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## An Overview On Certain Anticancer Natural Products

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### ABSTRACT

Cancer is the second leading cause of death in developed and developing countries. It may be caused due to incorrect diet, genetic predisposition or environmental factors. At least 35% of all cancers worldwide are caused by incorrect diet. The plant kingdom has a great place in the treatment of diseases with no ill effect. Numerous plant products are now used for the remedy of cancer. According to WHO estimates, more than 80% people in developing countries depend on traditional medicine for their primary health needs. Consumption of large amount of vegetables and fruits can prevent the development of cancer. Several natural products are available as chemoprotective agents against various types of cancer. These chemoprotective agents are present in fruits, vegetables, plant extracts, herbs, microbes and marine organisms. A host of natural product constituents could be responsible for the protective effect against cancer. Although the mechanism of the protective effect is unclear, nevertheless, the consumption of natural products lowers the incidence of cancer. A major group of these products are the powerful antioxidants, others are phenolic in nature and the remainder includes reactive groups. This article emphasizes many anticancer natural products obtained from plant, microbe and marine sources, which possess potent anticancer activity.

**Keywords:** Antioxidants; anticancer activity; cancer; anticancer natural products

### INTRODUCTION

Cancer is the second leading cause of death in developed and developing countries. It may be caused in one of the three ways : incorrect diet, genetic predisposition and through the environment. At least 35% of all cancers worldwide are caused by incorrect diet, and in the case of colon cancer, diet may account for 80% of the cases. When one adds alcohol and cigarettes to the diet, the percentage may increase to 60%. The genetic predisposition gives rise to 20% cancer cases. Thus the majority of cancers are being associated with a host of environmental carcinogens. As long ago as 480 BC, Hippocrates recognized that several aspects of what we now call 'lifestyle' must come together to produce a healthy body. He said, 'Positive health requires a knowledge of man's primary constitution and the powers of various foods, both those natural to them and those resulting from human skill.' What Hippocrates called 'man's primary constitution,' we today call 'genetics', and we can infer that foods 'resulting from human skills' can be equated with today's diet [1].

The plant kingdom has a great place in the treatment of diseases with no ill effect. Numerous plant products are now used for the remedy of cancer. According to WHO estimates, more than 80% people in developing countries depend on traditional medicine for their primary health needs [2-4]. In India, about 15-20 thousand plants have

good medicinal value, out of 45,000 plant species identified. However, traditional communities use only about 7000-7500 plants, Siddha system of medicine uses about 600, Ayurveda 700, Unani 700 and modern medicine about 30 medicinal plants for treating various diseases in man and animal. However, only few medicinal plants have attracted the interest of scientists to investigate the remedy for cancer [2-3].

Some medicinal plants and their products, including vegetables, fruits and crops may prevent from cancer. Consumption of large amount of vegetables and fruits has been reported to prevent the growth of cancer. Many doctors recommend that people wishing to reduce the risk of cancer eat large amount of fruits and vegetables every day. Thus, many plant-derived products have shown potent antitumour activity against several cancer cell lines [2-3, 5].

### CERTAIN ANTICANCER NATURAL PRODUCTS

Several natural products have been reported to act as chemoprotective agents against various types of cancer. These natural products are present in fruits, vegetables, plant extracts, herbs, microbes and marine organisms. A host of natural product constituents could be responsible for the protective effect against cancers, and it is likely that many of them play an important role. Although the mechanism of the protective effect is unclear, nevertheless, the consumption of fruits and vegetables lowers the incidence of cancer. A major group of these products are the powerful antioxidants, others are phenolic compounds and the remainder includes reactive groups

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Table 1 : Some anticancer plants

