

Medicinal Plants and Anticancer Treatment

Introduction

Terrestrial plants and their anticancer properties

Cancer has been a constant battle globally with a lot of development in cures and preventative therapies. The disease is characterized by cells in the human body continually multiplying with the inability to be controlled or stopped. Consequently, forming tumors of malignant cells with the potential to be metastatic.

Current treatments include chemotherapy, radiotherapy and chemically derived drugs. Treatments such as chemotherapy can put patients under a lot of strain and further damage their health. Therefore, there is a focus on using alternative treatments and therapies against cancer. For many years herbal medicines have been used and are still used in developing countries as the primary source of medical treatment. Plants have been used in medicine for their natural antiseptic properties. Thus, research has developed into investigating the potential properties and uses of terrestrial plants extracts for the preparation of potential nanomaterial based drugs for diseases including cancer.

Medicinal plants have been used for thousands of years in folk medicines in Asian and African populations and many plants are consumed for their health benefits in developed nations. According to the World Health Organisation (WHO) some nations still rely on plant-based treatment as their main source of medicine and developing nations are utilizing the benefits of naturally sourced compounds for therapeutic purposes. Compounds which have been identified and extracted from terrestrial plants for their anticancer properties include polyphenols, brassinosteroids and taxols.

Polyphenols

Polyphenolic compounds include flavonoids, tannins, curcumin, resveratrol and gallatechins and are all considered to be anticancer compounds. (A.S Amzi) Resveratrol can be found in foods including peanuts and grapes and red wine. Gallatechins are present in green tea. It is thought including polyphenols in a person's diet can improve health and reduce risk of cancers by being natural antioxidants. (A. Apostolou) The cytotoxicity of polyphenols on a range of cancer cells has been demonstrated and their antioxidant properties determined. Polyphenols are thought to have apoptosis inducing properties showing anticancer properties which can be utilized. Cancer agents may be altered through the polyphenol regulating acetylation, methylation or phosphorylation by direct bonding. For example, curcumin treated cancer cells in various cells lines have shown suppression of the Tumour Necrosis Factor (TNF) expression through interaction with various stimuli [1-8].

Flavonoids

Flavonoids are from the polyphenolic compounds and constitute a large family of plant secondary metabolites with 10,000 known structures. (J. Cao) They are physiologically active

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agents in plants and becoming of high interest scientifically for their health benefits. (G.Agati) There is a high content of flavonoid compounds such as anthocyanins, flavones, flavonols, chalcones and many more which can be found in just one structure of the plant like its seed. (L.Wen) With mitochondria damage to cells the cancer cells cannot survive. (A.S Pathania) Other studies have looked at flavonoid extracts from fern species and found that even in low concentrations they still demonstrate high percentage of anticancer activity. (X.Xia)

Brassinosteroids

Brassinosteroids (BRs) are naturally occurring compounds found in plants which play roles in hormone signaling to regulate growth and differentiation of cells, elongation of stem and root cells and other roles such as resistance and tolerance against disease and stress. (G.J Bishop) BRs are another naturally occurring compounds which have demonstrated therapeutic significance in the cause against cancer. BRs have been used in investigations to treat a range of cancer cell lines which include; T-lymphoblastic leukaemia CEM, multiple myeloma RPMI 8226, cervical carcinoma HeLa, lung carcinoma A-549 and osteosarcoma HOS cell lines. (J.Malikova)

Enhancing drug administration

With advancements and discoveries in naturally derived drugs new technologies are emerging for the application and dosage of these anticancer compounds. Administration of new drugs needs to be effective for the compound to be a successful alternative to current treatments such as chemotherapy. Through the field of nanotechnology the use of nanoparticles (NPs), as a delivery system for drugs to reach target sites, is developing. Some compounds that have demonstrated anticancer activities may be limited in their clinical development due to the need for high dosages. (P. Bhatnagar) A research investigating application using nanocochleates and nanoliposomes demonstrates achievement in anticancer activities through oral or inhalable intake. (A.W Pawar)

Paclitaxel taken orally is most cost effective and more comfortable for the patient. A formulation of Paclitaxel-loaded

nanochleates which can be administered orally showed controlled drug release and effective activities against lung, ovarian and breast cancer cell lines. (A.W.Pawar)

