Impact of different phytochemical classes and *Ayurvedic* plants in battle against cancer

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Cancer is believed the most dangerous diseases throughout the world. *Ayurvedic* texts have mentioned this disease as *arbuda* and plants are also listed for treatment. Coordination between the *ayurvedic* and modern framework can be helpful for future studies regarding the drug discovery from these plants. In recent years, many plants have been screened for anticancer activity and numerous potential dynamic constituents have also been confined from them. This survey highlights the fundamental phytochemical classes taking part effectively against malignancy. The present paper discusses the current status of researches in the field of cancer with repect to *Ayurvedic* plants and focuses on the phytochemical classes potentially active as anticancer.

Introduction

Cancer remains one of the leading causes of morbidity and mortality globally. Amongst the noncommunicable diseases, cancer is the second leading cause of death, after cardiovascular disease. Cancer is responsible for one in eight deaths worldwide—more than AIDS, tuberculosis, and malaria together . Globally, the number of cancer death is projected to increase from 7.1 million in 2002 to 11.5 million in 2030.[1] Cancer is the uncontrolled growth of abnormal cells in the body. Cancerous cells are also called malignant cells. Although cancer can develop in virtually any of the body's tissues, and each type of cancer has its unique features, the basic processes that produce cancer are quite similar in all forms of the disease.[2]

Ayurveda, the oldest Indian indigenous medicine system of plant drug is known from very early times for preventing or suppressing various tumors using these natural drugs. And nowadays scientists are keener to researches on complementary and alternative medicine for the management of cancer. In *Ayurvedic* concept, according to '*Charaka*' and '*Sushruta Samhitas*' cancer is described as inflammatory or non-inflammatory swelling and mentioned either as '*Granthi*'(Minor neoplasm) or '*Arbuda*'(Major neoplasm).[3] *Ayurvedic* literature defines three body-control systems, viz., the nervous system (*vata* or air), the venous system (*Pitta* or fire) and the arterial system (*Kapha* or water) which mutually coordinate to perform the normal function of the body. In benign neoplasm (*Vataja, Pittaja or Kaphaja*) one or two of the three bodily systems are out of control and is not too harmful because the body is still trying to coordinate among these systems. Malignant tumors (*Tridoshaja*) are very harmful because all the three major bodily system lose mutual coordination and thus cannot prevent tissue damage, resulting in a deadly morbid condition.[4]

Plants are natural sources of phytochemicals which are helpful to fight against diseases. The major phytochemicals to produce a significant pharmacological actions are tannins, alkaloids, flavonoids and flavones, steroids and sterols, phytohormones, terpenoids, natural pigments such as carotenoids, alpha and beta carotenes, saponins and sapogenins, cardiac glycosides etc. These phytochemicals play crucial role in fighting against the one of the dangerous disease cancer.

The anticancer activities of number of plants are still being actively researched and some have shown promising results. Here some most frequently examined plants are reviewd regarding their effect on cancer. Table 1 illustrates list of plants which have proven anticancer activity.

