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Targeting Different Types of Cancer: Molecular Factors and Therapeutic Applications of Phyto Compounds

Shouvik Kumar Nandy[1]* and Shikha Thakur[2]

[1]Department of Pharmacy, Burdwan Institute of Pharmacy, West Bengal, India

[2]Department of Pharmacy, Bengal College of Pharmaceutical Sciences and Research, West Bengal, India

ABSTRACT

Cancer is still the second most common cause of death because of genetic mutations in DNA (deoxyribonucleic acid) sequences. The standard target-directed strategy, which is one of the biggest hurdles in anti-cancer research is dealing with the significance of target function in healthy cells. Cancer cells also suffer from a variety of mutations, alterations in gene duplication, and chromosomal abnormalities, all of which have an immediate impact on the effectiveness of anticancer medications at various developmental stages. Cancer medicine development is challenging due to a combination of these characteristics, which also contribute to lower clinical licensure success rates than in other therapeutic categories. The pathophysiology and molecular characteristics of prevalent cancer types are the main topics of the current review. The search for herbal-based alternatives that lessen resistance brought on by cancer therapy and exert chemo-protective properties is motivated by the fact that the currently available chemotherapeutic medications, also known as combination chemotherapy, are linked to a number of negative effects. This review revised the list of important substances that may improve the effectiveness of cancer treatment in order to offer fresh perspectives.

***Corresponding author**

Shouvik Kumar Nandy, Department of Pharmacy, Burdwan Institute of Pharmacy, West Bengal, India.

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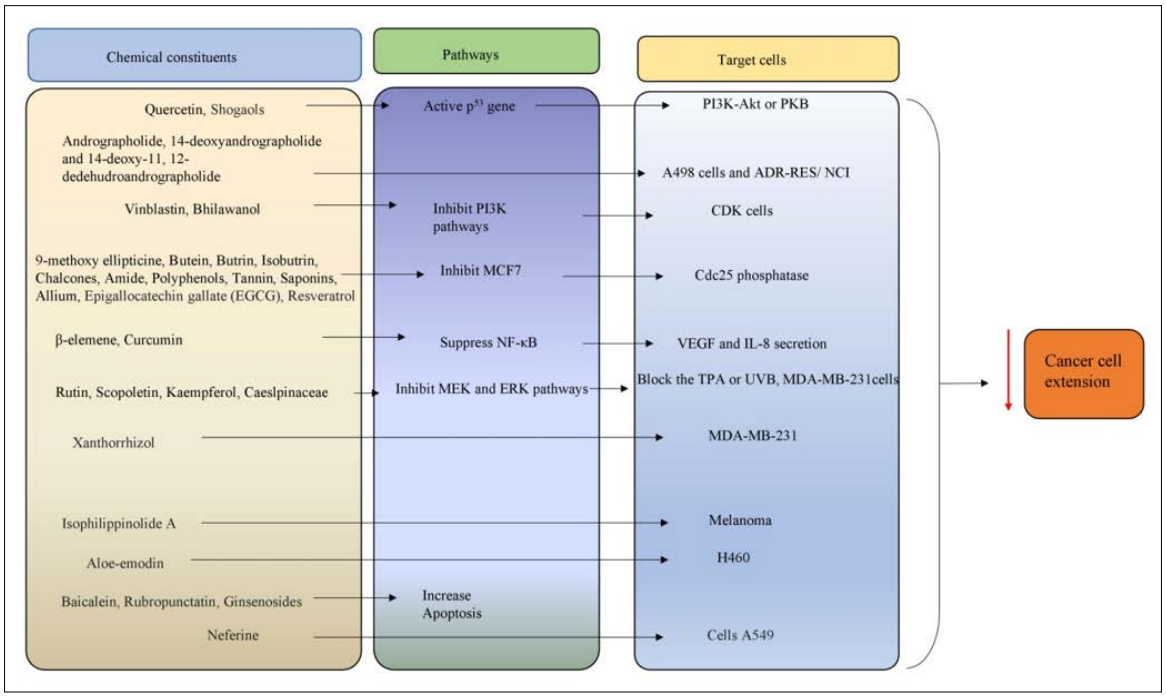
Introduction

The second most common cause of mortality throughout human history, cancer is a major issue that negatively impacts human health. The prevalence of cancer has greatly increased in 2014; there were around 1,665,540 cancer patients in the United States alone, and 585,720 of them died from the disease that year [1].

