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Importance of Medicinal plants having anticarcinogenic and antioxidant activities used in Ayurvedic Medicinal System

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ABSTRACT:

Internationally malignant growth is a sickness which seriously impacts the human populace. New treatments to treat and prevent this deadly disease are always in high demand. Natural compounds are getting more attention from scientists and researchers because they are thought to have fewer harmful side effects than current treatments like chemotherapy. The Plant Realm delivers normally happening auxiliary metabolites which are being explored for their anticancer exercises prompting the improvement of new clinical medications. New technologies are emerging to further develop the field as a result of these compounds' success as standard cancer treatments. Nanoparticles for nanomedicines are one example of a new technology that aims to control the release of plant-derived drugs and investigate novel administration strategies to enhance their anticancer properties. The demand for medicinal plant-derived naturally-derived compounds and the properties that make them potential targets for anticancer treatments are the subject of this review.

Key words: anticancer, secondary metabolites, polyphenols, cytotoxicity, epigenetics

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INTRODUCTION

There has been a lot of progress made in cancer treatment and prevention over the years. The disease is characterized by uncontrollable and unstoppable cell proliferation throughout the body. Thusly, shaping cancers of threatening cells with the possibility to be metastatic. Chemotherapy, radiation therapy, and drugs derived from chemicals are some of the current treatments. Chemotherapy, for example, can put patients under a lot of stress and make their health worse. As a result, alternative cancer treatments and therapies are prioritized. In developing nations, herbal medicines have been and continue to be the primary source of medical treatment for many years. Because of their natural antiseptic properties, plants have been used in medicine. As a result, research has focused on the potential properties and applications of extracts from terrestrial plants for the preparation of nanomaterial-based drugs for diseases like cancer. Numerous plant species are already being used to treat or stop cancer from growing. Plant species with anticancer properties have been identified by a number of researchers, with an emphasis on those that have been utilized in herbal medicine in developing nations. The ability of certain compounds, which are specific to the plant kingdom and are necessary for the survival of plants as well as the "housekeeping" of the organism, to stop cancerous cells from growing and start apoptosis is the subject of research. The purpose of this article is to provide an overview of the latest developments in the field and plant-derived compounds with anticancer therapeutic properties.

EPIGENETIC PROPERTIES

The control of hypermethylation of tumour-suppressor genes on CpG islands is deregulated in cancer cells, which is the first step in the path that leads to the development of cancer. Tumor-suppressor genes may become silenced or inactivated as a result. Recent years have seen the development of medications that can either inhibit or reverse epigenetic changes. Chemically derived epigenetic drugs like 5-azacitidine (azacitidine;) have been developed and tested. Vidaza) and 5-aza-2'-deoxycytidine, also known as decitbine; Dacogen), which are both DNMTi 11 and HDACi, such as FK228 (Romidespin, Istodax) and suberoyanilde hydroxamic acid (SAHA, Vorinostat, Zolinza). However, it is challenging to engineer a chemically derived drug that is specific for the cytotoxicity of cancer cells and non-toxic to normal cells. As a result, there is a growing demand for the development and research of naturally derived compounds that can be used to treat cancer, particularly those derived from plant species and their natural products. There are many different kinds of cancer in the human population, but they all have the same characteristics or genotypes, like being unable to respond to signals that stop cell growth and make their replication endless. Cancer cells are able to survive because angiogenesis is maintained within the tumor tissue and apoptosis is never triggered in them. Compounds derived from plants have been shown to inhibit cancer cell activity, inhibiting cancer cell proliferation and triggering apoptosis.

PLANT COMPOUNDS WITH ANTICANCER PROPERTIES

In Asian and African populations, medicinal plants have been used as folk remedies for thousands of years, and many plants are consumed for their health benefits in developed nations. The World Health Organization (WHO) says that some countries still use plant-based treatments as their primary medicine, and developing countries are using the benefits of naturally derived compounds for treatment. Polyphenols, brassinosteroids, and taxols are examples of compounds with anticancer properties that have been identified and extracted from terrestrial plants.

