal plants orally has limitations in increasing bioavailability and stability. Therefore, this study aims to formulate and characterize the SNEDDS preparation of a combination of *B. medicinalis* and *M. oleifera* leaves extracts as a potential drug delivery system that can increase the bioavailability and stability.

Methods

Design

This experimental study was conducted in the laboratory using a combined 70% ethanolic extract of *B. medicinalis* herb and *M. oleifera* leaves, which was then formulated into a solid-SNEDDS preparation.

Materials

B. *medicinalis* herb was obtained from Toddopoli village, Soyojaya district, North Morowali, Central Sulawesi Province, while kelor (M. oleifera) leaves were collected from Sibedi village, Marawola District, Sigi Regency, in February 2022. Each sample was identified at UPT Herbarium, Tadulako University with the number: 253/UN.28.UPT-SDHS/LK/2021. The materials used included Aquadest, 70% ethanol, Oleum Rosae, Virgin Coconut Oil (VCO), Castor, Olive, Sesame, and Sun Flower oil, Oleic Acid, Fennel Oil, Labrasol, Isopropyl myristate, Capryol 90. Cremophor RH40, Tween 80, Tween 20, PEG 400, and Propylene glycol.

SNEDDS dosage formulation

Oils, surfactants, and co-surfactants were selected as carriers due to their ability to provide the best solubility for the *B. medicinalis* and *M. oleifera* extract. To test for solubility, 100 mg of extract was dissolved in each carrier, beginning with the smallest volume and progressing sequentially from 0.1, 0.25, 0.5, 0.75, 1.0, 1.25, to 1.5 mL. The sample with the smallest amount but the greatest solubility was selected as the carrier. Formulas optimised by using ternary phase diagram were prepared by mixing SNEDDS with a volume of 5 ml (without active substance) as well as concentrations of oil (10-50%), surfactant (10-80%), and co-surfactant (10-40%) with oil: smix ratio (1 9, 2:8, 3:7, 4:6, 5:5). Visual observations of nanoemulsion formation with clarity parameters were carried out. In contrast, UV-Vis spectrophotometer (Shimadzu 1800, Japan) at 650 nm was used to measure transmittance. A ternary phase diagram was created by inputting the oil phase, surfactant, and co-surfactant data into Triplot Software (Fitria *et al.*, 2021).

SNEDDS preparation of combined ethanol extract of *B. medicinalis* and *M. oleifera* leaves was carried out by weighing 100 mg of extract (100 mg/mL) with a mixture of oil, surfactant, and co-surfactant using ultrasonication (model 300 V/T, USA) until a homogeneous sample was formed (Fitria *et al.*, 2021).

Characterisation and evaluation of SNEDDS formula

The SNEDDS formula was characterised by 100-fold dilution using aquabidest. The measurement of % transmittance was carried out using a UV-Vis spectrophotometer (Shimadzu UV 1800, Japan) at a wavelength of 650 nm with aquabidest as a blank. The particle size, zeta potential, and polydispersity index were determined using the Dynamic Light Scattering (DLS) method on a Particle Size Analyzer (Horiba SZ 100, Japan) (Inugala *et al.*, 2015; Fitria *et al.*, 2021).

Thermodynamic stability test

Thermodynamic stability examination included centrifugation, heat-cold cycling, and freeze-thaw cycling tests. Formulas were prepared with 25× dilutions using distilled water, then the centrifugation test was performed at 3500 rpm for 15 minutes. Heat and cooling cycles were carried out in three cycles at a temperature range of 4°C and 45°C for a minimum storage duration of 48 hours. The freeze-thaw cycle test was conducted in three freeze-thaw cycles at temperatures between -20°C and +25°C with storage at each temperature not less than 48 hours followed by centrifugation for 15 minutes at 3500 rpm (Inugala *et al.*, 2015; Fitria *et al.*, 2021).

Robustness to dilution and accelerated stability test

Samples were diluted 25, 50, 100, and 250 times using distilled water, then the changes in % transmittance value, particle size, polydispersion index, and zeta potential value were evaluated (Fitria *et al.*, 2021).

The accelerated stability test was conducted by placing the formulations into a climatic chamber at high temperature (40° ± 2°C) and relative humidity (75 ±

5%). The changes in characteristics such as % transmittance, zeta potential, and particle size were measured using a UV-Vis spectrophotometer and particle size analyser in weeks 0, 1, 2, 3, and 4 with 100x dilution (Fitria *et al.*, 2021).

