A REVIEW ON HERBS OF THE ZINGIBERACEAE FAMILY WITH BENEFICIAL EFFECTS ON CARDIOVASCULAR DISEASES.

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ABSTRACT
Cardiovascular disease (CVD) is the most common cause of death worldwide and is expected to be more prevalent as the population ages. Obesity, hypertension, hyperlipidemia, diabetes, endothelial dysfunction and oxidative stress are the major pathologies involved in CVDs. Though many synthetic drugs have been developed and are found to be very effective in the treatment of cardiovascular diseases, herbs still continue to be the mainstay in orthodox medicine. Herbs in the Zingiberaceae family finds greater importance in the treatment of CVDs. Family Zingiberaceae consists of the large group of rhizomatous medicinal plants characterised by the presence of volatile oils, oleoresins and terpenoids. The important genera in the family Zingiberaceae - *Alpini, Amomum, Curcuma, Hedychium, Kaempferia, Zingiber* were evaluated for their beneficial effect on cardiovascular diseases. There are still several species which have not explored so far. This family is a treasure trove of plants with a rich potential for use in cardiac disorder.

KEYWORDS: Cardiovascular disease, Zingiberaceae, *Alpini, Amomum, Curcuma, Hedychium, Kaempferia, Zingiber*.

INTRODUCTION
Cardiovascular disease (CVD) is the most common cause of death worldwide and is expected to be more prevalent as the population ages. The underlying pathology is the development of atheromatous vascular plaques, resulting in coronary artery disease (CAD), cerebrovascular disease and the subsequent development of heart failure and cardiac arrhythmias.[1] Obesity, hypertension, hyperlipidemia, diabetes, endothelial dysfunction and oxidative stress are the major pathologies involved in CVDs. Impaired endothelial function followed by inflammation of vessel wall leads to atherosclerotic lesion formation which causes
myocardial infarction and stroke. Heart failure can occur as a consequence of large myocardial infarctions or can be caused by genetic predisposition. Due to the rising age of the population, the incidence of heart failure is further increasing. In its more severe stages, heart failure patients have a life expectancy similar to aggressive cancers.\cite{2}

Though many synthetic drugs have been developed and are found to be very effective in the treatment of cardiovascular diseases, herbs still continue to be the mainstay in orthodox medicine for the treatment of various heart problems. Plants that contain cardiac glycosides are used for the treatment of heart failure and some arrhythmias. In such conditions these herbs increase the strength of heart beat and normalize the rate of beat. Among these, herbs in the Zingiberaceae family finds greater importance in the treatment of CVDs.\cite{3}

Family Zingiberaceae consists of the large group of rhizomatous medicinal plants characterised by the presence of volatile oils, oleoresins and terpenoids. India is one of the richest and diverse regions for Zingiberaceae. There are about 20 genera and more than 200 species of Zingiberaceous plants available in India. Generally, the rhizomes and fruits are aromatic, tonic and stimulant. Some are used as food as they contain starch in large quantities while others yield an astringent and diaphoretic juice. Various plants belonging to the Zingiberaceae family are utilized as ornamentals, medicines or food (vegetables or spices). Rhizome extracts of some members of the medicinal Zingiberales are widely used in dietary intake as well as in the traditional system of medicine. Many terpenoids compounds with varied physiological activities-antimicrobial, antiarthritic, antioxidant, anticancer, antiinflammatory, cardioprotective, anti arrhythmic, antidiabetic, anti-HIV and neuroprotective have been identified in the essential oils of Zingiberaceous plants.\cite{4}

**TAXONOMY**\cite{4}

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
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<tbody>
<tr>
<td>Sub-kingdom</td>
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<td>Division</td>
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<td>Subdivision</td>
<td>Angiospermae</td>
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<tr>
<td>Order</td>
<td>Scitaminales</td>
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<td>Family</td>
<td>Zingiberacea</td>
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The important genera belonging to the family Zingiberaceae with cardioprotective activity are Alpini, Amomum, Curcuma, Hedychium, Kaempferia, Zingiber.\[5\]