Table 1. Anticancer activity of plants

Sr. No.	*Ayurvedic* Name	Scientific Name	Family	Cancer cell line/Anticancer activity	References
1.	*Gunja*	*Abrus precatorius*	Leguminosae	Yoshida sarcoma (rats) Fibro sarcoma(mice), Ascites tumors cells	5
				Human breast cancer cell line MDA-MB-231	6
2.	*Bilva*	*Aegle marmelos*	Rutaceae	Ehrlich ascites carcinoma	7
				Breast cancer cell lines MCF7, MDA-MB-231	8
				Human cancer cell lines of lung (A549), colon (CoLo05), ovary (IGROV1), prostrate (PC3), leukaemia (THP1) and breast(MCF7) cancer	9
3.	*Ajmoda*	*Apium graveolens*	Umbelliferae	Dalton's lymphoma ascites (DLA) cells, L929 cell lines (Lung fibroblast)	10
4.	*Rasna*	*Alpinia galangal*	Zingiberaceae	A549(lung adenocarcinoma cells), CRL2522(normal fibroblast cells),MCF-12A(normal epithelial cells derived from breast), CRL2321(mammary carcinoma cells) and CRL2335(mammary carcinoma cells)	11
5.	*Shirish*	*Albizzia lebbeck*	Mimosaceae	Sarcoma 180 (mice)	5
6.	*Palandu*	*Allium cepa*	Liliaceae	Human breast cancer MDA-MB-231 cells	12
7.	*Rasona*	*Allium sativum*	Liliaceae	Sarcoma (rat)	5
8.	*Kumari*	*Aloe vera*	Liliaceae	Yoshida AH-130 ascites hepatoma (pleural tumour) human neuroectodermal tumors	5
	Saptaparna	*Alstonia scholaris*	Apocyanaceae	HSI human sarcoma	5
				Benzo(a)pyrene induced forestomach carcinoma	13
				Skin carcinogenesis(Mice)	14
9.	*Surana*	*Amorphopallus campanulates*	Araceae	Colon carcinoma cell line HCT-15	15
10.	*Kalmegh*	*Andrographis paniculata*	Acanthaceae	Neuroblastima (IMR-32) And Human Colon (HT-29) Cancer Cell Line	16
11.	*Lakshamanaphala*	*Annona muricata*	Annonaceae	Breast cancer, T37D cell line	17
				Capan-1 Cells	18
				Skin Papillomagenesis in Mice	19
				HeLa cervical cancer cell	20
				Cell lines of EACC, MDA and SKBR3	21
12.	*Shatavari*	*Asparagus racemosa*	Liliaceae	Human epidermoid carcinoma	5
				UOK146 renal cell carcinoma cell line	22
13.	*Neem*	*Azadirachta indica*	Meliaceae	Prostate cancer, buccal carcinogenesis, , breast cancer, gastric carcinogenesis and B12 melanoma	23

14.	*Brahmi*	*Bacopa monnieri*	Scrophulariaceae	Walker carcinosarcoma 256 Human breast cancer (MCF7 and MDAMB 231) cell lines	5 24
15.	*Amritavallari*	*Basella rubra*	Basellaceae	Colon carcinogenesis Human cervical carcinoma	25 26
16.	*Kanchnar*	*Bauhinia variegata*	Caesalpinaceae	Prostrate (DU-145), lungs (HOP-62), ovary (IGR-OV-1), breast (MCF-7), and leukemia (THP-1) cell lines	27
17.	*Daruharidra*	*Berberis aristata*	Berberidaceae	Human epidermal carcinoma of the nasopharynx, *N*-nitrosodiethylamine induced Carcinogenesis	5
18.	*Shallaki*	*Boswelia serrata*	Burseraceae	Human epidermal carcinoma of the nasopharynx, Leukemia and brain tumors	5
19.	*Arka*	*Calotropis gigantea*	Asclepiadaceae	Human epidermal carcinoma of the Nasopharynx1	5
20.	*Senna*	*Cassia angustifolia*	Caesalpinaceae	Colorectal cancer	28
21.	*Indravaruni*	*Citrullus colocynthis*	Cucurbitaceae	Hepatocarcinoma(Hep G2 cell line)	29
22.	*Nimbuka*	*Citrus medica*	Rutaceae	Human astrocytoma cancer cell line (line1321)	30
23.	*Kesar*	*Crocus sativus*	Iridaceae	Gastric cancer, Colorectal cancer, Hepatic cancer, Pancreatic cancer, Prostate cancer, Cervical, ovarian, and breast cancer, Skin cancer, Lung cancer, Leukemia	31
24.	*Haridra*	*Curcuma longa*	Zingiberaceae	Fibro sarcoma, Preclinical and clinical trials B164A5 murine melanoma cells Dalton Lymphoma ascites (DLA) tumor model in Swiss Albino mice	5 32 33
25.	*Musta*	*Cyperus rotundus*	Cyperaceae	L1210 cells murine lymphoblastic leukaemia K562 and L1210 cell lines K562 erythroleukemia cells	34 35 36
26.	*Dhatura*	*Datura metel*	Solanaceae	Human epidermal carcinoma of the Nasopharynx	5
27.	*Amalaki*	*Emblica officinalis*	Euphorbiaceae	Skin carcinogenesis Cervical and ovarian cancer cells, human liver cancer cell line HepG2 Human Ovarian Cancer Cell Proliferation	37 38 39
28.	*Paribhadra*	*Erythrina suberosa*	Leguminosae	Sarcoma 180	5
29.	*Dugdhika*	*Euphorbia hirta*	Euphorbiaceae	Freund virus leukemia	5
30.	*Udumbar*	*Ficus racemosa*	Moraceae	Renal carcinogenesis	40
31.	*Ashwatha*	*Ficus religiosa*	Moraceae	Human breast cancer cell line	41
32.	*Langli*	*Gloriosa superba*	Liliaceae	Human hepatoma cell lineHepG2 cells	42
33.	*Jimutaka*	*Luffa echinata*	Cucurbitaceae	colon cancer cells (HT-29)	5
34.	*Kampilak*	*Mallotus philippinenis*	Euphorbiaceae	A-549, COLO-205, DU-145, HEP-2, HeLa, IMR-32, KB,	43

