



## RESEARCH ARTICLE

## ANTIHYPERLIPIDEMIC EFFECT OF THE ETHANOLIC EXTRACT OF *SCAEVOLA TACCADA* (GAERTN) ROXB. LEAVES

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## Abstract

**Objective:** The research aimed to determine the effect of ethanolic extract of *Scaevola taccada* (Gaertn.) Roxb leaves in hyperlipidemic rats WITH Cholesterol and triglyceride parameter.

**Methods:** The research used 30 samples divided into 6 groups: group I (negative control) was given Sodium Carboxymethyl cellulose of 1% w/v, group II (positive control) was given simvastatin of 1.023 mg/kg Body weight, Group III was given gemfibrozil 167.60 mg/kg Body Weight, group IV, V and VI were respectively given ethanolic extract of *Scaevola taccada* (Gaertn) Roxb with the doses of 700 mg/kg body weight 900 mg/kg body weight, and 1100 mg/kg body weight. The sample was fed a high-fat diet during treatment and induced pure cholesterol for 28 days, the provision of dosage form was done orally once a day for 14 days and the measurement of rat cholesterol and triglycerides, level was done on day 0, 29, and 43. The research data were processed statistically by one way ANOVA test followed by Post Hoc Bonferroni test.

**Results:** The result showed that the positive control group had no significant effect compared on ethanol extract *Scaevola taccada* (Gaertn.) Roxb. group ( $p > 0.5$ ).

**Conclusion:** The conclusion is the ethanolic extract of *Scaevola taccada* (Gaertn.) Roxb. leaves had an activity in reducing cholesterol and triglyceride level in rat hyperlipidemia and with an effective dose of 1100 mg/kg body weight

**Keywords:** Antihyperlipidemia, ethanolic extract, *Scaevola taccada* (Gaertn.) Roxb.

## INTRODUCTION

Cardiovascular disorders (CVD) are major non-communicable diseases worldwide and atherosclerosis is the major risk factor for morbidity and mortality associated with CVD<sup>1</sup>. Dyslipidemias, are major causes of increased atherogenic risk; both genetic disorders and lifestyle contribute to the dyslipidemias seen in developed countries around the world<sup>2</sup>. It has been estimated that, by 2030, more than 24 million people per year will suffer from cardiovascular problems<sup>3</sup>. Several studies have proven that traditional plants are efficacious in lowering cholesterol levels, one of which is the leaves of *Scaevola taccada* (Gaertn.) Roxb. which can treat various diseases including swelling, diabetes mellitus, eye infections, headaches, swelling of the skin, feet, aches, coughs and flu. *S. taccada* (Gaertn.) Roxb has active compounds, namely scaevolin glycosides, alkaloids, flavonoids, phenols and saponins<sup>4</sup>. Flavonoid compounds have been shown to inhibit the oxidation of LDL which is the beginning of the formation of atherosclerosis. Previous data of *S.*

*taccada* (Gaertn.) Roxb can reduce cholesterol level in concentration 7% of the extract *S. taccada* (Gaertn.) Roxb. In Rahmawati's research using ethanol extract of *S. taccada* (Gaertn.) Roxb leaves has potential as an antioxidant with an ES50 value of 78.98 ppm<sup>5</sup> and in the research of Sukmawati using diethyl ether fraction on 3% *S. taccada* (Gaertn.) Roxb leaf has activity as free radicals or antioxidants with a value of 0.054<sup>6</sup>. From the description above, a research was carried out on the activity of *S. taccada* (Gaertn.) Roxb based ethanol extract to reduce cholesterol and triglyceride levels in hyperlipidemic rats.

## MATERIALS AND METHODS

The tools used are a set of glass tools, stirring rod, watch glass, beaker, scissors, human analyzer (Microlab 300), mouse cage, cannula, filter paper, micropipette, oven, tweezers, mouse restrainer, centrifuges, spoits, Eppendorf tubes, analytical scales (OHaus), animal scales, rotary evaporators, micropipette tips, and vortices (Mixer). The materials

used are ethanol, *S. taccada* (Gaertn.) Roxb, Natrium CMC 1%, high fat diet feed, total cholesterol testing reagent, simvastatin and gemfibrozil

#### Plant Material

The harvested leaves from Pinrang Regency, South Sulawesi Province of Indonesia. The plant identified by Research Center for Biology, Indonesian Institute of Science.

