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Bioprospecting plants for natural antioxidants: An overview

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ABSTRACT

Reactive oxygen species damage cellular proteins and lipids or form DNA adducts when present in high concentration that promotes carcinogenic activities. Plants have been the primary therapy for such ailments since ancient times. This paper reviews some medicinal plants having antioxidant activities useful for healing cancer, cardiovascular diseases and neuro-protection. A brief overview of the use of medicinal plants and their main constituents effective against reactive oxygen species-based diseases are presented. This overview will attract the interest of investigators aiming at the design of novel therapeutic approaches for the treatment of various reactive oxygen species-based conditions.

1. Introduction

Reactive oxygen species (most commonly H_2O_2, O_2^-, and OH^-) are produced during normal cellular processes that promote carcinogenic activities. Antioxidants play an important role to prevent reactive oxygen species concentrations from reaching a high level within a cell[1]. Antioxidant-based drug formulations are employed for prevention and treatment of such diseases[2]. Synthetic antioxidants, *e.g.* butylated hydroxyanisole and tylated hydroxytoluene, are reported to be the basis of liver damage[3]. This fright has increased the interest in the role of natural antioxidants. A plant-based diet safeguards oxidative stress-related diseases. Dietary plants contain different chemical families and concentrations of antioxidants[4]. Plants are sources of natural antioxidants and therefore take on significant part in chemoprevention of diseases[5].

Despite many plants being reported to have antioxidant potential by *in vitro* assays, only a few of these antioxidant activities have been investigated *in vivo*. Moreover, several phytochemicals have been found to have antioxidant activity within *in vitro* assays. However, only a few of these have been shown to be therapeutically useful under *in vivo* conditions[6-8]. This review aims to enlist the natural compounds with promising *in vitro* and *in vivo* antioxidant activities.

2. Anticancer activity

Cancer is among one of the most severe diseases in developing as well as developed countries. Some of the common symptoms of cancer are oxidative stress, DNA damage and chronic inflammation[9]. Formal treatment of cancer includes surgery, psychosocial support, chemotherapy and radiotherapy[10]. Due to the adverse effect of these treatments, there is a need to discover anticancer agents from natural resources. Medicinal plants are potential sources of anticancer compounds[11]. Screening of anticancer agents in medicinal plaants was started in 1950s with the discovery of vinblastine, vincristine, *Vinca alkaloids* and the isolation of cytotoxic podophyllotoxins[12]. Recently, more than 3 000 plants in the world have been reported for anticancer

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properties. The prevalence of products derived from plants for the treatment of cancer is from 10% to 40% and this rate now reaches up to 50% in Asiatic patients[13-15]. Approximately 60% of the drugs for cancer treatment have been isolated from natural products[16].

Various anticancer compounds have been isolated from plants, *e.g.* crocetin is a potential antitumor agent isolated from *Crocus sativus* (*C. sativus*)[17], and eupatoriopicrin isolated from *Eupatorium cannabinum* shows anticancer properties on fibrosarcoma cells[18] and withaferin A from *Withania somnifera* has a 70% volume reduction of tumor in mice[19]. There was an increased attention for the isolation of novel anticancer and therapeutic agents from natural products over the past 30 years[20,21]. Among these compounds, flavopiridol and meisoindigo isolated from *Dysoxylum binectariferum* and *Indigofera tinctoria* respectively have been considered to possess anticancer properties with low toxicity than conventional drugs[22]. The derivatives of stilbene, cassiagrol A and resveratrol isolated from *Cassia garrettiana* exhibit antitumor activity in *in-vivo* and *in-vitro* models through the inhibition of neovascularization. Two chalcone derivatives from the roots of *Angelica keiskei* also inhibited the growth of tumor in tumor-bearing mice[23]. Various other compounds like hyperforin and hypericin in *Hypericum perforatum* (*H. perforatum*)[24], maslinic acid in *Olea europaea*[25] and silymarin isolated from *Silybum marianum* contributed to the reduction of cell proliferation. Silymarine contains flavolignans, silybin A and B (silibinin), isosilybin A and B, silydianin and silychristin[26,27]. Silybinin is involved in the activation of apoptotic pathways in response to ultraviolet B-induced DNA damage[28]. Capillin from *Artemisia monosperma*[29], 1,8-cineole from *Origanum dayi*[30], carvacrol from *Origanum dayi*[31], cannabinoids from *Cannabis sativa*[32], epigallocatechin-3-gallate from *Camellia sinensis*[33], calotropin from *Calotropis procera*[34], curcumin from *Curcuma domestica*[35], schischkinnin from *Centaurea schischkinii*, montamine from *Centaurea montana*[36], tubeimoside V from *Bolbostemma paniculatum*[37], salgraviolide-A from *Centaurea ainetensis*[38] have been associated with the induction of apoptosis and growth suppression of cancer cell lines. Recent advances in the development of chemotherapeutic agents from plants are the development of a class of molecules called texanes[39]. In France, elliptinium is now available in the market for the treatment of breast cancer[40]. It was found that S-allylcysteine derived from garlic inhibits the growth of tumor in several animal models[41]. Another important class of therapeutic components is acetogenins found in graviola. Some acetogenins are considered as very toxic for different types of cancer cell lines[42] (Table 1).

3. Cardioprotective activity

Cardiovascular diseases are the major cause of death worldwide[60]. Hypertension is the commonest cardiac disease followed by ischemic heart disease. Recently, in 2013 it was estimated by the World Health Organization that 17.3 million people died from cardiovascular diseases and it was predicted that by 2030 the mortality rate will reach up to 23.3 million[61]. Conventional drug therapy has been utilized for the treatment of cardiovascular diseases such as antiplatelet agents, vasodilators, diuretics, anticoagulants and β-blockers[60]. Herbal products are used routinely by patients to treat cardiac complications[62]. Various plant-based extracts have been approved for the use in developed countries, *e.g.* use of ginseng root in Germany, and *H. perforatum*, *Plantago major* and *Matricaria chamomilla* in France[63]. Herbal medicines contain biologically active natural products which are used for the preparation of commercial drugs, *e.g.* digitoxin from *Digitalis purpurea*, reserpine from *Rauwolfia serpentina*, ephedrine from *Ephedra sinica* and salicin from *Salix alba*[64].

