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Review Article

A Review of Medicinal Plants Used in Therapy of Cardiovascular Diseases

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ABSTRACT

Phytochemicals are present in fruits and vegetables, it is important the consumption by the effects in protection of cardiovascular diseases mainly because these diseases are the first cause of death in world. This study is a review of principal phytochemicals present in plants (that are used in meals or not), mainly: *Allium cepa*; *Allium sativa*; *Citrus limon* and *Citrus sinensis*; *Coffea arabica* and *Coffea liberica*; *Ginkgo biloba*; *Digitalis purpurea* and *Digitalis lanata*, between others. The substances in these plants have a therapeutic effect in cardiovascular diseases (CVDs) like as: hypertension, atherosclerosis and stroke, between others. By other side, we can conclude that principal compounds are flavonoids; antioxidants (action in oxidative stress); ouabain; cardenolide glicosides; lanatosides; tannins; sesquiterpenoids and phenolic compounds.

Keywords: cardiovascular diseases (CVDs); hypertension; phytochemicals; cardenolide glicosides; lanatosides; tannins; phenolic compounds.

INTRODUCTION

Cardiovascular diseases (CVDs) are the first cause of death in world[1]. In 2012, an estimated 17,5 million people died from CVDs, representing 31% of all global deaths[1]. The principles diseases between CVDs are: coronary heart disease (7,4 million deaths, of CVDs deaths) and stroke (6,7 million deaths, of deaths of CVDs)[1,2]. The prevalence increase with age being 5% at 20 years to 75% at 75 years[3]. CVDs can be prevented by an intervention on behavioral risk factors: tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol[1]. Others risk factors are hypertension, diabetes, hyperlipidaemia or already established disease[1,4]. Diabetes mellitus and hypertension are increasing, being a major public health problems[4]. A high-glycemic index (by a higher postprandial blood glucose and insulin levels) affect the CVDs risk[5]. CVDs include: coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease and hypertension[1,6]. The nutrients has an important association with CVDs, someone have an association of risk, others cause a reduction of CVDs incidence[2]. The dietary factors are important to protect coronary heart disease, such as antioxidants (minerals: selenium and zinc; compounds: flavonoids), that are presents on fruit and vegetables[2]. In addition, other important substances are vitamin B6, B12, C and E, carotenoids (mainly β-carotene), folate[2].

Arrhythmias

Ventricular arrhythmias can occur with or without a cardiac disorder[7]. Clinical presentations of ventricular arrhythmias are: asymptomatic individuals with or without electrocardiographic abnormalities; people with symptoms potentially attributable to ventricular arrhythmias (palpitations, dyspnea, chest pain, syncope and presyncope); ventricular tachycardia (that can be hemodynamically stable or not); cardiac arrest (asystolic; ventricular tachycardia or fibrillation; pulseless electrical activity)[7].

Atherosclerosis

Atherosclerosis is the main cause of cardiovascular disease[8]. It is a disease that is characterized by a damaged intima the platelets again adhere to the wall of a blood vessel and to each other[9,10]. When the wall of a blood vessel is injured, aggregation of platelets is immediately and to each other to form aggregates on damaged intima[9,11]. When this happen, tend to seal the opening and help to arrest bleeding[9]. Aggregation of platelets is one of immediate causes of thrombosis and is mediated by cellular adhesion molecules and expressed on the vascular endothelium[9-11]. The secretion of nitric oxide (NO) and prostacyclin are potent inhibitors of aggregation[11]. Endothelial cells have a special role on regulation of blood platelet functions[11]. Levels of soluble adhesion molecules are a risk predictors of cardiovascular events[10].

Hypertension

Hypertension is one cause of cardiovascular complication and a chronic disease[12,13]. The pathophysiological mechanism behind this disorder is multifactorial such as: oxidative stress, inflammation, renin-angiotensin system and autoimmune vascular dysfunction[13,14]. This disorder can be reduced by some phytochemicals acting like an anti-hypertensive medication (as angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, β-blockers, Ca-channel blockers, direct renin inhibitors,

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direct vasodilators or diuretics)[12-14]. These compounds can attenuate the increase of blood pressure levels and also can prevent the cardiovascular disorders associated with hypertension[12].

Stroke

Stroke or cerebrovascular disease is responsible of mortality and morbidity in many industrialized countries, being the third leading cause of death in the United States[15,16]. This disease is more frequent on patients with cardioembolic stroke than among patients with stroke of other causes[17]. The clinical features of stroke are the size and site of the ischemic lesion[17]. Acute ischemic stroke is classified by: large-artery atherosclerosis (embolus or thrombosis); cardioembolism (high-risk or medium-risk); stroke of other determined etiology and stroke of undetermined etiology (two or more causes identified; negative evaluation and incomplete evaluation)[17].

Phytochemicals

These substances are presents in fruits and vegetables, when ingested can have a potential for modulating human metabolism being favorable on the prevention of chronic and degenerative diseases[18]. For thousands of years, the plants have used for food and medicinal purposes, by that reason the scientists have studied extensively their properties and bioactive compounds[19,20]. In various parts of the world, traditional medicinal plants have been used to treat some diseases and nowadays they have an important role in some cultures and traditions of developing countries[19,21]. Traditional medicine is used by 80% of the world's population, by WHO[19]. The bioactive compounds can be used as food addictives, functional food ingredients and nutraceuticals[20]. Some studies reported a significant protective association of consumption of fruits and vegetables or surrogate nutrients with stroke[2]. The fruits and vegetables present a protective effect against cardiovascular diseases[22]. Drugs have common substances from plants[23]. It's very important to identify available plants or plants extracts that could be used[23]. Others studies reveled a possible change of homocysteine blood levels by folate, vitamin B6 and B12, being protective[2]. By this reason is important know which are the principal substances that have an action in therapy of cardiovascular diseases and the respective plants. Cardiac glycosides (Figure 1) are a family of natural compounds that bind to and inhibit Na^+/K^+-ATPase[24]. They are used for the treatment of heart failure and atrial arrhythmia, having a mechanism of positive inotropic effect[24,25]. These substances have a steroid nucleus, a lactone moiety and a sugar moiety[24]. The cardiac glycosides can be classified on cardenolides (Figure 2) or bufadienolides (Figure 3)[24]. Flavonoids are phenolic compounds with a wide range of applications (physiology, biochemistry and chemical ecology (ultraviolet (UV) protection))[26]. Phenolic compounds present a relationship between her increase of consumption and a reduced risk of cardiovascular diseases[27,28].

Centella asiatica

Centella asiatica commonly known as Gotu Kola[21,29]. It belongs to Apiaceae family[29,30]. This plant is known as a herbal medicine with excellent pharmacological effects[30-33]. One of mainly compounds is asiatic acid (AA), a triterpenoid component[30,32]. This plant also contains madecassic acid (MA); asiaticosides (AD); madecassosside (MD); essential oils; amino acids[30,34]. *Centella asiatica* has been shown to prevent: blood coagulation and alleviation of oxidative stress[30,31]. This plant can be used as hypotensive[35].

Convallaria majalis

This plant is a member of the family Liliaceae, having cardenolide glycosides (Figure 4) on rhizomes[36,37]. The principal substance with cardiotonic action is convallatoxin (a cardiotonic heteroside)[23,37-39]. The others substances presents in this plant are: convallasaponin A, free flavonoids and by heterosides (3-methylquercetin) and mineral salts[38]. Convallatoxin is used as cardiotonic[39]. The principal medical use is in cardiac insufficiency, arrhythmias and edema[38].

Digitalis purpurea L. and *Digitalis lanata*

These plants are a member of Scrophulariaceae family[24,36,40,41]. The extracts of these plants have cardiac glycosides (digoxin (Figure 5), digitoxin (Figure 6), cardenolides) on the treatment of heart disorders like as was described in 1785 by William Withering[23,24,39-42]. Other compounds that are in both plants are: glucoevatromoside; glucodigifucoside; glucogitoroside; digitalinum verum; glucolanadoxin; glucoverodoin; tigogenin; gitogenin; digitogenin; apigenin; anthraquinones (1-methoxy-2-methyl anthraquinone; 3-methoxy-2-methyl anthraquinone and 1,4,8-thihydroxy-2-methyl anthraquinone); digitollytein; 3-methylalizarin; caffeic acid (Figure 7); ferrulic acid; P-coumaric acid and chlorgenicacid[40,42]. *Digitalis purpurea* L. has also digitalin and gitalin[23,39,42]. This plant has also glycogitaloxin, flavonoids, saponosides and triterpenes[40,42]. Used in cardiac insufficiency, being a cardiotonic action by increase of heterosides on cardiac contractility and decrease of excitability, conductivity and rhythm, decrease the requirement of oxygen for cardiac work[42,43]. The plant has also a diuretic action by flavonoids and minerals salts[42]. The plant is also used in tachyarrhythmia and systolic dysfunction[42,43]. *Digitalis lanata* has acetyldigoxin, deslanoside and lanatosides A, B, C, D and E (Figure 8; Figure 9; Figure 10; Figure 11 and Figure 12)[23,39,40,42]. This plant has the same uses that *Digitalis purpurea* L.[42]. Digoxin is a common medication for heart failure[3]. By study of Dean T. Mason in 1964, it has been revealed that Digitalis has a positive inotropic effect on cardiac output and tissue perfusion; blocks adrenergic action (vasodilatation); decrease preload and afterload; increase of blood flow; decrease of peripheral resistance, central venous pressure and cardiac frequency[25,43]. However, when administrated at patients with normal systolic function, the effect is an increase of peripheral resistance, a decrease of cardiac output and blood flow[43]. Acetyldigoxin, deslanoside, digitalin, digitoxin, digoxin, gitalin and lanatosides A-C are used as cardiotonic[39].