Medicinal plant demands

With successful clinical trials drugs being developed from plant origins are popular for clinical development. Their non-toxic effects on normal cells and their cytotoxic effects on cancer cells put them in high demand. A lot of the species investigated are selected from developing countries in Africa and Asia where herbal therapies are practiced and medicinal plants are relied upon for primary treatment. (C.N Kimwele) There is a huge demand for medicinal plants in developing countries putting high pressure on the plant populations. Many medicinal plants are cultivated from wild populations for informal trade but this cultivation is not regulated. With rapid population growth, deforestation and increasing urbanization the protection of medicinal plants is becoming an issue in need of addressing. (S.Parveen)

With constant increase in demand, high-value medicinal plants are threatened by extinction if over exploitation continues. Conservation of these plants is vital. When wild medicinal plants are harvested only specific parts of the plant are used in treatment such as the bark of a tree or bulbs and tubers from bulbous and tuberous plants. Extracting only segments of a plant may damage and reduce its survival. (S. Zschocke) To increase the sustainability of medicinal plants in developing countries, utilization of all parts including the stem, leaf, root and bark should be included in the treatment. Cultivating sustainable species may release pressure on other wild species and prevent loss of plant biodiversity. However, mass cultivation could lead to strain on land available for other resources in agriculture. Attention is being drawn towards foods with medicinal properties, such foods include cruciferous vegetables and fruit berries. (A.L Huntely) Raw by-products from industries could be utilized extract anticancer agents from sources possess these agents. For example, one of the biggest crops grown globally are grapes (*Vitisvinifera*) and 'grape seed extract' is often added in ingredients of food products due to its human health benefits. In the winery industry grape stems are a raw by-product of wine making. This high organic load can be acidic to the environment surrounding the winery. However, its high polyphenolic content make it advantageous for anticancer drug development and make a profitable scheme to solve environmental issues. Grape stem extracts have demonstrated to have antioxidant properties, prevent DNA damage from reactive oxygen species and shown anti-carcinogenic potential against an array of cancer cell lines from cervical cancer, thyroid cancer and many more. (D.Stagos)

Some plant-derived drugs in research and clinical trials:

i. Anticancer agent: Sulphoraphane; Isolated or derived from: Isotiocyanate in cruciferous vegetables 'Brassia'; Compound activity: Induces phase 2 detoxification enzymes,

inhibits tumor growth in breast cancers, antiproliferate effects; Research & Clinical development: Clinical trials with oral administration of cruciferous vegetable preparation with sulphoraphane. (A.Sobolewski, B.S. Cornblatt)

ii. Anticancer agent: Paclitaxel (Taxol); Isolated or derived from: Taxane, *Taxusbrevifolia* L; Compound activity: Microtubule disruptor, block mitosis, induce apoptosis, microtubules are polymerized and stabilized, disruption of spindle formation; Research & Clinical development: In clinical use, Phase I,III clinical trials, early treatment settings, non-small lung cancer, breast cancer, ovarian cancer, Kaposi sarcoma. Research and development in alternative drug administration using nanoparticles, nanochealtes and nanoliposomes.(M.A Jordan, E. Che, A.P Pawar)

iii. Anticancer agent: Vincristine; Research & Clinical development: Lymphomas, Sarcomas and Leukaemias, in clinical use, combination trials (A.Amin, M.A Jordan)

iv. Anticancer agent: Vinblastine; Isolated or derived from: Vinca Alkaloids; Compound activity: Microtubule inhibitor, pro-apoptotic properties and induce cell cycle arrest, antitumor activity; Research & Clinical development: Testicular cancer, Hodgkin's disease and Lymphoma, in clinical use, combination trials (A.Amin, M.A Jordan)

v. Anticancer agent: Pomiferin; Isolated or derived from: Isoflavonoidisolatated from *Maclurapomifera*, *DereisMalaccensis*; Compound activity: Pro-apoptotic effects, DNA fragmentation, inhibits oxidative damage of DNA, antioxidant activity, cytotoxicity of cancer cells; Research & Clinical development: Growth inhibition in six human cancer cell lines ACHN (kidney), NCI-H23 (lung), PC-3 (prostate), MDA-MB-231 (breast), LOX-IMVI (Melanoma), HCT-15 (colon) (A. Amin, I.H Son).

Acknowledgement

None.

Conflict of Interest

None.

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