#### Preparation of ethanolic extracts

The simplicia of the *S. taccada* (Gaertn.) Roxb is weighed as much as 500 g then put into a maceration container and soaked with 96% ethanol solvent until all the simplicia is immersed. Soak the simplicia for the first 6 hours, stirring occasionally, and then let stand for 18 hours. The simplicia that has been soaked is filtered to obtain macerate and the resulting residue is remacerated 2 times with new solvent. The macerate obtained was collected and then evaporated using a rotary vacuum evaporator to obtain a thick ethanol extract.

#### Preparation of 1% Sodium Carboxymethylcellulose (Na-CMC) suspension

Na-CMC is weighed as much as 1 gram, and put little by little into 50 mL of heated aquadest (70°C) while stirring with a stirring rod until homogeneous. Enough volume up to 100 mL, then put into a container and labelled.

#### Preparation of simvastatin suspension 1.023 mg/kgBW

Simvastatin® tablets were weighed as many as 10 tablets and the average weight was calculated. After that, the tablet is crushed in a mortar and then weighed as much 24.112 mg of simvastatin powder, then suspended with 10 mL of Na-CMC 1% w/v.

#### Preparation of gemfibrozil suspension

Gemfibrozil tablets were weighed as many 10 tablets and their average weight was calculated. The tablets are crushed in a mortar until smooth then the powder is weighed which is equivalent to 167.60 mg of gemfibrozil. then tablet suspended with Na-CMC 1% w/v to 10 mL<sup>7</sup>.

#### Manufacture of high fat diet feed

A high-fat diet, each 1 kg is prepared by mixing 150 g/kg wheat flour, 540 g/kg corn flour, 100 g/kg green bean flour, 10 g/kg duck egg yolk, and 200 g/kg beef fat. After all the ingredients are evenly mixed, the dough is made in small parts and then dried in the oven<sup>8</sup>.

#### Making pure cholesterol at a dose of 200 mg/kgBW

Pure cholesterol is weighed as much as 800 mg and then dissolved in 40 mL of quail eggs

#### Preparation of ethanol extract suspension Beruwas laut (*S. taccada* (Gaertn.) Roxb.)

The suspension of the ethanol extract of leaves of Beruwas laut (*S. taccada* (Gaertn.) Roxb.) at a dose of 700 mg/kgbw, 900 mg/kgbw, and 1100 mg/kgbw were made by weighing each extract as much as 700 mg, 900 mg, and 1100 mg. then suspended with 10 mL of Na-CMC 1% w/v.

#### Treatment of test animals

The Rats were adapted for ±14 days. Initial cholesterol levels were measured before induction on day 0. Then,

the rats were grouped into 5 groups with 5 rats per group. The rats were induced by pure cholesterol orally and were given high fat diet (DTL) ad libitum for 35 days. On the 35<sup>th</sup> day, the cholesterol levels of the rats were measured after being induced<sup>3</sup>. Then, the rats were treated with oral test preparation and DTL feed ad libitum once a day until the 48<sup>th</sup> day. The test preparations given are as follows:

Group I (negative control), was given Na-CMC 1%.

Group II (positive control), was given simvastatin dose of 1.023 mg/kgbw.

Group III (positive control), was given gemfibrozil dose of 167.60 mg/kgbw.

Group IV, given the ethanol extract of *S. taccada* (Gaertn.) Roxb leaves at a dose of 700 mg/kgbw.

Group V, given the ethanol extract of *S. taccada* (Gaertn.) Roxb leaves at a dose of 900 mg/kgbw.

Group VI, given the ethanol extract of *S. taccada* (Gaertn.) Roxb leaves at a dose of 1100 mg/kgbw.

On the 48<sup>th</sup> day, the cholesterol levels of the rats were measured after being given uji (end). The rats were fasted for 14-18 hours before each blood draw.

#### Blood sampling process

Blood was drawn through the lateral vein in the tail of the rat. Blood was collected in an Eppendorf tube as much as 0.5 mL, and then centrifuged for 10 minutes at 3000 rpm, then the serum (clear layer) was taken.

#### Measurement of rat blood cholesterol levels

The rat blood serum was taken as much as 3 µL, then added with 300 µL of cholesterol reagent, vortexed and incubated for 5 minutes 25 seconds. Cholesterol levels were measured using a Human Analyzer (Microlab 300) at a wavelength of 500 nm.

#### Measurement of rat blood triglyceride levels

Rat blood serum with a volume of 3 µL was added with 300 µL of triglyceride reagent, then vortexed and incubated for 7 minutes 5 seconds.

The mixture was put into a Human Analyzer to measure its triglyceride level at a wavelength of 505 nm

#### Data analysis

Cholesterol level data obtained from the research results, we presented in the table for easy comparison. The Data will be statistical analyzed using the One Way ANOVA test and followed by the Bonferroni Post Hoc test.

