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ANTICANCER DRUGS: A REVIEW ARTICLE

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ABSTRACT

Anticancer drugs research and development have been the largest market area in the pharmaceutical industry in terms of the number of project, clinical trials and spending. In the last 10 - 30 years, targeting therapy for cancers has been developed and achieved enormous clinical effectiveness by transforming some previously deadly malignancies into chronically manageable conditions, but cure problem still remains. This mini review outlined the current status of anticancer drugs development and hinted the opinions of how to further increase the accuracy and efficacy of discovery for cancer treatment. Chemotherapy is major therapeutic approach the treatment of both localized and metastasized cancers. Since anticancer drugs are neither specific nor targeted to the cancer cells, improved delivery of anticancer drugs to be a reasonable and achievable challenge. Scientist are working to increase the availability of drug for tumor uptake by -

- 1) delaying the release preparations for long - lasting actions.
- 2) Using liposome - entrapped drugs for prolonged effect or reduced toxicity.
- 3) Administrating inert, non- toxic Prodrug for specific activation at the tumor site.
- 4) Delivering the antibody - mediated drugs or
- 5) conjugating site - specific carriers to direct the drug to the tumor target. The latter depends heavily on pharmacokinetic investigations.

INTRODUCTION

Cancer is a disease characterized by uncontrolled multiplication and spread of abnormal forms of the body's own cells. The branch of medicine concerned with study, diagnosis, treatment and prevention of cancer is Oncology. Cancer may affect people at all ages, even foetuses, but the risk of most varieties increase with age. (1) All cancers begin in cells, the body's basic of life.

The body is made of many types of cells. These cells grow and divide in controlled way to produce more cells as they are required to keep the body healthy. When cell become old or damaged, they die and are replaced with new cells. However, sometimes this orderly process goes wrong . The genetics material [DNA] of a cell can become damaged, producing mutations that affect normal cell growth and division. When this happens, cells form when the body does not need them. The extra cells form a mass of tissue called a tumour. Targeted drug delivery is considered as a method in which drug - carrier complex, delivers drug to the pre- selected cell in a specific manner. The drug should reach the target cells [s] with the maximum concentration or with maximum effect. [2, 3]

Cancer is an uncontrolled growth of cells resulting in lack of differentiation and ability to invade local tissues and metastasis which are reproduce individually throughout the body. During metastasis, cancer cells enter the blood stream and are carried to distant parts of the body where they form other similar growths. Synthetic drugs are available for treatment of cancer buy they are not free from unfavourable effects. Chemotherapy and radiation therapy are major clinical treatment used for the control of early stages of tumour but these methods has severe side effects. Nature has provides human a variety of useful sources mainly plants for discovery and development of drugs against dreadful diseases. Traditional herbs as an effective system of treatment of cancer Drugs from medicinal plants are found to be comparatively less toxic and side effects. [4]

Nanoparticles:

Nanoparticles are solid colloidal particles ranging from 10 to 1000 nm in size, they consist of macromolecular materials in which the active ingredients [drug or biological active material] is dissolved, entrapped, encapsulated, adsorbed, or attached. [5] Nanospheres have a monolithic- type structure in which drugs are dispersed or adsorbed into their surfaces or encapsulated within the particles. Nanocapsules are the vesicular system in which the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane.

In this case the active substance is usually dissolved in the inner core, but may also be adsorbed to the capsule surface. Apart from this, nanoparticles have some following advantages: provide a targeted delivery of the drug , protect drug from degradation , Decrease of toxic side effects , Improve the bioavailability of the drug cheaper and stable , provide patient compliance.

Nanotechnology:

Nanotechnology is the preparation of nanosized structure containing the API. Nanotechnology is defined as the study and use of structures in the size range of 1 to 100 nm. The goal of nanotechnology is to diagnose as accurately and early as possible and adverse effects using controlled and targeted drug delivery approach. Important Drugs delivery system developed using Nanotechnology principles, Nanosuspension, Nanoemulsion, Nanocrystals.

Nanoparticles are the nanosized particles, which transport pharmaceutical agents to achieve better or enhanced pharmacological effects. The use of nanotechnology effects the use of nanotechnology with combination chemotherapy provides synergistic in drug delivery.

