Original Research Article

FORMULATION AND EVALUATION SERUM EXTRACT ETHANOL ARBENAN LEAVES [Duchesneaindica (Jacks.) Focke] PHARMACEUTICALY STABLE

ABSTRACT

Objective: Arbenan plants contain saponins, flavonoids, and tannins which have antioxidant activity. The purpose of this research is to perform formulation and evaluation Extract Ethanol of Arbenan leaves in the form of serum which is pharmaceutically stable.

Method: The composition of the serum extract of Arabenan leaves was carried out by optimization of the base formula to obtain the appropriate base based on the desired serum characteristics.

Result: Formulations ofleaf extract of Arabenan [*Duchesneaindica*(Jacks.) Focke] with four variations bases have shown to have good stability after stress condition. It can be seen from the evaluation result areorganoleptics, homogeneity, viscosity, rheology, and pH.

Keyword: Extract EtanolArbenan Leaves, Serum, HPMC, Na-CMC

A. INTRODUCTION

Molecular damage in the body can be induced by molecules called free, radicals[11]. Free radicals can be formed due to internal and external sources of free radicals. Internal sources of free radicals are factors derived from normal metabolite processes in the human body, namely phagocytes, xanthine oxidase, arachidonic pathways, peroxisomes, inflammation and others. External sources of free radicals are factors that originate outside the human body, namely cigarette smoke, environmental pollution, sunlight, chemicals, ozone, several types of drugs, pesticides and others. Excessive levels of free radicals are a trigger for various degenerative diseases and conditions[4]. Antioxidants can inactivate the development of oxidation reactions by binding to free radicals and highly reactive molecules so that cell damage can be inhibited[29].

The use of natural materials that have biological activity is the motivation for further research, after synthetic compounds that have biological activity such as synthetic antioxidant compounds Butylated Hydroxyanisole (BHA) and Butylated Hydroxytoluene (BHT) are restricted because they are carcinogenic[1].There is concern about the possible side effects of synthetic antioxidants causing natural antioxidants to become alternatives that need to be developed[26].

One of the plants that can be used as medicine is a plant (Duchesneaindica (Jacks.) Focke) known as Arbenan. The community uses this plant as a fever, anti-infection and stimulant (Hutapea, 1991). In addition, Arbenan is also used for cancer treatment, anti-inflammatory, stop bleeding, destroy blood clots, and reduce swelling[5].

According to Hutapea (1991), all parts of the Arbenan plant contain saponins, flavonoids, and tannins. Flavonoids are compounds that have antioxidant activity due to the presence of a hydroxy group in their molecular structure so they are called bioflavonoids. Likewise, some tannins have been shown to have antioxidant activity, inhibit tumor growth and inhibit enzymes such as reverse

transcriptase and DNA topoisomerase. While some saponins work as antimicrobials[3].

However, the use of Arbenan as an antioxidant for the skin is not widely known by the public. Aesthetic use certainly does not provide comfort. If further research is carried out, Arbenanplants can be formulated to facilitate their use. Preparations, especially cosmetic preparations, have developed into several dosage forms aimed at increasing convenience for their use, one of which is serum. Serum is a preparation that has more bioactive components. Serum has the advantage that it can provide a more comfortable effect and is easier to spread on the skin surface because its viscosity is not too high[10].

Serum or called concentrate, contains ten times more biologically active substances than cream preparations, so it is faster and more effective. Serum has fast absorption properties and the ability to penetrate into the deeper layers of the skin. The selection of serum preparations is motivated by the form of preparation that is easy to make, practical to use, easily absorbs into the skin and gives a soft and moist feeling after use[17]. Serum works locally on different parts of the body, face, neck, eyelids. This preparation can be used regardless of age[25].

Based on the explanation above, a research will be conducted on the formulation and evaluation of the ethanol extract serum of Arbenan [Duchesneaindica (Jacks.) Focke] leaves which are pharmaceutically stable.