Polyphenols

Flavonoids, tannins, curcumin, resveratrol, and gallacatechins are all polyphenolic compounds that are regarded as anticancer compounds. Red wine, grapes, and peanuts are all sources of resveratrol. Green tea has gallacatechins in it. Because they are natural antioxidants, it is thought that including polyphenols in one's diet can improve one's health and lower one's risk of developing cancer. Polyphenols' antioxidant properties have been determined and their cytotoxicity on a variety of cancer cells has been demonstrated. Polyphenols are thought to have anticancer properties that can be used by inducing apoptosis. Polyphenols are thought to initiate apoptosis by controlling the mobilization of copper ions that are bound to chromatin and cause DNA fragmentation. This is thought to be the mechanism by which polyphenols initiate apoptosis. Resveratrol was found to be capable of DNA degradation when Cu(II) was present. Plant polyphenols also possess the ability to inhibit cancer cell growth and interfere with proteins found in these cells. Through direct bonding, cancer agents can be altered by the polyphenol regulating acetylation, methylation, or phosphorylation. Through interaction with a variety of stimuli, curcumin-treated cancer cells in a variety of cell lines have demonstrated suppression of tumor necrosis factor (TNF) expression.

Flavonoids

With 10,000 known structures, flavonoids belong to the polyphenolic compounds and are a large family of secondary metabolites found in plants. They are physiologically active substances found in plants and are gaining scientific attention due to their potential health benefits. Different plants have been examined for their flavonoid content and what these mixtures mean for malignant growth cells, for example, greenery species and plants utilized in customary Chinese medications like the litchi leaf. Anthocyanins, flavones, flavonols, chalcones, and a slew of other flavonoid compounds can all be found in the plant's seed, which is just one of its many structures. Coa and other, 2013, identified and investigated the anticancer effects of flavonoids on the Dryopteris erythrosora fern cell line (A456 human lung cancer cell line). They discovered that flavonoids had high free radical scavenging activity and cytotoxicity against cancer cells. Additionally, purified flavonoids have demonstrated anticancer properties against the following human cancers: cervical carcinoma (Hela), hepatoma (Hep-G2), and breast cancer (MCF-7) It was demonstrated that the flavonoids (4'-Methoxy licoflavanone (MLF) and Alpinumi soflavone (AIF) extracted from Erythrina suberosa stem bark had cytotoxic effects on HL-60 cells (human leukemia). Through both intrinsic and extrinsic signaling pathways, MLF and AIF induced apoptosis. The induction of apoptotic proteins results in a significant decrease in the mitochondrial membrane potential. Cancer cells cannot survive when mitochondria are damaged. Flavonoid extracts from fern species have been the subject of additional research, and their anticancer activity was found to be high even at low concentrations. Polyphenols, as previously stated, have the ability to inhibit or alter the regulation of proteins and other agents, which may be contributing to cancer cell survival. Anti-apoptotic Signal Transducer and Activator of Transcription (STAT) proteins aid in cancer cell proliferation. By preventing the phosphorylation of the members of this family of proteins, which is necessary for the survival of cancer cells, MLF and AIF inhibit them. Additionally, these flavonoids prevent the expression of NF-B, which is necessary for the survival, angiogenesis, and proliferation of cancer cells.

