Treatment of cancer with native plant species of Rajasthan

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ABSTRACT *Cancer is development of malignancy and known to be multi-factorial in origin. Radiation, carcinogens, mutagens, smoking, improper diet, virus infections etc. are the few major agents among various causing cancer agents. The cancer cells produce various metabolites over and above the optimum level of their requirements. Reactive oxygen species (ROS) play very important role in various intra-cellular activities including apoptotic signalling and in cancer cells increase level of ROS has been observed. The elevated ROS promote tumour development and progression thus accelerates the development of malignancy. The tuning of ROS signalling in cancer cells or developing malignancy can avoid the built up of intra-cellular ROS. This could help to reduce the ROS-induced tumour progression, thus tuning of intra-cellular offer an opportunity for development of novel therapeutic strategies. Antioxidants are compounds having potential to sequester the excess ROS thus these may prevent early events in tumour development. Plants are natural factories of antioxidants and synthesize varying level of antioxidants under different growing conditions. Further plants of stressed regions (i.e. arid and semi-arid regions of Rajasthan) are rich in antioxidants. Plants from our own state Rajasthan possess potential to be used to cure or treat the cancer and develop the preventive drugs to treat cancer in an AYUSH mode. The strategy involves screening of plant extracts for anti-cancerous activity through metabolic profiling and in vitro cell toxicity assay. Once suitable plant species in selected further detailed investigation can be performed. The potential plant product can be further tested in vivo and drugs can be developed. The plant-derived drugs are natural, safe and do not have risks of any side-effects. We hereby propose screening of native plant species of Rajasthan to search anti-cancerous activity and development of preventive drugs to treat cancer in AYUSH mode.*

Keywords: *Cancer, Causes, ROS, Antioxidants, Anticancer plants*

Introduction

Cancer is an abnormal growth of cells that grows and spreads through uncontrolled cell division. These 'malignant' cells may invade other tissues and spread (metastasize) to more distant parts of the body. Cancer is not one disease but group distinct disorders. It is the world's second biggest killer after cardiovascular disease and was responsible for the death [1]. Of all new cancer cases, it is estimated that one third could be cured if they were adequately diagnosed and treated [2]. It is believed that cancer will be soon a global problem with its entire consecutive burden. Cancer therapy is, therefore, in the focus the world over. For the time being the treatment of any malignancy is based on surgery, radiotherapy and drug therapy. This complex approach is capable of curing approximately half of the cancer patients. While the other half of the affected individuals may have only prolonged survival or even no benefit at all from the treatment. While the results obtained by surgery and radiotherapy (which are loco regional interventions) are close to their maximum accomplishment, success of drug therapy, the only systemic approach, is far from satisfactory [3].

Cancer may affect people of all ages, but risk tends to increase with age, due to the fact that DNA damage becomes more apparent in aging DNA. Statistics indicate that men are largely plagued by lung, colon, rectum, and prostate cancer, whilst women increasingly suffer from breast, colon, rectal, and stomach cancer. Despite many therapeutic advances in the understanding of the processes in carcinogenesis, overall mortality statistics are unlikely to change until, it is believed, there is a reorientation of the concepts for the use of natural products as new chemo preventive agents [4].

Natural Plant compounds are highly varied in structure; many are aromatic substances, most of which are phenols or their oxygen-substituted derivatives. However, there is an increased attention on extracts and biologically active compounds isolated from plant species used in herbal medicine, due to the side effects and the resistance that pathogenic micro-organisms build against the antibiotics. Plants generally produce many secondary metabolites which are biosynthetically derived from primary metabolites and constitute an important source of microbicides, pesticides and many pharmaceutical drugs. From a long period of time medicinal plants or their secondary metabolites have been directly or indirectly playing an important role in the human society to combat diseases [5]. Even though there are number of synthetic antitumor agents

available, efforts are still on to search for effective naturally occurring anticarcinogens that would prevent, slow or reverse cancer development. Plants have a special place in the treatment of cancer. It is estimated that plant derived compounds constitute more than 50% of anticancer agents [6, 7]. Extracts of plants were used for the treatment of various diseases and this forms the basis for all Indian systems of Medicine. However, this area is not much developed when compared to modern system of medicine, mainly because of the lack of scientific documentation in this field [8]. In this paper we report the information earlier on plant species which are used in the treatment of cancer.