Two primary groups of constituents usually found in herbs are beneficial for cardiovascular diseases, which are triterpenes and flavonoids. Triterpenes are very important components of ginseng and have a role in lowering blood pressure and enhancing the utilization of oxygen and have protective effect for the treatment of cardiovascular disease and reducing free radical damage. Flavonoids are the active constituents of two herbs widely used in Europe which are *Crataegus* and gingko leaf[65]. Polyphenols are very important compounds in plants and flavonoids constitute the largest class of polyphenols. Among the flavonoids, flavonols are widely dispersed in nature and present in significant amounts in vegetables and fruits. Flavonols have wide range of biological activity and they may be potential drug for cardiovascular diseases[66]. Common forms of isoflavones are daidzein and genistein which possess lipid-lowering properties, especially in the case of hypercholesterolemia[67]. Polyphenols have free radical scavenging activity and help in reducing the chances of heart diseases[68]. Furthermore, many antioxidant compounds like vitamins C and E, and β-carotene are considered as possible therapeutic agents in cardiovascular disorders and oxidative stress[69]. The metabolites of isoflavones derived from legumes *cis*- and *trans*-tetrahydrodaidzein, dihydrodaidzein and dehydroequol have been reported as capable of provoking contractile activity, protecting endothelium and possessing cardioprotective properties[70]. Some components of pomegranate have been regarded as very efficacious for the prevention of low density lipoprotein oxidation and atherosclerosis[71]. Cardioprotective potential of *Bombax ceiba* has been reported. The chemical compounds present in the aqueous extract of *Bombax ceiba* are flavonoids, tannins and glycosides[72]. It was found that ginseng has a potential cardioprotective agent and that's why it has anti-arrhythmic property[73,74]. Legumes contain many compounds like isoflavonoids, flavanoids, coumestans, polyphenols and lignans which are helpful in reducing the risk of atherosclerosis[75]. Isoflavones are also reported in soybeans and it has a beneficial effect on the cardiovascular system[76]. Tea is a rich source of antioxidants, *e.g.* kaempferol, epigallocatechin gallate, quercetin and marketing and polyphenols comprise 35% dry weight of tea leaves[76]. In previous studies, it was observed that higher dietary intake of flavonoids reduces the occurrence of coronary heart disease[77-79]. Ferulic acid is a nitrite scavenger which is a cardioprotective agent in hemodynamics and ischemia-reperfusion injury[80,81]. Hydroxysafflor yellow A also protects the heart against ischemia-reperfusion injury by reducing the mitochondrial permeability transition pore opening[81]. Medicinal and dietary phytochemicals

Table 1
Natural anticancerous compounds.

Botanical names	Common name	Family	Chemical constituent(s)	Reference
Aegle marmelos	Bael	Rutaceae	Lupeol	[43]
Agapanthus africanus	African Lily, Lily of the nile	Agapanthaceae	Isoliquiritigenin	[44]
Ailanthus altissima	Tree of heaven, China sumac, varnishtree	Simaroubaceae	Ailanthone	[45]
Allium cepa	Garden onion	Liliaceae/Alliaceae	Allicin alliin, diallyl disulphide, quercetin	[43]
A. sativum	Garlic	Liliaceae	Alliin, allicin alliin, alliinase, S-allylcysteine, diallyl disulphide, diallyl trisulphide, methyl allyl trisulfide	[46,47]
Aphanamixis polystachya	Rohituka tree	Meliaceae	Amooranin	[43]
Apium graveolens	Wild celery	Umbelliferae	Apigenin	[48]
Azadirachta indica	Neem tree	Meliaceae	Limonoids, limbolide	[43]
Bauhinia variegate	Orchid tree, camel's foot tree, kachnar	Caesalpiniaceae	Cyanidin glucoside, malvidin and peonidin, glucoside, kaempferol	[43]
Berberis vulgaris	Barberry	Berberidaceae	Berberine	[43]
Bleekeria vitensis	–	Apocynaceae	Ellipticine	[12]
Brucea antidysenterica	Nux vomica	Simaroubaceae	Bruceantin	[12]
Camptotheca acuminata	Tree of life	Nyssaceae	Campothecin	[12]
Catharanthus roseus	Madagascar periwinkle	Apocynaceae	Vinblastine, vincristine, alstonine, ajmalicine and reserpine	[12,49,50]
Cephalotaxus harringtonia	Yew	Cephalotaxaceae	Homoharringtonine	[12]
Diphylleia grayi	Umbrella leaf	Berberidaceae	Diphyllin	[12]
Dysoxylum binectariferum	Black bean	Meliaceae	Rohitukine	[12]
E. officinalis	Gooseberry	Euphorbiaceae	Ellagic acid, gallic acid, quercetin, emblicanins A and B	[43]
Fragaria vesca	Woods strawberry	Rosaceae	Borneol, ellagic acid	[43]
Morinda citrifolia	Great morinda, Indian mulberry	Rubiaceae	Damnacanthal, rubiadin 1-methyl ether, alizarin, morindone and anthragallol-2,3-dimethyl ether, damnacanthol	[43]
Nigella sativa	Black cumin, black caraway	Ranunculaceae	Thymoquinone, dithymoquinone	[43]
Ocimum sanctum	Holy basil	Lamiaceae	Eugenol, orientin and vicenin	[43]
Oldenlandia diffusa	Snake needle grass	Rubiaceae	Ursolic acid	[43]
Prunella vulgaris	Self-heal, common selfheal	Lamiaceae	Ursolic acid, oleanolic acid	[43]
Psoralea corylifolia	Babchi, bakuchi	Fabaceae	Bavachinin and psoralen, psoralidin	[43]
Rubia cordifolia	Indian madder	Rubiaceae	Rubidianin, rubiadin, rosemary acids, purpurin, alizarin, xanthopurpurin	[43]
Saussurea lappa	Costus, kut root	Asteraceae	Cynaropicrin, costunolide dehydrocostus lactone, shikokio	[43]
Tinospora cordifolia	Heart-leaved moonseed	Menispermaceae	Berberin, tinosporin, giloin, giloinin	[43]
Viscum album	Mistletoe	Viscaceae	Lectin, propionyl choline, lupeol, viscotoxin, digallic acid	[43]
Annona glabra	Pond apple	Annonaceae	Acetogenins	[51]
Aralia nudicaulis	Wild sarsaparilla	Araliacea	Sarsasapogenin, smilagenin, smilasaponin, smilacin, sarsaparilloside	[52]
Taxus brevifolia	Pacific yew tree	Taxaceae	Taxol	[53]
Xanthium strumarium	Cocklebur	Asteraceae	Xanthatin, xanthinosin	[54]
Taraxacum officinale	Dandelion	Asteraceae	Inulin, caffeic acid	[55]
Pyrus malus	Apple	Rosaceae	Quercetin, catechin, phloridzin and procyanidin	[56]
Lantana camara	*Lantana*, tick berry	Verbenaceae	Camerine, isocamerine, micranine, lantanine, lantadene	[57-59]

A. sativum: *Allium sativum*; *E. officinalis*: *Emblica officinalis.*

play an important role in reducing the incidence of cardiovascular disease[82]. The estrogenic activity of isoflavones is because of their structural similarity to steroidal estrogens[83]. Endogenous steroidal estrogens have been considered as a potential cardioprotective agent, *e.g.* 17b-oestradiol acts as a vasorelaxant[84,85] (Table 2).

4. Neuroprotective activity

Neuroprotection is a mechanism within the central nervous system which protects neurons from apoptosis in case of acute brain injury and chronic neurodegenerative diseases[102]. Various neuroprotective compounds have been isolated from plants and are considered to be very effective in neuropathic condition. Polyphenols have a therapeutic potential for neurodegenerative diseases, *e.g.* curcumin is a natural polyphenol found in curry spice turmeric and plays an important role in various neuronal disorders. Resveratrol is another polyphenol in grapes and red wines, which has pharmacological effects and is helpful to release neurotrophic factors[103]. Ginseng

Table 2
Natural cardioprotective compounds.

