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Antihyperlipidemic activity of the medicinal plants among Kadazan and Dusun communities in Sabah, Malaysia: a review

Khaled Mohamed Mohamed Koriem[1,2*]

[1]*Medical Physiology Department, National Research Centre, Dokki, Giza, Egypt*

[2]*Integrative Medicine Cluster, Advanced Medical and Dental Institute (AMDI), Universiti Sains Malaysia (USM), Malaysia*

PEER REVIEW

Peer reviewer

Dr. Lilia Wassilewa, Professor of Biochemistry, Institute of Microbiology, Bulgarian Academy of Science, Sofia, Bulgaria.
Tel: +3592 8843636
E-mail: lwassilewa@yahoo.com

Comments

This is a well described and satisfied study in which the author reported the lipid lowering activities of the medicinal plants found in Dusun communities in Sabah, Malaysia. This article is capable to be useful to both phyto-protection and new medications develop in CVD.
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ABSTRACT

Sabah is one of the 13 states within the Federation of Malaysia and is located in the northernmost part of Borneo. It is the second largest state in Malaysia with a landmass of approximately 7.4 million hectares. The total forested area is 4.7 million hectares. Sabah, being part of Borneo, is rich in plant biodiversity. There is also an abundance of medicinal plants and other plants for everyday use. There is a great awarness regarding association between low density lipoprotein reduction and decreased cardiovascular disease mortality. The antihyperlipidaemic activity of herbs plays an important role in the reduction of cardiovascular diseases, which is the top disease that causes mortality all over the world. Lipid-lowering activity of medicinal plant for phytomedicine research and drug development for such a disease are now focused all over the world. A plant-based diet rich in fruit, vegetables, and legumes and low in saturated fat is an effective prescription for anyone with more severe atherosclerosis. However, there are few herbs available that provide some protection for persons with the above disease. The antihyperlipidaemia property in plant plays a vital role to reduce atherosclerosis. Thus, there is an increasing search for the lipid lowering agents from natural origin. In this review an attempt has been made to give an overview of the antihyperlipidemic activity in traditional medicinal plants found widely in Kadazan and Dusun communities in Sabah, Malaysia. The antihyperlipidemic activity of the traditional medicinal plants in these communities is more helpful for the development of new drugs used in the protection against dyslipidemia or atherosclerosis.

KEYWORDS

Medicinal plants, Sabah, Hyperlipidemia, Cardiovascular disease

1. Introduction

Sabah is one of the 13 states within the Federation of Malaysia and is located in the northernmost part of Borneo. It is the second largest state in Malaysia with a landmass of approximately 7.4 million hectares. The total forested area is 4.7 million hectares. The climate is marine equatorial with an average temperature of 74-88 °F (23-32 °C). The rainy season, locally called "Musim hujan", is around November to February. This is also known as the north-east monsoon. The south-west monsoon, which is less wet, is from May to October, making the annual rainfall 60-120 inches (1 525-3 050 mm, or sometimes up to 4 500 mm). Sabah, being part of Borneo, is rich in plant biodiversity. There is also an abundance of medicinal plants and other plants for everyday use.

*Corresponding author: Dr. Khaled Mohamed Mohamed Koriem, Medical Physiology Department, National Research Centre, Dokki, Giza, Egypt.
Tel: 202233371433/604-5622413
Fax: 202233370931/604-5622349
E-mail: kkoriem@yahoo.com
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The quest for finding the new safe and effective drug for dyslipidaemia in order to protect against cardiovascular disease (CVD) is going to be a continuous process amongst the scientific fraternity. Herbs have been used as food and for medicinal purposes for centuries. Research interest has been focused on various herbs possessing hypolipidemic property to reduce atherosclerosis that may be useful adjuncts in helping reduce the risk of CVD. Apart from the synthetic modern drugs like clofibrates, statins, there are efforts to find out herbal drugs possessing lipid lowering activities.

A plant-based diet rich in fruit, vegetables, and legumes and low in saturated fat is an effective prescription for anyone with more severe atherosclerosis. In addition, there are few herbs avaliable that provide some protection for persons with the above disease[1].

This review should act to stimulate a thought process on the importance of the antihyperlipidemic activity in traditional medicinal plants found widely in Kadazan and Dusun communities in Sabah, Malaysia.

2. Myrtaceae and musaceae

Family Myrtaceae has a wide distribution in tropical and warm-temperate regions of the world, and is typically common in many of the world's biodiversity hotspots containing over 3 100 species. It is divided into two subfamilies. The first subfamily is the Myrtoideae with 32 genera and 2 400 species; where 200 species are found in Asia. The second subfamily the Leptospermoideae comprises Leptospermae with 28 genera and 700 species and the Chamaelauciae with 12 genera and 165 species. This family includes 644 plants[2,3]. Family Musaceae is native to the tropics of Asia and Africa. The plants that have a large herbaceous growth habit with leaves with overlapping basal sheaths that form a pseudostem making some members appear to be woody trees are made up of three genera, *Musa*, *Ensete* and *Musella*. *Musa* is the largest group with about 35 species[4,5]. In this review three plants-*Eugenia jambolan* (*E. jambolan*), and two species of banana, *Musa paradisiaca* (*M. paradisiaca*) and *Musa acuminata* (*M. acuminata*) were chosen due to their higher antihyperlipidemic activities and wide distirbution in the two communities under investigation.

2.1. E. jambolana and M. paradisiaca

Mallick *et al*. evaluated the hyperlipidemia activity of both plants in experimental diabetic rats[6]. They found that total cholesterol (TC), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc) and triglyceride (TG) in diabetic rats' sera were corrected significantly after co-administration of the extract of the seed of *E. jambolan*a and the root of *M. paradisiaca*. Furthermore, serum TC, TG, HDLc, and the TC/HDLc ratio were significantly decreased following administration with ethanolic seed extract of *E. jambolan*a in diabetic rabbits[7].

