JNPDD
Journal of Natural Product for Degenerative Diseases
https://journal.univpancasila.ac.id/index.php/Natural

Formulation and Test of Antioxidant Activity from Serum Gel of the Extract Chrysanthemum Flower (*Chrysanthemum Indicum* L.)

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Received: 29 February 2024 / Accepted: 30 March 2024

ABSTRACT: Skin as the outermost layer of the body will be first exposed to UV light, and pollution which may form free radicals and lead to premature aging, so the application of antioxidants is indispensable. One of the skin cares that are in great demand is serum. A plant that has a high content of antioxidants and is widely cultivated in Indonesia is the chrysanthemum flower (Chrysanthemum indicum L.). Previous research stated that the IC_{50} value of chrysanthemums was 43.34 ppm. This study aimed to determine the IC_{50} value contained in chrysanthemum flower extract and formulate it into serum gel that contains antioxidants and meets physical parameters. The method used in determining the IC_{50} value is the DPPH method. The formulation was carried out by adding different levels of chrysanthemum flower extract to the formula. The evaluation test includes organoleptic, pH, spreadability, viscosity, and antioxidant activity and stability test at room temperature (25^{o}C) and high temperature (40^{o}C). The results obtained were IC_{50} values of chrysanthemum flower extracts was 32.78 ± 0.01 ppm while the IC_{50} of serum gel were 109.10 ± 0.1 ppm (F1) and 73.51 ± 0.08 ppm (F2) and after 4 weeks stored at room temperature the IC_{50} 114.02 ± 0.09 ppm (F1) and 76.39 ± 0.06 ppm (F2). The conclusion is that chrysanthemum flower extract has a very strong antioxidant activity, and the serum gel has a strong antioxidant activity and is stable at both room temperature and 40^{o}C for 4 weeks.

KEYWORDS: Antioxidants; DPPH method; chrysanthemum flower; *Chrysanthemum indicum* L.; serum

1. INTRODUCTION

Chrysanthemum indicum L. often known as chrysanthemum is a flower that has a variety of beautiful shapes and colors, making it attractive to cultivate. Initially, chrysanthemums had their natural habitat in mainland China and began to be cultivated in Japan in the 4th century and then entered Indonesia in the early 1800s. In Indonesia, chrysanthemums were only developed commercially in 1940 [1].

In 2013, the Ministry of Agriculture in 2013 released the data about chrysanthemum production experienced an average growth of 43.2% per year. Meanwhile, the data from the Central Statistics Agency states that until the last two years, the largest production of floriculture plants was chrysanthemums with a figure of 383,466,100 stalks in 2020 [1,2]. However, chrysanthemum flowers in Indonesia are mostly used as decorative flowers for decoration purposes, flower arrangements, souvenir decorations, and prayer media for Chinese people [1]. Chrysanthemum flowers contain many antioxidants, including flavonoids and triterpenoids [3].

Antioxidants are compounds that can inhibit the oxidation process by binding free radicals. Humans have natural antioxidants produced by the body, but nowadays exposure to free radicals cannot be avoided so the antioxidants found naturally in the body are not enough [4]. Exposure to ultraviolet light, air pollution, and cigarette smoke can trigger the formation of free radicals also known as reactive oxygen species (ROS). This exposure will first affect human skin as the outermost organ of the body, so the use of additional

How to cite this article: Shelly T,Dellia NR, and Diah KR Formulation and test of antioxidant activity from serum gel of the extract Chrysathemum flower (*Chrysanthemum İndicum* L.). JNPDD. 2024; 1(2): 57-66.

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https://doi.org/10.58511/jnpdd.v1i1.5317
ISSN: 3031-6847

antioxidants is important [5]. However, the use of synthetic antioxidants such as Terbutylhydroxyquinone (TBHQ), Butylated Hydroxyanisole (BHA), and Butylated Hydroxytoluene (BHT) needs to be limited because they can disrupt cell genomic stability [4]. Therefore, the antioxidants contained in plants can be explored for binding the free radicals by formulating them into cosmetic preparations. Chrysanthemum flower extract can be added to cosmetic formulations because of its antioxidant potential [3,6]. Research conducted by Zhu Sunying, et al. (2004) stated that chrysanthemum flowers (*Chrysanthemum indicum* L.) contain essential oils [7]. This is in line with research conducted by Fadia S. Youssef, et al. (2020) who compared the chemical content of essential oils contained between chrysanthemum flowers and the species *Chrysanthemum indicum* L. and *Chrysanthemum morifolium*. The results of the research showed that *Chrysanthemum indicum* L. has essential oil with more effective antimicrobial, antiviral, antimycobacterial, anti-Helicobacter pylori, anti-trypanosomal and antioxidant properties [6].

