OXIDANTS AND HUMAN DISEASES: ROLE OF ANTIOXIDANT MEDICINAL PLANTS - A REVIEW.

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Summary

Free radical production occurs continuously in all cells as part of normal cellular function. However, excess free radical production originating from endogenous or exogenous sources might play a role in many diseases. However, due to many environmental, lifestyle, and pathological situations, excess radicals can accumulate, resulting in oxidative stress. Oxidative stress has been related to cardiovascular disease, cancer, and other chronic diseases that account for a major portion of deaths today. Antioxidants are compounds that hinder the oxidative processes and there by delay or prevent oxidative stress. This article examines the process of oxidative stress and the pathways by which it relates to many chronic diseases. We also discuss the role that endogenous and exogenous antioxidants may play in controlling oxidation and review the evidence of their roles in preventing disease. In this review, we highlighted list of some major role of medicinal plants with potent antioxidant activity have been reviewed against chronic diseases induced by oxidative stress.

Keywords: Free radical; Reactive oxygen species; Human diseases; Antioxidant; Medicinal plants

Introduction

Oxygen is an element indispensable for life. When cells use oxygen to generate energy, free radicals are formed as a consequence of adenosine triphosphate (ATP) production by the mitochondria. These by-products are generally called as Reactive Oxygen Species (ROS) as well as Reactive Nitrogen Species (RNS) that result from the cellular redox process. At lower concentrations or moderate levels, ROS & RNS exert beneficial effects as cellular response and immune function. At high concentrations, they generate oxidative stress, a deleterious process that can damage all cell structures [1-6]. Oxidative stress plays a major role in the development of chronic and degenerative diseases such as cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurodegenerative disorders.

Reactive oxygen species (ROS) and Reactive Nitrogen Species (RNS) are the terms collectively explaining free radicals and other non-radical reactive derivatives also called as oxidants. Radicals are less stable than non-radical species, but their reactivity is generally stronger.
A molecule with one or more unpaired electron in its outer shell is called as free radical [1]. Free radicals are formed from molecules via the breakage of a chemical bond such that each fragment keeps one electron, by cleavage of a radical to give another radical and also via redox reactions. Free radicals includes hydroxyl ($OH^{\cdot}$), superoxide ($O_2^{\cdot-}$), nitric oxide ($NO^{\cdot}$), nitrogen dioxide ($NO_2^{\cdot}$), peroxyl ($ROO^{\cdot}$) and lipid peroxyl ($LOO^{\cdot}$). Also hydrogen peroxide (H_2O_2), ozone (O_3), singlet oxygen ($^{\cdot}O_2$), hypochlorous acid (HOCl), nitrous acid (HNO_2), peroxy nitrite ($ONOO^-$), dinitrogen trioxide (N_2O_3), lipid peroxide (LOOH) are called oxidants, but can easily lead to free radical reactions in living organisms [7]. Biological free radicals are highly unstable molecules that have electron available to react with various organic substrates such as lipids, proteins and DNA. In this review, the role of free radicals in these diseases has been briefly reviewed. Plants with potent antioxidant activity have been reviewed for their parts and active constituents.

Oxidative stress and human diseases

Cancer

The development of cancer in human is a complex phenomenon including cellular and molecular changes mediated by diverse endogenous and exogenous stimuli. It is well established that oxidative DNA damage is responsible for cancer development [8]. Cancer initiation and promotion and oncogene activation induced by free radicals. A common form of damage is the formation of hydroxyl bases of DNA which are considered an important event in chemical carcinogenesis [1]. Oxidative DNA damage also produces a multiplicity of modifications in the DNA structure including base and sugar lesions, strand breaks. DNA-protein cross links and base-free sites. The highly significant correlation between consumption of fats and death rates from leukemia, breast, ovary and rectum cancers among elderly patients may be a reflection of greater lipid.