Botanical names	Common name	Family	Chemical constituent(s)	Reference
Aesculus hippocastanum	Horse-chestnut	Hippocastanaceae	Hydroxycoumarin	[86]
A. sativum	Garlic	Liliaceae	Allicin	[87]
Camellia sinensis	Tea	Theaceae	Catechins	[88]
Cinnamomum tamala	Malabar leaf	Lauraceae	Cinnamaldehyde	[89]
Commiphora wightii	Guggal	Burseraceae	Guggulipid, guggulsterone	[90]
Crataeva nurvala	Varuna	Capparaceae	Lupeol	[91]
C. sativus	Saffron	Iridaceae	Crocin and safranal	[92,93]
Digitalis purpurea/lanata	Foxglove	Plantaginaceae	*Digitalis*, digitoxin, digoxin	[94]
E. officinalis	Amla	Euphorbiaceae	Vitamin C, gallic acid	[91]
Erythroxylum coca	Coca plant	Erythroxylaceae	Cocaine, tropacocaine, cinnamoylcocaine	[86]
Ginkgo biloba	Ginkgo	Ginkgoaceae	Ginkgolides A and B, bilobalide	[95]
Glycine max	Liquorice	Papilionaceae	Protein, lecithin, saponins	[86]
Hordeum vulgare	Barley	Poaceae	Vitamin C, β-glucan-enriched fraction	[86]
Nelumbo nucifera	Lotus	Nelumbonaceae	Quercetin, luteolin	[96,97]
Psidium guajava	Guava	Myrtaceae	Quercitin	[91]
Punica granatum	Pomegranate	Punicaceae	Punicalagin, punicalin, ellagic acid	[91]
Raphanus sativus	Radish	Brassicaceae	Caffeic acid	[98]
Rosa damascene	Rose	Rosaceae	Lycopene, rubixanthin, zeaxanthin, quercetin, kaempferol, cyanidin	[86]
Stachytarpheta jamaicensis	Blue snakeweed	Verbenaceae	Friedelin, stigmasterol, ursolic acid, hispidulin, scutellarein, choline	[99]
Tinospora cordifolia	Guduchi	Menispermaceae	Columbin, chasmanthin, palmarin, tinosporon, tinosporic acid, tinosporol	[100]
Vitis vinifera	Grapevine	Vitaceae	Procyanidin	[101]

Table 3
Natural neuroprotective compounds.

Botanical name	Common name	Family	Chemical constituent(s)	Reference
Acorus calamus	Sweet flag	Acoraceae	A and B-asarone	[121,122]
Achillea millefolium	Yarrow	Asteraceae	Borneol	[123]
Allium cepa	Onion	Amaryllidaceae	Allicin	[124]
A. sativum	Garlic	Amaryllidaceae	*Allium*	[124]
Bacopa monnieri	Brahmi	Plantaginaceae	Bacosides A and B	[125]
Centella asiatica	Manimuni	Apiaceae	Asiaticoside, centelloside, madecassoside, asiatic acid	[126]
Coffea spp.	Coffee	Rubiaceae	Caffeine	[127,128]
Cornus officinalis	Japanese cornel	Cornaceae	Ursolic acid, *p*-coumaric acid, gallic acid	[129]
Corydalis ternata		Papaveraceae	Protopine	[130]
Crinum jagus	Christopher Lily	Amaryllidaceae	Lycorine, vitattine	[131]
C. sativus	Saffron	Iridaceae	Crocetin, dimethylcrocetin, crocin	[132-134]
Curcuma longa	Turmeric	Zingiberaceae	Curcumin	[135]
E. officinalis	Amla	Phyllanthaceae	Vitamin C, phyllemblin	[136]
Evolvulus alsinoides	Dwarf morning glory	Convolvulaceae	Betaine, sankhapushpine, evolvine	[137]
Ginkgo biloba	Ginkgo	Ginkgoaceae	Bilobalide	[138]
Panax ginseng	Ginseng	Araliaceae	Ginsenosides	[139-141]
Glycyrrhiza glabra	Liquorice	Leguminosae	Glycyrrhizin	[142]
Hippophae rhamnoides	Sea buckthorn	Elaeagnaceae	Polyunsaturated fatty acids	[143]
Huperzia serrata	Club moss	Lycopodiaceae	Huperzine A	[144,145]
H. perforatum	Saint John's wort	Asteraceae	Quercetin, biapigenin, hyperoside	[145-148]
Ilex paraguariensis	Yerba mate	Aquifoliaceae	Chlorogenic acid caffeine, theophylline, theobromine quercitin, kaemferol	[149]
Lavandula angustifolia	Lavender	Lamiaceae	Linalool	[150]
Lepidium meyenii	Maca	Brassicaceae	Macamides	[151]
Magnolia officinalis	Magnolia bark	Magnoliaceae	4-O-Methylhonokiol, honokiol, magnolol	[124]
Morinda citrifolia	Noni	Rubiaceae	Rutin, scopoletin, quercetin	[152]
Morus alba	Mulberry	Moraceae	Cyanidin-3-o-b-d glucopyranoside	[153]
Olea europea	Olive	Oleaceae	Oleuropein	[154]
Polygonum cuspidatum	Japanese knotweed	Polygonaceae	Polynapstilbene B	[81]
Ricinus communis	Castor plant	Euphorbiaceae	Ricin, ricinine, undecylenic acid	[155,156]
Scutellaria baicalensis	Baikal skullcap	Lamiaceae	Baicalein, baicalin, wogonin	[157]
Solanum nigrum	Black nightshade	Solanaceae	Caffeic acid	[158]
Uncaria rhynchophylla	Gambir vine	Rubiaceae	Rhynchophylline, corynoxine, isorhynchophylline, isocorynoxiene	[124]
Withania somnifera	Winter cherry	Solanaceae	Sitoindosides VII-X, withaferin, withanoside IV	[159,160]
Zingiber officinale	Ginger	Zingiberaceae	Gingerol, shogaol, zingerone	[124]
Zizyphus jujube	Ennab	Rhamnaceae	Spinosin	[161]
Zizyphus spinosa	Jujube	Rhamnaceae	Jujubosides A and B	[124]

is a Chinese medicine which contains active constituents such as polysaccharides, ginsenosides and peptides with beneficial effects. It plays a neuroprotective role in neuroinflammatory processes, regulation of synaptic plasticity and release of neurotransmitter[104]. Hesperidine is a flavanone mostly occurring in citrus plants. It is isolated from the peels of *Citrus sinensis* (sweet

orange), *Citrus aurantium*, *Citrus unshiu* and has a significant neuroprotective activity[105,106]. A novel neuroprotective compound, 1-methoxyoctadecan-1-ol has been identified in *Uncaria sinensis*.

Phenylpropanoids were isolated from medicinal plants and they have a neuroprotective mechanism. Caffeic acid[107], *E-p*-methoxycinnamic acid, buergeriside A1 and ferulic acid[108] were isolated from *Scrophularia buergeriana* and have a role in inhibition of calcium influx and β-induced neurotoxicity. Caffeic acid phenethyl ester was obtained from the extract of propolis and has a neuroprotective role[109,110]. Echinacoside from *Cistanche salsa* plays an important role to inhibit caspase-3 activity[111]. Verbascoside from *Syringa vulgaris* is a neuroprotective agent[112]. Coumarins are another group of neuroprotective agents *e.g.* osthol from *Cnidium monnieri*[113] and decursin, decursinol, 4"-hydroxydecursin, (2"S,3"S)-epoxyangeloyldecursinol, (2"R,3"R)-epoxyangeloyldecursinol and 4"-hydroxytigloyldecursinol from *Angelica gigas* provide neuroprotection against excitotoxicity[114]. Lignans also have a neuroprotective role. Licarin A, isoguaiacin, *meso*-dihydroguaiaretic acid and (+)-guaiacin from *Machilus thunbergii* have significant neuroprotective activity[115,116]. Sauchinone from *Saururus chinensis*[97] and sesamin from *Sesamum indicum*[117] act as a neroprotective agent. Stilbenoids and other phenolic compounds were also obtained from medicinal plants and have a neuroprotective mechanism. Curcumin and Z-ligustilide were isolated from *Curcuma longa* and *Angelica sinensis*, respectively[118,119]. Cell-based assays were also performed for the identification of compounds in plant extracts to treat Alzheimer's disease. A potential alkaloid vocamine was isolated from *Voacanga africana* and had a neuroprotective activity[120] (Table 3). Reactive oxygen species based ailments are leading cause of deaths all worldwide. Mostly ROS induced diseases are associated with lethal cancers, brain and heart associated disorders. As bioprospecting based approach particularly in drug development along agrochemicals has been the focus of mankind since ancient times, plants remained to be the main focus in both cases. Today, there is plethora of literature reporting antioxidant properties of thousands of plants. Many isolated compounds are also cited in various research studies. Plants discussed in current review exhibited significant antioxidant activity. Potential isolated compounds of antioxidant activity are also discussed. It is now suggested to evaluate the synergistic effects of natural known antioxidants. Dose standardization and dosage regimen may contribute crucial role in mankind therapeutics.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1] Seifried HE, Anderson DE, Fisher EI, Milner JA. A review of the interaction among dietary antioxidants and reactive oxygen species. *J Nutr Biochem* 2007; **18**: 567-79.

