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The Formulation of Rambutan Leaf (Nephelium lappaceum L.) Extract on Syrup Preparation

Derry Evianna Pratiwi[1], Iwan Setiawan[2]

1. D3 Pharmacy, Sekolah Tinggi Kesehatan Nasional Surakarta
Surakarta, Central Java, Indonesia
pratiwide08@gmail.com
2. D3 Pharmacy, Sekolah Tinggi Kesehatan Nasional Surakarta
Surakarta, Central Java, Indonesia

Abstract

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia due to the abnormal metabolism of carbohydrates, fats, and proteins. Flavonoids are compounds that can reduce glucose levels in the blood. Rambutan leaves (Nephelium lappaceum L) are one of the plants that contain flavonoids. This research is an experimental study at producing concentrations of syrup for diabetes treatment with various propylene glycol as cosolvent. Rambutan leaves were extracted using the maceration method with 96% ethanol. Rambutan leaf extract made syrup preparations using propylene glycol with concentrations of 0%, 11%, 12%, and 13%. Syrup obtained by testing included: organoleptic, homogeneity, BJ, pH, viscosity, displaced volume, and acceptability. Based on the research on rambutan leaf extract formulation on syrup preparations showed that the addition of propylene glycol has an effect on taste which is giving a sweet taste so that the addition of propylene glycol can improve the taste in the preparation of rambutan leaf extract syrup. The concentration of propylene glycol 11% produced a preparation of rambutan leaf extract with the best physical stability.

Keywords: Rambutan leaves, propylene glycol, antidiabetic

INTRODUCTION

World Health Organization or WHO (2016) states that this disease is diabetes characterized by the appearance of typical symptoms, namely polyphagia, polydipsia, and polyuria, and some experience weight loss. Diabetes mellitus (DM) is a chronic disease that needs to be taken seriously. Uncontrolled diabetes mellitus can cause several complications such as damage to the eyes, kidneys, blood vessels, nerves, and heart. Based on data obtained from the International Diabetes Federation (IDF), the global prevalence rate of people with diabetes mellitus in 2012 was 8.4% of the world's population and increased to 382 cases in 2013.

IDF estimates that in 2035 the number of diabetes mellitus incidents will increase to 55% (592 million) among people with diabetes mellitus, namely 40-59 years. Indonesia

is the 7th country with the highest incidence of diabetes mellitus with a total of 8.5 million sufferers (IDF, 2013).

According to Susilawati's research (2017) rambutan leaf extract can reduce blood sugar levels in mice that have been induced by alloxan effectively at a dose of 25 mg/kg BW, as a comparison control using glibenclamide at a dose of 65 mg/kg BW. The effect of decreasing blood glucose levels is thought to be through the repair of cells by the components contained in the rambutan leaf extract. The chemical content of flavonoids in rambutan leaves can regenerate pancreatic cells and help stimulate insulin secretion. According to Leni's research (2017), rambutan leaf extract can reduce blood sugar levels well at a dose of 10 mg/kg BW in mice that have been induced with glucose, as a comparison control using metformin 65 mg/kg BW.

According to Kusuma's research (2017) rambutan leaf extract has the potential to reduce fasting blood glucose levels in male rats induced by alloxan at a dose of 200 mg/kg BW has the same ability as glibenclamide.

The syrup is a concentrated solution of sugar or other suitable sugar to which medicine or perfume is added, is a clear solution of sweet taste. Syrup unless otherwise stated, the content of saccharose ($C_{12}H_{22}O_{11}$) is not less than 64% and not more than 66% (Depkes RI, 1978). Most syrups contain the following components in addition to purified water and all existing medicinal substances: Sugar, usually sucrose or a sugar substitute used to impart a sweet and thick taste, antimicrobial preservative, flavoring agent, colorant.

Sweeteners function to improve taste and aroma, improve physical and chemical properties, as preservatives, develop types of beverages and foods with controlled calorie counts, and as main sweetener substitutes. Sucrose was the first sweetener to be used commercially because it was the most economical to use (Cahyadi, 2008).

Sucralose has a relative sweetness level of 600 times the level of sweetness of sucrose with no calorific value because sucralose is not used as an energy source by the body because it decomposes like sucrose. Therefore, sucralose is included in the GRAS (Generally Recognized as Safe) group, meaning that this substance has no toxic effect so it is safe for human consumption and is very useful as a sugar substitute for people with diabetes both types I and II (Cahyadi, 2008).