Results

Solubility test and optimisation of oil, surfactant and co-surfactant resulted in isopropyl myristate, sun flower oil and VCO as oil phase, Tween 80 as surfactant and Propylene glycol as co-surfactant which gave the best solubility. The composition of each phase is presented in the form of a ternary phase diagram in Figure 1. The nanoemulsion region is illustrated in the blue symbol and the turbid microemulsion region is shown in the red symbol. The phase mixtures with the largest nanoemulsion area are Isopropyl, Tween 80 and Propylene glycol.

The characterisation results show that 12 formulas have a percent transmittance value above 80% so that it can be said that the solution is clear and the particle size is below 100 nm (Table I). The polydisperty index value obtained from the SNEDDS formula is in the range of 0.31-0.66. The zeta potential results in the table indicate that the preparation has a value of -12.27 mV to -41.97 mV. There are 11 formulas that have zeta potential values above -30 mV, based on the previous explanation, it shows that the SNEDDS formula is stable. Based on the characterisation results, 12 best formulas were obtained which will be evaluated in the thermodynamic stability test.

The thermodynamic test results found 5 stable formulas, namely F2, F4, F5, F6 and F9, which were characterised by no precipitation and phase separation. Formulas that are stable in the thermodynamic stability test will be tested for dilution resistance.

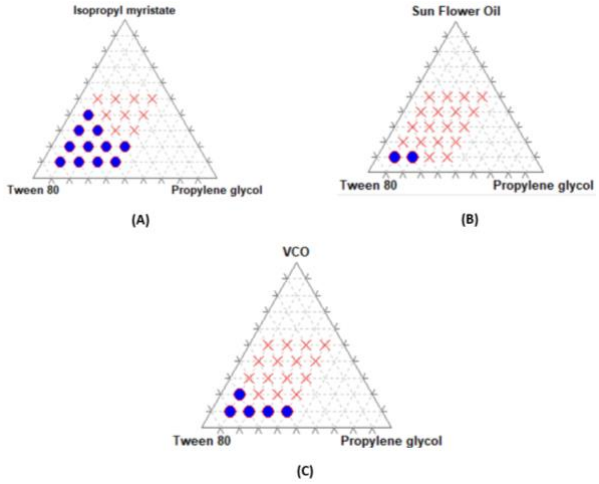

Figure 1: Pseudo ternary phase diagram showing the o/w nanoemulsion regions (A); Isopropyl myristate, Polysorbate 80 and Propylenglycol (B); Sun Flower Oil, Polysorbate 80 and Propylenglycol (C); VCO, Polysorbate 80 and Propylenglycol

Table I: Characterisation and stability test of SNEDDS formulas of combined extract of *B.medicinalis* and *M. oleifera* leaves

Formulation	Characterisation				Stability test		
	Transmittance (%)	Particle size (nm)	Polydispersity index	Zeta potential (mV)	Centrifugation test	Heating-cooling cycle test	Freeze-thaw cycle test
F1	87.67±0.06	16.43±0.40	0.48±0.04	-41.97±0.21	Precipitate	ND	ND
F2	84.77±0.04	17.53±0.45	0.57±0.02	-34.07±0.32	Stable	Stable	Stable
F3	83.53±0.05	18.27±0.46	0.53±0.01	-33.10±0.36	Precipitate	ND	ND
F4	83.79±0.27	18.67±0.21	0.66±0.01	-39.20±0.20	Stable	Stable	Stable
F5	87.78±0.15	17.33±0.06	0.31±0.02	-32.13±0.47	Stable	Stable	Stable
F6	83.19±0.31	18.47±0.21	0.62±0.01	-32.90±0.46	Stable	Stable	Stable
F7	84.28±0.20	23.70±0.66	0.40±0.01	-36.33±0.25	Precipitate	ND	ND
F8	84.86±0.18	20.53±0.15	0.66±0.03	-31.17±1.10	Precipitate	ND	ND
F9	86.81±0.16	24.40±0.10	0.46±0.004	-37.73±0.32	Stable	Stable	Stable
F10	82.67±0.11	26.53±0.95	0.40±0.004	-29.00±0.61	Stable	Unstable	Unstable
F11	80.21±0.72	51.33±0.46	0.41±0.01	-30.53±0.35	Stable	Unstable	Unstable
F12	26.26±0.58	113.53±0.15	0.50±0.002	-18.33±1.38	ND	ND	ND