Table 1. Formula Serum Extract ArbenanLeavesMasterOptimization

Materials	Formula 1 (%b/v)	Formula 2 (%b/v)	Formula 3 (%b/v)	Formula 4 (%b/v)	Function
Extract Arbenan Leaves	0,302 %	0,302 %	0,302 %	0,302 %	Zataktif
HPMC	0,5 %	1 %	-	-	Base
Na CMC	-	-	0,5 %	1 %	Base
Propyl paraben	0,02 %	0,02 %	0,02 %	0,02 %	Preservative
Methyl paraben	0,02 %	0,02 %	0,02 %	0,02 %	Preservative
Propylen Glycol	5 %	5 %	5 %	5 %	Humectant
α −tocoferol	0,03 %	0,03 %	0,03 %	0,03 %	Antioksidant
Aquadest add	100 %	100 %	100 %	100 %	Solvent

SUBJECTS AND METHODS

Sampling

The sample used was the leaves of Arbenan [Duchesneaindica (Jacks.) Focke] taken from Mount Bawakaraeng, Gowa Regency, South Sulawesi.

Preparation Sample

The collected samples of Arbenan [Duchesneaindica (Jacks.) Focke] were cleaned of dirt adhering to the leaves using running water and then dried by aerating. After drying the sample is then mashed.

Extraction Method

Arbenan leaf powder is weighed as much as 300 grams, put in a maceration container then 2700 mL of 70% ethanol solvent is added until the sample is submerged, then left for 3-4 days while stirring repeatedly, then filtering and obtaining residual and liquid ethanol extract. Furthermore, the liquid ethanol extract that has been obtained is evaporated using a Rotary Vacum Evaporator to obtain a thick ethanol extract.

The use of extract percentage in formulas based on IC50 Arbenan leaf ethanol extract is = 30.20µg / mL[28].Increase the concentration of the extract to 100x times that of IC50 in order to qualify as a serum with high concentrated skin preparations.

Preparation of Serum Extract EtanolArbenan Leaf

Prepared tools and materials. Weigh all ingredients to be used. The suitable basic formulation is selected from the optimization results. The base is dispersed in heated aquadest and added with propyl paraben and methyl paraben which have been dissolved in propylenglycol, added tocopherol then homogenized[2].

Characterization of Serum Extract EtanolArbenan Leaf

Organoleptic

Organoleptic tests are performed visually on serum preparations which include shape, color, and smell[25].

Homogeneity

The preparation is placed between two glass slides and then the presence of coarse particles or inhomogeneity under the light is observed[10].

Measurement of Viscosity and Flow Properties

Viscosity measurements were carried out using a Brookfield viscometer. The preparation is put into a measuring cup then the appropriate spindle is lowered until the spindle limit is immersed into the preparation. Then the motor and spindle are started. Player speed is set 0.5 successively; 2; 5; 10; and 20 rpm is then reversed from 20; 10; 5; 2; and 0.5 rpm. The viscosity number indicated by the red needle is noted. Then it is multiplied by the correction factor in the table on the tool brochure. The viscosity value is calculated and then the data obtained are plotted against shear stress (dyne / cm^2) and shear speed (rpm)[10].

Stability Test

Evaluation of the stability of the preparation is carried out before and after the conditions are imposed. The condition was enforced by storing the preparation as much as ±100.00 mLat a temperatureof 5°C and 35 °C alternatelyfor 12 hourseachfor 10 cycles.

Deployment Ability

A total of 0.5 mL of the preparation was placed on a diameter of 15 cm round glass, another glass was placed on it and allowed to stand for 1 minute. Then, a 50 gram load is added and allowed to stand for 1 minute and then a constant diameter of 5-7 cm is measured, showing a semisolid consistency which is very comfortable to use[25].

pH (Potential Hydrogen)

The pH examination of serum preparations was carried out before and after the conditions were forced using a pH meter. The pH meter is immersed into the serum preparation to the limit of the mark and the pH

value of the serum preparation will be read [19].

PEMBAHASAN

Molecular damage in the body can be induced by molecules called free radicals[11]. Free radicals can be formed due to internal and external sources of free radicals. Excessive levels of free radicals are a trigger for various degenerative diseases and conditions[4].