Shin Youn Joo (2013) also tested the antioxidant activity of several medical plant extracts in Korea, one of which was chrysanthemum flower extract (*Chrysanthemum indicum* L.) using 70% ethanol as a solvent. The test results using the DPPH method showed a very strong IC_{50} result of 43.34 ppm [8]. Antioxidant activity is categorized as very strong if it has an IC_{50} value of less than 50 ppm, strong if the IC_{50} value is between 50 - 100 ppm, moderate if the IC_{50} value is between 100 - 150 ppm, and weak if the IC_{50} value is between 100 - 200 ppm [9].

The Korean cosmetics industry has begun research to develop cosmetic products using chrysanthemum flower extract (*Chrysanthemum indicum* L.) such as research conducted by Keun Taek Choi et al. (2016) who formulated water extract of chrysanthemum flowers (*Chrysanthemum indicum* L.) into a facial cream preparation. Before formulation, Keun Taek Choi et al. (2016) first examined the content of phenolic acids and flavonoids. From the results of his research, it was found that luteolin and akasetin-7-O-rutinoside were the main flavonoids [10].

Beauty and personal care products have become daily necessities, especially among women. One cosmetic preparation that is in great demand by users of facial care products is serum. Serum is characterized by having more concentrated active substances compared to other types of preparations. So it can provide more effective results in managing skin problems because the ability of active substances penetrate deeper into the skin [11].

Based on the description above, the use of chrysanthemum flower extract as a raw material for cosmetics in Indonesia has not yet been carried out much in Indonesia. Infact, chrysanthemum flower extract has potential to be formulated into cosmetic preparations because of its antioxidant activity. Therefore, this reaserch will determine IC_{50} value of chrisanthemum flower extract, formulate it into serum gel and evaluate the serum gel.

2. MATERIALS AND METHODS

2.1. Material and Equipment

The chrysanthemum flower is collected from Cipanas – Cianjur, ethanol 70%, methanol pro analyses, aqua, 1,2-diphenyl-2-picrylhydrazyl (DPPH) Sigma Aldrich, glycerin, carbomer 940, methyl paraben, propylene glycol, natrium metabisulfite, TEA, Folin Ciocalteu reagent, natrium carbonate, dan gallic acid. The equipment used are macerator, vacuum rotary evaporator Buchi, water bath, analytical balance Sartorius, viscometer Brookfield, spektrofotometer UV-Vis Shimadzu, oven Memert, incubator, desicator, micro pippette, pH meter and Laboratory glass ware Pyrex.

2.2. Procedure

The experimental study was conducted at Faculty of Pharmacy of University Pancasila, Jakarta, and started with determination, preparation of simplicia, extraction of chrysanthemum flower, quality testing

covers phytochemical screening, and antioxidant activity test, preparation of serum gel with variety concentration of chrysanthemum flower extract, evaluation of serum and stability testing.

2.2.1 Determination of *Chrysanthemum indicum* L.

Determination was conducted at Herbarium Depokensis (UIDEP), at collection room of University of Indonesia (RKBUI) with No. 638/UN2.F3.11/PDP.02.00/2022.

