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RESEARCH ARTICLE

Characteristic and Formulation Turmeric Extract Nanoemulsion as Alternative Moisturizer in Atopic Dermatitis

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ABSTRACT:

Currently, many moisturizers are developed with anti-inflammatory ingredients intended for mild and moderate atopic dermatitis (AD). One of the ingredients that can be developed is turmeric (*Curcuma longa*), which has potent anti-inflammatory activity. However, turmeric topical treatments require nano formulas due to their limited skin absorption. This study aims to obtain the optimal formulation of turmeric extract nanoemulsion as an alternative moisturizer for AD. The nanoemulsions are made by a self-nanoemulsifying drug delivery system (SNEDDS) using a simplex lattice design (SLD). Based on the solubility test, the oil components were sunflower oil, tween 80 as a surfactant, and polyethylene glycol (PEG) 400 as cosurfactant with a ratio of 1:8:1. The SNEDDS formulation was analyzed using software design expert version 10.03. The optimum SNEDDS formulation characteristic included an average droplet size of 13.37nm, an average polydispersity index (PDI) of 0.179, an average transmittance of 81.53%, and an average zeta potential of -38.57mV. Based on these results, it can be concluded that the turmeric extract formula meets the nanoemulsion criteria because the average droplet size is <200nm, the droplet distribution is relatively homogeneous as illustrated by the small average PDI, the transmittancesare above 80%, and is relatively stable with a zeta potential >±30mV.

KEYWORDS: Turmeric extract, PEG 400, SNEDDS, Sunflower oil, Tween 80.

INTRODUCTION:

Atopic dermatitis (AD) is a chronic inflammatory skin disorder that can affect patients' and their families' quality of life, as well as social and economic issues.

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The skin barrier dysfunction is an early step in the development of AD,[1] which facilitates the entry of allergens, resulting in the initiation and sensitization of allergies and exacerbations of inflammation.[2] Various therapeutic guidelines consistently recommend the use of moisturizers to maintain the skin barrier and prevent AD.[3]

Recently, many moisturizers with anti-inflammatory ingredients have been developed to reduce mild-to-moderate AD symptoms. Adding active ingredients to the moisturizer can improve the skin barrier function and control skin dryness.[4] One of the anti-inflammatory ingredients that might be added to a moisturizer is turmeric (*Curcuma longa*). Turmeric contains curcuminoids, such as curcumin (CUR), demethoxycurcumin, and bisdemethoxycurcumin.[5] Curcumin possesses potent anti-inflammatory properties,[6] inhibiting inflammatory enzymes, cytokines, transcription factors, and intercellular signaling proteins.[7]

One of the disadvantages of using turmeric in topical preparations is CUR's poor solubility in water and low absorption on the skin,[8] so it needs to be made in nanoparticles or nanosystems. Nanosystems can increase the solubility of hydrophobic drugs and drug bioavailability.[9] Nanoemulsion, a dispersion of water and oil phases stabilized by surfactants, is one type of nanosystem.[10] The advantages of nanoemulsion is increasing the solubility and bioavailability of lipophilic compounds, having a small droplet size, and being transparent.[11] In the case of AD, no research has ever been conducted on the use of nanoemulsions of turmeric extract in moisturizing preparations. This research aims to examine the best formulation of turmeric extract nanoemulsion as an alternative moisturizer for AD.

MATERIALS AND METHODS:

Materials:

a) Research tools and materials:

The tools in this study were analytical balance, measuring cup, magnetic stirrer, overhead stirrer (IKA RW 20), conical flask, water bath, micropipette (Eppendorf), sonicator, stopwatch, UV-Visspectrophotometer (thermogenesis 10), viscotester Rion VT- 6, particle size analyzer (Horiba, Japan), GC-MS-QP2010S, pH meter, vortex mixer (Ohaus). Research materials include turmeric powder (Materia Medika Batu, Malang), 70% ethanol, oleic acid, tween 80, tween 20, span 20, propylene glycol, PEG 400, and distilled water (PT. Brataco), grape seed oil, rice bran oil, isopropyl myristate, sunflower oil, olive oil, and virgin coconut oil (VCO).

b) Turmeric extract Preparation:

A 500g of turmeric powder was macerated in 1000mL of 70% ethanol and allowed to stand for 24hours. The extract was filtered, and the filtrate was obtained first. Then, the simplicia dregs were added again with 1:2 solvent and allowed to stand for 24 hours. The procedure was repeated until the filtrate was obtained for three days. Finally, the whole filtrate was spun by evaporation using a rotatory vacuum evaporator at 60ºC to obtain a thick extract. The content of curcuminoids in turmeric extract was examined using the high-performance thin-layer chromatography (HPLC) method.

c) Turmeric extract solubility test:

The solubility test was carried out by dissolving 100 mg of turmeric extract into 1mL of carrier oil, surfactant, or cosurfactant; the mixing was performed using a magnetic stirrer at 2500 rpm for five minutes. Then, the test material was centrifuged at 6500rpm for 10 minutes and allowed to stand for 24 hours. The amount of dissolved extract was calculated based on the difference in the weight of the initial extract added and the weight remaining after centrifugation.

d) Determination of the self-nanoemulsifying drug delivery system (SNEDDS) turmeric extract components:

The SNEDDS turmeric extract was made by stirring several oils, surfactants, and cosurfactants at a rate of 700rpm for one hour at a temperature of 40ºC. (mixture A). Next, 100mg/mL SNEDDS-concentrated Turmeric ethanol extract was added to mixture A by stirring (700rpm; 40ºC) for 2 hours.

e) Optimization of SNEDDS composition of turmeric extract:

The SNEDDS composition was optimized by determining the upper and lower limits of surfactants and cosurfactants. The upper and lower limits of optimization values are then entered into the Design-Expert software version 10.03 on the simplex lattice design (SLD) menu.

f) Determination of the optimum formula for SNEDDS turmeric extract:

Selection of the optimum formula based on droplet size parameters, polydispersity index (PDI), transmittance, andzeta potential through the optimization menu in the software. Transmittance was assessed using a UV-Vis spectrophotometer (thermogenesis 10), with a wavelength of 650nm, and distilled water as a blank. The Horiba SZ-100 particle size analyzer (PSA) assessed droplet size, PDI, and zeta potential. The criteria for the optimum formula are SNEDDS produced by changes in the composition of surfactants and cosurfactants from the formula with the smallest droplet size and PDI and the largest zeta potential and transmittance value.

Methods:

This research is an experimental study using the simplex lattice design (LSD) technique conducted at the Department of Pharmacology and Therapy, Faculty of Medicine, Udayana University, and College of Pharmacy Mahaganesha, Denpasar, Bali, Indonesia. In addition,Curcuminoid content was examined at the Integrated Research and Testing Laboratory Technical Implementation Unit, Airlangga University, Surabaya, East Java, Indonesia.The turmeric extract nanoemulsion was produced via the self-nano emulsification drug delivery system (SNEDDS).In addition, the droplet size, transmittance, PDI, and zeta potential of turmeric extract SNEDDS were examined at the Islamic University of Indonesia, Yogyakarta, Indonesia. The research was conducted between October 2020 and April 2021.

RESULTS AND DISCUSSION:

Turmeric extract curcuminoids:

The HPLC analysis showed that each mg of turmeric extract contained 68.842±0.874% curcuminoids, consisting of bis-dimethoxy, dimethoxy curcumin, and curcumin. The turmeric extract chromatogram analysis results are listed in (Figure 1).

Turmeric extract solubility test:

The solubility test of turmeric extract was tested on several oils, surfactants, and co-surfactants. The composition of sunflower oil as an oil component, tween 80 as a surfactant, and PEG 400 as a co-surfactant were determined based on the solubility test of turmeric extract.

Determination of SNEDDS constituent components of turmeric extract:

After getting the solubility test results, the mixing test was conducted to determine the composition ratio and transmittance.(Table 1). The appearance of SNEDDS turmeric extract is shown in Figure 2.

