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SHORT COMMUNICATION

Phytotherapeutic potential of natural polyphenols used in alleviating cancer

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Abstract: These days, cancer is still the second biggest cause of death and causes serious issues with public health. The largest class of phytochemicals present in fruits, vegetables, and spices are called polyphenols. Secondary metabolites called polyphenols are used to treat a number of illnesses, including diabetes mellitus, hypertension, cancer, and osteoporosis. Additionally, they function as antioxidants and antimicrobials, extending the shelf life of food items. In this article, we primarily examine the role that polyphenols play in cancer therapy via molecular signaling pathways. In addition, multiple studies have shown that natural polyphenols have potential use in cancer prevention and treatment. These mechanisms may include antioxidant, anti-inflammatory, and anti-microbial effects on the carcinogenesis process. Prior to COVID-19, despite the serious side effects of antibiotics, people gave them a lot of importance. The world needs to know that natural plant sources have been used historically to heal a variety of illnesses. As technology advances, more users of natural therapy are turning to pharmaceuticals made of chemicals. Covid-19 has a significant influence on the use of plant sources in therapeutics. This review provides examples of how polyphenols are used to treat cancer.
Keywords: Apoptosis; Cell Proliferation; Polyphenols; Oxidative stress; Isoflavonoids

1. Introduction

Compounds with an aromatic ring and one or more hydroxyl groups are referred to as polyphenols. They are frequently present in tea, fruits, vegetables, and spices [1]. By encapsulating and shielding the polyphenols, nanocarriers improve their water solubility and bioavailability[2]. These are plant-extracted secondary metabolites. In addition to treating cancer, it is also used to treat a number of other illnesses, including diabetes mellitus, osteoporosis, hypertension, heart failure, Parkinson's and Alzheimer's disease, and neurodegenerative diseases. This article provides a brief detail about the natural polyphenols and their uses in the cancer treatment

Natural polyphenols can be divided into four Classes as shown in Figure 1 below:

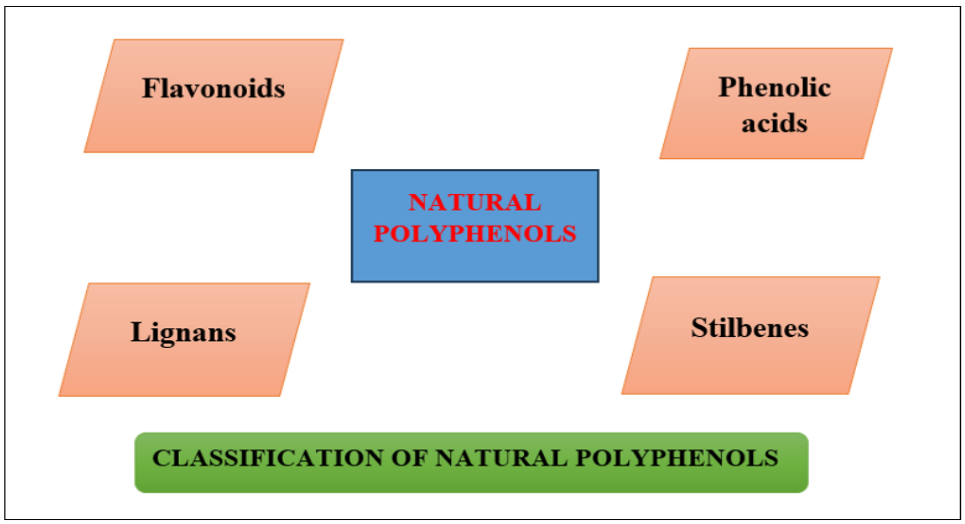

Figure 1. Classification of Polyphenols

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Moreover, polyphenols are added to diet and utilized as supplements[3]. Utilizing polyphenols as bio-preservatives extends the shelf life of food items. Polyphenols has antibacterial and antioxidant qualities. It acquires antioxidant properties as a result of the suppression of free radical production. Phenolic molecules are present and contribute to the antibacterial properties. Nitrate and sorbate preservatives have been linked to health problems such as asthma, cancer, hypersensitivity, and neurological damage. [4] The mechanism of action of polyphenols is shown in Figure 2.

