

CANCER: A REVIEW ARTICLE

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ABSTRACT-

One of the most common illnesses with a high fatality rate worldwide is cancer. Due to the limitations of traditional treatments like radiation and chemotherapy, as well as each one's unique set of risks, clinical management of cancer is still a challenging task. The two biggest risk factors for cancer are pollution and tobacco use, however risk can be reduced by leading a healthy lifestyle. Many innovative technologies are presently undergoing clinical trials, some of which have already been approved. This review offered an update on recent advancements and discoveries in cancer therapy. It may be possible to treat or prevent cancer by using natural antioxidants, which have demonstrated promise in identifying free radicals and lessening their harmful effects. An increasingly popular minimally invasive technique for burning or freezing malignancies without open surgery is ablation therapy.

Keywords: Carcinogens, . Stem Cell Transplant, Grading , Anticancer, Apoptosis, Tumors

1. Introduction –

Cell maturation and growth are typical processes in the development of organs during embryogenesis, growth, tissue healing, and post-injury remodeling. Loss of control over cell division, growth, and confinement in space can arise from perturbations in the regulation of individual processes. All disorders marked by aberrant cell proliferation, disruption of tissue homeostasis, and deformed architecture are together referred to as human neoplasia. Researchers refer to this new growth as a tumor or neoplasm. (1). A benign tumor, like a typical skin wart, stays in its original position and does not spread to other parts of the body or invade nearby normal tissue. On the other hand, a malignant tumor has the ability to metastasize, or spread throughout the body by the lymphatic or circulatory systems, as well as invade nearby normal tissue. The term "cancer" should only be used to refer to malignant tumors (2).

2. Cancer Grading And Staging

Once a malignant tumor is identified, two systems are used to forecast tumor behavior and direct therapy: "grading" and "staging." Grading refers to the tumor's macroscopic and gross degree of differentiation, whereas staging describes the tumor's internal tumor spread. So, although staging is clinical, grading is histologic (3).

A. Cancer grading-

- ✓ Grade I: Well-differentiated [less than 25% anaplastic cells].
- ✓ Grade II: Moderately-differentiated [25-50% anaplastic cells].
- ✓ Grade III: Moderately-differentiated [50-75% anaplastic cells].
- ✓ Grade IV: Poorly-differentiated or anaplastic [more than 75% anaplastic cells](4).

B. Staging-

The extent of spread of cancers can be assessed by 3 ways— by clinical examination, by investigations, and by pathologic examination of the tissue removed.

TNM staging. [T for primary tumour, N for regional nodal involvement, and M for distant metastases] was developed by the UICC [Union Internationale Contre Cancer, Geneva].

For each of the 3 components namely T, N and M, numbers are added to indicate the extent of involvement, as under:

- ✓ T0 to T4: In situ lesion to largest and most extensive primary tumour.
- ✓ N0 to N3: No nodal involvement to widespread lymph node involvement.
- ✓ M0 to M2: No metastasis to disseminated haematogenous metastases (5).

3. Causes Of Cancer-

Genetic damage, generally acquired but sometimes congenital, is the basic cause of all cancers. Generally speaking, the activation of growth-promoting oncogenes and/or the deletion or inactivation of growth-inhibiting tumor suppressor genes cause the genetic instability that leads to unchecked cell proliferation. The term "infective" refers to a number of broad categories that include viruses, chemicals (including occupational, environmental, and medicinal ones), electromagnetic radiation (such as ultraviolet, X-ray, and gamma rays), and immunosuppressive drugs (such as HIV) (6). These are

- I. Chemical Carcinogens- Human carcinogenicity has been demonstrated for several hundred substances. These chemical carcinogens can cause harm through environmental exposure (alcohol, tobacco), occupational exposure (asbestos, aniline dyes), or iatrogenic exposure (chemotherapy). The majority of carcinogens are activated by exposure to reactive metabolites, which cause genetic damage, even though many of them are directly mutagenic to DNA(7).
- II. Tobacco and alcohol consumption- Although tobacco use is thought to be the main risk factor for malignancies in this region, it also has a potent carcinogenic effect when combined with alcohol. The intensity (i.e., quantity and duration) of the drinking and smoking habits prior to the development of the first neoplasm determines the likelihood of acquiring a second primary (8).
- III. Pollution- There is considerable confusion regarding the role that man-made contaminants play in cancer prevention. The main way it gets into dwellings is through soil-drawn air. An estimated 15,000 lung cancer cases occur in the US each year as a result of high radon

exposure, especially in smokers. However, research on radon exposures in houses has not conclusively shown an increased risk.(9).