2.2. M. acuminata

The pulp of *M. acuminata* fruit was examined by Horigome *et al*. for its cholesterol-lowering effect with male rats fed on a diet containing lard (50 g/kg body weight) and cholesterol (5 g/kg body weight)[8]. Freeze-dried *M. acuminata* pulp showed a marked cholesterol-lowering effect when incorporated into a diet at the level of 300 or 500 g/kg body weight, while the banana pulp dried in a hot-air current (65 °C) did not. Starch and tannin prepared from banana pulp were not responsible for the cholesterol-lowering effect. The results also suggest that banana lipids did not affect the concentration of serum cholesterol. Feeding of dopamine, N-epinephrine and serotonin tend to raise the concentration of serum cholesterol. Thus, all the substances tested which were thought to be susceptible to influence by hot-air drying were unlikely to be responsible for the hypocholesterolaemic effect. However, both soluble and insoluble fibers fractionated from banana pulp had a cholesterol-lowering effect, with the exception of cellulose. It was assumed that a browing reaction undergone during hot-air drying might be related to the disappearance of the hypocholesterolaemic effect of banana pulp dried in a hot-air current. The results obtained support the conclusion that soluble and insoluble components of dietary fibre participated in the hypocholesterolaemic effect of *M. acuminata*.

3. Fabaceae

The Fabaceae or Leguminosae family, commonly known as the legume, pea, or bean family, is a large and economically important family of flowering plants. The group is the third largest land plant family, behind only the Orchidaceae and Asteraceae, with 730 genera and over 19 400 species[9,10]. The largest genera are *Astragalus* (over 2 400 species), *Acacia* (over 950 species), *Indigofera* (around 700 species), *Crotalaria* (around 700 species), and *Mimosa* (around 500 species). Plants of this family are found throughout the world, growing in many different environments and climates. A number of species are important agricultural plants, including *Glycine max* (*G. max*) (soybean), *Phaseolus* (beans), *Pisum sativum* (pea), *Cicer arietinum* (chickpeas), *Medicago sativa* (alfalfa), *Arachis hypogaea* (peanut), *Ceratonia siliqua* (carob), and *Glycyrrhiza glabra* (licorice), which are among the best known members of Fabaceae. The family includes three subfamilies: (1) Mimosoideae: 80 genera and 3 200 species, mostly found in tropical and warm temperate Asia and America; (2) Caesalpinioideae[9,11,12]: 170 genera and 2 000 species and (3) Faboideae: 470 genera and 14 000 species. Five plants were chosen due to the high antihyperlipidemic activities of these plants, high distirbution in the two communities under investigation and more publications of these plants from different Malaysian universities.

3.1. Ougeinia oojeinensis

Velmurugan *et al*. studied the hyperlipidemic activity of ethanolic extract of *Ougeinia oojeinensis*[13]. They found significant reduction in TC, LDL, TG, very low-density lipoprotein (VLDL) levels by 59.91%, 64.85%, 22.58% and 22.36%, respectively after extract administration compared to the decrease in TC, LDL, TG, VLDL levels by 66.55%, 79.50%, 26.68% and 26.57%, respectively of standard drug used. However, the HDL level increased with treatment of extract and glibenclamide drug group, respectively.

3.2. Tephrosia purpurea

Pavana *et al*. reported the plasma lipids and lipoproteins pattern (TC, TG, phospholipids, free fatty acids, HDLc, LDLc and VLDL-cholesterol) in diabetic animals[14]. All the lipid parameters except HDLc were significantly increased in streptozotocin induced diabetic animals as compared to control animals. However, oral administration of *Tephrosia purpurea* leaf extract to diabetic animals brought back all the values to near normal range.

3.3. Sesbania grandiflora (S. grandiflora)

S. grandiflora leaves aqueous extract at a dose of 200 μg/kg (*p.o.*) to the triton induced hyperlipidemic rats showed a significant decrease in the levels of serum cholesterol, phospholipid, TG, LDL, VLDL and significant increase in the level of serum HDL. Aqueous extract of leaves of *S. grandiflora* was investigated for its hypolipidemic activity on triton induced hyperlipidemic profile. Aqueous extract fraction decreased serum level of TC by 69.72%. On the other hand, aqueous extract of *S. grandiflora* increased the serum HDL level by 24.11%. The reduction of LDL level by aqueous extract was 30.31%[15].

3.4. Pterocarpus marsupium

This study on *Pterocarpus marsupium* Roxb. described that serum lipid levels in rats with hyperlipidaemia induced by diet as well as by triton were determined after oral administration of ethyl acetate extract of hearwood and its flavonoid constituents, marsupsin, pterosupin and liquiritigenin. Administration of ethyl acetate extract of hearwood for 14 consecutive days produced a significant reduction of serum TG, TC, LDL and VLDL-cholesterol levels without any significant effect on the level of HDLc. Liquiritigenin and pterosupin were able to produce a significant fall in serum cholesterol, LDLc and atherogenic index. Pterosupin was additionally effective in lowering serum triglycerides[16].

