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Formulation And Physical Evaluation Of Cream Preparations Collagen With Concentration Variations Trietanolamine As an Emulgator

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Abstract

Indonesia is a country that has a climate with an average temperature above 18 ^{O}C, thus allowing the skin of the Indonesian people to be exposed to sunlight more often. Skin that is often exposed to sunlight causes skin condition to darken and causes a number of skin injuries. To improve the layer structure of the skin, collagen is needed. Collagen is a type of structural protein composed of several amino acids. Collagen is a protein that can be found in skin, tendons, cartilage, and organs by contributing about 30% or more of the total protein.

The research method used was an experimental method by making collagen cream preparations with varying concentrations of triethanolamine as an emulsifier of 2%, 3% and 4%. Testing the physical properties of the cream includes testing organoleptic, homogeneity, pH, type of cream, spreadability, adhesion, viscosity, irritation, and hedonic.

The results of the physical evaluation of the cream on the three formulas, namely F1, F2, and F3 respectively, namely the spreadability test F1 5.72 ± 0.36; F2 6.08 ± 0.35 and F3 7.16 ± 0.58. F1 adhesion test 8.38 ± 0.27; F2 6.78 ± 0.31 and F3 5.76 ± 0.61. F1 Viscosity Test 3927.52 ± 17.07; F2 3912.76 ± 0.36 and F3 3854.96 ± 42.88. The results of a good physical evaluation of collagen cream in the hedonic test were obtained in formula 3 which was the most preferred by the panelists. Based on the results of the One Way ANOVA and Kruskal-Wallis tests, it can be concluded that variations in the concentration of triethanolamine emulsifier have a significant effect on physical evaluation which includes pH, adhesion, spreadability, viscosity, and hedonic tests.

Key words: *Skin, Collagen, Cream, Physical Evaluation.*

1. Introduction

Indonesia is a country that has a tropical climate with an average temperature above 18^{O}C, thus allowing the skin of the Indonesian population to be exposed to sunlight more often. Skin that is often exposed to sunlight causes skin conditions to darken and cause a number of skin damage.

Nowadays people are increasingly concerned about the health of the body, especially skin health. The outermost layer of the human body that is in direct contact with the environment is the skin. Therefore, the skin is sometimes prone to damage to the skin structure and injury. To improve the layer structure of the skin, collagen is needed[1].

Collagen is a type of structural protein consisting of several amino acids. Collagen is a protein that can be found in skin, tendons, cartilage, and organs and contributes around 30% or more of the total protein. This lack of collagen can cause disturbances in the body such as skin aging, inflammation, and slow wound healing[2].

Cream is a semi-solid preparation containing one or more drugs dissolved in a suitable base and containing at least 60% water, formulated as a water-in-oil emulsion or as an oil-in-water emulsion. Making collagen cream preparations is an interesting thing because collagen plays a role in skin health[3].

Cattle (Bos indicus) are livestock kept for the use of milk and meat. Cattle live in the wild or are raised in a traditional way and are easy to find in almost all parts of Indonesia. In addition to animal husbandry, cattle are also used for agriculture (pulling plows and others).[4]. Beef contains an average composition consisting of protein varying between 16-22%, fat 1.5-13%, inorganic compounds 1%, carbohydrates 0.5%, and water between 65-80%[5].

According to the research journal Kirana (2017), one of the beef components that has the potential to be developed is skin, because it contains 89% collagen. The proportion of skin from a cow is 6.84 - 8.11%. The high content of collagen in cows opens up opportunities for formulation[6].

Collagen is an important component of protein (25-30%) in bones, skin and connective tissue of animals[1]. Hydrolyzed collagen powder (hydrolyzed collagen) is obtained by hydrolyzing gelatin with acid and is available with molecular weights from 500 to 20,000 Da. As a raw material for preparations, the use of hydrolyzed collagen with low molecular weight (2,000-5,000 Da) is preferred because it prevents precipitation and turbidity problems in the preparation. The characteristics or characteristics of collagen are white, fibrous, or look like interlocking fibers. The benefit of collagen in the skin is that it works as an absorber of water through hydration so that it keeps the skin moisturised, thereby helping the skin to regenerate quickly[7].

