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Review Article

Role of natural products in cancer management: a comprehensive review

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Globally incidences of cancer-associated morbidity and mortality are still increasing. Despite tremendous innovations in the development of many chemically developed anti-cancer drugs the unsatisfactory prognosis of the disease still remains a major challenge. The most widespread negative aspects of conventional cancer treatments are the formation of drug resistance eventually leading to the termination of chemotherapy. Moreover, most patients in developing countries are unable to afford the high cost of sophisticated target-specific therapies like stem cells and immunotherapy. Therefore, to supplement the present cancer therapy treatments, new and less costly therapeutic strategies need to be developed. The use of natural products in cancer management has gained significant attention due to their diverse mechanisms of action and potential therapeutic benefits. Phytochemicals are bioactive compounds produced naturally by plants and have great potential in human health and disease. Natural Products have antioxidant, immunomodulatory, and antiproliferative properties. Phytochemicals are highly beneficial in managing a variety of diseases, including cancer, immunological disorders, and cardiovascular disease. They reduce reactive oxygen species (ROS), stop cancer from spreading, alter the immune system, and cause cancer cells to undergo apoptosis or autophagy. Investigating natural products is an effective way to find compounds that are biologically active and have unique structures and modes of action. Natural products represent a rich source for the discovery and development of cancer preventive and anticancer drugs. This comprehensive review explores the role of natural products in various aspects of cancer management and the development of anticancer drugs.

Keywords: *natural products, phytochemicals, cancer, therapeutic potential, mode of action*

Introduction

Cancer remains one of the most formidable health challenges worldwide, accounting for a significant burden of morbidity and mortality. Despite advancements in conventional cancer treatments, including chemotherapy, radiation therapy, and targeted therapies, the quest for novel and effective therapeutic strategies persists. In recent years, natural products have emerged as promising candidates in cancer management due to their diverse chemical compositions and multifaceted biological activities. From plant-derived phytochemicals to marine compounds and microbial metabolites, natural products offer a vast array of potential anticancer agents. Their mechanisms of action range from inducing apoptosis and inhibiting proliferation to modulating immune responses and angiogenesis. Cancer is considered as a biggest cause of death worldwide (Antoni et al., 2017). Tracheal, Bronchus and Lung cancer put out a high disease burden worldwide (Wang et al., 2023). After Bronchus and Lung cancer, Liver cancer is the third most common cause of cancer death. High HDI (high development index) countries shows the largest burden in liver cancer cases and deaths with having 60.6% of new cases and 63.2% of deaths globally (Rumgay et al., 2022). The most commonly diagnosing cancer worldwide is breast cancer, 1 in 8 cancer diagnoses is of breast cancer. Over 2.3 million new cases and 6,85,000 deaths are due to breast cancer, accounts for 11.6% of all new cases in 2020 (Arnold et al., 2022; Wu et al., 2023). With

high mortality and low survival rate, brain and central nervous system cancer is an important public health issue worldwide (Sung et al., 2021). In 2019, about 3,47,992 new cases and 2,64,253 deaths of brain cancer were recorded globally (Ilic & Ilic, 2023). According to a study the socioeconomic factors associated with onset of breast cancer over attributed to the process of economic development in different countries. The economies of Japan and Singapore are among the world's leading economies, consequently, its Age Standerdise Incidence Rate is also relatively high among other countries (Mubarik et al., 2022). Global demographic trends indicate that there will likely be a rise in cancer rates over the coming decade, with projections suggesting that more than 20 million new cancer cases will occur annually by the year 2025 (Zugazagoitia et al., 2016). Nowadays many treatments are present in the medicos for treating cancer, like CAR (Chimeric Antigen Receptor)-T cell therapy, Photodynamic therapy (PDT), Brachytherapy, Conventional adjuvant chemotherapy, Liquid Biopsis, Radiotherapy, Robot-assisted radical prostatectomy (RAPR) and Nanoparticle drug delivery although all of these treatments are efficient in curing cancer but every treatment has limitations and side effects. As if we talk about CAR-T cell therapy it has many limitations like Antigen escape, On-target off-tumor effect, Antigen escape, CAR-T cell associated toxicities, Tumor infiltration and Immunosuppressive microenvironment. (Sterner & Sterner, 2021). Side effects most commonly caused by PDT are mucosal sloughing and photosensitivity other than that it also causes bronchitis, hemoptysis, severe endotracheal candidiasis and pneumonias (Mudambi et al., 2017). Conventional adjuvant chemotherapy has very low possibility of curing the TNBC (Triple-negative breast cancer) (Kang et al., 2023). Liquid biopsis face problems in specificity and sensitivity issues as well as the impact of tumor location (Raez et al., 2023).