Fraxinus excelsior

This plants is a member of Oleaceae family[44-46]. This plant present two phenolic compounds mainly iridoids and

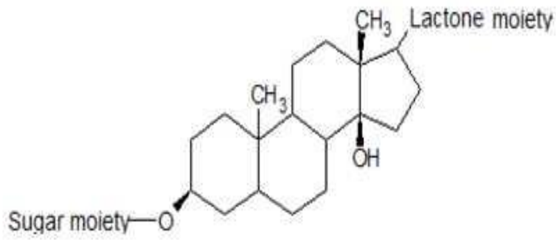

Figure 1: Cardiac glycosides structure

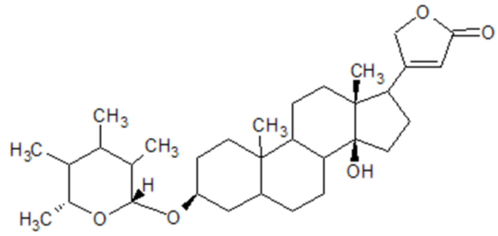

Figure 2: Cardenolides structure

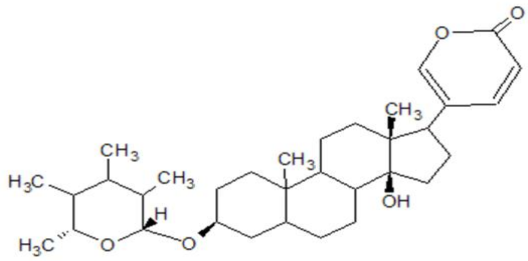

Figure 3: Bufadienolides structure

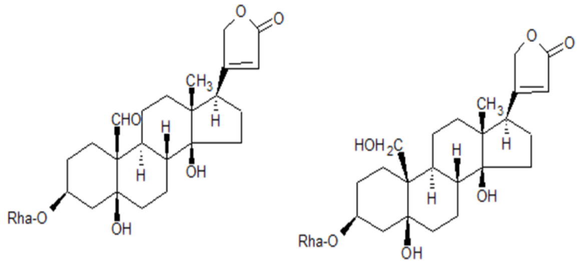

Figure 4: Cardenolide glycosides structure

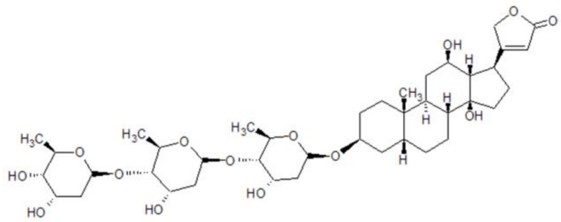

Figure 5: Digoxin structure ($C_{41}H_{64}O_{14}$)

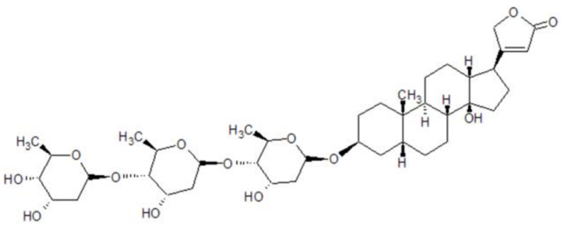

Figure 6: Digitoxin structure ($C_{41}H_{64}O_{13}$)

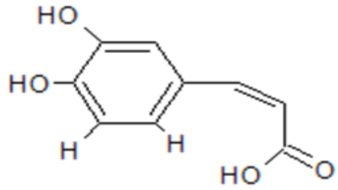

Figure 7: Caffeic acid structure

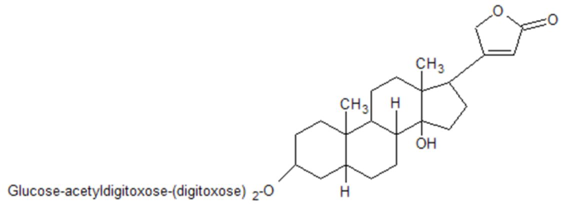

Figure 8: Lanatoside-A structure

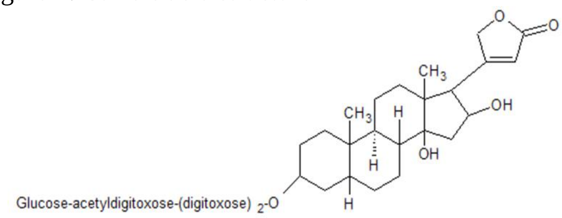

Figure 9: Lanatoside-B structure

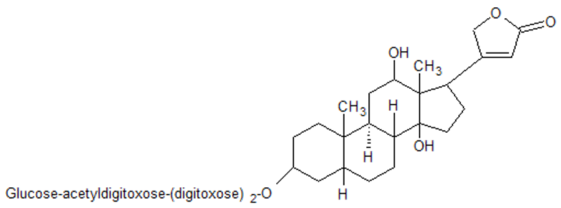

Figure 10: Lanatoside-C structure

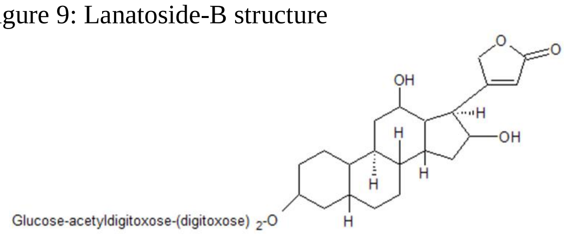

Figure 11: Lanatoside-D structure

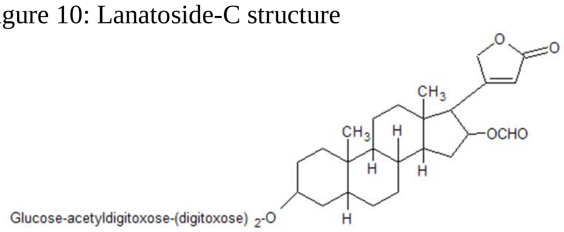

Figure 12: Lanatoside-E structure

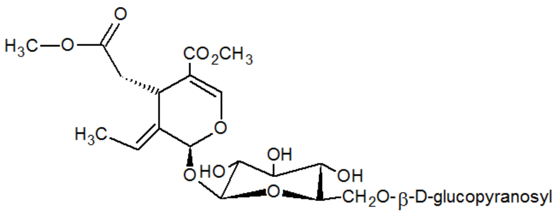

Figure 13: Elcelside A structure ($C_{24}H_{36}O_{16}$)

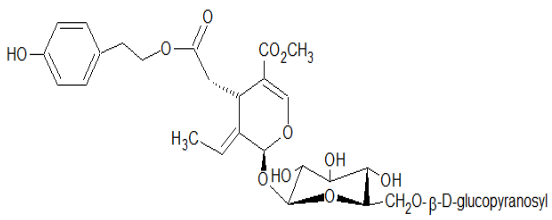

Figure 14: Elcelside B structure ($C_{31}H_{42}O_{17}$)

secoiridoid glucosides[12,45]. The principals secoiridoids are new escelsides A (Figure 13) and B (Figure 14); nuzhenide (6,8%) (Figure 15); GI3 (5,8%) (Figure 16); GI5; ligstroside; oleoside-11-methyl ester; oleoside dimethyl ester; 1'''-*O*-β-D-glucopyranosylformoside and phenylethanoid salidroside[12,45-47]. A natural extract of this plant is glucevia[46]. This extract has coumarins (fraxin, fraxetin, esculin, esculetin, cichoriin, scopolin and fraxidin glucoside)[46]. The leaves present tannins (8%); iridoids; coumarins; flavonoids; mannitol (16% to 28%) and mucilages (10% to 20%)[48]. This part of plants can be used as vasoprotective and venotonic[48]. This plant has an antihypertensive effect[12,46,49].

Hamamelis virginiana

This plant also called hazel[50]. This plant belongs to Hamamelidaceae, used in traditional medicine with a history in pharmaceutical therapy[50,51]. The leaves of this plant has phenolic compounds such as hydroxycinnamic acids and flavonoids[50]. The studies revealed that hydroalcoholic extracts has procyanidin and prodelphinidin oligomers (19,8% expressed as catechin units (Figure 17))[50]. This plant has also hydrolysable tannin that is composed of glucosylated gallates with five to ten galloyl moieties (such as hamamelitannin (Figure 18) and pentagalloylglucose (Figure 19)); quercetin, kaempferol, myricetin and their glycosides; caffeic, quinic, chlorogenic and gallic acids (Figure 20)[50,52]. This plant is used for varicose veins[53].

Nerium oleander

This plant is a member of Apocynaceae family[24,54-56]. This plant has ouabain (Figure 21); oleandrin (Figure 22); neriifolin (Figure 23) and neriine[24,54,55,57,58]. This compounds are cardiac glycosides, cardenolides[24,57-61]. The mechanism of action is the inhibition of plasma membrane Na+/K+-ATPase, which leads to alteration in the intracellular potassium, sodium and calcium levels[58]. However, this compounds present a toxicity[58,59]. The leaves and flowers are used for the treatment of heart diseases[56,60].

