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Review of Phytochemicals and Pharmacology of Medicinal Plants to Lower Blood Fat Levels

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Abstract

This review aims to seek information about the phytochemical and pharmacological activities of plants used traditionally to reduce blood lipid levels. The way to find information is to conduct literature studies to find sources or literature in primary data or official books and national and international journals in the last ten years (2010-2020). In doing this review, the search for data using online media with keywords is Phytochemical, Pharmacology, Lowering Blood Fat Levels. Search for the primary references used in this review article's production through trusted websites, namely Google Scholar, Science Direct, NCBI, ResearchGate, and other published and reliable journals. The results show that six herbs are used traditionally to lower blood lipid levels. The six plants contain carbohydrates, tannins, alkaloids, steroids, triterpenoids, flavonoids, glycosides, phenolics, saponins, polyphenols, quercetin, terpenoids, sterol glycosides, flavonols, and formic acid. These six herbs have been shown to work as anti-hypercholesterolemic agents. Thus, it can be concluded that six plants in Indonesia can be developed into phytopharmaca as anti-hypercholesterolemic drugs.

Keywords: Antihypercholesterolemia, medicinal plants, phytochemicals, pharmacology, lowering blood lipid levels.

1. Introduction

According to the Food and Drug Administration of the Republic of Indonesia (2011) [1], blood fats consist of triglycerides and cholesterol. Cholesterol is a fat-like substance (lipid) found in cell membranes and is a precursor to bile acids and steroid hormones. Cholesterol in the blood circulation is bound to lipoproteins. There are two kinds of lipoproteins: high-density lipoprotein (HDL), good cholesterol, and Low-Density Lipoprotein (LDL), known as bad cholesterol. LDL carries cholesterol from the liver to the body's parts where it is needed, while HDL carries excess cholesterol in the blood to the liver for reprocessing.

Also, there is something called triglycerides, which are excess calories stored in fat cells in the blood. The body needs normal levels of triglycerides. Total cholesterol contains 60-70% LDL, 20-30% HDL and 10-15%

triglycerides. Under normal circumstances, cholesterol is needed by the body for the growth of brain and nerve tissue, the formation of body cells, and a precursor for the formation of bile acids and steroid hormones. However, if the amount of LDL and triglycerides is excessive, the lipoproteins will stick to the coronary blood vessels' walls and can cause plaque known as atherosclerotic plaque. Hypercholesterolemia or also known as high cholesterol, is the presence of high cholesterol levels in the blood. It is a form of hyperlipidemia, high blood lipids, and hyperlipoproteinemia (increased lipoproteins levels in the blood) [2].

Many people use plants as a traditional medicine to reduce blood lipid levels because chemical drugs have many side effects from medications. Therefore, it is necessary to look for medicinal plants that can reduce blood lipid levels. The POM RI has determined that the plants Salam (*Syzygium polyanthum*), Alang-Alang (*Imperata cylindrica* L), Pegagan (*Centella asiatica* L), Sambiloto (*Andrographis paniculata*), Sweet Potatoes (*Ipomoea batatas*), and Sambung Nyawa (*Gynura procumbens*) can be used as an herb to lower blood fat levels [1]. Therefore, it is necessary to collect phytochemical and pharmacological information from these plants.

2. Method of data collection

In compiling this review article, the technique used is to use literature studies by finding sources or literature in primary data or the shape of official books and international journals in the last ten years (2010-2020). The search for data used online media with keywords such as phytochemistry, pharmacology, and lowering blood fat levels in doing this review. Search for the primary references used in this review article's production through trusted websites, namely Google Scholar, Science Direct, NCBI, ResearchGate, and other published and reliable journals.

3. Medicinal plants used to lower blood lipid levels

According to the POM RI [1], six medicinal plants can lower blood lipid levels. The six plants are Salam (*Syzygium polyanthum*), Alang-Alang (*Imperata cylindrica* L), Pegagan (*Centella asiatica* L), Sambiloto (*Andrographis paniculata*), Sweet Potatoes (*Ipomoea batatas*), and Sambung Nyawa (*Gynura procumbens*). Each plant will be described both phytochemical and pharmacological activities, especially in reducing blood lipid levels.