Acesulfame potassium is widely used in beverages, cosmetics, food, and pharmaceutical formulations, which are generally considered to be relatively non-toxic and harmless. The approximate strength of the sweetener is 180-200 times that of sucrose, so it can improve the taste system and can be used to mask some unpleasant taste characteristics. Pharmacokinetic studies have shown that acesulfame potassium is not metabolized and is rapidly excreted unchanged in the urine. Studies show long-term administration to mice and dogs is not mutagenic or carcinogenic. WHO (World Health Organization) has set an acceptable daily intake for acesulfame potassium up to 15 mg/kg BW (Rowe, 2006).

Likewise with previous research by Thitilertdecha et al (2008), that rambutan skin contains compounds from the tannin, polyphenol and saponin groups. Rambutan leaves have secondary metabolites of saponins, terpenoids, flavonoids, phenolics, and tannins

(Pratiwi, 2015). Rambutan seeds have secondary metabolites of phenols, flavonoids, and tannins (Yuda et al., 2015). While the bark contains tannins, saponins, and flavonoids (Dalimartha, 2005).

The hypoglycemic effect of rambutan has been demonstrated both in vivo and in vitro. Ethanol extract of rambutan rind (Nephelium lappaceum Linn) carried out on alloxan-induced mice has the efficacy of lowering blood glucose levels at a dose of 400 mg/kg BW (Aldina, 2015) and a dose of 500 mg/kg BW (Muhtadi et al., 2014). This ability was equivalent to glibenclamide which was used as a positive control. In addition, the ethanolic extract of rambutan peel can regenerate the pancreatic islets of Langerhans tissue at a dose of 400 mg/kg BW with the lowest percentage of damage to the islets of Langerhans at 7.96% (Aldina, 2015). The alleged mechanism of action of flavonoids is by regenerating and stimulating the release of insulin by pancreatic cells (Dheer and Bhatnagar, 2010). Other than that, The active substance contained in the skin of rambutan fruit that has antidiabetic activity is Geraniin. Geraniin has the highest inhibitory activity in inhibiting-glucosidase and -amylase with IC50 of 0.92 g/ml and aldose reductase with IC50 of 0.14 g/ml (Palanisamy et al., 2011).

Therefore, researchers want to make an alternative treatment for DM from rambutan leaf material in the form of syrup as an alternative treatment other than chemical drugs with syrup formulations that can be accepted by DM sufferers.

METHODS

The research includes experimental research. The formulation of the syrup preparation of rambutan leaf ethanol extract by maceration extraction with 96% ethanol solvent. Syrup preparations were made with various concentrations of propylene glycol as a cosolvent. The resulting syrup was tested for quality and observed syrup preparations from the 0, 7th, 14th, 21st, and 28th days. The research was conducted at the Laboratory of Traditional Medicine and Pharmaceutical Technology of the National College of Health Sciences from November 2018 to January 2019. The tools used in this study were: Shimadzu moisture balance, PH meter (pHep®), pycnometer (Ecolab), Ostwald Viscometer (Pyrex). The ingredients used are rambutan leaves obtained at the homes of residents of the Sondakan area, Laweyan, citric acid, propylene glycol.

Table 1. Rambutan leaf extract syrup formulation

Ingredients	Concentration			
	Formula I	Formula II	Formula III	Formula IV
Rambutan leaf thick extract	9.69 g	9.69 g	9.69 g	9.69 g
Propylene glycol	-	11%	12%	13%
Nulife (maltodextrin, Acesulfame K, Sucralose, corn starch)	0.20%	0.20%	0.20%	0.20%
citric acid	0.30%	0.30%	0.30%	0.30%
Aquedest to	150ml	150ml	150ml	150ml

Ways of working:

1. Simple making
2. Determination of drying shrinkage
3. Determination of drying shrinkage by using a moisture balance: Weigh two grams of Simplicia input in the tool, set at a temperature of 1050C, then closed, read the results on the tool.

