COMBINATION CREAM FORMULATION OF CITRONELLA AND KECOMBRANG FLOWER AND ANALGETIC TEST ON MICE WITH INFRA RED METHOD

Maya Handayani Sinaga[1], Tri Bintarti[2]
Pharmacy Departmen, Medan Health Polytechnic of Ministry of Health

ABSTRACT . Traditionally, citronella leaves and Kecombrang flowers have been empirically proven to cure various diseases, and can relieve pain (analgesic), but this has not been scientifically proven. This is closely related to the content of various secondary metabolites and other chemicals in citronella and flowers. kecombrang include polyphenolic compounds and steroids/triterpenoids. This study tested the phytochemical screening and analgesic effectiveness test of the combination of ethanol extract of citronella and Kecombrang flower extract in the form of a cream preparation which was carried out topically on the feet of male mice induced by stimulation with infrared light on the Plantar test. The aim is to obtain alternative analgesic drugs from natural ingredients that are rational and economical.Citronella extract was prepared by percolation using 80% ethanol. Phytochemical screening was carried out on the ethanol extract of citronella (EESW) and Kecombrang flower extract (SBK). The combination of EESW and SBK was formulated into cream preparations with variations in concentration (5:5)%; (7.5:2.5)%; (2.5:7.5)%; (10:0)%; (0:10)%, physical tests were carried out, and analgesic effectiveness tests were carried out on male mice induced by infrared light on the Plantar test device, observed pain response resistance time after being given a cream preparation that had been formulated, and Hot in cream as a comparison, every 15 minutes for 180 minutes. The data obtained were calculated as analgesic power. And the data were analyzed statistically with ANOVA and Tukey tests.The results showed that the ethanol extract of citronella and Kecombrang flower extract contained secondary metabolites of alkaloids, flavonoids, steroids/triterpenoids, saponins, glycosides, and essential oils. The best cream preparation is the EESW:SBK (5:5)% formula because at 135 minutes, it has an analgesic effect that is not significantly different from cream (7.5:2.5)% and with Hot In Cream® preparations circulating in Indonesia. market.

Keywords: *Citronella, Kecombrang flower, Cream Preparation, Analgesic Effectiveness, Plantar Test*

BACKGROUND

Pain is in most cases just a symptom that serves as a danger signal about a tissue disorder, such as inflammation (rheumatism, gout), microbial infection or muscle spasms. Pain caused by mechanical, chemical or physical stimulation of heat, electricity can cause tissue damage. These stimuli trigger the release of certain substances called pain mediators, including histamine, bradykin, leukotrienes, and prostaglandins (Tjay and Rahardja, 2007).

Analgesics are drugs or compounds that are used to reduce pain or pain without losing consciousness. Currently on the market there are many analgesic drugs circulating from synthetic chemicals, but they often cause various side effects, it is necessary to look for alternative analgesic drugs from natural

ingredients with relatively mild side effects. In a research journal (Widowati et al., 1999) it is known that a class of volatile oil compounds such as terpenoids and terpineol are useful for reducing fatigue and alertness. Essential oils of the terpenoid and terpineol groups are widely contained in various types of plants. Fragrant citronella (Cymbopogon nardus L. Rendle) contains many essential oils, namely citronella, citronellol and geraniol. In addition, sitral compounds, nerol, eugenol, farnesol. Kecombrang flowers (Etlingera elatior Jack) also contain relatively high essential oils of about 17%, in addition to the content of saponins, flavonoids, and polyphenols.