				MCF-7, NCI-H23, OVCAR-5, SiHa, SK-N-MC, SW-620 AND ZR-75-1 cancer lines	
				HL-60 Leukemia cells	44
35.	*Amra*	*Mangifera indica*	Anacardiaceae	Adenocarcinoma cell lines	5
				Human breast cancer (MCF-7 and MDA-MB-231 cell lines)	45
				Human proximal tubule cell line	46
36.	*Karvellak*	*Momordica charantia*	Cucurbitaceae	A-549, COLO-205, MCF-7, NCI-H322, PC-3, THP-1 AND U-87MG	47
37.	*Shigru*	*Moringa oleifera*	Moringaceae	Human epidermoid lymphocytic leukemia Skin Papillomagenesis	5
				Cervical carcinoma, HeLa cell line	29
38.	*Karveer*	*Nerium indicum*	Apocyanaceae	Erlish ascites carcinoma	5
39.	*Kallonji*	*Nigella sativa*	Ranunculaceae	Lewis lung carcinoma, Colon cancer	5
				Breast cancer cells	29
40.	*Tulsi*	*Ocimum sanctum*	Labiatae	Skin and liver tumors	29
				Dalton Lymphoma ascites (DLA) tumor model in Swiss Albino mice	35
41.	*Shyonak*	*Oroxylum indicum*	Bignoniaceae	HeLa cells	48
42.	*Gandhaprasarini*	*Paederia foetida*	Rubiaceae	Human epidermoid carcinoma of the Nasopharynx	5
43.	*Katuki*	*Picrorrhiza kurroa*	Schrophulariaceae	Hepatic cancers	5
44.	*Bhumi amalaki*	*Phyllanthus niruri*	Phyllanthaceae	Skin melanoma and prostate cancer cells	49
45.	*Kankola*	*Piper cubeba*	Piperaceae	Breast cancer cell lines (MCF-7, MDA-MB-231, MDA-MB-468)	50
46.	*Pippali*	*Piper longum*	Piperaceae	DU-145 prostate, A549 lung, THP-1 leukemia, , IGR-OVI-1 ovary and MCF-7 breast cancer cell line	51
47.	*Chitrak*	*Plumbago zeylanica*	Plumbaginaceae	Hepatoma	5
48.	*Ashoka*	*Polyalthia longifolia*	Annonaceae	Ehrlich's ascites tumor and Dalton's solid tumor, HeLa and MCF-7 cells	52
				HL-60 cells	53
49.	*Dadima*	*Punica granatum*	Punicaceae	Prostate cancer cell line	54
				Human breast cancer	55
				Mammary organ culture (mouse)	56
50.	*Mulaka*	*Raphanus sativum*	Cruciferae	MDA-MB-231 human breast cancer cells	57
51.	*Revandachini*	*Rheum emodi*	Polygonaceae	Breast cancer cells (MDA-MB-231)	58
				MDA-MB-435S(human breast carcinoma), Hep3B (human hepatocellular carcinoma) and PC-3 (human prostate cancer)	59
				MDA-MB-435S and Hep3B cell lines	60
52.	*Eranda*	*Ricinus communis*	Euphorbiaceae	SKMEL28 human melanoma	61