According to Bayarjargal's research (2021) entitled "Antioxidant and Antihypertensive Activities of Collagen and Elastin Hydrolyzate with Different Molecular Weights". This study aims to determine the antioxidant activity and inhibitory activity of angiotensin-converting enzyme (ACE) and antioxidant properties of collagen elastin hydrolyzate, and their peptide fractions (<5 kDa, 5-10 kDa, 10-100 kDa). Collagen antioxidant activity test was carried out by fractionating hydrolyzed collagen at different molecular weights determined at the same concentration (4%) used for the ACEI test. The results are expressed as IC concentrations50, where 50% at a molecular weight of ≤ 5 kDa scavenged ABTS radicals of 5.2 mg/ml and DPPH free radicals of 39.0 mg/ml had strong antioxidant properties and it was concluded that hydrolyzed collagen has a perspective as a bioactive[8].

Meanwhile, another study was conducted by Jumasni Adnan (2019) entitled "The Effect of Triethanolamine Concentration as an Emulgator on the Stability of the Physical Quality of Cream of Papaya Fruit Extract (Carica papaya L.)", the purpose of this study was to find out the comparison of the use of variations in the amount of triethanolamine 2%, 3%, and 4% on the stability of the physical quality of papaya fruit extract cream. Preparation of cream by varying the concentration of triethanolamine. The results showed that the organoleptic test, pH, homogeneity, cream washability, and emulsion type showed that formula 3 with 4% triethanolamine concentration had good physical properties stability, while when the spreadability test was carried out it showed formula 1 with 2% triethanolamine concentration and formula 2 with 3% triethanolamine concentration has good stability[9].

Many research journals have examined collagen as a wound healing potential in the skin, both as a cosmetic, biomedical, and supplement. Some of the existing journals, not many journals have conducted research on cream formulations using collagen, based on this the author wants to do a final project research entitled "Formulation and Physical Evaluation of Collagen Cream with Triethanolamine Variations as an Emulgator".

2. Method

The research was conducted from February 2023 to April 2023 and was carried out at the Pharmacy Technology Laboratory of the Indonusa Polytechnic Surakarta and took Bovine collagen from PT. Source Food, Istanbul.

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This type of research is the experimental method. The experimental method is a study in which the researcher treats research subjects and analyzes the effect of a treatment on the independent variable on the dependent variable by observing, noting the reactions that arise from the subject. This experimental study was to determine the effect of varying the concentration of triethanolamine in collagen cream.

The tools used include digital scales, mortar and pestle, measuring cup, beaker, dropper pipette, horn spoon, stirring rod, pH meter, porcelain dish, petri dish, object glass, watch glass, water bath, millimeter block, stopwatch, thermometer , Brookfield viscometer, test tube clamp and adhesion test kit.

The materials used include bovine collagen obtained from PT. Food sources, stearic acid, cetyl alcohol, methyl paraben (nipagin), propyl paraben (nipasol), triethanolamine (TEA), methyl blue, green tea essence, and distilled water (aquadest).

Table 1. Formulation of Collagen Cream

Material	Function	F1 (%)	F2 (%)	F3 (%)
Stearic acid	Oil Phase Emulgator	17	17	17
Cetyl alcohol	Emollient (Moisturizing)	2	2	2
Nipagin	Water Phase Preservative	0.1	0.1	0.1
Nipasol	Oil Phase Preservative	0.1	0.1	0.1
Collagen	Active Ingredients	4	4	4
Triethanolamine	Water Phase Emulgator	2	3	4
Jasmine Perfume	Additives	3 drops	3 drops	3 drops
Distilled water	Solvent	ad 100	ad 100	ad 100

Information :

(Each formula is made 70 grams)

F1 : Triethanolamine Formula(TEA) 2%.

