A Review Article on Anticancer Natural Drugs

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Abstract- *Cancer it's an abnormal growth of cells in body that can lead to death & globally the numbers of cancer patients are increasing day by day. There are several medicines available in the market to treat the various types of cancer but no drug is found to be fully effective and safe. Many natural products and their analogues have been identified as potent anti-cancer drugs and day by day the anti- cancer property of various plants is being identified. New drug discovery is time consuming process. So anticancer activity of certain natural products & their analogues can be enhanced by synthesizing new derivatives based on active models; drug resistance & solubility & metabolic limitations can be overcome by appropriate molecular modification, Medicinal plants with their isolated lead molecules are also used as an alternative medicine for treating neoplastic cells. Neoplastic cells are the anomalous proliferation of cells in the body which cause cancer. Diverse efficient compounds derived from natural products have been isolated as anticancer agents.*

Keywords- Cancer, Chemotherapy, cancer cells, natural plants, Medicinal plants, Herbal medicine.

I. INTRODUCTION

Natural products especially plants have been used for the treatment of various diseases for thousands of years. Some plants have been used as medicines in Egypt, China, India and Greece from ancient times & an impressive number of modern drugs have been developed from them. The 1st written records on the medicinal uses of plants was observed in about 2600 BC from the Sumerians and Acadians. Among the human diseases cancer is one, probably the most important genetic disease which can be treated with medicinal plants. Every year, millions of people are diagnosed with cancer, leading to death in a majority of the cases. Cancer is the abnormal growth of cells in our bodies that can lead to death. Cancer cells usually invade and destroy normal cells. These cells are born due to imbalance in the body and by correcting this imbalance, the cancer may be treated. Billions of dollars have been spent on cancer research and yet we don't understand exactly what cancer is. Every year, millions of people are diagnosed with cancer, leading to death. According to the American Cancer Society deaths arising from cancer constitute 2-3% of the annual deaths recorded worldwide. Thus cancer kills about 3500 million people annually all over the world. Several chemo preventive agents are used to treat cancer, but they cause toxicity that prevents their usage.Of over 2069 anti-cancer clinical trials recorded by the National Cancer Institute as being in progress as of July 2004, over 160 are drug combinations including these agents against a range of cancer.

Cancer and its Classification:-

Cancer is a general term applied of malignant diseases that may affect different parts of body. These diseases are characterized by a rapid and uncontrolled formation of abnormal cells, which may mass together to form a growth or tumour, or proliferate throughout the body, initiating abnormal growth at other sites If the process is not arrested, it may progress until it causes the death of the organism. The main forms of treatment for advance stage cancer in humans are surgery, radiation and drugs (cancer chemotherapeutic agents) Cancer chemotherapeutic agents can often provide temporary relief of symptoms, prolongation of life, and occasionally cures. In recent years, a lot of effort has been applied to the synthesis of potential anticancer drugs. Many hundreds of chemical variants of known class of cancer chemotherapeutic agents have been synthesized but have a more side effects. A successful anticancer drug should kill cancer cells without causing excessive damage to normal cells. This ideal is difficult, or perhaps impossible, to attain and is why cancer patients frequently suffer unpleasant side effects when under-going treatment. However, a waste amount of synthetic work has given relatively small improvements over the prototype drugs. There is a continued need for new prototype-new templates to use in the design of potential chemotherapeutic agents natural products are providing such templates Recent studies of tumor-inhibiting compound of plant origin have yielded an impressive array of novel structures.

