

Study of Medicinal Plants and their Anti-Cancer Activity. A Review

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Abstract

Medicinal plants serve as the major source for their unique featured chemical substances and the active ingredient possessed by some medicinal plants capable line in the field of research against

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cancer. In addition to this the chemotherapeutic agents used against cancer for treatment show very high potential of adverse drug reactions. However, plants and products derived from plant shows revolutionary results in medical field because of low-cost Simplicity, safety margin, less toxicity and eco-friendly than that of method of conventional treatment. Similarly, phytochemical substances are assumed to be the best suited class of substances for drug development against cancer because of having numerous method of action on targeted cell because of their pleiotropic actions. Many researches on photochemical have been conducted and are in process for the preparation and the discovery of the substances that have the higher potential against the growth of the cancerous cell and have the safe usage profile. Many chemical compounds belong to the group of phytochemicals and their derivatives are identified and are found to have the potential against therapy of cancer. The recent and modern development and progress made in the field of anticancer drugs from medicinal plants using phytochemicals are highlighted in this review.

Keywords: Cancer, Chemotherapeutic agents, phytochemicals, Medicinal plants.

INTRODUCTION

Cancer is unvarying combat worldwide with increase in advancement regarding anticipatory therapies and treatment cures. Cancer is a disease which is characterized as the continual, uncontrolled and abnormal multiplication of human cells which cannot be controlled that results in the condition called metastatic that forms malignant and non-malignant tumors in the body [1]. Recent treatments strategies involve the practice of include chemotherapy, chemically derived compounds and radiotherapy. 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 [2]. Herbal origin medicines are still used as the primary cure against disease in many regions of the world like the

ancient time when use of herbal medicines and crude herbs were common practice. Many plants have the antiseptic properties and are used as antiseptics. With the development and advancement in discovery of new medicine many drugs substances from the plant source are discovered to have the potential against many complicated diseases like cancer [3]. Several species of plants are used to prevent and treat cancer. In the developing countries many researchers have identified the plants species which potential against cancer and have anticancer properties these are herbal medicines [1, 4].

Medicinal plants play very important role internationally now a day. It has been proved since past decades that these plants have good impacts on health and trade worldwide. These are constantly used in developing countries due to the expensiveness of pharmaceutical medicines. The chance of identification, development and economic importance of these plants have been found on large scale in both developing and as well as industrial countries. Therefore, these plants are being used worldwide [5].

Cancer is a genetic disease that affect millions of the population most of cases are found in the form of death. This fatal disease can be treated with natural plants known as medicinal plants. A report presented by American cancer society showed that most of the deaths annually are the consequences of cancer. Breast cancer has been reported on large scale internationally, but African women have been found the most affected with breast cancer which has gained second position in whole world [6].

Most of the deaths in women in Pakistan have been found the consequences of breast cancer since last five years. A report by Sarwar and his coworker showed 119,710 cases [7]. Different studies showed various sources of breast cancer for the last five years. It has found that the genetic mutation is the main cause which inherited [8]. The recent research study conducted by Majeed and his coworker detected the genetic factor in the form of BRCA1 mutation for breast cancer in Pakistan. According to them, examining the BRCA1 together BRCA2 mutation is very essential at early stage to control the deaths due to breast cancer in Pakistan [9].

The compounds which are necessary for the growth, development of the whole kingdom plantae are identified and tested to reveal the capability to restrain development and commence apoptosis of cells causing cancer [3].

Epigenetic properties

The stride towards the expansion in cancer includes complex change and adulteration in the processes of epigenetic and its deregulation [10]. The deregulation of the cancer cells genes presents on CpG islands loss the command of hyper methylation of tumor-suppressor signals. The deregulation results in inactivation and gene silencing [11]. In the recent years many drugs have been developed which have the ability to reverse or inhibit alterations of epigenetic [5].