[2] Devasagayam TP, Tilak JC, Boloor KK, Sane KS, Ghaskadbi SS, Lele RD. Free radicals and antioxidants in human health: current status and future prospects. *J Assoc Physicians India* 2004; **52**: 794-804.

[3] Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. *Food Bioprod Process* 2011; **89**: 217-33.

[4] Sharma SK, Singh L, Singh S. A review on medicinal plants having antioxidant potential. *Indian J Res Pharm Biotechnol* 2013; **1**: 404-9.

[5] Khalaf NA, Shakya AK, Al-Othman A, El-Agbar Z, Farah H. Antioxidant activity of some common plants. *Turk J Biol* 2008; **32**: 51-5.

[6] Chand S, Dave R. *In vitro* models for antioxidant activity evaluation and some medicinal plants possessing antioxidant properties: an overview. *Afr J Microbiol Res* 2009; **3**: 981-96.

[7] Badarinath AV, Rao KM, Madhu C, Chetty S, Ramkanth S, Rajan TVS, et al. A review on *in-vitro* antioxidant methods: comparisons, correlations and considerations. *Int J Pharm Tech Res* 2010; **2**: 1276-85.

[8] Kasote DM, Katyare SS, Hegde MV, Bae H. Significance of antioxidant potential of plants and its relevance to therapeutic applications. *Int J Biol Sci* 2015; **11**: 982-91.

[9] De Flora S, Ferguson LR. Overview of mechanisms of cancer chemopreventive agents. *Mutat Res* 2005; **591**: 8-15.

[10] World Health Organization. Cancers NMH facts sheet. Geneva: World Health Organization; 2010. [Online] Available from: http://www.who.int/nmh/publications/fact_sheet_cancers_en.pdf [Accessed on 1st August, 2016]

[11] Mantle D, Wilkins RM. Medicinal plants in the prevention and therapy of cancer. In: Yaniv Z, Bachrach U, editors. *Handbook of medicinal plants*. New York: The Haworth Press; 2005, p. 281-318.

[12] Cragg GM, Newman DJ. Plants as a source of anti-cancer agents. *J Ethnopharmacol* 2005; **100**: 72-9.

[13] Tascilar M, de Jong FA, Verweij J, Mathijssen RH. Complementary and alternative medicine during cancer treatment: beyond innocence. *Oncologist* 2006; **11**: 732-41.

[14] Cassileth BR, Deng G. Complementary and alternative therapies for cancer. *Oncologist* 2004; **9**: 80-9.

[15] Molassiotis A, Browall M, Milovics L, Panteli V, Patiraki E, Fernandez-Ortega P. Complementary and alternative medicine use in patients with gynecological cancers in Europe. *Int J Gynecol Cancer* 2006; **16**(Suppl 1): 219-24.

[16] Gordaliza M. Natural products as leads to anticancer drugs. *Clin Transl Oncol* 2007; **9**: 767-76.

[17] Gutheil WG, Reed G, Ray A, Anant S, Dhar A. Crocetin: an agent derived from saffron for prevention and therapy for cancer. *Curr Pharm Biotechnol* 2012; **13**: 173-9.

[18] Woerdenbag HJ. *Eupatorium cannabinum* L. A review emphasizing the sesquiterpene lactones and their biological activity. *Pharm Weekbl Sci* 1986; **8**: 245-51.

[19] Munagala R, Kausar H, Munjal C, Gupta RC. Withaferin A induces p53-dependent apoptosis by repression of HPV oncogenes and upregulation of tumor suppressor proteins in human cervical cancer cells. *Carcinogenesis* 2011; **32**: 1697-705.

[20] Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981–2002. *J Nat Prod* 2003; **66**: 1022-37.

[21] Newman DJ. Natural products as leads to potential drugs: an old process or the new hope for drug discovery? *J Med Chem* 2008; **51**: 2589-99.

[22] Saklani A, Kutty SK. Plant-derived compounds in clinical trials. *Drug Discov Today* 2008; **13**: 161-71.

[23] Kimura Y. New anticancer agents: *in vitro* and *in vivo* evaluation of the antitumor and antimetastatic actions of various compounds isolated from medicinal plants. *In Vivo* 2005; **19**: 37-60.

[24] Martarelli D, Martarelli B, Pediconi D, Nabissi MI, Perfumi M, Pompei P. *Hypericum perforatum* methanolic extract inhibits growth of human prostatic carcinoma cell line orthotopically implanted in nude mice. *Cancer Lett* 2004; **210**: 27-33.

[25] Reyes-Zurita FJ, Rufino-Palomares EE, Lupiáñez JA, Cascante M. Maslinic acid, a natural triterpene from *Olea europaea* L., induces apoptosis in HT29 human colon-cancer cells via the mitochondrial apoptotic pathway. *Cancer Lett* 2009; **273**: 44-54.

[26] Scambia G, De Vincenzo R, Ranelletti FO, Panici PB, Ferrandina G, D'Agostino G, et al. Antiproliferative effect of silybin on gynaecological malignancies: synergism with cisplatin and doxorubicin. *Eur J Cancer* 1996; **32**: 877-82.

[27] Zi X, Feyes DK, Agarwal R. Anticarcinogenic effect of a flavonoid antioxidant, silymarin, in human breast cancer cells MDA-MB 468: induction of G1 arrest through an increase in Cip1/p21 concomitant with a decrease in kinase activity of cyclin-dependent kinases and associated cyclins. *Clin Cancer Res* 1998; **4**: 1055-64.

[28] Deep G, Oberlies NH, Kroll DJ, Agarwal R. Isosilybin B and isosilybin A inhibit growth, induce G1 arrest and cause apoptosis in human prostate cancer LNCaP and 22Rv1 cells. *Carcinogenesis* 2007; **28**: 1533-42.

[29] Whelan LC, Ryan MF. Effects of the polyacetylene capillin on human tumour cell lines. *Anticancer Res* 2004; **24**: 2281-6.

[30] Moteki H, Hibasami H, Yamada Y, Katsuzaki H, Imai K, Komiya T. Specific induction of apoptosis by 1, 8-cineole in two human leukemia cell lines, but not a in human stomach cancer cell line. *Oncol Rep* 2002; **9**: 757-60.

[31] Koparal AT, Zeytinoglu M. Effects of carvacrol on a human non-small cell lung cancer (NSCLC) cell line, A549. *Cytotechnology* 2003; **43**: 149-54.