Types of Cancers :-

1) Cancers of Blood and Lymphatic Systems
a) Hodgkin's disease, b) Leukemia's, c)Lymphomas, d) Multiple myeloma,
2) Skin Cancers
a) Malignant Melanoma

3) Cancers of Digestive Systems

a) Oesophageal cancer b) Stomach cancer c) Cancer of pancreas d) Liver cancer e) Colon and Rectal cancer 1) Anal cancer

4) Cancers of Urinary system

a) Kidney cancer b) Bladder cancer c) Testis cancer d) Prostate cancer

5) Cancers in women

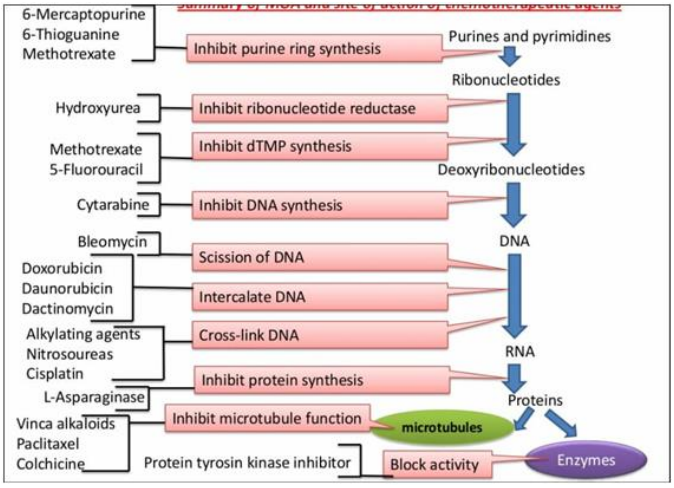
a) Breast cancer b) Ovarian cancer c) Gynaecological cancer

6) Miscellaneous cancers

a) Brain cancer b) Bone cancer c) Characinoid cancer d) Nasopharyngeal cancer e) Retroperitoneal sarcomas Soft tissue cancer g) Thyroid cancer

Breast cancer is the most common form cancer in worldwide Amongst south African women, breast cancer is likely to develop in one out of every 31 women in the country. Breast cancer in India is the second most common cancer in women after the cancer of uterine cervix.

Mechanism of cancer therapy:-



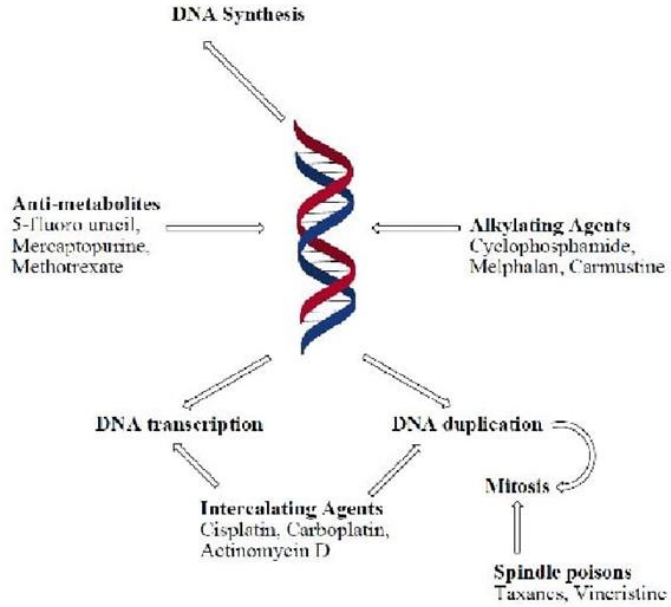


Fig. 1: Sites of action of cytotoxic agents.

Chemotherapy:-

The excessively active growth-signaling pathways in cancer cells makes them susceptible to a wide range of drugs which target growth-signaling molecules and/or processes involved in cellular replication and expression. Cells which are normally actively dividing, in particular the bone marrow constituents and those of the intestinal lining, are particularly susceptible. Disregulated cell cycle events, due to mutations in cancer cells, do sometimes offer opportunities to target those cells without affecting normal cells. The relatively wide spectrum of activity of cytotoxic drugs makes them a rather harsh and non-specific form of treatment that can only be tolerated for short periods. Indeed the effects of the treatment may sometimes cause more distress than the disease. These side-effects include dry flaky skin, loss of hair, nausea and vomiting, changes in taste and appetite, blood clotting problems. fatigue, depressed immune system and possible sterility.