Chemically derived epigenetic drugs which are derived chemically are developed and are passed through clinical trials for example 5-aza-2'-deoxycytidine 5-azacytidine, suberoylanilide hydroxamic acid and FK228 [10]. Conversely, it rendered very complicated to wangle a chemically derived drug which have no toxicity towards normal healthy cells and act against only specific cytotoxic cells in case of cancer cells. Consequently, it is becoming high demand and trend for the research in natural origin compounds and their development of drugs for treatment of cancer. The main focus of the researchers now is totally on the compounds extracted from plants and their natural products.

There are found many kinds of cancer that are common in human some have the comparable genotypes and characteristics. Apoptosis is a condition that attack and in no way induced in cancer cells. The cancerous cell activity like inhibition in the proliferation of cells in cancer and induction of cell death by the process of apoptosis can be inhibited by the extract and chemicals derived from plants [11].

CAUSES OF CANCER

The damage of DNA known as mutation of a cell become the cause of cancer. The division and growth of cell depends upon the instruction of DNA. DNA of Normal cell mostly shows Mutation. But, most of the

cells have tendency to repair the mutation. The mutations which are not repaired give birth to the cancer. As consequence, the accumulation of cancer cells take place [12]. It has been observed that environmental factors such as diet, smoking, chemicals, workplace, radiation etc. were responsible for the cause of cancer. Cancer in Pakistan affects the families in both economically as well as socially. Most of the population of the country live in remote areas where access to hospital for better treatment is very difficult. In such areas, mostly females are affected with cancer because they don't have any information about their hygienic conditions due to lack of education. Mostly, breast cancer has been observed in the women of such remote areas in Pakistan [13].

According to a report, 60% population was affected with lung cancer, esophagus cancer and cervix uteri cancer. The factors considered responsible for these cancers were low consumption of vegetables, smoking, alcohol and sexual interactions of HPV. Whereas, 13% joint PAFs (colorectal cancer) and 9% leukaemia were due to undetermined factors for which genetic problems could be supposed [14].

NATURAL PRODUCTS

Therapeutic plants are being used from ancient times in the populations belonging to continent of Africa and Asia. Several shrubberies are frenzied for the physical condition reimbursement in developed nations. According to report of World Health Organization (WHO) some regions still rely on plant treatment because the plants are considered as their main source for obtaining treatment against diseases. Many modern countries nowadays are opted toward the use of natural medicinal plants are to get the therapeutic benefits due to the pharmacological actions of compounds present in plants [15].

Azadirachta indica

The tropical countries are rich of *Azadirachta indica* plant. Homemade medicines are prepared traditionally from various parts of this plant since ancient times for the treatment of different diseases. neem is widely applied in India. Though, many research articles are present on

neem such as molecular mechanism studies. According to the report by National Research Institute in 1992, the neem tree has been found fruitful for the treatment of different diseases in India. With regards to other researchers, it can be used for the cure of various kinds of cancer. In spite of having few side effect, the neem is used widely due to low cost and easy availability [16]. Neem tree (*Azadirachta indica*) has been found rich with medicinal properties internationally. Different diseases such as inflammation, infections, fever, skin diseases and dental disorders have been treated with all segments of this neem tree. Leaf of this tree have shown antibacterial, antioxidant and anti-carcinogenic properties. It concluded that neem tree consists of many active compounds that function together through various mechanisms. Apoptosis is one of the mechanisms that eradicates and destroys the cancer cells. Mostly, it has been proved for the cure of lung, skin, prostate, and liver and breast cancers [17].

Ocimum sanctum

The bushy plant, *Ocimum sanctum*, which belongs to Labiatae family has various therapeutic properties. All the parts such as stem, leaves, roots, seeds etc. have been found to be used as antidiabetic, antifertility and anti-cancer agents. Fever, arthritis and bronchitis have also been treated with this Tulsi herb [18]. *Ocimum sanctum* plant were tested against human fibro-sarcoma (HFS cells) in culture. From the morphology of these cells, it has been found that the cells contain contracted cytoplasm and condensed nuclei. The extract used for the cure of HFS cells indicated high level of lipid per oxidation products and low intracellular glutathione. The ethanolic extract of this plant was found effective on sarcoma-180 tumor affected mice in the form enhancing lifespan and decreasing tumor. These all tests showed the presence of anti-cancer activity in *Ocimum* plant [19].