The bioavailability of poorly water-soluble drugs,such as curcumin from turmeric,can be improved by formulating them as a self-nano-emulsifying drug delivery system.[12,13]SNEDDS is a single-phase and thermodynamically stable isotropic system consisting of emulsifying oils, water, surfactants, co-surfactants, amphiphilic molecule, and aqueous phases.[14,15]Oil, surfactants, and co-surfactants are essential components of the SNEDDS formulation.[16]Surfactants reduce the tension interface by absorbing into the droplet surface as a monomolecular film and preventing the joining of oil droplets.[11,17]The most common use of surfactants is nonionic surfactants with high hydrophilic-lipophilic balance (HLB) values because they can help the formation of oil emulsion droplets quickly in the water media.[11]Nonionic surfactants are inexpensive and non-toxic biodegradable materials that have recently gained wide popularity for developing improved drug delivery systems.[18]Co-surfactants can decrease interfacial tension between oil and water, adjust the flexibility of the interfacial membrane, and sometimes reduce the amount of surfactant, so it is expected to improve drug solubility and bioavailability for poorly soluble and slowly absorbable drugs.[12]Co-surfactant to the nanoemulsion formula can increase drug loading, speed up emulsification time, and adjust the droplet size.[11]The oil phase can impact nanoemulsion formation and stabilization.[17]

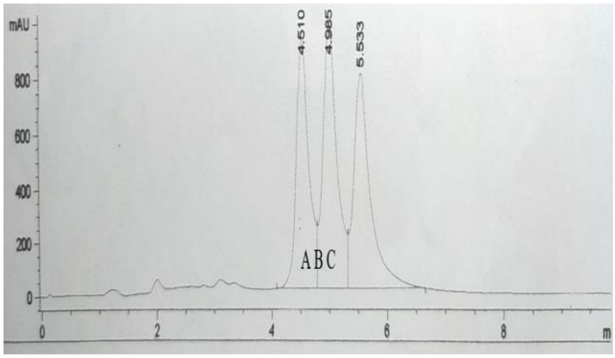

Figure 1: Results of the chromatogram of turmeric extract samples. A: Curcumin (area 15742.0); B: Demethoxycurcumin (area 13938.2); C: Bis-demethoxy curcumin (area 16428.8).

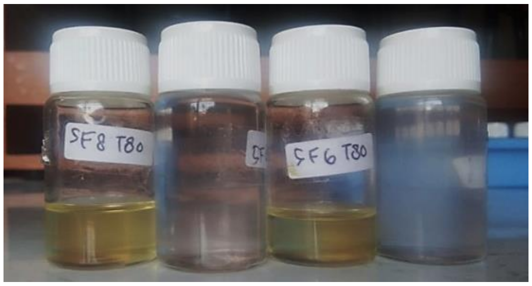

Figure 2: The appearance of SNEDDS turmeric extract

The components of SNEDDS turmeric extract are selected based on the effect of each element when applied to the skin. Sunflower oil is natural oil produced from sunflower seeds containing high essential fatty acids, especially linoleic acid, which can improve skin barrier function.[19,20] Sunflower oil application to the skin has been shown to maintain the integrity of the stratum corneum, increasing skin hydration without causing erythema.[19] Tween 80 is a hydrophilic nonionic surfactant with a high HLB value,[11]with relatively low toxicity,low irritation potential, and widely used in pharmaceutical microemulsion preparations.[21]

Table 1: Comparison of the results of the SNEDDS turmeric extract

Code	Ratio			Composition (mL)			Mixture	(%T) 100x dilution
	Oil	S	Co	Oil	S	Co		
SFO4	1	4	1	0,833	3,333	0,833	Separate	-
SFO6	1	6	1	0,625	3,750	0,625	Homogenous	65,95
SFO8	1	8	1	0,500	4,000	0,500	Homogenous	83,62*

Note: SFO = Sunflower oil; S (surfactant) is Tween 80; Co (cosurfactant) is PEG 400, %T= transmittance

Table 2: Determination of the upper and lower limits of surfactant optimization and SNEDDS cosurfactant turmeric extract

Code	Ratio			Comparison S: Co (%)	Composition (mL)			% T 20x df
	Oil	S	Co		Oil (SFO)	S (*Tween* 80)	Co (PEG 400)	
F1	1	8,550	0,450	95:5	0,5	4,275	0,225	87,495
F2	1	8,325	0,675	93:8	0,5	4,163	0,338	83,384
F3	1	8,100	0,900	90:10	0,5	4,050	0,450	83,011
F4	1	8,00	1,00	89:11	0,5	4,000	0,500	82,992
F5	1	7,875	1,125	88:13	0,5	3,938	0,563	80,924
F6	1	7,65	1,350	85:15	0,5	3,825	0,675	77,452

Note: SFO = Sunflower oil; S (surfactant) is Tween 80; Co (cosurfactant) is PEG 400, %T= transmittance; df= dilution factor

Polyethylene glycol (PEG) 400 is a hydrophilic nonionic surfactant with an HLB value of 11.6,[11] short-chain alcohol that can increase drug absorption, making it suitable for use as a co-surfactant.[22]Previous studies showed that curcumin nanoemulsions with clove oil, tween 80, and PEG 400 combination, produced highly transparent nanoemulsions.[23] Based on the results of mixing and clarity of SNEDDS, the selected components of SNEDDS were SFO (oil), tween 80 (surfactant), and PEG 400 (cosurfactant) with a composition of 1:8:1.