Oncogenes and tumour suppressor genes:

Two sets of genes are controlling cancer development. Oncogenes are the first set of genes and are involved in different cell activities including cell division. However, over expression of these genes transforms a normal cell into a cancer cell. On the other hand, the second set of genes (tumor suppressor genes) inhibits cancer cell formation by different mechanisms. Tumor suppressor genes are under expressed in cancer cells while, oncogenes are over expressed". Table 1 summarizes the main oncogenes and tumor suppressor genes and their role in cancer development. Oncogenes and their products represent good targets for

Cancer therapy. Other targets include enzymes involved in cell division like topoisomerases that unwind the DNA during replication. The diversity of plant derived natural products can provide therapeutic products attacking different targets in cancer cells.

Plant Derived Anti-Cancer drugs:-

1. **Vinca Alkaloids:** The first agents introduced in clinical use were vinca alkaloids, vinblastine (VLB) and vincristine (VCR), isolated from the *Catharanthusroseus*(Apocynaceae). While research investigators couldn't confirm this activity, it was noted that plant extracts reduced crucially white blood cell counts and also caused bone marrow depression in rats. Plant extract also enhance the life of mice, bearing a transplantable lymphocytic leukemia. The plant was originally native to Madagascar, but the samples used in the discovery of vincristine and vinblastin were collected in Philippines and Jamaica. Recently semi-synthetic equivalent of vinca alkaloids are vinorelbine (VRLB) and vindesine (VDS). VLB is used for the treatment of lymphomas, leukemias, breast cancer, testicular cancer, lung cancers, and Kaposi's sarcoma. VCR had also showed efficacy against leukemia, particularly acute lymphocytic leukemia in childhood".

2. Podophyllotoxin Derivatives: The species of Podophyllaceae family such as *PodophyllumpeltatumLinn* . Podophyllumemodii have been reported with a therapeutical use, including the treatment of skin cancers and warts. Podophyllumpeltatum have been used by the Americans for the treatment of cancer. It was promoted by the observation in the 1940s that an alcohol extract of the dried roots (called podophyllin) cures venereal warts by topical application. The chief cytotoxic therapeutic constituents were identified as podophyllotoxins&have been 1st isolated in 1880, but its correct structure could only be elucidated in the 1950s with the advancement in spectroscopic techniques Other closely related podophyllotoxins like lignans were also isolated during this period and became introduced into clinical trials, but they were dropped due to lack of efficacy and unacceptable toxicity. Extensive research studies at Sandoz Laboratories in Switzerland in the 1960s and 1970s led to the development of etoposide and teniposide as clinical agents which are used in the treatment of lymphomas and bronchial and testicular cancers.

3. Allium Sativum (Allicin):*Allium sativum* (garlic, lasun) is used to treat many diseases in India. Allicin is a major component of raw garlic &ajoene is a product of the rearrangement of allicin. Its cytotoxic effect has been tested using human primary fibroblasts, a permanent, non-tumorgenic cell line derived from baby hamster kidney cells and a tumorgenic lymphoid cell line derived from a Burkitt lymphoma. The cytotoxic action was in the range 2-50 ug/ml. Some organo-sulfur compounds from garlic, such as S-allylcysteine, are reported to retard the growth of chemically induced & transplantable tumors in several animal models. Administration of garlic (250 mg/kg, p.o., thrice a week) in male wistar rats, has been significantly suppressed 4-nitro quinoline-1-oxide induced tongue carcinogenesis as revealed by the absence by the carcinomas in the initiation phase and their reduced incidence in the post initiation phase. Thus the consumption of garlic may be effective for providing some kind of protection from cancer.

