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DETAILED REVIEW ON PHYTOCHEMICALS FOR VARIOUS TYPES OF CANCERS

Jeevana Jyothi B.[1*] and Ramya K.[2]

[1]Sri Padmavati Mahila Visvavidyalayam.
[2]Vikas Institute of Pharmaceutical Sciences.

***Corresponding Author: Jeevana Jyothi B.**
Sri Padmavati Mahila Visvavidyalayam.

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ABSTRACT

Cancer is the global alarming issue and has become highly hazardous, highly prevalent health worry worldwide. Several strategies are developed to combat cancer with the aim of minimizing toxicity. Large research is done on medicinal plants and their bioactive phytochemicals which would show potential therapeutic efficacy and with minimal side effects compared to anticancer drugs of synthetic origin. Researchers are now focussed their research on development of formulations of chemotherapeutic drugs either by combining them with phytochemicals or by using herbal drugs alone mainly to provide treatment with minimal side effects. Therefore the aim of the present article is to present detailed account of various phytopharmaceuticals that are used for treatment of different types of cancers. This article can become a ready reference for search of anticancer drugs of herbal source with information on source, mechanism of action and their specific uses *etc.*

KEYWORDS: Phytochemicals, Uses, Prevalence, better therapy, cancers.

INTRODUCTION

In India it is estimated that around 2.25 million people are living with cancer. Every year over 11,57,294 lakh new patients are being diagnosed with cancer. In the year 2018, a total of 7, 84,821 deaths were recorded out of which 4,13,519 were male and 3,71,302 were female.[1] In India every 8 minutes one woman dies of cervical cancer. Cancers of oral cavity and lungs account for over 25% of cancer deaths in males and cancer of breast and oral cavity account for 25% cancers in females.[2] The commonly occurring cancers in male and females in India are given in **Table 1.**

Table 1: commonly occurring cancers in males and females in India.

MALE	FEMALE
Lip, oral cavity	Breast
Lung	Lip, oral
Stomach	Cervix
Colorectal	Lung
Esophagus	Gastric

On a global scale also cancer is a leading cause of mortality. In 2018, around the world 9.6 million deaths were recorded. The most common cancers are

- Lung (2.09 million cases)
- Breast (2.09 million cases)
- Colorectal (1.80 million cases)
- Prostate (1.28 million cases)
- Skin cancer (non melanoma) (1.04 million cases)
- Stomach(1.03 million cases)

Surgical removal of cancerous tissues, radiation therapy, chemotherapy and immunotherapy are various treatment options available for the treatment of cancer. However, the success of cancer treatment depends on the type and stage of cancer.

Due to heavy demand for cost effective and affordable therapeutic strategies, researchers have now focused on the development of anticancer drugs of herbal source. India being gifted with the knowledge of Ayurveda, has ample information on various herbal drugs. Researchers have discovered and are still discovering new herbal drugs which would have lower side effects compared to synthetic drugs and are equally effective. Herbal or natural drugs would also help the researchers in overcoming the problem of resistance to anticancer drugs.

At this context, formulations of phytopharmaceuticals may be a better choice for improved therapeutic measures for cancers with many side effects. Hence the present paper presents a review on methods of Nanotechnology and information on phytopharmaceuticals for treatment of various cancers.

Phytochemicals in cancer therapy

Since ancient times Plants and their bioactive compounds are in medicinal practices. Several medicinal plant species and their phytochemicals inhibit the progression and development of cancer. It has been reported that of the 250000 plant species available only 10% have been studied for cancer treatment of different diseases.[3] Constituents such as alkaloids, flavonoids, lignans, saponins, terpenes, taxanes, vitamins, minerals, glycosides, gums, oils, inhibit cancer cell activating proteins, enzymes and signaling pathways or act by activating DNA repair mechanism (p21, p27, p51, p53 genes and their protein products), which stimulate the formation of protective enzymes (Caspase-3, 7, 8, 9, 10, 12), inducing antioxidant action (antioxidant enzymes e.g. GSH, GST and GPxn).[4]