## RESULTS AND DISCUSSION

Hyperlipidemia is a characterized by dyslipidemia in serum. Increased levels of cholesterol, triglycerides, LDL and decreased HDL levels are major factors in the development of diseases related to blood lipid levels, namely cardiovascular disease, atherosclerosis and obesity<sup>9</sup>. Hyperlipidemia with diabetes, hypertension, weight gain were one of the major risk factors of cardiovascular disease, a leading cause of death<sup>10</sup>. One of the traditional plants that can be used to lower cholesterol levels is Beruwas laut (*S. taccada* (Gaertn.) Roxb).

**Table 1: Results of measurement of the average cholesterol level of test animals.**

Cholesterol (mg/dL)	Group 1	Group 2	Group 4	Group 5	Group 6
Baseline (Day 0)	44.80±4.66	44.20±3.56	44.20±7.33	44.60±5.77	40.80±8.76
Induction (HFD)	85.60±10.21	86.20±7.12	86.60±4.16	89.40±3.78	83.40±7.13
Days 14 (Treatment)	77.60±7.30	25.80±8.76	28.20±11.71	26.40±5.86	23.60±5.86
Percentage Reduction	8.80*	69.93#	67.75#	70.48#	71.64#

The groups 1 and 2 received suspension Na. CMC 1% w/v and Simvastatin 1.023 mg/kgbw; groups 4, 5, and 6 are 700, 900 and 1100 mg/kgbw of ethanol extract of Leaves *S. taccada* (Gaertn.) Roxb, respectively, \*  $p < 0.05$  significantly group 1 compared to groups 2, 4, 5, and 6, #  $p > 0.05$  nonsignificantly group 2 compared to groups 4, 5 and 6

This plant contains chemical compound flavonoids, alkaloids, steroids and saponins<sup>11</sup>. Empirically, the people of South Sulawesi, Pinrang Regency uses the Beruwas laut (*S. taccada* (Gaertn.) Roxb.) as an antidiabetic<sup>4</sup>. Rahmawati (2013) found that the ethanol extract of Beruwas laut (*S. taccada* (Gaertn.) Roxb.) was potential as an antioxidant with an ES50 value of 78.98 ppm and antioxidant activity was also present in diabetic rats by reducing the malondialdehyde value by 58.98%, and this activity was the same with vitamin

E<sup>11,12</sup>. This study to evaluate the effectiveness of *S. taccada* (Gaertn.) Roxb. extract as an antihyperlipidemia by measuring the biochemical parameters cholesterol and triglycerides. The variation of concentration 700 mg/kgbw; 900 mg/kgbw and 1100 mg/kgbw in this research based on previous data showed a concentration of 7% could reduce cholesterol levels in test rats, which were then converted into a dosage equal to 700 mg/kgBW.

**Table 2: Results of measurement of the average triglyceride level of test animals.**

Triglyceride (mg/dL)	Group 1	Group 3	Group 4	Group 5	Group 6
baseline (Day 0)	79.33±13.91	86.33±7.93	87.66±6.59	78±12.08	77±11.34
Induction (HFD)	186.33±9.84	182.66±2.62	185±5.71	182±11.86	185.66±6.79
Days 14 (Treatment)	187.33±8.57	65.66±11.02	137.66±10.20	112.33±6.23	101.33±17.13
Percentage Reduction	-0.53 %*	64.10 %#	25.53 %*	37.86 %#	45.19 %#

The groups 1 and 3 received suspension Na. CMC 1% w/v and Gemfibrozil 167.60 mg/kgbw; groups 4, 5 and 6 are 700, 900 and 1100 mg/kgbw of ethanol extract of leaves *Scaevolataccada* (Gaertn.) Roxb, respectively, \*  $p < 0.05$  significantly group 1 compared to group 3, 4, 5, and 6, #  $p > 0.05$  non significantly group 3 compared to 5 and 6