[32] Guzmán M. Cannabinoids: potential anticancer agents. *Nat Rev Cancer* 2003; **3**: 745-55.

[33] Ho YC, Yang SF, Peng CY, Chou MY, Chang YC. Epigallocatechin-3-gallate inhibits the invasion of human oral cancer cells and decreases the productions of matrix metalloproteinases and urokinase-plasminogen activator. *J Oral Pathol Med* 2007; **36**: 588-93.

[34] Willaman JJ, Li HL. Alkaloid-bearing plants and their contained alkaloids. *Lloydia* 1970; **33**(3A): 1-286.

[35] Hong RL, Spohn WH, Hung MC. Curcumin inhibits tyrosine kinase activity of p185neu and also depletes p185neu. *Clin Cancer Res* 1999; **5**: 1884-91.

[36] Shoeb M, Celik S, Jaspars M, Kumarasamy Y, MacManus SM, Nahar L, et al. Isolation, structure elucidation and bioactivity of schischkiniin, a unique indole alkaloid from the seeds of *Centaurea schischkinii*. *Tetrahedron* 2005; **61**: 9001-6.

[37] Yu L, Ma R, Wang Y, Nishino H. Potent anti-tumor activity and low toxicity of tubeimoside 1 isolated from *Bolbostemma paniculatum*. *Planta Med* 1994; **60**: 204-8.

[38] El-Najjar N, Dakdouki S, Darwiche N, El-Sabban M, Saliba NA, Gali-Muhtasib H. Anti-colon cancer effects of salograviolide A isolated from *Centaurea ainetensis*. *Oncol Rep* 2008; **19**: 897-904.

[39] Kingston DGI. Taxol and its analogs. In: Cragg GM, Kingston DGI, Newman DJ, editors. *Anticancer agents from natural products*. Boca Raton: CRC Press; 2005.

[40] Itokawa H, Ibraheim ZZ, Qiao YF, Takeya K. Anthraquinones, naphthohydroquinones and naphthohydroquinone dimers from *Rubia cordifolia* and their cytotoxic activity. *Chem Pharm Bull (Tokyo)* 1993; **41**: 1869-72.

[41] Thomson M, Ali M. Garlic (*Allium sativum*): a review of its potential use as an anti-cancer agent. *Curr Cancer Drug Targets* 2003; **3**: 67-81.

[42] Medical Health Guide. Graviola herbal medicine – graviola uses, health benefits and side effects. USA: Medical Health Guide; 2011. [Online] Available from: http://www.medicalhealthguide.com/herb/graviola.htm [Accessed on 12th July, 2016]

[43] Govind P. Some important anticancer herbs: a review. *Int Res J Pharm* 2011; **2**: 45-52.

[44] Srinivas K, Grierson DS, Afolayan AJ. Ethnobotanical information of medicinal plants used for treatment of cancer in the Eastern Cape Province, South Africa. *Curr Sci* 2007; **92**: 906-8.

[45] Chang M. *Anticancer medicinal herbs*. Changsha: Hunan Science & Technology Press; 1992.

[46] Belman S. Onion and garlic oils inhibit tumor promotion. *Carcinogenesis* 1983; **4**: 1063-5.

[47] Milner JA. Garlic: its anticarcinogenic and antitumorigenic properties. *Nutr Rev* 1996; **54**(11 Pt 2): S82-6.

[48] Sultana S, Ahmed S, Jahangir T, Sharma S. Inhibitory effect of celery seeds extract on chemically induced hepatocarcinogenesis: modulation of cell proliferation, metabolism and altered hepatic foci development. *Cancer Lett* 2005; **221**: 11-20.

[49] Noble RL. The discovery of the *Vinca alkaloids* – chemotherapeutic agents against cancer. *Biochem Cell Biol* 1990; **68**: 1344-51.

[50] Jordan MA, Thrower D, Wilson L. Mechanism of inhibition of cell proliferation by *Vinca alkaloids*. *Cancer Res* 1991; **51**: 2212-22.

[51] Cochrane CB, Nair PK, Melnick SJ, Resek AP, Ramachandran C. Anticancer effects of *Annona glabra* plant extracts in human leukemia cell lines. *Anticancer Res* 2008; **28**: 965-71.

[52] Wang J, Li Q, Ivanochko G, Huang Y. Anticancer effect of extracts from a North American medicinal plant – wild sarsaparilla. *Anticancer Res* 2006; **26**: 2157-64.

[53] Biswas R, Mandal SK, Dutta S, Bhattacharyya SS, Boujedaini N, Khuda-Bukhsh AR. Thujone-rich fraction of *Thuja occidentalis* demonstrates major anti-cancer potentials: evidences from *in vitro* studies on A375 cells. *Evid Based Complement Alternat Med* 2011; **2011**: 568148.

[54] Ramirez-Erosa I, Huang Y, Hickie RA, Sutherland RG, Barl B. Xanthatin and xanthinosin from the burs of *Xanthium strumarium* L. as potential anticancer agents. *Can J Physiol Pharmacol* 2007; **85**: 1160-72.

[55] Ovadje P, Chatterjee S, Griffin C, Tran C, Hamm C, Pandey S. Selective induction of apoptosis through activation of caspase-8 in human leukemia cells (Jurkat) by dandelion root extract. *J Ethnopharmacol* 2011; **133**: 86-91.

[56] Madhuri S, Pandey G. Some anticancer medicinal plants of foreign

origin. *Curr Sci* 2009; **96**: 779-83.

[57] Kalita S, Kumar G, Karthik L, Rao KVB. Phytochemical composition and *in vitro* hemolytic activity of *Lantana camara* L. (Verbenaceae) leaves. *Pharmacologyonline* 2011; **1**: 59-67.

[58] Ghangale GD, Tambe RY, Gaykar AJ, Dama GY. Antimitotic activity of *Lantana camara* flowers. *Int J Inst Pharm Life Sci* 2011; **1**: 1-6.

[59] Patel S. A weed with multiple utility: *Lantana camara*. *Rev Environ Sci Biotechnol* 2011; **10**: 341-51.

[60] Zheng CS, Xu XJ, Ye HZ, Wu GW, Xu HF, Li XH, et al. Computational pharmacological comparison of *Salvia miltiorrhiza* and *Panax notoginseng* used in the therapy of cardiovascular diseases. *Exp Ther Med* 2013; **6**: 1163-8.

[61] World Health Organization. Cardiovascular disease. Geneva: World Health Organization; 2013. [Online] Available from: http://www.who.int/cardiovascular_diseases/en/ [Accessed on 29th March, 2015]

[62] Cohen PA, Ernst E. Safety of herbal supplements: a guide for cardiologists. *Cardiovasc Ther* 2010; **28**: 246-53.

[63] Anonymous. IARC monographs volume 82. Geneva: World Health Organization; 2002. [Online] Available from: http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-6A.pdf [Accessed on 12th April, 2015]

[64] Lin MC, Nahin R, Gershwin ME, Longhurst JC, Wu KK. State of complementary and alternative medicine in cardiovascular, lung, and blood research: executive summary of a workshop. *Circulation* 2001; **103**: 2038-41.

[65] Schmidt U, Kuhn U, Ploch M, Hübner WD. Efficacy of the hawthorn (*Crataegus*) preparation LI 132 in 78 patients with chronic congestive heart failure defined as NYHA functional class II. *Phytomedicine* 1994; **1**: 17-24.

