



An Overview on Cancer: Its Causes and Treatment Approaches

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Abstract

Cancer is a combinatorial disease characterized by uncontrolled cellular proliferation. It is caused when normal cells do not follow the pathway of cell cycle. It can be caused by several internal as well as external factors which include genetic abnormality, cellular damage, smoke, radiations etc. These factors are technically termed as carcinogens. Cancer is the second most leading cause of mortality globally next to cardiac diseases. It can only be controlled by early diagnosis, awareness and prevention. Several therapies are currently available; including chemotherapy and radiation being the most effective ones, but the side effects associated with them is also highest. Hence, the researchers are trying to explore a suitable alternative which could have minimum side effect and maximum efficacy. Thus, there is a zest for natural compound which could act as potent anti-cancer agent. The current paper is an attempt to address the cause of cancer, treatment approaches, mechanism underlying them, side effects associated with them.

Keywords: Carcinogen, Chemotherapy, Diagnosis, Side effects, Natural

1. INTRODUCTION

Cancer is a multi-factorial metabolic disorder that is characterized by uncontrolled, unchecked cellular proliferation and spread of these abnormal cells in distant locations of the body. If the spread of these abnormal cells is not timely restricted, it can even be fatal. According to American Cancer Society Report 2022, 1,918,030 new Cancer cases and 609,360 deaths are likely to occur in United States in the year 2022 [1]. India ranks third in the world for highest number of cancer cases. Over 13 lakhs Indians suffer from Cancer every year, according to National Cancer Registry Programming

report. The Indian Council of Medical Research (ICMR) estimates that there will be 12% rise in Cancer cases in India in the coming 5 years. Any individual can develop this disease. Since, the risk of this disorder being diagnosed increases with the age, most cases are reported to occur in older or middle age group adults. Approximately, 77% of all cancers are reported to be diagnosed in people who are above the age of 55 years (American Cancer Society 2014) [2]. Present article describes a general overview of causes and precautionary aspects regarding various types of cancer faced in modern society due

to change in life styles and hereditary reasons.

2. Causes and treatment

Cancer is known to occur by both external (pathogenic microbes, chemicals, exposure to radiations and tobacco consumption) as well as internal factors (hormones, inheritable mutations, weakened immune systems, and mutations resulting during metabolism). These causative agents can act synergistically or in series one after the other for causing the progression and development of cancer. It can be cured with radiation, surgery, chemotherapy, immune therapy, hormone therapy and targeted therapy [2]. Cancers of all types involve abnormal functioning of normal genes that are involved in division and growth of cell. Only few cancers are hereditary, wherein a specific genetic alteration is passed on from one generation to another thus, leading to increased risk of cancer development. Inherited factors play a vital role to detect risks involved in some types of cancers (e.g., Breast, Prostate and Colorectal) amongst others. It is now believed that many familial cancers develop from the interaction between common gene alterations and environmental or lifestyle risk factors. However, majority of them arise from damaged genes that occur because of the risk factors being exposed in the life time of an individual due to their lifestyles and not from inheritance of altered genes [2]. The agents that cause cancer are known as carcinogens. They can be present in environment (i.e., food, water, air, sunlight and also in certain chemicals that an individual gets exposed during routine activities). More significantly, globalization leading to unhealthy lifestyles, specifically

cigarette smoking and adoption of modern western diet (low fibre and high fat content) have caused increased incidence of cancer to a greater extent. Carcinogens interact with the individual's genetic composition, both inherited and acquired, creating higher risk probable factors for induction of cancer. The risk of cancer development is dependent on how an individual's constituents interact with carcinogen or convert these causal agents into a form which is not harmful before they could cause any genetic alteration or damage, [3].

Although cancer is not gender specific, but Dr. Rakesh Kapoor from radiology department of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh stated that "Women need greater medical attention in their entire life in comparison to men. Women easily get investigated during pre-natal check-up, menopausal problems and menstrual disorders and hence, by default get detected with cancer. Therefore, cancers are diagnosed at an earlier stage and mortality rate is comparatively lesser in women (American Cancer Society, 2018) [4].

3. Prevention and Care

Significant reduction in occurrence of cancer cases could be achieved by taking several precautionary measures. All cancers that are caused by smoking cigarette and excessive consumption of alcohol can be completely prevented. World Cancer Research Fund has also predicted that about one-third of the total cancer cases, that occur in economically developed country like US is mainly associated with obesity or overweight, physical inactivity, and/or poor nutrition, and hence can be prevented.

Some cancers are associated to occur by

infectious organisms like, Hepatitis B Virus, Hepatitis C Virus, Human Papilloma Virus, Helicobacter pylori and Human Immunodeficiency Virus. Many of these cancers can be prevented by adapting changes in the life-style or by using vaccines or antibiotics as protective measures. About 3 million cases of skin cancer could be prevented every year by avoiding tanning and protecting skin from getting exposed to intense solar radiations (American Cancer Society, 2018) [4].