Rauvolfia serpentina

This plant is a member of the Apocynaceae family[62,63]. *Rauvolfia serpentina* is an important tropical medicinal plant, known as Sarpagandha and native to India[64]. This plant present between 0,5% to 2,5% of total alkaloids like as reserpine (Figure 24), ajmalicine (Figure 25) and ajmaline[39,62,64-66]. Other important substance present on this plant is rescimamine[23,39]. Reserpine is used for hypertension by her sympatholytic effect[39,62,64-67]. Ajmalicine is an α-adrenergic blocking spasmolytic, reversing high doses into adrenalin effects, decreasing the activity on blood vessels (vasomotor) on bulbar center[39,65]. Ajmaline has an antiarrhythmic action but it is not common used by her toxicity[65]. Ajmalicine is used on circulatory diseases[39]. Rescimamine is an antihypertensive[39].

Rhododendron molle

This plant is a member of Ericaceae family[68-70]. This plant has rhomitoxin as substance and is used for hypertension and heart rate, being contraindicated in low blood pressure[23,39,68,70]. This plant also has flavonoids, diterpenoids, triterpenoids, lignans, phenolic glycosides, coumarins, quinones and steroids[68]. The major compound in flowers are flavonoids[68]. Another compounds present are grayanane diterpenoids (rhodojaponin-III (Figure 26)); phenolic glycosides, rhodomolleins F and G (Figure 27 and Figure 28)[69-71].

Stephania tetrandra

This plant belong to Menispermaceae family[72]. This plant has bisbenzylisoquinoline alkaloids (tetrandrine (TET) (Figure 29) and fangchinoline (FAN) (Figure 30)), biflavonoids (stephanflavone A and B (Figure 31 and Figure 32)) and β-sitosterol (Figure 33)[23,73-75]. Tetrandine used for hypertension by her hypotensive effects[23,76-78]. In China, these compounds are used to decrease portal venous pressure and blood pressure[73].

Strophanthus gratus

This plant is a member of Apocynaceae family[79]. This plant has a substance with cardiotonic effect, that is ouabain (Figure 21) (cardiac glycoside, cardenolide)[23,24,39]. This plant has lignans (pinoresinol (Figure 34), 8-hydroxypinoresinol (Figure 35) and olivil (Figure 36)) that were isolated from leaves[79]. Ouabain is a cardiotonic[39].

Urginea maritima

This plant belong to the family Liliaceae[80]. This plant has scillaren A as substance with cardiotonic effect[23,80]. This plant is used as cardiotonic for the treatment of cardiac marasmus and edema[80]. The compounds in bulbs of this plant are: scillarin A (Figure 37); scillirubroside; scilliroside; scillarenin 3-O-β-D-glucopyranoside; 6-desacetyl-scilliroside; scillarenin bis-rhamnoyranoside; 5-α-4,5-dihydro-scillaren A; proscillaridin A; 5-α-4,5-dihydro-scillirosidn 3-O-β-D-glucopyranoside; scillirosidin 3-O-α-L-rhamnopyranoside and 5-α-4,5-dihydro-scillirosidin 3-O-α-L-quinovopyranoside (knew as bufadienolide glycosides)[39,80,81]. The major compounds are scillaren A; scilliroside and proscillaridin A[80].

Scillarin A is a cardiotonic[39].

Veratrum album

This plant is a member of Liliaceae family[82]. This plant has esteralkaloids (protoveratrine A (Pro A) and protoveratrine B (Pro B)) as substance and is used for hypertension[23,82-84]. Other compounds of this plant are steroidal alkaloids and glycosides[82]. The chemical composition of the extracts of this plant are aliphatic alcohol (octason-1-ol), fatty acid (stearic acid), steroids and steroid glycosides (β-sitosterol (Figure 33); β-sitosterol 3-O-β-D-glucopyronoside (Figure 38); diosgenin (Figure 39); and diosgenin 3-O-α-L-rhamnopyranosyl-(1->2)-β-D-glucopyronoside (Figure 40)), stilbenoids and their glycosides (resveratrol (Figure 41); oxyresveratrol (Figure 42); oxyresveratrol 3-O-β-D-glucopyranoside (Figure 43) and wittifuran X (Figure 44)), steroidal alkaloids (jervine (Figure 45); pseudojervine (Figure 46) and 5,6-dihydro-1-hydroxyjervine (Figure 47)) and carbohydrate (saccharose)[82,83]. This plant present also veratridine (Figure 48) and cevanine (Figure 49)[83,84]. The rhizomes of this plant have the following compounds: diosgenin, wittifuran X; diosgenin 3-O-α-L-rhamnopyranosyl-(1->2)-β-D-glucopyronoside and oxyresveratrol 3-O-β-D-glucopyranoside[82]. This plant is also used for antithrombotic activity[82]. These type of

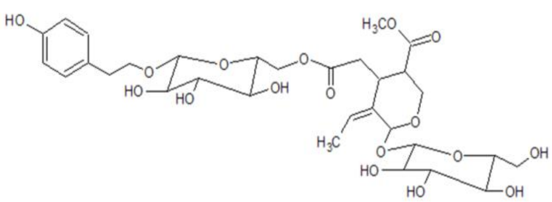

Figure 15: Nuzhenide structure

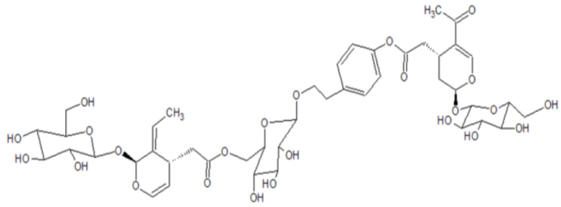

Figure 16: GI3 structure

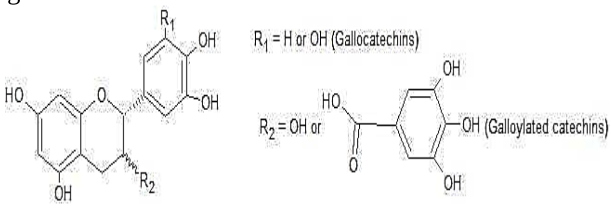

Figure 17: Monomeric catechins structure

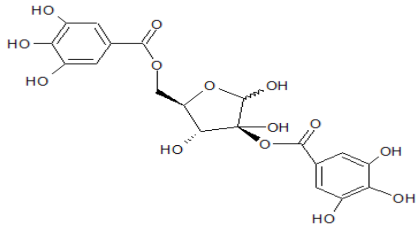

Figure 18: Hydrolysable tannin structure

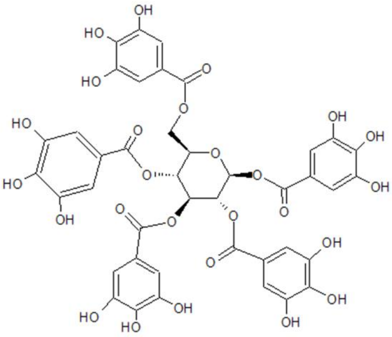

Figure 19: Pentagalloylglucose structure

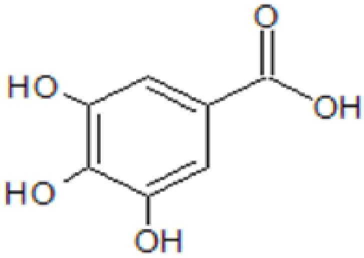

Figure 20: Gallic acid structure

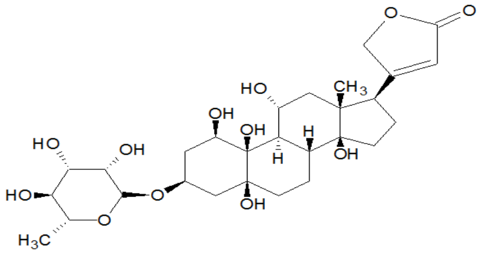

Figure 21: Ouabain structure ($C_{29}H_{44}O_{12}$)

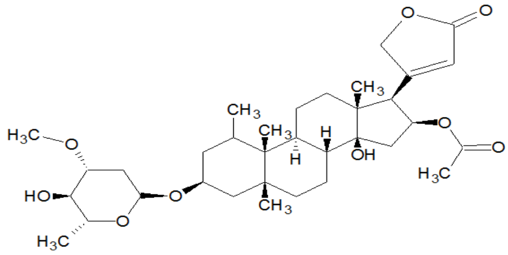

Figure 22: Oleandrin structure ($C_{32}H_{48}O_9$)

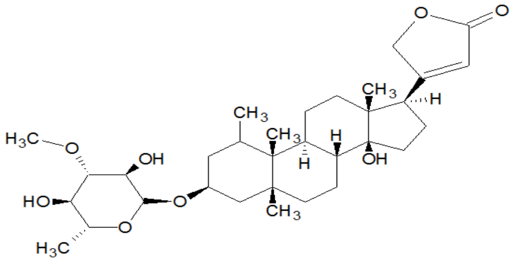

Figure 23: Neriifolin structure ($C_{30}H_{46}O_8$)