[66] Laskar MA, Choudhury MD, Chetia P. In silico screening of cardioprotective activity of some flavonols. *Int J Pharm Pharm Sci* 2014; **6**: 528-31.

[67] Park D, Huang T, Frishman WH. Phytoestrogens as cardioprotective agents. *Cardiol Rev* 2005; **13**: 13-7.

[68] Quiñones M, Miguel M, Aleixandre A. Beneficial effects of polyphenols on cardiovascular disease. *Pharmacol Res* 2013; **68**: 125-31.

[69] Kumar SV, Saritha G, Fareedullah M. Role of antioxidants and oxidative stress in cardiovascular diseases. *Ann Biol Res* 2010; **1**: 158-73.

[70] Chin-Dusting JP, Fisher LJ, Lewis TV, Piekarska A, Nestel PJ, Husband A. The vascular activity of some isoflavone metabolites: implications for a cardioprotective role. *Br J Pharmacol* 2001; **133**: 595-605.

[71] Fuhrman B, Volkova N, Aviram M. Pomegranate juice polyphenols increase recombinant paraoxonase-1 binding to high-density lipoprotein: studies *in vitro* and in diabetic patients. *Nutrition* 2010; **26**: 359-66.

[72] Vieira TO, Said A, Aboutabl E, Azzam M, Creczynski-Pasa TB. Antioxidant activity of methanolic extract of *Bombax ceiba*. *Redox Rep* 2009; **14**: 41-6.

[73] Zhou W, Chai H, Lin PH, Lumsden AB, Yao Q, Chen CJ. Molecular mechanisms and clinical applications of ginseng root for cardiovascular disease. *Med Sci Monit* 2004; **10**: RA187-92.

[74] Howard BV, Kritchevsky D. Phytochemicals and cardiovascular disease. A statement for healthcare professionals from the American Heart Association. *Circulation* 1997; **95**: 2591-3.

[75] Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995; **333**: 276-82.

[76] Ho CT, Lee C, Huang MT, Balentine AD. *Phenolic compounds in food and their effects on health*. Analysis, occurrence, and chemistry, Vol. 1. Washington, D.C.: ACS; 1992, p. 103-17.

[77] Hertog MG, Kromhout D, Aravanis C, Blackburn H, Buzina R, Fidanza F, et al. Flavonoid intake and long-term risk of coronary heart disease and cancer in the seven countries study. *Arch Intern Med* 1995; **155**: 381-6.

[78] Hertog MG, Feskens EJ, Hollman PC, Katan MB, Kromhout D. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen elderly study. *Lancet* 1993; **342**: 1007-11.

[79] Geleijnse JM, Launer LJ, Hofman A, Pols HA, Witteman JC. Tea flavonoids may protect against atherosclerosis: the Rotterdam study. *Arch Intern Med* 1999; **159**: 2170-4.

[80] Huang X, Zang Y, Wang Y, Niu G, Wen A, Ren P. Effects of tetramethylpyrazine phosphate and sodium ferulate alone or in combination on hemodynamics in anesthetized dog. *Am J Chin Med* 1996; **24**: 169-76.

[81] Liu F, Li F, Feng Z, Yang Y, Jiang J, Li L, et al. Neuroprotective naphthalene and flavan derivatives from *Polygonum cuspidatum*. *Phytochemistry* 2015; **110**: 150-9.

[82] Owen PL, Johns T. Antioxidants in medicines and spices as cardioprotective agents in Tibetan highlanders. *Pharm Biol* 2002; **40**: 346-57.

[83] Clarkson TB, Anthony MS. Phytoestrogens and coronary heart disease. *Baillieres Clin Endocrinol Metab* 1998; **12**: 589-604.

[84] Jiang CW, Sarrel PM, Lindsay DC, Poole-Wilson PA, Collins P. Endothelium-independent relaxation of rabbit coronary artery by 17 beta-oestradiol *in vitro*. *Br J Pharmacol* 1991; **104**: 1033-7.

[85] Freay AD, Curtis SW, Korach KS, Rubanyi GM. Mechanism of vascular smooth muscle relaxation by estrogen in depolarized rat and mouse aorta. Role of nuclear estrogen receptor and Ca^{2+} uptake. *Circ Res* 1997; **81**: 242-8.

[86] Arya V, Gupta VK. Chemistry and pharmacology of plant cardioprotective: a review. *Int J Pharm Sci Res* 2011; **2**: 1156-67.

[87] Isensee H, Rietz B, Jacob R. Cardioprotective actions of garlic (*Allium sativum*). *Arzneimittelforschung* 1993; **43**: 94-8.

[88] Li N, Zhao Y, Liang Y. Cardioprotective effects of tea and its catechins. *Health* 2013; **5**: 23-30.

[89] Dhulasavant V, Shinde S, Pawar M, Naikwade NS. Antihyperlipidemic activity of *Cinnamomum tamala* Nees. on high cholesterol diet induced hyperlipidemia. *Int J PharmTech Res* 2010; **2**(4): 2517-21.

[90] Anurekha J, Gupta VB. Chemistry and pharmacological profile of guggul – a review. *Indian J Tradit Knowl* 2006; **5**: 478-83.

[91] Vikrant A, Kumar GV. Review on some cardioprotective plants from Ayurveda. *Int J Res Ayu Pharm* 2011; **2**: 80-3.

[92] Hosseinzadeh H, Noraei NB. Anxiolytic and hypnotic effect of *Crocus sativus* aqueous extract and its constituents, crocin and safranal, in mice. *Phytother Res* 2009; **23**: 768-74.

[93] Mehdizadeh R, Parizadeh MR, Khooei AR, Mehri S, Hosseinzadeh H. Cardioprotective effect of saffron extract and safranal in isoproterenol-induced myocardial infarction in wistar rats. *Iran J Basic Med Sci* 2013; **16**: 56-63.

[94] Walden R, Tomlinson B. Cardiovascular disease. In: Benzie IFF, Wachtel-Galor S, editors. *Herbal medicine: biomolecular and clinical aspects*. 2nd ed. Boca Raton: CRC Press; 2011.

[95] Pietri S, Maurelli E, Drieu K, Culcasi M. Cardioprotective and anti-oxidant effects of the terpenoid constituents of ginkgo biloba extract (EGb 761). *J Mol Cell Cardiol* 1997; **29**: 733-42.

[96] Lee HJ, Chen CC, Chou FP, Wu CH, Lai FS, Yang MY, et al. Water extracts from *Nelumbo nucifera* leaf reduced plasma lipids and atherosclerosis in cholesterol-fed rabbits. *J Food Biochem* 2010; **34**: 779-95.

[97] Choi IY, Yan H, Park YK, Kim WK. Sauchinone reduces oxygen-glucose deprivation-evoked neuronal cell death via suppression of intracellular radical production. *Arch Pharm Res* 2009; **32**: 1599-606.

[98] Zaman R. Study of cardioprotective activity of *Raphanus sativus* L. in rabbits. *Pak J Biol Sci* 2004; **7**: 843-7.

[99] Okwu DE, Ohenhen ON. Isolation and characterization of steroidal glycosides from the leaves of *Stachytarpheta jamaicensis* Linn Vahl. *Der Chemica Sinica* 2010; **1**: 6-14.

[100]Rao PR, Kumar VK, Viswanath RK, Subbaraju GV. Cardioprotective activity of alcoholic extract of *Tinospora cordifolia* in ischemia-reperfusion induced myocardial infarction in rats. *Biol Pharm Bull* 2005; **28**: 2319-22.