Formulation	Characterisation				Stability test		
	Transmittance (%)	Particle size (nm)	Polydispersity index	Zeta potential (mV)	Centrifugation test	Heating-cooling cycle test	Freeze-thaw cycle test
F13	85.01±0.27	57.07±0.84	0.47±0.01	-35.87±1.90	Stable	ND	ND
F14	27.55±0.48	131.60±0.56	0.38±0.01	-22.77±0.64	ND	ND	ND
F15	3.62±0.04	148.47±1.98	0.38±0.01	-18.60±0.26	ND	ND	ND
F16	0.37±0.01	166.77±4.18	0.50±0.02	-13.10±0.36	ND	ND	ND
F17	6.78±0.32	126.90±0.56	0.34±0.01	-19.57±0.84	ND	ND	ND
F18	0.68±0.01	137.57±1.40	0.36±0.02	-12.67±0.61	ND	ND	ND
F19	0.95±0.03	146.43±0.57	0.41±0.01	-12.27±0.55	ND	ND	ND
F20	1.18±0.06	213.03±2.63	0.47±0.01	-13.23±0.60	ND	ND	ND

ND: Not Determined

The SNEDDS formulation of the combination of B. *medicinalis* and M. *oleifera* leaf extracts to resemble in-vivo conditions is carried out with double dilution 25, 50, 100, and 250 times. Formulations that are stable in thermodynamic stability evaluation, namely F2, F4, F5, F6 and F9, are tested for dilution resistance. Based on the table, five stable formulas were obtained against several levels of dilution, namely F2, F4, F5, F6 and F9. Stable formulas will be continued in accelerated stability testing (Table II).

The accelerated stability test results show that 3 formulas, F2, F4, and F6, were stable during the 4-week stability test process. The formulas did not experience significant changes from their original state and did not exceed the ideal criteria for a nanoemulsion to be declared stable.

Table II: Robustness to dilution test and accelerated stability test of SNEDDS formulas of combined extract of *B.medicinalis* and *M. oleifera* leaves

Formulation	Dilution	Robustness to dilution test			
		Transmittance (%)	Particle size (nm)	Polydispersity index	Zeta potential (mV)
F2	25	63.87±0.12	20.07±0.61	0.51±0.02	-17.63±0.45
	50	77.41±0.48	19.97±0.45	0.48±0.01	-21.90±0.36
	100	83.39±0.17	20.70±0.26	0.52±0.02	-30.23±0.31
	250	94.29±0.08	18.77±0.32	0.51±0.03	-34.23±0.90
F4	25	58.12±0.08	21.67±0.31	0.46±0.004	-16.80±0.70
	50	74.29±0.11	21.30±0.36	0.52±0.01	-22.60±0.53
	100	83.12±0.14	23.03±0.21	0.58±0.02	-35.53±0.25
	250	94.31±0.52	22.17±0.71	0.28±0.08	-36.03±0.35
F5	25	68.13±0.10	19.57±0.15	0.39±0.01	-20.60±0.89
	50	78.99±0.25	19.63±0.21	0.36±0.01	-28.03±0.25
	100	85.49±0.15	18.83±0.64	0.36±0.01	-29.50±0.36
	250	93.86±0.19	18.20±0.10	0.46±0.03	-34.40±1.25
F6	25	56.70±0.35	170.00±5.86	0.74±0.04	-15.50±0.70
	50	75.85±0.38	29.30±0.70	0.78±0.01	-21.33±0.15
	100	82.86±0.29	28.70±0.50	0.68±0.02	-27.23±0.25
	250	94.29±0.20	27.43±0.06	0.71±0.03	-33.87±0.45
F9	25	67.02±0.33	110.73±0.68	0.49±0.002	-22.17±0.25
	50	77.34±0.40	68.93±0.64	0.68±0.01	-22.03±0.67
	100	86.71±0.25	75.20±0.44	0.45±0.04	-36.13±0.85
	250	94.06±0.14	68.13±0.90	0.48±0.01	-33.73±2.57

		Accelerated stability test			
Formulation	**Weeks**	**Transmittance (%)**	**Particle size (nm)**	**Polydispersity index**	**Zeta potential (mV)**
F2	4	83.08±0.14	21.33±0.51	0.56±0.04	-30.70±0.46
F4	4	83.40±0.45	20.77±0.57	0.42±0.03	-31.03±0.55
F5	4	91.65±0.35	14.50±0.70	0.14±0.03	-24.17±0.87
F6	4	83.27±0.34	20.83±0.32	0.35±0.01	-29.53±0.64
F9	4	88.18±0.54	19.93±0.21	0.31±0.18	-26.4±1.05

Discussion

Solubility test

The oil selection process plays an important role in SNEDDS formulation to ensure the production of a stable preparation. Superior solubility of the drug in the carrier is essential to maintain the dissolved form and avoid precipitation upon dilution in the intestinal lumen (Khan *et al.*, 2015). The oil solubility test results based on the optimisation results were VCO, isopropyl myristate and sunflower oil. The surfactant that could dissolve both extracts was tween 80 as the most effective solvent for solubility. Meanwhile, the co-surfactant Propylene glycol could solubilise both extracts, with propylene glycol showing the highest solubility. Tween 80 is a nonionic surfactant widely used in cosmetics, food products, and pharmaceutical formulations. Tween 80 tends to be safer to use as it is non-toxic and non-irritating. Propylene glycol is used in various pharmaceutical formulations and is generally considered a relatively non-toxic ingredient (Kassem *et al.*, 2016).