4. Flavonoid test: 1 ml of liquid extract was added with magnesium powder and concentrated HCl then shaken until well mixed. A positive result is the attraction of red-yellow color (Depkes RI, 1995).
5. Extract using the maceration method with 96% ethanol, 900 g of Simplicia powder, put in a glass beaker, add 6.75 liters of 96% ethanol as a solvent, stir and then close the lid. Let stand five days and be protected from sunlight. Stir every day for five days. Sekai, squeeze, wash the dregs with a liquid filter to obtain 9 liters. Transfer to a closed container, in a cool place protected from sunlight for two days, set and filtered (Depkes RI, 1979). Concentration was carried out on a water bath to obtain a thick extract.
6. Formulation
   According to Susilawati's research (2017), the most effective dose of lowering blood glucose is 9.69 g/70 kg BW converted to humans. The syrup is made for use 3 times a day with a dose of 50 ml each containing the active substance of rambutan leaf extract of 3.23 g. Dissolve rambutan leaf extract with propylene glycol in a mortar, add hot water and stir until homogeneous. Sucralose and citric acid are dissolved in water, add in a mortar, stir until homogeneous, add distilled water to 150 ml.
7. Acceptability: This is done by giving several people a questionnaire with predetermined criteria and asked to taste and assess the color, taste, aroma, viscosity, and after taste of the syrup preparation sample.
8. Test the quality of the syrup preparations, including specific gravity, homogeneity, organoleptic, pH test, viscosity, volume transferred.

RESULTS AND DISCUSSION

Simplicity Making

Rambutan leaves weighing 900 grams that have been harvested are subjected to wet sorting to separate tree branches and impurities carried during the harvesting process. Washing is done using running water to remove impurities attached to the rambutan leaves. The clean rambutan leaves are dried in the sun with a black cloth-covered to avoid direct contact with the light to produce dry simplicia that are not easily damaged and can withstand long storage from damage caused by microorganisms. The dried rambutan leaves are subjected to dry sorting to remove contaminants during the drying process or those left behind during wet sorting. Dry and clean rambutan leaf simplicia was ground to obtain simplicia powder. Pollination of rambutan leaf simplicia using a blender.

Determination of Drying Loss

Rambutan leaf simplicia powder was subjected to a drying shrinkage test. Drying shrinkage is a measurement of the remaining substance after drying at a temperature of 105oC expressed as a percent value. The drying shrinkage test aims to provide a maximum limit for the number of compounds lost in the drying process. From the tests that have been carried out, the results of drying shrinkage are 7.654%. This shows that the drying shrinkage of rambutan leaf simplicia meets the requirements, which is less than 10% (Ministry of Health RI, 1995).

Flavonoid Test

Testing the chemical content that acts as an antidiabetic in rambutan leaf simplicia is the flavonoid content. The flavonoid test was carried out using rambutan leaf simplicia powder added in 96% ethanol then added Mg sulfate powder and concentrated sulfuric

acid to obtain a yellow solution. This shows that rambutan leaf simplicia contains flavonoids.

Extraction

Extraction of rambutan leaf simplicia using the maceration method. Maceration is a simple extraction, carried out by immersing simplicia powder in a filter search. The advantage of this method is that it is simple and easy to operate and use. The solvent used is 96% ethanol. Ethanol 96% is a solvent that has been commonly used, is polar which can extract secondary metabolites in simplicia which are polar. Flavonoids are compounds that are polar so that the filter used can maximally take up flavonoid compounds. Maceration was carried out twice because the extract obtained in the first maceration could not meet the dosage to make syrup. The macerate was concentrated on a water bath until a thick extract was obtained. From the results of another similar study conducted by Leni (2017), the yield was 19.3%. While in this study, the results of the viscous extract were weighed, and the percentage of yield calculated was 14.50%. The difference in yield is influenced by the time of extraction. The second extraction was not remaceration so that the obtained macerate was not maximal. The following is the yield calculation:

$$\text{Rendemen} = \frac{\text{the weight of total extract}}{\text{macerated powder weight}} x\ 100\%$$

$$\text{Rendemen} = \frac{130{,}5\ \text{gram}}{900\ \text{gram}} x\ 100\% = 14{,}50\%$$

