



# Medicinal Plants and their Phytochemical: A Critical Look on the Potential Benefits of Medicinal Plants on Cardiovascular Disease

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## ARTICLE INFO

### Article history:

Received on: October 28, 2023

Revised on: September 05, 2024

Accepted on: September 20, 2024

Published on: October 01, 2024

### Keywords:

Anti-inflammatories

Antioxidants

Cardio-protective properties

Cardiovascular diseases

Medicinal plants

Phytochemicals

## ABSTRACT

Throughout human history, from ancient civilisations to the present day, individuals have sought the healing properties of medicinal plants, commonly referred to as medicinal herbs. These natural botanical resources are used for therapeutic purposes owing to their efficacy, widespread availability in various regions across the globe, and cost-effectiveness. This paper helps to focus on medicinal plants that help treat cardiovascular diseases. Phytochemicals are the key botanical components that allow plants to have secondary metabolites that help protect them from environmental hazards and cardiovascular disease. There are several classifications of phytochemicals, some of which include phenols, flavonoids, nonflavonoids, and alkaloids. The purpose of this research is to identify plant species rich in phytochemicals that may help treat cardiac-related diseases. The plants, seeds and plant extracts mentioned include banana, hawthorn, flaxseed, spinach, arjuna and grapefruit extracts. These plants possess one or more properties of antioxidant, anti-inflammatory, cardioprotective, hypolipidemic, antihepatotoxic, and reduced dietary fat absorption. They have also been found to contain phytochemicals such as flavonoids, phenols, tannins, polyphenols, phenols, and flavonoids, which can be found in a variety of geographical locations across the world.

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## INTRODUCTION

Medicinal plants are diverse types of plants used for therapeutic purposes; many plants have medicinal activities. They are an abundant source of components useful in drug discovery and synthesis (Balunas & Kinghorn, 2005). Medicinal plants also known as medicinal herbs is any plant which, one or more of its organs (stem, bark, leaf, and root) contains compounds that possess therapeutic characteristics or can be used to manufacture drugs. This illustration is helpful in differentiating plants with well documented

therapeutic qualities from plants that are considered medicinal but has not been put to a rigorous scientific study (Sofowora, et al., 2013). Aspirin, Morphine, Physostigmine, Atropine, Artemisinin, Colchicine, Taxol, Tubocurarine, Vincristine Digoxin, Ephedrine, Pilocarpine, Quinine, Quinidine, Reserpine and Vinblastine are drugs derived from plant sources (Khamkar, et al., 2015).

### Properties of Medicinal Plants

Certain biological active compounds are credited with a plant's therapeutic potential. Flavonoids is

#### How to Cite:

Oyewole, O. M., Oke, G. O., Ogunniyi, T. J., Olayiwola, A. O., Dalhatu, A., & Ademikanra, A. F. (2024). Medicinal Plants and their Phytochemical: A Critical Look on the Potential Benefits of Medicinal Plants on Cardiovascular Disease. *Biomedicine and Chemical Sciences*, 3(4), 129–146. <https://doi.org/10.5281/zenodo.15777143>

#### Publisher's Note:

International Research and Publishing Academy (iRAPA) stands neutral with regard to jurisdictional claims in the published maps and institutional affiliations.

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an example which elicits a strong antifungal and antibacterial effect against some human pathogenic fungi and bacteria. Tannins, terpenoids, alkaloids, flavonoids which are secondary metabolites found in medicinal plants play a pivotal role in their therapeutic effectiveness. Flavonoids and tannins have been shown to have antibacterial characteristics that are effective against disease causing bacteria such as *Bacillus cereus*, *Staphylococcus aureus* amongst others (Kumar et al., 2008).

## Phytochemicals

The pharmacological and therapeutic effects are due to secretion of secondary metabolites in the plants which are known as phytochemicals (Dar et al., 2017). Phytochemicals are compounds found in plants and possess biological activity that are of immense importance to humans as food and medicine (Hasler & Blumberg, 1999). In general, phytochemicals provide protection against a wide range of environmental stress such as drought, UV radiation and pathogenic invasion (Gibson, et al., 1998). According to Saxena et al., 2013, phytochemicals are not essential nutrients, but they help treat and prevent some frequent diseases. Phytochemicals are stored in plants organs, for example, the roots, leaves, stems, blossoms, or seeds and are normally bountiful in the external layers of a few plant tissues. Factors such as plant types, processing and cooking technique and environmental conditions affect the number of phytochemicals in different plants (King & Young, 1999).

## Classification of Phytochemicals

Phytochemicals classification is based on its contribution to plant metabolism which may be essential or secondary. Essential parts are comprised of sugars, purines and pyrimidines of nucleic acids, amino acids, chlorophyll and so on. The secondary parts are made up of terpenes, flavonoids, phenolics, alkaloids, ligands, plant steroids, curcumins, saponins, flavonoids and glucosides (Lampe & Messina, 1998).

### Phenolics

The most prevalent and widely spread secondary metabolites in plants are phenolic phytochemicals. Flavonoids, phenolic acids, and polyphenols are examples of dietary phenolics compounds. Phenolics have hydroxyl groups (-OH) that connect to an aromatic hydrocarbon group directly. They are complex chemical compounds discovered in plants (Walton, Mayer and Narbad, 2003). Phenolics have several properties that benefit humans. Flavonoids as a group have been extensively studied (Dai & Mumper, 2010). The purple

colour which is because of anthocyanins presence, the phytoestrogens isoflavones from soy, and the tannins in tea are phenolics compounds. Polyphenols are characterized by the presence of phenol rings (Springob and Kutchan, 2009). The molecular structure of phenolics can be from simple compounds with low molecular-weight and an aromatic ring to complex high molecular weight tannins and polyphenols and their derivatives. Carbon atom count and configuration can be the basis of their classifications. Conjugation to sugars and organic acids are also prevalent. Flavonoids and the non-flavonoids are the two main classes of phenolics compounds (Crozier, et al., 2006).

### Flavonoids

Flavonoids are a group of polyphenolics that have two aromatics rings and fifteen carbon atoms. This structure is characterized by a succession of rings connected by a bridge made up of three carbon atoms. Leaves and fruit's skin have extreme amounts of flavonoid. They participate in processes that protect plants from ultraviolet light and disease, and stimulate nitrogen-fixing nodules (Koes, et al., 1994) The primary category of flavonoids includes anthocyanidins, isoflavones, flavanols, flavan-3-ols, flavones and flavanones (Figure 1). Dihydroflavonols, chalcones, dihydrochalcones, flavan-3,4-diols, coumarins, and aurones are other flavonoid classes (Figure 2.2). Numerous different substituents may be included into the flavonoid structure. The fourth, fifth and seventh carbon atoms often contain hydroxyl groups. Most naturally occurring flavonoids which are often in the form glycosides have sugar moiety as a common property. The solubility of flavonoids in water is increased by the hydroxyl and sugar entity while the lipid solubility is influenced by entities, such as methyl groups and isopentyl units (Crozier, et al., 2006).