Research in 2017 on Kecombrang that still fresh and dried at a temperature of around 600C, contains the same class of chemical compounds, namely: flavonoids, glycosides, anthraquinones, saponins, and tannins (Tri Bintarti et al.) dried at about 600C. Can be formulated into a toothpaste preparation, which is homogeneous, pH is around 5, has a good odor and color, good consistency (Tri Bintarti 2018 et al)

Empirically it is known that Citronella and Kecombrang flowers, have been proven and used as body warm rubs and pain relievers, aches and pains and are symptoms of rheumatism (Sastroamidjojo, 2001). In addition, these two plants because they contain a lot of 3-7 % aromatic essential oils can also be used as scents and mosquito repellents (Agoes, 2010). in a dosage form that is easy to use, practical, and easy to distribute and store with rational efficacy. One of them is made in the form of cream preparations (Wyatt et al., 2001). In connection with the above, the researchers conducted a phytochemical screening of the ethanol extract of citronella and Kecombrang flower extract, and formulated the combination of citronella extract and Kecombrang flower extract into a cream preparation. The cream preparation obtained was then tested for its effectiveness as an analgesic against white male mice using the infra red (plantar test) method, and as a comparison, Hot In Cream® which was circulating in the market was used as a comparison.

METHODS

This research method is experimental. Variations in concentration of ethanol extract of citronella leaves and Kecombrang flower extract in cream preparations were formulated as independent variables, and various test parameters as dependent variables. The design of this study consisted of the following stages: preparation of samples of citronella and Kecombrang flowers, preparation of research materials, extraction of citronella, and Kecombrang flower extract, phytochemical screening, formulation of cream preparations combination of ethanolic extract of citronella and fresh Kecombrang flower extract, examination of the homogeneity of the preparation. , measuring the pH of the preparation, determining the type of emulsion of the preparation, determining the stability of the preparation, testing irritation on volunteers, and testing the effectiveness of analgesics.

1.Tools and Materials

1.1 Tools

The tools used consist of: laboratory glassware, water bath, oven (Memmert), pH meter, object glass, water content determination tool (Azeotropy), rotary evaporator (Eyela), and plantar test infra red.

1.2 Ingredients

The ingredients used are citronella, Kecombrang flower, Hot In Cream® as a comparison, stearic acid, cera alba, triethanol amine, glycerin, liquid paraffin, methyl paraben, menthol, camphor, methanol, concentrated hydrochloric acid, anhydrous sodium sulfate, acetic acid, sodium hydroxide, concentrated sulfuric acid, iron (III) chloride, iodine, mercury (II) chloride, bismuth (III) nitrate, glacial acetic acid, alpha naphthol, ethyl acetate, potassium iodide, distilled water, ethanol 80% .

2. Animal Test

This study used 35 male mice (Mus musculus), body weight 30-40 g aged 2-3 months. Mice were adapted for 14 days in cages. so that mice can adjust to the new environment and reduce stress. During adaptation, observations were made on general conditions and weighing to select healthy mice and then used them in experiments (Depkes RI, 1979).

3. Volunteer

Volunteers in the irritation test are the closest people and are in the vicinity of the test so they are easier to monitor and observe if a reaction occurs on the skin being tested, totaling 6 people with the following criteria (Directorate General of POM, 1985):

1. Women aged between 20-30 years

2. There is no history of disease related to allergies
3. Willing to volunteer
4. Physically and mentally healthy

4. Preparation of Reagent Solution

4.1 Hydrochloric Acid 2N

A total of 17 mL of concentrated hydrochloric acid was put into a glass beaker containing 25 mL of distilled water, waited for it to cool and diluted with distilled water to 100 mL (Depkes, 1978).

4.2 Sulfuric Acid 2N

A total of 8.4 mL of concentrated sulfuric acid was put into a glass beaker containing 25 mL of distilled water, diluted with distilled water to 100 mL (Depkes, 1978).

4.3 Iron (III) Chloride 1% w/v

Weighed 1 g of iron (III) chloride then dissolved with distilled water to a volume of 100 mL (Depkes, 1978).

4.4 Lead(II) Acetate 0.4 M

A total of 15.17 g of lead acetate was weighed, then dissolved in carbon dioxide-free distilled water to a volume of 100 mL (MOH, 1978).