3.5. G. max

G. max is the scienific name of soybean. Soy protein with isoflavones intact was asociated with significant decreases in serum TC (by 0.22 mmol/L, or 3.77%), LDLc (by 0.21 mmol/L, or 5.25%), and triacylglycerol (by 0.10 mmol/L, or 7.27%) and significant increases in serum HDLc (by 0.04 mmol/L, or 3.03%). The reductions in total and LDLc were larger in men than women. Studies with intakes >80 mg showed better effects on the lipid profile. The strongest lowering effects of soy protein containing isolflavones on TC, LDLc, and triacylglycerol occurred within the short inital period of intervention, whereas improvements in HDLc were only observed in studies of >12 week duration. The lipid-lowering activity of isoflavones in soy protein related to the level, duration of intake, sex and inItital serum lipid concentrations of the subjects[17]. Choi *et al*. showed a decrease in body weight and adipose tissue after soybean administration[18]. They also recorded that plasma lipid concentrations, hepatic fatty acid synthase and glucose-6-phosphate dehydrogenase activities were significantly lowered following soybean administartion in high-fat treated C57BL/6N mice.

4. Amaranthaceae

The Amaranthaceae, the amaranth family, represent the most species-rich lineage within the flowering plant order of Caryophyllales. Including the goosefoot family (Chenopodiaceae), the extended family contains approximately 180 genera and 2 500 species. This is a widespread and cosmopolitan family from the tropics to cool temperate regions. The Amaranthaceae (sensu stricto) are predominantly tropical, whereas the former Chenopodiaceae have their centers of diversity in dry temperate and warm temperate areas[19,20]. Many of the species are halophytes, tolerating salty soils, or grow in dry steppes or semideserts. Most of these species are annual or perennial herbs or subshrubs, some are shrubs; very few species are vines or trees. Some species are succulent. Many species have stems with thickened nodes. The wood of the perennial stem has a typical "anomalous" secondary growth, only in subfamily Polycnemoideae there is normal secondary growth. The flowers are solitary or aggregated in cymes, spikes, or panicles and typically perfect (bisexual) and actinomorphic[21,22]. *Amaranthus spinosus* (*A. spinosus*) and *Achyranthes aspera* (*A. aspera*) species were chosen in this review due to their high antihyperlipidemic activitities and wide distribution of the two plants in the communitities under investigation.

4.1. A. spinosus

Balakrishnan and Panhare investigated the methanol extract of *A. spinosus* which was administered daily at single doses of 250 and 500 mg/kg, *p.o.* to diabetes-induced rats for a period of 15 d[23]. The serum lipid profiles [TC, TG, phospholipids (LDL, VLDL and HDL)] were determined. The activities were also compared to the effect produced by a standard anti diabetic agent, glibenclamide. The extract-

treated rats had significantly decreased TC, TG, LDL and VLDL cholesterol, and significantly increased HDLc.

4.2. A. aspera

The alcoholic extract of *A. aspera* at 100 mg/kg body weight dose lowered serum cholesterol (TC), phospholipid, TG and total lipid levels by 60%, 51%, 33% and 53%, respectively in triton induced hyperlipidaemic rats. The chronic administration of this drug at the same doses to normal rats for 30 d lowered serum TC, phospholipid, TG and total lipid by 56%, 62%, 68% and 67%, respectively followed by significant reduction in the levels of hepatic lipids. The faecal excretion of cholic acid and deoxycholic acid increased by 24% and 40%, respectively. The possible mechanism of action of cholesterol lowering activity of *A. aspera* may be due to rapid excretion of bile acids causing low absorption of cholesterol[24]. Moreovere, *A. aspera* decreased LDL and VLDL while increased HDL in sesame oil fed rats[25].

5. Apiaceae

The Apiaceae (or Umbelliferae), commonly known as carrot or parsley family, is a group of mostly aromatic plants with hollow stems. The family is large, with more than 3 700 species spread across 434 genera, and it is the sixteenth largest family of flowering plants[26,27]. Most species belonging to Apiaceae are annual, biennial or perennial herbs (frequently with the leaves aggregated toward the base), though a minority are shrubs or trees. Their leaves are of variable size and alternately arranged, or alternate with the upper leaves becoming nearly opposite. In some taxa the texture is leathery, fleshy, or even rigid, but always with stomata. There are petiolate or perfoliate and more or less sheathing. The blade usually dissected and pinnatifid, but entire in some genera. Most commonly crushing leaves emits a marked smell, aromatic to foetid, but absent in some members. The flowers are nearly always aggregated in terminal umbels, simple or compound, often umbelliform cymes, rarely in heads. The fruits are non-fleshy schizocarp of two mericarps, each with a single seed; they separate at maturity and are dispersed by wind. Some fruit segments like those in *Daucus* spp. are covered in bristles and spread via external transport. The seeds have an oily endosperm and generally contain large quantities of fatty oils[28-31], with the fatty acid petroselinic acid occurring universally throughout the family while rarely being found outside of the Apiaceae. *Apium graveolens* (*A. graveolens*) and *Ammi majus* (*A. majus*) plants were chosen due to their antihyperlidemic activities and the abundance of both in the two communitities under investigation.

5.1. A. graveolens

Tsi *et al*. studied the antihyperlipidemic property of aquous extract of celery[32], *A. graveolens* Linn. (Badi Ajmod) in rats. A significant reduction was reported by them in the serum TC, LDLc and TG concentrations in rats. However, the concentration of hepatic TG was significatly higher in the celery-treated group than in the control group. Hepatic triacylglycerol lipase activity was found to be significantly lower in the celery-treated rats while the reverse was observed for the hepatic microsomal P450 content. Analysis of an ethereal extract of the aqueous extract of celery by thin layer chromatography with two different solvent systems showed that the extract did not contain 3-n-butylphthalide, a unique compound in celery that has previously been reported to have lipid lowering action. Their study indicates that other active principle(s) could be responsible for the observed effects of aqueous celery extract on serum and hepatic levels. Furthermore, ethanolic extract of *A. graveolens* seeds inhibited the TC, TG, LDL level, and significantly increased HDL level and this effect is dose dependant in olive oil induced hyperlipidemic rats[33].