Evaluation of the relationship between the intake of flavonoid found in food and cardiovascular disease implies that different flavonoids share an inverse relationship with the likelihood of cardiovascular disease when compared to a significant and low intake. A close relationship is reported for flavanol consumption and cardiovascular disease probability. A 10mg/d increase in flavanol consumption implies a 5% reduction in the possibility of developing cardiovascular disease. According to research, consumption of the six groups of flavonoids—flavanols, anthocyanidins, proanthocyanidins, flavones, flavanones, and flavan-3-ols—has been linked to a significantly lower risk of cardiovascular disease (Wang et al., 2014). In older women, a higher intake of foods high in flavonoids,

such as fruits, red wine, tea, vegetables, and chocolate, is associated with a lower risk of mortality. Flavonoids

may offer benefits to the investigation of cancer and cardiovascular disease (Ivey et al., 2015).

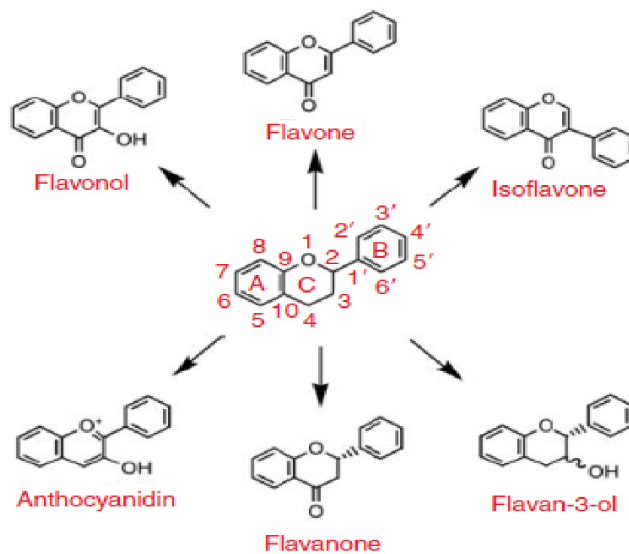


Fig. 1. Major flavonoid structures, adapted from Crozier et al. (2006).

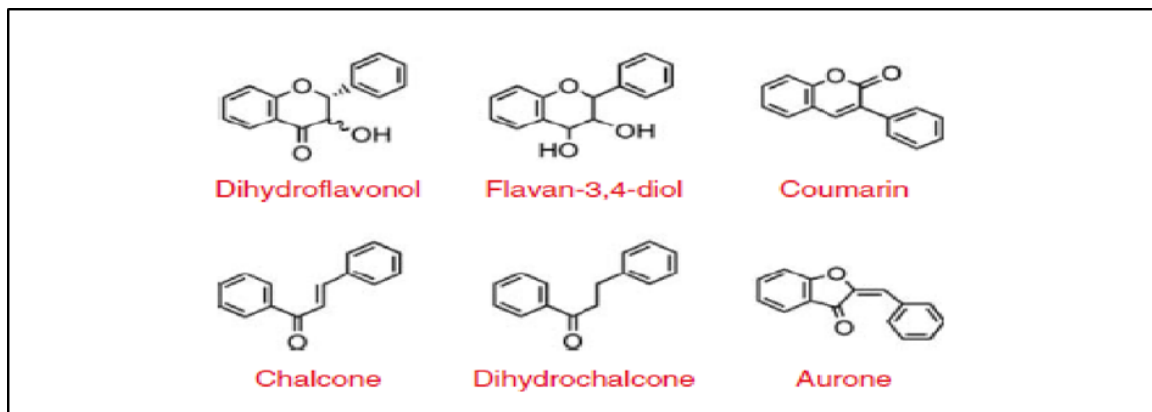


Fig. 2. Minor flavonoid structures

### Flavonols

Apart from fungus and algae, flavonoids, or flavonols, are the most widely dispersed group of plant compounds. In depth descriptions of flavonols' broad existence and structural variety may be found in scholarly literature. Isorhamnetin, myricetin, quercetin, and kaempferol are O-glycoside flavonols (Figure 2.3). The carbon ring's third position is where the bonding activity is most frequently seen, however positions three, four, five, and seven of the carbon rings

can also experience replacement. Even though there are only a few aglycones, several sugar conjugates of flavonols have been found, with kaempferol containing over 200 distinct sugar combines (Cerrato et al., 2020). The number of flavonoids in commonly consumed vegetables, fruit, and beverages is also listed (Cao et al., 2010). Due to the large variances in the quantity available, seasonal shifts and differences between varieties are feasible (Crozier, Jaganath and Clifford, 2006).

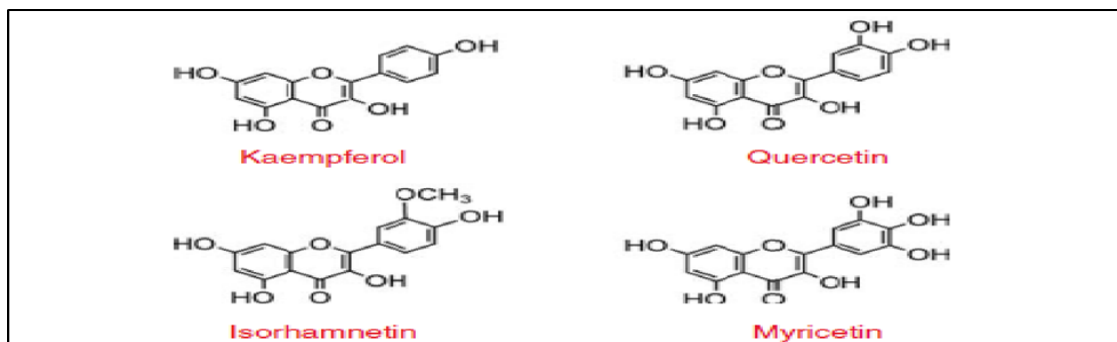
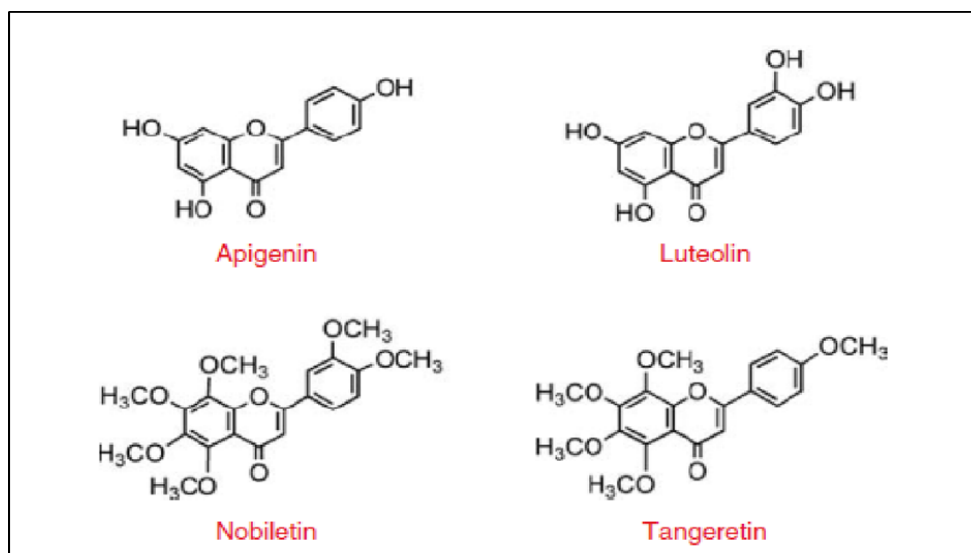


Fig. 3. The flavanol, aglycones, kaempferol, quercetin, isorhamnetin, and myricetin.

