REVIEW ARTICLE

A Review on Anti-cancer and Antioxidant Potentials of Plants with Mode of Action

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ABSTRACT
Cancer is an intensifying health problem, and after myocardial infarction, it is the most common reason for death among people. The current review aimed to highlight the anti-cancer and antioxidant potential of plant-derived natural bio-active compounds. Plants investigated so far with enriched anti-cancer, and antioxidant potential was traced out from previously published literature to present in one document for the ease of the scientific community and researchers working on it. The phytochemicals extracted from herbs have executed numerous healing effect by preventing cancer stimulating hormones and enzymes, exciting DNA reparation mechanisms, endorsing the production of shielding enzymes, persuading antioxidant action, and augmenting immunity, hence presenting the anti-cancer effect. Epidemiological studies suggest that regular intake of anti-cancerous food prevents the onset of many types of cancers. Antioxidant with scavenging properties and free radicals, are predictable to play significant roles in inhibiting ROS induced sicknesses, including cancer, because they can hamper oxidation route by responding with free radicals and chelating free catalytic metals; also by serving as O^2 scavengers.
Keywords: Anti-cancer plants, Antioxidants, DNA Reparation, Phytochemicals

INTRODUCTION

Cancer is an intensifying health problem, and after myocardial infarction, it is the most common reason for death among people[1]. The scientific community has shown interests in pharmacological studies of plant compounds to be used as cancer suppressants[1]. Plant products also perform in synergy with chemotherapeutic drugs by reducing cell resistance to them and cause them to effect efficiently[2]. Cancer could also be prevented by consuming diets that have anti-cancerous properties[3]. Epidemiological studies suggest that regular intake of anti-cancerous food prevents the onset of many types of cancers[4].

Normally human antioxidant system can rummage these hazardous radicals to keep the balanced oxidation and anti-oxidation. However, excessive contact with cigarette smoke, alcoholic beverages, hazardous radiation, xenobiotics may enhance the production of unnecessary ROS that can disturb the equilibrium of oxidation and anti-oxidation process, resulting chronic and degenerative disorders[5]. To prevent undesirable effects of oxidative stress, boosting of anti-oxidant defensive system of the body is much required with supplementation of exogenous antioxidants[6]. Anti-oxidants are also synthesized in-vivo or administrated orally antioxidants. Plants are potential source of exogenous (i.e., oral administration) antioxidants from a long period.

The current review article was aimed to highlight the anti-cancer and antioxidant potential of plant-derived natural bio-active compounds. Plants investigated so far with enriched anti-cancer and antioxidant potential were traced out from previously published literature to present in one document for the ease of the scientific community and researchers working on it. In this review, edible parts of plants with anti-cancer and antioxidant activity were presented for the information of the community to aware them with the medicinal benefits of commonly available plants.

Mechanism of Antioxidant Action

Normally, anti-oxidants defense system counter to free radicals prompted oxidative damages[7]. When we look on mood of action, anti-oxidants might be categorized as; free radical terminator, a chelator, or O_2 scavengers[8]. Free radical terminator act as a primary antioxidant reacts with higher energy lipid radicles and converts them into a thermodynamically more stable product. It contributes hydrogen/electron from phenolic hydroxyl groups, which either prevent the initiation or propagation step given in equations below[9]. An anti-oxidant (AH) reacts with radicals formed during autoxidation. The antioxidants free radicle presented in below equations are low energy free radicles which don't allow initiating the chain propagation reactions but entering into a termination reaction with lipid radicals to form lipid anti-oxidant products[8].