Pulmonary diseases

There is now substantial evidence that inflammatory lung diseases such as asthma and chronic obstructive pulmonary disease (COPD) are characterized by systemic and local chronic inflammation and oxidative stress [9-12]. Oxidants may play a role in enhancing inflammation through the activation of different kinases and redox transcription factors such as NF-kappa B and AP-1 [11,12].

Nephropathy

Oxidative stress plays an important role in a variety of renal disorders such as glomerulonephritis and tubulointerstitial nephritis, chronic renal failure, proteinuria and uremia [3,13]. The nephrotoxicity of certain drugs like cyclosporine, gentamycin, bleomycin, vinblastin is mainly due to oxidative stress via lipid peroxidation [14].

Ophthalmic Disorders

Oxidative stress is implicated in age related macular degenerative disorder and cataracts by altering various cell types in the eye either photochemically or non-photochemically [15]. Under the action of free radicals, the crystalline proteins in the lens can crosslink and aggravate, leading to the formation of cataracts. In the retina, long term exposure to radiation can inhibit mitosis in the retinal pigment epithelium and choroids, damage the photoreceptors outer segment and has been associated with lipid peroxidation [16-17].

Arthritis and inflammation

Rheumatoid arthritis is an autoimmune disorder characterized by chronic inflammation by the joints with infiltration of macrophages and activated T cells [18-19]. The pathogenesis of the disease is due to the generation of nitric oxide along with superoxide and the products of their interaction. Likewise, the neutrophils too produce oxidants and release granular constituents comprising of lytic enzymes performing important role in inflammatory injury [20]. Oxidative damage and inflammation in various rheumatic diseases were proved by increased levels of isoprostanes and prostaglandins in serum and synovial fluid compared to controls [19].

Cardiovascular diseases

Cardiovascular disease is of multifactorial etiology associated with a variety of risk factors for its development including hypercholesterolemia, hypertension, smoking, diabetes, poor diet, stress and physical inactivity [21-22]. Evidence suggests that damage to the myocardial cell induced by the cycle of ischemia and reperfusion may be due to the generation of toxic reactive oxygen species such as superoxide radical, hydrogen peroxide and the hydroxyl radical [23-25]. Nitric oxide (NO) has recently emerged as an important mediator of cellular and molecular events which impacts the pathophysiology of myocardial ischemia. Recently have been reported that nitric oxide and peroxy nitrite could contribute to cardiac dysfunction in situation such as hypoxia/reoxygenation [26].

The importance of oxidative stress in the development of atherosclerosis seems to be widely accepted. The statement that free radicals are involved throughout the atherogenic process, beginning from endothelial dysfunction up to the rupture of a lipid rich atherosclerotic plaque leading to acute myocardial infarction or sudden death has been reported [27].

Superoxide radical, hydrogen peroxide, hydroxyl radical and oxidized low density lipoproteins may play a critical role in the pathology of hypertension as well in other conditions such as atherosclerosis, reperfusion injury and myocardial infarction. However the relationship between oxygen free radicals and essential hypertension has received relatively limited attention [28].

Neurodegenerative disorders

Oxidative stress has been investigated in neurological diseases including Alzheimer's disease, Parkinson's disease, multiple sclerosis, memory loss and depression [29-32]. In disease such as Alzheimer's, numerous experimental and clinical studies have demonstrated that oxidative damage plays a key role in the loss of neurons and the progression to dementia. The production of β-amyloid, a toxic peptide often found present in Alzheimer's patient's brain, is due to oxidative stress and plays an important role in neurodegenerative process. The neuropathological changes observed during brain injury, trauma, stroke, and epileptic associated brain damage have all been ascribed to enhanced oxidative stress and related lipid protein and DNA molecules. This has been well demonstrated in severe experimental animal model systems. Kainic acid (KA) is an agonist of NMDA receptor, and the systemic administration of this drug resulted in the brain injury. The successive release of this excitatory amino acid neurotransmitter glutamate and oxidative stress are two mechanisms through which kinate induces brain injury. Kainic acid binds with and stimulates a subtype of ionotropic receptor that results in transmembrane ionic imbalance causing increased calcium influx. This results in cascade of events like activation of protein kinase, phospholipases, protease nitric oxide synthetases, all leading into impairment of mitochondrial function and release of oxygen free radicals. These free radicals attack lipid protein and DNA molecules causing extensive lipid peroxidation, structural and functional changes of protein molecules causing loss of enzyme activity, DNA strand breaks, nuclear fragmentation and neuronal damage.