5.2. A. majus

The effect of two dose levels (50 and 100 mg/kg body weight) of the *A. majus* Linn. total ethanolic extract on the serum levels of cholesterol, TG, HDL, and LDL in induced hyperlipidemic rats was comparable with the drug atorvastatin (1 mg/kg body weight). It clearly revealed that there was a significant decrease in the levels of cholesterol, TG and LDL. On the other hand, the level of HDL concentrations was found to be elevated after extract administration. These results were dose dependant for the alcoholic extract. Ethanolic extract in a dose of 100 mg/kg body weight exhibited a greater increase in the HDL than that of 50 mg/kg body weight after two months of administration. Administration of 100 mg/kg body weight of the extract showed better improvement for HDL value, which is considered a beneficiary effect in the treatment of dyslipidemia condition[34].

6. Zingiberaceae

Zingiberaceae, or the ginger family, is a family of flowering plants consisting of aromatic perennial herbs with creeping horizontal or tuberous rhizomes, comprising about 52 genera and more than 1 300 species, distributed throughout tropical Africa, Asia, and the Americas. Many species are important ornamental plants, spices, or medicinal plants[35]. Large herbaceous plants with distichous leaves with basal sheaths overlap to form a pseudostem. The plants are either self-supporting or epiphytic. Flowers are hermaphroditic, usually strongly zygomorphic, in determinate cymose inflorescences, and subtended by conspicuous, spirally arranged bracts. The perianth is composed of two whorls, a fused tubular calyx, and a tubular corolla with one lobe larger than the other two. Flowers typically have two of their stamenoids (sterile stamens) fused to form a petaloid lip, and have only

one fertile stamen. The ovary is inferior and topped by two nectaries, the stigma is funnel-shaped[36,37]. *Zingiber officinale* (*Z. officinale*) medicinal plant was chosen in this review due to antihyperlipidemic activity and its distribution in the two communities under investigation.

The lipid lowering and antioxidant potential of ethanolic extract of ginger, *Z. officinale* was evaluated in streptozotocin-induced diabetes in rats by Bhandari *et al*[38]. Ethanolic extract of ginger (200 mg/kg) fed orally for 20 d produced significant antihyperglycaemic effect in diabetic rats. Further, the extract treatment also lower serum TC, TG and increased the HDLc levels when compared with pathogenic diabetic rats. Streptozotocin treatment also induced a statistically significant increase in liver and pancrease lipid peroxide levels as compared to normal health control rats. Ginger extract treatment lower the liver and pancrease thiobarbituric acid reactive substances (TBARS) values as compared to pathogenic diabetic rats. The results of test drug were comparable to gliclazide (25 mg/kg body weight, orally), a standard antihyperglycaemic agent. The results indicate that ethanolic extract of ginger can protect the tissues from lipid peroxidation. The extract also exhibit significant lipid lowering activity in diabetic rats. This was the first pilot study to assess the potential of *Z. officinale* in diabetic dyslipidaemia. In addition, Al-Noory *et al*. revealed that *Z. officinale* ginger extract induced a decrease in the levels of TC and LDL[39]. A reduction in TG, and a clear increase in HDL were also recorded in the extract-treated groups.

7. Combretaceae

Combretaceae is a family of flowering plants in the order Myrtales. The family includes about 600 species of trees, shrubs, and lianas in 18 genera. The family includes the leadwood tree and *Combretum imberbe*[40]. Three genera, *Conocarpus*, *Laguncularia* and *Lumnitzera*, grow in mangrove habitats (mangals). Combretaceae are widespread in the subtropics and tropics[40]. From this family *Terminalia arjuna* (*T. arjuna*) medicinal plant was chosen for its higher antihyperlipidemic activity.

The hypocholesterolemic effects of *T. arjuna* was evaluated compared with a known antioxidant, vitamin E. Rsearchers performed a randomized controlled trail with 105 successive patients with coronary heart disease presenting to their centre recruited, and using a Latin-square design divied them into 3 groups of 35 each. The groups were matched for age, lifestyle and dietary variables, clinical diagnosis and drug treatment status. None of the patients was on lipid-lowering drug. Supplemental vitamins were stopped for one month before study began and American Heart Association step II dietary advice was given to all. At baseline, TC, TG, HDLc and LDLc, and lipid peroxide estimated as TBARS were determined. Group I receiced placebo capsules; Group II vitamin E capsules (400 units/day) and Group III received finely pulverized *T. arjuna* powder (500 mg) in capsules daily. Lipids and lipid peroxides levels were determined at 30 d follow-up. Response rate in various groups varied from 86% to 91%. No significant changes in TC, HDLc, LDLc and TG levels were seen in Groups I and II. In Group III there was a significant decrease in TC and LDLc. Lipid peroxide levels decreased significantly in both the treatment groups. This decrease was more in vitamin E group as compared to *T. arjuna* group. Thus, one may conclude that, *T. arjuna* powder has significant antioxidant action that is comparable to vitamin E. In addition, it also has a significant hypocholesterolaemic effect[41].

8. Euphorbiaceae

Euphorbiaceae, the spurge family is a large family of flowering plants with 300 genera and around 7500 species. Most are herbs, but some, especially in the tropics, are also shrubs or trees. Some are succulent and resemble cacti. This family occurs mainly in the tropics, with the majority of the species in the Indo-Malayan region and tropical America. There is a large variety in tropical Africa, but it is not as abundant or varied as in these two other tropical regions[42]. However, *Euphorbia* also has many species in non-tropical areas such as the Mediterranean Basin, the Middle East, South Africa, and Southern USA. The leaves are alternate, seldom opposite, with stipules. The family contains a large variety of phytotoxins (toxic substances produced by plants), mainly diterpene esters, alkaloids, glycosides, and ricin-type toxins. A milky sap or latex is a characteristic of the subfamilies Euphorbioideae and Crotonoideae[43]. *Phyllanthus niruri* (*P. niruri*) was chosen for reviw due to its higher antihyperlipidemic activity and its distribution in the two communitities under investigation.

