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Original Article

HMG-CoA Reductase Inhibitory Activity of *Garcinia latissima* Miq. Mesocarp Water Extract for Herbal Tea

Herra Williany Monalissa, Berna Elya*, Nuraini Puspitasari

ABSTRACT

Context: High cholesterol in the blood is a risk factor for atherosclerosis that causes various diseases. The main pharmacologic intervention to reduce cholesterol levels is inhibiting the HMG-CoA reductase enzyme. One of the genera of Garcinia, *Garcinia dulcis*, has potential as an anti-cholesterol. Based on chemotaxonomy, *Garcinia latissima* Miq. is also estimated to have a potency as anti-cholesterol. **Aims:** This study aims to test the inhibition of HMG-CoA reductase water extract activity of *G. latissima* fruit flesh with different duration of infusions. **Materials and Methods:** *Garcinia latissima* Miq. mesocarp was extracted using infusion method with different duration of infusions. Each of extracts was tested the inhibitory activity of HMG-CoA reductase as well as the determination of total flavonoid and total phenol content. In addition, the simplicia of the mesocarp of *G.latissima* Miq. will be made as a herbal tea and a hedonic test is performed to find out the degree of liking for the tea. **Result:** The test results showed the inhibitory activity of 100 ppm *G. latissima* Miq. mesocarp water extract with infusion for 5, 10 and 15 min respectively 11.32; 29.02; 13.03%. The 10 min extract with the largest enzyme inhibition had total flavonoids content of 31.24 mg QE / gram extract and total phenol content of 4.64 mg GAE/ gram extract. The result of the hedonic test for the colour, aroma, flavour of herbal tea formula A respectively 30; 30; 20% and formula B respectively for 40; 33.3; 50%. **Conclusion:** The water extract of *G.latissima* Miq mesocarp has a low potency in HMG-CoA reductase inhibitory activities.

Key words: Anti Cholesterol, *Garcinia latissima,* Herbal Tea, HMG-CoA reductase, Mesocarp.

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INTRODUCTION

Cholesterol has an important role in life. High levels of total cholesterol in the blood or hypercholesterolemia play a role in the pathology process as a risk factor for atherosclerosis that causes various diseases such as, cerebrovascular, coronary and peripheral blood vessels.[1] The main pharmacologic intervention used to reduce cholesterol levels is to inhibit the HMG-CoA enzyme that catalyses HMG-CoA changes to mevalonate in the cholesterol biosynthesis pathway.[2]

Indonesia has a high variety of Garcinia (Garcinia spp.) Species.[3] Garcinia plants have been utilized by the community empirically in various forms such as the utilization of Garcinia plants as tea. A tea has been made from the fruit of *G. mangostana* which can be used as a tonic to overcome fatigue.[4] Tea can improve the taste of the ingredients used without reducing the efficacy.[5]

The efficacy of the garcinia plant is not only proven empirically but also scientifically. From several studies that have been conducted on various types of Garcinia plants, Garcinia has a variety of pharmacologically useful activities for the treatment of certain diseases. Pharmacologic activity in Garcinia is antidiabetic and antioxidant, anticancer, antimalarial, antifungal, anti-bacterial, anti-inflammatory, as well as for the treatment of dysentery, diarrhoea and ulcers.[6] Research on the anti-cholesterol activity of Garcinia plant that can be used in helping the treatment of hypercholesterolemia is still rarely studied. One of Garcinia plant that has been studied is *Garcinia dulcis*. Biflavonoid from *Garcinia dulcis* has a constant inhibitory activity against HMG-CoA reductase enzyme of 80.87 ± 0.06 μm.[7]

Based on the above description, it is necessary to do further research on the activity of anti-cholesterol from *Garcinia latissima* Miq. and herbal tea will be made from the plant. Based on the consideration of chemotaxonomy, *Garcinia latissima* Miq. Is expected to inhibit HMG-CoA enzyme activity.

This study aims to determine the inhibitory of HMG-CoA reductase activity of *G. latissima* fruit water extract with different duration of infusion, as well as the determination of total flavonoid and phenol contents in the extract. In addition, simplicia *G. latissima* Miq. mesocarp will be made in the form of tea and a hedonic test is performed.