Brassinosteroids

Brassinosteroids (BRs) are naturally occurring substances found in plants. They play a role in hormone signaling to control cell growth, differentiation, and elongation, as well as in disease and stress resistance and tolerance. Additionally, BRs regulate plant senescence. They are necessary for the growth and development of plants. Another naturally occurring compound known as BRs has been shown to have therapeutic value in the fight against cancer. In studies with cancer cells, two natural BRs have been utilized to demonstrate these compounds' anticancer properties. 28-homocastasterone (28-homoCS) and 24-epibrassinolide (24-epiBL) have been shown to be effective at micromolar concentrations against various cancer cell lines. Cancer cells are unique in that they do not naturally undergo apoptosis and continue to multiply indefinitely. By interacting with the cell cycle, BRs can elicit responses necessary for growth inhibition and apoptosis. BRs have been used to treat a variety of cancer cell lines in research, including; Multiple myeloma RPMI 8226, T-lymphoblastic leukemia CEM, cervical carcinoma HeLa, lung carcinoma A-549, and osteosarcoma HOS cell lines Prostate and breast cancer cell lines are also included. Due to their abundance in breast cancer cells like MCF-7, MDA-MB-468, T47D, and MDA-MB-231, estrogen receptor (ER), epidermal growth factor receptor (EGFR), and human EGFR-2 (HER-2) are some of the essential proteins that are targeted in the treatment of the disease. The androgen receptor (AR), which shares a structure with ER, is a crucial protein in the development of prostate cancer cells (LNCaP and DU-145 cell lines). BRs will inhibit the growth of both hormone-sensitive and hormone-insensitive cancer cells by interacting with or binding to these proteins' receptors. Additionally, BRs may cause cell cycle disruption. When breast cancer cell lines were treated with 28-homoCS and 24-epiBL, the cyclin proteins that are involved in the G1 phase of the cell cycle were reduced. Treatment with BRs induces apoptosis at this stage, which cancer cells would not be able to do naturally without treatment. At this point in the cell cycle, cells will either undergo repair or enter apoptosis. In prostate malignant growth cell lines, LNCaP and DU-145, the equilibrium of apoptotic proteins which advance cell endurance and those which actuate modified cell passing changes with BRs treatment. After treatment with BRs, levels of the pro-apoptotic protein Bax rise, while anti-apoptotic proteins like Bcl-2 decrease. In addition to their anticancer properties, BRs produce distinct responses in cancer and normal cells. The agent must not be cytotoxic to normal

cells and must be cell specific to cancer cells in order to be effective as an anticancer treatment. This is where the therapeutic properties of BR agents originate.

Anticancer plant-derived drugs

Because they are natural and readily available, drugs derived from plants are desired for cancer treatment. They can be easily taken by mouth as part of a patient's diet. Additionally, because they are naturally derived compounds from plants, they are generally less harmful to human cells. However, cyanogenetic glycosides, lectins, saponins, lignans, lectins, and some taxanes are exceptions. Plant-derived drugs can enter clinical trials for further therapeutic development if they can demonstrate selectivity in research, non-toxicity to normal cell lines, and cytotoxicity to cancer cell lines. Drugs derived from plants can be divided into four groups based on how they act: inhibitors of the enzyme methytransferase, antioxidants or drugs that prevent DNA damage, histone deacetylase (HDAC) inhibitors, and mitotic disruptors HDAC inhibitors are substances like sulforaphane, isothiocyanates, isoflavones, and pomiferin. They prevent cancer-causing proteins from working. Sulforaphane, for instance, has been shown to inhibit important targets in the proliferation of breast cancer. Sulforaphane treatment of breast cancer cell lines inhibited HDAC, which led to a decrease in the expression of ER, EGFR, and HER-2. HDAC inhibitors reactivate epigenetically silenced genes that are necessary for chromatin acetylation in cancer cells, allowing the cells to enter programmed cell death (apoptosis). Chemotherapeutic sensitivity in human cancers may be enhanced by plant-derived compounds that inhibit HDAC. Vincristine, vinblastine, vinorelbine, vindesine, and vinflunine are drugs that inhibit microtubule dynamics by binding to -tubulin. These drugs are derivatives of vinca alkaloids. Microtubule disruption is also caused by taxanes like paclitaxel and its analog, docetaxel. Cell cycle arrest and apoptosis are caused by these compounds' inhibition of metaphase to anaphase phase transitions. Paclitaxel reduces cancer cell replication by stabilizing or polymerizing microtubules in the cells. Vincristine and vinblastine were two of the first drugs to be isolated, and paclitaxel was one of the first drugs to have a significant impact on cancer treatment. Plant extracts containing vinca alkaloids, Taxus diterpenes, Podiphyllum lignans, and Camptotheca alkaloids may be more effective as therapeutic agents and have stronger anticancer effects when combined. Separates from Urtica membranaceae, Artemesia monosperma and Origanum dayi Post in Solowely et al., 2014 were looked into to see how they worked on a variety of cancer cell lines, including lung, breast, colon, and prostate cancer cell lines. The investigation revealed that plant extracts containing a combination of anticancer compounds could kill cancer cells only, without harming normal human lymphocytes or fibroblasts. Because of this, plant extracts are more appealing as therapeutic agents than chemically derived ones, which can lead to toxic side effects during cancer treatment. An increased population of cells in the sub-G1 phase with a lower DNA content and condensation of chromatin was evidence of the plant extracts' induction of apoptosis. After extract treatment, a crucial stage in apoptotic cell death, caspase 3 activation also increased.