[101]Nassiri-Asl M, Hosseinzadeh H. Review of the pharmacological effects of *Vitis vinifera* (grape) and its bioactive compounds. *Phytother Res* 2009; **23**: 1197-204.

[102]Vasudevan SK, Gupta V, Crowston JG. Neuroprotection in glaucoma. *Indian J Ophthalmol* 2011; **59**: 102-13.

[103]Zhang F, Wang YY, Liu H, Lu YF, Wu Q, Liu J, et al. Resveratrol produces neurotrophic effects on cultured dopaminergic neurons through prompting astroglial BDNF and GDNF release. *Evid Based Complement Alternat Med* 2012; **2012**: 937605.

[104]Kim HJ, Kim P, Shin CY. A comprehensive review of the therapeutic and pharmacological effects of ginseng and ginsenosides in central nervous system. *J Ginseng Res* 2013; **37**: 8-29.

[105]Crozier A, Jaganath IB, Clifford MN. Dietary phenolics: chemistry, bioavailability and effects on health. *Nat Prod Rep* 2009; **26**: 1001-43.

[106]Cho J. Antioxidant and neuroprotective effects of hesperidin and its aglycone hesperetin. *Arch Pharma Res* 2006; **29**: 699-706.

[107]Sul D, Kim HS, Lee D, Joo SS, Hwang KW, Park SY. Protective effect of caffeic acid against beta-amyloid-induced neurotoxicity by the inhibition of calcium influx and tau phosphorylation. *Life Sci* 2009; **84**: 257-62.

[108]Kim SR, Kim YC. Neuroprotective phenylpropanoid esters of rhamnose isolated from roots of *Scrophularia buergeriana*. *Phytochemistry* 2000; **54**: 503-9.

[109]Altuğ ME, Serarslan Y, Bal R, Kontaş T, Ekici F, Melek IM, et al. Caffeic acid phenethyl ester protects rabbit brains against permanent focal ischemia by antioxidant action: a biochemical and planimetric study. *Brain Res* 2008; **1201**: 135-42.

[110]Khan M, Elango C, Ansari MA, Singh I, Singh AK. Caffeic acid phenethyl ester reduces neurovascular inflammation and protects rat brain following transient focal cerebral ischemia. *J Neurochem* 2007; **102**: 365-77.

[111]Deng M, Zhao JY, Tu PF, Jiang Y, Li ZB, Wang YH. Echinacoside rescues the SHSY5Y neuronal cells from TNFalpha-induced apoptosis. *Eur J Pharmacol* 2004; **505**: 11-8.

[112]Esposito E, Dal Toso R, Pressi G, Bramanti P, Meli R, Cuzzocrea S. Protective effect of verbascoside in activated C6 glioma cells: possible molecular mechanisms. *Naunyn Schmiedebergs Arch Pharmacol* 2010; **381**: 93-105.

[113]Wu SN, Lo YK, Chen CC, Li HF, Chiang HT. Inhibitory effect of the plant-extract osthole on L-type calcium current in NG108-15 neuronal cells. *Biochem Pharmacol* 2002; **63**: 199-206.

[114]Kang TH, Hur JY, Kim HB, Ryu JH, Kim SY. Neuroprotective effects of the cyanidin-3-O-beta-d-glucopyranoside isolated from mulberry fruit against cerebral ischemia. *Neurosci Lett* 2006; **391**: 122-6.

[115]Ma CJ, Kim SR, Kim J, Kim YC. Meso-dihydroguaiaretic acid and licarin A of *Machilus thunbergii* protect against glutamate-induced toxicity in primary cultures of a rat cortical cells. *Br J Pharmacol* 2005; **146**: 752-9.

[116]Ma CJ, Sung SH, Kim YC. Neuroprotective lignans from the bark of *Machilus thunbergii*. *Planta Med* 2004; **70**: 79-80.

[117]Khan MM, Ishrat T, Ahmad A, Hoda MN, Khan MB, Khuwaja G, et al. Sesamin attenuates behavioral, biochemical and histological alterations induced by reversible middle cerebral artery occlusion in the rats. *Chem Biol Interact* 2010; **183**: 255-63.

[118]Yazawa K, Kihara T, Shen H, Shimmyo Y, Niidome T, Sugimoto H. Distinct mechanisms underlie distinct polyphenol-induced neuroprotection. *FEBS Lett* 2006; **580**: 6623-8.

[119]Kuang X, Du JR, Liu YX, Zhang GY, Peng HY. Postischemic administration of Z-ligustilide ameliorates cognitive dysfunction and brain damage induced by permanent forebrain ischemia in rats. *Pharmacol Biochem Behav* 2008; **88**: 213-21.

[120]Currais A, Chiruta C, Goujon-Svrzic M, Costa G, Santos T, Batista MT, et al. Screening and identification of neuroprotective compounds relevant to Alzheimer's disease from medicinal plants of S. Tomé e Príncipe. *J Ethnopharmacol* 2014; **155**: 830-40.

[121]Paithankar VV, Belsare SL, Charde RM, Vyas JV. *Acorus calamus*: an overview. *Int J Biomed Res* 2011; **2**: 518-29.

[122]Pattanaik J, Kumar Y, Khatri RS. *Acorus calamus* Linn: a herbal tonic for central nervous system. *J Sci Innov Res* 2013; **2**: 950-4.

[123]Alikhanzade M, Tehranipour M, Khayatzade J. The neuroprotective effect of alcoholic and aqueous extracts of *Achillea biebersteinii* leaves on spinal motoneurons denegation after sciatic nerve compression in rats. *Adv Herb Med* 2015; **1**: 8-16.

[124]Kumar GP, Khanum F. Neuroprotective potential of phytochemicals. *Pharmacogn Rev* 2012; **6**: 81-90.

[125]Singh HK, Dhawan BN. Neuropsychopharmacological effects of the Ayurvedic nootropic *Bacopa monniera* Linn. (Brahmi). *Indian J Pharmacol* 1997; **29**: 359-65.

[126]Nalini K, Aroor AR, Rao A, Karanth KS. Effect of *Centella asiatica* fresh leaf aqueous extract on learning and memory and biogenic amine turnover in albino rats. *Fitoterapia* 1992; **63**: 231-8.

[127]Cauli O, Morelli M. Caffeine and the dopaminergic system. *Behav Pharmacol* 2005; **16**: 63-77.

[128]Gu L, Gonzalez FJ, Kalow W, Tang BK. Biotransformation of caffeine, paraxanthine, theobromine and theophylline by cDNA-expressed human CYP1A2 and CYP2E1. *Pharmacogenetics* 1992; **2**: 73-7.

[129]Hong SY, Jeong WS, Jun M. Protective effects of the key compounds isolated from Corni fructus against β-amyloid-induced neurotoxicity in PC12 cells. *Molecules* 2012; **17**: 10831-45.

[130]Kumar V. Potential medicinal plants for CNS disorders: an overview. *Phytother Res* 2006; **20**: 1023-35.

[131]Cortes N, Posada-Duque RA, Alvarez R, Alzate F, Berkov S, Cardona-Gómez GP, et al. Neuroprotective activity and acetylcholinesterase inhibition of five Amaryllidaceae species: a comparative study. *Life Sci* 2015; **122**: 42-50.

[132]Ahmad AS, Ansari MA, Ahmad M, Saleem S, Yousuf S, Hoda MN, et al. Neuroprotection by crocetin in a hemi-parkinsonian rat model. *Pharmacol Biochem Behav* 2005; **81**: 805-13.