MATERIALS AND METHODS

Materials

Garcinia latissima Miq. fruit collected from Bogor Botanical Garden, Indonesia and determined by

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Lembaga Ilmu Pengetahuan Indonesia, Bogor. Pravastatin (Sigma Aldrich), Quercetin (Sigma Aldrich) and Galic Acid (Sigma Aldrich), HMG-CoA reductase assay Kit CS 1090 (Sigma Aldrich), aquadest, chloroform P, acetone P, formic acid P, methanol P, ethanol P, folin-ciocalteu phenol LP, chloride acid LP, potassium phosphate, potassium dihydrogen phosphate and NaOH.

Preparation of Simplicia

Garcinia latissima Miq. fruit collected and sorted wetly from dirt. Fruits were separated from seeds and fruit flesh. Fruit fleshes were picked and dried in the drying cupboard. After drying, simplicia were sorted dryly to separate simplicia with other material. Then simplicia was powdered.

Characterization of Simplicia

Organoleptic test

Simplicia powder of *Garcinia latissima* Miq. was described as shape, colour and taste using the sensory.[8]

Water soluble extract

Five g of simplicia powder was weighed and put in a clogged flask, add 100 mL water-chloroform P shaken constantly for the first 6 h, then left for 18 h. 20 ml of filtrate were evaporated in a tared flat dishes, the rest of filtrate was heated in 105°C until constant mass.[8]

Ethanol soluble extract

Five gram of simplicia powder was weighed accurately and put in a clogged flask, add 100 mL ethanol 95% P, shook constantly for the first 6 h, then left for 18 h. 20 ml of filtrate were evaporated in a tared flat dishes, the rest of filtrate was heated in 105°C until constant mass.[8]

Total ash content

Two gram of simplicia powder was weighed accurately and put in a tared silica crucible, incinerate gradually until free from carbon, cool in the desiccator and weighed. Total ash content is calculated from the weight of the sample was taken and expressed in % w/w.[8]

Acid-Insoluble Ash Content

Boil the ash obtained as directed in Total ash with 25 mL diluted hydrochloric acid for 5 min. The insoluble matters were collected and filtered through the ashless filter, washed with hot water, ignite in the crucible until constant weight. Acid-insoluble ash was calculated from the weight of the sample was taken and expressed in % w/w.[8]

Loss on drying

The weighing bottle was prepared and heated at 105°C for 30 min, then weighed. The bottle was heated again at 105°C for 30 min the weighed until constant mass. After that, simplicia powder was weighed 1 g accurately than was heated at 105°C for 5 h and was weighed again. Drying process was continued and was weighted again for one hour until the difference in two successive weighings is less than 0,25%.[8]

Extraction

Each two gram simplicia powder extracted using infusion method for 5, 10 and 15 min. After extraction, the result was filtered and was dried using freeze dryer to obtain a dry extract.

HMG-CoA Reductase Inhibitory Activity Test

The commercially available HMG-CoA reductase assay kit from Sigma-Aldrich was used to screen HMG-CoA reductase inhibitory activity. The test was performed three repetitions using microplate reader at 37°C. Each extract was added DMSO then dissolved in phosphate buffer solution pH 7,4. A 0.2 mL reaction mixture containing 1 mL of the solutions of the extracts, 4 mL of reconstituted NADPH, 12 mL of HMG-CoA solution and 2 mL HMG-CoA reductase was shaken mechanically in the plate reader for 10s. Then, the solution was measured its absorbance at 340 nm every 20 sec for 10 min. HMG-CoA reductase inhibitory activity was calculated using the following formula:

$$\%\ \text{HMG}-\text{CoA reductase inhibitory activity}: \frac{(A-B)-(C-D)}{A-B}\times 100$$

A = Δ Positive blank absorbance; B = Δ Negative blank absorbance, C = Δ Sample absorbance, D = Δ Sample blank absorbance

Thin Layer Chromatography Profile

Thin Layer Chromatography was performed with mobile phase Chloroform P-Acetone P-Formic Acid (10:2:1), stationary phase Silica gel 60 F_{254}. Sample solution 5% in ethanol P and standard solution 0,01% in ethanol P. Spotted volume of sample solution 30 µL and standard solution 5 µL. The chromatogram was sprayed with Aluminium chloride 5% and identified using UV detection at 365 nm.