Diabetes

It gas been postulated that the etiology of the complications of diabetes involves oxidative stress perhaps as a result of hypoglycemia. Glucose itself and hyperglycemia-related increased protein glycosylation are important sources of free radicals. Elevated glucose causes slow but significant non-enzymatic glycosylation of proteins in diabetes. Glucose auto-oxidize in the presence of transition metal ions generating oxygen free radicals, which make the membrane vulnerable to oxidative damage. The significance of oxidative stress in the disease pathology is uncertain but is frequently proposed to be related to hyperglycemia[20].

Diseases in premature infants

Premature infants are probably developmentally unprepared for extrauterine life in an oxygen rich environment and exhibit a unique sensitivity to oxidant injury. Diseases associated with premature infants, including bronchopulmonary dysplasia, periventricular leukomalacia, intraventricular hemorrhage, retinopathy of prematurity and necrosizing enterocolitis have been linked to free radical mediated cell and tissue injury [33].

Pathophysiology of male reproduction

The excessive generation of reactive oxygen species by abnormal spermatozoa and contaminating leucocytes has been defined as one of the few etiologies for male infertility. Administration of antioxidants in patients with 'male factor' infertility has begun to attract considerable interest. Mammalian spermatozoa membranes are very sensitive to free radical induced damage mediated by lipid peroxidation, as they are rich in poly unsaturated fatty acids. Reactive oxygen species attacks the fluidity of the sperm plasma membrane and the integrity of DNA in the sperm nucleus. ROS induced DNA damage accelerate the germ cell apoptosis [34].

Gastrointestinal disorders

Peptic ulcer and gastritis has multietiopathological factors. It is widely accepted that a major underlying factor of this disorder is the generation of free radicals. There is substantial evidence that oxygen derived free radicals plays an important role in the pathogenesis of the injury of various tissues, including the digestive system [35-36]. In addition, involvement of oxygen derive free radicals such as superoxide anion, hydrogen peroxide and hydroxyl radical are well established in the pathogenesis of ischemic injury of gastrointestinal mucosa [37]. The lipoxygenase pathway and the activated inflammatory cells could be involved in the pathogenesis of mucosal damage. Gastric mucosal cells metabolize arachidonic acid via both the cyclo-oxygenase and lipoxygenase pathways and the presence of inflammatory cell infiltrates in the gastric mucosa [37].

Antioxidants

Till date as such no set definition of antioxidants exists. Scientists are still striving hard to find out the role of particular dietary supplements in body that have potent health benefits. Since, different antioxidant compounds found in diet considerably vary from one another; it is a difficult task to identify the role of a single compound. In simple words, *"Antioxidants are a type of complex compounds found in our diet that act as a protective shield for our body against certain disastrous enemies (diseases) such as arterial and cardiac diseases, arthritis, cataracts and also premature ageing along with several chronic diseases. "*

The above definition gives an idea about what actually an antioxidant is as still a lot of work has to be carried on getting exact information about antioxidants, their exact amount in one's diet and their function. The recent researches on free radicals promise a revolutionary improvement in health and life-style of humans.

Types of antioxidants: Basically these are classified into three categories

Enzymatic and Non-enzymatic antioxidants: They are found both in extra cellular as well as intracellular environment. These are tactically arranged within the cell in order to provide maximum protection against free radicals.