3.1 Salam or Bay (*Syzygium polyanthum*)

Bay leaves and flowers that can be used to lower blood lipid levels are shown in Figure 1 below.

Figure 1: Leaves and flowers of Salam (*Syzygium polyanthum*) [3]

This study aims to extract the phytochemical compounds in *S. polyanthum* leaves using ultrasound-assisted extraction (UAE) and identify them with Gas Chromatography-Mass Spectrometry (GC-MS) analysis. The leaves were consecutively soaked with n-hexane, ethyl acetate, and methanol in a sonicator bath to obtain

extracts of n-hexane (HSP), ethyl acetate (EASP), and methanol (MSP) of *S. polyanthum* leaves (Table 1), then the extract was carried out. GC-MS analysis. Compared with the Wiley, NIST, and FNSCC libraries for compound identification, the peak mass spectral databases were compared. GC-MS analysis of HSP, EASP, and MSP revealed the presence of heights of 21 peaks, respectively (Figure 2, Table 2), 27 peaks (Figure 3, Table 3), and 31 peaks (Figure 4, Table 4). The main compounds for HSP (31,912%), EASP (27,042%), and MSP (22,386%) are unknown compounds detected at retention times between 61.980 and 62.29 minutes so they require further characterization. Squalene and phytol were among the other main compounds present in all three extracts. Several compounds identified in extracts such as squalene, phytol, hentriacontane, palmitic acid, α -pinene, nerolidol, linalool, α -tocopherol, and β -tocopherol are known to be bioactive compounds. Thus GC-MS analysis of n-hexane (HSP), ethyl acetate (EASP), and methanol (MSP) from *S. polyanthum* leaf extract has revealed the presence of several known bioactive compounds of therapeutic importance [5].

Table 1: Percentage yield of n-hexane, ethyl acetate, and methanol extracts from *S. polyanthum* leaves [5]

Batch No.	Fresh weight (kg)	Yields After Drying		Final Yield					
		Dry Weight (kg)	% (Wet basis)	HSP		EASP		MSP	
				Weight (g)	% (Dry basis)	Weight (g)	% (Dry basis)	Weight (g)	% (Dry basis)
1	0.7	0.30	42.86	3.39	1.13	6.65	2.22	16.49	5.50
2	0.6	0.30	50.00	6.89	2.30	15.03	5.01	21.81	7.27
Total				1.72 $\pm$ 0.83		3.62 $\pm$ 1.97		6.39 $\pm$ 1.25	

Note: Final results are expressed as percentage mean $\pm$ standard deviation. HSP: *S. polyanthum* leaf n-Hexane extract, EASP: *S. polyanthum* leaf ethyl acetate extract, and MSP: *S. polyanthum* leaf methanol extract.

Figure 2: GC-MS chromatogram of *S. polyanthum* leaf n-hexane extract.

Table 2: Phytochemical compounds in the n-hexane extract of *S. polyanthum* leaves [5]

Name	Peak %	Chemical Classes	Molecular Formula	Retention Time (min)
α -Pipene	4.921	Monoterpene	$C_{10}H_{16}$	8.072
Octanal	0.573	Aldehyde	$C_8H_{16}O$	11.083
Linalool	0.448	Oxygenated monoterpene	$C_{10}H_{18}O$	15.366
α -Cubebene	3.633	Sesquiterpene	$C_{15}H_{24}$	28.330
2-Isopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalene	0.558	-	$C_{15}H_{24}$	33.258
Azulene	1.255	Sesquiterpene derivatives	$C_{15}H_{24}$	33.538
Valencene	1.097	Sesquiterpene	$C_{15}H_{24}$	33.620
β -Panasinsene	3.990	Volatile compounds	$C_{15}H_{24}$	33.892
δ -Cadinene	0.737	Bicyclic sesquiterpene	$C_{15}H_{24}$	34.670
α -Panasinsen	1.515	Sesquiterpene,	$C_{15}H_{24}$	34.848
Nerolidol	2.845	Sesquiterpene	$C_{15}H_{26}O$	36.417
Humulene epoxide II	2.060	Peroxide	$C_{15}H_{24}O$	38.772
Caryophyllene oxide	0.846	Oxygenated terpenoid/ sesquiterpene	$C_{15}H_{24}O$	39.679
Farnesol	0.715	Acyclic alcoholic sesquiterpene	$C_{15}H_{26}O$	42.619
Phytol	8.409	Diterpene alcohol	$C_{20}H_{40}O$	56.147
RT:62.093	31.912	-	-	62.091
Squalene	8.776	Triterpene	$C_{30}H_{50}$	75.442
β -Tocopherol	0.934	Tocopherol (methylated phenols)	$C_{28}H_{48}O_2$	80.906
γ -Tocopherol	0.934	Tocopherol (methylated phenols)	$C_{28}H_{48}O_2$	81.301
α -Tocopherol	0.340	Tocopherol (methylated phenols)	$C_{29}H_{50}O_2$	83.063
β -Sitosterol	0.676	Steroidal	$C_{29}H_{50}O$	87.992
Total = 77.174 %