2.2.2 Preparation and extraction of Chrysanthemum flower (*Chrysanthemum Indicum* L.)

First, the simplicia was dried in oven at 40°C, then the dried simplicia was made into powder form using blender, and sifting using mesh 4 and 18 where all powder can pass through mesh 4 but not more than 40% through mesh 18. The extraction was using kinetic maceration with ethanol 70% as solvent, filter then the filtrate was evaporated by rotary evaporator [12]. The yield was calculated with below equation 1 and 2:

$$\text{DER-Native} = \frac{weigh\ \ of\ Simplisia}{weight\ of\ extract} \quad (1)$$

$$\text{Yield} = \frac{weight\ of\ extract}{weigh\ \ of\ simplicia}\ x\ 100\% \quad (2)$$

2.2.3 Quality test of the extract

The quality test conducted on the concentrated extract is following Farmakope Herbal Indonesia, but focus more on organoleptic, water content, phytochemical screening [13]. In order to make a homogeneous serum, we need to know solubility of extract referring to FI ed VI

2.2.4 Antioxidant Activity Test by DPPH method

The antioxidant activity was conducted by preparing 0.4 mM stock solution of DPPH, vitamin C solution as standard reference, and stock solution of extract. After the max wave length, operating time were obtained, then measure blank solution, series of sample solution and series of vitamin C solution as control positive (1 ppm, 2 ppm, 3 ppm, 4 ppm and 5 ppm). Calculation of antioxidant activity was evaluated by this equation 3.

$$\%\ \text{Inhibition} = \frac{Absorbance\ blanko - Absorbance\ sample}{Absorbance\ blanko}\ x\ 100\% \quad (3)$$

The IC_{50} value was calculated from the curve concentration (x) and % inhibition (y) using regression line with the equation of $y = a + bx$ where IC_{50} is stated as x.

2.2.5 Formulation of Serum gel

The formula of base serum was adopted from Rahayu with some adjustment [14]. As the aim of the study is to make formulation of serum which has strong antioxidant activity, then 2 formula were developed using the IC_{50} value of *Chrysanthemum flower extract*, as in Table 1 below, the formulae FI contains of 100 x IC_{50} and FII contains 150 x IC_{50} as stated in Table 1.

https://doi.org/10.58511/jnpdd.v1i2.6376
JNPDD 2024; 1(2): 57-66

Table 1. Formulation of serum gel of *Chrysanthemum flower extract*

Material	Formula (%)		
	0	**I**	**II**
Chrysanthemum flower extract	-	100 x IC_{50}	150 x IC_{50}
TEA	0.2	0.2	0.2
Carbomer 940	0.5	0.5	0.5
Glycerin	5	5%	5
Propylene glycol	5	5%	5
Methyl paraben	0.1	0.1	0.1
Natrium metabisulfite	0.02	0.02	0.02
Aquadest	Ad 100	Ad 100	Ad 100

2.2.6 Preparation of serum gel

The preparation of serum gel was begun with preparing solution A by dispersing 0.5 g Carbomer 940, into 10 ml of hot water 50°C then leaving it to swell. Then TEA was added to solution A stirred using a homogenizer until a thick mass was formed. Then solution B was prepared by adding 0.1 g methyl paraben in hot water, and then prepared solution C by dissolving 0.02 g sodium metabisulfite in water and mixed solution B and C, and added to the solution A gently and stirred at constant speed using a homogenizer until homogeneous. Chrysanthemum flower extract was mixed with 5 mL of glycerine until completely mixed, then 5 mL of propylene glycol was added and mixed until homogeneous. The mixture was then added to the thick mass little by little while stirring using a homogenizer at constant speed until homogeneous. The preparations were then subjected to evaluation tests and antioxidant activity tests.

2.2.7 Evaluation of serum gel of chrysanthemum flower extract

The evaluation of serum gel includes organoleptic; homogeneity test; pH, viscosity and rheology, spread ability test. Additionally, antioxidant test was conducted for base serum gel (F0) and F I and F II. The evaluation of serum gel was also observed per week for 4 weeks stability test.

2.2.8 Antioxidant Test of serum gel

The antioxidant activity test was evaluated with the same procedure for testing antioxidant activity for extract, but the series for sample solution was difference where the concentration are in the range of 20 ppm up to 120 ppm. The calculation of antioxidant activity activity was evaluated by this equation 3.

2.2.9 Stability testing

The stability testing was conducted for 4 weeks where the serum gel was stored at room temperature (25°C) and at 40°C. The parameter testing are organoleptic, viskosity and rheology, pH, spread ability, homogenity for the formulae.