$R^{\circ} + AH. \longrightarrow RH + A^{\circ}$ (Inhibition of the propagation step)
$R^{\circ}\, OO^{\circ} + AH \longrightarrow ROOH + A^{\circ}$ (Involvement in termination reaction)
$RO^{\circ} + AH \longrightarrow ROH + A^{\circ}$ (Involvement in termination reaction)
$R^{\circ} + A^{\circ} \longrightarrow RA$
$R^{\circ} + A^{\circ} \longrightarrow ROA$

1. Electron to active-radical leads to cation and anion radical formation, which is flourished by transfer of proton from cation to anion radical.
2. H^+ transfers from anti-oxidant to active-radicles
3. Deprotonation leads to electron transfer by subsequent anion to active-radicle
4. Proton (electron coupled) transfers for phenolic anti-oxidant

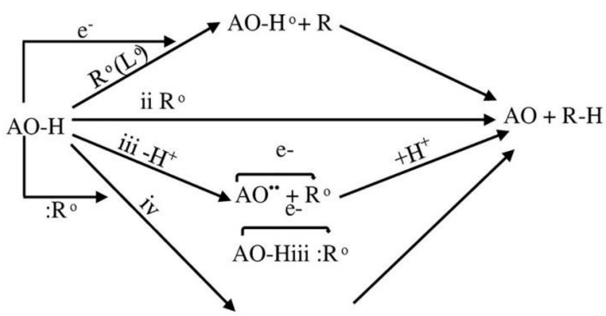

Fig. 1: Process of radical scavenging by an antioxidant[8].

TYPES OF ANTIOXIDANTS

Non-enzymatic Antioxidants

Non enzymatic defensive systems alongside oxidative stress comprising on antioxidants; viz, α-tocopherol, phenolic compounds, carotenoids, glutathione and ascorbic acid[10], which are liable for scavenging free radicals presence in plants by donating electron/ hydrogen[11].

Ascorbic-acid

Mitochondria are its production house from where it is transported to other constituents of the cell by mechanism of facilitated diffusion[12]. Generally, it exists in condensed form, where its concentrations within cell range from 20 mM and 20–300 mM in cytosol and stroma (chloroplast), respectively[13]. It protects plants alongside ROS produced by photosynthetic and respiratory activities[11]. Physiological processes like growth regulation, plants metabolism and differentiation process is influenced by ascorbic acids.

Glutathione

Low molecular weight tri-peptide (γ-glutamylcysteinylglycine) having non-protein thiols, exists in virtually all components of cell, specifically ETRs (endoplasmic reticulum), mitochondria, chloroplast and chloroplasts. As a major source of thiol, glutathione serves extensive variety of biological and chemical function in living organisms. The neutrophilic properties of thiol are prime group in creation of mercaptide bonding with metals and reaction with some electrophiles[13]. Glutathione is involved in various cellular processes like regulation of enzymatic activity, cell growth/division, cell differentiation, cell death and senescence, detoxification of xenobiotics, regulation of sulfate transport, production of proteins and nucleotides, synthesis of phytochelatins, conjugation of metabolites, and expression of stress-responsive genes[14].

Carotenoids

Carotenoids are natural lipophilic pigments produced from phytoene[15] found in plastids. Carotenoids are also present in microorganisms[14]. More than 600 types of carotenoids exist in nature, with β-carotene the most abundant among others (Olson & Krinsky, 1995). Carotenoids prevent cellular lipid and membrane damage by scavenging peroxyl radicals produced during lipid peroxidation of cell membranes[15-16]. Different studies indicated that carotenoids constrain various kinds' age-related muscular degeneration, cancer types, atherosclerosis, and some other disorders[13].

α-Tocopherols

Tocopherols are a lipid-soluble antioxidant present in almost all plant parts including algae. There are four α, β, γ, and δ isomers of tocopherols, where α-tocopherols are the most abundant and active antioxidants in the chloroplast membrane (where there is one molecule of α-tocopherol for ten molecules of chlorophyll) and protect it against photo-oxidative damage[13]. It works as a well-organized 'chain breaker' while lipid peroxidation process occurring in cell membranes and other lipid particles, consisting of LDL (low density lipoprotein). Maize, wheat germs and cottonseeds and sunflower oil contain higher level of tocopherols and others like as tocols and tocotrienols; these are required to protect seed during germination from lipid peroxidation and for longevity of seed[17].

Phenolic Compounds

A group of secondary metabolites in plants cells, including flavonoids, tannins, hydroxycinnamates esters and lignins. Phenolic acids also include in phenolic compounds antioxidants; it includes the byproducts of cinnamic acid benzoic acid [18]. It is responsible for H_2O_2 scavenging.