Dorland (2011, p. 74) explains that it prevents or prevents oxidation, or natural or synthetic substances. Antioxidants can inactivate the development of oxidation reactions by binding to free radicals and highly reactive molecules so that cell damage can be inhibited[29].Synthetic compounds that have biological activity such as synthetic antioxidant compounds Butylated Hydroxyanisole (BHA) and Butylated Hydroxytoluene (BHT) because of their use because they are carcinogenic[1]. Therefore, natural antioxidants are an alternative that needs to be developed[26].

One of the uses of natural materials that have biological activity is Arbenan plants. All parts of the Arbenan plant contain saponins, flavonoids, and tannins. Flavonoids are compounds that have antioxidant activity due to the presence of a hydroxy group in their molecular structure so they are called bioflavonoids.

However, the use of Arbenan as an antioxidant for skin is not widely known by the public. Aesthetic use certainly does not provide comfort. Therefore it is necessary to develop Arbenan as a serum preparation. Serum dosage forms are easy to make, practical to use, easy to penetrate into the skin and provide a soft and moist feeling after use. Besides, it can provide a more comfortable effect and spread more easily on the surface of the skin because the viscosity is not too high[10,17].

The extract was made by maceration method using 70% ethanol as the solvent. In the formulation, the HPMC and Na-CMC bases were optimized. As for the variation, the concentration of HPMC used was 0.5% and 1%, while the Na-CMC base used concentrations of 0.5% and 1%. This variation is carried out to optimize the basis that is effective to meet the criteria for pharmaceutical sedioan physical properties and can survive the shelf life through stability testing. The testing is based on physical parameters including organoleptic examination, homogeneity, viscosity measurement, flow type determination, pH measurement, dispersion and drying time.

Stability testing is carried out using the stress condition method using a climatic chamber. The tested preparations were stored at 5 °C and 35 °C for 10 cycles, each cycle lasting 12 hours. The purpose of this test is to determine the physical stability of the preparation. The resulting formulation was then evaluated pharmaceutically.

The first evaluation was carried out by organoleptic testing to determine whether there was a change in color, odor and consistency that occurred during storage. Organoleptic examination of serum preparations showed that the viscosity enhancing concentration was physically stable because it did not experience changes in color, odor and consistency, before and after the conditions were imposed. The results of organoleptic observations can be seen in table 2.

Table 2. Organoleptic observations of the serum formula for Arabenan leaf extract before and after the conditions were imposed

Formula	Type of examination	Condition	
		Before	After
1	Smell	Typical	Typical
	Color	Light Brown	Light Brown
	Concistency	A Little thick	A Little thick
2	Smell	Typical	Typical
	Color	Light Brown	Light Brown
	Concistency	A Little thick	A Little thick
3	Smell	Typical	Typical
	Color	Light Brown	Light Brown
	Concistency	A Little thick	A Little thick
4	Smell	Typical	Typical
	Color	Light Brown	Light Brown
	Concistency	A Little thick	A Little thick

Information :
F1: Formulation with a concentration of 0.5% HPMC
F2: Formulation with a concentration of 1% HPMC
F3: Formulation with a concentration of 0.5% Na CMC
F4: Formulation with a concentration of 1% Na CMC

The homogeneity test was carried out to see a homogeneous serum composition. The compositionofthe serum issaidtobehomogeneousifthereisanevencol orequationandnodifferentparticles are found[22].Homogeneityobservations were carried out visually with a glass object, where smearing the serum sample on a glass object was observed. The results of the homogeneity test observations can be seen in table 3.

Table3. The results of the observation of the homogeneity test of the formula serum extract Arabenan leaf before and after the conditions were forced

Formula	Homogenety Test	
	Before	After
1	Homogeny	Homogeny
2	Homogeny	Homogeny
3	Homogeny	Homogeny
4	Homogeny	Homogeny

Information :
F1: Formulation with a concentration of 0.5% HPMC
F2: Formulation with a concentration of 1% HPMC
F3: Formulation with a concentration of 0.5% Na CMC
F4: Formulation with a concentration of 1% Na CMC

From the results of testing the homogeneity of F1, F2, F3 and F4 before and after the forced conditions on the serum formula of Arabenan leaf extract

showed that the formula was homogeneous which was marked by the absence of coarse particles in the preparation.