3. RESULTS

3.1 Extract of chrysanthemum flower

Extraction of chrysanthemum flower was done with kinetic maceration. It was obtained 188.6 g concentrated extract with the value of DER-*native* = 3.1431 and yield was 31.81% as shown in Table 2. The minimum requirement of yield of chrysanthemum flower extract in The Farmakope Herbal Indonesia should not less than 22.7% [13].

Table 2. Result of Extraction

Weight dried sample (g)	Weight of concentrated extract (g)	DER-*native*	Yield (%)
592.8	188.6	3.1431	31.81

3.2 Qualitative parameter of extract

The result of quality test on concentrated extract as in Table 3, below

Table 3. Result of qualitative parameter of concentrated extract

Parameter testing	Observation
Organoleptic	The color of extract is yellow brownish and has specific aroma.
pH	5.31
Dissolve in solvent	
- Water	1 : 10
- Glycerin	1 : 10
- Propylene glycol	1 : 100
Water content	7.51%
Total ash	9.07%
Screening phytochemical	
- Flavonoid	+
- Saponin	+
- Tanin	+
- Polyphenol	+
- Alkaloid	+
- Steroid	-
- Triterpenoid	+
Total phenolic compound	5.98 % ± 0.001

3.3 Antioxidant activity of extract

The antioxidant activity of chrysanthemum flower extract was shown in Table 4.

Table 4. Antioxidant activity of chrysanthemum flower extract

Extract	Concentration (ppm)	Absorbance		Inhibition (%)	IC_{50} (ppm)	Linear regresion
		Blank	Extract			
Series I	10	0.7319	0.6362	13.08	32.79	y = 1.5070x + 0.5930 R^2 = 0.9901
	20		0.4806	34.34		
	30		0.3924	46.39		
	40		0.2982	59.26		
	50		0.1759	75.97		
Series II	10	0.7318	0.6361	13.08	32.79	y = 1.5056x + 0.6259 R^2 = 0.9901
	20		0.4805	34.34		
	30		0.3923	46.39		
	40		0.2981	59.26		
	50		0.1764	75.90		
Series III	10	0.7321	0.6362	13.10	32.76	y = 1.5066x + 0.6365 R^2 = 0.9901
	20		0.4804	34.38		
	30		0.3922	46.43		
	40		0.2980	59.30		
	50		0.1759	75.97		
Average IC_{50} (ppm)					32.78	
SD					0.01	

The measurement of antioxidant activity of extract chrysanthemum flower showed IC_{50} value was 32.78 ± 0.01 ppm.

3.4 Serum Gel Formulation and its Evaluation

The result of serum gel was shown in Figure 1. The evaluation of serum gel of chrysanthemum flower extract as seen in Table 5.



F0 – Basis serum gel **Serum gel F1** **Serum gel F2**

Figure 1. Serum gel chrysanthemum flower

Table 5. Evaluation of serum gel of chrysanthemum flower

Parameter Testing	F0	F1	F2
Organoleptic (color, aroma)	Clear and specific aroma	Yellow and specific aroma	Dark yellow and specific aroma
Texture	Thicker	Thick	Slightly thick
Homogeneity	Homogeny	Homogeny	Homogeny
pH	5.30	5.20	4.77
Spread ability (cm^2)	5.47	6.70	7.44
Viscosity (cps) at 20 rpm	28,500	7750	5000

3.5 Antioxidant activity of serum gel

The result of antioxidant activity of serum gel was shown in Table 6.

Table 6. Antioxidant activity of serum gel with chrysanthemum flower extract

A. Formulae		IC_{50} (ppm)	
	week-0	**week-4 at room temperature**	**week 4 at 40°C**
F0 (Basis	147.98 ± 0.9	152.18 ± 0.03	156.08 ± 0.02
F1 (100 x IC_{50})	109.10 ± 0.1	114.02 ± 0.09	118.64 ± 0.20
F2 (150 x IC_{50})	73.51 ± 0.08	76.39 ± 0.06	81.20 ± 0.03

The data was prsented in mean ± SD, n=3.