Reactive Oxygen Species and their importance with respect to Cancer

Reactive oxygen species are radicals, ions or molecules that have a single unpaired electron in their outermost shell of electrons. Due to this character, ROS are highly reactive. ROS Can be categorized into two groups: free oxygen radicals and non-radical ROS. Free oxygen Radicals include superoxide (O_2 •−), hydroxyl radical (•OH), nitric oxide (NO•), organic Radicals (R•), peroxyl radicals (ROO•), alkoxyl radicals (RO•), thiyl radicals (RS•), sulfonyl Radicals (ROS•), thiyl peroxyl radicals (RSOO•), and disulfides (RSSR). Non-radical ROS Include hydrogen peroxide (H_2O_2), singlet oxygen (O_2), ozone/trioxygen (O_3), organic hydro peroxides (ROOH), hypo chloride (HOCl), peroxynitrite (ONO−), nitroso peroxy carbonate anion (O=NOOCO_2−), nitro carbonate anion (O_2NOCO_2−), di nitrogen dioxide (N_2O_2), nitronium (NO_2+), and highly reactive lipid-or carbohydrate derived carbonyl compounds. Among them, superoxide, hydrogen peroxide and hydroxyl radicals are the most well studied ROS in cancer.

In cancer cells high levels of reactive oxygen species can result from increased metabolic activity, mitochondrial dysfunction, peroxisome activity, increased cellular receptor signaling, oncogene activity, increased activity of oxidases, cyclooxygenases, lipoxigenases and thymidine phosphorylase, or through cross talk with infiltrating immune cells [9–11]. Many cancers arise from sites of chronic irritation, infection, or inflammation. Macrophages induce the generation of ROS within tumor cells through secretion of various stimuli, such as TNFα [1]. Production of ROS by neutrophils and macrophages as a mechanism to kill tumor cells is well established. In these cells, a rapid burst of superoxide formation primarily mediated by NAPDH oxidase leads to subsequent production of hydrogen peroxide [12-13]. Furthermore, during inflammation processes, activated macrophages also generate nitric oxide which reacts with superoxide to produce peroxinitrite radicals that are similar in their activity to hydroxyl radicals and contribute to tumor cell apoptosis [14].

Antioxidants and their importance with respect to cancer

An antioxidant is any substance which is capable of preventing the oxidation of other molecule [15-18]. In biological system they protect cells from damage that is caused by unstable molecules known as free radicals. Antioxidants interrupt the chain reactions by removing intermediates of free radical, and inhibit other oxidation reactions by being oxidizing themselves. They help in preventing the growth of many chronic diseases. Antioxidants are emerging as prophylactic and therapeutic agents.

Antioxidants have natural activity of preventing neuronal loss and damage caused due to oxidative stress. Many antioxidants have been observed to cross the blood-brain-barrier (BBB) and have neuro protective effect in humans as well as in animal models. But the main drawback of antioxidants is their low biological half-life and low bioavailability at the sites reactive oxygen and nitrogen species generation [19-22]. Antioxidants are the substances whose presence in low concentrations inhibits the rate of oxidation significantly.

A process called oxidation causes damage of important molecules in the body and can result in harmful processes like neuronal damage and carcinogenesis [23-26]. Oxidation is a natural process that occurs any time a when substance combines with oxygen. Antioxidants are chemicals that block this process. Scientific research now confirms that free radicals results in the development of cancer, heart disease, cataracts and impairment of the immune system. The use of antioxidants as an adjunct alternative cancer therapy is an area of intense research [27-30]. Antioxidants are molecules that can safely react with free radicals to neutralize or terminate the chain reaction before vital molecules are damaged. They exert their defense mechanisms in a number of ways:

1) Enzymatic systems which catalyze removal of free radicals and ROS, e.g. catalase and superoxide dismutase. 2) Sacrificial anti-oxidants which donate oxygen to free radicals, such as vitamin C and vitamin E. 3) Proteins that minimize the availability of prooxidants, such as transferrin, heptoglobins, haemopexin and metallothionein. 4) Proteins that protect molecules by other mechanisms, e.g. heat shock protein.

An overview of potential native plant species rich in antioxidants

Prosopis

Prosopis cineraria is the botanical name of the khejri.khejri is the state tree of the rajasthan. The importance of khejri is increased due to the socio economic development of the india specially thar desert in the rajasthan. Khejri is also known as "Kalpatru" which means "the king of desert"due to its food,feed and medicinal value. Kh ejri is worshipped by a number of communities. *Prosopis cineraria* is cultivated in a number of countries in all over the world but it is specially cultivated in western and southern Asia including Afganistan,Iran India,Oman,Saudi Arabia and Pakistan.The crude extracts of *Prosopis cineraria* shows positive results in supporting of health benefits and in prevention of wide range of illness includes protein and mineral deficiency. Prosopis is extensively planted as fast growing and drought tolerant fuel and fodder tree but in a large number of countries it spreads readily without control as invasive weed.

The leaves of the prosopis have some fungicidal and insecticidal activity.Bark of the prosopis used as a source of tannin, dye and fibers so it is used for the preparation of medicines mostly for stomach, skin and eye problem. Prosopis cineraria have a number of chemical constituents that have nutritional value and also have certain action in the prevention and treatment of the disease. The medicinal value of the plants are increased randomly in the treatment of the cancer due to antioxidant activity. The methanolic extract of the leaves of Prosopis cineraria are used which shows significant radical scavenging activity. The extract inhibits cell proliferation by inducing cell death and the extent of cell proliferation16.