F2 : Triethanolamine Formula(TEA) 3 %.

F3 : Formula Triethanolamine (TEA) 4 %.

2.1 How Formulas Work

Weigh all the ingredients, separate the ingredients into two, namely the water phase and the oil phase. The oil phase which includes stearic acid and cetyl alcohol is dissolved over a water bath (mass 1). The water phase consisting of triethanolamine and methyl paraben is dissolved in hot water which has been measured at 70°C on a hotplate (mass 2). Soaking mortar and stamper in hot water, drying. Enter mass 1 and mass 2 into the mortar, grind until homogeneous and add propyl paraben. After a homogeneous creamy mass is formed, gradually add the bovine collagen, crushed until the creamy mass is homogeneous. Add 3 drops of perfume then homogenize with the remaining distilled water until a cream forms. The procedure was repeated for all formulations with different variations of triethanolamine concentrations[10].

2.2 Evaluation of Cream Preparations

2.2.1 Organoleptic Test

Examination of the physical properties of the cream preparations, including: Form: examination of the shape / consistency of the cream. Color: cream color check. Smell : check the scent of the cream[11].

2.2.2 Homogeneity Test

This homogeneity test was carried out by applying the cream obtained on the glass slide, then covering it with another glass. Check whether the cream applied to the slide has homogeneous properties, the surface is smooth and the color is even.

2.2.3 pH test

Cream measured its pH with a pH meter. Examination of the pH of the cream was carried out by means of a pH meter calibrated with a buffer solution of pH 4 and 7. Then 1 gram of cream sample was mixed with 1 ml of distilled water, then measured the pH. The pH of the skin is 4.5-6.5.

2.2.4 Cream Type Test

The method used to observe the type of emulsion is the color dispersion method, by adding a few drops of methyl blue to a beaker containing the cream sample. If the blue color is directly mixed in the emulsion, the type of cream is oil in water (M/A) and vice versa, if the blue color is not completely mixed the type of cream is water in oil A/M[11].

2.2.5 Spreadability Test

Place the transparent glass on the millimeter block paper. Give 0.5 grams of cream sample on top, cover with another glass then let stand for 1 minute to get cream with a certain diameter. Then load it on the glass with a load of 50 g to 250 g and observe the diameter of the distribution obtained. A good cream is a cream that spreads easily and evenly[13].

2.2.6 Stickiness Test

This test is done by placing 500 mg of cream sample on a glass object, then covering it with a second glass object and pressing it with a 1 kg load for 5 minutes. The glass object is placed on the test stand, the 80 g weight is removed and the time it takes for the two objects to be released is recorded. Replicated 3 times. Repeat test on other formulas[13].

2.2.7 Viscosity Test

Cream viscosity was measured using a BrookField viscometer, by pouring 50 grams of cream into the ointment pot. Run spindle no. 3 with a rotor speed of 30 rpm. Test results are recorded[11].

2.2.8 Irritation Test

Irritation testing was carried out on 9 adult female and male panelists. The test is carried out on the arm behind the earlobe for 24 hours, if an itchy or reddish reaction does not occur then the cream is safe to use[14].

2.2.9 Hedonic Test

Hedonic testing on 20 male and female volunteers for the cream preparations that had been made and asked to assess the cream preparations which included color, texture, and ease of being

spread. The test parameters were measured at the panelist's level of preference for the preparation[15].

2.2.10 Data analysis

The test data was analyzed using the Statistical Package For The Social Sciences (SPPS), which is a program used on computers for data analysis. The data tested in the first SPSS uses the normality test to see if the data is normally distributed or not based on its significance value, if the data obtained has a significance value > 0.05, which means that the data is homogeneously distributed, then parametric statistical tests are used with the Analysis of Varience (ANOVA) One test. Way whereas if the results obtained have a significance value of <0.05 which means the data is not distributed homogeneously then a nonparametric statistical test is used with the Kruskal wallis test[16].