## Flavones

Flavones and flavanols have similar structural makeups (Figure 2.1). Apigenin and luteolin are two examples of flavones that do not include oxygen at carbon position three despite having A- and C-ring replacements (Figure 2.4). Flavones can undergo a variety of modifications, including hydroxylation, meth-

ylation, O- and C-alkylation, and glycosylation. Plants commonly contain flavones in the 7-O-glycoside form. There are just a few foods that have been documented to contain a significant quantity of flavones, including celery, parsley, and certain herbs. Nobiletin and tangeretin, two polymethoxylated flavones, are present in citrus fruits (Gaitan et al., 1989).



**Fig. 4.** The polymethoxylated flavones nobiletin & tangeretin, as well as the flavones apigenin & luteolin

## Flavan-3-ols

The flavonoids subclass known as flavan-3-ols, which ranges from simple molecules like (+)-catechin and its isomer (-)-epicatechin to complex proanthocyanidins that are oligomers and polymers, is characterized by complexity (Figure 2.5). Flava-3-ols and flavanones differ from flavones, flavanols, anthocyanidins, and isoflavones by having a saturated carbon 3 position in the heterocyclic C-ring and non-planar properties. For each degree of B-ring hydroxylation, flavan-3-ols shows two chiral centers at carbon 2 and carbon 3, and four isomers are produced. According to research, (+)-catechin and (-)-epicatechin are the two isomers that are most frequently found in nature, whereas (-)-catechin and (+)-epicatechin are the uncommon isomers (Yilmaz & Toledo, 2004).

Proanthocyanidins feature an additional chiral center at carbon 4, whereas flavanones only have a single chiral center at carbon 2. Although reversed phase HPLC columns are frequently employed, they cannot always identify enantiomeric pairing and as a result are readily missed. The different levels of chirality have a significant impact on the molecules' three-dimensional structure. The influence on their redox characteristics or the capacity of radicals to scavenge is negligible, but the binding qualities, which are crucial

to the phenomena of "lock-and-key," may have a more noticeable effect (Hazra, et al., 2008). interactions between an enzyme and its substrate, an enzyme and its inhibitor, or a receptor and its ligand. When people eat (-)-epicatechin, they also excrete some (+)-epicatechin, which leads to the opening of rings and racemization in the digestive system (Crozier, et al., 2009). Transformation can also result via food preparation (Seto et al., 1997).

The oligomeric or polymeric units of type B proanthocyanidin are produced by the oxidative coupling of (+)-catechin and (-)-epicatechin at the Carbon 4 of the heterocycle and the Carbon 6 or Carbon 8 site of the neighboring unit (Figure 2.5). Proanthocyanidins of type A have an additional ether bond between carbons 2 and 7. Proanthocyanidins' polymeric units can be up to 50 units long. In addition to transforming flavan-3-ols into gallic acid (Figure 2.5). Procyanidins, which are highly dispersed polymeric units of proanthocyanidins, are known as pure (epi)catechin polymers. Propellerargonidins and prodelfphinidins are the unusual forms of proanthocyanidin polymers for (epi)afzelechin and (epi)gallicocatechin, respectively (Balentine, et al., 1997).

Dark chocolate is a good source of procyanidins,

which are also found in oligomeric procyanidins and prodelphinidins found in the seeds of black grapes (Jin et al., 2012). Green tea (*Camellia sinensis*) has a high concentration of flavan-3-ols, particularly (-)-epigallocatechin gallate, (-)-epigallocatechin, and (-)-epicatechin gallate (Figure 5). The content of catechins decreases because of the fermentation process for tea

leaves. Black tea's primary constituents are thearubigins (Figure 5), which have a high molecular weight, and theaflavins, which have a lower molecular weight (Tanaka and Matsuo, 2020). Despite being made up of two flavan-3-ol units, theaflavins are not strictly dimers (Crozier, et al., 2006).

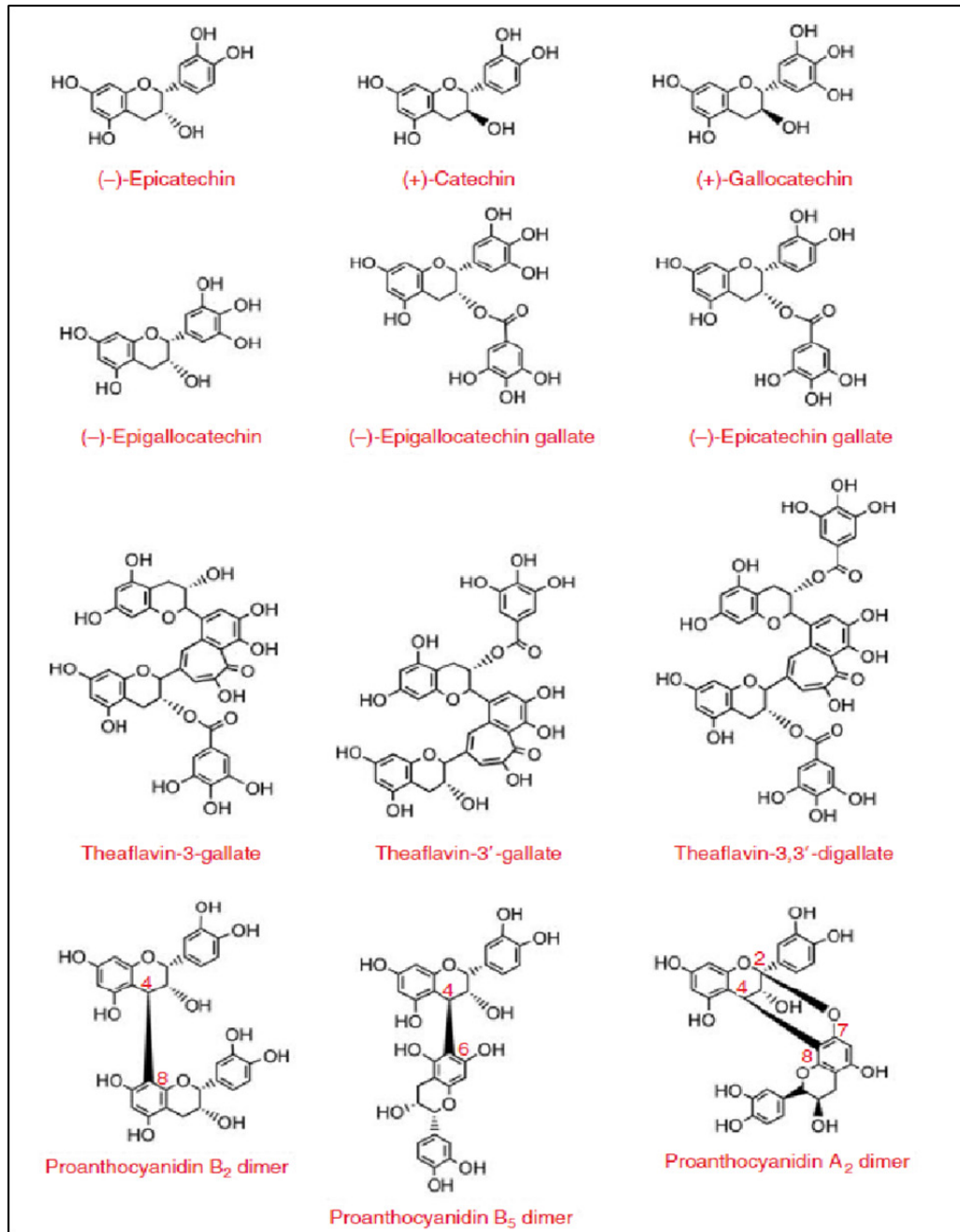


Fig. 5. Flavan-3-ol structural details

### Anthocyanidins

A wide variety of the plant kingdom contains anthocyanidins and its conjugated derivatives, anthocyanins. It is present in fruit and flower tissue because of red, blue and purple colours which it is responsible for. Equally visible in the tissue of leaves, stems, seeds, and roots, they provide defense against intense solar ex-