IV. Physical Carcinogenesis - There are two categories of physical agents involved in carcinogenesis:

1. The most significant physical agent is radiation, which includes both ionizing and ultraviolet light. The following recessive hereditary illnesses, which are linked to a high incidence of cancer and are characterized by a deficiency in the DNA repair system, provide evidence in favor of the mutagenic effect of UV radiation:

- Xeroderma pigmentosum is predisposed to skin cancers at younger age [under 20 years of age].
- Ataxia telangiectasia is predisposed to leukaemia(10).

2. Non-radiation physical agents: It has been suggested that physical injury to tissues, such as kidney or gallstones, or old scars from burns or accidents, increases the chance of cancer in those tissues. To be sure, though, there isn't enough evidence. Inert materials such as plastic or glass that are inserted into the body, such as in prosthetics, are another example of anything that can cause cancer. In addition, foreign objects can occasionally cause tumors in lab animals. However, these substances hardly ever cause cancer in people (11).

V. Microbe-Induced Cancers - Cancers Induced by Microbes Both native and exogenous (foreign) pathogenic microorganisms exist, albeit it's not always clear how to distinguish between the two (12). There are three types of bacteria that cause cancer.

- Class A microbes induce cancers including lymphomas by targeting immunocytes leading to immunosuppression(13)..
- Class B microbes induce This immunosuppression also contributes to the cancer-inducing effects of class B microbes, which include local effects on parenchymal cells and induction of host responses (14).
- Class C microbes are a postulated class in which a microbe produces local effects on epithelial tissues that change the regulation of a systemic operator [e.g., a hormone] that promotes cancer at a distant site (15).

4. Treatment-

A. Radiation therapy- Nowadays, radiation accounts for almost half of all cancer therapies. It works by introducing energy directly into the tumor tissue. Ions and photons can both directly damage DNA or other parts of the cell, such as the mitochondria. Additionally, they have the ability to ionize the surrounding media, producing reactive species such as secondary electrons and radicals that, once they diffuse, may cause indirect harm. The medium may interact with secondary electrons to generate more radicals(16).. The most effective treatment for primary non-metastasised solid tumours is radiotherapy; nevertheless, combination chemotherapy techniques are sometimes employed for brain tumours, deep-seated cancers, especially those associated with major blood arteries, or patients with co-morbidities who cannot undergo surgery. In addition to ion radiotherapy, novel sensitizers—such as nanoparticles—have shown promise in amplifying locally the harmful effects of

photon and ion radiation administered to the tumor site(17). Due to a number of advantages, such as their biocompatibility, the ability to coat their surface with a wide variety of molecules to partially control properties like surface charge or interaction with serum proteins, and synthesis techniques that have been shown to produce nanoparticles in a broad range of sizes, gold nanoparticles are one of the most widely used nanoparticle systems currently available (18).

B . Stem Cell Transplant- Stem cells are a population of undifferentiated cells that can proliferate into highly specialized, functioning progeny cells and undergo unending self-renewal throughout the body. Hematopoiesis is a continuous process of development that gives HSCs the ability to select certain cell fates, resulting in the various blood lineages. For autologous or allogeneic transplantation, HSC products from bone marrow (BM), peripheral blood, or umbilical cord blood (UCB) are available. (19). The posterior iliac crests are removed for their marrow while sedated. It is possible to remove more bone marrow from the anterior iliac crest or sternum. Large-bore needles and heparinized syringes are used to gather BM. BM can be stored at 4°C for an entire day without affecting the stem cells' viability. A dosage of 2×10^8 /kg of nucleated cells is generally considered sufficient for stable long-term engraftment. The National BM Donor Program guidelines limit the withdrawal of BM to 15 mL/kg of donor weight. Marrow is screened to remove any small particles or clots prior to intravenous administration (20).