4.5 Mayer's reagent

A total of 1.36 g of mercury (III) chloride was dissolved in distilled water to 60 mL. In another container weighed 5 g of potassium iodide dissolved in 10 mL of distilled water. Then both are mixed, made up to 100 mL (Depkes, 1978).

4.6 Molish reagent

A total of 3 g of alpha-naphthol was dissolved in 0.5 N nitric acid to taste and added with distilled water up to 100 mL (Depkes, 1978).

4.7 Bouchardat's reagent

A total of 4 g of potassium iodide was dissolved in sufficient distilled water then added 2 g of iodine, then added distilled water up to 100 mL (Depkes, 1978).

4.8 Dragendorph's reagent.

A total of 0.85 g of bismuth (III) nitrate was weighed, dissolved in 100 mL of glacial acetic acid and added 4 mL of distilled water. In another container weighed as much as 8 g of potassium iodide dissolved in 20 mL of distilled water. Then the two solutions were mixed equally, then added 20 mL of glacial acetic acid and diluted with distilled water to 100 mL (Depkes, 1978).

4.9 Chloralhydrate Reagent Solution

70 g of chloral hydrate crystals were weighed and then dissolved in 30 mL of distilled water (Depkes, 1995).

4.10. Liebermann-Burchard reagent

A total of 20 parts of acetic anhydride are mixed with 1 part of concentrated sulfuric acid. This solution must be made fresh. (Ministry of Health, 1995).

5. Sample Processing of Citronelle and Kecombrang flowers

Fresh citronella that has been collected is cleaned of impurities by washing with clean water, then drained, then dried in a dryer. The sample is considered dry if it is crushed. Furthermore, it is mashed using a blender, and the simplicia citronella powder is obtained, then stored in a container.

5.1 Determination Water Content of Citronella Simplicia

Determination of the water content of simplicia was carried out to determine the simplicia obtained met the requirements for a good simplicia water content, which was not more than 10%. Performed by the azeotropic method as follows:

In a round bottom flask, 200 mL of toluene and 2 mL of distilled water were added, distilled for 2 hours, until all the distilled water was obtained, the toluene was saturated. After that, the toluene was cooled and set aside a little for rinsing, the volume of water in the receiving tube was read as the initial volume of water.

Then, into a flask containing saturated toluene, 5 g of citronella simplicia powder was carefully weighed, then heated carefully for 15 minutes. After the toluene boils, adjust the drip rate to approximately 2 drops per second until most of the water is distilled off. Then the distillation speed was increased to 4 drops per second. After all the water has been distilled, the inside of the cooler is rinsed with saturated toluene. Distillation was continued for 5 minutes, then the receiving tube was allowed to cool to room temperature. After the water and toluene were completely separated, the volume of water was read to an accuracy of 0.05 mL as the final water volume. The difference between these two volumes is read and calculated the water content contained in citronella simplicia

(Ministry of Health RI, 1989). Percent water content is calculated by the following formula :

$$\% \text{ Moisture content} = \frac{\text{(Final volume of water - Initial volume of water (mL))}}{\text{(Simple weight (g))}} \times 100\%$$

5.2 Manufacture of Citronella Ethanol Extract

A total of 3 kg of simplicia citronella powder was put into a covered vessel and 80% ethanol was added, until it was submerged for 3 hours. The mass is transferred into the percolator while being pressed, then the filter fluid is poured until there is a layer on top of the simplasia. The percolator is closed and left for approximately 24 hours. Then the percolator tap is opened and the liquid is allowed to drip at a rate of 20 drops per minute. The filter fluid is added through the reservoir, and the drops that enter the simplicia are the same as the drops that come out of the simplicia, so that there is always a layer of filter fluid on top of the simplicia.