posure and are crucial to pollination. Pelargonidin, peonidin, petunidin, cyanidin, delphinidin and malvidin are popular types of anthocyanidins. Anthocyanins are present as a sugar conjugate of anthocyanidins. Malic and acetic acids are anthocyanins conjugates of hydroxycinnamates and organic acids which often occur on carbon 3, but also occur on carbon 5 and carbon 7.

Fully matured red wines and ports undergo chemical and enzymatic changes that significantly enhance the quantity of “anthocyanin-derived polyphenols,” which raises the overall intake of edible phenols (Crozier, et al., 2006).

### *Flavanones*

Flavanones may be identified by the chiral centre at carbon 2 as well as the lack of a double linkage at site 2 and 3. The C-ring is often connected to the B-ring at carbon 2 in the *-*configuration in naturally occurring flavanones. Due to the reactive nature of flavanone, it can undergo hydroxylation, glycosylation, and O-methylation processes. They are present at concentrated levels in citrus species as dietary components. Citrus peel has one of the highly popular flavanone glycosides which is hesperetin-7-O-rutinoside (hesperidin) and exhibits tastelessness. Example of glycoside with a discernible flavour profile include the flavanone neohesperidoside conjugates neohesperidin also referred to as hesperetin-7-O-neohesperidoside, it is found in naringin, also known as naringenin-7-O-neohesperidoside, and bitter orange (*Citrus aurantium*). which has an extremely bitter taste, a derivative of grapefruit peel (*Citrus paradisi*). A similar chemical, neohesperidin dihydrochalcone, is used as a sugar substitute in non-alcoholic beers (Crozier, et al., 2006).

### *Isoflavones*

Isoflavones' B-ring is connected at carbon 3 as opposed to carbon 2. As with other members of the legume family, soyabean (*Glycine max*) is a legume plant with high isoflavone levels (Crozier, et al., 2006). The reproductive function of ruminant animals like cows and sheep may be affected by isoflavones genistein and daidzein. They are termed phytoestrogen since they share structural similarities with steroidal hormone estradiol that may inhibit ovulation. This highlights the importance of isoflavonoid-deficient legumes that have been modified genetically.

Breast and prostate cancer risk have been linked to intake of soy products that contain genistein and daidzein. The androgenic hormone testosterone affects and is necessary for the growth of prostate cancer cells, but oestradiol production has the opposite impact. Insufficient natural oestradiol can be substituted with isoflavones to affect a reduced androgen level and inhibit tumor development. The progression of Breast cancers depends upon the level of oestrogens that can be competitively inhibited in the presence of Isoflavones ultimately interrupting tumor growth (Crozier, et al., 2006).

In comparison to baseline values, the bone resorption marker urine deoxypyridinoline (DPD) dropped by 23% and bone mineral density increased by 54% in women who drank soy isoflavone. It was shown that postmenopausal women who took isoflavone dosages more than 75 mg/d had the largest weighted mean difference when the effect of isoflavones on bone mineral density was evaluated in connection to menopausal status and isoflavone dosage. According to research, soy isoflavone consumption significantly increases bone mineral density and lowers the bone resorption marker urine deoxypyridinoline (Wei et al., 2012). Consuming isoflavones was found to significantly increase lumbar spine bone mineral density, even if the effect was not seen at whole hip regions femur neck area, or trochanter density of bone minerals. The lumbar spine's bone mineral density is significantly and favourably affected by soy isoflavone ingestion after six months. According to a study, soy isoflavone consumption during menopause may reduce bone loss and increase bone density following menopause. The lumbar spine's bone mineral density increases, and the bone resorption marker urine deoxypyridinoline decreases as a result (Taku et al., 2011).

### **Non-Flavonoids**

The most significant non-flavonoids in the diet are the carbon-6-carbon-1 phenolic acids, gallic acid, one that is an intermediate to hydrolysable tannins, and the carbon-6-carbon-3 hydroxycinnamates and their recombination product. Also, of relevance are C6-C2-C6-structured polyphenolic stilbenes.

### *Phenolic Acids*

Chemical compounds with a carboxylic acid group are referred to as phenolic acids. The well-known hydroxybenzoic and hydroxycinnamic acids are included in it. According to research, phenolic substances from plants come in a variety of molecular forms with hydroxylated aromatic rings (Ahmed, et al., 2020). They have antioxidant characteristics that protect against oxidative harm, which causes several destructive illnesses, such as cancer, inflammatory disorders, and cardiovascular diseases. Because they produce more reactive oxygen species (ROS) than normal cells, tumor cells are more susceptible to oxidative damage (Mandal, et al., 2010). The potential application of this natural antioxidant as a food additive underlines the advantages of its antioxidant properties (Lafay & Gil-Izquierdo, 2008). Phenolic acids serve as a precursor for high molecular weight compounds like proanthocyanidins. They can also occur as glycosides or esters along with sterols, alcohols, glucosides, and

hydroxy fatty acids. Phenolic acids have several biological properties, including antiulcer, antioxidant, anti-inflammatory, cytotoxicity as well as antitumor, antispasmodic, and antidepressant properties. These biological activities include Improved bile secretion, reduction of triglyceride level and blood cholesterol and antimicrobial activity (Ahmed, et al., 2020).

### *Hydroxycinnamates*

Cinnamic acid has the chemical formula C<sub>6</sub>-C<sub>3</sub>, and several other hydroxycinnamates can be produced through the metabolism of phenylpropanoids. P-coumaric, caffeic, and ferulic acids are prominent examples of hydroxycinnamates because they chemically transform into the tartrate esters, coumaric, caffeic, and ferulic acids. Quinic acid is conjugated to caffeine to generate 3-, 4-, and 5-O-caffeoylquinic acid, which is frequently found in fruits and vegetables. Chlorogenic acid, also known as 5-O-Caffeoylquinic acid, is present in both the foliage of green mate (*Ilex paraguariensis*) and the fresh beans of Coffee canephora (commonly known as robusta coffee). It constitutes approximately 10% of the composition in each. According to a study by (Crozier, et al., 2006), individuals who consume regular coffee may exceed a daily intake of 1g of caffeine.