Phytochemicals from plants and their mechanism on tumor tissues

1. Vinca alkaloids (VA)

These are group of phytochemicals isolated from *Catharanthus roseus* (C. roseus) (Apocynaceae) and are employed in the cancers therapies of breast, liver, leukemia, testes and lung. Vinorelbine, vindesine, vincristine and Vinblastine are the four main VA in use. Of these alkaloids, Vincristine and vinblastine are found to bind to a specific site termed as tubulin heterodimers or vinca-binding site and they help in disrupting the functions of microtubules or by arresting cell cycle at metaphase.[5]

2. Taxanes

Taxanes are potent anticancer agents. Their main mechanism of action is by binding to microtubules and play an important role in cell division. Docetaxel and paclitaxel are first-generation taxanes which are considered as strong anticancer agents. Both the drugs are highly effective on its different molecular targets. Paclitaxel (taxol) which is extracted from the bark and leaf of *Taxus baccata* (T. baccata) and *T. canadensis*, Corylus avellana and is used to cure a wide range of cancers including ovarian, breast and lung cancer. Paclitaxel mechanism of action is it binds with β-tubulin in the lumen of microtubules and leads to decrease in microtubule dynamics and stops cell cycle at M phase.[6] Docetaxel is a semi synthetic derivative from T. baccata which is primarily used in breast, pancreas, prostate and lung cancers therapies.

3. Camptothecin derivatives

Campothecin are clinically-active chemotherapeutic agents which are reported to possesses strong anticancer potential inhibiting topoisomerase I in a large number of cancers.[7] It was first isolated from Camptotheca acuminata (Nyssaceae). Topotecan, which is a camptothecin derivative is used to treat ovarian and lung cancer and another derivative Irinotecan is used in treatment of colorectal cancer.

4. Cephalotaxus

Cephalotaxus alkaloids are also a group of phytochemicals that are used against wide range of cancer including A-549 lung cancer, HeLa, SGC-7901 gastric cancer cell lines. They act by inhibiting protein synthesis and aim at the molecular events in synthesis of protein such as initiation of protein synthesis, release of nascent peptide, polyribosome degradation but do not show any effect on elongation of new peptide chain.[8]

5. Colchicine

Colchicine is isolated from Colchicum autumnale (Colchicaceae) and is reported to treat crystal arthritis, cirrhosis, gout by binding to tubulin, stabilizes microtubule formationand hence arrest cell cycle at different phases and induces apoptosis. It will act by targeting the rapidly dividing normal cells and arrest their cell cycle. Colchicin derivatives such as colchicinamide, deacetylcolchicine are less toxic and and can be used to treat variety of cancers including colorectal (HCT-116), chronic granulocytic leukemia, melanoma, central nervous system and breast cancers.[9]

6. Ellipticine

It is naturally occurring anticancer compound which is extracted from the stem, bark, leaf and root of Bleekeria vitensis and *Ochrosia elliptica*. It is generally found along with another phytochemical elliptine. It shows its activity on tumor cells by inhibiting topoisomerase II. It also intercalates with DNA and avoids proliferation.[10]

7. Berberine

It is isolated from the root and rhizome of *Tinospora cordifolia*, Berberis vulgaris, *Berberis aquifolium* and *Rhizoma coptidis*. From the clinical trails data it is proved to be a strong and effective anti cancer compound. It is used for the treatment of breast, prostate and colorectal cancer. In case of breast and colorectal cancer it induces apoptosis and arrests the cell cycle at G2/M phase and in liver cancer it inhibits anti-apoptotic proteins c-IAP1and Bcl-2, and simultaneously activate pro-apoptotic proteins such as p21, p53, caspase-3 and caspase-9.[11]

8. Combretastatins

The ideal feature of these phytochemicals is that they specifically suppress tumor angiogenesis. Hence these belong to the class of anti – angiogenic agents. These are isolated from Combretum caffrum. These phytochemicals belong to the family of stilbenes and due to its anti angiogenic property they act by causing tumor necrosis.