Botanical name (with common name)	Main active components	Mechanism of action	Cancer in which used <sup>[Ref.]</sup>
<i>Acanthopanax gracilistylus</i>	---	Antioxidant	Liver cancer cells <sup>[9]</sup>
<i>Allium cepa</i> Linn. (Piyaz), <i>A. porrum</i> (leek)	Diallyl disulphide, quercetin flavonoid, Allicin & allin	Detoxifies carcinogen, inhibits <i>Helicobacter pylori</i> , arrests cell cycle from S to G2M phase	Cancers of lung & other <sup>1</sup> organs <sup>[2, 6]</sup> , stomach cancer <sup>[10]</sup>
<i>Azadirachta indica</i> Juss. (Neem)	Polyphenolic myoinositol & dexamethasone	Cytotoxic, antioxidant	Various cancers <sup>[11]</sup> , lung tumour & liver cancer <sup>[12]</sup>
<i>Camellia sinensis</i> (Green tea, black tea)	Polyphenols	Apoptosis induction, cell cycle arrest	Tumour cells <sup>[13]</sup>
<i>Corioliolus versicolor</i> (Chinese herb)	Bisbenzyliso-alkaloids, berberine, bufalin & tetrandrine	Apoptosis induction, complexes with DNA	HL-60 & U937 cells <sup>[14]</sup>
<i>Cytopia intermedia</i> (honeybush tea)	Polyphenolic compounds	Antioxidant, antimuta- genic, alters P450- mediated metabolism	Various cancers <sup>[15]</sup>
<i>Emblca officinalis</i> Gaertn. (Amla)	Valepotriates Ascorbic & phyllembic acids	Cytotoxic Antioxidant, antitumour & immunomodulatory	Various cancers <sup>[16]</sup> Breast, gastric & uterine cancers <sup>[2, 4]</sup>
<i>Eucalyptus grandis</i> <i>Fragaria vesca</i> Linn. (Strawberries)	Euglobal-G1 Vitamin C, bioflavo- noids & chalcones	---	Various cancers <sup>[17]</sup> Various cancers <sup>[18]</sup>
<i>Gymnosporia rothiana</i> Laws	GCE	DNA/RNA & protein synthesis inhibited after treatment for 12-36 hr	Leukemia in mice <sup>[19]</sup>
<i>Malus domestica</i> (Apple)	---	Antioxidant	Various cancers <sup>[20]</sup>
<i>Ocimum sanctum</i> Linn. (Tulsi)	Flavonoids (orientin, vicenin, eugenol) & oleanic acid	Antioxidant, antitumour & immunomodulatory	Various cancers <sup>[2, 4, 21]</sup>
<i>Olea europaea</i> Linn. (Olives)	Polyphenols	Antioxidant	Various cancers <sup>[22]</sup>
<i>Ornithogalum spp.</i>	Cholestane glycoside	Apoptosis induction	HL-60 cells <sup>[23]</sup>
<i>Pinus pinaster</i> (maritime)	Polyphenolic fraction, ferrulic acid, bioflavonoids, proanthocyanidins & procyanidin pycnogenol b-Elementene	Antioxidant, increases activity of NK cells, modulates mitogenic signaling, induction of G1 arrest & apoptosis Cell cycle arrest from S to G2M phase	DU145 cells, & prostrate & skin cancers <sup>[24]</sup>
<i>Rhizoma zedoariae</i>	---	---	Cancers <sup>[25]</sup>
<i>Ricinus communis</i> Linn. (Arand)	Ricinine & ricinoleic acid	---	Various tumours <sup>[2]</sup>
<i>Rubia cordifolia</i> (Rosemary)	Carnosic acid & rosemary acid RC-1	Forms DNA adducts	P388 cells, L1210 cells & <sup>1</sup> B16 melanoma <sup>[26]</sup>
<i>Scutellariae radix</i> , <i>S. indica</i>	Flavonoids	Prostaglandin E2 production	Rat C6 glioma cells <sup>[27]</sup>
<i>Solanum spp.</i>	Flavonoid (quercetin)& alkaloids (solasodine, solanine, solamargine)	---	Various tumours <sup>[2, 21]</sup>
<i>Swertia chirata</i> Buch- Ham. (Chirayita)	Swertianin, swertinin chiratanin & swertenol	---	Various tumours <sup>[2]</sup>
<i>Triticum aestivum</i> Linn. (Wheat)	Ellagic, linolenic & oleic acids, sterols, phytases, & vitamin E	Protects against lipid peroxidation	Skin cancer <sup>[2, 17]</sup>
<i>Uncaria tomentosa</i> <i>Undaria pinnatifida</i> (Seaweed)	---	Apoptosis induction Prophylactic	Tumour cells <sup>[28]</sup> Lewis lung cancer in mice <sup>[29]</sup>
<i>Viscum album</i> , <i>Viscum var. coloratum</i> (Korean mistletoe)	Lectin alkaloids	Caspase-3 activation, lectin 11-induced apoptosis, inhibition of telomerase via mitochon- drial controlled pathway independent of p53	U937, HL-60, lymphoblastoid & hepatocarcinoma cells <sup>[30]</sup>
<i>Vitis rotundifolia</i> (Muscadene berries)	Hexamethylene bioacetamide Resveratrol	p53-dependent apoptosis, induction with telomerase Antioxidant	Human colon carcinoma & leukemic cells <sup>[31]</sup> Lung tumour in A/J mice <sup>[12]</sup>
<i>Withania somnifera</i> Dunal (Ashwagandha)	Withanolides (withaferin A, withanolide D)	Antioxidant, antitumour & immunomodulatory	Various cancers <sup>[21, 32]</sup>