Determination of Total Flavonoid Content

Samples were analysed spectrophotometrically for the contents of total flavonoid using FHI method and quercetin as standard. Sample solutions were added internal standard. Each 0,5 mL standard and sample solution were separately mixed with 1,5 mL ethanol P, 0,1 mL $AlCl_3$ 10% (w/v), 0,1 mL Natrium acetate 1 M and 2,8 mL aquadest. After incubation at room temperature for 30 min, the absorbance of the mixture was measured at a maximum wave. Each mixture was measured in three repetitions.

Determination of Total Phenolic Content

Samples were analysed spectrophotometrically for the contents of total phenolic using Folin Ciolcalteu method and gallic acid as standard. Sample solutions were added internal standard. Each one mL standard and sample solution were separately diluted in 5 mL Folin-ciocalteu LP (7,5 % in aquadest). The mixture was allowed to stand for 8 min, then the mixture was added 4 mL NaOH 1 %. After incubation at room temperature around 1 h, the absorbance of the mixture was measured at a maximum wave. Each mixture was measured in three repetitions.

Formulation of Herbal Tea and Preparation of Hedonic Test

Two formulas of *Garcinia latissima* Miq Mesocarp herbal tea were made for the hedonic test. Formula A contained ± 2 g simplicia powder. Formula B contained ± 2 g simplicia powder and ±0,35 g stevia. For hedonic test, 100 mL hot water was used to brew the tea. The herbal tea was brewed for several min adapted to duration of extract that had highest inhibitory activity.

Hedonic test

The hedonic test was performed with 30 untrained panellists. There is three parameter which will be valued namely taste, fragrance and colour. This hedonic test was used 6 hedonic scaled. 0 = dislike; 1 = neutral; 2 = like slightly; 3= like; 4 like very much; 5=like extremely. Each panellists had herbal tea formula A and B in a plastic glass, mineral water as blanko and The assessment sheet. Data were analysed stastically with Mann-Whitney test using SPSS 20.0 Program.

RESULT

Characterization of Simplicia

The result of characterization of simplicia can be seen in Table 1.

Table 1: The result of Characterization of Simplicia.

No	Parameter	The test result
1.	Organoleptic	
	Shape	Dry powder
	Colour	Pink
	Odor	Specific odor
	Taste	Sour
2.	Water-Soluble Extract	29,17 ± 0,34 %
4.	Total Ash Content	4,80 ± 0,13 %
5.	Acid-insoluble ash content	0,34 ± 0,04 %
6.	Loss on drying	3,13 ± 0,27 %

Table 2: Yield presentation of *G. latissima* Miq. Mesocarp.

Duration	Extract Weight (gram)	Simplicia Extract (gram)	Yield (%)
5 Minutes	0,61	2	30,5
10 Minutes	0,7	2,01	34,83
15 Minutes	0,68	2,01	33,83

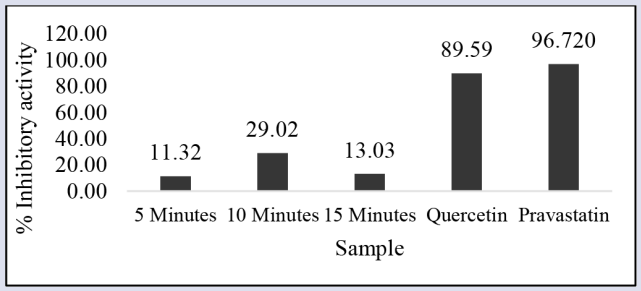

Figure 1: Graph of HMG-CoA Inhibitory activity percentage.

Extraction

10 min infusion extract had optimal yield presentation. Yield presentation decrease on extract with 15 min infusion. Yield presentation of all infusion can be seen in Table 2.