Radiotherapy or RAPR (Robot-assisted radical prostatectomy) has the risk of side effects when used for treatment of prostate cancer. Treatment related side effects consist of erectile dysfunction, urinary incontinence, and rectal toxicity, which impacts the life quality (Van Riel et al., 2023). Nowadays nano material drug delivery is used for treating brain cancer as it is the effective way to cross BBB (blood-brain barrier) which is difficult to cross for drugs (Neganova et al., 2022). However this is very costly as it needs certain ingredients and tools and also, the use of nano material can lead to immediate and direct neurotoxic effects (Cheng et al., 2021). As all the treatments are costly and some have side effects we should move towards natural products for the treatment of cancer. Products present in nature have played an important role in the treatment of human ailments since 2600 BC in Mesopotamia (Mali, 2023). Traditional medicine is commonly used in China, India, Japan, Iran, and Saudi-Arabia in which plant and animal derived natural products are used for the treatment of diseases. By following the idea, we can use these products for the treatment of altered protein homeostasis of cancer (Sak, 2022). Natural products are rich resources for uncovering anticancer drugs as supported by the fact that 113 (accounting 83%) of the total 136 validated small molecules, anticancer compounds for clinical uses are either natural products or derived from natural products (Champiat et al., 2016). When traditional Chinese medicine (TCM) treatment of primary liver cancer (PLC) is compared to current advanced treatment (Hepatic artery profusion) the survival and PFS (progression-free survival) were longer in the traditional Chinese medicine treatment group (Chen et al., 2012). Ayurveda, a traditional Indian medicine system describes a disease as an exploitation of nature's law causing upset of the human body's system and can be cured by nature as a physician. Ayurvedic plant drugs have been eminent from ancient times to prevent and suppress various tumors using a line of treatment (Balachandran & Govindarajan, 2005). Secondary metabolites are the products produced by plants which are not essential for their life but helps in surviving stress or pathogenic attacks (Yang et al., 2023). The secondary compounds found in plants, whether individually or collectively, offer the potential for crafting personalized cancer prevention strategies (Table 1).

Table 1. Plant based natural compounds used for cancer management

Plant source	Phytochemical	Type of Cancer	Mode of action	References
Aconitum sinomontanum	Lappaconitine	Liver	Downregulation of Bcl-2 and upregulation of P53 and Bax expression	Song et al., 2021
Alliaria petiolata	Benzyl isothiocyanate	Colon	MAPK and PKC pathways inhibition	Ranjan et. al., 2019
Allium cepa	Quercetin	Thyroid	Pro—NAG-1/GDF15 pathways upregulation	Hong et al., 2021
Artemisia annua	Artemisinin	Breast	G2/M (cell cycle) arrest, autophagy, antiproliferative, apoptosis	Guan & Guan, 2020
Camellia sinensis	Catechins	Prostate	Increased expression of cytochrome c and decreased expression of B-cell lymphoma-2 induced apoptosis	Chen & Tsai, 2016
Cannabis sativa	Cannabinoids	Liver	Anti-apoptotic	Hussein et al., 2014