Triticum aestivum

In plants, Wheatgrass, a particular type of grass, contains vast contents of chlorophyll. The structure of chlorophyll resembles to blood and it is very useful for both plant and animals due to having a large number of amino acids and enzymes. The juice (2.5 pounds) of wheatgrass is same

as raw vegetables. It can be used as a natural food due to containing minerals, amino acids, vitamins, enzymes etc. Therefore, the daily use of its fresh juice promotes the maintenance of healthy cells. Healthy cells can prevent the formation and growth of cancer cells. As a result, cancer is inhibited. Its juice is taken on empty stomach to gain extra energy for metabolism process [20].

Cancer cells have defensive coating due to which immune system can't recognize them easily and their growth becomes out of control. Wheatgrass root contains the compounds namely abscisic acid and P4D1. These compounds are effective in removing the coating of the cancer cells and they become visible for immune system to be inhibited. P4D1 can also act as an anti-aging agent to repair the injured DNA. Wheatgrass plant also contains Superoxide dismutase acting as an antioxidant agent. It gives protection to the cells from the destruction produced due to radiation, irritant, free radicals, infections and inflammations [6].

Taxol, polyphenols and Brassinosteroids are the compounds that are obtained and extracted from plant source are known to possess the potential against cancer [3].

Polyphenols

Polyphenol include tannins, flavonoids, curcumin, gallatechins and resveratrol. These are the compounds which are considered as anticancer substances. Resveratrol is present in foods including grapes, red wine and peanuts. Gallatechins can be found in green tea. It is assumed that the presence of polyphenols in our daily diet can help in improvement of health and also cause the reduction in the risk of developing cancers because these are the naturally occurring antioxidants [10, 21].

The cytotoxicity caused by polyphenols on cancer cells is verified and the antioxidant property of these compounds are also evaluated. Polyphenols are assumed to possess ability of inducing apoptosis that results in development of anticancer properties. The mechanism of action of polyphenols involves the mobilization of copper ions which are attached to chromatin inducing DNA fragmentation which accomplishes apoptosis initiation is through regulating the DNA

chromatin. In the presence of Copper ion DNA degradation starts by resveratrol. Another property of the plant polyphenols is the ability to hinder in proteins which are the part of cancer cells and promote the growth. Cancer causing agents are assumed to alter by polyphenol that regulates the process of phosphorylation, acetylation or methylation or by the process of direct attachment. For example, Tumor Necrosis Factor (TNF) expression is suppressed by curcumin to treat cancer by interacting with different stimulus [22].

Flavonoids

Polyphenolic compounds which are referred as flavonoids belongs to the great family of secondary metabolites of plant constituents which have more than 10,000 recognized isomeric structures. These are the compounds which are considered physiologically active ingredients of plants and are now of the high scientific interest due to their healthiness advantages and benefits [21].

Brassinosteroids

Brassinosteroids are the natural compounds present in plants and play important roles in differentiation of cells and growth regulation by signaling of hormones. They are also involved in the, elongation of roots and stem cells, growth and protective functions like tolerance and resistance against ailment and anxiety. They play an important role in the development and growth of plants. Brassinosteroids have the therapeutic significant anti-cancer activity and these are naturally occurring compounds [2].