Unfortunately, because this illness shows up at the tissue level, it is very challenging to diagnose and effectively treat [2, 3]. While females are more likely to develop breast cancer, men are more likely to develop prostate cancer than women [4]. Cancer is a condition marked by aberrant cell division that spreads via the lymphatic and vascular systems. The main causes of cancer are tobacco smoking, excessive alcohol and opiate use, environmental contaminants, and UV radiation exposure [5]. Adenocarcinomas, squamous, basal, and transitional cell carcinomas are among the subtypes of carcinomas. Other subtypes of cancer include myeloma and lymphoma leukaemia, bone and soft tissue sarcomas, myeloma, and malignancies of the brain and spinal cord. Changes in DNA sequences result in several types of proteins that cause cerebrovascular disease in the brain (CVD) [6,7]. These patients have aberrant central nervous system (CNS) activity, as well as nerve metastases and bleeding [8-10]. In addition to surgery, synthetic drugs can be used to treat cancer. Drugs are being created to stop the unchecked expansion of B cells. Numerous drugs, including abemaciclib, ribociclib, palbociclib, and imatinib, can be used to treat cancer. These therapies come with side effects include nephrotoxicity, myelosuppression, leukopenia, neutropenia, thrombocytopenia, oral mucosal membrane inflammation, haemoglobin deficiency, inanition, general ill health with emaciation, loose movements, and nausea in addition to being pricey [11]. As a result, researchers found a number of natural substances that may interact with different proteins and target specific routes to stop the spread of cancer. Natural substances don't have the same adverse effects as conventional medications, and separating chemical compounds from plants is simpler than creating synthetic medications in labs. Quercetin, andrographolide, 14-deoxyandrographolide, vinblastine, β-elemene, curcumin, berberine, baicalein, and other phytochemicals are a few examples. These substances may be able to directly regulate both the development of tumours and the proliferation of cells during unchecked cell growth. Nuclear factor kappa- B (NF-KB) transcription factor is inhibited by curcumin extract from the rhizome of the Curcuma longa L. plant, which causes cell death [12,13]. One of the well-known natural substances with anticancer effects is berberine. It comes from a variety of plant species, including Coptis japonica, Chinese schneid, and Berberis aristata. By modifying the proteins NF-B, MMP-2, and MMP-9, it targets the AMPK (Adenosine monophosphate activated protein kinase) and mTOR (mammalian or mechanistic target of rapamycin) signaling pathways to control the growth of tumors. The potential of all such natural substances that can be used to target cancer is summarized in this paper [14].



Compounds from Nature with Cancer-Preventive Qualities

Quercetin

Flavonoids and polyphenols are examples of natural substances that have been shown to have anti-cancer properties and can be utilised to treat different types of cancer. Regarding this, quercetin is widely found in common foods including teas, vegetables, nuts, and various plants. By interfering with the uPA/ uPAR systems, NF-Kβ, AMPK (adenosine monophosphate-activated protein kinase), ERK1/2, and PKC, quercetin inhibits the growth of Gastric cancer (GC) metastases cells (Protein kinase C). The effects of quercetin on colorectal cancer (CRC) cells with the KRAS mutant gene suggested that it might boost cancer apoptosis. In various myeloma cell lines, it prevents the growth of ARP-1, MM.1R, and RPMI8226 by causing apoptosis and cell cycle arrest in the G2/M phase. It inhibited the NF-KB and COX-2 pathways, the Akt/ERK1/2 signalling system, hTERT (telomerase reverse transcriptase) through the AP-2/hTERT, and COX-2 (cyclooxygenase 2). It has anticancer properties and targets AMPK-α, PI3K-Akt, Akt/ERK 1 and 2, NF- Kβ, COX-2, ARP-1, and RPMI8226.

Andrographolide and 14-Deoxyandrographolide

Andrographis paniculata, which belongs to the Aceanthaceae family, is the source of andrographolide and 14-deoxyandrographolide. They are said to possess anti-cancerous qualities. Andrographolide and 14-deoxyandrographolide are present in ethanol, dichloromethane, methanol, and water extracts of this plant that inhibit telomerase and fight cancer [16]. They prevent TRAP in MCF-7 cells (telomerase using the repeated amplification protocol). According to studies, they each suppressed telomerase by 73.7, 77.5, 78.5, and 80.3 percent, respectively [17]. In addition, the flow cytometry study showed that methanol and water extracts increased the rates of overall apoptosis by 25% and 32.8%, respectively, in comparison to dichloromethane (10.07%) and ethanolic extracts (10.7%), which both induced lower rates of apoptosis [18].