The percolation process was terminated until the last drop that came out of the percolator was colorless, and one mL of the last drop was evaporated in a vaporizer dish leaving no residue. Then the percholate was distilled under low pressure at a temperature of not more than 50^0C using a rotary vacuum (rotavapour) to obtain a thick juice. Then it was dried in a freeze dryer at a temperature of -40^0C at a pressure of 2 atm for ± 24 hours to obtain a citronella extract, called citronella ethanol extract (Dit.Jend POM 1979).

5.3 Kecombrang flower Sample Processing

A total of 3 kg of fresh Kecombrang flowers, mashed with a blender without the addition of water. The result is squeezed using a white cloth, the sari is obtained. Then the dregs are given a little water and squeezed again. This is repeated until the juice is colorless. The collection of juice was evaporated in an evaporating dish at low temperature over a water bath until a thick juice was obtained and it was called Kecombrang flower essence (Dit. Jend POM 1979).

6. Phytochemical Screening

Phytochemical screening was carried out to determine the class of secondary metabolite chemical compounds in the ethanolic extract of citronella and fresh Kecombrang flower extract including examination of alkaloids, flavonoids, tannins, saponins, steroids/triterpenoids, glycosides, saponins, and essential oils (Depkes, 1978). So that it can be seen the potential of ethanol extract of citronella and fresh Kecombrang flower extract as an analgesic.

6.1 Alkaloids

A total of 0.5 g of citronella extract and fresh kecombrang flower extract were each put into a test tube and then 1 mL of 2N hydrochloric acid and 9 mL of distilled water were added, heated on a water bath for 2 minutes then cooled and filtered. The filtrate was used for the following experiments:

a. As much as 1 mL of filtrate is added 2 drops of Mayer's reagent, a white or yellow precipitate will form if it contains alkaloids

b. As much as 1 mL of filtrate is added 2 drops of Bouchardat reagent, a brown to black precipitate will form if it contains alkaloids

c. As much as 1 mL of filtrate is added 2 drops of Dragendorff's reagent, a red to brown precipitate will form if it contains alkaloids.

But if reactions 1 and 2 only occur turbidity proceed with the following examination:

A total of 8 mL of the filtrate was added with 5 mL of concentrated ammonia and shaken with 10 mL of the ether-chloroform mixture (3:1) and allowed to separate, the ether-chloroform layer was taken, added a little anhydrous sodium sulfate, filtered and the filtrate was evaporated in a watch glass over a water bath, dissolved. residue with a small amount of 2N hydrochloric acid. Alkaloids are positive if there is a precipitate or turbidity in at least two reactions from the three experiments above (Directorate General of POM, 1989).

6.2 Flavonoid Examination

A total of 10 g of citronella extract and fresh kecombrang flower extract were each put into an Erlenmeyer flask with 10 mL of methanol added, refluxed for 10 minutes. Heat filtered through filter paper. The filtrate is diluted with 10 mL of water, after cooling 5 mL of kerosene ether is added, shaken carefully and allowed to stand. The methanol layer is taken, then evaporated at 400C, the remainder is dissolved in 5 mL of ethyl acetate, then filtered. The filtrate was used for flavonoid assay as follows:

a. A total of 1 mL of the filtrate was evaporated to dryness, the rest was dissolved in 2 mL of 96% ethanol and then added 0.5 g of zinc powder and 2 mL of 2N hydrochloric acid, left for 1 minute. Add 10 drops of concentrated hydrochloric acid. if within 2-5 minutes an

intense red color occurs, it indicates the presence of flavonoids (glycosides-3-flavonols) b. A total of 1 mL of the filtrate was evaporated to dryness, the remainder was dissolved in 1 mL of 96% ethanol then added 0.1 g of magnesium powder and 10 drops of concentrated hydrochloric acid. If the red orange to red purple color shows the presence of flavonoids (Directorate General of POM, 1989