3. Result and Discussion

The purpose of the physical evaluation of collagen cream with triethanolamine variations is to determine the quality of the cream produced with variations in emulsifier concentrations. Physical evaluation of cream preparations consisted of: organoleptic test, homogeneity, pH, type of cream, spreadability, adhesion, viscosity, irritation, and hedonic.

3.1 Organoleptic Test

Table 2. Organoleptic Test Results

Formulas	Smell	Color	Consistency
F1	Jasmine Perfume	White	Half Solid
F2	Jasmine Perfume	White	Half Solid
F3	Jasmine Perfume	White	Half Solid

The organoleptic test aims to determine the appearance of the cream by examining the color, smell and consistency of the preparation[11]. Based on the obtained test results, there is a difference in the consistency of the cream, namely in formulation 1 the consistency of the cream produced is semi-solid but thicker in texture, while formulation 2 is semi-solid and formulation 3 has a semi-solid consistency. The three formulas produce a different cream consistency in each

formulation where the more triethanolamine (TEA) content, the resulting cream texture will be slightly thinner. In the organoleptic test for odor, all formulas have the same smell, which is typical of jasmine perfume. In the organoleptic test the consistency of all formulations obtained thick cream that is relatively liquid.

3.2 Homogeneity Test

The purpose of the test is to find out whether the collagen cream can be mixed evenly in the cream preparation or not. The test was carried out by placing a small amount of cream on a glass plate and cupping the other plate, then observing whether there were coarse grains and an even color in the cream. The test results of the three formulas are homogeneous, no coarse grains and uniform color.

3.3 pH Test

The purpose of testing the pH is to ensure that it is not harmful to use the preparation on the skin. Testing the pH by dipping the pH meter into the cream preparation then looking at the results of the pH measurement printed on the pH meter. The pH test results obtained were F1 pH 5.68, F2 pH 6.4, and F3 pH 6.6. The observation results for formulations 1 and 2 have met the quality requirements, while formulation 3 does not meet the requirements for good cream quality because it produces a pH > 6.5. There is a significant difference in pH between the three formulas, this could be due to triethanolamine having an alkaline nature with a pH of 10.5 so where the higher the concentration of triethanolamine, the resulting pH will be even higher[17]. Cream preparations are expected to meet the pH requirements for good cream preparations, namely pH 4.5-6.5.

Table 3. pH Test Results

Formula	pH
F1	5,68 ± 0,46
F2	6,40 ± 0,06
F3	6,60 ± 0,07

3.4 Cream Type Test

The test which aims to examine the type of cream in this formulation has 2 methods, namely the dilution method and the color dispersion method. The type of cream test that has been carried out is by using the color dispersion method, namely by giving a few drops of methylene blue into

a beaker containing a sample of cream. If the blue color is immediately dissolved in the emulsion then the type of cream is oil in water (o/m) and vice versa, if the blue color is not completely dissolved then the type of cream is water cream in oil w/o[11]. The results of the cream test from the three formulas, namely the type of m/a, the three cream formulas are distributed in blue overall. Based on the formula design, the overall collagen cream formulation is dominated by the water phase category where the drug substance dissolves in water which is alkaline. In addition, the M/A type has a high water content because the oil is distributed in water so it can provide a hydrating effect to prevent the skin from drying out.

3.5 Spreadability Test

The purpose of this test is to measure how well a sample of the cream spreads on the skin. The results of the spreading power test were F1 5.72; F2 6.08; and F3 7.16cm. There is a difference in the spreadability of the cream which is affected by variations in the concentration of the emulsifier, this is because the triethanolamine before it is formulated is in the form of a liquid and slightly viscous, so it can be concluded that the higher the triethanolamine level, the greater the spreadability value because the resulting preparation is more liquid and easier spread. Formulas 1 and 2 meet the requirements for good cream spreadability, which is between 5-7cm[18], while Formula 3 exceeds 7 centimeters.