Antioxidant derived from natural and dietary sources: Plants develop several antioxidants that aid in antioxidant defense system, protecting plants against damage caused by active O_2 formed due to exposure to ultraviolet radiation. Certain seaweeds also function as antioxidants. Our daily diet contains vegetables, fruits, tea, wine, etc. which possess compounds rich in anti oxidative properties.

Antioxidants from natural sources

Secondary products of plants which are functioning as antioxidant are

i. Chlorophyll derivatives
ii. Essential oils
iii. Carotenoids
iv. Alkaloids
v. Phytosterols
vi. Phenolics- coumarines, flavonoids
vii. Polyphenolics - tannins, proanthocynidine
viii. Nitrogen containing compounds- alkaloids, indoles.
ix.

Dietary antioxidants: These reduce the free radical formation as well as oxidative stress & reduce the possibility of cardiovascular diseases. Several compounds such as phenolic diterpenoids- camosol, rosmanol, camosoic acid, etc. obtained from several aromatic plants possess strong antioxidant properties [38-39].

Antioxidants based on defense mechanism: *These* are of four types:

a. Preventive antioxidants - These suppress the free radical formation. ex. Enzymes such as peroxidase, catalase, lactoferrin, carotenoids, etc.
b. Radical scavenging antioxidants - These suppress the chain initiation reaction. ex Vitamin-C & Carotenoids.
c. Repair and de novo antioxidant- It comprise of proteolytic enzymes and repair enzymes of DNA and genetic materials.
d. Enzyme inhibitor antioxidants- These induce production and reaction of free radicals and the transport of appropriate antioxidants to appropriate active site.

Functions of Antioxidants:-

i. Antioxidants such as Vitamin-C & E boost immune system.
ii. Certain phytochemicals have beneficial effect on heart diseases.
iii. Antioxidants lower the level of Low-density lipoprotein (LDL) cholesterol, thus preventing plaque deposition in the blood vessels.
iv. It is beneficial in cancer prevention.
v. Antioxidants neutralize substances that can damage the genetic material by oxidation.

Compounds that function as Antioxidants

Vitamins

Vitamin C - It prevents free radical damage due to its property of donating free radicals. It is beneficial in boosting immune system. The main source of Vitamin-C is carrots, peaches, sweet potatoes, oranges, broccolis, etc [40].
Vitamin E - Both plants and animals serve as a source of vitamin E. It has been found beneficial against certain types of cancer & cardiac problems. It is known as *'scavenger of free radicals'*. Vitamin E is mainly present in nuts, whole cereal grains, almonds, vegetable oils etc.
Phytochemicals- Plants contain certain chemicals such as carotenoids, flavonoids, biflavonoids, phenols, phytosterols, etc. that possess antioxidative properties.
***Carotenoids* -** These are a group of antioxidant nutrients present in many fruits and vegetables and are found effective if taken with dark coloured fruits such as carrots, tomatoes, beets, etc. These are further composed of α- carotene, β- carotene, Cryptoxanthin, Lycopene, Lutein & Zeaxanthin. They are present in red, dark orange & yellow fruits such as carrots, peaches, broccoli, pumpkins, sweet potatoes etc
***Flavonoids* -** Plants contain flavonoids like quercetin, kaempferol which scavenge free radicals and combat pathological disorders generated by Reactive Oxygen Species (ROS).
Phenols - Prevent oxidative damage of tissues from ROS of DNA, RNA, enzymes and proteins and has anti-inflammatory properties.
Minerals - Selenium is an essential component of several enzymes that prevent free radical formation & their removal from blood stream. It occurs in grains, low-fat dairy products, poultry, organ meat, seafood etc.