				cells	
53.	*Manjishtha*	*Rubia cordifolia*	Rubiaceae	P-388, L-1210, B-16 melanoma, colon 388, Lewis lung carcinoma, mammary carcinoma	5
54.	*Bhallataka*	*Semecarpus anacardium*	Anacardiaceae	Leukemia, melanoma and glioma, hepatocarcinoma	62
55.	*Kakamachi*	*Solanum nigrum*	Solanaceae	Human Leukemic Cell Lines	63
				HepG2 and CT26 cancer cell lines	64
				Human endometrial carcinoma cell lines, HEC1A, HEC1B, and KLE	65
56.	*Kantakari*	*Solanum xanthocarpum*	Solanaceae	leukemia (THP1) and lung cancer (HOP62) cell lines	66
57.	*Lavanga*	*Syzygium aromaticum*	Myrtaceae	Colon, Lung, and Breast Cancer Cell Lines	67
				MCF7 human breast cancer cell lines	68
				MCF-7 human estrogen dependent breast cancer and MDA-MB-231 human estrogen independent breast cancer cell lines (ATCC)	69
				Lung cancer	70
58.	*Jambu*	*Syzygium cumini*	Myrtaceae	Cervical cancer cell lines	71
				Skin papillomagenesis (mice)	72
				Gastric carcinogenesis(mice)	73
59.	*Talisapatra*	*Taxus baccata*	Taxaceae	Cytotoxic against various tumors	5
				HepG2 (Human hepatocarcinoma) and SKOV3 (Human ovary carcinoma)	74
				Human gastric and colon tissue	75
60.	*Sarpunkha*	*Tephrosia purpurea*	Fabaceae	MCF-7 cell line	29
				Human breast cancer cell line	41
61.	*Arjuna*	*Terminalia arjuna*	Combretaceae	Hepatocellular carcinoma	76
62.	*Bibhitaki*	*Terminalia bellerica*	Combretaceae	human cancer cell lines, including cancers of lung (A549), prostate (PC-3), breast (T47D and MCF-7), colon (HCT-16 and Colo-205) and leukemia (THP-1, HL-60 and K562)	77
63.	*Haritaki*	*Terminalia chebula*	Combretaceae	Lung Cancer Cells (A549) and mouse lung cancer cell line LLC	78
64.	*Guduchi*	*Tinospora cordifolia*	Menispermaceae	Dalton Lymphoma ascites (DLA) tumor model in Swiss Albino mice	35
65.	*Gokshur*	*Tribulus terrestris*	Zygophyllaceae	Liver cancer cells	79
				Papillomagenesis, HepG2 cells, human skin fibroblasts	80
66.	*Methika*	*Trigonella foenum-graecum*	Fabaceae	T-cell lymphoma	81
				(TCP), B-cell lymphomas, Thyroid Papillary carcinoma (FRO) and breast cancer (MCF7)	
				Hepatocellular Carcinoma Cell Line, HepG2	82

				Breast, pancreatic and prostate cancer cell lines	83
67.	*Sadapushpi*	*Vinca rosea*	Apocyanaceae	P-1534, carcinoma of the breast, cervix, kidney, lung and ovary	5
68.	*Nirgundi*	*Vitex negundo*	Verbenaceae	Human hepatoma cells	84
				Brine shrimp lethality bioassay	85
69.	*Draksha*	*Vitis vinifera*	Vitaceae	Skin Cancer Cell Lines A431	86
				Oral squamous cell carcinoma	87
70.	*Ashwagandha*	*Withania somnifera*	Solanaceae	Lung adenomas(Mouse)	88
				Prostate(PC3), ovary(A2780), breast(MCF7), oral(DWD), lungs(Hop62) and colon(Colo205)	89
71.	*Sunthi*	*Zingiber officinalis*	Zingiberaceae	B164A5 murine melanoma cell line	90
				Human colorectal cancer cells, human breast cancer cell lines (MCF-7 and MDA-MB231) and human hepatocellular carcinoma (HepG-2)	91
				Liver cancer(Rats)	92
				Human breast carcinoma cell lines	93
72.	*Badar*	*Ziziphus mauritiana*	Rhamnaceae	Dalton Lymphoma ascites (DLA) tumor model in Swiss Albino mice	35

Phytochemical classes and cancer

Alkaloids

Alkaloids are one of the major classes of compounds possessing anticancer activity. Several alkaloids isolated from natural herbs exhibit antiproliferation and antimetastasis effects on various types of cancers both *in vitro* and *in vivo*.[94] One of the oldest and most important anticancer drugs found from the plant *Vinca rosea* i.e.Vinca alkaloids. Some other alkaloids colchicine, morphine, berberine etc found active against cancer.