The lipid lowering activity of *P. niruri* has been studied by Khanna *et al*. in triton and cholesterol fed hyperlipidaemic rats[44]. Serum lipids were lowered by *P. niruri* extract (250 mg/kg body weight) orally fed to the triton WR-1339 induced hyperlipidaemic rats. Chronic feeding of this drug (100 mg/kg body weight) in animals stimultaneously fed with cholesterol (25 mg/kg body weight) for 30 d caused lowering of the lipids and apoprotein levels of VLDL and LDL in experimental animals. The antilipidemic activity of this drug is mediated through inhibition of hepatic cholesterol biosynthesis, increased faecal bile acids excretion and enhanced plasma lecithin: cholesterol acyltransferase activity. Also, the leaf and seed aqueous extract of *Phyllanthus amarus* decreased total glycerides, TC, LDLc, and atherogenic indices in rats[45], while the treatment with *Phyllanthus emblica* extract significantly decreased the lipid profile in the patients with type 2 diabetes mellitus[46].

9. Arecaceae

Arecaceae or Palmae (also known by the name Palmaceae, or by the common name palm tree), is a family of flowering

plants, the only family in the monocot order Arecales. It contains 202 genera with around 2 600 species currently known, most of which are restricted to tropical, subtropical, and warm temperate climates. Most palms are distinguished by their large, compound, evergreen leaves arranged at the top of an unbranched stem. However, many palms are exceptions, as palms in fact exhibit an enormous diversity in physical characteristics. As well as being morphologically diverse, palms also inhabit nearly every type of habitat within their range, from rainforests to deserts. Whether as shrubs, trees, or vines, palms have two methods of growth: solitary or clusters. The common representation is that of a solitary shoot ending in a crown of leaves[47].

This monopodial behavior may be exhibited by prostrate, trunkless, and trunk-forming members. Some common palms restricted to solitary growth include *Washingtonia* and *Roystonea*. Palms may instead grow in sparse to dense clusters. The trunk will develop an axillary bud at a leaf node, usually near the base, from which a new shoot emerges. The new shoot, in turn, produces an axillary bud and a clustering habit results. Exclusively sympodial genera include many of the rattans, *Guihaia* and *Rhapis*. Several palm genera have both solitary and clustering members. Palms which are usually solitary may grow in clusters, and vice versa. These aberrations suggest the habit operates on a single gene[48]. The Arecaceae are notable among monocots for their height and the size of their seeds, leaves, and inflorescences. *Ceroxylon quindiuense*, Colombia's national tree, is the tallest monocot in the world, reaching heights of 60 m[49]. The Coco de Mer (*Lodoicea maldivica*) has the largest seeds of any plant, 40-50 cm in diameter and weighing 15-30 kg each. Raffia palms (*Raphia* spp.) have the largest leaves of any plant, up to 25 m long and 3 m wide. The *Corypha* species have the largest inflorescence of any plant, up to 7.5 m tall and containing millions of small flowers. *Calamus* stems can reach 200 m in length[50]. *Cocos nucifera* was chosen for this review due to its high antihyperlipidemic activity and wide distribution in the two communitites under investigation.

Cocos nucifera is the scientific name of coconut. A study was conducted by Nevin and Rajmohan to investigate the effect of consumption of virgin coconut oil (VCO) on various lipid parameters in comparison with copra oil[51]. In addition, the preventive effect of polyphenol fraction from test oils on copper induced oxidation of LDL and carbonyl formation was also studied. After 45 d of oil feeding to Sprague-Dawley rats, several lipid parameters and lipoprotein levels were determined. Polyphenol fraction was isolated from the oils and its effect on *in vitro* LDL oxidation was assessed. Thus, it was found that VCO obtained by wet process has a beneficial effect in lowering lipid components compared to copra oil. It reduced TC, TG, phospholipids, LDLc and VLDL cholesterol levels and increased HDL cholesterol in serum and tissues. The polyphenol fraction of VCO was also found to be capable of preventing in vitro LDL oxidation with reduced carbonyl formation. The results demonstrated the potential beneficiary effect of VCO in lowering lipid levels in serum and tissues as well as LDL oxidation by physiological oxidants. This property of VCO may be attributed to the biologically active polyphenol components in the oil.

10. Linaceae

The Linaceae is a family of flowering plants. The family is cosmopolitan, and includes approximately 250 species. There are 14 genera, classified into two subfamilies: Linoideae and Hugonioideae (often recognized as a distinct family, the Hugoniaceae). Leaves of Linaceae are always simple; arrangement varies from alternate (most species) to opposite (in *Sclerolinon* and some *Linum*) or whorled (in some *Hesperolinon* and *Linum*). The hermaphroditic, actinimorphic flowers are pentameric, or very rarely tetrameric (*e.g. Radiola linoides*, *Linum keniense*)[52].

In Linoideae, the largest genus is *Linum*, the flaxes, with 180-200 species including the cultivated flax, *Linum usitatissimum* (*L. usitatissimum*). Members of Linoideae include herbaceous annuals and perennials as well as woody subshrubs, shrubs, and small trees (*Tirpitzia*) inhabiting temperate and tropical latitudes of Eurasia, Africa, Australia, and the Americas. The largest genus of Hugonioideae is *Hugonia* (~40 spp.); Hugonioideae are woody vines, shrubs, and trees and are almost entirely tropical in distribution. In addition to their growth habits and geographic distributions, Linoideae and Hugonioideae can be differentiated by the number of fertile stamens (5 in Linoideae, 10 in Hugonioideae) and fruit type (capsules in Linoideae, fleshy drupe-like fruits in Hugonioideae)[53]. *Linum usitatissimum* was choosen in this review due to its wide distribution in the two communitites under investigation and higher antihyperlipidemic acitivity.