Advantages of Nanoparticle - based drug delivery therapy are:

1. It enhances therapeutic effectiveness
2. Reduces side effects of the drug payloads by improving their pharmacokinetics properties
3. Provides long circulation half lives
4. Enhanced permeation and retention effect
5. Drug safety
6. Patient compliance

This study is carried to perform brief description about cancer, medicinal plants and cancer drugs that have anticancer activity. Study reviewed of cancer, anticancer drugs and anticancer medicinal plants like Turmeric, Vinca and Wheat grass, Neem, Taxus and Aloe Vera in treatment or chemoprevention of cancer.

Facts about Cancer:

1. Cancer figure among the leading causes of morbidity and mortality worldwide , with approximately 14 million new cases and 8.2 million cancer related deaths in 2012.
2. The number of new cases is expected to rise by about 70% over the next 2 decades.

3. Among men, the 5 most common sites of cancer diagnosed in 2012 were lung, prostate, stomach, and liver cancer.
4. Among women the 5 most common sites diagnosed were , colorectum , lung, cervix, breast and stomach cancer.
5. Cancer deaths are due to the 5 leading behavioral and dietary risks: high body mass index, low fruit and vegetable intake , lack of physical activity, tobacco use , alcohol use.
6. Tobacco use is the most important risk factor for cancer causing around 20% of global cancer deaths and around 70% of global lung cancer deaths.
7. Cancer causing viral infection such as HBV and HPV are responsible for up to 20% of cancer deaths in low and middle income countries.
8. More than 60% of world's total new annual cases occur in Africa, Asia, and Central and South America . These regions account for 70% of world's cancer deaths.
9. It is expected that annual cancer cases will rise from 14 million in 2012 to 22 within the next 2 decades.

Table 1: Types of cancer

Type	Site of cancer
Carcinomas	Cells that cover internal and external parts of the body such as lung, breast, and colon cancer.
Sarcoma	Bone, cartilage, fat, connective tissue, muscle and other supportive tissues.
Lymphomas	Lymph nodes and immune system tissue.
Leukaemias	Bone marrow and often accumulate in the bloodstream.
Adenomas	Thyroid, the pituitary gland, the adrenal gland and other glandular tissues.

Sign and symptoms:

You should know some signs and symptoms of cancer. But remember, having any of these does not mean that you cancer - many other things cause these sign and symptoms, too.

1. Unexplained weight loss
2. Fever
3. Fatigue
4. Pain
5. Skin changes

6. Change in bowel habits or bladder function
7. Sores that do not heal
8. White patches inside the mouth or white spots on the tongue
9. Unusual bleeding or discharge
10. Thickening or lump in the breast or other parts of the body indigestion
11. Recent change in a wart or mole or any new skin change

Diagnosis:

If you have a symptom or your test result suggests cancer , the doctor must find out whether it is due to cancer or some other cause. The doctor may ask about your personal and family medical history and do a physical exam. The doctor also may order lab tests , scans , or other tests or procedures.

Factors Influencing Cancer:

Age:

Cancer most commonly develops in older people 78% of all cancer diagnoses are in people 55 years of age or older. Anyone can develop cancer. However, the risk of being diagnosed with cancer increases significantly with age.

Obesity and physical activity:

Obesity and lack of physical activity are associated with increased risk at various cancer sites, including breast and endometrial cancer.

Tobacco and Smoking:

The consumption of tobacco is the leading cause of cancers. The regular use of tobacco via smoking, chewing, sniffing which is responsible for 65% to 85% cancer incidences in men and women respectively

Alcohol consumption:

Alcohol consumption has been considered as one of the major causes of colorectal cancer as per a recent monograph of WHO. Annually, about 9.4 % new colorectal cancer cases are attributed to the consumption of alcohol, globally.

Radiation:

In the developed and developing countries, the radiations are also notorious carcinogens. About 10% cancer occurrence is due to radiation effect, ionizing and non - ionizing. The major sources of radiations are radioactive compounds, ultraviolet [UV] and pulsed electromagnetic fields.