Numerous chemotherapeutic agents are used for cancer treatment. These agents are categorised into antimetabolites, anthracyclines, alkylating agents, alkaloids, topoisomerase inhibitors, and other antitumour agents. Majority of them act by affecting the different phases of cell cycle while few show their action by generating free radicals or active oxygen compounds. Alkylating agents add alkyl groups to molecules with negative charge. These agents inhibit tumour proliferation by covalently binding guanine nucleotides in DNA strands, which cause the DNA to damage directly by restricting its uncoiling and separation. These attacked cells cannot replicate, neither do they die nor proliferate. 5 major categories of alkylating agents are of remarkable importance: nitrogen mustards, alkyl sulphonates, aziridines, platinum-containing drugs and nitroso ureas (Siddik, 2002) [5]. Daunorubicin and its 14-hydroxy derivative doxorubicin are anthracycline antibiotics secreted by fungus *Streptomyces peuceticus*. It damages DNA by intercalation, chelation

of metal ions or by producing free radicals. It is also known to inhibit the enzymatic action of DNA topoisomerase II which plays a crucial role in functioning of DNA. The most common side effects for doxorubicin include myelosuppression, bleeding, elevated Liver Function Tests (LFTs), alopecia, anorexia, rashes, diarrhoea and cardiotoxicity (CCO Formulary, 2017) [6].

Anthracyclines are a group of chemotherapeutic agents used in cancer therapy, usually extracted from bacterium *Streptomyces*. The three modes of action of Anthracycline are as follows: (a) Inhibits nucleic acid synthesis by intercalating nitrogenous bases, thus blocking the replication of rapidly-dividing cancer cells, (b) Inhibits topoisomerase II which in turn restricts DNA replication and transcription and (c) Produces iron-mediated free radicals of oxygen thus impairing cell membranes and DNA of the cancer cell (Nepomuceno, 2011) [7].

The traditional cancer chemotherapy suffers with the problem of Multi Drug Resistance (MDR). It is caused by over expression of membrane transporters like P-gp (P-Glycoprotein) that decreases the intracellular concentration of anticancer drugs thus increasing its rate of accumulation. Cells reported to show MDR develop resistance towards different structurally and mechanically distinct chemotherapeutic drugs. Many studies related to the developing of new drugs are reported that are capable of overcoming MDR. [8-10].

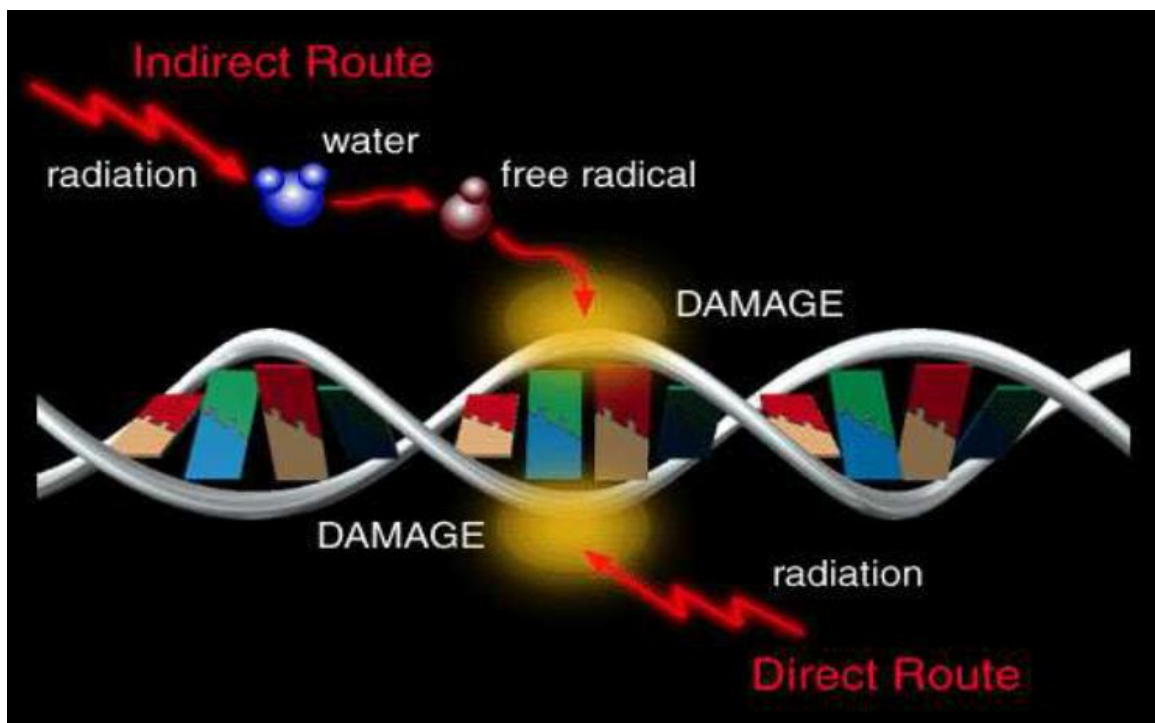


Fig 1: DNA damage of living cells by radiation (Indirect and Direct Ionization)