### *Stilbenes*

Polyphenolic compounds, stilbenes, are characterized by the molecular formula C<sub>6</sub>-C<sub>2</sub>-C<sub>6</sub>. Plants respond to attack by pathogens by secreting stilbenes and can be regarded as phytoalexin compounds. The most common stilbene is Resveratrol which has a cis and the trans isomeric form. Trans-resveratrol-3-O-glucoside, sometimes referred to as polydatin and piceid, is an illustration of one of these isomers frequently found in plants. Viniferines are a kind of polymer that belongs to the resveratrol family (Crozier, et al., 2006).

### **Alkaloids**

Nitrogen-containing organic molecules with low molecular weight are known as Alkaloids. The existence of a heterocyclic ring that includes nitrogen is responsible for their alkaline nature. Classification of alkaloids is based on their precursors which are more than 20 classes, the classes are dependent on their heterocycles structure. They have various structures and anabolic pathways (Yang & Stöckigt, 2010). Acid-base extraction is a standard technique for refining crude alkaloid extract and they are toxic to a wide variety of species. Many drugs are used for therapeutic and recreational purposes, cocaine, caffeine, and nicotine are local anesthetic and stimulants, morphine is an analgesic, vincristine is an anticancer chemical, reser-

pine is an antihypertensive agent, quinidine is an antiarrhythmic compound, ephedrine is an anti-asthma therapeutic agent, and quinine is an antimalarial drug. Bitter to the tongue palate, alkaloids affect various metabolic processes in the body (Springob & Kutchan, 2009). Alkaloids enhance defense mechanisms against biotic and abiotic stresses and thereby improve plant pollination. Defense mechanisms like the use of their bitterness and toxicity to repel predators and ability to repair damages to the antioxidant system (del Pilar Vilariño & Ravetta, 2008). Parent plant plus the characteristic physiological activity is used in the nomenclature of members. The categorization of alkaloids by their heterocyclic ring system are enumerated below (Saxena et al., 2013):

- Pyrrolidine alkaloids: Hygrine found in *Erythroxylum coca* leaves is an example of this alkaloid type and they are characterized by pyrrolidine (tetrahydropyrrole) ring systems.
- Pyridine alkaloids: Coniine, piperine and isopelletierine possesses a piperidine(hexahydropyridine) ring system
- Pyrrolidine-pyridine alkaloids: This category of alkaloids is distinguished by the presence of a heterocyclic chain. Myosmine, a nicotine alkaloid identified in the plant that produces tobacco (*Nicotiana tabacum*), is a common instance.
- Pyridine-piperidine alkaloids: A distinguishing characteristic is the existence of a pyridine circle linked to a piperidine loop system. The most basic alkaloid, anabasine, is separated from the deadly Asian herb anabasis aphyllan.
- Quinoline Alkaloids: Quinoline, an elementary heterocyclic structure is observed within only quinoline alkaloids. Quinine, which is naturally present in the bark of cinchona trees, has been used for ages as an antimalarial agent. Primaquine, a synthetic drug, is the replacement of quinine as an anti-malarial.
- Isoquinoline alkaloids: Nicotine, papaverine, morphine, codeine, and heroine are opium and examples of isoquinoline alkaloids have heterocyclic ring structures.
- Phenanthrene alkaloids: Compounds belonging to phenanthrene alkaloids have three fused benzene rings and are therefore categorized as polycyclic aromatic hydrocarbons. Poppy seeds derivatives are effective as pain relievers and narcotics. Morphine is very effective in relieving pain but is also highly addictive. Derivatives of phenanthrene have anticancer therapy potential

due to its ability to induce apoptosis. Such examples include members of the Orchid family (Roy et al., 2019).

- Phenylethylamine alkaloids: They are primary amines in which the ethyl group is attached to the benzene ring and the amino group. They are neuromodulators or neurotransmitters and are used in asthma treatment. Ephedra contains phenylethylamines ephedrine, pseudoephedrine, norephedrine, as well as amines catecholamine (dopamine) and Phenethylamine (monoamine) also known as  $\beta$ -phenylethylamine or 2-phenylethylamine. Microbial fermentation of chocolate produces a great quantity of this alkaloid. Its presence can be observed in mistletoe (*Viscum album*), cabbage, cauliflower, and kale (Roy et al., 2019)
- Tropolone alkaloids: This is a chemical compound that is referred to as a cyclic ketone because of

its seven-membered aromatic ring structure. Its unusual electronic structure makes it useful as a precursor of a ligand. It shares similarities to a variety of naturally occurring chemicals with antifungal properties. Derivatives of Tropolone may suppress histone deacetylase (HDAC), an important enzyme in carcinogenesis (Ononye et al., 2013).

- Steroidal alkaloids: The steroidal characteristics are influenced by having a tetracyclic cyclopentanophenanthrene backbone. Alkaloids of solanum which are present in potatoes, tomatoes and cherries are solanidine and chaconine while *Veratrum* alkaloids may be present roots of veratridine, cyclopamine and nervine are the two main classes of steroidal alkaloids. Anti-inflammatory, antimicrobial and anti-estrogenic properties have been identified in steroidal alkaloids (Roy et al., 2019).

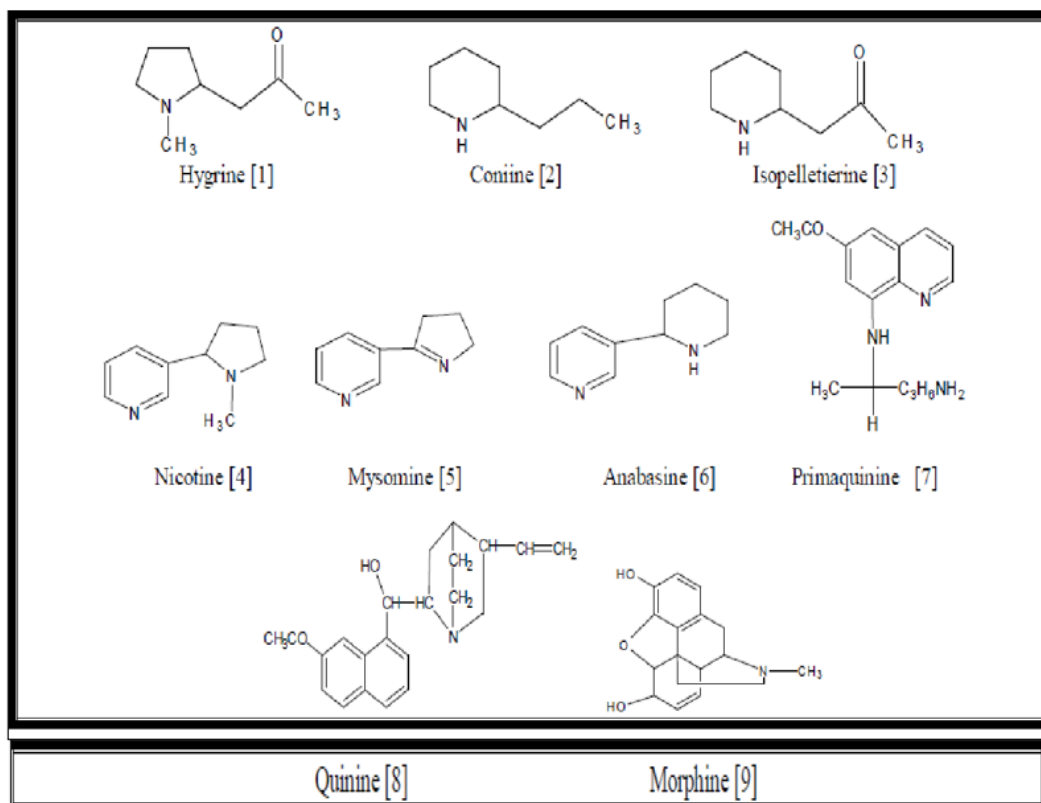


Fig. 6. Important naturally occurring alkaloids' structures

## Saponins

Glycosylated steroids, triterpenoids, and steroid alkaloids are chemical constituents of saponins. The main triterpene aglycone is a derivative of oleanane (Bohlmann, Meyer-Gauen and Croteau, 1998). A sapogenin (aglycone) has a simple sugar (such as glucose, galactose, xylose, arabinose, rhamnose, or glucuronic acid) connected to it via a glycosidic bond.