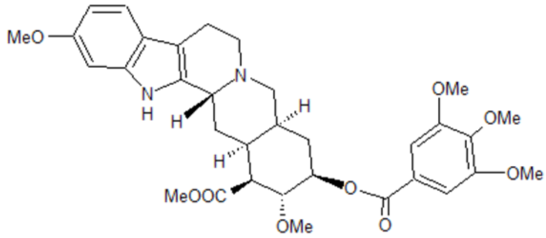

Figure 24: Reserpine structure

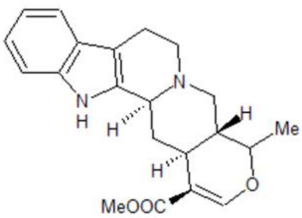

Figure 25: Ajmalicine structure

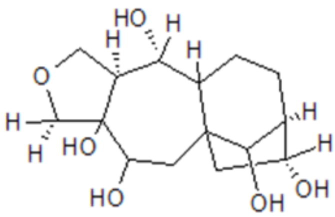

Figure 26: Rhodojaponin-ɪɪɪ structure

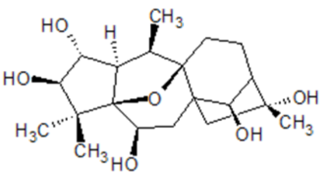

Figure 27: Rhodomolleins F structure

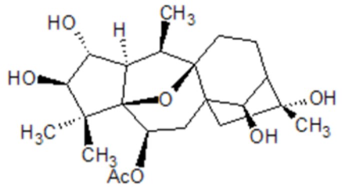

Figure 28: Rhodomolleins G structure

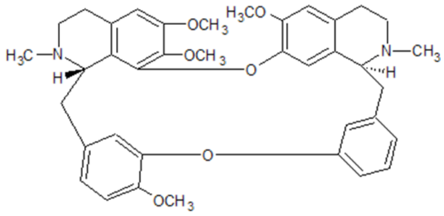

Figure 29: Tetrandrine structure ($C_{38}H_{42}O_6N_2$)

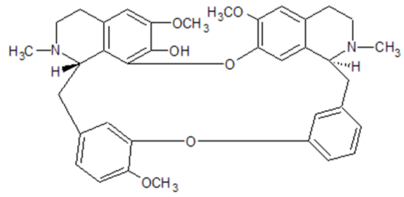

Figure 30: Fangchinoline structure ($C_{37}H_{40}O_6N_2$)

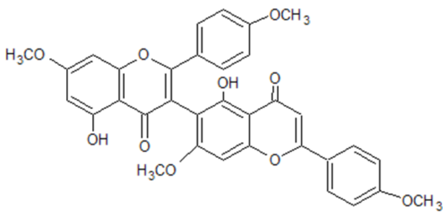

Figure 31: Stephaflavone A structure ($C_{34}H_{26}O_{10}$)

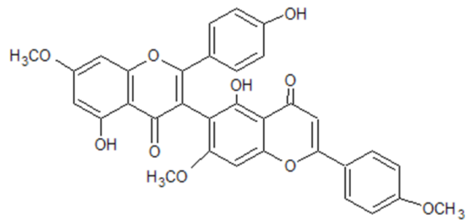

Figure 32: Stephaflavone B structure ($C_{33}H_{24}O_{10}$)

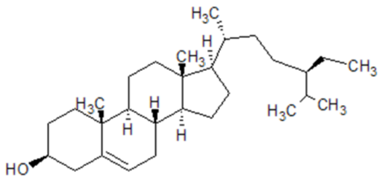

Figure 33: β-sitosterol structure

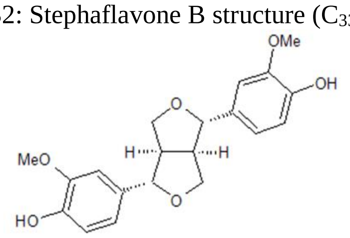

Figure 34: Pinoresinol structure

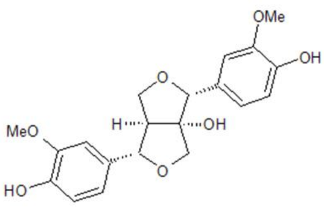

Figure 35: 8-hydroxypinoresinol structure

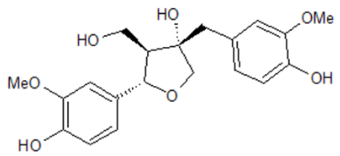

Figure 36: Olivil structure

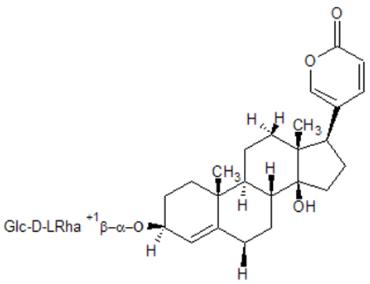

Figure 37: Scillaren A structure

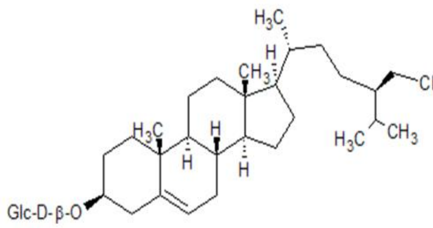

Figure 38: β-sitosterol 3-O-β-D-glucopyronoside structure

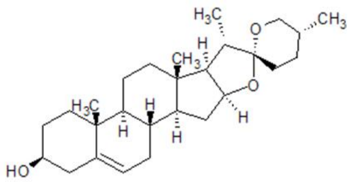

Figure 39: Diosgenin structure

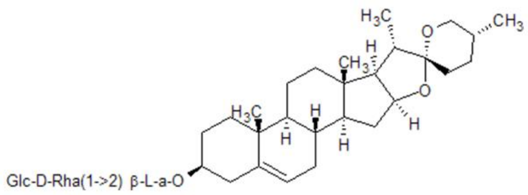

Figure 40: Diosgenin 3-O-α-L-rhamnopyranosyl-(1->2)-β-D-glucopyronoside structure

substances are also present in some food, drinks, nutritional supplements or teas.

Aesculus hippocastanum

Commonly known as horse chestnut[85,86]. This plant belongs to Hippocastanaceae family[85,87,88]. This plant contains gallic acid (Figure 20) and tannic acids being used in industrial applications[89]. Other compounds of this plant are flavonoids (mainly glycosides of quercetin and kaempferol) and coumarins (esculetol)[87]. This plant has been employed, more precisely the leaves of these plants, on venous insufficiency[87,89,90]. The leaves present hydroxycoumarin heterosides (esculosid, fraxoside); flavonoids (quercetol and kaempferol derivates); tannins; escin; phytosterols (sitosterol)[91]. By other side, the seeds of this plant have been used as treatment of heart diseases[89]. The fruit presents triterpenoid saponins 10% (mainly aescin (Figure 50)); coumarins (esculin and fraxetin); flavonoids (8 to 28%); tannins; pectin; mucilages; sugar; carbohydrates (40 to 50%) and glyceride oil[88,90,91]. Aescin is composed by triterpene saponins, which consist of A, B, C and D aescin[92]. The shells present hydroxycoumarin heterosides (2 to 3%, esculosid and fraxoside); flavonoids (kaempferol, free quercitin and heteroside quercitin); triterpenic saponosides (3 to 5%, escin); tannins and phytosterols[91].

This plant is traditionally used to treat varicose veins, venous congestion and chronic venous insufficiency[86,87,93]. This activity is caused by the acylated triterpene glycosides – saponins[93]. Escin (Figure 51) is a saponin present on this plant (seeds), is a mixture of more than 30 triterpene saponin isomers, that exists in two forms: α-escin and β-escin (they have different aqueous solubility, melting point, specific rotation and haemolityc index)[86,93]. Escin has pharmacological actions such as venotonic properties and possess an efficiency in prevention and treatment of vascular disorders[93]. Between venotonic properties they exist protective properties of capillary blood vessels (antiedematogenic, prevents fluid build-up) and anti-exudative (prevents the overflow of blood elements out of vessels)[86,91].

Allium cepa

Usually known by onion, her bulbous plants[94]. This plant belongs at Liliaceae family[95-97]. The compounds of this plant are: essential oil (substances from allicin hydrolyze); sulphurized compounds (allicin and cycle derivates of hexane and butane); fructosans between 10% to 40%; flavonoids (quercitin (Figure 52) and kaempferol (Figure 53)) mineral salts, carbohydrates (mono and disaccharides, pectin, inulin), amino acids, vitamins, enzymes and saponins of sterol nucleus[94,98]. The sulphurized compounds have an inhibitory action on platelet aggregation, hypotensive and other actions or effects[94]. The principal medical use is arterioscleroses prevention and hypertension by her hypotensive action[94]. This plant is also used on prevention of cardiovascular diseases (inhibition of cholesterol synthesis, platelet aggregation, arterial smooth muscle, cell proliferation)[96,98,99]. Others effects of this plant are anti-inflammatory, antioxidant and hydrogen sulfide-mediated vasodilator effects[96].