Capsicum annuum	Capsaicin	Breast	NF-kB inactivation mediated by the FBI-1 downregulation	Chen et al., 2012
Capsicum frutescens	Capsaicin	Pancreatic	ß-catenin/TCF-1 signaling inhibition-mediated apoptosis	Chapa-Oliver & Mejía-Teniente, 2016
Carica papaya	Benzyl isothiocyanate	Pancreatic	FOXO/PI3K/AKT pathways-mediated tumor apoptosis	Mahrous & Noseer, 2023
Chamaemelum nobile	Phenolic compounds	Breast	Mitochondrial pathway activation-induced apoptosis	Kandelous et al., 2016
Citrus limon	Hesperidin	Breast	NF-kB and Akt downregulation-mediated PD-L1 expression inhibition	Kongtawelert et al., 2020
		Prostate	ROS-induced apoptosis	Ning et al., 2020
Crocus sativus	Safranal	Prostate	Downregulation of NF-kB and AKT signaling pathways	Jiang et al., 2020
Cucumis sativus	Cucurbitacin B	Neuroblastoma	MAPKs- and JAK2/STAT3-mediated apoptosis	Zheng et al., 2014
	Cucurbitacin B (in combination with gefitinib	Colorectal	JAK/STAT and EGFRinduced apoptosis	Yar Saglam et al., 2016
Denrobium chrysotoxum	Erianin	Breast	PI3K/Akt pathway activation	Xu et al., 2021
Eclipta alba	Luteolin	Breast	Intrinsic apoptotic pathway activation	Arya et al., 2015
Galanthus nivalis	Gallic acid	Colon	EGFR and SRC phosphorylation inhibition	Lin et al., 2021
		Liver	Wnt/_-catenin pathway suppression	Shi et al., 2021
Glycyrrhiza glabra	Licochalcone A	Lung	JNK suppression, P38 and ERK activation	Luo et al., 2021
Gossypium hirsutum	Gossypol	Skin	Mitochondrial apoptosis	Haasler et al., 2021
		Cervical	FAK pathway inhibition and TGF-_1-mediated EMT reversal	Jia et al., 2023
		Colon	Downregulation of FAS, CLAUDIN1, GAPDH, ELK1, ZFAND5, IL2, and IL8 expression	Cao et al., 2021
Lagerstroemia speciosa	Corosolic acid	Bladder	SQSTM1/P62, UBB, and NBR Upregulation	Cui et al., 2021
		Liver	YAP/CDK19/OGlcNAcylation Inactivation	Zhang et al., 2021
Mortonia greggii	Pristimerin	Lung	MMP2 and integrin _1 expression downregulation	Li et al., 2020
Myrica nagi	Myricetin	Lung	FAK-ERK pathway inhibition	Kang et al., 2020
Nelumbo nucifera	Hyperoside, rutin	Colon	Mitochondrial pathway activation-induced apoptosis	Guon & Chung, 2016
Panax ginseng	Ginsenosides	Breast	VEGF-R2 pathway inhibition correlated with anti-angiogenesis	Kim et al., 2021
			ROS generation, mitochondrial dysfunction, apoptosis	Kim et al., 2020
Papaver somniferum	Noscapine	Colon	AKT/PI3K/mTOR pathway inhibition	Tian et al., 2020
Perovskia abrotanoides	Tanshinones	Hella cell lines	Antiproliferative, apoptosis	Geryani et al., 2016
Piper longum	Piperlongumine	Prostate	DNA damage-mediated proliferation inhibition	Zhang et al., 2021
		Lung	mTOR/AKT/PI3K pathway inhibition-induced apoptosis	Wang et al., 2015