Anti-oxidative properties of polyphenols are due to

i) hydrogen or electron contributors donating high reactivity,
ii) stabilization and delocalization properties to electron un-pairing
iii) Chelating ability for transmission metal ion
iv) Reduction of fluidity of membrane

Enzymatic Anti-oxidants

Enzymes existent in different sub-cellular components as a part of anti-oxidant machanism including superoxide-dismutases, catalases, ascorbate-peroxidase, mono dehydro-ascorbate reductases, dehydro-ascorbate reductases, glutathione-reductases, and guaiacol-peroxidases[14].

Superoxide-dismutase (SODs)

Superoxide dismutase is a part of metalloenzymes family and forms frontline defense against reactive oxygen species[14-19]. SODs found in various creatures, like bacteria, yeasts, different animals, and plants. Plants carry numerous genes encoded SODs, which may be accomplished by expansion, and environmental signs[19]. Larson, 1998 reported that activity of superoxide dismutase and catalase have been shown to decline in older leaves of tobacco plants, which indicates signs of membrane damage[20].

Catalase (CAT)

Catalase was ever first characterized antioxidant enzyme[15]. Catalase is tetrameric heme-containing enzyme, present in peroxisomes- a hotspot of H_2O_2 production. It is found in peroxisomes of leaves and eliminates H_2O_2 formed during the process of photo-respiration via alteration of glycolate to glyoxylate[11]. This enzyme involves voguish scavenging of H_2O_2, which can diffuse from the cytosol. There are three isoforms of catalase, CAT1, CAT-2 and CAT-3 found in mitochondria, chloroplast and cytosol but slight tendency to organic peroxide(s) (R-O-O-R)[14].

Peroxidases

Number of iso-enzymes of peroxidase (POD) plays an important role during normal conditions and in response to environmental stresses. There are four types of peroxidases encoded by the plants present in different cell components, including chloroplast and mitochondria[17]. Ascorbate peroxidase (APX) and guaiacol peroxidase (GPX) are most important peroxidases present in plants defense systems against reactive oxygen species. Ascorbate peroxidase is the essential ingredient of ascorbate glutathione cycle. It executes similar functions as catalase like, scavenging of H_2O_2, but at a different location in cytosol and chloroplast[21].

MODE OF ACTION AND MOLECULAR TARGETS OF PHYTOCHEMICALS WITH ANTI-CANCER POTENTIALS

Medicinal herbs have been observed to impart therapeutic effect to prevent and treat cancer. Herbal treatment reduces the negative effect, cancer-related problems, and enhances the healing process[22]. Anti- cancerous phytochemicals extracted from plants retard the development of normal cells into the malignant tumor and persuade apoptosis of neoplastic cells along with the prevention of metastasis and angiogenesis[1].

PLANTS WITH ANTI-CANCER PROPERTIES

Infusions made from herbs with greater potential to cure cancer work effectually through several bio-chemical paths and effects, various organ structures and nurture of body by subsidiary system[23]. Various plants have been identified to be beneficial to prevent and treat cancer such as; Aronia melanocarpa, Camellia sinensis, Catharanthus roseus, Datura metel, Momordica charantia, Curcuma longa, Gymnema sylvestre, Stevia rebaudiana, Scutellaria, Nelumbo nucifera, Oroxylum indicum e.t.c[23-24-25- 26]. Species of plants with anti-cancer potential are given in Table-I.

Table-I: Anti-cancer potential of plant species with bioactive compound and site of action