Optimization of the composition of SNEDDS turmeric extract:

After obtaining the SNEDDS composition, the upper and lower limits of surfactant and co-surfactant optimization were determined (Table 2).

Table 2 shows that the surfactant (tween 80) concentration of 85-95% and the cosurfactant (PEG 400) of 5-15% can form an emulsion with good clarity, so this concentration is used as the upper and lower limits of optimization.

Determination of the optimum formula for SNEDDS turmeric extract:

The upper and lower optimization values were entered into the software design expert version 10.03 on the SLD menu, and 8 SNEDDS optimization formulations were tested for transmittances, droplet size, PDI, and zeta potential. The measurement data for the eight optimum formulations are presented in (Table 3).

Based on table 3, it was found that the eight SNEDDS formulas produced a relatively clear emulsion system with transmittance values ranging from 77.452 - 87.495%. The surfactant and oil components affect the percentage of transmittance, especially the surfactant component. Surfactants can increase the clarity rate because the primary function of surfactants is to reduce the surface tension between the oil and water phases so that a tinynanoemulsion droplet is got to produce a transparent nanoemulsion liquid.[11] The eight optimization formulas resulted in an emulsion system with droplet sizes ranging from 12.30 - 15.80nm, which were by the nanodroplet size target (<200nm).In SNEDDS, the droplet size of the emulsion was a crucial factor in self-emulsification performance because it determines the rate and extent of drug release and absorption.[24] A broad droplet size distribution in nanoemulsion shows significant variations in drug loading and release, bioavailability, and efficacy.[11] Droplet size <90nm can increase the stability of nanoemulsion against sedimentation.[17] The droplet size test in this study showed that the eight nanoemulsion systems formed had droplets with relatively homogeneous sizes, as illustrated by the small value of the PDI.

Table 3: Results of characterization of eight optimization formulas for turmeric extract SNEDDS

run	Composition (%) Total volume 4,5 mL		SFO (mL)	Turmeric extract (mg/mL)	Size (nm)	PDI	Zeta Potential (mV)	%T df 20x
	S	Co						
1	95	5	0,5	100	12.70	0.132	-14.9	87.495
2	87,5	12,5	0,5	100	12.30	0.179	-13.0	80.924
3	90	10	0,5	100	12.80	0.196	-28.2	83.011
4	95	5	0,5	100	15.80	0.112	-26.8	85.593
5	92,5	7,5	0,5	100	12.70	0.122	-30.9	83.384
6	85	15	0,5	100	13.80	0.192	-30.8	83.153
7	85	15	0,5	100	13.60	0.318	-41.9	77.452
8	90	10	0,5	100	12.30	0.159	-42.0	80.134
Formula optimum								
rep	Composition (%) Total volume 4,5 mL		SF0 (mL)	Turmeric extract (mg/mL)	Size (nm)	PDI	Zeta Potential (mV)	%T df 20x
	S	Co						
1	91.94	8.06	0,5	100	13.9	0.185	-38.3	81.375
2	91.94	8.06	0,5	100	13.5	0.132	-39.4	80.782
3	91.94	8.06	0,5	100	12.7	0.220	-38.0	82.457
mean			0,5	100	13.9	0.185	-38.3	81.375

Note: S= surfactant; Co= cosurfactant; SFO=Sunflower oil; %T= transmittance; PDI= polydispersity index; df= dilution factor

Table 4: Results of the mathematical model of the relationship between independent variables and optimization parameters

Parameter (y)	Model	Actual equation	Lack of fit
Droplet (size)	Quadratic (p= 0.0008)	Y= + 0.24A + 8.09B – 0.1AB	p= 0.0963
PDI	Linear (p= 0.0170)	Y= +0.00045A + 0.01B	p= 0.8751
Zeta potential	Cubic (p=0.3941)	Y=+2.15A-1966.33B +32.53AB -0.1 AB(A-B)	p =0.0627
%Transmittance	Linear (p= 0.0236)	Y= +0.88A +0.278B	p=0.8620

