

Antihypercholesterol activity of *Costus speciosus* water extract

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Received: Aug 09, 2017

Accepted: May 15, 2018

Published: May 15, 2018

Keywords:

Antihypercholesterol, *costus*, water extract, PTU

ABSTRACT

Introduction: Hypercholesterolemia is one of the causes of cardiovascular disease. *Costus speciosus* (CS) is known empirically as an antihypercholesterol remedy. **Material and Method:** This study was conducted to determine the effect of water extract of CS on cholesterol blood serum level of rat induced-propylthiouracil (PTU). The antihypercholesterol activity performed on male Wistar rats which induced 0.01% PTU (mixed in drinking water, 14 day-induction) was followed by the administration of CS for 14 days. The animals were randomly divided into seven groups: Solvent control (carboxymethylcellulose 0.5% w/v in water), positive control (simvastatin at dose 7.2 mg/kg BW), negative control (water), CS extract 50, 100, and 200 mg/kg, and normal control. The cholesterol levels were measured at day 0th, 14th, and 28th. **Result and Conclusion:** Results showed that administration of CS extract 200 mg/kg can reduce the total serum cholesterol equal to simvastatin 7.2 mg/kg.

INTRODUCTION

Cardiovascular disease is a degenerative disease which is leading killer worldwide. Most of the cardiovascular diseases such as coronary heart disease are closely related to atherosclerosis [1]. One of the factors that cause atherosclerosis is a condition of dyslipidemia, which is characterized by increased levels of total blood cholesterol (hypercholesterolemia, triglycerides [hypertriglyceridemic], low-density lipoprotein cholesterol, and decreased levels of high-density lipoprotein cholesterol). The development of atherosclerosis increases with an increase in the quantitative degree of dyslipidemia [2,3].

Many synthetic drugs have been used in hyperlipidemia therapy, such as statin groups and fibrates, but their usage still provides considerable side effect. It has become a challenge for researchers to look for another resource for overcoming this problem. Indonesia has many resources for medicine, especially from a plant. *Costus speciosus* (CS) was empirically used as an antihypercholesterol remedy.

CS grows as weeds in the yard or in the garden. CS has hypolipidemic, hepatoprotective, antifertility, antioxidant, and antifungal activities. Traditionally, the plant is also

known to have a role in treating arthritis, rheumatic, bronchial asthma, and leprosy [4]. It has been reported that 50% ethanol extract of the rhizome CS can inhibit the production of spermatozoa irreversibly [5]. Sari *et al.* reported that CS water extract can reduce 16-38% of spermatozoa without changing its morphology and viability [6]. A chemical compound which is assumed to be closely related to antispermatogetic effect, diosgenin, is present in several parts of the CS plant. Diosgenin is present in the CS rhizomes by 0.2% while the leaves by 0.37%, 0.65% at the trunk, and the highest is at the flower at about 1.21% [4]. Water extract of the leaves and rhizomes of CS contains steroids, tannins, and phenolics [7].

People used the decoction of CS in the traditional remedy. To our knowledge, there was no research about the effectivity of water extract in CS in the form of antihypercholesterol activity on male rats. The aim of this study was to observe the antihypercholesterol activity of CS water extract on propylthiouracil (PTU)-induced male rats.

Thyroid hormones play an important role in regulating the synthesis, metabolism, and lipid mobilization. Disruption of lipid profile occurs in hypothyroid condition. PTU is a drug used to treat hyperthyroidism. Prescribing 0.01% PTU

in drinking water in animal model showed higher cholesterol serum level than normal control [8].

MATERIALS AND METHODS

The main material was aerial part of CS herb, obtained from Berbah, Kalasan, Sleman, Yogyakarta Region, Indonesia.

Chemicals: Aquadest and formaldehyde were obtained from local distributor, PTU tablets (PT. Kimia Farma), Simvastatin tablets (PT. Dexa Medica), carboxymethylcellulose (Bratachem), and the CHOD-PAP enzymatic reagent kit were obtained from Dyasis.