The results of measurements of cholesterol levels before induction, after induction, treatment and percentage reduction of ethanol extract of leaves *S. taccada* (Gaertn.) Roxb leaves can be seen in Table 1. The results of the average cholesterol measurement in table 1 show that there is an increase in cholesterol levels with a range of 40.8 - 44.8 mg/dl to a range of 83.40-89.40 mg/dl after the induction of a diet high in cholesterol and pure cholesterol for 35 days. This shows that giving a diet high in fat and pure cholesterol will cause an increase in the amount of fat in the form of triglycerides. The lipid will be deposited in adipose tissue, especially those under the skin and in the abdominal cavity and will be used as material for the formation of VLDL and LDL in the liver so that it can affect total cholesterol levels. All test groups except the control group Natrium CMC 1% w/v after giving therapy for 14 days experienced a decrease in cholesterol levels with a large decrease occurring in the simvastatin group and the EEDBL group at a dose of 1100 mg/kgBW. Based on the results of the ANOVA statistical test and Bonferonni follow-up test, the percent reduction in cholesterol levels showed that the simvastatin control group against the EEDBL group at doses of 700, 900 and 1100 mg/kgbw was not significantly different ( $p < 0.05$ ). This means that EEDBL has the same effect as simvastatin in reducing cholesterol levels. By looking at the percent reduction in cholesterol levels, the largest was the EEDBL group with a dose of 1100 mg/kg BW. The use of simvastatin as a cholesterol drug in this study because it is a statin drug class with a mechanism of inhibiting the 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase HM G-CoA reductase in the cholesterol synthesis process in

the liver<sup>1</sup>. The results of measurements of triglyceride levels before induction, after induction, treatment and percentage reduction of ethanol extract of *S. taccada* (Gaertn.) Roxb leaves can be seen in Table 2.

The results of the measurement of the average triglycerides in Table 2 show that there is an increase in triglyceride levels with a range of 77.00 - 87.66 mg/dL to a range of 182.00-186.33 mg/dL after the induction of a high cholesterol and pure cholesterol diet for 35 days. This shows that giving a diet high in fat and pure cholesterol will cause an increase in the amount of fat in the form of triglycerides. The more fat levels are consumed; the triglyceride synthesis in the body will also increase<sup>13</sup>. All test groups except the control group Natrium CMC 1% w/v after giving therapy for 14 days experienced a decrease in triglyceride levels with a large decrease occurring in the simvastatin group and the EEDBL group at a dose of 1100 mg/kgBW. Based on the results of the ANOVA statistical test and the continued bonferonni test, the percent reduction in triglyceride levels showed that the simvastatin control group against the EEDBL group at doses of 900 and 1100 mg/kgBW was not significantly different ( $p < 0.05$ ). This means that the EEDBL doses of 900 and 1100 mg/kg have the same effect as simvastatin in reducing triglyceride levels according to the percent reduction in cholesterol levels, the largest in the EEDBL group at a dose of 1100 mg/kgBW. The use of gemfibrozil as an anti-hyperlipidemia in this study because it is a class of fibrate Fibrates reduce triglycerides through PPAR $\alpha$ -mediated stimulation of fatty acid oxidation, increased LPL synthesis, and reduced expression of apoC-III<sup>14</sup>. The results of measuring cholesterol and triglyceride

levels from the ethanol extract of Beruwas laut (*S. taccada* (Gaertn.) Roxb.) showed that the doses of 900 and 1100 mg/kgBW were effective doses. This is thought to be due to the chemical content of flavonoids, saponins and alkaloids from Beruwas laut (*S. taccada* (Gaertn.) Roxb.). Alkaloids have hypolipidemic activity by inhibiting fatty acids which are the basic ingredients for the formation of triglycerides. Flavonoids are the constituents of Beruwas laut (*S. taccada* (Gaertn.) Roxb.)<sup>10</sup>. Numerous studies have been approved the potential role of flavonoid as antidiabetic, antihyperlipidemic and antioxidant<sup>13,15</sup>. Saponins can reduce triglyceride by inhibited pancreatic lipase activity<sup>16</sup>. Flavonoids and saponins are antioxidants that can help lower triglyceride levels by increasing the activity of the lipoprotein lipase enzyme which works to convert triglycerides into free fatty acids<sup>17</sup>.

## CONCLUSIONS

The conclusion of this study is that the ethanol extract of *S. taccada* (Gaertn.) Roxb. leaves has an effect on reducing cholesterol levels in hyperlipidemic rats. The concentration of ethanol extract from *S. taccada* (Gaertn.) Roxb. leaves which is the most effective in reducing cholesterol and triglyceride levels of hyperlipidemic rats is ethanol extract of *S. taccada* (Gaertn.) Roxb. leaves with a dose of 1100 mg/kgbw

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## AUTHOR'S CONTRIBUTION

**Rahmawati:** writing original draft, clinical work. **Aulia Wati A:** methodology, formal analysis, conceptualization. **Santi I:** editing, methodology. **Jafar J:** investigation, conceptualization. **Sangaji AP:** data curation, investigation. All authors revised the article and approved the final version.

## DATA AVAILABILITY

Data will be made available on reasonable request.

## CONFLICT OF INTEREST

None to declare.

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