Derivatives of spirostan and furostan are the two known classes of steroid aglycones. Monodesmoside Saponins are linked at the carbon 3 site while bidesmoside saponins which translate to a saponins with a minimum of two sugars, are linked carbon-3 and carbon-22 (Lásztity, et al., 1998). The growth of bacteria can be retarded by a variety of saponins due to its antimicrobial activities Saponins classification as

a phytoanticipins or Phyto-protectants is because of its involvement in the defense mechanism of plants (Lacaille-Dubois & Wagner, 2000). Several biological effects can be seen when consumption of saponins by animals happens. The properties of Saponins such as membrane-permeability, activation of the immune system, hypocholesterolemic, and antitumor activities have been subject of much study. Animal development, feed intake, and procreation have been greatly influenced positively by studies on saponins. Saponins can behave like a nutrient inhibitor by preventing protein digestion and vitamin and mineral absorption in the GIT, can act as antioxidants, possess antifungal and antiviral capabilities and induces hypoglycemia (Saxena et al., 2013).

## **MEDICINAL PLANTS IN MANAGEMENT OF CARDIOVASCULAR DISEASE**

### **Banana**

The common name for so many hybrids in the genus *Musa* is banana. Conventionally, a variety of banana species are used to treat conditions like diarrhea, hypertension, diabetes, inflammation, and dysentery (Pereira & Maraschin, 2015). Due to its antioxidant properties, *Musa paradisiaca* peel extract possesses cardioprotective potential. The existence of ascorbic acid, tocopherols,  $\beta$ -carotene, and dopamine were linked to its antioxidant potentials, and it is widely consumed without showing any signs of toxicity. According to a study, *Musa paradisiaca* peels account for about 40% of the weight of the fresh fruit overall and exhibit feasible antioxidant actions in both water-soluble and ethyl acetate extracts (Vijayakumar, et al., 2008). Additionally, flavonoids, phenols, tannins, alkaloids, and glycosides, were isolated from banana peels, indicating their anti-inflammatory and antioxidant properties (Pereira & Maraschin, 2015). A study found that pre-treatment with *Musa paradisiaca* peel extract increased the electrolytes  $\text{Na}^+$  and  $\text{K}^+$ , indicating receptiveness of electrical conductivity of the heart, in rats that had been given isoproterenol. Following the administration of isoproterenol, serum levels of both  $\text{Na}^+$  and  $\text{K}^+$  decreased, which can be attributed to ongoing oxidative damage brought on by the attack of free radicals on the  $\text{Na}^+/\text{K}^+$  pump, which impairs it (Suleiman et al., 2021). Electrolyte stability, which is essential for healthy bodily cells and organ function, including that of the heart, was achieved through the course of treatment. Normal levels of calcium, potassium, and sodium are necessary

for controlling heart conductivity, while calcium, magnesium, and phosphorus are required for ideal heart contraction (Alizadehasl et al., 2008).

The vulnerability of hearts to oxidative injury due to myocardial membrane damage from increased free radical production is further highlighted by increased lipid peroxidation, as shown by elevation of malondialdehyde in Isoproterenol-induced myocardial infarction using rats (Wong, et al., 2017). Observing rats with isoproterenol-induced myocardial infarction, pre-treatment with *Musa paradisiaca* peel extract reduced the elevation of malondialdehyde relative to aspirin, demonstrating its cardioprotective effect, which is probably achieved by scavenging accumulated free radicals because of isoproterenol administration (Pereira & Maraschin, 2015). Several phenolic antioxidants, such as catechol, (-)epicatechin, kaempferol 3-O-sophoroside, and quercetin 3-O-[2-O-b-D-glucopyranosyl], are present in *Musa balbisiana*. The favourable effects of the supplement on heart health may be attributed to the ingredients L-rhamnopyranoside, rutin, apigenin-6-C-glucoside-7-O-glucoside, and chlorogenic acid. Some authors claim that the anti-inflammatory and antioxidant activities of phenolic compounds account for the beneficial characteristics of these compounds (Wang et al., 2014). Following the decrease of inflammation and oxidative stress within the hypertrophied heart, the powdered form of banana fruit pulp is viewed as a promising option in avoiding cardiac hypertrophy (Kumari et al., 2020).

### **Hawthorns**

The Rosaceae family includes a sizable genus of prickly shrubs and trees known as hawthorn. There are 280 species of shrubs and they are based in the temperate zones of North America, eastern Asia, and Europe. According to Yang et al. (2013) (Yang et al., 2013), chronic heart disease and having a stroke have historically been two of China's main killers. China had an aggregate rise in cardiovascular disease fatalities of 46%, which is four times greater than the US and Western nations due to its rapidly aging population. Since the first decade, hawthorn has been used to treat cardiac problems. In the early 1800s, American physicians started treating cardiovascular and respiratory problems. The berries have historically been used therapeutically for various heart problems such as arrhythmia, heart disease, hardening of arteries, exorbitant blood flow, and chest discomfort. Till date, its flowers coupled with leaves are still utilized medically. There is also evidence of the use of hawthorn in treating mild to moderate heart disease.

In traditional Chinese medicine, there's a theory that also says it focuses on strengthening spleens to clear congestion, stimulate blood flow and gastrointestinal function (Ekor, 2014).

Hawthorn extracts are becoming increasingly popular due to their anti-atherosclerotic properties and serum lipid-lowering effect, antioxidant effect and cardiovascular protective effect. Interestingly, fresh hawthorn fruit is said to contain polyphenols, including up to 20.5% pectin as reported by Wang (Wang et al., 2018). Antioxidant action, lipid-lowering action, anti-glycation action, antibacterial action is found in pectin oligosaccharides with 2–11 polymers (Zhu et al., 2019). According to Liu et al. (Liu et al., 2016), hawthorn contains about 150 phenolics, including procyanidin B2, B5, and C1, flavonoids like epicatechin, hyperoside, quercetin, rutin, and isoquercitrin, and triterpenoid acids including ursolic, corosolic, oleanolic, and maslinic acid. Other species, such as *C. Monogina* and *C. azarulus*, also contain phenolic chemicals of a similar sort, which have been divided into four subcategories. Anthocyanins like cyanidin glycosides, of which cyanidin-3-O-glu is one, phenolic acids like hydroxycinnamic acids, flavonoids, the most prevalent component, including flavones and flavanols, and flavonoids (the most abundant component) are all present in phenolic compounds. Recent studies confirm that numerous fruits, leaf and flower extracts of Hawthorn contain medicinal and biological compounds, which also includes cardiovascular protection, hypolipidemic action, and antioxidant capacity. These properties are growing global interest (Zhang et al., 2014).