Animals: The animal test was performed on male Wistar rat stains obtained from the Laboratory of Pharmacology, Faculty of Pharmacy, UGM.

Method

The plant was identified and authenticated by an expert in botany, Djoko Santosa, MSc, Department of Biology Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia. This is evidenced by certificate No. BF/37/Ident/Det/II/2016.

The collected aerial part of herb was shade dried and powdered in a mixer grinder to get the coarse powder. The water extract of CS was obtained by infundation method [8] followed by freeze drying. The antihypercholesterol activity performed on male Wistar rats which induced 0.01% PTU (mixed in drinking water, 14 day-induction) [9] was followed by the administration of CS for 14 days.

The animals were randomly divided into seven groups: Solvent control (carboxymethylcellulose 0.5% w/v in water), positive control (simvastatin 7.2 mg/kg), negative control (water), CS 50, 100, and 200 mg/kg, and normal control. The cholesterol levels were measured at day 0th, 14th, and 28th. The blood serum was taken from sinus orbital of eye followed by vortexing it for several seconds. The serum layer was separated by pipetting the supernatant after centrifuging it. The total cholesterol serum level was measured enzymatic-spectrophotometrically based on CHOD-PAP method [10].

The data obtained were analyzed using ANOVA ($P < 0.05$).

The liver of the animals was collected at the end of this treatment. The liver was fixed using formaldehyde and prepared for the histopathology scanning. The rat liver tissue histopathology made preparations with hematoxylin-eosin staining method (HT). Observations were made with an optical microscope Olympus BX-51. Changes were observed in fatty liver hepatocyte cells.

The experimental protocol was approved by UAD Animal Ethics Committee, Ethical Approval Number: 011505046.

RESULT AND DISCUSSION

The antihypercholesterol activity performed on male Wistar rat induced 0.01% PTU (mixed in drinking water, 14 day-induction). The 14-day induction increased the total cholesterol level ($P < 0.5$). The CS extract treatment 200 mg/kg can

Table 1: The serum cholesterol level before and after treatment

Groups	Cholesterol level (mg/dL) day of:		
	0 th	14 th	28 th
Negative control	60.62±7.40	120.24±8.98	149.72±7.07
CMC Na	75.21±11.52	107.06±11.96	108.50±11.36
Simvastatin 7.2 mg/kg	65.82±9.93	118.45±18.32	99.79±21.79*
CS 50 mg/kg	84.68±13.83	104.98±28.91	118.81±18.75
CS 100 mg/kg	75.87±11.11	106.94±18.78	106.34±12.72
CS 200 mg/kg	69.14±2.84	130.07±3.12	108.73±17.34*
Normal	101.19±9.08	106.01±12.31	119.51±10.38

Data were presented as mean±SD. * ($P < 0.05$) compared with the same group at 14th day. SD: Standard deviation

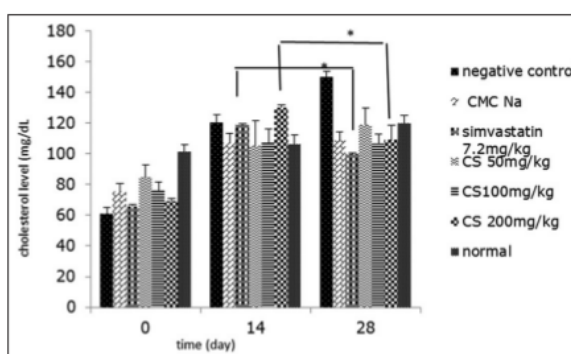


Figure 1: The profile of cholesterol level of each group on 0th, 14th, and 28th days * ($P < 0.05$)

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reduce the cholesterol level after inducing PTU, the results are shown in Table 1 and Figure 1.

Figure 1 shows that the cholesterol level of the animals increased after inducing PTU. The effectivity of simvastatin (as the positive control) and the extracts was determined by calculating the % decrease of cholesterol level 28th day against the 14th day. The CS extract 200 mg/kg can reduce the cholesterol level as well as simvastatin 7.2 mg/kg, while the CS extract 50 and 100 mg/kg have not been able to lower the cholesterol level yet.