[133]Papandreou MA, Kanakis CD, Polissiou MG, Efthimiopoulos S, Cordopatis P, Margarity M, et al. Inhibitory activity on amyloid-beta aggregation and antioxidant properties of *Crocus sativus stigmas* extract and its crocin constituents. *J Agric Food Chem* 2006; **54**: 8762-8.

[134]Pitsikas N, Boultadakis A, Georgiadou G, Tarantilis PA, Sakellaridis N. Effects of the active constituents of *Crocus sativus* L., crocins, in an animal model of anxiety. *Phytomedicine* 2008; **15**: 1135-9.

[135]Rajakrishnan V, Viswanathan P, Rajasekharan KN, Menon VP. Neuroprotective role of curcumin from *Curcuma longa* on ethanol-induced brain damage. *Phytother Res* 1999; **13**: 571-4.

[136]Joseph JA, Shukitt-Hale B, Casadesus G. Reversing the deleterious effects of aging on neuronal communication and behavior: beneficial properties of fruit polyphenolic compounds. *Am J Clin Nutr* 2005; **81**(1 Suppl): 313S-6S.

[137]Gupta P, Akanksha, Siripurapu KB, Ahmad A, Palit G, Arora A, et al. Anti-stress constituents of *Evolvulus alsinoides*: an Ayurvedic crude drug. *Chem Pharma Bull (Tokyo)* 2007; **55**: 771-5.

[138]Chandrasekaran K, Mehrabian Z, Spinnewyn B, Chinopoulos C, Drieu K, Fiskum G. Neuroprotective effects of bilobalide, a component of ginkgo biloba extract (EGb 761) in global brain ischemia and in excitotoxicity-induced neuronal death. *Pharmacopsychiatry* 2003; **36**(Suppl 1): S89-94.

[139]Tawab MA, Bahr U, Karas M, Wurglics M, Schubert-Zsilavecz M. Degradation of ginsenosides in humans after oral administration. *Drug Metab Dispos* 2003; **31**: 1065-71.

[140]Radad K, Gille G, Liu L, Rausch WD. Use of ginseng in medicine with emphasis on neurodegenerative disorders. *J Pharmacol Sci* 2006; **100**: 175-86.

[141]Rausch WD, Liu S, Gille G, Radad K. Neuroprotective effects of ginsenosides. *Acta Neurobiol Exp (Wars)* 2006; **66**: 369-75.

[142]Dhingra D, Parle M, Kulkarni SK. Memory enhancing activity of *Glycyrrhiza glabra* in mice. *J Ethnopharmacol* 2004; **91**: 361-5.

[143]Yang B Kallio HP. Fatty acid composition of lipids in sea buckthorn (*Hippophaë rhamnoides* L.) berries of different origins. *J Agric Food Chem* 2001; **49**: 1939-47.

[144]Liu JS, Zhu YL, Yu CM, Zhou YZ, Han YY, Wu FW, et al. The structures of huperzine A and B, two new alkaloids exhibiting marked anticholinesterase activity. *Can J Chem* 1986; **64**: 837-9.

[145]Liu L, Sun JX. [Advances on study of organophosphate poisoning prevented by huperzine A]. *Wei Sheng Yan Jiu* 2005; **34**: 224-6. Chinese.

[146]Silva BA, Dias AC, Ferreres F, Malva JO, Oliveira CR. Neuroprotective effect of *H. perforatum* extracts on beta-amyloid-induced neurotoxicity. *Neurotox Res* 2004; **6**: 119-30.

[147]Silva BA, Oliveira PJ, Cristóvão A, Dias AC, Malva JO. Biapigenin modulates the activity of the adenine nucleotide translocator in isolated rat brain mitochondria. *Neurotox Res* 2010; **17**: 75-90.

[148]Zeng KW, Wang XM, Ko H, Kwon HC, Cha JW, Yang HO. Hyperoside protects primary rat cortical neurons from neurotoxicity induced by amyloid β-protein via the PI3K/Akt/Bad/Bcl (XL)-regulated mitochondrial apoptotic pathway. *Eur J Pharmacol* 2011; **672**: 45-55.

[149]Prediger RD, Fernandes MS, Rial D, Wopereis S, Pereira VS, Bosse TS, et al. Effects of acute administration of the hydroalcoholic extract of mate tea leaves (*Ilex paraguariensis*) in animal models of learning and memory. *J Ethnopharmacol* 2008; **120**: 465-73.

[150]Koulivand PH, Khaleghi Ghadiri M, Gorji A. Lavender and the nervous system. *Evid Based Complement Alternat Med* 2013; **2013**: 681304.

[151]Alquraini A, Waggas D, Bohlke M, Maher T, Pino-Figueroa A. Neuroprotective effects of *Lepidium meyenii* (Maca) and macamides against amyloid-beta (25-35) induced toxicity in B-35 neuroblastoma cells (657.13). *FASEB J* 2014; **28**(Suppl 1): 657.13.

[152]Pachauri SD, Tota S, Khandelwal K, Verma PR, Nath C, Hanif K, et al. Protective effect of fruits of *Morinda citrifolia* L. on scopolamine induced memory impairment in mice: a behavioral, biochemical and cerebral blood flow study. *J Ethnopharmacol* 2012; **139**: 34-41.

[153]Kang SY, Lee KY, Sung SH, Kim YC. Four new neuroprotective dihydropyranocoumarins from *Angelica gigas*. *J Nat Prod* 2005; **68**: 56-9.

[154]Omar SH. Cardioprotective and neuroprotective roles of oleuropein in olive. *Saudi Pharm J* 2010; **18**: 111-21.

[155]Ferraz AC, Angelucci ME, Da Costa ML, Batista IR, De Oliveira BH, Da Cunha C. Pharmacological evaluation of ricinine, a central nervous system stimulant isolated from *Ricinus communis*. *Pharmacol Biochem Behav* 1999; **63**: 367-75.

[156]Lee E, Eom JE, Kim HL, Kang DH, Jun KY, Jung DS, et al. Neuroprotective effect of undecylenic acid extracted from *Ricinus communis* L. through inhibition of μ-calpain. *Eur J Pharm Sci* 2012; **46**: 17-25.

[157]Lai MY. Chen CC, Hsiu SL, Chao DL. Analysis and comparison of baicalin, baicalein and wogonin contents in traditional decoctions and commercial extracts of *Scutellariae radix*. *J Food Drug Anal* 2001; **9**: 145-9.

[158]Singh A, Singh S, Krishna G, Pandey AK. Traditional knowledge and ethnopharmacological perspectives of herbal medicine in India: a review. *J Med Plants Stud* 2014; **2**: 89-96.

[159]Schliebs R, Liebmann A, Bhattacharya SK, Kumar A, Ghosal S, Bigl V. Systemic administration of defined extracts from *Withania somnifera* (Indian ginseng) and shilajit differentially affects cholinergic but not glutamatergic and GABAergic markers in rat brain. *Neurochem Int* 1997; **30**: 181-90.

[160]Singh N, Pandey BR, Verma P. An overview of phytotherapeutic approach in prevention and treatment of Alzheimer's syndrome & dementia. *Int J Pharm Sci Drug Res* 2011; **3**: 162-72.

[161]Ko SY, Lee HE, Park SJ, Jeon SJ, Kim B, Gao Q, et al. Spinosin, a c-glucosylflavone, from *Zizyphus jujuba* var. *spinosa* ameliorates Aβ1-42 oligomer-induced memory impairment in mice. *Biomol Ther (Seoul)* 2015; **23**: 156-64.