HMG-CoA Reductase Inhibitory Activity Test

HMG-CoA Reductase Inhibitory Activity was done for each of samples and standard solution. There are 5 min infusion extract, 10 min infusion extract, 15 min infusion extract, quercetin and pravastatin. A preliminary test on pravastatin was performed to determine IC_{50} was also performed. The standard solution, pravastatin, was diluted into several concentrations and the calibration curve was made. The regression equation obtained is y = 0,2716 x + 29,169 with regression coefficient is 0,99984. The calibration curve of pravastatin can be seen in Figure 2 and the dose of Pravastatin that used in the preliminary test can be seen in Table 3. IC_{50} was obtained from the test is 76,72 nM. IC50 pravastatin from previous is 66,5 nM,[9] 70 nM[10] dan 87,76 nM.[11]

Based on the result,10 min infusion extract of *G. latissimia* Miq. mesocarp has the highest percentage HMG-CoA reductase inhibitory activity. Inhibitory activity percentage of all infusions extract, quercetin and pravastatin can be seen in Figure 1. Therefore, at Thin layer Chromatography profile was used 10 min infusion extract and at hedonic test duration of brewing is 10 min.

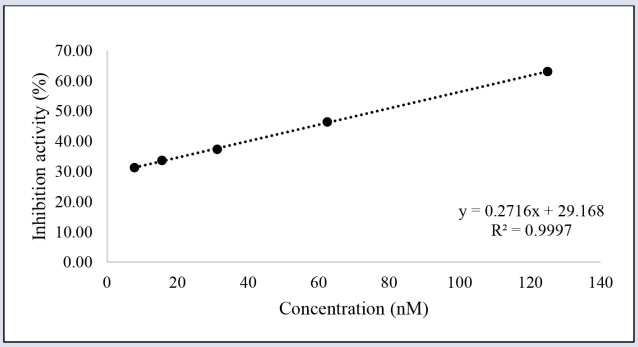

Figure 2: Calibration Curve of Pravastatin in λ_{max} 366 nm.

Table 3: The Dose of Pravastatin In The Preliminary Test.

Concentration (nM)	Inhibitory Activity (%)
125	63,07
62,5	46,36
31,25	37,30
15,625	33,64
7,8125	31,25

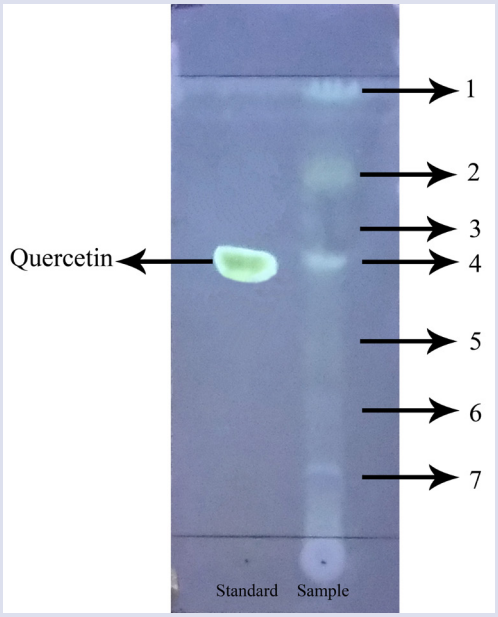

Figure 3: Chromatogram Profile of Quercetin and 10 min infusion water extract *G. latissima* Miq. mesocarp using mobile phase chloroform: acetone: formic acid (10:2:1) after was sprayed AlCl3 on UV 366 nm.

Chromatogram Profile

The result of chromatogram can be seen in the Figure 3 and Table 4. Based on chromatogram profile at 10 min infusion water extract *G. latissima* Miq. Rf value of Quercetin is 0,58 and has yellow spot colour. The sample also had the same Rf value with Quercetin. There is an identical spot with standard and sample, so it can be concluded that 10 min infusion water extract contained flavonoid quercetin.

Table 4: Chromatogram Profile of Quercetin and 10 min infusion water extract *G. latissima* Miq. mesocarp using mobile phase chloroform: acetone: formic acid (10:2:1) after was sprayed $AlCl_3$ on UV 366 nm.