6.3 Glycoside

A total of 3 g of citronella extract and fresh kecombrang flower extract were extracted with 30 mL of a mixture of 7 parts 96% ethanol and 3 parts distilled water, respectively. Then concentrated sulfuric acid was added and refluxed for 10 minutes, then cooled and filtered. Then 20 mL of the filtrate was taken, added 10 mL of distilled water and 10 mL of 0.4 M lead (II) acetate, shaken, allowed to stand for 5 minutes and then filtered. The filtrate was extracted with 20 mL of a mixture of chloroform and isopropanol (3:2), repeated 3 times. Further tested as follows :

1. Test on sugar compounds

a. Taken as much as 1 mL of the top layer (water extract) is evaporated on a water bath. The remaining evaporation is added 2 mL of water and 5 drops of Molish reagent solution, and carefully added concentrated sulfuric acid, a purple ring is formed at the liquid boundary, this reaction indicates the presence of sugar bonds.
b. Take 1 mL of the top layer (water extract) and evaporate on a water bath. The remainder is added Fehling A and Fehling B (1:1), heated. Formation of a brick red color precipitate indicates reducing sugar

2. Test on non-sugar compounds

Take as much as 1 mL of the bottom layer (organic solvent extract), evaporated over a water bath at a temperature of not more than 600C. The remainder is dissolved in 2 mL of methanol, added 20 drops of glacial acetic acid and 1 drop of concentrated sulfuric acid (Lieberman-Bouchard reagent), if a blue, green, red purple, or purple color occurs, positive for nonsugar (MMI vol VI, 1995) .

6.4 Saponins

A total of 0.5 g of citronella extract and fresh kecombrang flower extract were each put into a test tube, then 10 mL of hot water was added, cooled and then shaken vigorously for 10 seconds. If a foam is formed as high as 1-10 cm, it is stable for not less than 10 minutes and when the addition of 2N hydrochloric acid does not disappear, it indicates the presence of saponins (Ditjen POM, 1989).

6.5 Steroids/Triterpenoids

As much as 1 gram of citronella extract and fresh kecombrang flower extract were each macerated with 20 mL of ether and then filtered. Taken as much as 5 mL of the ether solution was evaporated over a water bath, then added 20 drops of glacial acetic acid and 1 drop of concentrated sulfuric acid (Liebermann-Bouchard reagent). Formation of blue or green color indicates the presence of steroids, and if formed red or purple color indicates the presence of triterpenoids (Ditjen POM, 1989).

6.6 Tannin

A total of 1 g of citronella extract and fresh kecombrang flower extract were each boiled for 3 minutes in 100 mL of distilled water, cooled and filtered. Add 1-2 drops of 1% iron (III) chloride reagent to the filtrate. a blackish blue or blackish green color occurs indicating the presence of tannins (Directorate General of POM, 1978).

6.7 Essential oil

A total of 1 g of citronella extract and fresh kecombrang flower extract were each macerated in 20 mL of n-hexane for 2 hours and then filtered. 5 mL of filtrate was evaporated in an evaporating dish to dryness. To the residue was added 20 drops of anhydrous acetic acid and 1 drop of concentrated sulfuric acid (Lieberman-bouchard reagent). The appearance of blue or blue green indicates the presence of steroids, while red, pink or purple colors indicate the presence of triterpenoids (Harborne, 1987).

7. Formulation of Creams

The cream preparation was formulated using a cream base and added a combination of ethanol extract of citronella (EESW) and fresh kecombrang flower extract (SBK) in various combinations of concentrations.

a. Cream Base Making

The basic formula of the cream is based on the Indonesian Cosmetics Formulary (1985), with the following formula :

R/ Stearic acid 60

Cera Alba	50
Triethanolamine	10
Liquid paraffin	250
Glycerin	200
Methyl Paraben	0.15
Aquades ad	1000

Liquid cream base made of 1000 grams was used for the manufacture of cream preparations with a combination of ethanol extract of citronella and fresh kecombrang flower extract

- F-1 (Citronella extract 5.0: Kecombrang flower powder 5.0) %,
- F-II (Citronella extract 7 ,5 : Kecombrang flower powder 2,5) %,
- F-III (Citronella extract 2,5 : Kecombrang flower powder 7,5) %,
- F-IV (Citronella extract 10 : Kecombrang flower powder 0)%,
- FV (Citronella extract 0 : Kecombrang flower powder 10) %., and
- blank (without using any test materials. Each formula is made as much as 100 grams, then it is made as follows.