Allium sativum

Usually known by garlic, that is a bulbous plant[95,100,101]. This plants belong at same family that *Allium cepa*[95,100,102]. This plant has alliin that after hydrolyze, by allinase enzyme originating volatile products between them allicin and sulphides soluble in water (Figure 54)[95,100,103]. The principal bioactive compound is allicin (allyl 2-propenethiosulfinate or diallyl thiosulfinate)[95]. This compound is present in the aqueous extract garlic[95]. Others compounds are 1-propenyl allyl thiosulfonate, allyl methyl thiosulfonate, (E,Z)-4,5,9-trithiadodeca-1,6,11-triene 9-oxide (ajoene) (Figure 55) and y-L-glutamyl-S-alkyl-L-cisteine[95,103,104]. *Allium sativum* present also fructosans in 75%, reducing sugars (15%), mineral salts, saponin and vitamin A, B and C[100]. Fructosans has as principal effect a diuretic action[100]. Garlic obtained by freeze-drying has a minimum 0,45% of allicin[100]. The sulphurized compounds are responsible by a decrease of platelet aggregation and an increase of fibrinolytic activity[100]. These compounds are very soluble in water[100]. The substances on this plant has also a hypoglycemic effect; a decreased of cholesterol; antiseptic, fungicides and antiviral properties[95,100,102,104-106]. The principal use of this plant is a reduction of risk factors for cardiovascular diseases (prevention of thromboembolic events and hypertension)[95,96,99,100,102,104-106]. The preparations with garlic have been recognized as agents for prevention and treatment of cardiovascular diseases[95,99,104,106]. These parameters were demonstrated by *in vitro* studies[106]. The studies were demonstrated that garlic as an effect on lowering blood pressure, inhibition of platelet aggregation, reduction in systolic and diastolic pressures[95]. The oral ingestion of garlic extract in hypertensive animals was demonstrated a decrease of blood pressure until normal level[95]. Clinical studies showed a reduction of blood pressure in more than 80% of patients with hypertension[95]. A trial study on 47 hypertensive patients reveled a reduction of mean systolic blood pressure by 12mmHg and 9mmHg for diastolic blood pressure versus placebo[95]. The mechanism of antihypertensive activity is probably due of prostaglandin-like effects and by consequence they cause a decrease peripheral vascular resistance[95].

Citrus limon and Citrus sinensis

These plants are known by their fruits lemon and orange and are the third and the second most important Citrus species[107].

These plants are from Rutaceae family[108]. Pericarp of lemon has an essential oil, that is composed by dipentenes (70%) (α-pinen, β-pinen, citral, between others); coumarins; flavonoids carotenoids; mucilages; calcium oxalate and pectins[109]. Lemon plant present organic acids (ascorbic, citric, malic) and sugars[109,110]. This species *Citrus* has a beneficial effect on health particularly in prevention of cardiovascular diseases and in lowering blood lipid levels[107,108,111,112]. Other compounds are polyphenols (hydroxycinnamic acids (Figure 56) and vitamin C)[108,111]. Flavonoids are composed of two aromatic rings[107]. Flavonoids can be classified into six classes: flavones (Figure 57), flavanones (Figure 58), flavonols (Figure 59), isoflavones (Figure 60), anthocyanidins (Figure 61) and catechins (Figure 62)[18,107,108,111].

Flavanones are weak acids and they can be converted to isomeric chalcones in alkaline or acid media[107]. The principal flavanone is hesperidin (Figure 63) having an influence on vascular permeability[110]. Between flavones, diosmin is distinguished[110]. Diosmin (Figure 64) is an active ingredient of certain drugs that are used in treatment of several diseases of the circulatory system[110]. Flavonoids of lemon plant have a venotonic activity[109]. Lemon juice

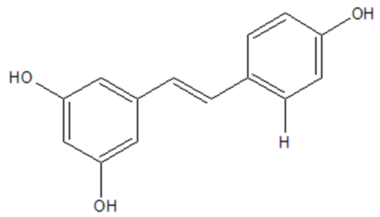

Figure 41: Resveratrol structure

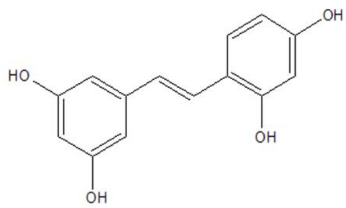

Figure 42: Oxyresveratrol structure

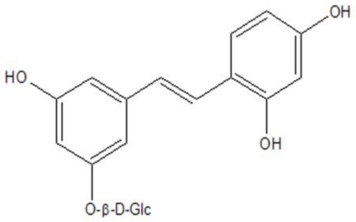

Figure 43: Oxyresveratrol 3-O-β-D-glucopyranoside structure

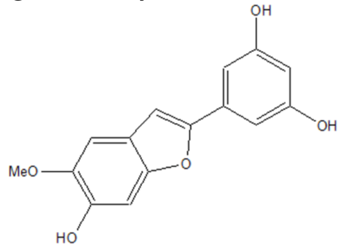

Figure 44: Wittifuran X structure

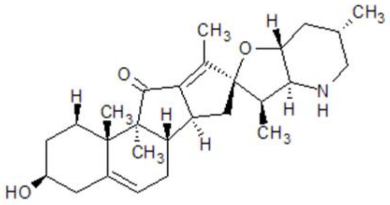

Figure 45: Jervine structure

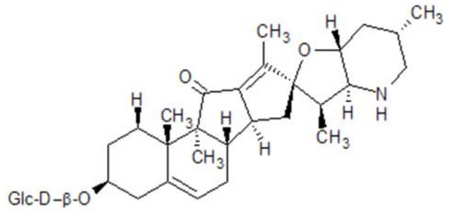

Figure 46: Pseudojervine structure

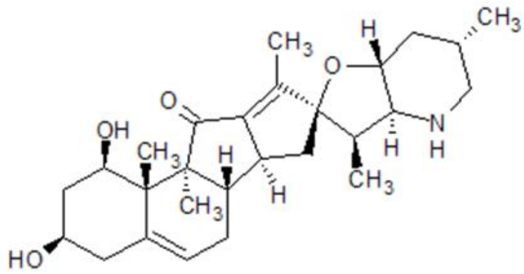

Figure 47:

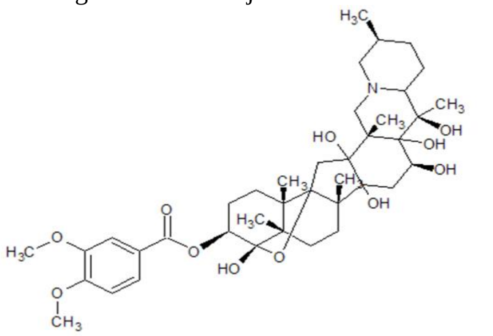

Figure 48: Veratridine structure

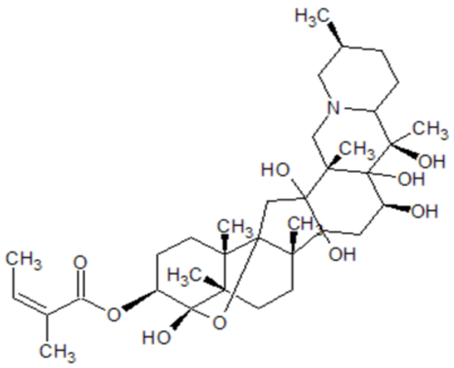

Figure 49: Cevanine structure

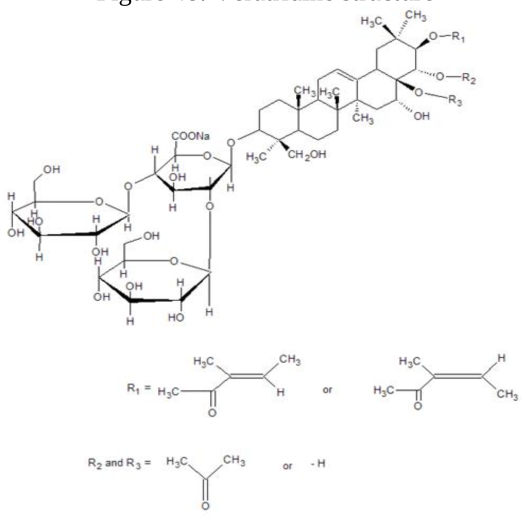

Figure 50: Sodium Aescinate structure

has an effect on blood pressure in treatment of hypertension like as clinical studies revealed[107,112]. Dietary flavonoid intakes and cardiovascular diseases have an inverse relationship like as epidemiological studies has revealed[18].

Coffea arabica and *Coffea liberica*

Usually known by her seeds, that supply commercial coffee[113]. *Coffea arabica* represents 70% of the world coffee production[113]. The substances present on this plant are purine bases as methylxanthine with presence of free and combined caffeine with chlorogenic acid[114]. Other constituents of this plant are phenolic acids (± 5%) like as caffeic acid (Figure 7), ferulic acid and esters of them; free diterpenes on carbohydrates forms and mineral salts[114,115]. By a study of Emure *et al.*, it was possible to identify other compounds like monoterpenes (geraniol; linalool and nerol); limonene; myrcene; β-ocimene; terpinolene and α-terpineol[113,115]. In the leaves of this plant it was identified