**Table 2 : Plant-derived anticancer agents**

Compound	Plant source	Mechanism of action	Cancer in which used <sup>[Ref.]</sup>
Docetaxel	Western yew tree (Taxanes)	Promotes tubulin assembly & inhibits microtubule depolymerization, also acts as a mitotic spindle poison & induces mitotic block in proliferative cells	Breast, ovarian, lung, head, neck & colorectal melanomas <sup>[21, 33]</sup>
Flavopiridol	<i>Dyboxylum binectiferum</i>	CDK modulator	Various cancers <sup>[34]</sup>
Irinotecan	<i>Camptotheca acuminata</i>	Inhibits action of topoisomerase I, prevents religation of DNA strand & results in cell death	Leukemia & liver, colorectal, & head & neck cancers <sup>[21, 31, 33]</sup>
Paclitaxel	Western yew tree (Taxanes)	Promotes assembly of microtubules, stabilizes them against depolymerization, inhibits cell replication & causes apoptosis	Breast & ovarian adenocarcinomas & other solid tumours <sup>[21, 33, 35]</sup>
Topotecan	<i>Camptotheca acuminata</i>	Inhibits topoisomerase I & repairs nuclear DNA	Ovary & lung cancers <sup>[21, 34-35]</sup>
Vinblastine	<i>Catharanthus roseus (Vinca rosea)</i>	Inhibits microtubule formation & arrests mitosis in metaphase	Breast, lymphoma, germ-cell & renal cancers <sup>[21, 34]</sup>
Vincristine	<i>Catharanthus roseus (Vinca rosea)</i>	Inhibits microtubule formation & arrests mitosis in metaphase	Leukemia, lymphoma, & cancers of breast & lung <sup>[21, 33]</sup>

**Table 3 : Microbe-derived anticancer agents** <sup>[33,36-39]</sup>

Compound	Microbial sources	Mechanism of action	Cancer in which used
Actinomycin	<i>Streptomyces spp.</i>	Blocks DNA dependent RNA synthesis	Sarcoma & germ-cell tumours
Bleomycin	<i>Streptomyces verticillus</i>	Metal chelating glycopeptide antibiotic & it degrades preformed DNA	Germ-cell, cervix, head & neck cancers
Daunomycin	<i>Streptomyces coeruleorubidus</i>	Blocks DNA dependent RNA synthesis	Leukemia
Doxorubicin	<i>Streptomyces Pneuceticus</i>	Binds with DNA, & inhibits DNA & RNA synthesis	Cancers of breast, ovary, lung & other organs
Epirubicin	<i>Streptomyces pneuceticus</i>	Binds with DNA, & inhibits DNA & RNA synthesis	Breast cancer
Geldanamycin	<i>Streptomyces Hygroscopicus</i>	Cell cycle disruption	Experimental
Idarubicin	<i>Streptomyces Pneuceticus</i>	Binds with DNA, & inhibits DNA & RNA synthesis	Breast cancer & leukemia
Mitomycin C	<i>Streptomyces caespitosus</i>	After enzyme activation acts as bifunctional alkylating agent	Gastric, colorectal, anal & lung cancers
Rapamicin	<i>Streptomyces hygroscopicus</i>	Immunosuppressant	Experimental
Streptozocin	<i>Streptomyces achromogenes</i>	---	Gastric & endocrine tumours
Wortmannin	<i>Talaromyces wortmanni</i>	Potent enzyme inhibitor	Experimental