The serum gel has IC_{50} value 109.10 ± 0.1 ppm (F1) and 73.51 ± 0.08 ppm (F2), The formula 2 has higher antioxidant activity compare than other formulae. After 4 weeks stored at room temperature the IC_{50} value shown in Table 6 has slightly decreassed into 114.02 ± 0.09 ppm (F1) and 76.39 ± 0.06 ppm (F2).

3.6 Stabilty test of gel

The stability of serum gel was stable at room temperature for 4 weeks. The result of stabilty test was shown in Table 7.

Table 7. The stabilty test of serum gel with chrysanthemum flower extract

	Organoleptic and Homogeneity									
Week	**0**		**1**		**2**		**3**		**4**	
Storage condition	25°C	40°C	25°C	40°C	25°C	40°C	25°C	40°C	25°C	40°C
F1	Yellow, specific aroma and thick. Homogeny	Yellow, specific aroma and thick. Homogeny	No change	No change	No change	No change	No change	No change	No change	No change
F2	Yellow, specific aroma and slightly thick. Homogeny	Yellow, specific aroma and slightly thick. Homogeny	No change	No change	No change	No change	No change	No change	No change	No change

pH										
F1	5.20	5.20	5.21	5.23	5.11	5.12	5.12	5.15	5.10	5.13
F2	4.77	4.77	4.79	4.76	4.72	4.71	4.73	4.72	4.71	4.73
Spread ability (cm^2)										
F1	6.70	6.70	6.68	6.68	6.71	6.73	6.72	6.71	6.70	6.71
F2	5.47	5.47	5.46	5.51	5.56	5.53	5.48	5.45	5.49	5.48
Viscosity (cps) at 20 rpm										
F1	7750	7750	8000	8000	8250	8250	8500	8500	8500	8500
F2	5000	5000	5250	5250	5250	5250	5500	5500	5750	5750

4. DISCUSSION

We have extracted the chrysanthemum flower with kinetic maceration. The ethanol 70% was used to extract the chrysanthemum flower, which is polar solvent. The yield has fulfilled the Herbal Farmakope Indonesia. Flower extraction by maceration with liquids of increasing polarity is the method most often employed. A classic and easy-to-implement method for non-targeted extraction, maceration aims to isolate and describe as many chemicals as feasible. Without the need for a lengthy heating process, this technique does not further harm the active compound [15]. Despite its prevalence, there is a dearth of research that can explain or improve upon this strategy for maximum output. Moreover, this extraction method is in need of improvement, mostly due to concerns regarding efficiency, the environment, and time constraints [16].

The phytochemical screening of extract showed the presence of polar secondary metabolite such as flavonoid, saponin, tanin, and polyphenol compounds. It also have semipolar compound such as alkaloid and non polar compound such as triterpenoid. The result of the phytochemical screening was simmilar with the previous research of *Chrysanthemum indicum* L flower which has bioactive constituents alkaloids, terpenoids flavonoids, saponins, terpenoids, cardiac glycosides and protein compounds [17]. There are polar compounds such as flavonoids like apigenin, luteolin, quercetin, and their derivatives like flavonoid glycoside, flavonols, and flavonol glycosides that are found in chrysanthemums [18]. Many researchers have found that flavonoids compounds of chrysanthemum can stop oxidation caused by a lot of lipid uptake and buildup in a way that depends on the dose [19]. It's possible that this effect is caused by flavonoids losing several phenolic groups. Since oxidation of lipids inside cells makes free radicals, these groups might react with the free radicals and stop the oxidation process. The flavonoid compound on this research has antioxidant activity regarding the content of TPC and the IC_{50}.

The antioxidant activity of the chrysanthemum flower extract was measured by DPPH methods Based on the IC_{50} value on DPPH tests, the chrysanthemum flower extract is a very strong antioxidant. The DDPH assay is a quick, easy, and cheap way to check the antioxidant power of natural products. It uses the free radical 2, 2-Diphenyl-1-picrylhydrazyl (DPPH), which is often used to see how well compounds can remove free radicals or donate hydrogen and check their antioxidant activity [20]. The DPPH assay method is based on DPPH, a stable free radical, being broken down [21]. Antioxidants found in natural products can help stop degenerative diseases by stopping the oxidation process, which is the first step in the development of many degenerative diseases and premature aging [22].