The mechanism on cancer therapy:

1. Inhibiting cancer cell production directly by stimulating macrophage phagocytises, enhancing natural killer cell activity.
2. Promoting apoptosis of cancer cells by increasing production of interferon - I , interleukin - 2 , immunoglobulin and complement in blood serum.
3. Enforcing the necrosis the tumour and spread by blocking the blood source of tumour tissue.
4. Enhancing the number of leukocytes and platelets by stimulating the haemopoietic function.
5. Promoting the reverse transformation from tumour cells into normal cells.
6. Promoting metabolism and preventing carcinogenesis of normal cells.
7. Stimulating appetite, improving quality of sleep, relieving pain, this benefiting patient's health.

Plant as a Source of Anti - Cancer Compounds:

Plant derived compounds, which are the important source of clinically useful anti - cancer drug, has shown to have Probable for treatment or prevention of cancer in humans. In the treatment of cancer, plants have a long history; more than 3000 plant species have been reported by Hartwell which are used in treatment of cancer. Plants as well as plant derived compounds have played significant role in development of number of clinically used anti - cancers agents.

Chemotherapy, being a major treatment used for the control of advanced stages of malignancies and as a prophylactic against possible metastasis, exhibits severe toxicity on normal tissues. Plants have been used for treating various diseases of human beings and animals. They maintain the health and vitality of individuals and also cure diseases including cancer without causing toxicity More than 50%of all modern drugs in clinical use are of natural products, many of which have the ability to control cancer cells.

Influence of Aging on Drug Pharmacokinetics:

With increasing age, multiple physiological parameters alter, which may substantially influence the PK of anticancer drugs. In elderly patients, the PK profile can be influenced by changed distribution, metabolism and elimination parameters, while changes in absorption rarely led to clinically - relevant differences changes in gastric pH may have variable impacts on anticancer drug absorption, while absorption of Class II oral therapeutic drugs, including

tyrosine kinase inhibitors and endocrine agents, increases with increasing gastric pH. Another example includes Capecitabine, with a higher absorption in elderly patients with a higher gastric pH, Similar to increased absorption In the fed compared to the fasted state. These multifactorial and complex changes make it difficult to predict the net effect of aging on the PK profile of a specific drug administered to elderly breast cancer patients. Besides these physiological changes, multiple other factors contribute to the complexity of anticancer drug treatment in the elderly patient. Firstly, elderly patients often have several comorbidities and receive comedication that may negatively affect anticancer treatment. For instance, patients with diabetes mellitus encountered more chemotherapy - related toxicities when receiving adjuvant chemotherapy for breast cancer compared to the non - diabetic control group. A higher fat proportion in the elderly patients may result in impaired anticancer drug disposition and increased toxicity from various chemotherapy regimens. Furthermore, comorbidities were determined to significantly influence mortality rates in elderly patients diagnosed with cancer.

List of Some Anticancer Drugs:

1. Docetaxel
 - 1.1 Paclitaxel
2. Anthracyclines
 - 2.1. Doxorubicin
 - 2.2. Epirubicin
3. Alkylating Agents
 - 3.1. Cyclophosphamide
4. Vinca - Alkaloids
 - 4.1. Vinorelbine [Intravenous]
5. Anti- Metabolites
 - 5.1. 5 - Fluorouracil
 - 5.2 Capecitabine

CONCLUSION:

Cancer after cardiovascular disease is the second leading cause of death. Cancer is the abnormal growth of cells in our bodies that can lead to death. For treatment of cancer there are very synthetic compounds are present but they have many adverse effects as compared to medicinal plants that have anticancer activity. Medicinal plants that have anticancer activity

has role in treatment as well as chemopreventive purpose for cancer. Some medicinal plant like turmeric, vinca, taxus, neem, aloe vera , broccoli, etc that have chemical constituents as curcumin, vincristine, vinblastine, taxol and various anticancer classes of constituents like vitamins, flavonoids, phenolic compounds, anthraquinones, carotenoids, coumarins, tannins, saponins and other miscellaneous compounds have their important role in treatment and in prevention of cancer.

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