Weigh the ingredients of the cream base. Liquid paraffin, stearic acid, cera alba were melted on a water bath (oil phase) at a temperature of 70-750C. Glycerin, methyl paraben and triethanolamine were dissolved in hot distilled water (aqueous phase). Then the oil phase was put into a hot mortar, added the still hot water phase and stirred constantly until a homogeneous cream base was obtained. This cream base is then used for the manufacture of cream preparations containing a combination of ethanol extract of citronella and kecombrang flower extract in various concentrations.

b. Cream Preparation

The cream contains a combination of ethanol extract of citronella and kecombrang flower extract. Because this cream is desired to give a warm feeling, then camphor, menthol are added with the following formula composition :

Table 1. Formula for Citronella Extract and Kecombrang Flower Extract.

Formula	Citronella Extract (g)	Kecombrang Flower Powder (g)	Kamfer (g)	Mentol (g)	Base cream (g)	Total (g)
Base cream 1	5,0	5,0	2,5	7,5	80,0	100
Base cream 2	7,5	2,5	2,5	7,5	80,0	100
Base cream 3	2,5	7,5	2,5	7,5	80,0	100
Base cream 4	10	-	2,5	7,5	80,0	100
Base cream 5	-	10	2,5	7,5	80,0	100
Base cream (Blank)	-	-	2,5	7,5	90	100

How to make it :

Menthol and Kamfer were put into a mortar, then dripped with sufficient ethanol and ground until homogeneous, then a combination of ethanol extract of citronella and fresh kecombrang flower extract was added according to the concentration of each formula, and added the cream base little by little which had been weighed according to each. -each formula. Then ground until homogeneous, stirred until homogeneous. Put in the container provided. Hereinafter referred to as F-1 (EESW 5.0 : SBK 5.0)%, F-II (EESW 7.5 : SBK 2.5)%, F-III (EESW 2.5 : SBK 7.5)%, F-IV (EESW 10 : SBK 0)%, FV (EESW 0 : SBK 10)%. Then the resulting cream preparation was evaluated with various test parameters, including: organoleptic test, homogeneity, pH, stability, emulsion type, irritation to volunteers, and effectiveness as an analgesic on test animals.

7.1 Evaluation of Cream Preparation

7.1.1 Organoleptic Test

The organoleptic test was carried out by visually observing the cream preparation produced from the shape, smell, and color of the observed preparation (Kurniati, 2011).

7.1.2 Examination for Homogeneity of Preparations

The homogeneity test was carried out by placing a small amount of cream on a piece of glass, then observing the presence of coarse particles or visual inhomogeneities. The homogeneity of cream preparations is related to the comfort parameter of the cream preparation user (Ansel, 2008).

7.1.3 Observation of Cream Stability

Observation of the stability of the preparation was carried out at room temperature storage by: Each cream preparation was put into a plastic pot, closed the top. Furthermore, observations were made when the new preparation was finished and after storage for

1, 4, 8, and 12 weeks. The things that were observed were phase separation, changes in color and odor of the preparation (Ansel, 2008).

7.1.4 Measurement of the pH of the preparation

Measurement of the pH of the preparation was carried out using a pH meter. The instrument was first calibrated using a neutral standard buffer solution (pH 7.01) and an acidic pH buffer solution (pH 4.01) until the instrument showed the pH value. Then the electrodes were washed with distilled water, then dried with a tissue. The sample was made in a concentration of 1%, which was weighed 1 g of the preparation dissolved in distilled water up to 100 mL, stirred. Then the electrode is dipped in the solution. The pH value guide is left until it is constant. The number shown by the pH meter is the pH of the preparation (Rawlins, 2003).