C. Surgery- Cancer surgery is the term for a procedure or therapy used to remove a tumor from the body. Every now and then, adjacent healthy tissue is also removed. It is still an effective treatment for a wide range of tumors and is the most conventional type of cancer care (21). Here are a few techniques:

- (I) Cryosurgery – This approach uses very cold materials, including liquid nitrogen, argon spray, or a cold probe. Tumor cells are destroyed by freezing in the cold. Effectiveness of cryosurgical tissue damage depends on four factors: excellent process monitoring, freezing quickly to a lethal temperature, thawing gradually, and repeating the freeze-thaw cycle (22). Open surgical procedures may reduce recovery time for liver or kidney cancers. On the other hand, percutaneous cryotherapy is less costly, less uncomfortable, and has fewer side effects because it just requires a small incision and doesn't damage healthy tissue. When treating fibroadenomas, cryotherapy leaves little scar tissue and no obvious post-treatment calcifications (23).
- (II) Laser surgery – Laser surgery is the process of using a laser beam's power to remove a skin tumor or cut through tissue without bleeding. Less invasive surgery is growing in popularity these days. In other surgical specializations, techniques have advanced to the point where very small or no incisions are required (24). There are many different types of lasers, and each one has its own power, coagulation, cutting, and evaporation capabilities as well as its own wavelength of light. Certain conditions that result in bleeding or obstruction are treated using lasers (25). Lasers can be used to minimize, eliminate, and eradicate tumors that are causing obstruction in the intestines or stomach. It is the most secure method of treating various organ system cancers. Laser ablation methods are used in the treatment of numerous superficial gastrointestinal malignancies, such as colorectal adenoma, early gastric tumors,

and superficial esophageal cancers. In certain cases, laser photodynamic treatment is effective for lung cancer lesions (26).

D. Chemotherapy –

In the early 1900s, renowned German chemist Paul Ehrlich started developing drugs to treat infectious diseases. He coined the term "chemotherapy," defining it as the administration of chemicals to treat disease (27). Furthermore, he was the first to document the efficacy of animal models in screening a variety of chemicals for potential anti-disease action; this finding has important ramifications for the advancement of cancer therapeutics. Ehrlich was particularly fascinated by anti-cancer drugs, albeit it appears that he had doubts about their efficacy. Examples of these drugs include the first crude alkylating compounds and aniline dyes. The goal of chemotherapy is to halt the growth and division of the tumor in order to stop invasion and metastasis (28). Chemotherapy can be applied to adjuvant, neoadjuvant, combination, and metastatic diseases. There are several ways to stop tumor growth, both inside the cell and outside of it. In order to affect the macromolecular production and function of neoplastic cells, conventional chemotherapy medications usually interfere with the creation of DNA, RNA, or proteins or modify the normal functioning of the preformed molecule. Cell death occurs due to either apoptosis or the direct effects of the chemotherapy agent when there is a severe disruption of macromolecular production or function (29).

Significance of Herbal medicine used in treatment of cancer-

A sizable portion of the global populace still primarily uses medicinal plants as a component of their healthcare regimen. The medical and financial advantages of plants are becoming more widely acknowledged and advanced, both in developing and industrialized nations (30). Any plant or part of a plant that is utilized for its flavor, scent, and/or therapeutic properties is referred to as a herb, often called a botanical. Plant-based products that are meant to maintain or improve health are referred to as botanicals, phytomedicines, or herbal supplements. Herbal remedies 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 (31)." The pharmacological treatment of illness began with the use of herbal remedies. Traditional herbal remedies have been used in local or regional healing cultures to treat illness. They are made from naturally existing plant ingredients that have undergone little to no industrial processing. Common concerns include disease prevention, inadequate results and few options for treating a serious illness, the belief that natural and herbal products are safer or better than conventional medicine, the weariness of conventional therapies, and the unhappiness or ineffectiveness of those therapies (32).

I. **Achillea wilhelmsii** - Botanical systematics classifies *Achillea* species as an Angiosperm plant, within the Eudicots clade, Campanulales order, Asteraceae family, Tubuliflorae subfamily, and Anthemideae tribe. It has antiproliferative and cytotoxic effects. The anti-proliferative properties of quercetagenin 3,3-dimethyl ether, centaureidin, and vitexicarpin that were extracted from *A. millefolium* flowers (33). Phytochemical studies have revealed the remarkable bioactivity of certain components derived from *Achillea* species. The genus *Achillea* produced the first naturally occurring proazulene, achillicin III, while *A. millefolium* L. supplied the first anti-spasmodic flavonoids, cynaroside I and cosmosiin II. Alkamides, such as p-hydroxyphenethylamide, lignans, terpenoids, and derivatives of amino acids are also present in addition to fatty acids. Monoterpenes are the

most distinctive metabolites identified in *Achillea* volatile oils. It has been shown that sesquiterpene concentrations are higher than monoterpene levels (34).