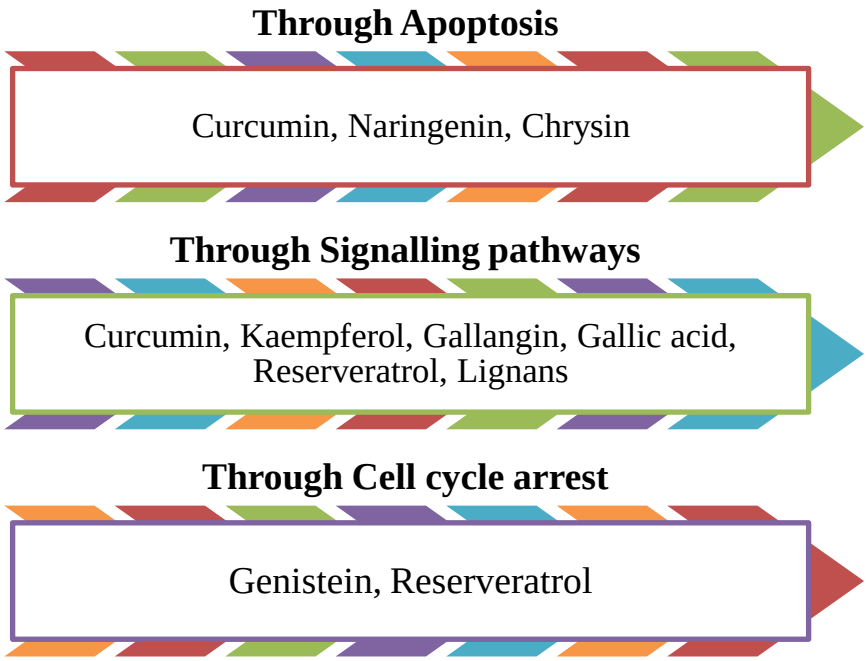

Figure 2. Mechanism of action of Polyphenols through signaling pathways

2. Types of polyphenols

2.1 Naringenin

The polyphenol naringenin is a member of the flavanone group. It is a source of several fruits, including tomatoes, cherries, citrus, and grapes. It demonstrates anti-inflammatory, anti-oxidant, and anti-cancer qualities. Cancer is treated with naringenin in its purest form. Carcinogens are rendered inactive by TGF-β signaling pathways, apoptosis induction, and cell cycle arrest. Treatment options include pancreas, liver, ovary, GIT, and breast cancer, among other cancers. An herbal remedy with numerous pharmacological and therapeutic properties is naringenin [5].

2.2 Hesperitin

Aglycone Hesperetin and hesperidin exhibit anti-cancer effects. It works in multiple ways, including oxidative status, glucose uptake, MRNA expression, DNA repair, and tumor suppressor p53. There are potential chemotherapeutic and chemo-sensitizing effects for both Hesperetin and hesperidin. When doxorubicin and hesperidin are combined, the effectiveness of pharmaceutically available drugs is increased [6].

2.3 Chrysin

Chrysin is extracted from honey and propolis. It shows anti-oxidant, anti-cancer and anti-inflammatory properties. It inhibits the cancer cells growth through multiple cell signaling pathways such as arresting cell cycle, metastasis, induction of apoptosis, inhibition of angiogenesis without disturbing the normal cells. These pathways are linked to various activities like survival, angiogenesis, growth, invasion, Metastasis of cancer cells. Anti-tumor activity of chrysin is having great value in cancer therapy because of its low side effects. Along with anti-cancer, Chrysin has other activities such as anti-allergic, anti-diabetic, anti-oxidant, anti-estrogenic, anti-tumor activities [7].

2.4 Curcumin

The turmeric's yellow pigment, curcuma longa, is used to extract curcumin. Depending on the kind of cell, it stops it at different stages of the cell cycle, which prevents cell proliferation. It causes cancer cells to undergo apoptosis through a mitochondria-mediated mechanism. The downregulation of anti-apoptotic proteins by anti-sense nuclear types is one of the mechanisms via which curcumin induces apoptosis[8].