Table 4. Spreadability Test Result

F1 (cm)	F2 (cm)	F3 (cm)
5.72 ± 0.36	6.08 ± 0.35	7.16 ± 0.58

3.6 Stickiness Test

This test aims to determine how long the preparation can stick to the skin, the higher the adhesion value, the longer the preparation will stick to the skin. The results of the cream test were F1 8.38 seconds, F2 6.78 seconds and F3 5.76 seconds. From the data obtained, it can be seen that there are differences in results where differences in triethanolamine concentrations affect the adhesion test, this is due to the characteristics of triethanolamine before it is formulated, which is in the form of liquid and slightly viscous, where the higher the concentration of triethanolamine, the lower the stickiness. So it can be concluded that the adhesive power is inversely proportional

to the spreading power. All three formulas have met the requirements for good adhesion of topical preparations, which is more than 4 seconds[18].

Table 5. Stickiness Test Results

F1 (Second)	F2 (Second)	F3 (Second)
8.38 ± 0.27	6.78 ± 0.31	5.76 ± 0.61

3.7 Viscosity Test

This test aims to determine the thickness of a preparation using a Brookfield viscometer. The results of the cream viscosity test on F1 were 3,927.516 cPs; F2 3913.753 cPs and F3 3854.953 cPs at 30 rpm. Of the three formulas, they meet the requirements for good cream viscosity, namely 2,000-50,000 cPs[18]. There is a difference in the resulting viscosity value because it is influenced by variations in the concentration of the triethanolamine emulsifier where the higher the triethanolamine concentration the lower the viscosity value because the resulting preparation will be more liquid.

Table 6. Viscosity Test Results

F1 (cPs)	F2 (cPs)	F3 (cPs)
3927.52 ± 17.07	3912.76 ± 0.36	3854.96 ± 42.88

3.8 Irritation Test

This test has the aim of knowing whether the preparations made cause irritation / serious side effects to the skin. This test is done by applying the cream behind the earlobe for 24 hours, if there is no itching or redness reaction, the cream is safe to use[14]. The test results of the three formulas met the requirements of a good cream, namely the three formulas did not cause itching or redness in 9 respondents.

3.9 Hedonic Test

This hedonic test was carried out to evaluate a sample by involving several panelists or volunteers who were then asked to give their opinions or comments on the quality of the sample. The hedonic test was carried out on 20 panelists (19 women and 1 man) on cream preparations that had been made and were asked to assess the cream preparations which included color, texture,

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and ease of smearing. The hedonic test results for the three formulations that the panelists liked the most were formula 3.

Table 7. Hedonic Test Results

Test Category	Subset Value Results			Best Formulas
	F1	F2	F3	
Color	3.80	3.70	4.00	F3
Texture	3.60	3.70	4.05	F3
Ease of Greasing	3.40	3.70	3.95	F3

3.10 Statistical Test of Physical Properties of Cream

Statistical results pH Fl = 0.486; F2 = 0.511 and F3 = 0.161. In the One Way ANOVA test, the pH of the cream yielded a value of 0.000 in significance which means <0.05 that the cream has a significant difference in the pH test.

The statistical results of the spreadability of Fl = 0.218; F2 = 0.327 and F3 = 0.583. In the One Way ANOVA test the spreadability of the cream yielded a value of 0.000 at significance which means <0.05 that the cream has a significant difference in the spreadability test.

The statistical results of stickiness Fl = 0.038; F2 = 0.084 and F3 = 0.001. In the Kruskal-Wallis test the adhesion of the cream yielded a value of 0.000 at a significance level which means <0.05 that the cream has a significant difference in the adhesion test.

The statistical results of the viscosity of Fl = 0.000; F2 = 0.319 and F3 = 0.000. In the Kruskal-Wallis test the viscosity yielded a value of 0.000 at a significance level which meant <0.05 that the cream had a significant difference in the viscosity test.

4. Conclusion

Based on the analysis of the One Way ANOVA and Kruskal-Wallis tests that have been carried out, it can be concluded that differences in varying triethanolamine concentrations significantly affect the physical evaluation which includes pH, adhesion, spreadability, and viscosity tests.

5. Acknowledgement

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