Figure 3: GC-MS chromatogram of ethyl acetate extract of *S. polyanthum* leaves.

Table 3: Phytochemical compounds in ethyl acetate extract of *S. polyanthum* leaves [5]

Name	Peak %	Chemical Classes	Molecular Formula	Retention Time (min)
Propylene glycol	0.144	Diol	C ₃ H ₈ O ₂	3.521
n-Heptanal	0.317	Aldehyde	C ₇ H ₁₄ O	7.207
α-Pinene	1.068	Monoterpene	C ₁₀ H ₁₆	8.076
Heptane	0.389	Alkane	C ₇ H ₁₆	9.992
Octanal	0.563	Aldehyde	C ₈ H ₁₆ O	11.093
β-linalool	0.468	Terpene alcohol	C ₁₀ H ₁₈ O	15.373
α-Cubebene	1.690	Sesquiterpene	C ₁₅ H ₂₄	28.333
α-Humulene	0.504	Monocyclic sesquiterpene	C ₁₅ H ₂₄	32.023
β-Selinene	0.735	Sesquiterpene	C ₁₅ H ₂₄	33.545
Valencene	0.548	Sesquiterpene	C ₁₅ H ₂₄	33.620
1H-Cyclopropa[a]naphthalene	2.226	Acyclic alkene	C ₁₅ H ₂₄	33.894
α-Panasinsen	0.887	Sesquiterpene	C ₁₅ H ₂₄	34.843
Nerolidol	3.085	Sesquiterpene alcohol	C ₁₅ H ₂₆ O	36.423
Humulene epoxide II	1.557	Sesquiterpene	C ₁₅ H ₂₄ O	38.782
Caryophyllene oxide	0.824	Oxygenated terpenoid	C ₁₅ H ₂₄ O	39.688
Farnesol	0.645	Acyclic alcoholic sesquiterpene	C ₁₅ H ₂₆ O	42.628
Neophytadiene	1.347	Terpenoid	C ₂₀ H ₃₈	46.723
Phytol	5.715	Diterpene alcohol	C ₂₀ H ₄₀ O	56.151
9,12,15-Octadecatrien-1-ol	1.037	Unsaturated alcoholic compound (Lignan)	C ₁₈ H ₃₂ O	57.341
Hentriacontane	0.303	Long chain alkane	C ₃₁ H ₆₄	58.758
RT:62.290	27.042	-	-	62.291
2-Cyclohexen-3-ol-1-one, 2-[1-iminoethyl]-	0.107	-	-	62.658
n-Pentacosane	0.472	Aliphatic hydrocarbon alkane	C ₂₅ H ₅₂	64.611
Squalene	8.345	Teriterpene hydrocarbon	C ₃₀ H ₆₂	75.455
β-Tocopherol	0.693	Tocopherol (methylated phenols)	C ₂₈ H ₄₈ O ₂	80.916
α-Tocopherol	4.660	Tocopherol (methylated phenols)	C ₂₉ H ₅₀ O ₂	83.081
β-Sitosterol	4.959	Steroidal	C ₂₉ H ₅₀ O	88.038
Total = 70.330 %

Figure 4: GC-MS chromatogram of *S. polyanthum* leaf methanol extract.

