

Mini-Review

Anticancer Effects of Chemotherapy and Nature ProductsShikha Rana¹, Savita Dixit^{1,*}, Alok Mittal^{1,*}¹Department of Chemistry, Maulana Azad National Institute of Technology, Bhopal, India.

Cancer is an anomalous growth of cells which originates from a single abnormal cell. These cells then move through the tissues, shift to various parts of the body and enhance the growth of new blood vessels thus acquiring nutrients. Cancerous cells can be evolved in body from any tissues. Various treatments are in force today but have serious side effects. These include surgery, radiation therapy, chemotherapy etc. Long back natural treatments were emphasized more. Also with the study of various side effects of various treatments scientists have shifted their interests towards herbs and plants. Vinca alkaloids, alkaloids in green tea, potatoes, egg plant, pomegranate, wheat grass etc have been studied for various results. Thus these can be a promising source for various leads beneficial in the formulation of anticancerous agents.

Keywords: Cancer, alkaloids, traditional methods, natural methods, herbs.

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Introduction

The use of natural products with curative properties is as archaic as human civilization and since long mineral; plant and animal products have always been the main sources of drugs. With the advances and augmentation of organic chemistry synthetic compounds are preferred more for pharmacological treatments as pure compounds can easily be gathered and can be conveniently modified structurally so that active and potent lead can be developed. Also these methods are cost effective.

“Cancer” can be said to be a general term that can be attributed to over 100 distinct diseases which affects various tissues and cell types. However, all forms of cancer are symbolized by anomalous cell growth which results from a comparatively small number of rooted or environmentally-induced genetic anomalies [1]. Understanding the mechanism of carcinogenesis can provide us with essential routes for cancer prevention. Most of the researches are based on the multistage carcinogenesis notion i.e. initiation → promotion → progression. Thus cancer chemoprevention can be interpreted as the usage of natural and synthetic chemical agents which can reverse or quench carcinogenesis so as to avert the advancement of nosy cancer.

In recent years, natural products especially those derived from natural plants are considered for alternative therapies [2]. India is a prosperous source of medicinal plants and various systems of medicine such as ayurveda, unani and siddha utilize these plants and their extracts to cure or prevent various diseases. Many natural products such as flavonoids, terpenoids and alkaloids have been extracted and have been exploited for various ailments due to their pharmacological diversity [3].

With the exploration of several protein/peptide receptors and tumor-related peptides and proteins may emerge as a “new wave” for impressive and discriminatory anticancer drugs snatching the largest share in cancer therapeutic market [4]. Plants are the wealthy sources of peptides with probable anticancer properties. Peptides from various plants possess different chemical structures and pharmacological actions thus these can be altered and can be considered for designing a lead compound. Till date only few plant derived peptides have been considered for studying various anticancer mechanisms. Therefore plant peptides can be explored more for anticancer activities [5].

Cancer and cancer treatment

Cancer is an anomalous growth of cells which has been derived from a sole abnormal cell. The cells at this stage lose its natural control mechanism and thus expand. These

*Correspondence: Savita Dixit, Department of Chemistry, Maulana Azad National Institute of Technology, Bhopal, India. Email: Savitadixit1@yahoo.com OR Alok Mittal, Department of Chemistry, Maulana Azad National Institute of Technology, Bhopal, India.

cells then breach contiguous tissues, drift to obscure parts of the body and boost the growth of new blood vessels from which these cells acquire nutrients. Cancerous cells can be evolved in body from any tissues [6].

Cancerous tissues can be those of the blood and it can also be blood forming tissues. These include leukemias and lymphomas and solid tumors which are generally termed as cancer. These can be carcinomas or sarcomas.

Blood forming cells form Leukemia. These cells can accumulate in the bone marrow and blood stream. The

cancerous cell from lymphomas produces large masses in armpit, groin, abdomen or chest due to expansion of lymph nodes (Fig. 1). The cancer cells of the lining of skin, lungs, digestive tract and internal organs cause carcinomas. Cancer of skin, lungs, colon, stomach, breasts, prostate and thyroid gland are its examples. The mesodermal cells, which are responsible for muscles, blood vessels, bone and connective tissues, cancer is termed as sarcomas. Leiomyosarcoma and osteosarcoma are its example [7].