<table>
<thead>
<tr>
<th>Genus</th>
<th>Species</th>
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<tbody>
<tr>
<td>Alpini</td>
<td>A. galanga, A. calcarata, A. allughas</td>
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<tr>
<td>Amomum</td>
<td>A. subulatum</td>
</tr>
<tr>
<td>Curcuma</td>
<td>C. amada, C. longa, C. zedoaria, C. aromatic</td>
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<tr>
<td>Kaempferia</td>
<td>K. rotunda, K. galangal</td>
</tr>
<tr>
<td>Zingiber</td>
<td>Z. officinale, Z. zerumbet</td>
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1. **Alpinia galanga**

*Alpinia galanga* Linn, is a perennial herb used in medication, cosmetics and for culinary purpose. The rhizomes have a pungent, hot and spicy taste with aromatic odour. The main chemical constituents of galangal are galangin (3, 5, 7-trihydroxyflavone), a flavonoid with medicinal property. Other flavonoids like kaemferide and alpinin are also present.\[6\] The various cardiovascular effects of *Alpinia galangal* are as follows.

**Hypolipidemic activity**

The hypolipidemic activity of ethanolic extract of *A.galanga* has been reported in rats when 20mg/kg was given for 4 week period. Treatment caused a reduction in serum levels of total cholesterol, triglycerides, low density lipoprotein and also increase in high density lipoprotein levels. The reduction in the levels of lipid levels is considered to be due to a decrease in the intestinal absorption of exogenous cholesterol.\[7\]

**Antihypertensive activity**

Data obtained from the study (Achuthan CR 1997) revealed the antihypertensive effect of extract of *Alpinia zerumbet* (EOAZ) and its main constituent, terpinen-4-ol (Trp-4-ol), in the experimental model of deoxycorticosterone-acetate (DOCA)-salt hypertensive rat. I.V. bolus injections of EOAZ (1-20 mg/kg) or Trp-4-ol (1-10 mg/kg) decreased mean aortic pressure (MAP) in a dose-related manner. These results show that I.V. treatment with either EOAZ or Trp-4-ol decreased the blood pressure in a dose dependent manner in conscious DOCA-salt hypertensive rats and this action is enhanced when compared with uninephrectomized controls. Enhancement could be related mainly to increase in EOAZ-induced vascular smooth muscle relaxation in this hypertensive model.\[8\]
Anti-atherosclerotic activity
An in vitro study was carried out using acetone extract of various parts like leaves, seeds and flowers, pericarp of *Alpinia zerumbet* to evaluate their ability to inhibit atherosclerosis. The seed extract had the strongest activity against tyrosinase, pancreatic lipase (PL), 15-lipoxygenase (15-LO) and LDL oxidation activities. Cholest-4-ene-3, 6-dione, a steroid present in the seed extract seems to be the compound responsible for the anti atherosclerotic activity.[9]

2. *Amomum subulatum*
*Amomum subulatum* is the most used species of the genus Amomum which is generally known as cardamom. It is used mainly used for culinary purpose and as a medicinal herb. *A. subulatum* mainly contains glycosides, cardomonin, flavanone, alpinetin and subulin. Volatile oil in seeds contains cineol, limonene, myrcene and alpha terpinene. The presence of polyphenols and antioxidants are responsible for the cardioprotective effect of amomum.[10]

Hypolipidemic activity
*Amomum subulatum* supplementation has shown to decrease the cholesterol levels in cholesterol fed rabbits. The oral administration of cardamom extract at dose of 150mg/kg and 250mg/kg for 90 days showed a significant reduction in serum lipid levels of LDL, TG, VLDL and increase in HDL when compared with control group. The hypolipidemic effect of *A. subulatum* is due to the increased uptake of cholesterol by the extrahepatic tissue, mainly as VLDL.[10]