Spot number	Rf value UV366 nm	Spot Colour
Quercetin	0,58	yellow
1	0,97	yellow
2	0,8	yellow
3	0,7	yellow
4	0,58	yellow
5	0,42	yellow
6	0,25	yellow
7	0,1	yellow

Table 5: Total Flavonoid Content of Water Extract of *G.latissima* Miq Mesocarp.

Duration	Total Flavonoid Content (mgQE/one gram extract)
5 Minutes	17,61
10 Minutes	31,24
15 Minutes	29,85

Table 6: Total Phenolic compound of Water Extract *G. latissima* Miq Mesocarp.

Duration	Total Phenolic Extract (mg GAE/one gram extract)
5 Minutes	12,04
10 Minutes	4,64
15 Minutes	21,61

Determination of Total Flavonoid Content

Determination of Total Flavonoid Content was calculated used quercetin as standard. A Six concentration quercetin solution was used to made curve calibration and was obtained quercetin calibration curve with y = 0,0618x + 0,0216 and correlation values (r) is 0,99919. Total flavonoid content was stated in QE (Quercetin Equivalent). Total flavonoid content of water extract of *G. latissima* Miq. mesocarp can be seen in Table 5. Based on the test, 10 min infusion water extract had highest total flavonoid content i.e 31,24 mg QE/one gram extract.

Determination of Total Phenolic Content

This test used Galic Acid as Standard Solution. A six standard solution concentration was used to determine gallic acid calibration curve and was obtained linear regression with y = 0,0855x + 0,0442 and r =0,99934. The total phenolic compound was stated as GAE (Galic Acid Equivalent). Total phenolic compound of water extract *G. latissima* Miq. Mesocarp can be seen in Table 6. Based on the test, 15 min infusion water extract had highest total phenolic content i.e 21,61 mg GAE/ one gram extract.

Hedonic test

Herbal tea of *G. latissima* Miq. mesocarp was made into two formula. Formula B was sweetener than formula A. The colour of formula A is pink and the colour of Formula B is yellowish pink. The odor of both formulas was similar. Based on statistics, it showed there was no significant difference to the colour, odor and taste of the two formula. Hedonic test result of Herbal Tea can be seen in Table 7.

Table 7: Hedonic test result of Herbal Tea.

Taste		
Hedonic Scale	**Formula A**	**Formula B**
Dislike	13 %	13 %
Neutral	24 %	13 %
Like slightly	30 %	7 %
Like	20 %	50 %
Like Very much	13 %	10 %
Like Extremely	0 %	7 %
Colour		
Hedonic Scale	**Formula A**	**Formula B**
Dislike	3 %	7 %
Neutral	0 %	3 %
Like slightly	17 %	20 %
Like	30 %	40 %
Like Very much	23 %	20 %
Like Extremely	27 %	10 %
Odor		
Hedonic Scale	**Formula A**	**Formula B**
Dislike	0 %	24 %
Neutral	37 %	3 %
Like slightly	23 %	13 %
Like	30 %	34 %
Like Very much	7 %	23 %
Like Extremely	3 %	3 %

DISCUSSION

Characterization of Simplicia

Characterization of simplicia was done to guarantee the quality of simplicia. Simplicia is a dry pink colour, sour taste and no odor. Determination of water soluble extract content was aimed to know an amount of the extract that can soluble in water.[12] Determination of ethanol soluble extract content was aimed to show an amount of the extract that can soluble in ethanol.[12] Determination of total ash was aimed to show the content of mineral content in simplicia. On this test, the sample was burned at a specific temperature where organic compound and its derivate are destructible and evaporate, so it remains mineral and inorganic content.[12] Determination of ash insoluble-acid showed the amount of mineral content that insoluble in acid. Determination of loss on drying was aimed to show the amount of compound that lost on drying. At *G. latissima* Miq. simplicia had the loss on drying valued around 3,13 ± 0,27 %. It was met the requirements of loss on drying of brewing simplicia powder i.e maximal 10%.[13]

Extraction

Extraction of *G. latissima* Miq. mesocarp using infusion method was done because this method is most closely related to the tea brewing process. A number of simplicia extracted and solvent used was adjusted to the content of simplicia powder in a tea bag and water used to brew tea.