Glycosides

In the 1960s inhibition of malignant cells of cardiac glycosides *in vitro* was reported and since then other anticancer effects of cardiac glycosides have been observed. Therapeutic effect of cardiac glycosides in breast cancer has been known from 1979.[95]

Flavonoids

A huge number of epidemiological studies have been conducted to prove the protective effect of flavonoids against cancer. Flavonoids greatly influence the cascade of immunological events associated with the development and progression of cancer. In vivo studies using animal models have suggested the protective effect of flavonoids against initiation as well as tumor progression.[96]

Phenolics

The antiproliferative effects (through apoptosis) induced by the phenolic agents on several cancer cell lines, for instance, were explained in terms of topoisomerase or phosphatidylinositol-3-kinase inhibition, or even cell cycle arrest. It is generally appreciated that the toxicity associated with some phenolic compounds is mediated by their oxidative activity, which can accelerate oxidative damage in vitro, either to DNA or to proteins and carbohydrates. Another possible, although insufficiently investigated, mechanism of phenol cytotoxicity may be associated with their pro-oxidant properties.[97]

Saponins

Modern research found that saponins have antitumor effect on many cancer cells. Several saponins inhibit tumor cell growth by cell cycle arrest and apoptosis with IC50 values upto 0.2 mM.[98]

Essential oils

A very promising field of treatment with essential oils is their application against tumors. Especially since the 1990s the anticancer properties of essential oils and/or their main constituents and/or metabolites have gained more and more interest, in as much as such a "natural" therapy is accepted all over the world by the patients.[99]

Terpenes

Terpenoids constitute the largest class of natural products and are a rich reservoir of candidate compounds for drug discovery. Recent efforts into the research and development of anti-cancer drugs derived from natural products have led to the identification of a variety of terpenoids that inhibit cancer cell proliferation and metastasis via various mechanisms.[100]

Steroids

Phytosterols possess anti-cancer effects against cancer of the lung, stomach, ovary and estrogen-dependent human breast cancer. It has been speculated that phytosterols inhibit the production of carcinogens, cancer-cell growth, invasion and metastasis, and promote apoptosis of cancerous cells.[101]

Table 2 presents list of few different active plant constituents with their phytochemical class and anticancer activity which give an outline about main fundamental phytochemical classes which have potent anticancer activity.

Table 2. Active comstituents with their anticancer activity

Active constituents	Plant source	Class	Activity	References
Berberine	*Berberis aristata*	Alkaloid	Human breast cancer T47D and MCF7 cell lines	102
			HONE1 cells (a human nasopharyngeal carcinoma cell line	103
Colchicine	*Gloriosa superba*	Alkaloid	Leukemic and solid tumors	104
Flavopiridol	*Amoora rohituka*	Alkaloid	Head and neck squamous cell carcinomas	105
			Bladder Cancer Cells	106
Morphine	*Papaver somniferum*	Alkaloid	Human lung and breast carcinoma cell lines	107
Piperine	*Piper longum*	Alkaloid	Lung cancer	108
			Human fibrosarcoma (HT1080) cell, human breast cancer with *HER2*, human rectal tumor (HRT)18 cells, human prostate cancer cells	109
Pippalartine	*Piper longum*	Alkaloid	Prostate cancer cells, colon cancer cell	109
Taxol	*Taxus baccata*	Alkaloid	HeLa Cervical carcinoma, A549 Lung adenocarcinoma, U373 Grade III astrocytoma, MCF-7 Breast adenocarcinoma, HT-29 Colon adenocarcinoma, OVG-1 Ovarian carcinoma, PC-Sh Pancreatic adenocarcinoma, PC-Zr Pancreatic adenocarcinoma	110
Vincristine,Vinblastine	*Catharanthus rosea*	Alkaloid	Urothelial tract, nonsmall cell lung cancer and carcinoma of the breast	111