9. Triterpenoid acids

They are reported to act against breast cancer, leukemia and pancreatic cancer. *Ziziphus mauritiana*, *Ziziphus rugosa* and *Ziziphus oenoplia and Betula Sp.* (Betulaceae) have betulinic acid in them, which is also a triterpenoid acid. It is also cytotoxic against a wide range of cancer including human melanoma.[12]

10. Capsaicin

Capsaicin is isolated from red pepper. Capsaicin is reported to exhibit several activities such as anti cancer, anti mutagenic, antimetastatic, anti-angiogenic. It is found effective in treatment of skin, liver, lung, bladder, colon, pancreatic, prostatic, and endothelial cell cancer. Capsaicin acts on different molecular targets like, caspase-3, reactive oxygen species (ROS), Rac1, and HER-2 ***etc***.[13]

11. Flavones/Flavonoids

These are secondary metabolites found in fruits, grains, tea, vegetables and soyabean. Around 8000 different compounds of flavones are reported so far. They generally act by inhibiting cyclin-dependent kinase in esophageal and gastric cancers.[14]

12. Cyanidin glycosides

Cyanidin glycosides are organic compounds which have multiple biological functions. They are isolated from apples, grapes, plums, blackberry, raspberry, red berries, cranberry, red onion and red cabbage. In colon cancer cells they inhibit cell growth and division through COX-2 and iNOS gene expression. In prostate cancer they induce apoptosis and in bladder and lung cancer they stop MMP-9 expression.[15]

13. Saffron (Crocetin)

Crocetin is isolated from dried stigmas of saffron which also has other potent anticancer compounds such as carotenoids, crocin and safranal. It acts on different types of cancers such as breast, colorectal, pancreatic, skin, liver and lung. Crocetin regulates various nuclear and cellular factors. It inhibits iNOS, COX-2 enzymes, TNF-α, cyclin B, cyclin A. It upregulates Bax/Bcl-2 ratio, regulate of caspase-3, 8 and 9 expression. It down-regulates MMP-2, MMP-9 expression. It induces apoptosis, targets microtubules and inhibits invasion and metastasis.[16]

14. Epigallocatechin gallate

Chemically it is a polyphenolic compound found in green tea. It has the ability to restore genes expression of tumor suppression such as retinoid X receptor alpha. This results in breast cancer inhibition. It binds to many high affinity target proteins such as 70 kDa, Zap-70 (a zeta-associated protein).[17]

15. Gingerol

Gingerol is extracted from the rhizome of Zingiber officinale and has (6)-gingerol, (8)-gingerol and (10)-gingerol. It is reported to possess anticancer effect in colon, pancreas, ovarian and breast cancers. It acts by suppressing NF-kB nuclear translocation and IkBa phosphorylation down regulates the expression of iNOS and TNF-alpha. (10)-gingerol has exhibited promising results in the treatment of MDA-MB- 231 and MDA-MB-468 breast cancer. By reducing the number of cell divisions, cell cycle arrest, inducing apoptosis and by releasing proapoptotic mitochondrial cytochrome c[18], (10)-gingerol exhibits inhibitory effect on MDA-MB-231.

16. Lycopene

It is a red pigment isolated from tomatoes, watermelons, red papayas and red carrot. It has potential anticancer activity and is reported to show its activity against pancreatic, stomach, breast, endometrial, prostate, colon and colorectal cancers. It targets on various signaling pathways such as PI3K/Akt (pancreatic and stomach cancers) and down regulates Erk and Bcl-2 protein. It removes oxidative damage by up regulating anti oxidant enzymes such as GSH, GST and GPxn (breast, endometrial, prostate and colon cancers). By acting on various signaling pathways like NF-kβ and JNK. It also effects cell proliferation and progression (colorectal cancer). Lycopene also causes inflammation and suppresses the expression of COX-2, iNOS IL-1b, IL-6, and TNF-α.[19]

17. Vitamin E from plant oil

Vitamin E represents a group of compounds consisting of both tocotrienols and tocophenols. Vitamin E is reported to exhibit anti tumor activity like pro apoptotic, anti proliferative effects in both in vitro and in vivo studies.[20] It is a fat soluble vitamin and is a potent anti oxidant. It is found in germ oil, safflower oil, sunflower oil and wheat.