that confer protective properties against cancers <sup>[2, 5-6]</sup>.

In view of the above facts, this review article has been presented to enumerate certain natural products with anticancer activity. These natural products are derived from plants, microbes and marine organisms (Tables 1-4). They have been found very effective in ex-

perimental as well as clinical cases of many cancers, e.g. sarcoma, lymphoma, carcinoma and leukemia. Some authors <sup>[7-8]</sup> have elucidated the main active components of anticancer plants as mentioned in Table 1; however, the mechanism of action of anticancer natural products and their uses in various cancers have been reported by other authors as cited in Tables 1 to 4.

**Table 4 : Marine organism-derived anticancer agents**

Compound	Mechanism of action and use in various cancer (with references)
Aplidine	Inhibition of cell-cycle progression has been observed experimentally <sup>[40]</sup>
Bryostatin 1	Activation of Protein kinase C (PKC) has been observed experimentally <sup>[41]</sup>
Citarabine	Inhibition of DNA synthesis used in leukemia & lymphoma <sup>[40]</sup>
Cryptophycin	Hyperphosphorylation of B-cell lymphoma 2 has been observed experimentally <sup>[40]</sup>
Discodermolide	Stabilization of tubulin has been observed experimentally <sup>[40]</sup>
Dolastatin 10	Inhibition of microtubules & pro-apoptotic effects have been observed experimentally <sup>[42-43]</sup>
Ecteinascidin 743	Alkylation of DNA has been observed experimentally <sup>[44]</sup>
Halicondrin B	Interaction with tubulin has been observed experimentally <sup>[40]</sup>

It has been reported <sup>[3,5-6]</sup> that medicinal plants contain many antioxidants such as vitamins (A, E, C, K), carotenoids, flavonoids, polyphenols, alkaloids, proteins, enzymes etc. as evident from Table 1. These antioxidants possess potent anticancer activities. The plant-derived anticancer agents (e.g. docetaxel, flavopiridol, irinotecan, paclitaxel, topotecan, vinblastine and vincristine; Table 2) and the microbe-derived anticancer agents (e.g. antibiotics of anthracycline, bleomycin, actinomycin, mitomycin and aureolic acid groups; Table 3) have different mechanism of action with high anticancer properties. However, the marine-derived anticancer agents (e.g. aplidine, bryostatin, cryptophycin, discodermolide, dolastatin, ecteinascidin and halicondrin B) have been shown to inhibit experimentally induced cancers.

## CONCLUSION

Natural products are the most important part of our life, many of which are consumed daily with the diet. They provide significant protection against various cancers and many other diseases. Consumption of natural products is widely accepted as lowering the risk of several cancers. The antioxidant medicinal plants and their products prevent from the cancer and other diseases by protecting cells from damage. Thus, consuming a diet rich in antioxidant fruits, vegetables, herbs etc. will certainly provide health-protective effects. Microbes and marine organisms also play an important role in the prevention and treatment of cancer. Conclusively, all the natural products described in this review article exhibit anticancer activities. Although many scientific studies have been performed to explore out the anticancer activities of several natural products, but no drug has been searched out to cure the cancer perfectly. Hence, there is an

urgent and great need for oncologists and pharmaceutical scientists to derive novel anticancer drugs from natural products, which have no or negligible toxicity unlike the allopathic drugs.

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