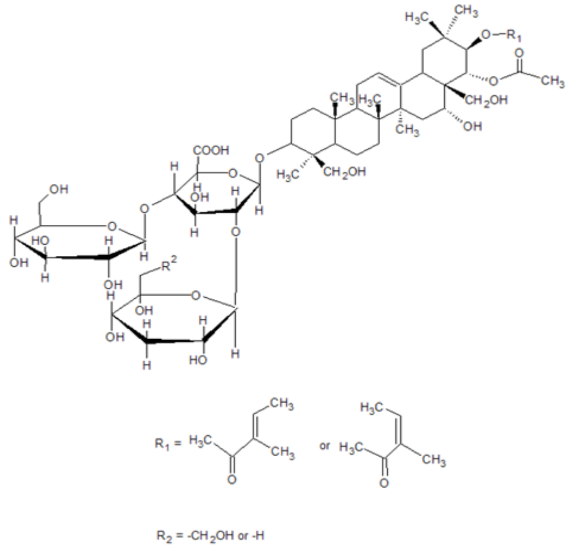

Figure 51: Escin structure

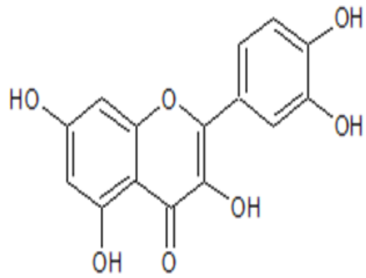

Figure 52: Quercetin structure

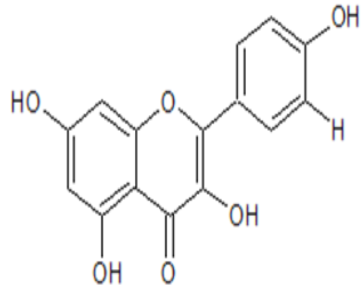

Figure 53: Kaempferol structure

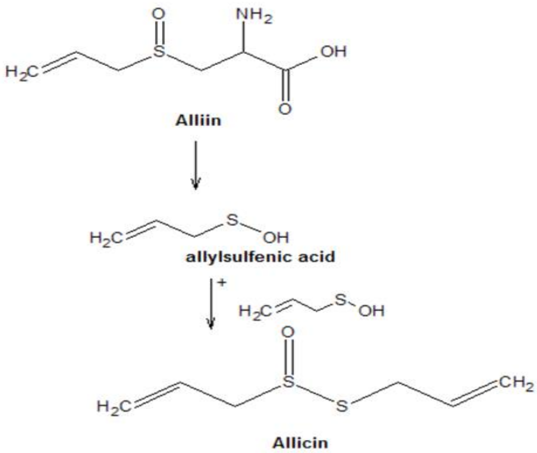

Figure 54: Metabolism of alliin

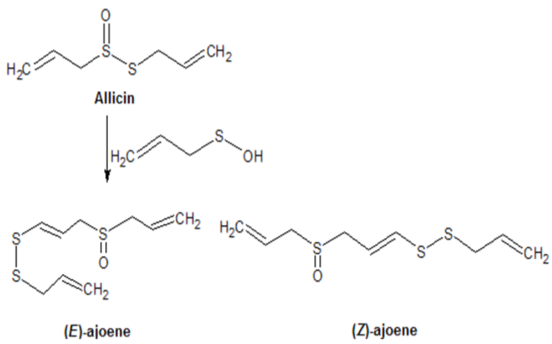

Figure 55: Metabolism of allicin

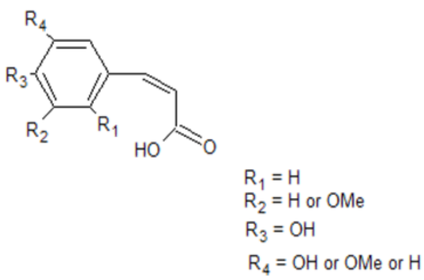

Figure 56: Hydroxycinnamic acids structure

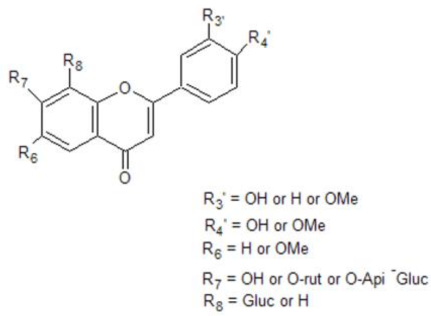

Figure 57: Flavones structure

anthocyanins (ANCs)[116]. On not roast seeds the chlorogenic acid is present in a rat e of 1 to 2,5% and a little quantity of purine bases as theobromine and theophylline[114]. By other side, on roast seeds are present aromatic compounds in a significant quantity and pigments with origin on carbohydrates, proteins and lipids that are formed over heating[114]. Caffeine is responsible by isotropic effect and on high concentrations, it causes a positive chronotropic effect on heart and is also a stimulant of SNC with delivery of catecholamine[114].

Corylus avellana

This plant belongs to the Betulaceae family[117-119]. This plant is known by her fruit, the hazelnuts[117,118]. This plant has nutritional and nutraceutical properties[120]. The compounds of this plant are tannins; flavonoids; essential oil; fat (mainly oleic acid); proteins; carbohydrates; dietary fibre; vitamins; minerals; phytosterols (mainly β-sitosterol) and antioxidant phenolics[120,121]. This plant has a venotonic action being used on varicose veins and edema caused by venous insufficiency[121-123]. Dietary fiber has an important therapeutic implication, as exhibit a protective effect against hypertension, chronic heart diseases[120]. The leaves of this plant contain phenolic compounds such as flavonoids, caffeic acid and diaryl ether heptanoids derivates (Figure 65; Figure 66 and Figure 67)[122].

Ginkgo biloba

The leaves of this plant are used as food in China, where is present 70% of ever Ginkgo of the World[124].

The substances present on her leaves are ginkgolides A (GA), B (GB), C (GC), J (GJ) and M; bilobalide (BB) (Figure 68)[125-127]. Ginkgolides are compounds with three lactonic cycles and a tetrafuran nucleus with a butyl radical[125]. She also has biflavonoids between 0,9% to 3,7% (ginkgetol; quercetin and kaempferol derivates); proanthocyanidins (Figure 69); carbohydrates; fat acids; phytosterols; proteins; vitamin C; riboflavin; isorhmnetin (Figure 70) and sesquiterpenes[124,125,127,128]. The extract contain flavonoids (22-24%) and terpene trilactones (5-7%)[127,128]. The compounds of extract increase blood flow through peripheral, cerebral blood vessels, reduce vascular permeability, selective antagonism of platelet activating factor, anti-ischemic and anticonvulsant[127,128]. This extract is used on cerebral vascular insufficiency and cardiovascular diseases[127]. This extract has a therapeutical application as an inhibition of platelet aggregation and stimulation the secretion of endothelial vasodilating factor[128]. The substances of this plant, increase the capillary resistance and tissues oxygenation; prevent the lipid peroxidation caused by free radicals; increase the resistance and decrease the vascular permeability[125]. She has also a peripheral vasodilator action and platelet aggregation[125].

Hordeum vulgare

This plant belongs to Poaceae family[129]. Until now, this plant is eaten by people as functional food[129]. It is present on beers, pasta and baked products[27,28,130]. This plant is known by her cereal grains (barley)[26]. The leaves of this plant has antioxidants (vitamin E, phytic acid, selenium, tocotrienols and phenolic acids) [26,129]. Barley contains phenolic compounds and vitamins[26]. Phenolic compounds include benzoic and cinnamic acid derivates, flavonoids (saponarin and lutonarin), proanthocyanidins (Figure 69), tannins and amino phenolic compounds; β-glucans and tocols[26,28,130]. As medicinal plant, it is used to protect against stroke and other diseases[129].

Melissa oficinallis

The leaves and flowers of this plant are usually consumed as an infusion[131]. This plant is from Lamiaceae family[131-133]. This plant is native from western Asia and southern Europe[132,134]. The substances present on this plant are flavonoids (luteolin-3'-*O*-glucuronide), phenol acids and esters, between them caffeic acid (Figure 7), rosmarinic acid (RA)[131,132,134,135].

Rosmarinic acid is a polyphenol, that is present in major quantity[132,133]. This compound is a potent antioxidant[133]. Sepand *et al.* studied that this compound inhibits oxidative stress and also apoptosis[133]. By another study (Dastmalchi *et al.*), revealed that this acid has a high anti-acetylcholinesterase activity[133]. The essential oil in a proportion between 0,02% to 0,2%, where are mainly 40%