It has been shown that the CS extract 200 mg/kg has similar capability as antihypercholesterol with simvastatin. It is assumed that the steroid contains in the water extract has contributed in the antihypercholesterol effect. Steroids were known as the raw material in the biosynthesis of cholesterol. Son *et al.* reported that 0.1% and 0.5% diosgenin added in the high cholesterol fed could decrease total cholesterol in plasma level to about 26.1% and 32.1%, respectively [11]. The ability of extracts in lowering cholesterol premises allegedly linked to the content of diosgenin which is a steroid saponin compound. Suspected steroid compounds within the extract can inhibit the synthesis of cholesterol in the body by inhibiting the action of the enzyme HMG-CoA reductase. The other possible antihypercholesterol activity was the role of diosgenin due inhibit gastrointestinal cholesterol absorption and increasing the serum lipase activity [12]. In addition, the content of flavonoids and polyphenols has

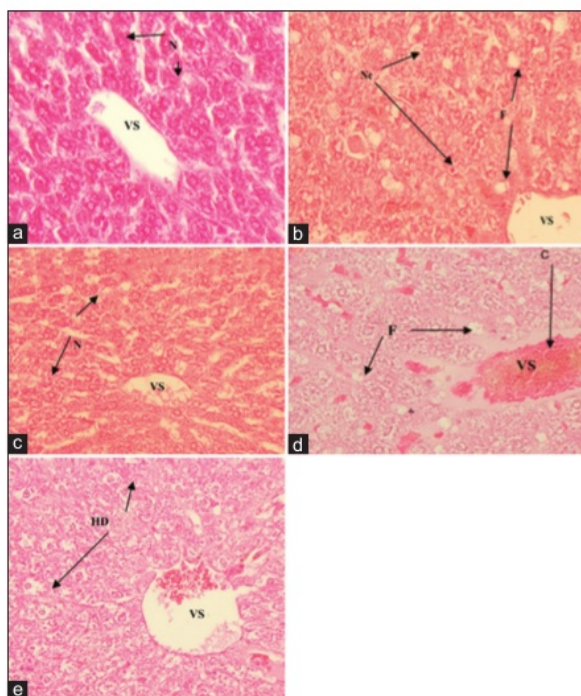


Figure 2: The histopathology profile of liver after treatment: Observation of changes in hepatocyte around central vein (VS). (a) Normal group showing normal cell (N), (b) negative control, necrosis (Nc) and fatty (F), (c) CS extract 200 mg/kg, showing normal cell, no specific pathological changes (N), (d) CS extract 100 mg/kg, fatty (F) and congestion (C) there is accumulation of blood cell in VS, (e) CS extract 50 mg/kg, hydropic degeneration (HD)-enlarged cells

antihyperlipidemic activity in rats induced by high-fat diet with a mechanism to decrease the activity of lipase enzymes involved in lipid absorption [13]. Tannin content in the CS in the body may precipitate mucosal proteins that exist on the surface of the small intestine so that it can reduce the effectiveness of cholesterol and fat absorption [14].

The histopathology profile of liver is shown in Figure 2.

The histopathologic profile (Figure 2) shows that there is no specific pathologic change just like normal cell at CS 200 mg/kg group. The positive control, i.e., simvastatin gives two different profiles. The first one was like a normal cell, but the other one shown fatty and necrosis condition as the negative control. Cell necrosis was characterized by cell nucleus (black). It was indicated that simvastatin at the high dose has the unexpected effect on the liver. The CS extract 100 mg/kg showed congestion and the CS extract 50 mg/kg showed a HD. It seems that the CS extract 100 and 50 mg/kg could not prevent the liver damage.

CONCLUSION

The water extract of CS 200 mg/kg has antihypercholesterol activity similar to that of simvastatin 7.2 mg/kg.

ACKNOWLEDGMENT

The authors acknowledge the receipt of financial support from the State Ministry of Research and Technology under the project PDD-002/SP3/III/2016. The authors also thank Djoko Santosa, MSc, for providing plant identification.

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