Formulation

The viscous extract obtained was formulated in a syrup preparation. A syrup is a concentrated solution of sugar or other suitable sugar to which medicine or perfume is added, is a clear solution of sweet taste. Syrups, unless otherwise stated, contain levels of saccharose ($C_{12}H_{22}O_{11}$) not less than 64% and not more than 66% (Depkes RI, 1978). The sweetener used in the syrup is sucralose. Sucralose is included in the GRAS (Generally Recognized as Safe) group, meaning that this substance has no toxic effect so it is safe for human consumption and is very useful as a sugar substitute for people with diabetes both types I and II (Cahyadi, 2008). Each formula contains Nulife containing the artificial sweeteners sucralose and acesulfame potassium. Nulife is used as much as 300 mg for 150 ml. According to the World Health Organization (WHO), The recommended use of sucralose and acesulfame potassium in a day is 15 mg/kg BW. Citric acid is used in the preparation of rambutan leaf extract syrup with a concentration of 0.3% per 150 ml of syrup. Citric acid was used as a buffer with a concentration of 0.1 – 2.0% (Rowe, 2006). The citric acid used meets the specified levels as a buffer. Propylene glycol in syrup preparation is used as a cosolvent. Propylene glycol is used to help the solubility of rambutan leaf extract because rambutan leaf extract is less soluble in water. The addition of propylene glycol is expected to improve the solubility of rambutan leaf extract in syrup preparations. Propylene glycol used was 11%, 12%, and 13%. The concentration level of propylene glycol for oral solution is 10% - 25% and can also be used as a preservative with levels of 15% - 30% (Rowe,

Acceptability

Each formulation of rambutan leaf extract syrup was tested for taste responsiveness to several respondents with an age range of 20 years to 30 years who had a better taste response as many as 10 people. Respondents were asked to taste each formula and fill out a questionnaire regarding taste, color, smell, viscosity, and after taste. The results showed that 10% chose formula 1, 60% chose formula 2 and 30% chose formula 3 and formula 4.

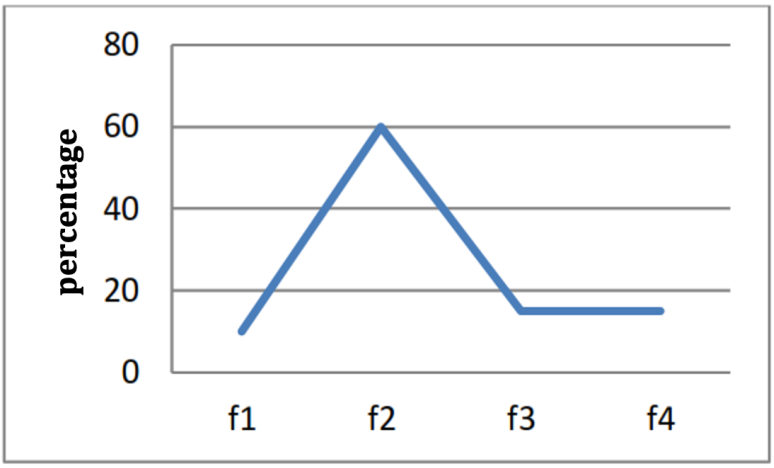

Figure 1. Percentage of Accessibility

The preparation of rambutan leaf extract syrup was tested for physical stability once a week for 28 days. Physical stability test consists of:

Organoleptic Test

Table 2. Organoleptic Test Results

Characteristics	FI	FII	FIII	FIV
Color	Dark green	Dark green	Dark green	Dark green
Flavor	Bitter, sour, bitter	Bitter, sweet, sour, bitter	Bitter, sweet, sour, bitter	Bitter, sweet, sour, bitter
Smell	Typical rambutan	Typical rambutan	Typical rambutan	Typical rambutan
Form	Liquid	Liquid	Liquid	Liquid

The organoleptic test consists of taste, color, smell, and shape. In formula 1 as a negative control that is without the addition of propylene glycol has a bitter, sour and bitter taste while in formula 2, formula 3, and formula 4 with the addition of propylene glycol at different concentrations has a bitter, sweet, sour and bitter taste. During 28 days of storage, the syrup preparation did not change in the organoleptic test. The addition of propylene glycol affects the taste, namely giving a sweet taste so that the addition of propylene glycol can improve the taste of the syrup preparations of rambutan leaf extract. This is following the characteristics that propylene glycol is a clear, viscous, colorless, odorless, hygroscopic liquid with a slightly sweet taste (Depkes RI, 1979), so it can increase the viscosity and improve the taste of the preparation.