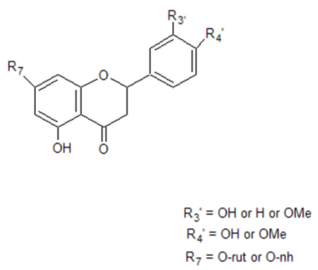

Figure 58: Flavanones structure

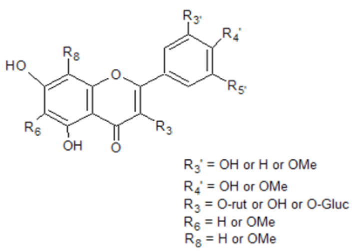

Figure 59: Flavonols structure

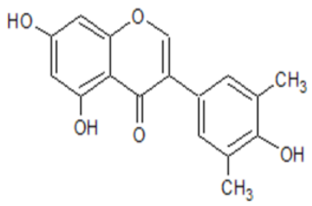

Figure 60: Isoflavones structure

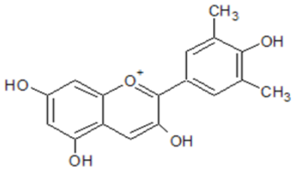

Figure 61: Anthocyanidins structure

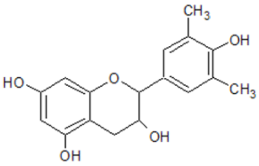

Figure 62: Catechins structure

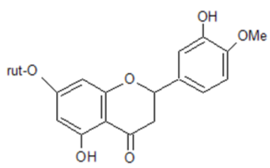

Figure 63: Hesperidin structure

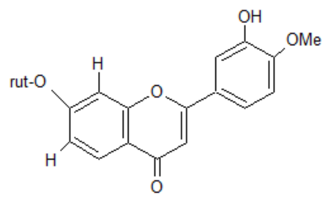

Figure 64: Diosmin structure

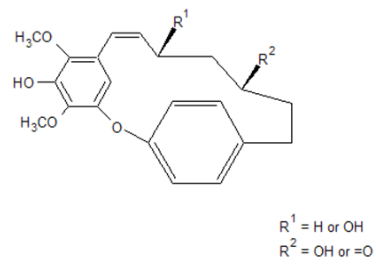

Figure 65 : Diaryl ether heptanoids derivates structure

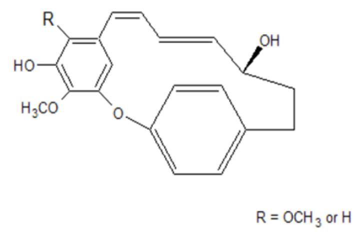

Figure 66: Diaryl ether heptanoids derivates structure

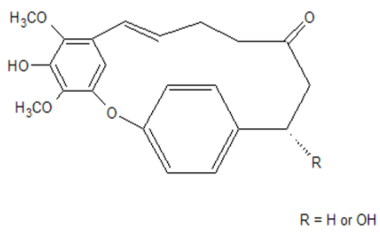

Figure 67: Diaryl ether heptanoids derivates structure

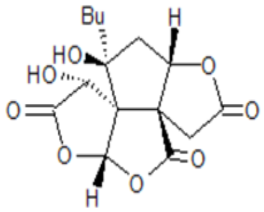

Figure 68: Bilobalide structure

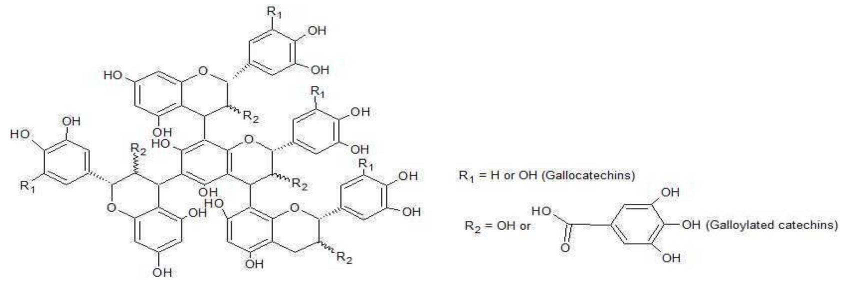

Figure 69: Proanthocyanidins oligomeric catechins structure

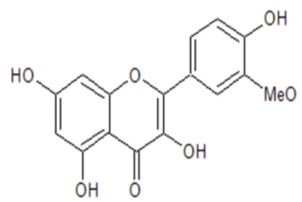

Figure 70: Isorhmnetin structure

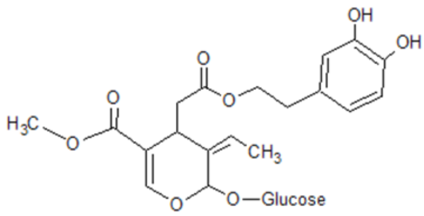

Figure 71: Oleuropein structure

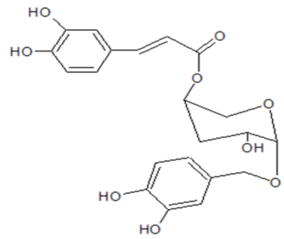

Figure 72: Verbascoside structure

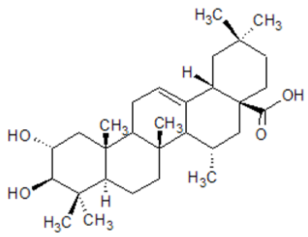

Figure 73: Maslinic acid structure

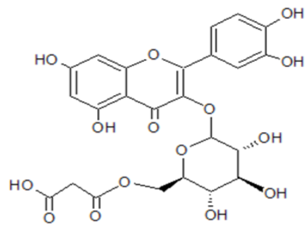

Figure 74: Quercetin-3-O-(6-malonyl)-glucoside structure

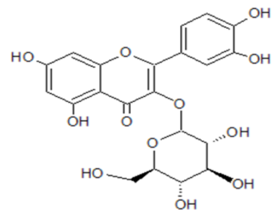

Figure 75: Quercetin-3-O-glucoside structure

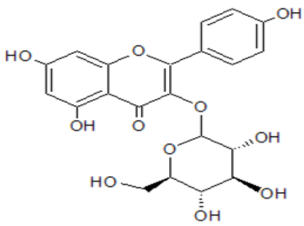

Figure 76: Kaempferol-3-O-glucoside structure

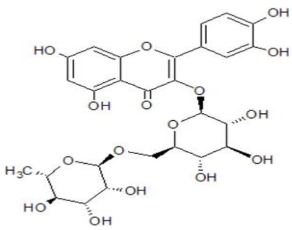

Figure 77: Quercetin-3-O-rutinoside structure

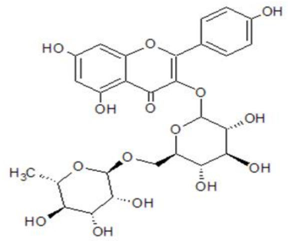

Figure 78: Kaempferol-3-O-rutinoside

monoterpenic aldehydes (citronellal and citral), others monoterpenes (linalool, geraniol, citronellol and α-terpineol) and 35% of sesquiterpenes (β-caryophyllene and germacrene D) and poliuronic mucilage[132-134]. The extract of this plant have an anticholinesterase activity[133]. This plant has as medical uses: hypertension, tachycardia and others[131,134]. Also, used for treatment of palpitation whatever it is the fraction[133].