Enhancing drug administration

New technologies for the application and dosage of these anticancer compounds are emerging as a result of developments and discoveries in naturally derived drugs. For a compound to be a successful alternative to current treatments like chemotherapy, its administration must be effective. The application of nanoparticles (NPs) as a drug delivery system to reach target sites is developing through the field of nanotechnology. Due to the requirement for high dosages, some compounds with demonstrated anticancer activities may be limited in clinical development. When formulated with NPs, the isolated bromleain from Aanas comosus was found to be more effective than free bromelain as an anticancer agent. Bromelain nanoparticles (NPs) were used in this study to demonstrate a biocompatible, secure strategy for maintaining drug release at the intended site while also protecting the drug. By controlling the expression of pro-apoptotic and anti-apoptotic proteins in mice undergoing two stages of skin tumorigenesis, these bromelain-loaded polyllactic-co-glycolic acid NPs (BL-PLCG NPs) were shown to induce apoptosis of benign cells more strongly than free bromelain. Other

synthesized NPs have also been studied, including; copper oxide NPs of Acalypha indica and gold NPs of the powdered extract of Antigono leptopus. MCF-7 breast cancer cell lines were cytotoxic by these formulations of plant extract and NPs. Paclitaxel has been tested in both early treatment settings and clinical trials. Utilizing magnetic mesoporous silica NPs with a gelatine membrane, research and development aims to control drug release and increase target specificity. A magnetic field can be used to manipulate paclitaxel from the outside. As the drug's distribution is controlled, this has been shown to be effective in increasing the drug's ability to inhibit tumor growth and reduce unwanted effects on other tissue areas. Utilizing superparamagnetic magnetite NPs, the drug quercetin has also been shown to be effective against breast cancer (MCF-7) cell lines. When compared to free or pure quercetin, the activities of the NPs in cytotoxicity of MCF-7 cells were found to be superior. As a natural alternative to current treatments, the use of NPs for cancer treatment is attracting increasing interest. Oral or inhaled administration of nanocochleates and nanolipososmes, on the other hand, has been shown to be effective in combating cancer. Oral administration of paclitaxel is more cost-effective and comfortable for the patient. A formulation of oral paclitaxel-loaded nanocochleates demonstrated effective activities against lung, ovarian, and breast cancer cell lines and controlled drug release. Due to its insoluble nature, noscapine was also restricted in clinical trials until derived analogues were developed. Jyoti and other, 2015 looked into the formulation of the noscapine analogue 9-bromo-noscapine with nanostructured lipid particles. They demonstrated enhanced cytotoxicity and apoptosis in lung cancer cell lines here, with the formulated noscapine analogue taking up more cancerous cells than the free drug.