Viscosity testing aims to determine the consistency of preparations that affect the skin. The higher the viscosity value, the more difficult it is to apply to the skin, the lower the viscosity, the easier it is to apply to the skin. The factors that affect viscosity are pressure, temperature, size and molecular weight[23]. The results obtained that the serum using HPMC had a higher viscosity than that of NaCMC. In measuring the viscosity of Arabenan leaf extract serum, a Brookfield Viscometer was used. The viscosity of the preparation was measured using a spindle number 62 with the rotating speed adjusted to 0.5 successively; 2; 5; 10; and 20 rpm is then reversed from 20; 10; 5; 2; and 0.5 rpm for four replications. The results obtained can be seen in table 4.

Tabel 4. Hasil pengukuran viskositas (*poise*) serum ekstrak daun Arabenan sebelum dan sesudah kondisi dipaksakan

Formula	Average Viscosity (Poise)	
	Before	After
1	127.6	126.3
2	754.3	752
3	33.6	33.3
4	144.6	143.3

Information :
F1: Formulation with a concentration of 0.5% HPMC
F2: Formulation with a concentration of 1% HPMC
F3: Formulation with a concentration of 0.5% Na CMC
F4: Formulation with a concentration of 1% Na CMC

The viscosity of the preparations before and after the conditions were forced there was a change in the decrease in the mean viscosity at F1, F2, F3 and F4. This may be because in the formulation there are variations in the concentration of the base used to improve the appearance of the preparation. The viscosity data obtained were analyzed statistically using the One-Way ANOVA method. The results of the analysis can be seen in table 4, which shows that for serum preparations, the viscosity of all formulas both F1, F2, F3 and F4 with a base concentration of 0.5% HPMC concentration, 1% HPMC concentration, 0.5% NaCMC concentrationand 1% NaCMC concentrationexperienced a slight significant change in the conditions before and after the conditions were imposed. This suggests that the existence of a force

condition greatly affects the viscosity of all norms.

In determining the flow type of Arabenan leaf extract serum, a Brookfield Viscometer was also used. The type of flow can be seen from the rogram and the yield value of the preparation. The yieldvalueisthepricethatmustbemet in order forthepreparationtoflow[23]. The yieldvalueisobtainedfrommeasuringthevisc osityofthepreparationatseveralrpm, thenthe data obtainedcanbedeterminedbyshearingstress andshearspeed (rateofshare). After creating a rogram linking the shearing stress and the shear speed (rate of share), the newton flow type is obtained which is formed from the four formulas, namely plastic flow. It is said to be plastic flow because the results of the rogram show that the rising and falling curves cut the yield value in the absence of a hysteresis loop. Flow types in F1, F2, F3 and F4 did not change the flow both before and after the accelerated condition. The resultsobtainedcanbeseen in therheogram.