Botanical Name	**Bio-active Compound**	**Specific Cancers Suppressed**
Aegle marmelos	Skimmianine	Liver cancer (Both in vitro and in vivo)[31]
Allium wallichii	Steroids, terpenoids, flavonoids, reducing sugars and glycosides	Prostate cancer, breast cancer, cervical cancer (In vitro)[25]
Aloe vera	Alexin B, emodin	Leukemia, stomach cancer (In vivo)[32]
Amoora rohituka	Amooranin	Lymphocytic leukemia (In vitro)
Annona crassiflora	Caffeic acid, sinapic acid, rutin	Glioma, renal, ovary cancer (In vitro)[33]
Argemone gracilenta	Argemonine and berberine	B-cell lymphoma, leukemia (In vitro)[34]
Artemisia annua	Artemisinin	Liver, breast and pancreatic cancer (Both in vitro and in vivo)[35]
Bleekeria vitensis	Elliptinium	Myelogenous leukemia and breast cancer (In vivo)[36]
Boerrhavia diffusa	Punarnavine	Malignant melanoma cancer (In vitro)[37]
Broussonetia papyrifera	2S-abyssinone Ⅱ verubulin	Glioblastoma and brain cancer (In vitro)[38]
Capsicum annuum	Luteolin	Colorectal cancer (Both in vitro and in vivo)[39]
Camelia sinesis	Epicatechingallate, picatechin, epigallocatechin, Theabrownin	Picatechin, epigallocatechin Lung, bladder, skin, prostate and breast cancer (Both in vitro and in vivo)[27]
Centella asiatica	Asiatic acid	Melanoma, glioblastoma and breast cancer (In vivo)[39]
Cicer arietinum	Bowman-Birk-type protease	Breast and prostate cancer (In vitro)[28]
Colchicum autumnale	Colchicine	Hodgkin's lymphoma, chronic granulocytic leukemia (Both in vitro and in vivo)[40]
Combretum caffrum	Combretastatins	Colon, and leukemia and lung cancer (In vivo)[35]
Crocus sativus	Crocetin	Hippocampal cell death and lung cancer (In vivo)[41]
Curcuma longa	Curcumin, ascorbic acid	Leukemia, glioblastoma, Colon adenocarcinoma, prostate esophagus, liver and skin cancer (In vitro)[30]
Debregeasia saeneb	Tannins	Internal tumors (In vitro)[10]
Dioscorea colletti	Dioscin	Liver and human gastric cancer (In vitro)[24]
Elusine coracana	Ragi bifunctional inhibitor	Myeloid leukemia cell and K562 cell line (Both in vitro and in vivo)[42]
Ginkgo biloba	Ginkgetin, ginkgolide A &B	Hepatocarcinoma, ovary, prostate, colon and liver cancer[43]
Glycyrrhiza glabra	Licochalcone-A, licoagrochalcone	Prostate, breast, lung, stomach and kidney cancer (In vivo)[29]
Gossypium hirsutum	Gossypol	Mice xenograft (HT-29) and colorectal cancer (Both in vitro and in vivo)[13]
Herba epimedii	Icariin, icaritin, icariside Ⅱ	Prostate, lung, kidney and gastric cancer (Both in vitro and in vivo)[24]
Morinda citrifolia	Damnacanthal	Lung cancer, sarcomas (In vitro)
Nigella sativa	Thymoquinone	Colon, prostate, breast and pancreas cancer[07]
Ocimum sanctum	Eugenol, orientin, vicenin	Breast, liver and fibrosarcoma cancer (In vitro)[44]
Oldenlandia diffusa	Ursolic acid	Lungs, ovary, uterus, stomach, liver, colon, rectum and brain cancer (Both in vitro and in vivo)[31]
Panax ginseng	Panaxadiol, panaxatriol	Human colon cancer (Both in vitro and in vivo), Breast, ovary, lung and prostate (In vitro)[29]
Panax pseudoginseng	Panaxadiol	Human colon cancer (Both in vitro and in vivo)[29]
Passiflora caerulea	Chrysin	Colorectal cancer (in vitro)[08]
Peganum harmala	Harmine	Breast cancer (Both in vitro and in vivo)[24]
Peltophorum dubium	Peltophorum dubium trypsin inhibitor	Rat lymphoma cells, human leukemia cells[02]