Redox imbalance contributes to cancer and other chronic diseases [11]. By causing DNA damage, oncogene activation and genomic instability, reactive oxygen species can initiate carcinogenesis [12]. Oxidative stress is known to be associated with several malignancies including brain, bladder, breast, gastric, cervical, liver, melanoma, lungs, multiple myeloma, lymphoma, leukemia, ovarian, oral, pancreatic, prostate cancers and sarcoma [13-14].

Several published reports show that oxidative stress is associated with cancer development, progression and its occurrence. During carcinogenesis, level of ROS in cancer cells increases and antioxidant concentration decreases. Increase of ROS in cancer cells is

dependent on both intrinsic and extrinsic factors. Cancer associated macrophages and fibroblasts; Hypoxia also contributes to increased production of ROS in cancer cells. Release of cytokines and matrix metalloproteinases induce migration and metastasis thus, leading to development and further progression of cancer [15].

In cancer cells, increased levels of ROS results from enhanced metabolic activity, peroxisome activity, mitochondrial disorders, oncogenic activity, increased signaling of cellular receptors, increased activity of cyclooxygenases, oxidases, thymidine phosphorylase and lipoxygenases or through crosstalk with infiltrating immune cells [16-18].

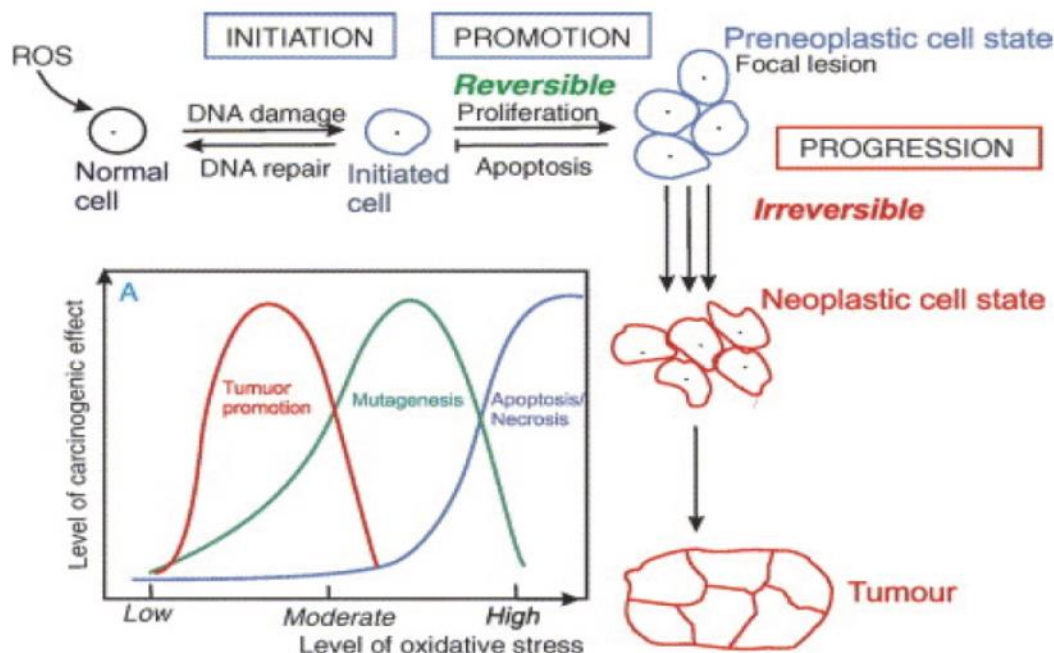


Fig 2: Three stages of carcinogenesis and the level of oxidative stress in each stage (Eerola, 2015 [22])

There is an emerging need for the development of new medicines, due to the side effects and resistance to available treatments. The natural products cover greater area of chemical space than the synthetic compound and also the property distribution is similar to drugs that are used presently. Approximately 50% of the drugs currently used for various treatments are

natural products and their analog or derived molecules, whereas with respect to anticancer drugs, 63% of them falls under this category [19-21].

Conflicts of interest: Authors have no conflict of interest to declare.

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