The most studied material is WS® 1442, which consists of a 45% ethanolic extract from *C. Monogina* leaves and flowers and 20% oligomeric procyanidins. According to the New York Heart Association (NYHA) classification, WS® 1442 is indicated for curing: In both US and Europe, stages I to III of heart failure (Pittler, et al., 2003). Consuming hawthorn extract may increase the quantity of post-thoracic discharge and after surgery bleeding, according to a research study of patients having heart surgery. Although, adverse events have not been reported currently in its clinical use. Additionally, hawthorn extract has been shown to be effective because it has an anti-apoptotic effect in ischemic myocardial injury, which is a general result of atherosclerotic lesions invading the coronary arteries (Ranjbar et al., 2018). This could be the result of the signaling pathways that are activated (Jayachandran et al., 2010). Therefore, hawthorn extract may be a promising addition to the treatment of cardiovascular

disease and recovery from myocardial infarction.

## Flaxseed

Flaxseed (*linus usitatissimum*) is a blue flowering crop that produces a small flat seed that ranges from yellow to red brown in colour. There are three main methods to consume it as meals: entire seeds, powdered seeds in a granular form, and oil made from flaxseed. Alpha linoleic acid (ALA), fibre, and lignans are some of the key ingredients in flaxseed (Dahal, 2020). Flaxseeds are rich in various bioactive components, including alpha-linolenic acid (ALA), unsaturated fatty acids such as oleic acid, linolenic acid, and linoleic acid. They also contain cellulose, a soluble flaxseed fibre that consists of compounds like d-Xylose, L-Galactose, L-Rhamnose, and d-galacturonic acid. Lignans, specifically secoisolariciresinol diglycoside (SDG), are another prominent component found in flaxseeds. Additionally, flaxseeds contain monoglycerides, triglycerides, free sterols, sterol esters, hydrocarbons, and derivatives of ballast phenylpropane. Of particular importance, flaxseeds are a valuable source of unsaturated fatty acids like ALA and linoleic acid, both of which are essential fatty acids (EFAs) necessary for human health (Fale et al., 2022). In addition to its usage as a laxative, research has shown that flaxseed may be able to treat, prevent, or manage illnesses of the circulatory system, cancer (including breast cancer), and diabetes. Its ability to reduce blood cholesterol, inflammatory indicators, platelet aggregation, and enhance glucose tolerance give it the potential to manage cardiovascular illnesses (Goyal et al., 2014).

High levels of low-density lipoprotein (LDL) and low levels of high-density lipoprotein (HDL) cholesterol are abnormal lipoprotein levels and are a high-risk factor for cardiovascular disease, when flaxseed oil (FO) supplementation was studied for 12 weeks, it was shown that risk factor low density lipoprotein cholesterol levels decreased by 25.8% and 21.2% after 4 and 12 weeks, respectively (Kawakami et al., 2015). Another study concludes that pure SDG and flaxseed have stronger lipid-lowering benefits in people (Prasad, et al., 2020). More than 25 g/day of -linolenic acid in flax oil therapy reduces serum lipids in people and has minor impact on other components. An essential process in the creation of hemostatic plugs and thrombosis is platelet aggregation, which occurs when platelets connect to one another at the site of vascular damage (Jackson, 2007). Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are precursors of alpha-linoleic acid. The properties of biological

membranes and their capacity to regulate the activities of membrane-associated proteins are influenced by polyunsaturated fatty acids (PUFA), particularly EPA and DHA (Bruno, et al., 2007). Due to its anti-platelet qualities, flax seed is now used therapeutically to treat thrombosis, the most prevalent underlying pathology that causes cardiovascular disease mortality (Adili, Hawley and Holinstat, 2018). The anti-platelet feature is a result of PUFA's capacity to lower von Willebrand factor, one of the platelet activation factors, whole blood viscosity, and positively influence red blood cell flexibility (DiNicolantonio and OKeefe, 2019). Another study demonstrates that males are more likely to respond favorably to dietary consumption of EPA than women are to DHA when it comes to the risk of thrombotic illness (Phang, Lincz and Garg, 2013).

Diabetes is an ongoing medical condition brought on by insufficient or poor insulin production, which results in elevated blood glucose levels and subsequent damage to several physiological systems, including the blood vessels and neurons (Galicia-Garcia et al., 2020). Additionally, obesity increases insulin resistance, which results in vascular damage. According to Javidi et al., daily intake of powdered flaxseed decreased blood pressure in those with prediabetes but did not improve glycemic and IR indices (Javidi et al., 2016). Long-chain n-3 polyunsaturated fatty acids (n-3PUFA) with concentrated blood levels were also strongly associated with a decreased prevalence of insulin resistance and obesity (Pan et al., 2018). According to a study's findings, oil from flaxseed supplements may be beneficial for boosting the antioxidant system and reducing the harm done by reactive oxygen species in adults. This suggests that flaxseed oil can control insulin resistance brought on by oxidative stress, eradicating the vascular damage brought on by hyperglycemia (Musazadeh et al., 2021).

## Spinach

Several supporting findings revealed that eating fruit and vegetables, particularly green leafy vegetables, lowers the risk of disease associated with coronary arteries. Antioxidant-containing compounds in Fruits and vegetables are of great benefit (Aune et al., 2017). Green leafy vegetable *Spinacea oleracea* (spinach), which is consumed all over the world, is said to have anti-diabetic, anti-hyperlipidemic, and antithrombotic properties thanks to several antioxidants Phytoconstituents collectively called NAO (natural antioxidant mixture). NAO contains polyphenols, folic acid and vitamins A, B, C, E, K, alongside flavonoids (rutin & flavonol glucuronides) (Panda and Shinde, 2017). Spinach possesses a variety of antioxidant

phytochemicals that give its powerful antioxidant and ROS scavenger properties. Consuming fresh products high in flavonoids, particularly quercetin and rutin, which are natural antioxidant phytoconstituents, are connected to reduced threat of cardiovascular disease (Khan et al., 2021). Recent research suggests that flavonoids can protect against myocardial ischemia/reperfusion (I/R) damage, rutin has been demonstrated in multiple studies to be cardioprotective in myocardial damage triggered by isoproterenol due to its great antioxidant capacity. Rutin decreased infarct size and lipid peroxidation in myocardial infarcted rats and replaced isoproterenol-depleted levels of lactate dehydrogenase, heart-specific creatine kinase, aspartate aminotransferase, superoxide dismutase, catalase, glutathione peroxidase, glutathione, and vitamin C. Through its antihyperlipidemic ability, NAOE and rutin significantly decreased the elevated plasma total triglyceride and cholesterol levels in rodents with myocardial infarction induced by isoproterenol (Karthick & Prince, 2006).