Two types of naturally occurring Brassinosteroids are investigated against cancer cells in order to confirm its anticancer properties possessed by these compounds. 24-epibrassinolide (24-epiBL) & 28-homocastasterone (28-homoCS) have showed action against cancer when tested against different cancer cell lines. These compounds are proved to be well effective in the treatment of cancer in very minimal amount of dose. One of the main characteristic shown by cancer cells can be elaborated as the cancer cells do not have the natural tendency to undergo proliferation and the process of apoptosis indefinitely. Brassinosteroids have the tendency to activate response

which is necessary in growth suppression and induction of apoptosis by its interaction with the cell cycle [10, 22]. Brassinosteroids can bind with receptors or interact with the proteins and cause inhibition in the hormone sensitive growth and hormone insensitive growth of cancerous cells. Also, Brassinosteroids can induce blockage of cell cycle. Along with the anticancer properties Brassinosteroids produce diverse responses in cancer and normal cells [9]. A major approach against anticancer management is that such compound is selected which do not have any cytotoxicity against normal healthy cells and should be specific for only cancer cells. The Brassinosteroids origin agents are believed to of great interest because of their therapeutic and pharmacological properties [22].

ANTI-CANCER DRUGS

The specialty and key importance of the use of plant-derived drugs as anticancer therapy is that these are readily easily available and are 100% natural. They can also be easily and readily administered as a part of patient diet through oral route. As these compounds are directly extracted from natural plants so they are considered to have no toxicity against human cells and they can be tolerated easily by patient. Conversely, the exceptions in the use of plant derives drugs are the use of substances like lectins, lignans, cyanogen etic glycosides, Texans, saponins etc. The drugs obtained from plant source are tested for toxicity studies and selectivity and cytotoxicity against the cancer cells if it gives successful results then these compounds are proceeded further for clinical trials for detection of therapeutic activity and dosage form development. Plant-derived drugs are classified into four major drugs classes which contain activities which are as follows:

- a. Mitotic disruptors
- b. Histone deacetylases (HDAC) inhibitors
- c. Methyl transferase inhibitors
- d. DNA damage preventive drugs or antioxidants

PHYTOCHEMICALS DEVELOPMENT STRATEGIES

The presence of quality as well as the quantity of active phytochemicals in the plants determines the therapeutic potential and importance of that medicinal plant. The quality and quantity of phytochemicals in medicinal plant depends on following factors:

Latitude of area of cultivation

- a. Age of plant
- b. Longitude of the cultivated region
- c. Altitude of the region
- d. Season or climate of that region
- e. Species of medicinal plant

The pharmacology, action and potential of the compound are different in different parts of plant. Against cancer the phytomolecules which are bioactive can be used. The strategies for purification of phytomolecules involve [15].

- a. Combinatorial chemistry
- b. Bioassay-guided fractionation isolation assays
- c. Bioassay guided fractionation

A variety of analytical techniques can be used to isolate different biological active substances and compounds from the mixture. The process of isolation is initiated with the preparation of natural extracts for testing (wet/dry plant) which have known biological activity. After this appropriate solvent are used in process of fractionation to obtain active extracts. Different analytical instruments and techniques for example FTIR, TLC, HPLC, NMR and Mass spectroscopy *etc.* are specifically used for isolation of active ingredient. The measures can be change depending on the bioactive compound's quality, purity and quantity. High quality, purity and quantity of bioactive compound can be achieved by the use of matrices, high quality solvents and careful handling. *In-vitro* or *In-vivo* anticancer activity can be evaluated after the purification of phyto molecules [10, 15].

CONCLUSION

The main aim purpose to review this was to inspect on anti-cancer activities of medicinal plant carried out by scientific studies that are gamely accessible and used in management and treatment of various disease conditions. A variety of studies are performed in different regions of many countries to assess the medicinal plants for containing any anti-cancer activity. This review reveals that extracts of plants be capable of imparting any anti-cancer behavior at different steps of the development involved in process of cancer development, tumor formation. Research conducted on medicinal plants having anti-cancer activities is the most rising topic in current bio-drugs. The need of the hour is to explore more medicinal plants for the assessment of anti-cancer activities.

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