Vinblastine

The semi-synthetic alkaloid vinblastine is obtained from the plant Catharanthus roseus, which belongs to the Apocynaceae family. In order to investigate the plant's anti-diabetic properties, this plant extract was given to rabbits, which demonstrated the plant's potential as a chemotherapeutic agent. Vinblastine was deemed to be effective against cancers of the WBC in the study, where rabbits died of bacterial infection as a result of a lack of WBC [19]. Vinblastine stops the development of microtubules, which leads cells to go towards the M phase. This substance has an impact on a number of biomolecules, including the metabolism of glutathione, cyclic AMP, amino acids, calmodulin-dependent Ca++ transport ATPase activity, cellular respiration, and lipid biosynthesis. Non-Hodgkin lymphomas, Hodgkin's lymphomas, breast cancer, renal cell carcinoma, Kaposi sarcoma, and testicular cancer can all be treated with vinblastine. It results in the usual side effects of myelo-suppression, fever, anaemia, alopecia, and mucositis as a result of unfavorable reactions [7,19].

β-Elemene

Traditional Chinese medicine uses the sesquiterpene natural substance β-elemene to cure a variety of cancers without any unfavourable side effects. It improves the sensitivity of the multidrug-resistant leukaemia (DNR/K562) and GS (glutamine synthetase) cell lines (ADR/SGC7901), inhibits the ABCB1 transporter efflux component that is over-expressed in KB-C2 cells, and down-regulates Akt signaling pathways. β- Elemene inhibits MCF-7 cells, boosts PTEN and Pgp expression, and enhances cell death to aid in the treatment of cancer. It exhibits anti-cancer properties by targeting DNR/K562, GS cell lines, ABCB1 transporters efflux part, and MCF-7 [20].

Curcumin

A naturally occurring anticancer substance called curcumin is obtained from the rhizome of the Zingiberaceae plant species Curcuma longa. It increases hypoxia-induced stress and the activation of beta-growth factor by blocking AP-1 and hypoxia-

inducible factors (TGF-β). HIF-1 encourages VEGF expression. HIF-1 encourages aggressive angiogenesis in malignancies. It decreases the expression of the proteins E-selectin, intracellular adhesion molecule-1, and vascular cell adhesion molecule-1, all of which are crucial for cellular adhesion. MMPs, ICAM-1, and VCAM (Vascular Cell Adhesion Molecule), which are all involved in metastasis and cellular adhesion, are all inhibited by curcumin [21]. Additionally, it raises various anti-metastatic proteins such E-cadherin, tissue inhibitor metalloproteinase (TIMP 2), and the non-metastatic gene NM23. There are claims that curcumin can prevent cancer in many organs [22].

Baicalein

One of the most significant active ingredients was identified from the roots of Scutellariae radix, often known as Chinese Huang Qin, and is called baicalein. By preventing cell cycle progression at the S/G1 phase of division by activating caspase-3 and caspase-9, upregulating Bax expression, and downregulating Bcl-2 expression, it inhibits Akt phosphorrylation and the development of T24 cells. Apoptosis is enhanced by baicalein [23]. By blocking the activation of cyclin B1 and CDC2, it also slows the spread of bladder cancer. By preventing 17-estradiol-induced trans activation, it significantly increased ER-positive MCF-7 cell death. It encourages the ERK/p38 MAPK pathway's activation, which aids in inhibiting breast cancer cell proliferation. Baicalein inhibits the Akt pathway to prevent the activation of MMP-9 and MMP-2 in colorectal cancer (CRC). Gastric cancer can also be treated with baicalein. Molecules linked to metastasis, including vimentin, N-cadherin, ZEB2, and ZEB1, had their expression levels decreased. The Akt, PTEN, and HIF-1 pathways are stimulated, which aids in reducing cell growth. Because baicalein aids in cell cycle arrest in the G1 phase, it can treat hepato-cellular cancer [24,25].

Conclusion

The main cause of death worldwide is cancer. The primary cause of this condition is excessive cell proliferation. Different types of causes are discovered by researchers that cause cancer. Anyone from a child to senescence can contract cancer because there is no upper age limit for the disease. Studies have shown that a gene mutation or change in a gene is what causes cancer. Numerous types of radiation and chemotherapy are offered commercially for the treatment of cancer. Even though there is currently no cure for cancer, taking drugs and getting radiation can add years to a person's life. Patients who take medication may experience adverse effects, and treatments can be costly for individuals living in rural and developing countries. Researchers discovered some naturally occurring substances that have anti-cancer action, such as plant extracts. This study summarizes a number of organic compounds that have been studied for their potential to fight cancer. These organic ingredients can be used to treat cancer. These components can control gene modifications, gene deletions, cell proliferation, genetic alterations, and excessive protein synthesis.

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