Table 4: Phytochemical compounds in the methanol extract of *S. polyanthum* leaves.

Name	Peak %	Chemical Classes	Molecular Formula	Retention Time (min)
Propylene glycol	0.272	Diol	C ₃ H ₈ O ₂	3.487
Octanal	0.354	Aldehyde	C ₈ H ₁₆ O	11.090
2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one	1.423	Flavanoid fraction	C ₆ H ₈ O ₄	17.841
α-Copaene	0.636	Sesquiterpene	C ₁₅ H ₂₄	28.333
Pyrogallol	5.247	Phenol	C ₆ H ₆ O ₃	28.727
α-Humulene	0.576	Sesquiterpene	C ₁₅ H ₂₄	32.031
β-Panasinsene	0.923	Sesquiterpene	C ₁₅ H ₂₄	33.554
Selina-4,11-diene	1.519	-	C ₁₅ H ₂₄	33.896
α-Panasinsen	0.677	Sesquiterpene	C ₁₅ H ₂₄	34.848
Nerolidol	2.267	Sesquiterpene	C ₁₅ H ₂₆ O	36.417
β-Selinene	0.321	Sesquiterpene	C ₁₅ H ₂₄	38.307
Humulene epoxide II	0.910	Epoxide	C ₁₅ H ₂₄ O	38.784
Caryophyllene oxide	0.943	Oxygenated terpenoid	C ₁₅ H ₂₄	39.698
Pentadecane, 2,6,10,14-tetramethyl-	0.386	Saturated terpenoid alkane	C ₁₉ H ₄₀	41.659
Farnesol	0.421	Acyclic Sesquiterpene	C ₁₅ H ₂₆ O	42.630
Neophytadiene	0.581	Terpenoid	C ₂₀ H ₃₈	46.735
Methyl palmitate	0.425	Palmitic acid ester	C ₁₇ H ₃₄ O ₂	50.092
Palmitic acid	2.378	Fatty acid	C ₁₆ H ₃₂ O ₂	51.507
Eicosane	0.294	Aliphatics alkane	C ₂₀ H ₄₂	52.398
Methyl oleate	0.343	Unsaturated fatty acid Methyl ester	C ₁₉ H ₃₆ O ₂	55.887
Phytol	4.952	Diterpene alcohol	C ₂₀ H ₄₀ O	56.137
9,12,15-Octadecatrien-1-ol	1.783	Unsaturated alcoholic compound	C ₁₈ H ₃₂ O	57.317
Stearic acid	0.604	Stearic acid	C ₁₈ H ₃₆ O ₂	57.963
		Saturated fatty acid		
Hentriacontane	0.674	Alkane	C ₃₁ H ₆₄	55.647
RT:61.980	22.386	-	-	61.975
Pentacosane	1.282	Aliphatic hydrocarbon	C ₃₁ H ₆₄	58.758
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)	0.525	Fatty acid	C ₁₉ H ₃₈ O ₄	68.232
Squalene	10.913	Triterpene	C ₃₀ H ₅₀	75.440
β-Tocopherol	0.548	Tocopherol compound (methylated phenols)	C ₂₈ H ₄₈ O ₂	80.903
α-Tocopherol	4.933	Tocopherol (methylated phenols)	C ₂₉ H ₅₀ O ₂	83.048
β-Sitosterol	5.560	Steroidal	C ₂₉ H ₅₀ O	87.988
Total = 75.056 %				

Hypercholesterolemia is a condition in which serum cholesterol levels increase, especially Low-Density Lipoprotein (LDL) levels that exceed normal limits. The antihypercholesterolemic effect of ceremai leaf extract and bay leaf extract has been tested with a combination of 1 dose of 30 mg/kg BW of ceremai leaf extract and 50 mg/kg BW of bay leaf extract, a combination of 2 doses of 15 mg/kg BW of ceremai leaf extract and 25 mg/kg BW of bay leaf extract given to hypercholesterolemic male white rats (*Rattus norvegicus*). Male white rats were given a high cholesterol diet. Data analysis using ANOVA method and KK advanced test. Based on the results of research that has been done, it shows that the combination of ethanol extract of ceremai leaves with a dose of 15 mg/kg BW and ethanol extract of bay leaves 25 mg/kg BW can reduce total blood cholesterol levels in white male rats which is comparable to the positive control simvastatin [6].