Olea europea

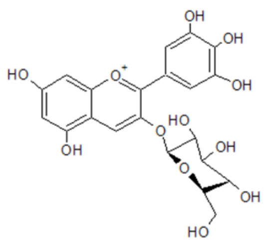

Figure 79: Delphinidin 3-glucoside structure

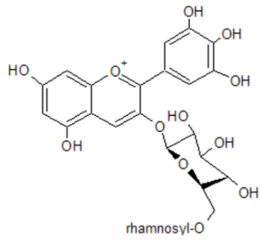

Figure 80: Delphinidin 3-rutinoside structure

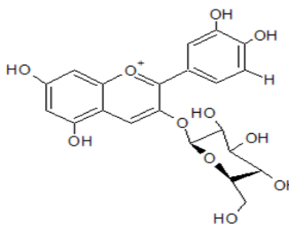

Figure 81: Cyanidin 3-glucoside structure

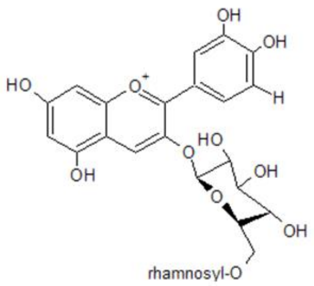

Figure 82: Cyanidin 3-rutinoside structure

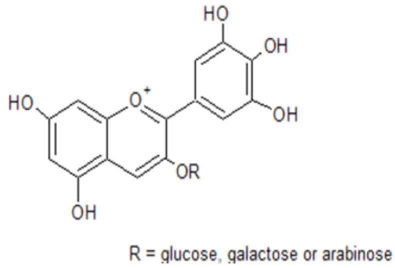

Figure 83: Delphinidin structure

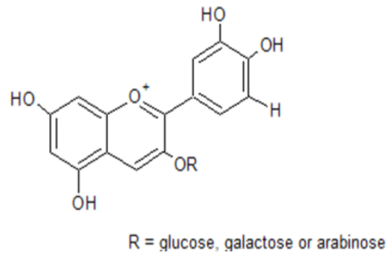

Figure 84: Cyanidin structure

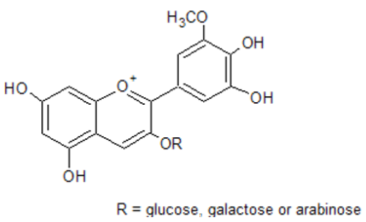

Figure 85: Petunidin structure

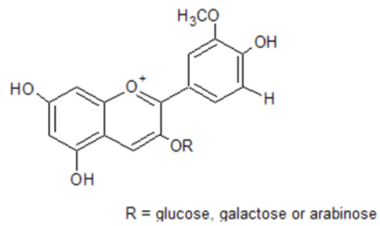

Figure 86: Peonidin structure

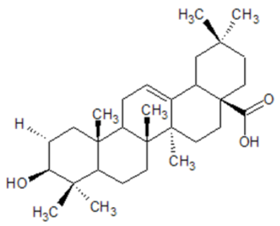

Figure 87: Oleanolic acid structure

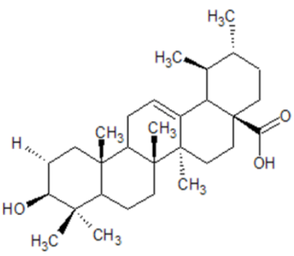

Figure 88: Ursolic acid structure

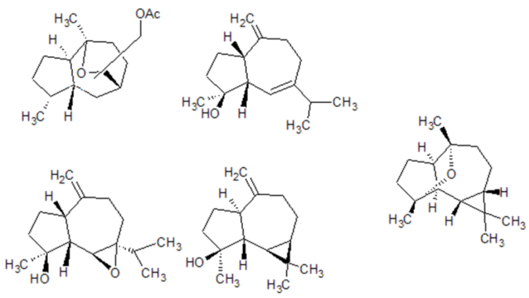

Figure 89: Sesquiterpenoids structures

This plant is usually known by her fruits, olives. This plant belongs to the Oleaceae family[136]. The olives tree contain bioactive compounds: oleuropeosides (oleuropein (Figure 71) and verbascoside (Figure 72)); flavonoids (luteolin, luteolin-7-O-glucoside, apigenin-7-O-glucoside, diosmetin-7-O-glucoside, diosmetin, rutin and catechin); simple phenolics (tyrosol, hydroxytyrosol, vanillin, vanillic acid and caffeic acid)[137-139]. Bourquelot and Vintilesco discovered oleuropein, in 1908[22]. Oleuropein can be act on the inhibition of platelet aggregation[22]. The leaves of olive tree present natural antioxidants (polyphenols, tocopherols and pigments) and phenolic compounds such as demethyloleuropein, oleuroside, verbascoside, non-glycosidic secoiridoids, ligstrosides, flavonoids and biflavonoids[137,140,141]. Olives has pentacyclic triterpenes such as oleanolic and maslinic acids[142]. Maslinic acid (Figure 73) is a natural triterpenoid[142]. This compound correspond for 80% of the wax in the olive skin, being an antioxidant[142]. Olive oil has fatty acids, polyphenols and sterols[143]. The consumption of this oil has been associated with the decrease of incidence of cardiovascular diseases in the Mediterranean area[143]. Virgin olive oil has a high content of phenolic compounds, α-tocopherol, carotenoids and monounstarurated fatty acids, oleic and linoleic acid[141]. Olive leaf extract has the capacity to lower blood pressure in animals and increased blood flow in the coronary arteries relieved arrhythmia[22].

Passiflora spp.

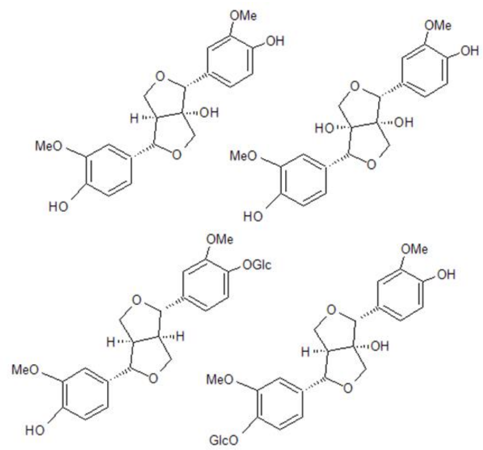

Figure 90: Lignans structures

Usually known by passion fruit, her fruit that can be consumed as fresh fruit, juice industries also is a natural resource for the pharmaceutical industries[144]. This plant belongs to Passifloraceae family[144]. Fruits have sugars (sucrose, glucose and fructose), ascorbic acid, organic acids and phenolic compounds (secondary metabolites naturally)[145]. Juice has essential nutrients as micronutrients such as minerals, fiber, phenolic compounds and ascorbic acid[145]. Phenolic compounds are responsible by reducing the risk of cardiovascular diseases[145]. Other compounds of this plant are alkaloids, phenols, cyanogenic compounds, glycosyl flavonoids, maltol, ethyl maltol, flavones (apigenin and luteolin) and antioxidant compounds (phenolic compounds, ascorbic acid, carotenoids and flavonoids) [13,146]. Phenolic compounds has an antioxidant action that improve endothelial function and normalize vascular tone resulting in antihypertensive effect[13]. This plant has also quercetin and caffeic acid[13]. This two compounds have been demonstrated an antihypertensive action on *in vivo* studies, being this effect related to their antioxidant activities[13]. However, the molecular mechanisms responsible by these effects are not fully known[13]. Studies revealed that this plant has an antihypertensive activity[13]. Another compound that can contribute to decreasing blood pressure is γ-aminobutyric acid, also present in this plant[13].

Ribes Nigrum

Usually known by black currant, her berries[147-149]. The substances present on her leaves are flavonoids (hyperoside, glucosides of quercetin and of kaempferol (quercetin-3-O-(6-malonyl)-glucoside (Figure 74); quercetin-3-O-glucoside (Isoquercitrin) (Figure 75); kaempferol-malonyl-glucoside; kaempferol-3-O-glucoside (Figure 76), quercetin-3-O-rutinoside (rutin) (Figure 77) and kaempferol-3-O-rutinoside (Figure 78))), a little quantity of essential oil, tannins, vitamin C and mineral salts[147,149]. The substances present on fruits are anthocyanosides at 0,3%; flavonoids; pectin; tannins; a high level of vitamin C, potassium salts, carbohydrates (10% to 14%) and organic acids[147,149]. This plant has ANCs (delphinidin 3-glucoside (Figure 79); delphinidin 3-rutinoside (Figure 80); cyanidin 3-glucoside (Figure 81) and cyanidin 3-rutinoside (Figure 82))[148]. The essential oil is mainly composed by α-pinene; sabinene; δ-car-3-ene; β-phellandrene; terpinolene and β-caryophyllene[150]. The oil present on seeds have an action as a platelet inhibitor and increase the anticoagulant effect by inhibition of fibrin formation[11]. This plant has also an action on serum lipid profile like an increase of HDL-cholesterol level and a decrease of triglyceride or total cholesterol[11]. The phenolic compounds have a vasomodulatory effect[149]. This plant is used at hypertension by compounds of leaves and capillary fragility by anthocyanosides action[11,147]. Some extracts are used in treatment of cardiovascular disorders and are reported to be free radical scavengers[148]. The oral administration of ANCs were found as intact anthocyanin glycosides in the blood[148].

Vaccinium myrtillos

This plant belongs to the family Ericaceae[151]. Usually known by wild blueberries, her fruits[152]. The fruit of this plant are tannins (about 10%), mainly soluble in water; oligomeric procyanidins; ANCs pigments (0,5%) by heterosides forms (delphinidin (Figure 83), cyanidin (Figure 84), petunidin (Figure 85), peonidin (Figure 86) and malvidin); organic acid; carbohydrates (oses, inositol); pectin; carotenes; flavonoids (rutin (Figure 77))[151-153]. This plant is a good natural source of ANCs[154]. The fruits have properties of vitamin P of ANCs, flavonoids pigments, phenolic compounds other than flavonoids (flavonols, phenolic acids and pro-anthocyanidins) and vitamins C and E that increase and decrease of capillary permeability[14,151,152,154]. They are medical use at venous insufficiency by varicose veins and hemorrhoids[152]. The leaves present tannins (between 5% and 10%); flavonoids (quercetin derivates); triterpenic acids (ursolic, oleanolic) (Figure 87 and Figure 88); phenolic acids and iridoids; ANCs pigments; mineral salts (iron, magnesium and chromium) and quinolizidine alkaloids[151,152,154]. Other compounds of this plant are catechins, pectins, myricetin, caffeic acid and ρ-coumaric acid[151]. Pharmacological studies have shown an effective treatment for vascular disorders[151,154]. Others studies shown that ANCs are responsible for a decrease of blood pressure in models of hypertension[14]. Mykkänen *et al.* study demonstrated that this plant can prevent the development of hypertension in a dose dependent manner[14].

Valeriana officinalis

Usually known as valerian, used as perfume added into food and drinks[155-157]. This plant is a member of Valerianaceae family, used as herb medicine[155]. Phytochemical compounds present in this plant are iridoids, sesquiterpenoids (guaiane-type: valerol A and kessyl 3-acetate) (Figure 89), flavone glycosides, lignans (Figure 90) and alkaloids[158]. Other compounds of this plant are madolin A, isobicyclogermacrenal, kissoone B and C, volatile oil, amino acids, germacrane-type sesquiterpenoids (volvalerenals A-G, volvalerenic acids A-D, valerianin A-B and heishuixiecaoline A-C) [156,158]. The mainly compounds are valepotriates, sesquiterpenes hydrocarbons (34,10%), monoterpene hydrocarbons (27,88%), oxigenated sesquiterpenes (18,14%), patchoulol (16,75%), α-pinene (14,81%), oxygenated monoterpenes (9,38%), β-humulene (8,19%) and α-bulnesene (7,10%)[159].

Roots and rhizomes has sesquiterpenes of the volatile oil (valerenic acid and its derivates, valeranone, valeranal, kessyl esters) and valepotriates (valtrate, didrovaltrate, acevaltrate, isovaleroxyhydroxyvaltrate), flavonoids, triterpenes, lignans and alkaloids[157]. Essential oil contain monoterpenes, sesquiterpenes and their oxygenated derivates[159]. Oil has as major compounds calarene (25,31%), aristolone (13,35%), α-selinene (7,32%), β-maaliene (6,70%) and spathulenol (6,28%)[159]. Animal and clinical studies has been demonstrated that this plant has a pharmacological activity[157]. This plant has been used in treatment of hypertension, agitation, palpitation and for others diseases[157]. Some extracts of this plant can cause coronary and systemic vasodilatation, possessing a coronary dilatory and hypotensive properties[157].

CONCLUSION

We can conclude that the substances in these plants have a therapeutic effect in cardiovascular diseases like as: hypertension, atherosclerosis and stroke, between others. By other side, we can conclude that principal compounds are flavonoids; antioxidants (action in oxidative stress); ouabain; cardenolide glicosides; lanatosides; tannins; sesquiterpenoids and phenolic compounds. Phytochemicals are present in fruits and vegetables, it is important the consumption of this products in meals by all benefices that they have. The consumption it is also important by the effects in protection of cardiovascular diseases mainly because these diseases are the first cause of death in world.

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