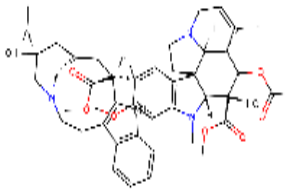
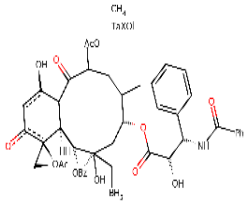
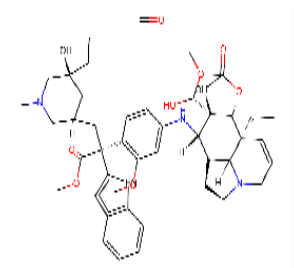
Piper nigrum	Piperine	Colon	Wnt/_-catenin pathway suppression	De Almeida et al., 2020
Polygonum uspidatum	Pterostilbene	Colon	DNA repairing by Top1/ Tdp1 pathway	Zhang et al., 2021
Pongamiopsis	Epipervilline	Ovarian	Antiproliferative	Harinantenain et al., 2010
Pueraria radix	Puerarin	Prostate	Keap1/Nrf2/Are pathway inhibition	Li et al., 2021
Quercus alba	Quercetin	Prostate	ROS modulation, AKT/NF-kB pathway activation	Ward et al., 2018
Reseda luteola	Luteolin	Lung	FAK-Src signaling inhibition	Masraksa et al., 2020
Rheum palmatum	Emodin	Lung	HAS2-HACD44/RHAMM signaling pathway suppression	Li et al., 2021
Ruta graveolens	Psoralens	Breast, colon, and prostate	Inhibits proliferation of cancer cells	Malik et al., 2016
Salvia involucrate	Hispidulin	Lung	ER stress activationinduced apoptosis	Lv et al., 2020
Solanum lycopersicum	Lycopene	Cervical	Bcl-2 downregulation and Bax upregulation	Aktepe et al., 2021
Solanum lycopersicum	Lycopene	Lung	Increase in RAR_ protein expression	Cheng et al., 2020
		Brain	Caspases activation	Czarnik-Kwaśniak et al., 2019
	Lycopene (in combination with quinacrine)	Breast	Wnt-TCF signaling inhibition	Preet et al., 2013
Sophora flavescens	Matrine	Liver	HOXD3 and circ-0027345 downregulation and miR-345-5p upregulation	Lin et al., 2020
Spinacia oleracea	Kaempferol	Pancreatic	ROS-induced Akt/mTOR signaling inactivation	Wang et al., 2021
		Breast	Upregulation of caspase-3 and -9 and H2AX expression	Zhu & Xue, 2019
Trianthema portulacastrum	Ecdysterone	Breast	_-catenin/Wnt signaling inhibition inducing pro-apoptotic and antiproliferative effects	Bishayee & Mandal, 2014
Vitis vinifera	Resveratrol	Breast	Cell cycle inhibition, apoptosis	Wu et al., 2019
		Osteosarcoma	STAT3 pathway and cell cycle inhibition	Peng & Jiang, 2018
		Colorectal	NF-kB pathway inhibition, apoptosis	Buhrmann et al., 2017
Zingiber officinale	Gingerol	Lung	A549 cells death by iron accumulation, USP14 expression inhibition	Tsai et al., 2020
		Breast	ROS generation, activation of p53 expression mediated apoptosis,	Sp et al., 2021

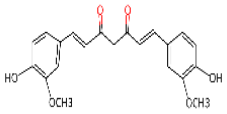
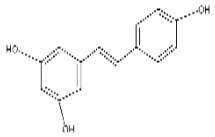
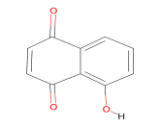
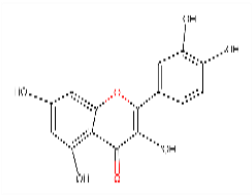
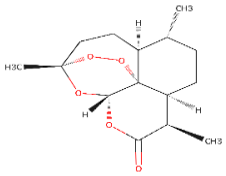
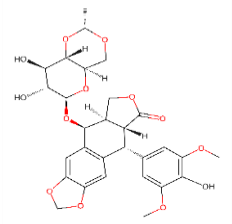
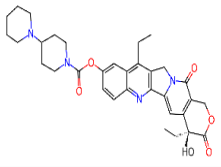
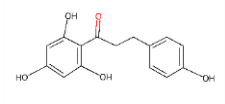
These bioactive substances from plants are valuable for their ability to provide essential genoprotective effects, including safeguarding DNA from damage in healthy cells. (Hossain et al., 2022; Salehi et al., 2019). Apart from plant-based products, we can also use compounds extracted from marine sources which include sponges, dinoflagellates, fishes, tunicates and mollusks (Suarez-Jimenez, 2012). Alkaloids are primary anticancer agents in the class of phytochemicals. The alkaloids represent a highly distinct group of compounds, around 3000 different alkaloids have been identified from plants, animals and fungi together (Salehi et al., 2018). The delay of DNA replication and cell death is caused by the restraining effect of alkaloids on the topoisomerase enzyme (Koklesova et al., 2020). Therefore, alkaloids have been a base for anti-tumor, and anti-inflammatory drug development (Habli et al., 2017).

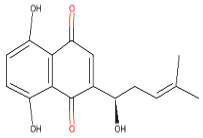
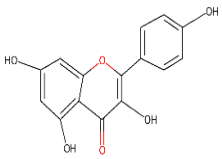
Mechanisms of action of anticancer natural products:

Natural products can affect a variety of signaling pathways, which in turn affects how cells behave molecularly (Figure 1). As a result, they may be employed as possible adjuvants in the treatment of cancer. Large-scale improvements have been made in the surgical, chemotherapeutic, and radio therapeutic treatment of malignant tumours. However, the emergence of invasive or widespread malignancies is frequently linked to inadequate patient diagnosis and continues to be a significant barrier to effective cancer treatment (Jemal et al., 2009). Recent investigations have shown that tumour recurrence and resistance to chemotherapeutic therapy are caused by (CSCs), which are capable of starting tumor and self-renewal (Li at al., 2011; Dick, 2008; Reya et al., 2001). Most naturally derived anticancer mediations e.g., curcumin, resveratrol, juglone and taxol exert their action by suppression of tumorigenesis and targeting abnormal cell signaling pathways in cancer. Natural products interact with cancer cell by induction of autophagy (LC3 conjugation to phosphatidylethanolamine), inhibition of angiogenesis (inhibit endothelial growth factor like VEGF), induction of apoptosis (reduced expression of Bcl-2 and increase the expression of Bcl-2 associated x- protein and activate caspase-3, cell cycle arrest, inhibition of EMT (epithelial to mesenchymal transition repress the mesenchymal markers e.g., N-cadherin, vimentin, snail and enlarge the appearance of epithelial marker E-cadherin) and inhibit pro inflammatory cytokines (interleukin-6 promotes growth and survivorship of multiple myeloma cells). These interaction helps in activation of several pathways like Wnt pathway, Notch pathway and Hedgehog pathway and some embryonic pathway which ultimately leads to suppression of tumorigenesis. Some of the anticancer compounds reported from important medicinal plants and their mode of action, structure and IUPAC name are tabulated in (Table 2).

Table 2. Some selected anticancer compounds, their unique structure and mode of action

Natural products	IUPAC Name	Structure	Mode of action	References
Vinblastine	dimethyl(2β,3β,4β,5α,12β,19α)-15-[(5s,9s)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2h-3,7-methanoazacycloundecino[5,4-b]indol-9-yl]-3-hydroxy-16-methoxy-1-methyl-6,7-didehydroaspidospermidine-3,4-dicarboxylate		Disrupting microtubule formation	Wang et al., 2023
Taxol	(2α,4α,5β,7β,10β,13α)-4,10-Bis(acetyloxy)-13-{[(2R,3S)-3-(benzoylamino)-2-hydroxy-3-phenylpropanoyl]oxy}-1,7-dihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl benzoate		Initiate or hinder the Bcl-2 proteins that are either anti-apoptotic (Bcl-2/MCL-1) or pro-apoptotic (BAX/BAK)	Lim et al., 2022
Vincristine	(3a R,3a1R,4R,5S,5a R,10b R)-Methyl4-acetoxy-3a-ethyl-9-((5S,7S,9S)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-2,4,5,6,7,8,9,10-octahydro-1H-3,7-methano[1]azacycloundecino[5,4-b]indol-9-yl)-6-formyl-5-hydroxy-8-methoxy-3a,3a1,4,5,5a,6,11,12-octahydro-1H-indolizino[8,1-cd]carbazole-5-carboxylate		Binds to tubulin dimers, preventing their polymerization into microtubules.	Jordan & Wilson, 2004

Curcumin	(1 E,6 E)-1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione		Suppresses the VEGF & NF-kB illustration	Li et al., 2018
Resveratrol	E -5- (4-hydroxystyryl) benzene-1,3-diol		Decrease glucose consumption; Influence Glut1, ROS passageway.	Brockmueller, et al., 2021
Juglone	5-hydroxy-1,4-naphthalenedione		Increase appearance of E-Cadherin, decreasing the Vimentin and N-cadherin.	Fang et al., 2018
Quercetin	2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy- 4H-chromen-4-one		Influence the p53pathways; Hindering the activities of cyclin A, cyclin B and CDK2.	Chou et al., 2010
Artemisinin	(3R,5a S,6R,8a S,9R,12S,12a R)-Octahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10(3H)-one		Trigger of BAX, IL6 activate STAT3.	Lu et al., 2009
Etoposide	4'-Demethyl-epipodophyllotoxin9-[4,6-O-(R)-ethylidene-beta-D-glucopyranoside],4'-(dihydrogen phosphate)		TOP2 Inhibitor, Break dsDNA during duplication.	Hainsworth & Greco, 1995
Irinotecan	(S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo1H-pyrano[3',4':6,7]-indolizino[1,2-b]quinolin-9-yl-[1,4'bipiperidine]-1'-carboxylate		activation to its active form, 7-ethyl-10-hydroxycamptothecin (SN-38), through the action of carboxylesterase 2.	Mathijssen et al., 2002
Phloretin	3- (4-Hydroxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one		Disrupts the activity of cyclins and cdk, activation of mitochondria-mediated cell death pathways.	Choi, 2019