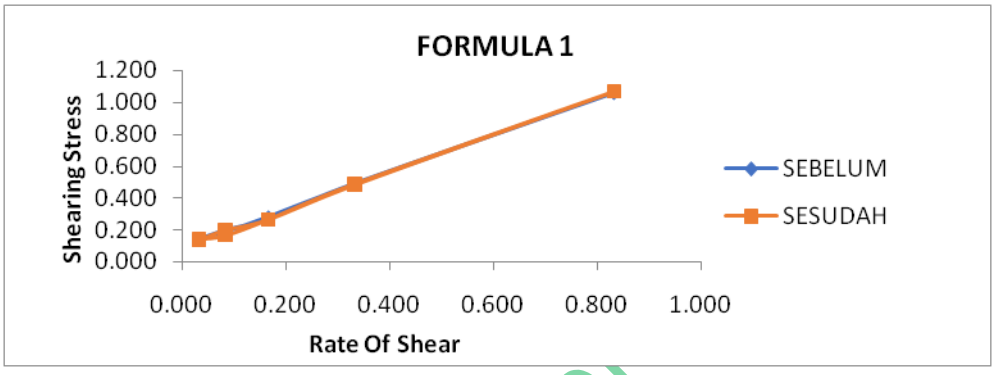

Figure 1. Formulation with a Concentration of 0.5% HPMC

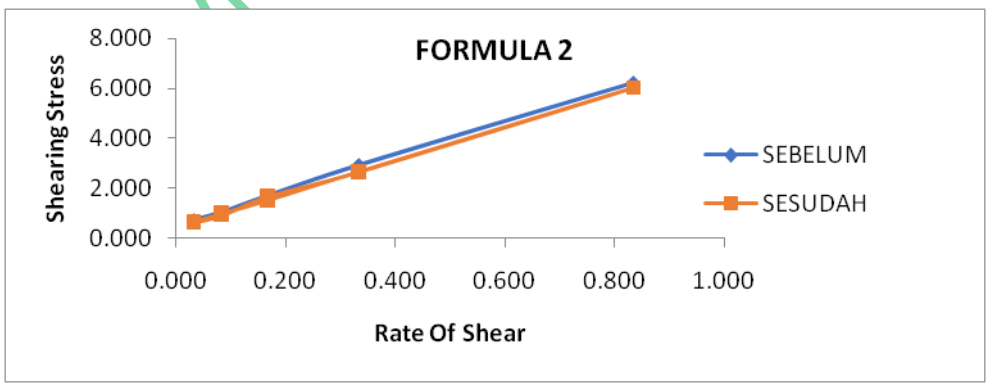

Figure 2. Formulation with a Concentration of 1% HPMC

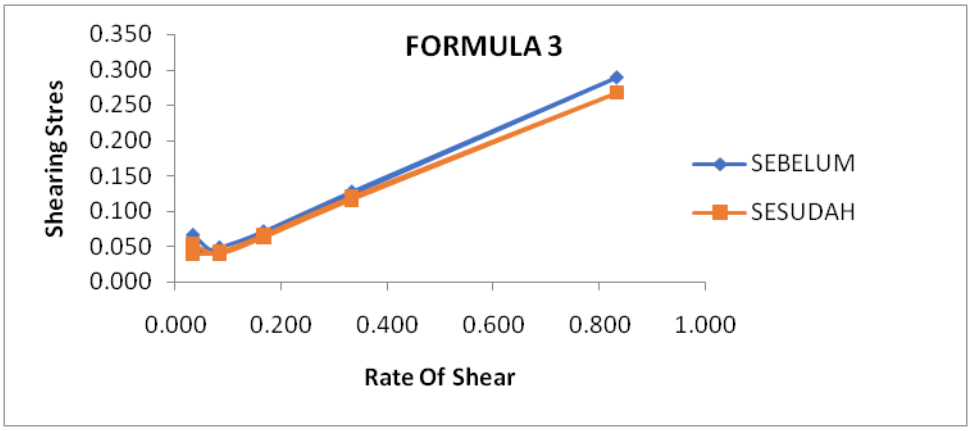

Figure 3. Formulation with a Concentration of 0,5% Na-CMC

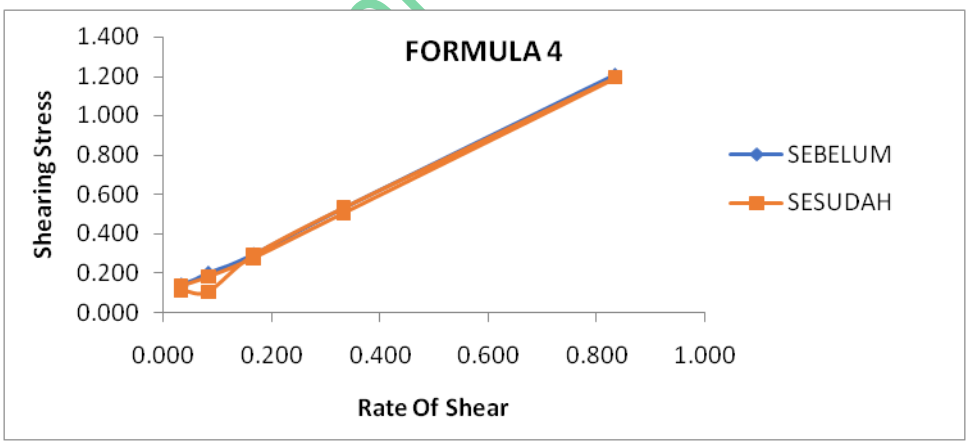

Figure 4. Formulation with a Concentration of 0,5% NaCMC

The spreadability test is carried out to determine how much the spreadability of the serum is, because it is a good preparation and is preferable if it can spread easily and is comfortable to use[30]. The greater the dispersibility value, the easier the serum will spread on the skin. From the test results the spreadability is inversely proportional to the viscosity of a preparation, the thicker the consistency, the smaller the dispersion power produced. The value of the scattering power whose consistency is very comfortable to use is 5-7 cm[22]. The results of the measurement of the scattering power can be seen in table 5.

Table 5. The results of the measurement of the dispersibility of the Arabenan leaf extract serum formula before and after the conditions were imposed

Formula	Diameter (Average)	
	Before	After
1	9.50	9.38
2	9.25	9.63
3	14.88	14.50
4	12.75	13.25

Information :
F1: Formulation with a concentration of 0.5% HPMC
F2: Formulation with a concentration of 1% HPMC
F3: Formulation with a concentration of 0.5% Na CMC
F4: Formulation with a concentration of 1% Na CMC

From the test results, the spreadability did not meet the good serum dispersion parameters. Literature studies were carried out in several journal base formulations with HPMC and NaCMC as the basis. Research on serum formulations with HPMC and NaCMC according to Shukr and Metwally (showed that the dispersibility produced by 0.5% and 1% HPMC and NaCMC concentrations of gel was 8 cm - 15 cm. In the Mappa study it was also said that the dispersibility The gel is not good because the viscosity of NaCMC is too high. When NaCMC is put into water, Na + is released and replaced with H + ions and forms HCMC which will increase the viscosity[15]. and Na-CMC also determines the viscosity stability and spreadability of the gel preparation so that further research is needed regarding the effect of differences in the concentration of additional strength of the gel on physical stability, with this study it is necessary to adjust the formula.