Behavior of Antioxidants
The free radicals play very important role in human health and beneficial in combating against several diseases. Before we understand the working, it is necessary to have a brief idea about free radicals. During a chemical reaction (oxidation), one reactant loses an electron and is called oxidant or free radical, while the other gains an electron. In living organisms oxygen in unstable form is the most common free radical. This is called Reactive Oxygen Species (ROS) and is generated during various metabolic activities. Contaminants in the environment as well as normal metabolism of a cell can change molecule into a free radical. The examples of ROS are OH, O_2, H_2O_2, O_3, HOCl, RO_2, and RO. Any molecule can become a free radical by either losing or gaining an electron. One initiated these free radicals get involved in chain reaction with stable types. The compounds thus formed have longer stability and in body and increase the potential for cellular damage. Free radicals damage the cell at the site of their operation causing serious disorders. Plaque may accumulate in arteries on oxidation. LDL Cholesterol functions as free radical and damages the free artery lining. It hampers the blood circulation which may lead to heart attack. However termination or neutralization of free radicals is achieved by antioxidants or enzymatic mechanism [41]. It is necessary to balance the free radical & antioxidant activity.

Requirement of antioxidants in the body
A number of processes are taking place in our body like breathing, breaking up of protein in the body or exposure of body to air pollution or UV radiation leads to the formation of free radicals that aid in the process of oxidation which further leads to several health problems. If the body is healthy it is capable enough to break down these free radicals before they become harmful. In case, the formation of the free radicals exceeds in the body, it can damage the cells and tissues.

This damage can be counteracted by antioxidants which prevent the free radical formation and if the formation occurs it helps in their removal from blood stream. Thus antioxidants play potentially beneficial role in the risk reduction and treatment of diseases.

Medicinal plants with antioxidant activity

Since time immemorial man has been using plant extracts to protect himself against several diseases and also to improve his health and life-style. No doubt, plants are serving several purposes whether health, nutrition, beauty or medicinal. With the development in techniques and recent researches, it has been proved that certain non-nutritive chemicals in plants such as terpenoids and flavonoids which were earlier thought to be of no importance to human diet possess antioxidant properties. The plants are susceptible to damage caused by active oxygen and thus develop numerous antioxidant defense systems resulting in formation of numerous potent antioxidants. Many aromatic, medicinal and spice plants contain compounds that possess confirmed strong antioxidative components. In traditional medicine, several plants and herbs have been used to treat free radical mediated diseases. Experimental evidence suggests that free radical and reactive oxygen species can be involved in high number of disease. As plants produce a lot of antioxidants to control the oxidative stress caused by sunbeams and oxygen, they can represent a source of new compounds with antioxidant activity. Number of herbal drugs has been reported to possess antioxidant activity (Table 1). In conclusion, the present review provided more information about medicinal plants having antioxidant properties. However, more detailed analytical information on the constituents mediating the observed biological effects are needed prior the promotion or development of effective and safe medicinal plants.

Table 1. List of medicinal plants and their antioxidant properties

Botanical Name (Family)	Plant parts used	Name of Extract	Active constituents	Ref
Lycopus lucidus Turcz (Lamiaceae)	Aerial Parts	Methanol	Flavonoids, Coumarins, Terpenoids and Tannins	[42]
Caesalpinia bonducella (Caesalpiniaceae)	Seeds	Ethanol	Phenolic compounds	[43]
Stevia rebaudiana Bert. (Asteraceae)	Leaves	Ethanol	Phenolic acids, flavonoids and tannins	[44]
Carduus pynocephalus L. (Asteraceae)	Stems	Hydro alcohol	Phenols, sterols, flavonoids	[45]
Cichorium intybus L. (Asteraceae)	Leaves and roots	Hydro alcohol	Phenols, sterols and flavonoids	[45]
Cynara cardunculus L. (Asteraceae)	Leaves	Hydro alcohol	Phenols, sterols and flavonoids	[45]
Echium vulgare (Boraginaceae)	Leaves and flowers	Hydro alcohol	Phenols, sterols and flavonoids	[45]
Foeniculum vulgare (Umbelliferae)	Leaves	Hydro alcohol	Volatile oils and terpenes	[45]
Lepidium sativum L. (Brassicaceae)	Leaves	Hydro alcohol	Sterols	[45]
Papaver rhoeas L. (Papaveraceae)	Leaves	Hydro alcohol	Alkaloids	[45]
Picris hieraciodies L. (Asteraceae)	Leaves	Hydro alcohol	Flavonoids	[45]
Sonchus oleraceus L. (Asteraceae)	Leaves	Hydroalcohol	Flavonoids	[45]