Shikonin	5, 8-dihydroxy-2-[(1R)-1-hydroxy-4-methyl-3-pentenyl]-1,4-naphthoquinone		inhibits the activation of the EGFR and PI3K/AKT signaling pathways, suppresses angiogenesis.	Wang, 2021
Kaempferol	3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one		overcoming resistance to 5-FU therapy through its modulation of the miR-326-hnRNPA1/A2/PTBP1-PKM2 axis.	Wu et al., 2022

(Sources: Phytochemical structures are adapted from Pubchem, IUPAC name referred from Pubchem)

Vinblastine

Vinblastine, a vinca alkaloid derived from *Catharanthus roseus*, was discovered as a natural compound. Primarily known for its effectiveness in treating Hodgkin's and Non-Hodgkin's lymphomas, breast cancer, sarcoma, and testicular cancer, its potential as a chemotherapeutic agent became apparent when it was tested in an experiment exploring the plant's potential anti-diabetic properties. Subsequently, these alkaloids have gained medical significance for their anti-tumor characteristics (Dhyani et al., 2022). Vinblastine causes disruption of microtubules by binding to them which causes cell death or apoptosis by arresting the cell cycle at the M phase (Trybus et al., 2022). Vinblastine disrupts microtubules, which are structural components of the cell's cytoskeleton. It attaches itself to the tubulin protein, which is responsible for microtubule formation and function. This disturbance obstructs the regular division of cells, which ultimately results in cell cycle arrest and a reduction in the growth of cancer cells (Jordan & Wilson, 1998). Vinblastine interferes with mitosis, the process of cell division, by interfering with microtubules. As a result, mitotic arrest occurs, which stops cancer cells from proliferating and dividing (Amos & Löwe, 1999). Cancer cells can engage in apoptosis when exposed to vinblastine. This process is aided by mitotic arrest and microtubule disruption (Dumontet & Jordan, 2010). To increase its efficacy, vinblastine is frequently used in conjunction with other chemotherapy medications. Combinations like these might work in concert to improve the patient's response to therapy as a whole (Bonate et al., 2012). Many diseases, such as lymphomas, leukaemia, testicular cancer, and certain solid tumours, can be treated with vinblastine. The kind and stage of cancer can affect vinblastine's efficacy. This study investigated the mechanism of action of vinblastine, a natural source-derived chemotherapeutic medication, in the treatment of aggressive juvenile brain cancers. It shown that vinblastine causes microtubule disruption, which results in apoptosis and cell cycle arrest (Lee et al., 2012).

Vincristine

Vincristine is a natural vinca alkaloid which is also called as leurocristine has $C_{46}H_{56}N_4O_{10}$ formula is obtained from *Catharanthus roseus* is commonly used for the treatment of myeloma, leukemia, breast cancer, neck cancer and head cancer (Dhyani et al., 2022). This alkaloid blocks cell cycle in metaphase with its anti-microtubule activity (Schiller et al., 2018). Vincristine functions by inhibiting tubulin polymerization, resulting in the cessation of microtubule synthesis and promoting the breakdown of already formed tubules. It disrupts nucleic acid and protein synthesis by impeding the utilization of glutamic acid (Martino et al., 2018).

Taxol

Taxol is a first generation taxanes i.e., paclitaxel which is obtained from the leaf and bark of *Taxus baccata*. Taxanes are potent anti-cancer drugs that operate by attaching to microtubules, which play a crucial role in cell division. They are utilized in treating various cancers such as breast, lung and ovarian cancer. The binding of paclitaxel to ß-tubulin within microtubules reduces microtubule dynamics, leading to cell cycle arrest at the M-phase. Docetaxel, a semi-synthetic compound derived from *Taxus baccata*, is predominantly employed in therapies for breast, pancreatic, prostate, and lung cancers. Analogues of paclitaxel currently in clinical trials encompass larotaxel, ortataxel, anilataxel and teretaxel. Larotaxel is administered alone or in combination with other treatments for urethral bladder, lung, pancreatic, and breast cancers (Xie & Zhou, 2017; Ojima et al., 2016). The chemotherapy medication Taxol, also known as paclitaxel, is frequently used to stop the development and spread of cancer cells. It is a member of the taxanes pharmacological class and works against cancer in a number of different ways. Taxol binds to microtubules, which are essential structural components of the cell's cytoskeleton. Unlike vinca alkaloids, which destabilize microtubules, Taxol stabilizes them.