18. Fisetin

It is isolated from strawberries, apple, grape and onion. Chemically it is a flavone. It has been reported to exhibit potential anti cancer activity (anti migration, anti proliferation, apoptosis). Fistein is used to treat human colon cancer, lung cancer and human oral cancer. It inhibits PI3K/Akt signaling pathway, MAPK signaling network. Through p53-mediated up regulation of DR5 expression, it also induces apoptosis in human renal carcinoma caki cells.[21]

19. Resveratrol

It is found in mulberries, blueberries, peanuts, grapes. It is a naturally occurring polyphenol. Resveratrol is reported to cure a wide range of cancers like breast cancer, liver, colorectal, pancreatic, prostate cancer and lung carcinoma. By reducing MAP kinase phosphorylation it suppresses VEGF protein and inhibits angiogenesis.[22] It upregulates p53 and Bcl-2 associated X proteins and down regulates MMPs, NFkB, AP-1, Bcl-2 and cyclins, cyclin dependent kinases and cytokines and COX 2 proteins.

20. Apigenin

It is isolated from celery, chamomile and parsley. It is a naturally occurring flavonoid. The special feature of this flavonoid is non mutagenic and less toxic and induces apoptosis. It targets leptin/leptin receptor pathway, activates caspase dependent extrinsic apoptosis pathway, activates transcription 3 (STAT3) signaling pathway and inhibits signal transducer.[23]

21. Curcumin

It is extracted from Curcuma longa and is a lead phytochemical. Curcumin acts on several nuclear and cellular factors. It regulates p16, p21, p53, Bcl-2 associated X protein, EIK-1, ErK enzyme, early growth response protein 1, c-Jun N-terminal kinase, Caspase-3, 8, 9 enzymes. It decreases the level of Bcl-2, mTOR, p65, protein kinase B (Akt), retinoblastoma protein (pRB), NF-kB, and cyclin D1 proteins.[24]

22. β-elemene

It is isolated from Curcuma wenyujin. It has promising effect against drug resistant tumors and is a potent anti cancer agent commonly used in traditional Chinese medicine. β-elemene acts by inducing apoptosis and cell death. It inhibits expression of VEGF and down regulates Akt phosphorylation and CD34 expression. It also suppress PI3K/Akt/ mTOR, MAPK and pathway. β-elemene also attenuates angiogenesis. It is reported to show its activity against human gastric cancer.[25]

23. Chalcone

It is a flavonoid isolated from fruits and vegetables and is reported to treat colon, lungs, breast, liver, prostate cancer.[26] It acts by up regulating proapoptotic proteins expression and decreases anti-apoptotic gene expression (Bcl-2).

24. Sesquiterpene lactones

These groups of compounds are isolated from several plant families. The most commonly used plants belong to the family of asteraceae. They are reported to treat a large number of cancers like prostate, liver, lung, breast and oesophageal. Sesquiterpene lactones acts by different mechanisms. They induce ROS, mitochondrial dysfunction, modulate Bcl-2 family proteins, arrest cell cycle. It inhibits STAT3 activation and NF-kβ.[27]

25. Chrysin

Chrysin is found in propolis, honey, blue passion flower and chamomile. Chemically these are 5,7-dihydroxyflavone. The important feature of chrysin is that being an effective anti cancer compound it shows very less side effects. This flavones induces apoptosis in SW480 (colorectal cancer), arrests the cell cycle at G2/M phase which would result in cleavage of DNA and apoptosis. It also increases ROS production and lipid peroxidation and stimulates MAPK, ERK ½ and P38 proteins (prostate cancer cells). Chrysin also suppresses the abundance of S6, AKT,P13K, P90RSK and P70S6K proteins.[28]

26. Oroxylin flavone

It is isolated from Scutellaria radix and is a potential flavones. It acts by down regulating the expression of COX-2 and iNOS genes. It also blocks NF-kβ. It also blocks IKβ degradation there by inhibiting the activation of LPS- induced NF-kβ.[29]

27. Kaempferol

It is isolated from propolis, black tea, grape fruit, broccoli and is a naturally occurring anticancer agent with significant antitumor activity on a large number of cancer cells. It shows its activity especially in colorectal cancer and HT-29 cancer cells by activating the expression of caspase -3 enzyme, P53 gene and its products. It also inhibits the activity of different enzymes (CDK2, CdC2 and CDK4) and arrests the cycle at G1 and G2/M phase.[30]

28. Genistein

It is isolated from soybeans, lentils and chickpeas. Chemically it is an isoflavone and possess proapoptotic function and is a potent antitumor agent. It upregulates the expression of pro apoptotic protein and antioxidant enzyme expression such as glutathione peroxidases.[31] It inhibits NF-kβ and topoisomerases II enzymes.