Psoralea corylifolia (Fabaceae)	Seeds	Methanol	Isoflavones	[46]
Moringa oleifera (Moringaceae)	Leaves	Methanol	Carotenoids, vitamins, amino acids, minerals, sterols, glycosides, alkaloids, flavonoids and phenols	[47]
Acacia confuse (Leguminosae)	Bark	Ethanol	Cinnamic acid and benzoic acid	[48]
Magnolia liliflora Desr. (Magnoliaceae)	Seeds	Chloroform, ethyl acetate and ethanol	Phenolic compounds	[49]
Arcangelisia flava (Menispermaceae)	Stem	Methanol	Berberin, palmatine and jatrorrhizine	[50]
Coscinium blumeanum (Menispermaceae)	Stem	Methanol and chloroform	Esters, phenols, flavonoids	[50]
Fibraurea tinctoria (Menispermaceae)	Stem	Methanol and chloroform	Isoquinoline alkaloids	[50]
Aloe ferox Mill (Asphodelaceae)	Leaves	50% methanol, dichloromethane, ethanol	Phenols Gallotannins	[51]
Carpobrotus dimidiatus (Mesembryanthemareae)	Leaves	50% methanol, ethanol	Phenols, gallotannins	[51]
Colocasia antiquorum (Araceae)	Tubers	50% methanol ethanol	Phenols, gallotannins	[51]
*Pyenostachys reticulate (E.mey.)*Benth (Lamiaceae)	Roots	Petroleum ether Dichloromethane, ethanol	Gallotannins, phenols	[51]
Senecio serratuloides DC. (Asteraceae)	Leaves	50%methanol Dichloromethane, ethanol	Gallotannins, phenols	[51]
Turraea floribunda Hochst (Meliaceae)	Roots	50%methanol Dichloromethane, ethanol	Flavonoids, Gallotannins, Phenols	[51]
Abuta grandiflora (Menispermaceae)	Bark	Aqueous	Phenols & Flavonoids	[52]
Anacardium excelsum (Anacardiaceae)	Leaf, stem	Aqueous	Phenols & Flavonoids	[52]
Anacardium occidentale (Anacardiaceae)	fruit	Aqueous	Phenols & Flavonoids	[52]
Bellucia grossularioides (Melastomataceae)	Fruit	Aqueous	Phenols & Flavonoids	[52]
Brownea rosademote (Caesalpiniaceae)	Bark	Aqueous	Phenols & Flavonoids	[52]
Crescentia cujete (Bignoniaceae)	Fruit	Aqueous	Phenols & Flavonoids	[52]
Cyperus prolixus (Cyperaceae)	Root	Aqueous	Phenols & Flavonoids	[52]
Eugenia stipitata (Myrtaceae)	Fruit	Aqueous	Phenols & Flavonoids	[52]
Irlbachia alata (Gentianaceae)	Leaf, Stem	Aqueous	Phenols & Flavonoids	[52]