L. usitatissimum is the scientific name of flaxseed. Flour derived from flaxseed or linseed is popular for use in bread and bakery products; it provides a nutty flavour and also increases the nutritional and health benefits of the final product. Flaxseed consumption may lower both TC and LDLc concentrations because of its low saturated fat content, high polyunsaturated fat and phytosterol content, and mucilage content[54,55]. When 15 patients with elevated blood cholesterol concentrations (>6.2 mmol/L, 240 mg/dL) consumed 15 g ground flaxseed and 3 slices of flaxseed-containing bread daily for 3 months, their TC and LDLc concentrations decreased by 10% and platelet aggregation decreased substantially, while their HDLc and triacylglycerol concentrations did not change significantly[56].

11. Ginkgoaceae

The Ginkgoaceae is a family of gymnosperms which appeared during the Mesozoic Era, of which the only extant representative is *Ginkgo biloba* Linn. (*G. biloba*), which is for this reason sometimes regarded as a living fossil. Formerly, however, there were several other genera, and forests of

ginkgo existed. Because leaves can take such diverse forms within a single species, these are a poor measure of diversity, but wood structure points to the existence of diverse ginkgo forests in ancient times[57]. *G. biloba* was choosen from this family due to its antihyperlipidemic acitivity and its distibution in the two communities under investigation.

It has been found that maidenhair tree (*G. biloba*) ethanol extract (761 mg/kg body weight) inhibits beta amyloid production by lowering the free cholesterol in animal models[58]. Also, *G. biloba* extract decreased lipid profile and lipid peroxidation in streptozotocin-induced diabetes in rats[59].

12. Liliaceae

The Liliaceae, or the lily family, is a family of monocotyledons in the order Liliales. Plants in this family have linear leaves, mostly with parallel veins but several have net venation (*e.g.* cardiocrinum, clintonia, medeola, prosartes, scoliopus, tricyrtis), and flower arranged in threes. Several have bulbs, while others have rhizomes. Shade-dwelling genera usually have broad, net-veined leaves, fleshy fruits with animal-dispersed seeds, rhizomes, and small, inconspicuous flowers. Genera native to sunny habitats usually have narrow, parallel-veined leaves, capsular fruits with wind-dispersed seeds, bulbs, and large, visually conspicuous flowers[60-62]. *Allium sativum* was chosen from this family due to the huge amount of publication related to its antihyperlipidemic activity and also its high distibution in the two communities under investigation.

Allium sativum is the scientific name of garlic. Epidemiologic studies have suggested that fresh garlic has lipid-lowering activity. Long-term dietary supplementation of fresh garlic may exert a lipid-lowering effect partly through reducing intestinal MTP gene expression, thus suppressing the assembly and secretion of chylomicrons from intestine to the blood circulation[63]. Another short-term supplementation of garlic in human subjects has demonstrated an increased resistance of LDL to oxidation. Theses data suggest that suppressed LDL oxidation may be one of the powerful mechanisms accounting for the antiatherosclerotic properties of garlic[64].

13. Burseraceae

The Burseraceae are distributed throughout the world and primarily in the tropics, especially Malaysia, Africa, Meso- and South America. Burseraceae is a moderate-sized family of 17-18 genera and about 540 species of flowering plants. The actual numbers differ according to the time period, in which a given source is written describing this family. The Burseraceae members are characterized by the non-allergenic resin they produce in virtually all plant tissue and the distinctive smooth, yet flaking aromatic bark[65,66]. The origins of the family can be traced to the Paleocene (~65 million years ago) when *Beiselia mexicana* first diverged in Mexico. The subsequent divergences in the family lineage and migration of the species in the Eocene (~53 million years ago) from North America have led to the current distributions of the species that are primarily associated with the tropics areas[67,68]. *Commipora mukul* Engl. (*C. mukul*) were chosen in this review due to its wide distribution in the two communities and their antihyperlipidemic activities.

The effects of the adminstration of 50 mg of *C. mukul* or pacebo capsules twice daily for 24 weeks were compared by Singh *et al*. as adjuncts to a fruit- and vegetable-enriched prudent diet in the management of 61 pateints with hypercholesterolaemia in a randomized, double blind fashion[69]. Guggulipid decreased the TC level by 11.7%, the LDLc by 12.5%, TG by 12.0%, and the TC/HDLc ratio by 11.1% from the post diet levels, whereas the levels were unchanged in the placebo group. The HDLc level showed no changes in the two groups. The lipid peroxides, indicating oxidative stress, declined 33.3% in the guggulipid group without any decrease in the placebo group. The compliance of patients was greater than 96%. The combined effect of diet and gugglipid at 36 weeks was as high as the reported lipid-lowering effect of modern drugs. Moreovere, *C. mukul* ethyl acetate extract possessed significantly higher antihyperlipidemic activity[70].