After the spreadability test, pH measurements were carried out which aims to see whether the pH on the preparation matches the pH on the skin. The pH measurement of the preparation was carried out before and after the conditions were imposed. This is related to the problem of stability and safety of using preparations to avoid irritation of the skin for its users, the pH of skin preparations should have a pH that is approximately the same as the pH of the skin, which is between 5-7[24]. The pH measurement results can be seen in table 6.

Tabel 6. Hasil Pengukuran pH sediaan formula serumformula serumekstrak daun Arabenan sebelum dan sesudah kondisi dipaksakan

Formula	pH (Average)	
	Before	After
1	6.02	6.07
2	5.6	5.5
3	6.17	6.02
4	6.03	6.12

From the results of pH measurement, the Arabenan leaf extract serum formula before and after the conditions were forced to meet the requirements because it had a pH between 5.6 to 6.17. A stable pH indicates that the components in the preparation are still in the pH range category and are not affected by temperature so that the preparation remains stable during storage. So that the results of pH measurements for each formula 1 and 2 on the basis of HPMC and formulas 3 and 4 on the basis of Na-CMC are concluded to remain stable and safe to use. Even though the pH has decreased and increased after the conditions are imposed, the indicated pH changes are very small and still acceptable because they still meet the pH range of the preparation for the skin.

CONCLUSION

results of the research that have been carried out can be concluded that :

1. Leaf extract of Arabenan [*Duchesneaindica*(Jacks.) Focke]can be formulated into a serum with various bases of HPMC and Na CMC
2. The serum formula forLeaf extract of Arabenan [*Duchesneaindica*(Jacks.) Focke]is stable and complies with the required parameters

AUTHORS CONTRIBUTION

All authors have worked equally for the literature survey, lab work and writing of the manuscript.

CONFLICT OF INTEREST

No conflict of interest, associated with this work.

ACKNOWLEDGMENTS

The authors would like acknowledge Indonesian Ministry of education and Culutre, and faculty of Pharmacy, Universitas Muslim Indonesia.

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