Based on the result, optimal yield presentation was obtained at 10 min infusion extraction and decreased on 15 min infusion. The same pattern also occurred in the previous study, in that study the extension of extraction time cause the yield to rise in the 15th min and then decreased at the 30th min.[14] It is suspected to occur because on 10 min infusions extract there are compounds in the plant that decomposes. In addition, it can also be due to errors during the extraction process ie there are extracts remaining in the container so that the yield obtained is reduced.

HMG-CoA Reductase Inhibitory Activity Test

A preliminary test to determine IC_{50} pravastatin was done to ensure the method used is valid. The low percentage of inhibitory activity may be caused by the lack of methods and solvents used, so the compound that could inhibit HMG-CoA reductase enzyme was not perfectly extracted.

Based on the result, a 10 min infusion extract had the highest inhibitory the activity and then decreased on 15 min infusion extract. This might happened because in 10 min infusion extract, the component that could inhibit activity of HMG-CoA reductase enzyme had been completely extracted and in a 15 min infusion extract the component had been degraded. In addition, the decreasing in inhibitory activity might be caused by decreasing of the compound content that might has inhibitory activity, such as flavonoid. Decreasing of the compound content is caused by prolonged extraction time.[15] Total flavonoid content in this study also had the same pattern with inhibitory activity percentage.

Chromatogram Profile

Chromatogram profile was aimed to show an overview of chemical content from the extract. Chromatogram profile was used quercetin as standard, silica gel 60 F_{254} as stationary phase, phase Chloroform P-Acetone P-Formic Acid (10:2:1) as mobile phase.The Plat that had been elucidated, it was sprayed by using $AlCl_3$ and was observed in UV Light 366 nm. $AlCl_3$ show all 5-hydroxy-flavonoid as fluorescence spot under UV light 366 nm.[16]

Determination of Total Flavonoid Content

Determination of Total Flavonoid Content was performed by using FHI method. Aluminium chloride and Sodium acetate were added in this method. Aluminium chloride forms acid stable complexes with C-4 keto group and also C-3 or C-5 hydroxyl group of flavones and flavonols. Aluminium chloride also forms acid labile with the ortho-dihydroxyl groups in the ring A-or B of flavonoids.[17] The addition of sodium acetate causes ionization of the most acidic hydroxyl groups of flavonoid, sodium acetate is used to detect free 7-hydroxyl group. In flavonol addition of Aluminium chloride will cause a bathochromic shift 35 to 55 nm, while the addition of sodium acetate will cause a 5 to 20 nm bathochromic shift.[16] The complexes between Aluminum chloride and flavonol in the C-3 and C-4 hydroxyl groups and also in the ortho-dihydroxyl group have maximum absorption at wavelengths of 415-440 nm.[17] In this study, the maximum wavelength obtained was at 437 nm.

Based on the result showed that the total flavonoid content in 10 min infusion extract is the highest total flavonoid content then total flavonoid content decreased in the extract of 15 min infusion extract. This might happen because in 10 min infusions had been completely extracted and in 15 min infusions extract the component had been degraded. Previous studies have shown that prolonged extraction time can reduce total flavonoid content, as in routine compounds[18] and also in catechins.[15]

Determination of Total Phenolic Content

Determination of total phenolic content was performed on all three extracts. In the Folin-Ciolcateu Phenol method, sample was added Folin-Ciolcalteu Phenol reagent, then was incubated for 8 min and then was added NaOH 1 %. Reagent Folin-Ciolcalteu Phenol contains tungstate and molybdate 6^+ oxidation number. When reagents was added to sample, molybdate will reduction so it will change from yellow to blue. The reaction occurs slowly in the acidic atmosphere.[19] The addition of NaOH 1% to sample will provides an alkaline atmosphere which accelerates the process of reduction reaction on molybdate.[19]