4. ApisMellifera: *Apismellifera* scientific name of honey bee. Honey is used for healing of skin wounds, ulcerations, and burns in Indian system of medicine. A protein from honeybee *Apismellifera*has been reported to enhance proliferation of primary-cultured rat hepatocytes and also suppresses apoptosis. It has also showed cytotoxicity in normal human lymphocytes & HL-60 cells Hamzaoglu et al. (2000) implanated cancer cell into neck wounds of mice, then mice is divided into two groups. A decrease in wound cancer tumors were observed in the groups of mice that were treated with surgical wounds coated with honey pre and postoperatively. This may have some application in human surgery.

5. Cannabis Sativa: In vitro studies of components of marijuana (*Cannabissativa*) indicates a potential to inhibit human breast cancer cells & to produce tumor eradications. In experiments introducing marijuana to malignant brain tumors, it was found that survival of animals was increased significantly. The active components of Cannabis sativa-cannabinoids. Cannabinoids & their derivatives have palliative effects in cancer patients by preventing nausea, vomiting and pain and also stimulated the appetite. These compounds have also been shown anti-tumor activity in cell culture and animal models by modulating key cell-signalling pathways.

6.GossypiumHirsutum:*Gossypiumhurustum*or*Gossypiumherbaceum*also called as Gossypol or cottonseed oil and used as a male contraceptive, in the treatment of metastatic carcinoma of endometrium or ovary and also used in HIV. Some in vivo & in vitro studies showed the antitumor properties of gossypol on many cytosolic and mitochondrial enzyme systems that is fundamental for tumor cell growth, including melanoma, endometrial, colon, lung prostate, breast, brain, and adrenocortical cancer. However no typical dose is yet suggested for the treatment of cancer & self-medication with gossypol is not safe because of it's potential toxicity.

7. ZingiberOfficinale: *Zingiberofficinale* ethanol extract was investigated to find out its antitumor effects. Pre-application of

*Zingiberofficinale*ethanol extract into the skin of mice resulted in significant inhibition of 12-0-tetradecanoylphorbol 13-acetate (TPA)-caused induction of epidermal ODC, cyclooxygenase, and lipoxygenase activities and ODC mRNA expression in a dose-dependent manner. Pre- application also resulted in a significant inhibition of TPA caused epidermal edema and hyperplasia. In prolonged time studies, topical application of *Zingiberofficinale*ethanol extract 30min prior to that of each TPA application to 7, 12-dimethylbenz(a) anthracene initiated mice caused protection against skin tumor incidence its multiplicity. Ginger's natural bio-actives, specifically ginger extract and 6-gigerol, have been investigated for their in vitro inhibition of two key aspects of colon cancer biology, cancer cell proliferation and angiogenic potential of endothelial cell tubule formation. These active ginger constituents are directly related to effect on cancer cells. Among other compounds, 6-gingerol was found to be more effective even at lower doses resulted in inhibition of endothelial cell tube formation. The suggested mechanism of action of Ginger extract on colon cancer cells may be its suppression and arresting the G0/G1-phase, reducing DNA synthesis and inducing apoptosis.

II. CONCLUSION

Medicinal plants maintain the health and strength of individual & also cure various diseases including cancer without causing toxicity. Natural products were discovered from medicinal plants have an important role in treatment of cancer. In this review article some anti cancer plants have been presented. These plants possess good immunomodulatry and antioxidant properties leading to anticancer activity, In conclusion this article provides the knowledge about anticancer medicinal plants which are used by people all over the world. Also its significance to exploit novel anticancer drugs from medicinal plants. Without this early warning system, the problem of overcoming development of chemoresistance is quite considerable. In an ideal situation, therapy would be tailored to suit the individual at the outset, this is unlikely at least for the very near future, despite rapid progress in pharmacogenomies. In the meantime, a better understanding of the mechanisms of resistance will at least allow the physician to modulate the therapy on a need to do basis. Medicinal plants have given a rich health to human beings. Plant extracts & their bioactive compounds which present in them are responsible for anticancer activity have to be screened for their valuable information. This review had given some of the plants with anticancer activity for various types of cancer.

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