The combination of *Andrographis paniculata* aqueous extract and aqueous *Syzygium polyanthum* (6: 1) was reported to reduce blood glucose in normal and alloxan rats. This combination also exerted a protective effect on the kidneys, liver and pancreas of tested animals against alloxan toxicity. Eighty male albino rats were divided into eight different groups: normal control, diabetes control, four groups of *Andrographis paniculata*

aqueous extract treatment groups, and *Syzygium polyanthum* and its combination, and standard drugs (metformin, insulin) as many as ten rats in each group. The extract and standard were given orally for seven days. On the 7th day of blood sampling, the serum was separated, and the levels of glucose, total cholesterol, LDL, HDL, triglycerides, and alkaline phosphatase were determined. Recording body weight on days 1 and 7. The data obtained showed that the aqueous extract of *Andrographis paniculata* (WAP), an aqueous extract of *Syzygium polyanthum* (WSP) and their combinations (1 WAP: 6 WSP; 6 WAP: 1 WSP)) reduced glucose levels. The treatment with this extract also significantly reduced LDL and triglyceride levels and alkaline phosphatase levels compared to the normal and diabetic groups. Aqueous extract of *Andrographis paniculata*, an aqueous extract of *Syzygium polyanthum*, and their combination have significant antidiabetic activity as well as antihypercholesterolemic activity [7].

3.2 Alang-Alang (*Imperata cylindrica* L)

The roots, leaves, and flowers of alang-alang that can be used to lower blood fat levels are shown in Figure 5 below.

Figure 5: Leaves and flowers of Alang-Alang (*Imperata cylindrica* L) [8]

Alang-Alang (*Imperata cylindrica* / *I. cylindrica*) from the Gramineae family is abundant in nature. The roots of this plant have several beneficial biological activities. This study aims to isolate and identify flavonoids from Alang-Alang roots and test their potential as hypocholesterolemic agents. Flavonoid compounds were isolated by the maceration method, followed by gravity column chromatography until pure compounds were obtained. The molecular structure of isolated compounds was determined using ^1H - nuclear magnetic resonance (NMR) and ^{13}C - NMR spectroscopy. *In vivo*, lipid-lowering tests used a group experimental design control was only randomized post-test in mice with hypercholesterolemia. The animals were divided into four groups: K0, negative control; K1, positive control; K2, the ethanol extract treatment group; and K3, the ethyl acetate fraction treatment group, and the lipid profile was examined at the end of the study. The compound isolated, 7,3',5'-trimethoxyflavonol, was collected in the form of a yellow powder; it proved to be a flavonoid and consists of 18 carbon atoms and 16 hydrogen atoms. *In vivo* tests showed that the ethanol extract 15 mg/200 g body weight (BW) significantly reduced total cholesterol levels ($P = 0.001$) but did not decrease low density lipoproteins (LDL) ($P = 0.109$) and high density lipoproteins (HDL) ($P = 0.003$). Ethyl acetate fraction given at 15 mg/200 g BW was able to significantly reduce total cholesterol levels ($P = 0.002$) and reduce LDL levels ($P = 0.006$) but was unable to increase HDL levels ($P = 0.190$). The *in vivo* test showed that the ethyl acetate fraction of *I. cylindrica* reduced total and LDL cholesterol levels more effectively than ethanol extract but did not affect HDL levels in hypercholesterolemic rats [9].

Imperata extract was studied to affect the absorption rate of cholesterol in mice (*Mus muscular*). Male mice (20-25 g) were divided into the control group and the previous treatment group. The treatment group was

further divided into two groups with different doses of Imperata extract (90 mg/kg and 115 mg/kg BW) for two weeks. The mice were fasted 12 hours before being given acute olive oil at a dose of 10 μ L / g, and blood was drawn at time points 0, 2, and 6 hours on the specified day. Blood is collected from the retroorbital plexus at a designated point in time. Total cholesterol levels were significantly ($p < 0.05$) decreased in both groups treated previously at 6 hours after acute olive oil administration. It can be concluded that the significant effect of Imperata extract on reducing serum cholesterol levels indicates its potential impact as an antihypercholesterolemic therapy [10].