Antihypertensive activity
Powdered cardamom has been shown to posses antihypertensive activity. At a dose of 3g, it has shown a decrease in diastolic pressure in hypertensive rats. It enhances fibrinolysis and improves antioxidant status. These effects are thought to be mediated through cholinergic and Calcium ion blocking mechanism.[11]

Cardioprotective effect
A study reported the cardioprotective effect of cardamom against isoprenaline (ISO)-induced myocardial infarction. Rats were treated with extract of cardamom (100 and 200 mg/kg per oral) or normal saline for 30 days with concomitant administration of isoprenaline (85 mg/kg, subcutaneous) on 29th and 30th days, at 24 h interval. Isoprenaline injections to rats caused cardiac dysfunction evidenced by declined arterial pressure indices, heart rate, contractility
and relaxation along with increased preload. All these changes in cardiac and left ventricular function as well as alterations in endogenous antioxidants, lipid peroxidation and myocyte enzymes were ameliorated when the rats were pretreated with cardamom for 30 days. Additionally, the proof of the protective effects were strengthened by improved histopathology and ultrastructural changes, which specifies the salvage of cardiomyocytes from the deleterious effects of Isoprenaline. The findings demonstrate that cardamom significantly protects the myocardium and exerts cardioprotective effects by free radical scavenging and antioxidant activities.[12]

3. Curcuma longa Linn

Turmeric (Curcuma longa Linn) is extensively used as a spice and used in traditional medicine as a remedy for various diseases. Curcumin is the active principle in turmeric. Desmethoxy curcumin and bis-desmethoxycurcumin are two major curcuminoids. Curcumin has antioxidant, anti inflammatory, antiviral, antifungal, hypolipidemic and cardioprotective activity. It is also effective in treating cough, diabetes, hyperlipidemia, hypertension and hepatic disorders.[13]

Hypolipidemic activity

Curcumin is reported to have hypolipidemic effect in cholesterol fed mice. This could be due to an increase in HDL cholesterol, indicating that curcumin acts by mobilizing cholesterol from extra hepatic tissues to the liver where it is catabolised. Curcumin is reported to activate cholesterol 7-α-hydroxylase the rate limiting step in cholesterol catabolism. Due to this, it stimulates the conversion of cholesterol to bile acid, an important pathway in the degradation of cholesterol.[14]

Antihypertensive activity

Data from the in vitro study by Yonggang Yao 2016 reported the antihypertensive effect of curcumin in A10 cell (a rat thoracic aorta cell line). The study showed that curcumin down regulates angiotensin II receptor (AT1 R) expression in A10 cells, thus decreasing AT1R mediated vasoconstriction thereby preventing the development of hypertension in angiotension II induced hypertensive model.[15]

Anti atherosclerotic activity

Antioxidants in turmeric have been shown to prevent the oxidation of LDL cholesterol thereby reducing the risk of atherosclerosis. Many animal studies have shown that curcumin
lowers LDL cholesterol and TG that circulates in blood stream by activating cholesterol 7 alpha hydroxylase. In a recent study of atherosclerosis, curcumin treated mice which were fed with atherogenic diet after four months showed a 20% decrease in blockage of arteries than mice fed without curcumin.[13]

**Cardioprotective activity**

In this study, cardioprotective role of curcumin was evaluated by investigating the preventive role of curcumin against doxorubicin induced myocardial toxicity in rats. The rats were pretreated with curcumin (200mg/kg) orally for 2 weeks and then for two more weeks alternatively with doxorubicin (15mg/kg). Curcumin pretreated rats protected myocardium from toxic effects of doxorubicin as indicated by reduction in elevated levels of biomarkers like LDH, AST, ALT. GSH, SOD and catalase and an increase in levels of MDA in cardiac tissues The cardioprotective effect of curcumin is attributed to its antioxidant property.[16]