The serum gel has a strong antioxidant activity with IC_{50} value below 100 ppm. The serum gel has a strong antioxidant activity with IC_{50} value below 100 ppm. The serum gel of chrysanthemum flower extract, which contains phenolic compounds, should penetrate the epidermis of the skin. Thus, it might prevent the oxidation process and reduce the risk of hyperpigmentation [23]. This result is lower than that research obtained with the serum gel of kojic acid with an IC_{50} value 12.20 ppm for antioxidant activity and serum gel with Angelıca keıskeı Leaf extract with IC_{50} value 16.68 ppm [24].

The stabilty of serum gel was stable at room temperature for 4 weeks. The flavonoid and phenolic content affects how stable the mixture is because they are easily oxidized at neutral pH. To keep the formula stable, we can put the mixture in a container that won't let light in or add anti-oxidants to stop oxidation [25]. This

result of antixodant activity demonstrated that the serum gel of chrysanthemum flower extract could be developed as face lightening lightening or anti aging products but need a clinical study. Therefore, we need to check both formulae are stable at room temperature during clinical study for 4 weeks.

5. CONCLUSION

The conclusion is that chrysanthemum flower extract has a very strong antioxidant activity, and the serum gel has a strong antioxidant activity and is stable at both room temperature and 40°C for 4 weeks. This study demonstrated that the serum gel dosage form of chrysanthemum flower extract could be developed as face lightening or anti aging products.

Acknowledgements:
The author thanks to the Pancasila University Laboratory for supporting the equipment of this research.
Author contributions:
Concept – ST, DKP; Supervision – ST; Resources – ST, DNR; Materials – ST, DNR; Data Collection and/or Processing – DNR; Analysis and/or Interpretation – ST, DNR, DKP; Literature Search – ST, DKP; Writing – ST, DKP; Critical Reviews – ST, DKP.
Conflict of interest statement: The authors declare no conflict of interest

REFERENCES

[1] Hadizadeh H, Samiei L, Shakeri A. Chrysanthemum, an ornamental genus with considerable medicinal value: A comprehensive review. South African J Bot. 2022;144:23–43.

[2] Apriliani E, Widyajayantie D, Hidayah UF, Yudha YS. Perbanyakan Tanaman Chrysanthemum pada Kondisi Fotoautotropik Secara in Vitro. Agric Biol Technol. 2023;1(1):1–9.

[3] Shao Y, Sun Y, Li D, Chen Y. *Chrysanthemum indicum* L.: A comprehensive review of its botany, phytochemistry and pharmacology. Am J Chin Med. 2020;48(04):871–97.

[4] Hutapea M, Swandiny GF, Syafawi MI, Putra FP, Kokadir S, Basilianus E, et al. The Latest Research on 3 (Three) Types of Sea Cucumber Extract from Tegal Mas Island, Lampung. J ILMU KEFARMASIAN Indones. 2023;21(2):165–71.

[5] Jaganjac M, Sredoja Tisma V, Zarkovic N. Short Overview of Some Assays for the Measurement of Antioxidant Activity of Natural Products and Their Relevance in Dermatology. Molecules. 2021;26(17):5301.

[6] Youssef FS, Eid SY, Alshammari E, Ashour ML, Wink M, El-Readi MZ. *Chrysanthemum indicum* and *Chrysanthemum morifolium*: chemical composition of their essential oils and their potential use as natural preservatives with antimicrobial and antioxidant activities. Foods. 2020;9(10):1460.

[7] Shunying Z, Yang Y, Huaidong Y, Yue Y, Guolin Z. Chemical composition and antimicrobial activity of the essential oils of *Chrysanthemum indicum*. J Ethnopharmacol. 2005;96(1–2):151–8.

[8] Joo SY. Antioxidant activities of medicinal plant extracts. J Korean Soc food Sci Nutr. 2013;42(4):512–9.

[9] Fauziah A, Sudirga SK, Parwanayoni NMS. Antioxidant Test Leunca Plant Leaf Extract (Solanum nigrum L.). Metamorf J Biol Sci. 2021;8(1):28. .