Note A= Tween 80; B=PEG 400

The PDI of the nanoemulsion system describes the droplet size distribution and the physical stability of a dispersion system.The high PDI indicates that the droplet size distribution is not uniformbecause the droplets aggregate form groups, so they are unevenly dispersed (polydisperse) and cause a decrease in the nanoemulsion stability.[17] A PDI value close to zero indicates a single dispersion system, while a PDI value close to 1.0 indicates that the emulsion has a wide size distribution. The desired formulation characteristic is the high stability of the two components, which cannot be mixed to remain miscible as a single-phase emulsion.[11] The good index value is between 0 (uniform size distribution) to 0.5 (wide size distribution).[17] The PDIfor all selected SNEDDS in this study was found to be below 0.5, which indicated good uniformity in droplet size distribution.

Zeta potential is an indicator that shows the stability of a system containing dispersed particles through repulsion between particles with the same charge when close together. When dissociated in the dispersing medium, the negative ions will approach the particle surface and act as a barrier that reduces the electrostatic attraction between the particles, which can cause the particles to coalesce.[11] The magnitude of the zeta potential value of a nanoparticle system can provide an overview of the stability of the nanoparticle system. The zeta potential value ensures the physical stability of the nanoemulsion must be far from zero, i.e., greater than 30mV or less than -30mV.[25] The zeta potential values for the eight optimization formulas in this study ranged from -13.0 to -42.0mV. A negative value on the results shows that the surface charge of the droplet is negatively charged. The value of zeta potential depends on the composition of the constituent and its dispersion medium.

Analysis with software design expert version 10.03 on the analysis menu was used to determine the effect of surfactants and cosurfactants on each parameter. The relationship is modeled by the mathematical equation shown in (Table 4) and the contour plot in (Figure 3).

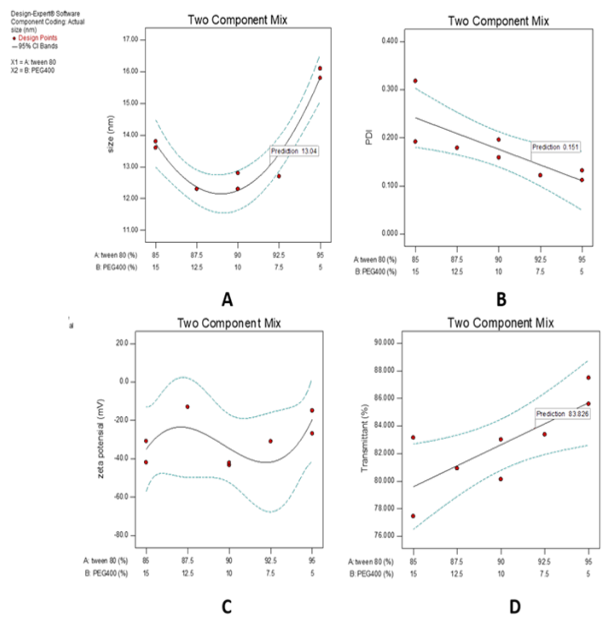

Figure 3: Contour plot of the relationship between the independent variable's tween 80 and PEG 400 with the physical quality parameters of turmeric extract nanoemulsion. Size (A); size uniformity (B); zeta potential (C); and clarity (D)

Table 4 and Figure 3 found that the relationship between the variables and the droplet size of the resulting emulsion was obtained; a quadratic equation was chosen, which showed that tween 80 and PEG 400 caused a decrease in particle size. PDI parameters follow a linear pattern, where an increase in the material will increase the PDI value. The transmittance data follows a linear pattern which shows that tween 80 and PEG 400 can increase the clarity of the solution. The zeta potential data follows the cubic pattern, which shows the stability pattern of the resulting emulsion droplets, but the significance value of the model ($p>0.05$), so the cubic equation cannot explain the resulting data pattern.