Plumbago zeylanica	Plumbagin	Liver, fibrosarcoma, leukemia and breast cancer (In vitro)[29]
Polygonum cuspidatum	Resveratrol	Colorectal, skin and liver cancer (In vitro)[42]
Psoralea corylifolia	Psoralidin, Bavachanin, corylfolinin, psoralen	Stomach, prostate cancer, Lung, osteosarcoma, fibrosarcoma and liver cancer (In vitro)[11]
Scrophularia Atropatana	dichloromethane extract of S. atropatana	breast cancer[21]
Solanum nigrum	Solamargine, solasonine	Breast, liver, lung and skin cancer (In vitro)[45]
Sylibum marianum	Silibinin, Silymarin	Lung, liver, skin, colon and prostate cancer, Colorectal cancer (Both in vitro and in vivo)[18]
Tylophora indica	Tylophorine	Breast cancer (In vivo)
Vaccinium macrocarpon	Hydroxycinnamoyl ursolic acid	Cervical, prostate cancer (In vitro)[14]
Vicia faba	Field bean protease inhibitors	Skin cancer (Both in vitro and in vivo)[02]
Vigna unguiculata	Black-eyed-pea trypsin/ Chymotrypsin inhibitor	Human breast cancer (In vitro)[34]
Vitis vinifera	Procyanidins	Human colon cancer (In vitro)
Withania somnifera	Withaferin A, D	Breast, cervix, prostate and colon cancer (In vivo)[29]
Zingiber officinale	6-Shogaol	Ovary cancer (In vitro)[33]
Ziziphus mauritiana	a-linolenic acid, Methyl stearate	Leukemia, human cervical and liver cancer (In vitro)[41]
Ziziphus spina-christi	Doxorubicin, spinanineA, rutnine, quercetin	Lung cancer and breast cancer (In vivo)[19]

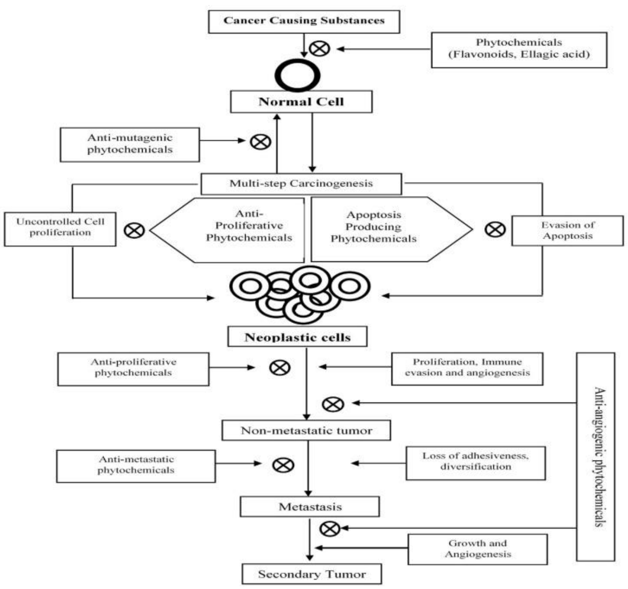

Fig. 2: Mode of action adopted by phytochemicals against cancer[1-23].

Allium wallaichii has moderate antioxidant and cytotoxic properties and includes many phytochemicals such as; steroids, glycosides, flavonoids and terpenoids. Allium wallaichii has the ability to be used as an anti-cancer agent[27]. Artemisia annua, also known as qinghao in China, where it has long been informed[28]. Artemisinin (ARS), is the active ingredient which is anti-cancerous against pancreatic cancer, liver cancer and, breast cancer.

Kumari[27] studied that green tea is obtained from new and soft leaves of Camelia sinesis. Study on Curcuma longa L has exposed for curcumin substantial potential against a varied type of both diseases (malignant and non malignant)[30]. Debregeasia saeneb suppresses internal tumors. Ginkgo biloba, Glycyrrhiza glabra, Peganum harmala L., Scrophularia Atropatana, Solanum nigrum, Vigna unguiculate, Withania somnifera (L.), Zizipus mauritiana Lam, Z. nummularia, Z. mauritiana and Z. jujuba are reported anticancer medicinal plants.

CONCLUSION

This review article describes the anti-cancer and antioxidant potential of plant-derived natural bio-active compounds. A number of medicinal plants edible parts carry anti-cancer and antioxidant activities; are presented here for information of community to aware them with medicinal benefits of commonly available plants. This article provides natural and plant base antioxidants list with their specific activity and mode of action and detail of bio-active compounds to suggest that the use of synthetic antioxidants for food preservation and medicinal purpose need to be restricted due to its toxic impacts.

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