Optimisation of SNEDDS formulation base

Optimisation was performed to determine the ideal oil for SNEDDS formulation. The exploration continued by creating a pseudo-ternary phase diagram. The creation of this diagram was facilitated using Triplot software. The pseudo-ternary phase diagram was created by mixing oil, surfactant, and co-surfactant (Fitria *et al.*, 2021). A total of 3 oils (Isopropyl myristate, VCO, and sunflower oil) were mixed with tween 80 (surfactant) and propylene glycol (co-surfactant), resulting in 20 formulas. Based on the results, the oil blend containing Isopropyl myristate emerged with the most extensive nanoemulsion domain. The blue marker indicates that the formulation produced a perfect nanoemulsion (Figure 1). The increase in nanoemulsion area is due to the increased adsorption of surfactant molecules at the oil-water interface, leading to decreased interfacial tension, facilitating the formation of smaller droplets. It also occurs due to the large volume of surfactant that diffuses from the oil phase to the water phase, thus forming finer oil droplets (Khan *et al.*, 2015).

Characterisation and stability test of SNEDDS formulation

The percentage transmittance is an important parameter to determine the isotropic properties of the system. Values close to 100% indicate an isotropic formulation and globular size in the nanometer range (Khan *et al.*, 2015). The presence of 12 formulations exhibiting transmittance values surpassing 80%, unequivocally indicating their clarity. Particle size is one of the most important nanoemulsion characteristics for stability evaluation and a crucial step in improving drug bioavailability (Kassem *et al.*, 2016). The term polydisperty index describes the degree of particle non-uniformity (Hayati *et al.*, 2021). The results obtained from the formulas ranged from 0.31-0.66, with a reference value below 0.7. This indicates that the particle size is well-distributed or homogeneous (Fitria *et al.*, 2021). Zeta potential indicates the degree of repulsion between adjacent similarly charged particles in a dispersion. Values higher than +30 mV or lower than -30 mV provide good stability by preventing particle aggregation due to high repulsive forces (Kassem *et al.*, 2016; Fitria *et al.*, 2021). The zeta potential results indicated that the formulations had a value of -12.27 mV to -41.97 mV.

Stability evaluation, in the form of thermodynamic stability studies, is carried out to determine the preparation's physical stability, including precipitation, creaming, and coalescence. These tests were carried out through centrifugation and heating-cooling and freezing-thawing cycles to evaluate stability with phase separation and precipitation parameters (Fitria *et al.*, 2021). The results showed five thermodynamically stable formulas (F2, F4, F5, F6, and F9) that did not experience precipitation and phase separation.

Robustness to dilution test and accelerated stability test

Robustness to Dilution Test aims to determine the resistance and uniformity of the character of several dilution levels. This test is used to assess the drug release rate and the possibility of dilution factors causing precipitation, which can interfere with the

process of drug absorption rate (Fitria *et al.*, 2021). Based on the results, formulas F2, F4, F5, F6, and F9 are stable preparations. No signs of precipitation or phase separation were observed at dilution. These results confirm the stability and suitability of the nano-emulsions formed for oral use (Abd-Elhakeem *et al.*, 2019). The accelerated stability test was conducted to evaluate the effect of storage conditions on the stability of SNEDDS formulations under controlled conditions at 40 ° C ± 2 ° C / 75% RH ± 5% RH (Fitria *et al.*, 2021). Three formulas remained stable during the four-week test period that are F2, F4, and F6. Formulations that showed minimal change from the initial conditions and remained within the desired parameters were stable nanoemulsions (Fitria *et al.*, 2021).

Based on the study's results, the combination of B. medicinalis extract and M. oleifera leaves can be developed into SNEDDS preparations. This preparation can increase its solubility and stability, and it can be continued to test its pharmacological activity so that it can be developed into a product.