It causes many tumor cell lines to undergo apoptosis. By reacting with the cells, it produces reactive oxygen species, which increases the expression of receptors on the tumor cell membrane. Curcumin induces apoptosis by upregulating P53 activity, which prevents tumor cells from proliferating. Curcumin also prevents NF-kB and COX-2 from acting. Apoptosis is induced by receptors such as transforming growth factor-beta and tumor necrosis factor-alpha [9].

2.5 Genistein

The most prevalent isoflavonoid found in soy and soy-based products is genistein [10]. It is used to treat cancer and as a preventative measure for chronic illnesses. On a variety of cancer cells, it exhibits oxidant activity [11]. It inhibits the immune system's humoral cells and cell mediators. It is utilized to stop the growth of cancer cells by causing apoptosis. Additionally, it keeps DNA from being damaged. Genistein, which causes addiction, is less harmful and lessens anthrogenic conditions[12]. The mice are administered 20 mg, 50 mg, or 80 mg kg/day of genistein. It shrinks from the size and weight of colon cancer. When genistein is given orally to mice at a dose of 50 mg kg/day, it suppresses the angiogenin and the growth of colorectal cancer. It inhibits the spread of liver cancer cells. [13].

2.6 Kaempferol

Among the natural flavonoids found in apples, beans, strawberries, and broccoli is kaempferol. It demonstrates anti-allergic, anti-diabetic, and anti-cancer effects. Kaempferol acts through inducing apoptosis and inhibiting the G2 or M phases of the cell cycle. It suppresses the HT-29 colon cancer cells by turning on the mitochondrial pathway[14]. It suppresses MMP-9 activity and prevents the growth of breast cancer cells. By blocking GLUT-1-mediated glucose uptake, kaempferol prevents cancer cells from proliferating. The anti-proliferative properties of kaempferol are evident [15].

2.7 Galangin

Alpinis officinarum and oregano are common sources of galangin, a naturally occurring flavonoid. It is primarily prevalent in Asian nations. Galangin strongly prevents chemically induced cell invasions and also prevents liver cancer cells from metastasizing via altering PKC/ERK pathways [16]. Galangin can stop hepatocellular carcinoma cells from proliferating by increasing endoplasmic reticulum stress [17].

2.8 Gallic Acid

Gallic acid is a phenolic acid that is frequently present in sumac, tea leaves, oak bark, and gallnuts. This review delves into the anti-tumor properties of gallic acid, along with the cellular pathways and molecular mechanisms that underlie them. It inhibits the growth of P13K/AKT cancer cells. Additionally, gallic acid can inhibit the growth of cancer [18] when used with chemotherapy drugs. Gallic acid's bioavailability is increased and its delivery is specifically targeted to the cancer site with the introduction of nano-vehicles. Additionally, when bioavailability rises, gallic acid enhances tumor suppression.

2.9 Resveratrol

The primary sources of resveratrol are red wine, berries, and grapes. Human non-small lung cancer cell lines' chemosensitivity to etoposide is enhanced when resveratrol suppresses the expression of XRCCI [19]. It greatly suppresses the invasion and metastasis of A549 lung cancer cells by blocking the EMT pathway. Senescence of the cells results from resveratrol's ability to stop gastric cancer cells in their G-phase. At greater doses, it causes DNA damage and death in human gastric cancer cells by encouraging the production of reactive oxygen species [20]. Damage to DNA results from species in colon cancer cells producing excessive amounts of reactive oxygen.

2.10 Lignans

The main sources of lignans include sesame, flax, and Artium lappa seeds. Flax seeds are high in secoisolariciresional diglucoside (SDG). In terms of structure, it resembles estradiol. The anti-estrogen action of SDG is used in the treatment of breast cancer [21].