Parameters such as droplet size, PDI, transmittance, and zeta potential are used in determining the optimum formula through the optimization menu in Design-Expert software version 10.03. The selected SNEDDS optimum criteria were changes in surfactant and cosurfactant composition from the formula with the smallest droplet size and Pdi and the largest zeta potential and transmittance value.The droplet size distribution test showed that the eight nanoemulsion systems formed had droplets with relatively homogeneous sizes, as illustrated by the small value of the PDI. The zeta potential values for the eight optimization formulas ranged from 13.0 - 42.0mV. The magnitude of the zeta potential value of a nanoparticle system can provide an overview of the stability of the nanoparticle system. A dispersion system such as a nanoemulsion will generally be more stable if it has a zeta potential more significant than 30mV or less than -30mV.[25] Based on the analysis results, it was found that the optimum formula for turmeric SNEDDS recommended by the software was composed of 91.94% tween 80 and 8.060% PEG with a total volume of 4.5 mL per 5mL SNEDDs. The desirability value of the optimum formula is 0.776, which is close to 1.

CONCLUSION:

On the basis of these results, it can be concluded that the turmeric extract formulation satisfies the nanoemulsion criteria, as the average droplet size is 200nm, the droplet distribution is relatively homogeneous, as evidenced by the small average PDI, the transmittance is greater than 80 percent, and the zeta potential is greater than -30mV.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this research**.**

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REFERENCES:

1. Kim BE, Leung YM. Significance of Skin Barrier Dysfunction in Atopic Dermatitis. Allergy, Asthma & Immunology Research. 2018; 10(3): 207-15.doi: 10.4168/aair.2018.10.3.207
2. Kim JE, Kim JS, Cho DH, Park HJ. Molecular Mechanisms of Cutaneous Inflammatory Disorder: Atopic Dermatitis. International Journal of Molecular Sciences. 2016; 17(8): 1234. doi: 10.3390/ijms17081234
3. Correa M, Nebus J. Management of Patients with Atopic Dermatitis: The Role of Emollient Therapy. Dermatol Res Pract. 2012; 1–15. doi:10.1155/2012/836931
4. Giam YC, Hebert AA, Dizon MV, Van Bever H, Tiongco-Recto M, Kim KH, et al. A review on the role of moisturizers for atopic dermatitis. Asia Pac Allergy. 2016; 6(2): 120-8. doi: 10.5415/apallergy.2016.6.2.120
5. Sharma J, Sherry, Bhatt S, Saini V, Kumar M. Development and Validation of UV-Visible Spectrophotometric method for the Estimation of Curcumin and Tetrahydrocurcumin in Simulated Intestinal Fluid. Research J Pharm and Tech. 2021; 14(6): 2971–5. doi: 10.52711/0974-360X.2021.00520
6. Nisar T, Iqbal M, Raza A, Safdar M, Iftikhar F, Waheed M. Estimation of Total Phenolics and Free Radical Scavenging of Turmeric (Curcuma longa). J. Agric. & Environ. Sci. 2015; 15(7): 1272-7.doi:10.5829/idosi.aejaes.2015.15.7.9527
7. Wojcik M, Krawczyk M, Wojcik P, Cypryk K, Wozniak LA. Molecular Mechanisms Underlying Curcumin-Mediated Therapeutic Effects in Type 2 Diabetes and Cancer. Oxidative Medicine and Cellular Longevity. 2018: 9698258. doi. 10.1155/2018/9698258
8. Marin E, Briceno M, George C. Method to Produce Curcumin Oil-in-Water Nanoemulsions as Templates for Drug Carriers. Journal of Biotechnology & Biomaterials. 2016; 6: 247. doi: 10.4172/2155-952X.1000247
9. Nastiti CMRR, Ponto T, Abd E, Grice JE, Benson HAE, Roberts MS. Topical Nano and Microemulsions for Skin Delivery. Pharmaceutics. 2017; 9(4): 37. doi: 10.3390/pharmaceutics9040037
10. Roberts MS, Mohammed Y, Pastore MN, Namjoshi S, Yousef S, Alinaghi A, et al. Topical and cutaneous delivery using nanosystems. Journal of Controlled Release. 2017; 247: 86–105. doi: 10.1016/j.jconrel.2016.12.022
11. Kresnawati Y, Shantiningsih R, Martien R. Optimization of Soybean Oil, Tween 80, PEG 400 in Formulation of Beta Carotene Nanoemulsion. Research J Pharm and Tech. 2020; 13 (12):5692–8. doi: 10.5958/0974-360X.2020.00991.9
12. Elsegaie D. Formulation and In-vitro Characterization of Self Nano-emulsifying Drug Delivery System (SNEDDS) for enhanced Solubility of Candesartan Cilexetil. Research J Pharm and Tech. 2019; 12(6): 2628–36. doi: 10.5958/0974-360X.2019.00440.2
13. Kartika C, Sureshkumar R, Upadhyay D, Janani S, Vasanthi J, Raja M, et al. Formulation Development and In vitro Characterization of Solid Self Nano Emulsifying Drug Delivery System for Curcumin to Target Colon Adenocarcinoma. Research J Pharm and Tech. 2019; 12(7): 3338–46.doi: 10.5958/0974-360X.2019.00563.8
14. Akiladevi D, Hari P, Biju G, Madumitha N. Nano-novel approach: Self Nano Emulsifying Drug Delivery System (SNEDDS) - Review Article. Research J Pharm and Tech. 2020; 13(2): 983–90. doi: 10.5958/0974-360X.2020.00183.3
15. Raghuveer P, Rani A. Design, Development and Characterization of Self Nano Emulsifying Drug Delivery Systems for Repaglinide. Research J Pharm and Tech. 2020; 13(11): 5283–8. doi: 10.5958/0974-360X.2020.00924.5
16. Shiyan S, Zubaidah, Pratiwi G. Chemometric Approach to Assess Response Correlation and its Classification in simplex centroid design for Pre-Optimization stage of Catechin-SNEDDS. Research J Pharm and Tech. 2021; 14(11): 5863-0. doi: 10.52711/0974-360X.2021.01020:5863–70
17. Suryani, Sahumena MH, Mabilla SY, Ningsih SR, Adjeng ANT, Aswan M, et al. Preparation and Evaluation of Physical Characteristics of Vitamin E Nanoemulsion using virgin coconut Oil (VCO) and olive oil as oil phase with variation Concentration of tween 80 Surfactant. Research J. Pharm. and Tech. 2020; 13(7): 3232-3236. doi: 10.5958/0974-360X.2020.00572.7
18. Kumar Y, Kumar K, Kishore V. Preparation and Evaluation of Diclofenac Niosomes by Various Techniques. Research J Pharm and Tech. 2013; 6(10):1097–101.
19. Lin TK, Zhong L, Santiago JL. Anti-Inflammatory and Skin Barrier Repair Effects of Topical Application of Some Plant Oils. International Journal of Molecular Sciences. 2017; 19(1): 70. doi:10.3390/ijms19010070
20. Dwiyana RF, Darmadji HP, Hidayah RMN, Hergyana F, Gondokaryono SP, Diana IA, et al. The Beneficial Effect of 20% Sunflower Seed Oil Cream on Mild Atopic Dermatitis in Children. Int J Pharm Pharm Sci. 2019; 11(2): 100–3. doi: 10.22159/ijpps.2019v11i2.30707
21. Ramly NH, Zakaria R, Naim MN. Characterisation of crude palm oil O/W emulsion produced with Tween 80 and potential in residual oil recovery of palm pressed mesocarp fibre. IOP Conf Ser: Earth Environ Sci. 2016; 36: 012033. doi:10.1088/1755-1315/36/1/012033
22. Shaker DS, Ishak RAH, Ghoneim A, Elhuoni MA. Nanoemulsion: A Review on Mechanisms for the Transdermal Delivery of Hydrophobic and Hydrophilic Drugs. Sci Pharm. 2019; 87(3): 17. doi:10.3390/scipharm87030017
23. Ahmad N, Ahmad R, Al-Qudaihi A, Alaseel SE, Fita IZ, Khalid MS, et al. Preparation of a novel curcumin nanoemulsion by ultrasonication and its comparative effects in wound healing and the treatment of inflammation. RSC Adv. 2019; 9:20192–206.
24. Patel P, Solanki S, Mahajan A, Mehta F, Shah K. Preparation and Characterization of Novel Self Nano Emulsifying Drug Delivery System of Allopurinol. Research J Pharm and Tech. 2021; 14(4): 2108–14. doi: 10.52711/0974-360X.2021.00373
25. Schreiner TB, Santamaria-Echart A, Ribeiro A, Peres AM, Dias MM, Pinho SP, et al. Formulation and Optimization of Nanoemulsions Using the Natural Surfactant Saponin from Quillaja Bark. Molecules. 2020; 25: 1538. doi:10.3390/molecules25071538