29. Silymarin

It is extracted from Sylibum marianum. It is a naturally occurring flavolignan which is a mixture of silydianin, silychrystin, silibin (silybin A and B) and isosilybin (A and B). It induces cell arrest and it acts on cyclin dependent kinases and induces apoptosis. It is used in the treatment of colorectal cancer along with other synthetic drugs paclitaxel and doxorubicin.[32]

30. Ursolic acid

silIt is the main chemical constituent in species of rosemary and basil. Chemically it is a triterpene and is apotent antioxidant compound. It plays a vital role in the modulation of cellular redox status of normal cells. On normal cells it exerts pro oxidative action. It exhibits pro apoptotic effects by reducing the level of pro-inflammatory NF-kB cytokine, survival effectors Bcl-2 and pro metastatic MMP-9 matrix metalloprotease.[33]

31. Ginsenosides

It is obtained from the roots of ginseng. They act on various tumors including liver, breast, gastric, ovarian, melanoma and colon cancer. Ginsenosides possess anti invasion and anti migration properties and they induce apoptosis and cell cycle arrest.[34]

32. Celastrol

It is isolated from bark of Tripterygium wilfordii. It is a strong anti cancer compound and it inhibits heat shock proteins and blocks its interaction with Cdc37, induces apoptosis via caspase-3 enzyme in ovary, colon, lungs, prostate, oesopharyngeal, glioblastoma, liver, skin, leukemia and gastric cancer.[35]

33. Gossypol

It is found in cotton seeds (gossypium) and Thespesia populnea. It exhibits potential anticancer activities and it has completed phase II clinical trails for treatment of human breast and prostate cancer. It suppresses self proliferation and induces apoptosis in colorectal cancer and other cancer cell lines.[36]

34. Isothiocyanates

It is found in vegetables belonging to the family Crusiferae such as watercress and broccoli. Without causing any toxic side effects it is reported to treat a wide variety of cancers namely colorectal, cervical, lung, prostate and also acts on human T-leukemia cells. They act by different mechanisms such as they induce apoptosis and ROS- mediated mechanisms, arrest the cell cycle at G2/M phase and also down regulates activated signaling cascade, inhibits cell proliferation, modulate epigenetic changes.[37]

35. Genipin

It is isolated from Gardenia jasminoides. It has anti proliferative property especially reported in the treatment of breast cancer. It down regulates Bcl-2 expression and upregulates Bax and caspase-3, pro-apoptotic signalling cascades (JNK, p38, MAPK).[38]

36. Denbinobin

It is isolated from the stem of *Ephemerantha lonchophylla* and Dendrobium moniliforme and is reported to possess multi functional properties such as anti cancer, anti- angiogenesis and apoptosis inducing properties. It inhibits SrC kinase activity, decreases iNOS there by inhibits metastasis and by suppressing NF-kB activation it inhibits COX-2 activity in concentration dependent manner.[39]

Detailed information about the medicinal plants, part used, the phytochemicals present and the specific cancer suppressed is given in **Table 2**.

Table 2: Medicinal plants and their phytochemicals for specific types of cancers.