The result showed that total phenol content decreased on 10 min infusion extract and increased on 15 min infusion extract. it was suspected that total phenol content in 10 min infusion extract had been degraded. The previous study showed that total phenolic compound in *Thymus vulgaris* had been decreased since the 5th min in the extraction condition at 100ºC.[14] Increasing total phenolic compound in 15 min infusion extracted might be caused by other components such as carbohydrates, that had been extracted and the component also affects total phenol content.[14] Folin-Ciolcateu also can react with other components such as protein, carbohydrate amino acid, nucleotide, unsaturated fatty acid, vitamin, amine, aldehyde and ketone.[20]

Hedonic Test

Herbal tea of *G. latissima* Miq. was made in two formula. Formula A was not added by sweetener and formula B was added by sweetener. Sweetener which was used is dry Stevia leaf (*Stevia rebaudiana*). Stevia leaves were chosen because stevia leaves were one of the natural sweeteners that have been widely used as sugar substitutes.[21] In this study required the amount of stevia which is equivalent to 10 g of sucrose. The stevia leaves have a sweetness level 20-30 times higher than sucrose.[21] Therefore, the required amount of stevia was about 0.333 - 0.5 g, so in the formula B added stevia as much as approximately 0.35 g.

The hedonic test was performed on non-standard panellist or untrained panellits. Non-standard panellists are people who have not been trained in organoleptic/sensory assessment. The minimum number of non-standard panellists on hedonist testing is 30 people, so in this study using non-standard panellists of 30 people.[22]

CONCLUSION

Based on this study, it can be concluded that water extract of *G. latissima* Miq mesocarp has a low potency in HMG-CoA reductase inhibitory activities.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

DMSO: Dimethyl sulfoxide; **NADPH:** Nicotinamide adenine dinucleotide Phosphate Hydrogen; **HMG-CoA:** 3-Hydroxy-3-methylglutaryl coenzyme A; **FHI:** Farmakope Herbal Indonesia.

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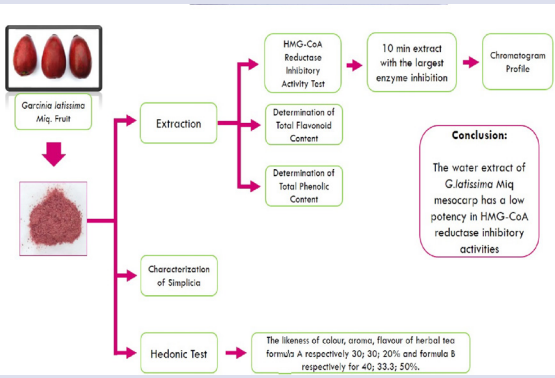
GRAPHICAL ABSTRACT



SUMMARY

- High cholesterol in the blood is a risk factor for atherosclerosis that causes various diseases. The main pharmacologic intervention to reduce cholesterol levels is inhibiting the HMG-CoA reductase enzyme. One of the genera of Garcinia, *Garcinia dulcis*, has potential as an anti-cholesterol. Based on chemotaxonomy, *Garcinia latissima* Miq. is also estimated to have a potency as anti-cholesterol. This study aims to test the inhibition of HMG-CoA reductase water extract activity of *G. latissima* fruit flesh with different duration of infusions. *Garcinia latissima* Miq. mesocarp was extracted using infusion method with different duration of infusions. Each of extracts was tested the inhibitory activity of HMG-CoA reductase as well as the determination of total flavonoid and total phenol content. In addition, the simplicia of the mesocarp of *G.latissima* Miq. will be made as a herbal tea and a hedonic test is performed to find out the degree of liking for the tea. The test results showed the inhibitory activity of 100 ppm *G. latissima* Miq. mesocarp water extract with infusion for 5, 10 and 15 min respectively 11.32; 29.02; 13.03%. The 10 min extract with the largest enzyme inhibition had total flavonoids content of 31.24 mg QE / gram extract and total phenol content of 4.64 mg GAE/ gram extract. The result of the hedonic test for the colour, aroma, flavour of herbal tea formula A respectively 30; 30; 20% and formula B respectively for 40; 33.3; 50%. The water extract of *G.latissima* Miq mesocarp has a low potency in HMG-CoA reductase inhibitory activities.

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