3.3 Pegagan (*Centella asiatica*)

Pegagan herbs that can be used to lower blood fat levels are shown in Figure 6 below.

Figure 6: Herbs of Pegagan (*Centella asiatica*) [11]

Centella asiatica is a herbaceous plant commonly known as Gotu Kola and belongs to the Apiaceae family. This plant is found in most tropical and subtropical countries that grow in swampy areas. This plant is a tasteless, odorless plant and is traditionally used for the treatment of various diseases. The leaves and roots are used as a vegetable and for medicinal purposes. Knowledge of their contribution to human nutrition and bioactive components' content is lacking and has limited their use. Therefore, this study evaluated the nutritional content and phytochemical composition of Gotu kola leaves using standard methods. Proximate analysis of this plant shows water content of $13.10 \pm 1.07\%$, ash $16.5 \pm 0.45\%$, protein $8.35 \pm 1.28\%$, fat $1.20 \pm 0.10\%$, fiber $17.00 \pm 1.87\%$ and carbohydrates $43.81 \pm 0.70\%$. The physicochemical analysis showed a saponification value of 238.43 mg / KOH. The fatty acid composition showed high palmitic acid concentrations (55.70%) as saturated acid and linoleic acid (17.50%) as unsaturated fatty acids. Meanwhile, the amino acid composition showed high glutamate levels (13.389 g / 100 g) as nonessential and histidine (11.64 g / 100 g) as an essential amino acid. The phytochemical composition indicates the presence of bioactive compounds such as; Proanthocyanin (11,964 μ g / g), Rutin (11.8883 μ g / g), Nannigenin (3.0122 μ g / g), Quinine (10.4490 μ g / g), Flav-3-ol (2,5900 μ g / g), Sparteine (3, 0122 μ g / g), Phenol (18.8713 μ g / g), Flavonones (2.1836 μ g / g), Steroids (18.8974 μ g / g), Kaempferol (0.7273 μ g / g), Phytate (1, 6851 μ g / g), Naringenin (2.7523 μ g / g), Resveratol (10.8596 μ g / g), Tannins (4,4377 μ g / g) and Ribalinidine (3.0500 μ g / g). These bioactive nutrients and phytochemicals in Gotu kola leaves make them useful in the pharmaceutical and food industries [23].

Phytochemical analysis of Gotu kola extract revealed various biochemical compounds such as alkaloids, flavonoids, glycosides, phenolic compounds, triterpenoids, and saponins. Phenolic compounds, triterpenoids, and flavonoids have extraordinary anti-inflammatory, anti-rheumatic and antioxidant activity. Evaluation of the in vitro anti-inflammatory activity, membrane stabilization Human Red Blood Cell (HRBC) was used to inhibit

HRBC-induced hypotonicity of membrane lysis. Percentage of Haemolysis was tested with a concentration of 50 $\mu\text{g} / \text{mL}$ to 2000 $\mu\text{g} / \text{mL}$, and the value decreased from 32.25% to 5.02%. On the other hand, the percentage of stabilization at the same concentration increased from 67.74% to 94.97%. Diclofenac sodium was used as a standard drug, and the same experiments were carried out at the same concentration range. And the percentage value of hemolysis was reduced from 47.18% to 1.24%, and the percentage of stabilization increased from 52.81% to 98.76% [12].