Antioxidants are the compounds that inhibits the oxidation of lipids and other molecules by inhibiting the oxidizing chain reaction. Redox property of the phenolic compounds are responsible for Antioxidant activity. It can play a major role in the adsorbing and neutralizing free radical and decomposing peroxides20.

Solanum

Solanum nigrum belongs to family: solanaceae. Commonly it is known as black night shade makoy, deadly night shade. It possess medicinal properties like antimicrobial, antioxidant, cytotoxic properties, anti ulcerogenic and hepato protective activity. *Solanum nigrum* is a potential herbal alternative as anticancer agent and one of active principles reported to be responsible for this action is Diosgenin. *Solanum nigrum* methanolic extract has significant cytotoxicity effect on HeLa cell Line.

Azadirachta

Neem (*Azadirachta indica*), a member of the Meliaceae family, is a fast growing tropical evergreen tree with a highly branched and stout, solid stem. Because of its tremendous therapeutic, domestic, agricultural and ethnomedicinal significance, and its proximity with human culture and civilization, neem has been called "the wonder tree" and "nature's drug store." All parts of this tree, particularly the leaves, bark, seed-oil and their purified products are widely used for treatment of cancer. Over 60 different types of biochemicals including terpenoids and steroids have been purified from this plant. Pre-clinical research work done during the last decade has fine-tuned our understanding of the anticancer properties of the crude and purified products from this plant. The anticancer properties of the plant have been studied largely in terms of its preventive, protective, tumor-suppressive, immunomodulatory and apoptotic effects against various types of cancer and their molecular mechanisms.

Capparis

Capparis sepiaria is widely distributed in India, Srilanka, Mayanmar and Pakisthan. It is a climbing shrub with curved thorns, elliptical leaves and simple flowers, fruits are in clusters,

pisiform and black. It is distributed throughout salty *ranges* of Andhra Pradesh, Maharashtra and Karnataka. Ethno botanical studies are stating that *C. sepiaria* used *as* blood purifier, stomachic, tonic and appetizer. Its flowers, leaves and roots are used in cough and toxemia and root powder is also used as a cure for the snake bite. It is also possesses febrifuge properties and also used to treat skin diseases, tumors and diseases of muscles. Various bioactive compounds can be seen in *Capparis sepiaria* like alkaloids, phenols, sterols or glycosides. ß-sitosterol, present in whole extracts of different parts of *Capparis* show biological activities against various diseases. *C. sepiaria* seed have been considered as antidote for snake bite. Stem root bark having therapeutic value in curing dropsy gout, apathies. This further suggests that *Capparis species* roots might have at chemical compound with anticancer properties.

Advantages of herbal drugs

Medicinal plants continue to play a central role in the health care system of large proportions of the world's population. Recognition and development of the medicinal and economic benefits of plants are on the

increase in both developing and industrialized nations. An herb (also called a botanical) is a plant or plant part used for its scent, flavor, and/ or therapeutic properties. Products made from botanicals that are used to maintain or improve health have been called herbal supplements, botanicals, or phytomedicines. The pharmacological treatment of disease began long ago with the use of herbal medicines are "crude drugs of vegetable origin utilized for the treatment of disease states, often of a chronic nature, or to attain or maintain a condition of improved health" or the herbal medicines can be defined as "Finished labeled medicinal products that contain ingredients from aerial or underground parts of plant parts or other plant material or combination in the crude state or as plant preparations. Traditional herbal medicines are naturally occurring plant-derived substances with minimal or no industrial processing that have been used to treat illness within local or regional healing practices. Common reasons for use of herbal drugs include health promotion, disease prevention, poor outcomes and limited treatment options for a serious illness, exhaustion of conventional therapies, dissatisfaction with, or lack of efficacy of conventional therapies, significant side effects or risks associated with conventional medicine, belief that herbal and natural products are better or safer.

Conclusion

Medicinal plants are rich sources of herbal properties contributing in the discovery of new drugs towards various disorders, diseases including cancer without showing no toxic effects on the individuals treated. Treatment of cancer by use of natural products and traditional medicine by applying the concepts of Ayurveda is attaining a great significance scope of cancer research. In this review author presented the importance of traditional medicine, medicinal plants in cancer treatment, anti cancer properties of natural products in brief. Medicinal plants contain good immunomodulatry and antioxidant properties which leads them to be a anticancer drug. Only few selected plants have been explored for biological activity from around 1000 species and much more, From this review, it can be concluded that cancer is the leading cause of death in developing countries like India. The less expensive herbal drug treatment may highly be recommended to the rural and poor people to treat effectively the cancers of various type is an ideal choice.

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