3. Molecular Targets of Cancer

Molecular targets include proteins, enzymes, receptors, and ion carriers. Anytime a drug molecule enters our body, it first binds to receptors before it can start working as a medication. Both at the molecular and cellular levels, medications and receptors interact with one another [22]. The greatest illustration of molecular interactions is seen in genes. Modern technology is developing to the point that researchers can now pinpoint the altered genes responsible for a wide range of illnesses. One of the newest methods in the modern world is bioinformatics, a technology that assists in identifying a molecule's biological information. Numerous bioinformatic methods are used to predict genes, proteins, and amino acid sequencing [24].

Identification of the various illness states is aided by the sequencing alignments of different macromolecules. One method is molecular docking, in which a ligand molecule is positioned against a target (a receptor) to determine the molecules' binding affinity. We can determine the interaction between ligands and receptors with the use of binding affinity [23]. All of these strategies work well when the molecular details of the targets are already known to us. Similar to how medication molecules target receptors, plant-based components like polyphenols also do the same. This review examines the molecular mechanisms and signaling pathways by which polyphenols function as anti-cancer drugs [25].

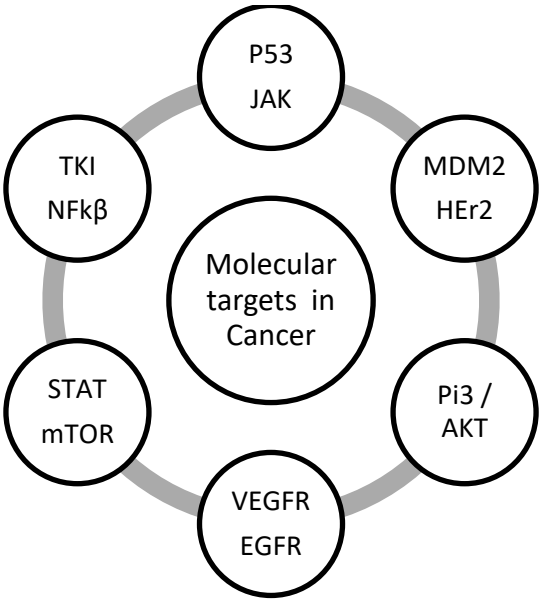

Fig 2: Cellular & Molecular targets of Cancer

4. Future Perspectives

Because of their stronger antioxidant activity, polyphenols have anti-cancer qualities. A few number of polyphenols have undergone clinical trials to demonstrate their efficacy as anti-cancer medicines. The field of molecular comprehension of the mechanism needs further investigation.

5. Conclusion

Many polyphenols which are naturally occurring have anti-cancer activity with the propounding research in molecular and cellular processes. They can exhibit their activity through anti-oxidant, anti-inflammatory and various signaling pathways. Further research has to be done in the core of evaluating therapeutic potential of various chemical constituents obtained from different natural sources of plants and highlighting their activity in the treatment of different types of cancers.

6. Abbreviations

TGF -Transforming growth factor
DNA -Deoxy ribonucleic acid
MRNA -Messenger ribonucleic acid
NF-kB - Nuclear factor kappa B
COX-2 - Cyclo oxeganase-2
MMP-9 - Matrix metalloproteinase-9

GLUT -1 Glucose transporter SDG- Secoisolariciresional diglucoside
EMT- Epithelial mesenchymal transition

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Author's short biography

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Area of Research interest include Insilco Research (Auto dock Vina, PYRX, QSAR tool box). Also interested in Invitro and In vivo works. Completed my M.Pharm in the Dept. of Pharmacology, Sri Padmavathi Mahila Viswavidyalayam, Tirupathi. Completed my internship at Pharma Deep Remedies, Hyderabad. Right now, serving as Assistant Professor in the Department of Pharmacology, Narayana Pharmacy College, Nellore, Andhra Pradesh, India. Myself certified in Clinical SAS. She had also completed a diploma course in "Food & Nutrition" in IGNOU, Vishakhapatnam. Given oral presentation on "Therapeutic Drug Monitoring" in the seminar – "Current Achievements, Challenges and Future Prospects of Drug Delivery" held at Gokula Krishna College of Pharmacy, Sullurpet.