Supplementing isoproterenol-administered ovariectomized rats with *A. tricolor* extract prevented the infiltration of inflammatory cells, the deposition of collagen, and the accumulation of ferric ions in the heart. The antioxidants present in *A. tricolor* extract, which reduce tissue inflammation and cardiomyocyte loss, are credited with this protective effect. In rats with ovariectomized hearts that had received isoproterenol administration, atenolol also prevented lipid peroxidation and inflammation (Nahar et al., 2018). *Amaranthus cruentus* extract administration in isoprenaline-treated animals demonstrated a significant defense to cardiocytes. Reduction was seen in very low-density lipoprotein and low-density lipoprotein cholesterol level, and a partial increase in high-density lipoprotein cholesterol level. Alanine aminotransaminase, aspartate aminotransferase, and alkaline phosphatase levels were restored. Additionally, administration of *Amaranthus cruentus* extract significantly increased the total protein level of cardiocytes (Bisen et al., 2020). Lower-density and very low-density lipoprotein levels were reduced, whereas high-density lipoprotein levels slightly increased. The levels of alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase were recovered. The total protein content of cardiocytes was also markedly raised after receiving *Amaranthus cruentus* extract (Bisen et al., 2020) (Bisen et al., 2020).

Treatment with *A. viridis*' increased the serum total protein, albumin, and globulin levels in isoproterenol-induced myocardial infarction rats because it can

sift radicals that are free and stop the oxidation of lipids. As a result of greater production of free radical brought on by the administration of isoproterenol, there is albumin and globulin reduction, and overall level of protein in rats with myocardial infarction caused by isoproterenol. All these reductions occur as a result from several oxidative processes, together with changes in vascular permeability that are brought on by vascular injuries (Shearman et al., 1988), or they can be a sign of increased lipoprotein oxidation (Saravanan and Ponmurugan, 2012).

## **Terminalia Arjuna**

The World Health Organization (WHO) reported that traditional herb supplements are still used by 80% of people worldwide ((Amalraj and Gopi, 2017)). With differences to synthetic medicines, medicinal plants are widely available, especially among low-income people. It is considered non-toxic and has few adverse effects. One of these traditional medicines is Terminal arjuna (TA), a member of the Combretta specie and it is majorly present in India. It is a perpetually green, blossoming tree that may reach heights of 20 to 30 meters and there are about 24 species in India. In the various plant parts, there are several therapeutic attributes found in the fruit, bark, leaf, seed, and root (Srivastava, Srivastava and Chouksey, 2001; Bagchi et al., 2003; Gopinath et al., 2014; Amalraj & Gopi, 2017; Goswami et al., 2020). Coupled with other numerous bioactive properties, like antioxidant, anti-inflammatory, cardio-protective, anti-atherosclerotic, and anti-tumor (Subramaniam et al., 2011; Kapoor, et al., 2014; Kasote et al., 2015). According to studies, phytochemicals that are isolated from TA contain a wealth of antioxidant capabilities, also, TA display a range of pharmacological capabilities for treating a number of clinical issues, such as cardiac difficulties, ischemia, cardiomyopathy, atherosclerosis, myocardial necrosis, tumor, viral infections, ulcer, and many more (Sarveswaran et al., 2016; Amalraj and Gopi, 2017). The herb TA has long been recognized as a cardio tonic, and today it is given more consideration and focused on the treatment of several cardiac issues. Lactones, flavonoids, phytosterol, phenolic compounds, glycosides, and tannins are all present in the alcoholic extract of TA and have strong antioxidant, anti-hyperlipidemic, and cardiovascular preventive properties (Shah et al., 2019). Cardiovascular disease is brought on by hyperlipidemia, hyperglycemia, inflammation, clotting factors, enhanced platelet activation, smoking, and oxidative stress.

The following are the mechanisms underlying the

cardioprotective function of TA.

- Flavonoids increase reverse vasorelaxation processes and reduce endothelial dysfunction and reduce artery pressure.
- Flavonoids also help absorb and excrete oxidized modifiers of low-density lipoprotein that damages the endothelial cells and leads to atherosclerotic plaque formation (Alique et al., 2015)
- Platelet control activation and prevention of platelet aggregation, as indicated. The bark extract and Gemmomodified extracts have strong therapeutic potential for treating myocardial infarction (Jahan et al., 2012).

Different other research observed that the cardioprotective impact of TA are caused by:

- The antioxidant capacity of tannins, and
- Oleanane triterpenoids that give rise to physiological antioxidants in the body (Pawar and Bhutani, 2005)

A Study Using Herbal Supplement Abana (Contains Herb Arjuna) on people with hypertension were found to have significantly reduced left echocardiographic SBP, wall and septal thickness, plus increased ejection fraction and other markers of cardiac function. Arjuna has recently been shown to be effective in reducing and improving SBP and cardiovascular endurance in healthy normal humans (Sandhu et al., 2010).

## **Grapefruit seed extracts (GSE)**

Polyphenolic chemicals may be found in abundance in grapes (*Vitis vinifera*). Grape seeds are a byproduct of the processing of grapes and make about 5% of the weight of grapes. Because of their potent antioxidant, anti-cancer, anti-microbial, anti-aging, anti-hepatotoxic, and anti-inflammatory properties, grapes are recognized as a food-based supplement (Nowshehri, et al., 2015). Grapefruit seed extract (GSE) has a far higher antioxidant potential than other renowned antioxidants like vitamin C and E (Bagchi et al., 2003). Since ethanol grapefruit seed extract inhibits lipase, it can help control obesity by preventing fat from being absorbed and from building up in adipose tissue (Moreno et al., 2003). A study report expresses that grape seed extract improves the antioxidant defense against reactive oxygen species generated under hyperglycemic conditions (Chis et al., 2009). This suggests defense against cardiovascular artery damage brought on by such hyperglycemia states. Temporary consumption of purple grape concentrate decreases coronary artery disease patients' levels of low-density lipoprotein (LDL) that is susceptible to oxidation

(Stein et al., 1999). Hypercholesterolemic Grape seed proanthocyanidin extract supplementation in human patients also results in decreased LDL oxidation susceptibility (Bagchi et al., 2003). An acceptable indicator of atherosclerotic damage is the presence of oxidized LDLs and the development of foam cells in the artery. Grapefruit seed extract reduces the sensitivity of LDL to oxidation, which suggests that it may be effective in the management or treatment of atherosclerosis (Delmas, et al., 2005).

## CONCLUSION

Medical plants are known to possess secondary metabolites which are referred to as phytochemicals. Plants are known to be protected against illnesses and harm from environmental risks by phytochemicals found in root systems, stems, foliage, fruit, flowers, or grains. These compounds also give plants their colour, scent, and flavour. Phytochemicals are not just important to plants; they are known to be of health benefit to humans. The health benefits of plants are due to the

phytochemicals they possess. The phytochemical has antioxidant, anti-inflammatory, antihypertensive, antiarrhythmic, antimicrobial, and anticarcinogenic effects which make medicinal plants a prospective treatment option. The paper also reviewed some plants which are helpful in preventing and treating cardiovascular illnesses. Based on the findings, some plants like Banana, Hawton, Spinach, Terminalia, and Grapefruit seeds have antioxidant properties that are of great benefit in clearing off free radicals that might be developed due to exposure to risk factors that can pose a great threat to the cardiovascular system. Also, the plants reviewed in this study are known to possess anti-atherosclerotic, anti-hyperlipidemic, reduced platelet aggregation, and lipid peroxidation levels which have proven essential to preventing and curing cardiovascular illnesses and improving human well-being which is a global issue cannot be undermined.

## Competing Interest

The authors had no competing interests.

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