Bullatacin	*Annona muricata*	Glycoside	Hepatocarcinoma	112
			Mammary adenocarcinoma	113
Curcumin	*Curcuma longa*	Phenolics	Colon Carcinogenesis	114
			Mammary tumor	115
Gingerol	*Zingiber officinalis*		cancer cell lines including prostate, gastric, and breast	116
Resveratol	*Vitis vinifera*	Polyphenolics	Prostate cancer cell lines	117
			Human mammary epithelial cells	118
Diosgenin	*Trigonella foenum graecum*	Saponin	Rat colon carcinogenesis, HT-29 human colon cancer cell line	119
			Gastric Cancer BGC-823 Cells	120
Terrestrosin D	*Tribulus terrestris*	Saponin	Human prostate cancer	121
Anethole	*Foeniculum vulgare*	Essential oil	Human skin fibroblasts	122
Eugenol	*Syzygium aromaticum*	Essential oil	HL-60 human promyelocytic leukemia Cells	123
Thymoquinone	*Nigella sativa*	Essential oil	Colorectal carcinoma, breast adenocarcinoma, osteosarcoma, ovarian carcinoma, myeloblastic leukemia, and pancreatic carcinoma	116
Chebulagic acid	*Terminalia chebula*	Phenolic	Retinoblastoma cells	124
Gallic acid	*Terminalia bellerica, Emblica officinalis*	Phenolic	A549,a human lung adenocarcinoma cell line	125
			Gastric cancer cells	126
Urushiol	*Semecarpus anacardium*	Oleoresin	Breast cancer cells, MCF-7 and MDA-MB-231 cell lines	127
Emodin	*Rheum emodi*	Anthraquinone	HepG2, MDAMB231 and NIH/3T3 cells lines	128
Aloe-emodin	*Aloe vera*	Anthraquinone	CH27 (human lung squamous carcinoma cell) and H460 (human lung non-small cell carcinoma cell)	129
			Prostate cancer	130
			Breast cancer MCF-7 cells	131
			Human colon carcinoma cells	132
Boswelic acid	*Boswelia serrata*	Resin	Human malignant glioma cells	133
			Colon cancer cells	134
			Human prostate cancer xenografts in mice	135
			Colorectal cancer	136
Gambogic acid	*Garcinia indica*	Resin	Human hepatoma, breast cancer, gastric carcinoma, and lung carcinoma	116
Podophyllotoxin	*Podophyllum hexandrum*	Resin	ovarian, renal and lung cancer cell lines	137

Abrin	*Abrus precatorius*	Protein	B-cell lymphocytic-leukaemia	138 139
			Human small cell lung cancer	140
			Dalton's lymphoma ascites model	141
			MCF-7 (breast carcinoma), HepG2(hepatocarcinoma), KB (nasopharyngeal carcinoma)	
Allicin	*Allium sativum*	Protein	colon cancer LoVo cell in vitro	142
			Human gastric cancer cell lines	143
			Human gastric cancer cell line SGC-7901	144
			Human ovarian cancer cell line	145
			Renal clear cell carcinoma	146
Ricin	*Ricinus communis*	Protein	Malignant Human B-Cells	147
			Human cervical cancer cells	148

Conclusion

Plants are good source of natural chemicals which are fruitful to fight against cancer. This paper reviews anticancer activity of different plants and group of phytochemicals representing good candidates for anticancer action. All compounds reviewed in the present work have a well documented anticancer activity in different cell lines. Phytochemicals possess multiple mechanisms to fight against cancer. By utilizing this compound as a part of the treatment survival rate of patient can be expanded. The main aim of the review fulfilled by the conclusion that the main phytochemical groups fighting against cancer with more number of candidates are alkaloids, phenolics and flavonoids. More research work can be performed towards these classes of phytochemicals and there is also scope to find out main active compound from the other plants which gave anticancer activity in crude extract form.

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