7.1.5 Determination of the type of emulsion preparation

A certain amount of preparation is placed on a glass object, added 1 drop of methyl blue, stirred with a stirring rod. Covered with a cover slip and observed. If the methyl blue is evenly distributed, it means that the preparation is an O/O emulsion type, but if only blue spots are present, it means that the preparation is an A/O emulsion type.

8. Volunteer Irritation Test

The irritation test of the cream preparation that has been formulated is carried out on 6 volunteers by: 500 mg of cream is applied behind the ear with a diameter of 2 cm, then left for 24 hours and the changes that occur in the form of redness of the skin, itching of the skin, skin becomes dry. rough (Tranggono and Latifah, 2007).

9. Analgesic Effectiveness Test

The working stages of the analgesic antifungal research in cream preparations containing a combination of ethanol extract of citronella and fresh kecombrang flower extract which have been formulated with various combinations of concentrations in male mice are as follows:

All test animals in the form of adapted male mice were weighed and given identification marks. divided into 7 groups and each group consisted of 5 mice. The provision of test materials for cream preparations and comparisons in mice was carried out topically with the following test groups :

1. Group I : Negative control (blank) was given cream base
2. Group II : The comparison is given Hot incream® which is circulating in the market
3. Group III : Given cream preparation F-1 (Citronella extract 5.0: Kecombrang flower powder 5.0) %,
4. Group IV : Given cream preparation F-II (Citronella extract 7.5 : Kecombrang flower powder 2.5) %,
5. Group V : Given cream preparation F-III (Citronella extract 2.5 : Kecombrang flower powder 7.5)%,
6. Group VI : Given cream preparations F-IV (Citronella extract 10: Kecombrang flower powder 0)%,
7. Group VII : Given F-V cream preparation (Citronella extract 0 : Kecombrang flower powder 10)%.

All mice that have been given as much as 500 mg of test material according to each group are topically on their feet, analgesia test is carried out by placing each animal on a Plantar test apparatus. The time (seconds) of the mice's ability to withstand pain responses caused by infrared stimuli was recorded. The pain response is characterized by the reaction of the mouse lifting, licking the soles of the feet or jumping.

Observation time on mice for 180 minutes with intervals: 15 minutes, 30 minutes, 45 minutes, 60 minutes, 75 minutes, 90 minutes, 105 minutes, 120 minutes, 135 minutes, 150 minutes, 165 minutes, and 180 minutes (Demirturk and Oner , 2003).

The data obtained in the form of time (seconds) the ability of mice to withstand pain responses from various treatment groups, were analyzed by statistical tests to see the distribution of the data and the homogeneity of the data. If the data obtained are normally distributed and homogeneous, then the one-way analysis of variance (ANOVA) test with a 95% confidence level uses SPSS version 20 for windows. The purpose of the ANOVA test was to determine whether or not there was a significant difference between the treatment groups, then continued with the Tukey test, to determine whether there was a significant difference (significance) or not between the two treatment groups being compared.

CONCLUSION

1. Ethanol Extract of Citronella and Kecombrang Flower Extract contains chemical compounds of the same class, namely alkaloids, flavonoids, tannins, glycosides, steroids/triterpenoids and saponins.
2. Cream preparations containing a combination of ethanol extract of citronella and kecombrang flower extract in various concentrations have an analgesic effect on male mice.
3. Cream formulations containing a mixture of ethanolic extracts of citronella extract and kecombrang flower extract in a concentration ratio of 5%: 5% are the best because at 120 minutes after use, the strength of the analgesic effect is not significantly different with a concentration ratio of 7.5: 2.5. and Hot In Cream on the market

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