14. Ranunculaceae

Ranunculaceae (buttercup or crowfoot family; Latin *Ranunculus* "little frog", from *Rana* "frog") is a family of about 1 700 species of flowering plants in about 60 genera, distributed worldwide. The largest genera are *Ranunculus* (600 species), *Delphinium* (365 species), *Thalictrum* (330 species), *Clematis* (325 species), and *Aconitum* (300 species). Ranunculaceae are mostly herbaceous plants. Leaves are usually divided or lobed, but are heart-shaped or narrow and undivided in some species of *Ranunculus*, and usually arise from the base of the plant, or alternately up the stem, but in *Clematis* they are opposite[71]. Perennial species form a small rhizomes or tubers which develop new roots each year. Flowers may be solitary, but are frequently found aggregated in cymes, panicles or spikes. Many species have no true petals, and the flower is formed by a brightly colored calyx. There are usually five sepals, although there are many which come in a wide variety of shapes. *Ranunculus* (buttercups) is the only genus in this family with a true calyx and petals. There are many stamens surrounding many fused carpels[54]. *Nigella sativa* Linn. is the most well known from this family, and together with its high antihyperlipidemic activity, also its wide distribution in the two coummunities investigation makes it the choice for this review.

Petroleum ether extract of *Nigella sativa* has

hypolipidaemic activity; data showed that *in vivo* treatment with the petroleum ether extract exerts an insulin-sensitizing action by enhancing the activity of the two major intracellular signal transduction pathways of the hormone's receptor[72].

15. Plantaginaceae

The Plantaginaceae are the most diverse, cosmopolitan family, occurring mostly in temperate zones. It consists of herbs, shrubs and also a few aquatic plants with roots (such as the genus *Callitriche*). Being so diverse, the circumscription of this family is difficult to establish. The leaves are spiral to opposite and simple to compound. Unusual in Lamiales is the absence of vertical partitions in the heads of the glandular hairs. The structure and form of the flowers can be very variable. Some genera are 4-merous (*i.e.* with 4 sepals and 4 petals), such as *Aragoa* (but this one has 5 sepals); others are 5-8-merous, such as *Sibthorpia*. The flowers of most genera are polysymmetric. The corolla is often two-lipped. In some taxa, the androecium is formed before the corolla. The fruit is a capsule that dehisces through the partitions between the cells. In *Veronica* this partition is in the length; in species of Antirrhineae the dehiscence releases the pollen through the pores at the tip of the anther; or it may come about through a transverse circular line around the capsule[73,74]. *Plantago psyllium* Linn. was chosen due to its antihyperlipidemic activity and its distribution in the two communities under investigation.

Hypocholesterolemic patients have benefited from the use of black psyllium (*Plantago psyllium*), a rich source of soluble fibre (10%-12% mucilage). When 5 g psyllium was given twice a day for 4 months to subjects with blood cholesterol concentration >5.7 mmol/L (220 mg/dL), their TC and LDLc concentrations dropped to an average of 0.26-0.39 mmol/L and 0.28-0.34 mmol/L, respectively (10-15 mg/dL and 11-13 mg/dL, respectively). Theses changes tend to be be greater in subjects consuming high-fat diets[75].

16. Lamiaceae

Lamiaceae or Labiatae, is a family of flowering plants. The family has a cosmopolitan distribution. The enlarged Lamiaceae contains about 236 genera and 6 900 to 7 200 species. The largest genera are *Salvia* (900), *Scutellaria* (360), *Stachys* (300), *Plectranthus* (300), *Hyptis* (280), *Teucrium* (250), *Vitex* (250), *Thymus* (220), and *Nepeta* (200) [76]. The plants are frequently aromatic in all parts and include many widely used culinary herbs, such as basil, mint, rosemary, sage, savory, marjoram, oregano, thyme, lavender, and perilla. Some are shrubs, trees, such as teak, or rarely, vines. Many members of the family are widely cultivated, owing not only to their aromatic qualities but also their ease of cultivation: these plants are among the easiest plants to propagate by stem cuttings. The flowers are bilaterally symmetrical with 5 united petals, 5 united sepals. They are usually bisexual and verticillastrate (a flower cluster that looks like a whorl of flowers but actually consists of two crowded clusters)[77]. *Ocimum sanctum* Linn. (*O. sanctum*) was chosen for this review due to its antihyperlipidemic activity and its distribution in the two communities under investigation.

Administration of *O. sanctum* leaves (1 g and 2 g) in 100 g of diet for four weeks brought about significant changes in the lipid profile of normal albino rabbits. This resulted in significant lowering in serum TC, TG, phospholipids, LDLc levels and increase in the HDLc and total faecal sterol contents[78]. *O. sanctum* extract decreased the high serum lipid profile and expressed antiartherogenic and cardioprotective actions against hyperlipidemia. The anti-hyperlipidemic action of *O. sanctum* extract mainly resulted from the suppression of liver lipid synthesis[79].

17. Myrsinaceae

Myrsinaceae, or the Myrsine family, is a rather large family from the order Ericales. It consists of 35 genera and about 1 000 species. It is a widespread family belonging to temperate to tropical climates. They are mostly mesophytic trees and shrubs; a few are lianas or sub-herbaceous. The leathery, evergreen leaves are simple and alternate, with smooth margins and without stipules. They are often dotted with glands and resinous cavities. The latter may take the form of secretory lines. The plants are mostly monoecious, but a few are dioecious. The small flowers are arranged in racemose terminal clusters, or in the leaf axils. The flowers are 4-merous or 5-merous, *i.e.* they have 4 or 5 sepals and petals. The floral envelope (perianth) has a distinct calyx and corolla. The calyx is regular and polysepalous. The non-fleshy petals of the corolla are more or less united, closely overlapping. There are 4 or 5 stamens, usually isomerous with the perianth. The carpel has one style and one stigma, with the ovary unilocular, superior or semi-inferior[80-82]. *Embelia ribes* (*E. ribes*) was chosen from this family due to its antihyperlipidemic activity and its wide distribution in the two communities under investigation.