Studies to evaluate carotid-femoral plaque echogenicity in asymptomatic subjects with increased oxidative stress and risk factors (mild hypertension, hypercholesterolemia) have been performed. Supplementation with the Pycnogenol-CA (Centella asiatica) combination on plaque echogenicity was assessed at six months (79 subjects). Standard management plans (SM) were used in all subjects (risk factor control, lifestyle changes); 36 subjects used supplement + SM; 43 BC only. The groups are comparable. High-resolution ultrasound evaluates the echogenicity and structure of plaque. Pycnogenol (150 mg / day) and CA (*Centella asiatica*, 450 mg / day) were used for 6 months. Cholesterol levels decreased ($p < 0.05$) in both groups (the difference between groups was not significant). At 6 months, plasma free radicals were decreased with supplementation (17.64%; $p < 0.05$; vs $< 2\%$ in controls). The plaque stability index increased from 11.22, 2.3 to 22.4, 1.1 ($p < 0.05$) with supplementation; no significant changes were seen in controls. Plaque echogenicity (% of the "whiter" component in the figure) increased with supplementation from 16.7 to 34.2, 2% ($p < 0.05$); no variation was observed in the controls. The maximum plaque height was decreased ($p < 0.05$) with supplementation. No significant variations were observed in the controls. Plaque length decreased ($p < 0.05$) in the supplement group without a change in controls. The amount of plaque (carotid, femoral bifurcations) decreases with supplementation; no significant changes were observed in the controls. No side effects, tolerability problems, or variation in routine blood tests were recorded. The Pycnogenol-CA combination appears to improve the plaque complex's echogenicity and stability at six months [13].

3.4 Sambiloto (*Andrographis paniculata*)

Sambiloto leaves and flowers that can be used to reduce blood lipid levels are shown in Figure 7 below.

Figure 7: Leaves and flowers of sambiloto (*Andrographis paniculata*) [14]

The chemical content of sambiloto (*Andrographis paniculata*) is diterpenoids, flavonoids, and polyphenols [14]. This plant, known as *Andrographis paniculata*, has many pharmacological properties used to treat several diseases. Leaf, stem, and root extracts prepared in chloroform, methanol, and petroleum ether are used to detect β -sitosterol from plants. The chromatography process was carried out on TLC plates coated with silica gel 60 F₂₅₄, and the solvent used for the mobile phase was toluene: ethyl acetate: formic acid (15: 4,5: 1,5). After development, the plates were derivatized with 10% methanol sulfuric acid, scanned, and measured at 510 nm. The results showed the presence of β -sitosterol in all sections with an R_f value of 0.62. The calibration curve was prepared, and the amount of β -sitosterol was calculated in the extract by comparing each peak area with

the standard. The correlation coefficient for β -sitosterol against the reference sample was significant ($r = 99.769057\%$) for the concentration range of 0.5 to 4.0 μg . The methanol extract of the leaves showed the highest β -sitosterol concentration, namely 147.6 $\mu\text{g} / \text{mL}$. The β -sitosterol extraction efficiency was more elevated in methanol, followed by petroleum ether and chloroform extract. Thus, this study suggests that *Andrographis paniculata* has a significant concentration of β -sitosterol, which may be useful for pharmacological applications against cancer, hypercholesterolemia, inflammation, and angiogenesis processes [15].

Cholesterol is one of the causes of coronary heart disease. In the experimental method using a completely randomized design (CRD) 3 replications, 6 treatments, namely: 1) D0 = normal control; 2) D1 = positive cholesterol control; 3) D2 = comparator simvastatin 2 mg / 200 g body weight; 4) D3 = dose of sambiloto 100 mg / 200 g body weight; 5) D4 = dose 200 mg of sambiloto / 200 g of body weight; 6) D5 = dose of 400 mg of sambiloto / 200 g of body weight. The mice that have been tested are white male Wistar rats aged two months weighing ± 200 g. Analysis using ANOVA, and further test using DMRT, $\alpha 5\%$. The results showed that the extract of sambiloto 100 mg / 200 g body weight, 200 mg / 200 g body weight, 400 mg / 200 g body weight, and the comparison of simvastatin 2 mg / 200 g body weight could all reduce the total blood cholesterol levels of rats made to become hypercholesterolemic. Interestingly, a dose of 400 mg / 200 g BW had the same ability as simvastatin at a dose of 2 mg / 200 g BW in reducing the total blood cholesterol levels of rats by 51%, considering the risk of hypocholesterolemia [16].

3.5 Sweet Potato (*Ipomoea batatas* L.)

Sweet potato leaves and flowers that can reduce blood lipid levels are shown in Figure 8 below.