II. **Zingiber officinale**- Ginger is from the *Zingiber officinale* family (Zingiberaceae), a versatile plant that has been used medicinally for over 2,000 years. Owing to its diverse biological activity, it is a widely used condiment for a range of dishes and drinks. Ginger's medicinal properties come from two shogaols: gingerol and paradol. Ginger's many health-promoting qualities are attributed to a variety of phytochemicals that it contains (35). Most of the ingredients that give ginger its therapeutic qualities are volatile and non-volatile compounds. The non-volatile component is composed of the oleoresin (4.0–7.5%). *Z. officinale* can prevent or control cancers of the colon, stomach, ovaries, liver, breast, and prostate, despite the fact that it contains bioactive chemicals such as 6-gingerole, 6-shogaol, 6-paradol, and zerumbone (36). Its anti-inflammatory and anti-tumorigenic qualities are also present. By activating enzymes such as glutathione reductase, glutathione transferase, and glutathione peroxidase, *Z. officinale* inhibits the growth of colon cancer (37).

III. **Curcuma longa** - Turmeric, a popular Indian spice that is a member of the ginger family (Zingiberaceae), contains curcumin as its primary curcuminoid. The other two curcuminoids are desmethoxycurcumin and bis-desmethoxycurcumin. Curcuminoids are a class of polyphenols that give turmeric its yellow hue. At least two types of curcumin are tautomeric: enol and keto (38). Turmeric's active components include the flavonoid curcumin, often referred to as diferuloylmethane, and several volatile oils, including tumerone, atlantone, and zingiberone. Among the extra constituents are proteins, carbs, and resins. Curcumin is the active component that has been studied the most; it makes up roughly 0.3–5.4 percent of raw turmeric. The anti-cancer properties of haridra may be due to the following mechanisms: antioxidant, NFκB inhibition, free radical scavenging, and anti-mutagenic properties. Curcumin induces apoptosis in cancer cell lines. Research on cell lines has shown that apoptosis is the catalyst for curcumin's anticancer activity. Tumor metastases grow less rapidly as a result of curcumin's inhibition of tumor angiogenesis (39).

IV. **Camellia Sinensis**- Tea produced from the leaves of the *Camellia sinensis* plant. The health advantages of green tea are mostly attributed to its polyphenols, which are compounds with potent antioxidant properties). As it turns out, polyphenols appear to be more potent antioxidants than vitamin C. Because of its polyphenols, green tea also has a little bitter taste. One kind of polyphenol present in teas is called catechins. The six primary catechin compounds included in green tea are gallaogatechin, epicatechin, epigallocatechin, epicatechin gallate, and apigallocatechin gallate (EGCG). Green tea is considered to be involved in the formation of cancer because tea catechins inhibit the growth of tumor cells and promote the death of leukemia cells (41).

V. **Saffron crocus**- The spice *Crocus sativus*, also referred to as saffron crocus, belongs to the iridaceae family of plants. Biochemically active compounds, such as safranal, crocetin, and crocin, are found in varied levels in different plant parts, such as the rind, peels, fruits, and seeds of *Crocus sativus*. (42). Saffron's active components have a major role in both preventing and treating tumor growth and metastasis. A range of malignant and nonmalignant prostate cancer cell lines were used to evaluate the antiproliferative effects of saffron extract and particular ingredients such crocin. Saffron contains over 150 volatile, non-volatile, and aroma-producing compounds. These consist of proteins, amino acids, minerals, musilage,

hydrophilic and lipophilic carbohydrates, vitamins (especially thiamine and riboflavin), and colors like zigzantin, carotene, lycopene, crocin, anthocianin, starch, and gums (43).

CONCLUSION-

This review looked at prospective treatment options, preventative measures, and the mechanisms behind the causes of cancer. It suggested including a few anticancer items in the diet because research has shown them to be helpful in slowing the spread of cancer cells and increasing the chances of survival for a variety of cancer forms. The extensive research on the connection between nutrition and cancer makes it abundantly evident that diet plays a major role in cancer development. A person's diet is simply one aspect of their lifestyle that affects their cancer risk; other lifestyle factors include obesity, smoking, consuming alcohol, and engaging in regular exercise.

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