Justicia pectoralis(Acanthaceae)	Leaf and Stem	Aqueous	Phenols & Flavonoids	[52]
Piper glandulosissimum (Piperaceae)	Leaf, Stem	Aqueous	Phenols & Flavonoids	[52]
Piper krukoffi (Piperaceae)	Leaf and Stem	Aqueous	Phenols & Flavonoids	[52]
Piper putumeyoense (Piperaceae)	Leaf and Stem	Aqueous	Phenols & Flavonoids	[52]
Senna reticulate (Fabaceae)	leaf	Aqueous	Phenols & Flavonoids	[52]
Solanum of grantiflorum (Solanaceae)	Stem	Aqueous	Phenols & Flavonoids	[52]
Solanum sessiliflorum (Solanaceae)	Fruit	Aqueous	Phenols & Flavonoids	[52]
Spathiphyllum spp (Areceae)	Leaf	Aqueous	Phenols & Flavonoids	[52]
Uncaria guianensis (Rubiaceae)	Stem	Aqueous	Phenols & Flavonoids	[52]
Vismia baccifera (Clusiaceae)	Stem	Aqueous	Phenols & Flavonoids	[52]
Fraxinus angustifolia (Oleaceae)	Bark	Chloroform extract	Phenols, Flavonoids, Tannins	[53]
Pistacia lentiscus (Anacardiaceae)	Leaves	Chloroform extract	Phenols, Flavonoids, Tannins	[53]
Clematis flammula (Ranunculaceae)	Leaves	Chloroform extract	Phenols, Flavonoids, Tannins	[53]
Bauhinia kockiana (Leguminosae)	Flowers Leaf	Methanol	Flavonoids, phenols, Anthocyanins	[54]
Caesalpinia pulcherrina (Leguminosae)	Flowers Leaf	Methanol	Flavonoids, phenols, Anthocyanins	[54]
Cassia surattensis (Leguminosae)	Flowers Leaf	Methanol	Flavonoids, phenols, Anthocyanins	[54]
Tanarix gallica (Tamaricaceae)	Leaves Flowers	Methanol	Phenols, Flavonoids, Tannins	[55]
Teucrimun polium (Lamiaceae)	Aerial parts	Ethanol	Phenols, Flavonoids	[56]
Cyperus rotundus (Cyperaceae)	Aerial parts	Ethanol	Phenols, Flavonoids	[56]
*Anethum graveolens (*Appiaceae)	Aerial parts	Ethanol	Phenols, Flavonoids	[56
Nasturtium officinali (Brassicaceae)	Aerial parts	Ethanol	Phenols, Flavonoids	[56]
Potentilla fulgens (Rosaceae)	Roots	Methanol	Phenolic contents (Vit C, pyrogallol, quercetin)	[57]
Lavandula stoechas L. (Lamiaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Melissa officinalis L (Lamiaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Teucrium polium L (Lamiaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
*Thymus capitatus(*L) Hoffm (Lamiaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]

Citrullus colocynthis (Cucurbitaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Aliium sativum L (Liliaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Scilla martima L (Liliaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Adoxa moschatellina L (Adoxaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Olea sylvestris Mill (Oleaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Phyllanthus emblica L (Euphorbiaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Terminalia citrine Roth (Combretaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Terminalia chebula Retz (Combretaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Matricaria chamomilla L (Asteraceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Acmella sp.murr (Asteraceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Cyclamen europaeum L (Primulaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Statice limonium L Gray (Plumbaginaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Mimusops schimperi (Sapotaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Semecarpus anacardium L (Anacardiaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Cupressus semperviens L (Cupressaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Amaranthus tricolor L (Amaranthaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Sinapis alba L (Brassicaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Sinapis arvensis L (Brassicaceae)	Aerial parts	Hydro alcohol	Phenolic contents	[58]
Teucrium polium L (Lamiaceae)	Aerial parts	Methanolic extract	Flavonoids	[59]
Allium paradoxum (Lilliaceae) (	Leaf	Methanol or water	Fibres, Flavonoids, phenolic	[60]
Allium rubellum (M.Bieb) (Lilliaceae)	Leaf	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Foeniculum vulgare Mill (Apiaceae)	Stem, leaf, seeds	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Mentha longifoliads(Lamiaceae)	Leaf	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Origanum vulgare L (Lamiaceae)	Leaf	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Prunus divaricata (Rosaceae)	Fruit	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Rubus sanctus schreber (Rosaceae)	Fruit	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]