This stabilization inhibits microtubule dynamics, preventing them from depolymerizing and disrupting the cell division process. As a result, cancer cells are apprehended in the G2/M phase of the cell division cycle, and this disruption of cell division leads to cell death (apoptosis) and inhibits cancer cell growth (Schiff et al., 1979). Additionally, Taxol possesses anti-angiogenic qualities. It obstructs angiogenesis, the process of forming fresh neo blood vessels that tumours need to get blood. Taxol helps starve the tumour by inhibiting the formation of new blood vessels, which limits the tumour's gain way in to nutrition and oxygen (Thigpen et al., 1994). Taxol has the ability to cause cancer cells to die. It stimulates biological pathways that result in programmed cell death by severing microtubules and interfering with the mitotic spindle (Yang et al., 2010). Research has indicated that Taxol stimulates the immune system. It may strengthen the body's natural defences against cancer by encouraging the release of cytokines and activating immune cells. The chemotherapy drug Taxol is frequently used with radiation treatment, targeted treatments, or other medications. These mixtures may work in concert to improve the overall efficacy of cancer treatment. The mechanisms of action and resistance to microtubule-stabilizing drugs such as docetaxel and paclitaxel are covered in detail in this thorough study. It draws attention to how they cause microtubule disruption, cell cycle arrest, and apoptosis (Dumontet, 2000).

Resveratrol (3,4 ,5–trihydroxy stilbene):

Through a variety of ways, Resveratrol has been demonstrated to begin cancer cells to go through apoptosis. Planned cell death, can result from the arousal of pro-apoptotic proteins like Bax and hampering of anti-apoptotic proteins like Bcl-2 (Athar et al., 2007). Resveratrol may stop unchecked cell division by arresting the cancer cell cycle at many stages, like the G1, S, and G2/M phases (Kozuki, 2001). Through its effects on several signalling routes, such as the PI3K/Akt passageway, which is important for cell growth and survival, Resveratrol can prevent the spread of cancer cells (Roy et al., 2021). Resveratrol causes mitochondrial dysfunction in cancer cells, which triggers the let-out cytochrome c and the starting the apoptotic pathway. Because of its antioxidant qualities, Resveratrol helps prevent oxidative stress and neutralize reactive oxygen species (ROS), both of which can promote the formation of cancer (Fulda & Debatin, 2004). Additionally, it possesses anti-inflammatory properties that may prevent the growth of tumours (Bishayee & Dhir, 2009). Resveratrol can prevent cancer cells from migrating, invading, and metastasizing by altering the expression of certain genes and proteins (Bai et al., 2016). Cancer cells can become more invasive through a process called epithelial-mesenchymal transition (EMT). By controlling the expression of EMT markers, Resveratrol has been demonstrated to reverse EMT and contribute to a less aggressive phenotype (Jiao et al., 2015). The effects of chemotherapeutic medications can be improved by Resveratrol. For instance, it has shown synergistic effects with docetaxel in prostate cancer, enhancing cell cycle arrest and death (Dona et al., 2004). Certain signalling pathways, which are frequently dysregulated in cancer, can be blocked by Resveratrol. For example, it has the ability to suppress the Wnt/β-catenin signaling route, linked to the proliferation and spread of cancer cells (Kim et al., 2004). The impact of resveratrol on malignant pleural mesothelioma cells was the main focus of this investigation. It was discovered that resveratrol prevented the growth of cells by focusing on the SP1 transcription factor, which controls a large number of cancer-related genes (Lee et al., 2012).