Conclusion

In conclusion, the optimal formula of SNEDDS preparation was achieved using isopropyl myristate (10%), tween 80 (50%), and propylene glycol (40%). The characterisation values obtained for optimal formula (F4) were as follows: transmittance (83.79±0.275%), particle size (18,66±0.208 nm), polydispersity index (0.66±0.0085), and zeta potential (-39.20±0.2 mV). This formula remained stable during the evaluation process, which included thermodynamic, durability, and accelerated stability tests conducted for four weeks.

Acknowledgement

Authors acknowledge The Directorate General of Higher Education, Research and Technology, The Ministry of Education, Culture, Research and Technology, Republic of Indonesia, for the financial support through *Penelitian Kerjasama Dalam Negeri 2023* grants with the contract number 1462.a/UN28.2/PL/2023 to author (Zubair, MS).

Source of funding

The Directorate General of Higher Education, Research and Technology, The Ministry of Education, Culture, Research and Technology, Republic of Indonesia.

References

Abd-Elhakeem, E., Teaima, M. H., Abdelbary, G. A., & El Mahrouk, G. M. (2019). Bioavailability enhanced clopidogrel -loaded solid SNEDDS: Development andin-vitro/in-vivo characterization. *Journal of Drug Delivery Science and Technology*, **49**(December 2018), 603–614. https://doi.org/10.1016/j.jddst.2018.12.027

Fitria, A., Hanifah, S., Chabib, L., Uno, A. M., Munawwarah, H., Atsil, N., Pohara, H. A., Weuanggi, D. A., & Syukri, Y. (2021). Design and characterization of propolis extract loaded self-nano emulsifying drug delivery system as immunostimulant. *Saudi Pharmaceutical Journal*, **29**(6), 625–634. https://doi.org/10.1016/j.jsps.2021.04.024

Harvey, A. L., Edrada-Ebel, R., & Quinn, R. J. (2015). The re-emergence of natural products for drug discovery in the genomics era. *Nature Reviews Drug Discovery*, **14**(2), 111–129. https://doi.org/10.1038/nrd4510

Hayati, F., Chabib, L., Sekarraras, F. D., & Faizah, W. S. (2021). Antihyperglycemic activity of Centella asiatica (L.) Urb. leaf ethanol extract SNEDDS in zebrafish (Danio rerio). *Open Chemistry*, **19**(1), 184–188. https://doi.org/10.1515/chem-2021-0200

Husni, E., Badriyya, E., Putri, L., & Aldi, Y. (2021). The effect of ethanol extract of moringa leaf (moringa oleifera lam) against the activity and capacity of phagocytosis of macrofag cells and the percentage of leukosit cells of white mice. *Pharmacognosy Journal*, **13**(3), 706–712. https://doi.org/10.5530/pj.2021.13.90

Inugala, S., Eedara, B. B., Sunkavalli, S., Dhurke, R., Kandadi, P., Jukanti, R., & Bandari, S. (2015). Solid Self-Nanoemulsifying Drug Delivery System (S-SNEDDS) of darunavir for improved dissolution and oral bioavailability: In vitro and in vivo evaluation. *European Journal of Pharmaceutical Sciences*, **74**, 1–10. https://doi.org/10.1016/j.ejps.2015.03.024

Kassem, A. A., Mohsen, A. M., Ahmed, R. S., & Essam, T. M. (2016). Self-Nanoemulsifying Drug Delivery System (SNEDDS) with enhanced solubilization of nystatin for treatment of oral candidiasis: Design, optimization, in vitro and in vivo evaluation. *Journal of Molecular Liquids*, **218**, 219–232. https://doi.org/10.1016/j.molliq.2016.02.081

Khan, A. W., Kotta, S., Ansari, S. H., Sharma, R. K., & Ali, J. (2015). Self-Nanoemulsifying Drug Delivery System (SNEDDS) of the poorly Wwater-soluble grapefruit flavonoid naringenin: Design, characterization, in vitro and in vivo evaluation. *Drug Delivery*, **22**(4), 552–561. https://doi.org/10.3109/10717544.2013.878003

WHO. (2019). *WHO Global report on traditional and complementary medicine 2019*. World Health Organization. https://apps.who.int/iris/bitstream/handle/10665/312342/9789241515436-eng.pdf?ua=1

Zubair, M. S., Alarif, W. M., Ghandourah, M. A., Anam, S., & Jantan, I. (2020). Cytotoxic activity of 2-o-β-glucopyranosil cucurbitacin d from benalu batu (Begonia sp.) growing in Morowali, Central Sulawesi. *Indonesian Journal of Chemistry*, **20**(4), 766–772. https://doi.org/10.22146/ijc.43626