MEDICINAL PLANT DEMANDS

Plant-based medicines are becoming increasingly popular for clinical development after completing successful clinical trials. They are in high demand due to their cytotoxic and non-toxic effects on cancer cells and normal cells. Most of the species studied come from developing countries in Asia and Africa, where herbal medicine is used as a primary treatment and medicinal plants are widely used. In 2007, the World Health Organization estimated that the trade in drugs derived from plants was worth $100 billion US. By 2050, the trade is expected to reach $5 trillion. In developing nations, there is a significant demand for medicinal plants, which puts a significant strain on plant populations. It is illegal to cultivate numerous medicinal plants from wild populations for informal trade. The protection of medicinal plants is becoming a problem that must be addressed in light of rapid population growth, deforestation, and growing urbanization. High-value medicinal plants are in danger of extinction if overexploitation continues, as demand for them continues to rise. It is essential to preserve these plants. The bark of a tree or the bulbs and tubers of bulbous and tuberous plants, for instance, are the only parts of wild medicinal plants that are utilized in treatment. Taking only portions of a plant can harm it and make it less likely to survive. Utilization of all plant parts, including the stem, leaf, root, and bark, ought to be incorporated into the treatment for the purpose of increasing the sustainability of medicinal plants in developing nations. Germplasm conservation is another method of conservation; cryopreservation, storing seeds that are viable; using tissue culture and liquid nitrogen to preserve biological material; clones mature plants of rare species quickly and can propagate plants in sterile conditions. In developed nations, these preservation techniques will also make industrial use possible. To meet the growing demand for natural alternatives to pharmaceuticals, some medicinal plants are being grown extensively in developed regions like Europe, India, and China. Plant biodiversity may be preserved and other wild species may be relieved of pressure by sustainable species cultivation. However, widespread cultivation may put a strain on the available land for other agricultural resources. Cruciferous vegetables and fruit berries, among others, are attracting attention for their medicinal properties. It is possible to extract anticancer agents from sources containing these agents using raw by-products from industries. For instance, grapes (Vitris vinifera) are one of the most widely grown crops in the world. Because of its positive effects on human health, "grape seed extract" is

frequently included in the ingredients of food products. In the winery business grape stems are a crude result of wine making. The winery's surrounding environment may become acidic as a result of this high organic load. However, its high polyphenolic content may make it a profitable strategy for addressing environmental issues and advantageous for the development of anticancer drugs. Antioxidant properties, DNA protection from reactive oxygen species, and anti-carcinogenic potential against a variety of cancer cell lines, including cervical cancer, thyroid cancer, and many others, have all been demonstrated by grape stem extracts.

CONCLUSION

In both developed and developing nations, cancer is gaining prominence. The World Health Organization (WHO) reported in 2007 that in 2005, cancer-related diseases caused the deaths of 7.6 million people, the majority of whom lived in low-income nations 49. Cancer accounts for one in four deaths in the United States, and more than 1.5 million new cases were estimated in 2010. According to Cancer Research UK, 8.2 million people worldwide died from cancer and 14.1 million adults were diagnosed with the disease in 2012. As a result, there is a tremendous demand for cancer treatments and prevention. Drugs derived from chemicals have been developed, and other cancer treatments are already available. However, current treatments like chemotherapy have drawbacks due to the toxic effects they have on non-targeted tissues, which exacerbate human health issues. As a result, there is a demand for alternative treatments that come from naturally occurring anticancer agents—ideally from plants. The potential of the secondary metabolites found in plants, such as polyphenols, flavonoids, and brassinosteroids, as anticancer agents has been investigated. Collectively, they have been shown to have the following anticancer properties: antioxidant power; a stop to the growth of cancer cells; triggering apoptosis; a focus on specificity; cytotoxicity of cancer cells Positive research results have led to the development of drugs derived from plants, which have now entered clinical trials. Vinca alkaloids were some of the first drugs used, and together with Pacitaxel and other cancer drugs, they are developing in clinical Phase III trials. These compounds are relatively non-toxic to healthy human cells and are readily available from the natural environment. Additionally, new technologies like nanoparticles are currently being developed for the administration of anticancer drugs and treatments. Their development could be used to control sustained drug release and aid in the development of tissue-specific drugs to lessen the severity of treatment-related side effects. High-value medicinal plants are under pressure and their biodiversity is at risk as a result of rising demand for plant-derived drugs. In developing nations, species extinction is exacerbated by population growth, urbanization, and deforestation. To help preservation of these species germplasm protection, cryopreservation, tissue societies and plant part replacement systems should be set up. The widespread cultivation of medicinal plant species and the industrial use of raw by-products may also contribute to conservation. Because they are potent inhibitors of cancer cell lines 3, plant-derived anticancer agents are in high demand. To meet demand and remain viable, these agents' exploitation must be controlled.

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