Juglone

Juglone is a natural compound found in walnut trees (genus Juglans) and other plant species. Juglone can switch on pro-apoptotic proteins and hindrance anti-apoptotic proteins, thus inducing apoptosis, or programmed cell death, in cancer cells (Sun, 2012). Juglone can cause DNA damage in cancer cells. This can trigger a DNA repair response or lead to cell cycle arrest and apoptosis (Campbell, 2003). Juglone has anti-angiogenic qualities, which means it can prevent the occurrence of fresh new blood vessels that provide tumours with nourishment, thereby restricting their growth (Ahmad & Suzuki, 2019). Tumour development and progression may be aided by persistent inflammation. Juglone anti-inflammatory qualities may be a factor in its anticancer characteristics. The NF-B and PI3K/Akt pathways, which are linked to cell survival, proliferation, and inflammation (Ahmad & Suzuki, 2019). Hsu, (2004), can be affected by juglone, as can other signaling pathways implicated in cancer. study scrutinize the effects of juglone on glioblastoma cancer cells and found that it suppressed cell proliferation by activating the p53 pathway, a key regulator of cell cycle arrest and apoptosis (Wang et al., 2017).

Curcumin

Curcumin is lead phytochemical obtained from *Curcuma longa* which is plant of Zingiberaceae family, a perennial plant that grows in humid and tropical climates and originates from the Indian subcontinent and southeast Asia (Zhang & Kitts, 2021; Kocaadam & Şanlier, 2017). It modulates various nuclear and cellular factors, also upregulates the expression of various genes and their product which act against the growth of human glioblastoma cells (Vallianou et al., 2015). It also induces apoptosis as it efficiently releases cytochrome c which activates caspase 3 and caspase 9 resulting into cell death (Kuttikrishnan et al., 2019). The natural substance curcumin, which is present in the spice

turmeric, has drawn a lot of interest due to its possible anticancer effects. Strong antioxidant curcumin can reduce oxidative stress and shield cells from DNA damage by neutralizing harmful reactive oxygen species (ROS) (Menon & Sudheer, 2007). Cancer is linked to chronic inflammation both during its initiation and progression. The anti-inflammatory qualities of curcumin may prevent the growth of cancer by lowering inflammation (Aggarwal et al., 2007). By starting pro-apoptotic proteins and hindrance anti-apoptotic proteins, curcumin leads cancer cells to go through programmed cell death (Jiao et al., 2009). Curcumin may limit the growth and spread of tumours by preventing the angiogenesis the process of creating fresh new blood vessel that provides the tumours with nutrition (Teiten et al., 2009). Curcumin has the ability to target multiple cancer-related signaling pathways, including those that control inflammation, cell survival, and proliferation, such as the PI3K/Akt, STAT3, and NF-κB passageway (Shakibaei et al., 2007; Aggarwal et al., 2005). Curcumin may affect the activation or suppression of genes implicated in the development of cancer by influencing the epigenetic regulation of gene expression (Yang et al., 2017). According to reports, curcumin enlarges the sensitivity of cancer cells to radiation, increasing the potency of these treatments (Kunnumakkara et al., 2007). Telomerase activity is essential for the immortalization of cancer cells, and curcumin has been demonstrated to inhibit it (Shay & Wright, 2006). Curcumin has the ability to control autophagy, a biological process that, depending on the situation, can either increase or decrease the ability of cancer cells to survive (Yamauchi et al., 2012). This study looked at curcumin's capacity to suppress laryngeal carcinoma cells occurrence of matrix metalloproteinase-2 (MMP-2), enzyme implicated in tumour invasion and metastasis. It revealed curcumin's potential function in inhibiting cancer cell invasion by suppressing MMP-2 expression and activity (Mitra et al., 2006).

Conclusion

In conclusion, the comprehensive review on the role of natural products from plants in cancer management highlights the vast potential of phytochemicals in various aspects of cancer prevention and treatment. The diverse bioactive compounds found in plants exhibit a wide range of anticancer properties, including antioxidant, anti-inflammatory, pro-apoptotic, and anti-angiogenic effects. These compounds not only target cancer cells directly but also modulate the tumor microenvironment, enhance immune responses, and mitigate chemotherapy-induced toxicity. Natural products from plants hold immense promise as adjunctive therapies or standalone treatments in personalized cancer care. Integrating these compounds into mainstream oncology practices could lead to significant advancements in precision medicine and integrative oncology, ultimately improving outcomes for cancer patients. Natural products can target various signalling pathways implicated in tumour development and progression. Additionally, their synergistic effects with conventional treatments offer opportunities for enhanced efficacy and reduced drug resistance. Their holistic and multifaceted benefits not only offer alternative therapeutic options but also contribute to a broader understanding of cancer biology and treatment paradigms. Collaborative efforts between researchers, healthcare professionals, and pharmaceutical industries are essential for translating these findings into clinical applications and improving cancer patient outcomes.

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