PLANT NAME	PART USED	PHYTOCHEMICALS	SPECIFIC CANCER SUPRESSED
Peganum harmala	Roots	Harmine	Breast cancer (Both in vitro and in vivo)
Curcuma longa	Rhizomes	Curcumin, ascorbic acid	Leukemia, glioblastoma and colon cancer (In vitro)
Allium wallichii	Whole plant	Steroids, terpenoids, flavonoids, reducing sugars and glycosides	Prostate cancer, breast cancer, cervical cancer (In vitro)
Camelia sinesis	Leaves	Epicatechingallate, picatechin, epigallocatechin	Lung, bladder, skin, prostate and breast cancer (Both in vitro and in vivo)
Ocimum sanctum	Leaves	Eugenol, orientin, Vicenin	Breast, liver and fibrosarcoma cancer (In vitro)
Camellia sinensis	Leaves	Theabrownin	Lung cancer (In vivo)
Solanum nigrum	Leaves	Solamargine, solasonine	Breast, liver, lung and skin cancer (In vitro)
Ziziphus spina-christi	Flowers, leaves	Doxorubicin, spinanine-A, rutnine, quercetin	Lung cancer and breast cancer (In vivo)
Glycyrrhiza glabra	Roots	Licochalcone-A, Licoagrochalcone	Prostate, breast, lung, stomach and kidney cancer (In vivo)
Nigella sativa	Seeds	Thymoquinone	Colon, prostate, breast and pancreas cancer
Moringa oleifera	Flowers, leaves	Moringa oleifera protease inhibitor (MoPI)	Abdominal cancer (Both in vitro and in vivo)
Glycine max	Seeds	Bowman-Birk inhibitors	Colorectal, prostate and colon cancer (Both in vitro and in vivo)
Withania somnifera	Roots	Withaferin A, D	Breast, cervix, prostate and colon cancer (In vivo)
Aegle marmelos	Bark, root	Lupeol	Lymphoma, melanoma, leukemia and breast cancer (In vitro)
Zingiber officinale	Ginger	Gingerol	Ovary, cervix, colon, liver and urinary caner (In vitro and in vivo)
Curcuma longa	Rhizomes	Curcumin, ascorbic acid	Leukemia, glioblastoma and colon cancer (In vitro)
Artemisia annua	Whole plant	Artemisinin	Liver, breast and pancreatic cancer (Both in vitro and in vivo
Camelia sinesis	Leaves	Epicatechingallate, picatechin, epigallocatechin	Lung, bladder, skin, prostate and breast cancer (Both in vitro and in vivo)
Herba epimedii	Leaves	Icariin, icaritin, icariside Ⅱ	Prostate, lung, kidney and gastric cancer (Both in vitro and in vivo)
Elusine coracana	Seeds	Ragi bifunctional Inhibitor	Myeloid leukemia cell and K562 cell line (Both in vitro and in vivo)
Psoralea corylifolia	Seeds	Psoralidin	Stomach and prostate cancer
Colchicum Autumnale	Leaves	Colchicine	Hodgkin's lymphoma, chronic granulocytic leukemia (Both in vitro and in vivo)
Curcuma longa	Dried rhizome	Curcumin	Colon adenocarcinoma (In vitro)
Ziziphus jujube	Fruits, seeds, leaves	Linoleic acids, triterpenoids	Breast cancer, human Jurkat leukemia T cells (Both in vitro and in vivo)
Podophyllum	Leaves	Podophyllotoxin	Breast, ovary, lung, liver, bladder and testis cancer