[10] Choi KT, Kim JH, Cho HT, Lim SS, Kwak SS, Kim YJ. Dermatologic evaluation of cosmetic formulations containing *Chrysanthemum indicum* extract. J Cosmet Dermatol. 2016;15(2):162–8.

[11] Khan N, Ahmed S, Sheraz MA, Anwar Z, Ahmad I. Pharmaceutical based cosmetic serums. In: Profiles of Drug Substances, Excipients and Related Methodology. Elsevier; 2023. p. 167–210.

[12] Gallo M, Formato A, Ianniello D, Andolfi A, Conte E, Ciaravolo M, et al. Supercritical fluid extraction of pyrethrins from pyrethrum flowers (*Chrysanthemum cinerariifolium*) compared to traditional maceration and cyclic

pressurization extraction. J Supercrit Fluids. 2017;119:104–12.

[13] Departemen Kesehatan RI. Farmakope herbal Indonesia. Jakarta: Kementerian Kesehatan RI; 2017. 1–506 p.

[14] Rahayu FS. Formulasi Dan Uji Efektivitas Sediaan Serum Ekstrak Etanol Kulit Kayu Manis (*Cinnamomum burmanni*) Sebagai Anti-Aging. Universitas Sumatera Utara; 2021.

[15] Gori A, Boucherle B, Rey A, Rome M, Fuzzati N, Peuchmaur M. Development of an innovative maceration technique to optimize extraction and phase partition of natural products. Fitoterapia. 2021;148:104798.

[16] Momchev P, Ciganović P, Jug M, Marguí E, Jablan J, Zovko Končić M. Comparison of Maceration and Ultrasonication for Green Extraction of Phenolic Acids from *Echinacea purpurea* Aerial Parts. Molecules. 2020;25(21).

[17] Kumar Hotta S, Neelapu N, Priyanka N. Phytochemical analysis of the flower of *Chrysanthemum indicum* L. and *Calendula officinalis*. Int J Pharmacogn Chem. 2021;2(1):35–41.

[18] Liang W-L, Gong D, Zhang WK. The Composition of chrysanthemum extracts and their pharmacological functions. STEMedicine. 2020 Dec 16;2(5 SE-Review articles).

[19] Xia DZ, Lv GY, Yu XF, Wang HM, Yang Q. Antagonism of total flavonoids from *Chrysanthemum morifolium* against lead induced oxidative injury in mice. Zhongguo Zhong yao za zhi= Zhongguo Zhongyao Zazhi= China J Chinese Mater Medica. 2008;33(23):2803–8.

[20] Pratami DK, Mun'im A, Sundowo A, Sahlan M. Phytochemical profile and antioxidant activity of propolis ethanolic extract from Tetragonula bee. Pharmacogn J. 2018;10(1):73–80.

[21] Han A-R, Nam B, Kim B-R, Lee K-C, Song B-S, Kim SH, et al. Phytochemical composition and antioxidant activities of two different color chrysanthemum flower teas. Molecules. 2019;24(2):329.

[22] Fernandez-Panchon MS, Villano D, Troncoso AM, Garcia-Parrilla MC. Antioxidant activity of phenolic compounds: from in vitro results to in vivo evidence. Crit Rev Food Sci Nutr. 2008;48(7):649–71.

[23] Syarifah A, Budiman A, Nazilah SA. Formulation and Antioxidant Activity of Serum Gel of Ethyl Acetate Fraction From Musa x paradisiaca L. In: 4th International Conference on Sustainable Innovation 2020–Health Science and Nursing (ICoSIHSN 2020). Atlantis Press; 2021. p. 310–5.

[24] Aulifa DL, Noerfitri RY, Tristiyanti D, Budiman A. Formulation of Serum Gel Containing *Angelica keiskei* Leaf Extract as an Antioxidant and Tyrosinase Enzyme Inhibitor. Int J Appl Pharm. 2020;12(3):108–11.

[25] Nur A, Rani R. The Potential of Tradescantia Spathaceae Leaves Infusion as Sunscreen Gel Use Spectrophotometric UV-Vis Method. J ILMU KEFARMASIAN Indones. 2022;20(1):6–13.