Figure 8: Sweet potato (*Ipomoea batatas* L.) leaves and flowers [17]

Sweet potato leaves are plant leaves containing chemicals such as polyphenols, flavonoids, quercetin, tannins, and fiber, which effectively reduce total cholesterol levels. Increased total cholesterol levels increase the risk of cardiovascular disease. To analyze the effect of ethanol extract of purple sweet potato leaves on serum total cholesterol levels, rats fed a high-fat diet. An experimental study with pre and post-test design was conducted on ten male Wistar rats (*Rattus norvegicus*) fed a high-fat diet, namely two groups: 1 hyper cholesterol control group and 1 group of ethanol extract of purple sweet potato leaves. The dosage is based on the quercetin leaf content, which is 2 mg/kg BW. The average ethanol content of quercetin purple sweet potato leaf extract was obtained at 14.08 mg / 100g. The ethanol extract of purple sweet potato leaves was given for 14 days using a sonde. Serum total cholesterol was determined by the CHOD-PAP method. The data obtained were analyzed descriptively. The results showed that the average total cholesterol level of white blood rats before giving ethanol extract of purple sweet potato leaves was 189.89 mg / dL. After giving ethanol extract of purple sweet potato leaves, a 2 mg/kg bb was 131.92 mg / dL. The decrease in white rats' total cholesterol level after giving ethanol extract of purple sweet potato leaves at a dose of 2 mg/kg body weight was 30.52% [18].

3.6 Sambung Nyawa or "life extension" (*Gynura procumbens*)

The "life extension" leaves that can be used to lower blood fat levels are shown in Figure 9 below.

Figure 9: Sambung Nyawa or "life extension" (*Gynura procumbens*) [19]

The leaves of Sambung Nyawa are non-toxic and exhibit antidiabetic, anti-inflammatory, antihypertensive, and wound healing properties. This plant extract contains active chemicals such as tannins, terpenoids, sterol glycosides, saponins, and flavonoids. Antioxidants work against oxidants and free radicals by donating their scoped electrons to radical molecules and neutralizing oxidation processes in biological systems [20].

Gynura procumbens has antihyperlipidemic, antioxidant, and cardioprotective properties. To determine the effect of 80% ethanol extract of *Gynura procumbens* on the lipid profile and oxidative status of hypercholesterolemic rats, postmenopausal (PM) Sprague-Dawley rats were ovariectomized and fed 2% cholesterol fortified with palm oil to develop hyperlipidemia status. Two doses of the extract (250 and 500 mg/kg) and atorvastatin (10 mg/kg) were given once daily by oral gavage for 24 weeks. Systolic blood pressure (SBP) increased during the first month in the postmenopausal group and decreased with *Gynura procumbens* supplementation. Lipid droplet accumulation was seen in the tunica media (TM) area of the aorta in the postmenopausal group and was reduced by *Gynura procumbens* supplementation. Total cholesterol (TC), total triglycerides (TG), low-density lipoprotein (LDL), and malondialdehyde (MDA) increased ($p < 0.05$) at 3 and 6 months in the postmenopausal group and were reduced by *Gynura procumbens* supplementation. *Gynura procumbens* also increased high-density lipoprotein (HDL) levels in the postmenopausal group. Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activity were reduced in the postmenopausal group compared to controls but increased ($p < 0.05$) with *Gynura procumbens* supplementation. It suggests that a higher dose of *Gynura procumbens* (500 mg/kg) gives a better effect. *Gynura procumbens* can reduce oxidative stress and prevent cell membrane damage by modifying antioxidant enzyme activity and changes in lipid profiles in postmenopausal mice associated with atherosclerosis [21].

4. Conclusion

Indonesian plants that have anti-hypercholesterolemic properties are Salam (*Syzygium polyanthum*), Alang-Alang (*Imperata cylindrica* L), Pegagan (*Centella asiatica* L.), Sambiloto (*Andrographis paniculata*), Sweet Potatoes (*Ipomoea batatas*), and Sambung Nyawa (*Gynura procumbens*). These plants contain various phytochemical compounds which are efficacious in reducing fat blood levels. Therefore, these six plants have the potential to be developed into phytopharmaca as anti-hypercholesterolemic herbal medicine.

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