E. ribes commanly known as vidang, is used for its anthelmintic activity. Antihyperglycaemic activity of decoction of *E. ribes* in glucose-induced hyperglycemic albino rabbits has also been reported, and the lipid-lowering and antioxidant activities potentially related to ethanolic extract of *E. ribes* in streptozotocin (40 mg/kg body weight, *i.v.*, single injection)-induced diabetes in rats were reported by Bhandari *et al*[83]. Twenty days of oral feeding the extract (200 mg/kg body weight) to diabetic rats resulted in significant decrease in blood glucose, serum TC, and TG but increase in HDLc levels when compared to pathogenic diabetic rats. The extract also lowered the liver and pancreas TBARS values when compared to TBARS values of liver and pancrease of pathogenic diabetic rats.

These results were compared to gliclazide (25 mg/kg body weight, orally), a standard antihyperglycaemic agent. The study provides biochemical evidence of potential of *E. ribes* in diabetic dyslipidaemia. Also, administration of the aqueous extract of *E. ribes* (100 and 200 mg/kg, *p.o.*) for 30 d, to hyperhomocysteinemic rats, significantly decreased the levels of TC, TG, LDLc and VLDL-cholesterol and increased the HDLc levels in serum[84]. Furthermore, the serum levels of apolipoprotein B, TC, TG, LDLc, HDLc were decreased after treatment with embelin from *E. ribes* in high-fat diet-induced obesity in rats[85].

18. Papaveraceae

Papaveraceae is widely distributed in Western Asia, Europe, North America and the Mediterranean. It includes 44 genera and 760 species; most of them are herbaceous plants, but the family includes some woody shrubs and a genus of small tropical trees. Most species are found in the Northern Hemisphere. All species in the family have bisexual, regular, dish-shaped flowers with one superior pistil and many stamens. The buds and flowers are usually large and often nodding. They have 2 or 3 many-seeded separate sepals and 4 to 12 or more separate, often crinkled petals. The fruit is a spherical or linear capsule. The leaves are usually deeply cut or divided into leaflets, and the sap is coloured[86]. *Chelidonium majus* (*C. majus*) was chosen from this family due to its antihyperlipidemic activity and its wide distribution in the two communities under investigation.

C. majus (4 mg/kg) reduces LDL, TC, TG levels while increases HDL level[87]. This activity related to its chelidonine alkaloid ingredient which inhibit cholesterol biosynthesis, so total plasma lipids and cholesterol in rats were reduced after oral administration of *C. majus* methol extract and this effect was found to be dose dependant[88].

19. Guttiferae

The Clusiaceae or Guttiferae Juss. is a family of plants including about 37 genera and 1 610 species of trees and shrubs, often with milky sap and fruits or capsules for seeds. It is primarily tropical. It shows a large amount of variation in plant morphology (for example, 3 to 10 petals, fused or unfused petals, and many other traits)[89]. *Garcinia cambogia* Linn. (*G. cambogia*) was chosen for this review due to its wide distribution in the two communities and its higher antihyperlipidemic activity.

Flavonoids from *G. cambogia* exerted hypolipidaemic activity in rats. Lipid lowering activity was reported maximum in rats administrated with flavonoids (10 mg/kg body weight) from *G. cambogia*. A dose response study revealed biphasic activity. Higher doses were less effective in reducing lipid levels in serum and tissues, although devoid of toxic effects[90].

20. Conclusions

The antihyperlipidaemic activity of plants plays an important role in the reduction of CVD; where this is the top disease that causes mortality all over the world. Thus we need to focus on lipid-lowering activity of herbs and should adopt a new approach to the protective role of these medicinal plants which depends on the reduction of LDL, so we can come out with more concrete solution on these plant lipid-lowering activity for phytomedicine research and drug development for such a disease. This review is an overview of the antihyperlipidemic activities in traditional medicinal plants in Kadazan and Dusun communities in Sabah, Malaysia as potential use for the development of new drugs used in the protection against dyslipidemia or atherosclerosis.

Conflict of interest statement

I declare that I have no conflict of interest.

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Comments

Background

CVD is the top disease that causes mortality all over the world. The lipid lowering activity of herbs plays an important role in the reduction of CVD; where there is a relation between LDL reduction and decreased CVD mortality. Consequently, Medicinal plant lipid-lowering activity for phyto-medicine research and drug development for such a disease are now focused all over the world. On the other hand, Sabah has a landmass of approximately 7.4 million hectares and a total forested area equal to 4.7 million hectares; in addition, the climate is marine equatorial and rainy season. So, Sabah state is rich in plant biodiversity which can be useful for medical and pharmaceutical researches.

Research frontiers

This review discusses in details the diversity of families occurr in Kadazan and Dusun communities in Sabah, Malaysia. And also the author concentrates on the antihyperlipidemic effects of the different medicinal plants belonging to these families under investigation. This article is a guide to new medications for atherosclerosis patients

especially in this area.

Related reports

The study stated in details the unique and different families in these two communities depending on the unique climate in this area, which is rainy equatorial season. All these factors make a diversity of medicinal plants in this area, so this study is very interesting to medical field in both phyto-protection and new medications for CVD.

Innovations and breakthroughs

This manuscript covers in details the lipid lowering activity of different medicinal plants in Kadazan and Dusun communities in Sabah, Malaysia. Furthermore, the author describes in details the each family found in these two communities. The article is a new research in these communities and is a good support for medical application.

Applications

From the literature survey it has been found that lowering lipid profile is greatly associated with decreasing CVD patients. The antihyperlipidemia effects of these medical plants under investigation are important in developing new medications. This study is a well documented study that satisfy carefully the medicinal plants' hyoplipidemic effects in these communities under concentration.

Peer review

This is a well described and satisfied study in which the author reported the lipid lowering activities of the medicinal plants found in Dusun communities in Sabah, Malaysia. This article is capable to be useful to both phyto-protection and new medications develop in CVD.

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