Hexandrum			(In vitro)
Panax ginseng	Roots	Panaxadiol	Human colon cancer (Both in vitro and in vivo)
Gossypium hirsutum	Cotton	Gossypol	Mice xenograft (HT-29) and colorectal cancer (Both in vitro and in vivo)
Glycyrrhiza uralensis	Roots	Isoliquiritigenin	Human lung cancer (In vitro)
Gossypium hirsutum	Whole plant	Gossypol	Breast, stomach, liver, prostate and bladder cancer (In vitro)
Aloe vera	Leaves	Alexin B, emodin	Leukemia, stomach cancer (In vivo)
Momordica Charantia	Leaves, Roots	Charantin, cucurbitanetype Triterpene	Colon cancer and breast cancer (In vitro)
Camellia sinensis	Leaves	Epigallocatechin gallate	Brain, prostate, cervical and bladder cancer (In vivo)
Ipomoea batata	Roots	Trypsin inhibitor protein	Promyelocytic leukemia cells (In vitro and in vivo)
Lens culinaris	Seeds	Lentil (Lens culinaris trypsin inhibitor)	Human colon cancer (Both in vitro and in vivo)
Pisum sativum	Pea	Protease inhibitors,rTI1B, rTI2B	Human colorectal and colon cancer (In vitro)
Phaseolus vulgaris	Seeds	Tepary bean protease Inhibitor	Leukemia L1210 and lymphoma MBL2 (In vitro)
Curcuma zedoaria	Whole plant	Curcumin	Colorectal cancer and B-16 melanoma cells (In vitro)
Clematis manshrica	Flower, Leaves	1,4-benzoquinone,5-oethyl-embelin, 15-carbon isoprenoid	Liver cancer and blood cancer (In vivo)
Hibiscus mutabilis	Pepper	Lectin	Liver, breast cancer (In vitro)
Smilax chinensis	Rhizomes	Tannin, saponins and Flavonoid	Sarcoma-180 and ascites sarcoma (Both in vitro and in vivo)
Allium sativum	Whole plant	Allin	Carcinoma of human (mammary) gland (Both in vitro and in vivo)
Aloe vera	Whole plant	Aloesin, emodin	Anti-angiogenic activity (In vitro)
Stevia rebaudiana	Leaves	Labdane sclareol Properties	Anti-tumorous and cytotoxic (In vitro)
Nelumbo nucifera	Embryos	Neferine	Liver cancer (In vitro)
Pleurotus sajor-caju	Fruiting bodies	Ribonucleases	Leukemia and liver cancer (in vivo)
Clematis manshrica	Flower, Leaves	1,4-benzoquinone,5-oethyl-embelin, 15-carbon isoprenoid	Liver cancer and blood cancer (In vivo)
Saffron crocus	Dry stigmas	Saffron	Liver, lung cancer and pancreatic cancer (In vitro)
Stevia rebaudiana	Leaves	Labdane sclareol Properties	Anti-tumorous and cytotoxic (In vitro)
Berberis vulgaris	Root, stem bark	Berberine, cannabisin	Breast, prostate and liver cancer (In vivo)
Colchicum Autumnale	Leaves	Colchicine	Multiple solid tumors (In vitro and in vivo)
C. roseus	Bark, leaves	Vindesine Vincristine, Vinblastine	Leukemias, testicular, breast and lung cancer (In vitro) Lymphocytic leukemia (In vivo)
Berberis vulgaris	Roots stem and bark	Berberine	Breast, liver, colon cancers (In vitro)
Citrus limon	Fruits	5-hydroxy-6,7,8,30,40-Pentamethoxyflavone	Human colon cancer (In vitro)
Moringa oleifera	Seed	Pterygospermin 4-(40-Oacetyl-a-Lrhamnopyranosyloxy), benzylisothiocyanate,4-benzylisothiocyanate	Lung, neuroblastima and colon cancer (In vitro)
Butea monosperma	Flower	Butrin, (7,30,40-trihydroxyflavanone-7,30-diglucoside)	Liver cancer (In vitro and in vivo)
Carissa spinarum	Fruit	Alkaloids, saponins, tannins, flavonoids	Nasopharyngeal carcinoma (In vitro)
Withania somnifera	Root stem and leaves	Adriamycin and 5-Fluorouracil	Human cervical cancer cell (In vitro)

CONCLUSION

Cancer is a fatal condition and the number of patients diagnosed is increasing by enormous numbers day by day. The current drugs available are having the major disadvantage of having side effects. Now, the world is moving towards natural products as they are available at low cost and comparatively the side effects produced are low. Safer anticancer drugs can be developed from bioactive phytochemicals and formulations. Extraordinary attention is received onto the field of nanotechnology and its application in cancer treatment. The major advantage of nanomaterials or nano carriers is that they can be tailored as per the requirement and can be targeted to specific sites.

In the present review various nanotechnological approaches have been briefed. It also included various phytochemicals and plant sources with their mechanism of action on the tumor cells. Nanotechnology can be utilized for herbal drugs to make them target specific. This combination of nanotechnology with phytochemicals poses various challenges for further study.

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