4. **Zingiber officinale**

*Zingiber officinale*, a member of Zingiberaceae family, is a popular spice and used as a medicine. The main chemical constituents of ginger rhizomes are essential volatile oils and non essential oil. The volatile oil mainly contains terpenoids, whereas gingerol and shogaols are major non volatile constituents found in fresh and dried rhizomes of ginger which are mainly responsible for the medicinal property. The high content of potassium in ginger protects against muscle weakness, bone fragility, paralysis, blood pressure and damage to heart. Antioxidant principles in the ginger is reported to play an important role in treatment of cardiovascular diseases.[5]

**Hypolipidemic activity**

Patrick Ambrose Teru *et al* (2015) evaluated the antihyperlipidemic effect of crude extract of ginger. Hyperlipidemia was induced by feeding high fat diet for 4 weeks followed by ginger treatment for 2 weeks at different doses (50mg/kg, 100mg/kg, 150mg/kg, 200mg/kg). The consumption of ginger at higher doses showed a marked decrease in LDL, TC, TG, VLDL and increase in HDL level when compared to the untreated group. This shows the antihyperlipidemic effect of ginger.[17]

**Antihypertensive activity**

M Mohan *et al* (2007) investigated the antihypertensive effect of petroleum ether extract of ginger rhizomes in deoxycorticosterone acetate salt induced hypertensive rats.
Deoxycorticosterone acetate (DOCA)- salt (25mg/kg once a week) was administered in uninephrectomised animals for 4 weeks. Treatment with petroleum ether extract of ginger 50mg/kg for 5 weeks showed a lowered blood pressure through a dual inhibitory effect mediated via stimulation of muscarnic receptor and blockade of calcium channels.[18]

**Anti-atherosclerotic activity**

The anti-atherosclerotic effect of ginger has been reported and it is considered to be mediated by inhibition of the LDL oxidation in atherosclerotic rats.[19]

**Cardioprotective activity**

Azza. A Galal et al (2013) studied the cardioprotective effect of ginger against doxorubicin induced cardiac damage in rats. Cardiac damage was induced by the administration of doxorubicin 15mg/kg i.p. for 2 weeks. Along with it one group of rats received vitamin E 100mg/kg which serves as positive control and another group received ginger extract 200mg/kg for 6weeks. The results revealed that doxorubicin administrated rats showed marked ECG alteration and reduction in catalase and increase in lipid peroxidation levels. Ginger and vitamin E treated group of rats showed an improved ECG tracing and decrease in the mortality rate. This reveals the cardioprotective effect of ginger.[20]

5. **Kaempferia galanga**

*Kaempferia galanga* is a plant with potent medicinal activities. The rhizome and root tubers of the plant possess a number of medicinal applications. The rhizomes are used for the treatment of psoriasis, bacterial infections, tumor and it is applied externally for abdominal pain in women and for treatment of rheumatism (Hirschhorn, 1983). The major chemical constituents are ethyl-p-methoxy cinnamate (31.77%), methyl cinnamate (23.23%), carvone (11.13%), eucalyptol (9.59%) and pentadecane (6.41%).[4]

**Hypolipidemic activity**

The rhizomes of *Kaempferia galanga* is widely used in the Ayurvedic medicine. A study evaluated the hypolipidemic action of the ethanolic extract of *Kaempferia galanga* in rats. Oral administration of the extract (20mg/day) effectively lowered the serum and tissue levels of total cholesterol, triglycerides, phospholipids and significantly increased the serum levels of high density lipoproteins (HDL) in the cholesterol fed rats over a period of 4 weeks. The results indicate the hypolipidemic activity of the plant.[7]
CONCLUSION

It is thus evident that Zingiberaceae family possesses beneficial cardioprotective effect. There are still several species which have not explored so far. This family is a treasure trove of plants with a rich potential for use in cardiac disorder.

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