Rumex tuberosus L (Polygonaceae)	Leaf	Methanol or water	Fibres, Flavonoids, phenolic compounds	[60]
Satureja mutica (Lamiaceae)	Aerial parts	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Spinacia turkestanica (Chenopodiaceae)	Leaf	Methanol or water	Fibres, flavonoids, phenolic compounds	[60]
Teucrium arduini L(Lamiaceae)	Leaves,flowers	Aqueous extract	Phenols, volatile oils, tannins, terpenoids, steroids	[61]
Acacia nilotica L Wild.Ex Delile (Fabaceae)	Leaves	Ethanol extract	Phenolic compounds, flavonoids, alpha tocopherol, carotenoids	[62]
Diospyros peregrine (Ebenaceae)	Fruits	Aqueous extract	Polyphenol	[63]
Clausena lansium (Rutaceae)	Fruit peel	Ethanol and ethyl acetate	8-hydroxy psoralen	[64]
Daucus carota L. (Apiaceae)	Peels	Ethanol	Polyphenol, flavonoids and anthroquinones	[65]
Luffa cylindrical (Cucurbitaceae)	Peels	Ethanol	Phenols and flavonoids	[65]
Pisum sativum (Fabaceae)	Peels	Ethanol	Phenolic compounds and flavonoids	[65]
Raphanus sativus (Brassicaceae)	Peels	Ethanol	Phenolic compounds and flavonoids	[65]
Trichosanthes dioica (Cucurbitaceae)	Peels	Ethanol	Phenols and flavonoids	[65]
Ricinus communis (Euphorbiaceae)	Leaves	Aqueous methanol	Gallic acid, quercetin, gentisic acid, rutin, epicatechin	[66]
Celastrus paniculatus (Celastraceae)	Seeds	n-Hexane	Sesquiterpene, alkaloids-celapanin, celapanigin and celapagin	[67]
Moringa oleifera (Moringaceae)	Leaves	Acidified aqueous methanol	Phenolic compounds	[68]
Phyllanthus niruri (Euphorbiaceae)	Leaves	Aqueous extract	Proteins	[69]
Chromolaena odorata (Asteraceae)	Leaves	Methanol & Petroleum ether	Alkaloids, tannins, flavonoids and phenolic compounds	[70]
Punica granatum (Puniaceae)	Fruit, peel	Methanol	Phenolic compounds, terpenes, flavonoids and anthocyanins	[71]
Solanum melogena (Solanaceae)	Fruits and entire plant	Methanol	Vitamins, Polyphenol, flavonoids, minerals	[72]
Gymnema montanum (Asclepidaceae)	Leaves	Petroleum ether	Phenolic compounds	[73]
Emblica officinalis (Euphorbiaceae)	Fruits	Ethanol	Phenols, Flavonoids	[74]
Terminalia bellerica (Combretaceae)	Fruits	Ethanol	Phenols, Flavonoids	[74]
Terminalia chebula (Combretaceae)	Fruits	Ethanol	Phenols and Flavonoids	[74]
Cydonia oblong (Rosaceae)	Leaves	Aqueous ethanol	Coumarins, lectins, tannins, lipids, proteins and carotenoids	[75]
Allium porrum (Liliaceae)	Bulbs	Aqueous ethanol	Coumarins, lectins, tannins, lipids, proteins and carotenoids	[75]
Helianthus tuberosus (Asteraceae)	Tubers	Aqueous ethanol	Coumarins, lectins, tannins, lipids, proteins and carotenoids	[75]

Foeniculum vulgare (Umbelliferae)	Leaves, stems, shoots	Methanol & diethyl ether	Vitamins, terpenoids and Flavonoids	[76]

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