Homogeneity Test

Table 3. Homogeneity Test Results

Formula	Results
I	Homogeneous
II	Homogeneous

III	Homogeneous
IV	Homogeneous

The homogeneity test is carried out to determine whether the preparations are homogeneous or not, this is to ensure that each use contains the same dose, not less or more than it should be, to produce a response as expected in use. The homogeneity test in Formula 1 as a negative control without the addition of propylene glycol contained many deposits. In formula 2, formula 3, and formula 4 with the addition of propylene glycol, fewer precipitates are formed because propylene glycol increases the solubility of rambutan leaf extract and the precipitation time is longer than formula 1.

Specific Weight Test

A specific gravity test was carried out to determine the purity of the preparations made. The test was carried out when the syrup of rambutan leaf extract was at a temperature of 25oC using a pycnometer. Specific gravity on day 0 to day 28 has the same value. In formula 1 with a specific gravity of 1.0083 g/ml. In formula 2, formula 3, and formula 4 with a specific gravity of 1.0190 g/ml. Based on the results of the One Way Anova test, the sig value of 0.000 < 0.005 means that there is a significant difference in specific gravity due to differences in the concentration of propylene glycol so that it affects the specific gravity of the syrup preparations of rambutan leaf extract. This is because propylene glycol has higher specific gravity than water, which is 1.035-1.040 (Rowe et al., 2006) so that formulations 2, 3, and 4 added with propylene glycol will have a higher specific gravity.

pH test

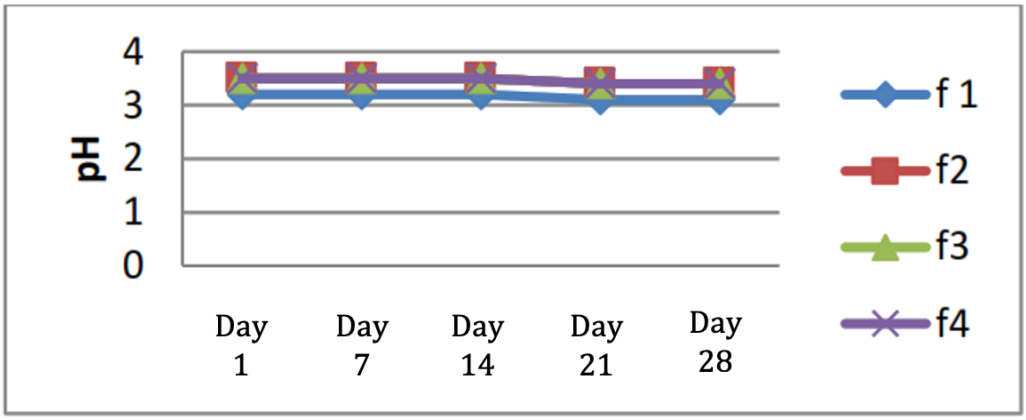

Figure 2. pH graph

The pH value test on the syrup preparations of rambutan leaf extract had a pH value between 3.2 - 3.5 on day 0 to day 14 after day 21 to day 28 the pH value dropped to 3.1 – 3.4 where the pH in the syrup of rambutan leaf extract is acidic with a low pH value, even a very small change in pH can have serious effects on organs. Testing the pH value of the solution of rambutan leaf extract before adding citric acid which functions as a buffer has a pH value of 4 so that with the addition of citric acid the pH value of the syrup of rambutan leaf extract decreases. Here the results are presented in a graph.

Viscosity Test

A viscosity test is carried out to determine the thickness of the preparations made, this is related to whether or not the preparations are easily poured into bottles and

whether or not they are easily dispersed into the body to work. From the tests that have been carried out, it was found that the viscosity of the preparations made was in the range of 1.5726 – 1.5963 cp. The preparations made have good viscosity and are easy to pour into bottles.

Transferred Volume Test

The transferred volume test is carried out to ensure that the prepared preparation has the volume as stated on the label. The results obtained in each formula ranged from 98.66% - 100%. The average volume obtained from 10 containers is not less than 100% and none of the containers is less than 95% of the volume stated in the label (MOH, 1995). This shows that the transferable volume test of rambutan leaf extract preparations meets the requirements.

CONCLUSIONS AND SUGGESTIONS

1. The addition of propylene glycol has a good effect on the stability of the syrup preparations of rambutan leaf extract in improving the taste of the syrup of rambutan leaf extract.
2. A concentration of 11% propylene glycol can produce a syrup preparation of rambutan leaf extract with the best physical stability.

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