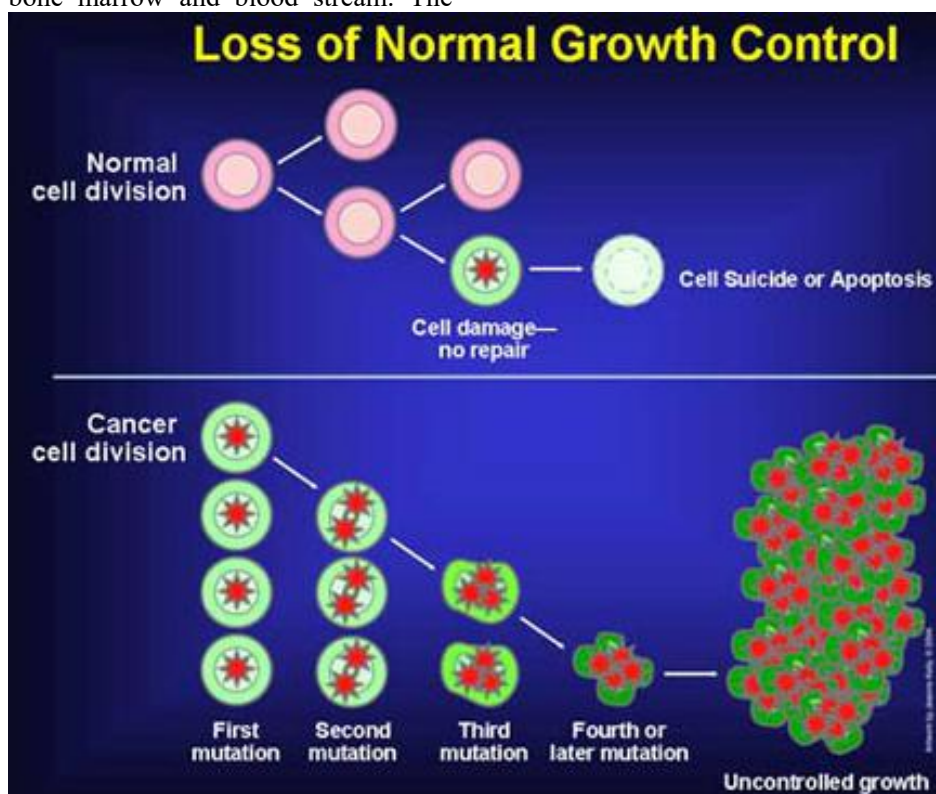


Figure 1. Leukemia development

Causes of Cancer

Bulk of the cancers is mainly caused due to various environmental factors and the rest are caused due to inherited genes [8]. Environmental factors include lifestyle, economic and behavioral factors. Various other factors such as usage of tobacco (causing 25-30% cancers), obesity (30-35% cancers), infections (15-20% cancers), radiations (causing upto 10 % cancers), stress, lack of physical activity and environmental pollution are some of the other prime factors responsible for cancer [9].

Traditional Treatments to cancers

Various treatments are followed today but with serious side effects. These treatments include surgery which is used in those cases in which the cancer is not spread in the body but is confined to a specific area. It is the most widely

used method to diagnose, cure and prevent cancer. Chemotherapy or Chemo is the treatment of cancer with chemicals. When high energy particles or waves are used to wipe out the cancerous cells then this technique is called the radiation therapy. A newly developed therapy is in more use known as the targeted therapy which includes the utilization of drugs to precisely attack the targeted cancerous cells which may sometime affect the normal cells too. This mode of therapy is known as the targeted therapy. When body's immune system is stimulated to fight against cancerous cell smartly or when some external immune system components are provided such as proteins for active working of immune system so as to fight cancerous cells then such a technique is known as immunotherapy. Another important therapy used today is

hyperthermia which is based on the idea that heat can be used to treat or kill cancer cells. In some therapies photosensitizing agents along with light are used to kill cancer cells. These agents are activated only when light is incident on it. Lasers are also being employed to treat these cancerous cells [10].

Major side-effects of the treatments

The abiding side effects of cancer are known as late effects. These effects depend on the type of cancers. The cancer cells grow fast and fast growing cells are killed by chemotherapy. But as the drugs pass through various pathways it influences other normal cells and damaging their natural working. Chemotherapy and other targeted therapies may lead to reduction of white blood cells thus increasing the chances of infection. Also these may lead to the reduction of red blood cells resulting into anemia. This may lead to the reduction of oxygen carrying capacity of the cells making an individual tired and breathless. The blood platelet count also decreases. The major side effect of using the traditional treatment is Hair loss. If chemotherapy is used then the hair loss is seen all over the body but if radiotherapy is used then hair loss is experienced at the area of treatment. The hair may either get thin or may drift permanently. Fatigue, sore throat, nausea, ulcers, loss of appetite, change in taste, constipation, diarrhea, change in skin color and various hormonal changes are other side effects which are observed during these treatments [11].

Small molecular drugs and natural products

Due to the detriment effects of the traditional therapies scientists are now moving towards the natural way for treating cancer with meager or no side effects. Classically natural products have been used religiously to treat various diseases and illness. Natural product chemistry techniques facilitated a vast multitude of bioactive secondary metabolites from which many of them have become present drug candidates [12]. The plant based drug discovery has led to the advancement of anticancer agents such as vincristine, vinblastine, etoposide, paclitaxel, camptothecin, topotecan and irinotecan. Also various fruits and vegetables can be used in anticancer therapy such as curcumin (turmeric), resveratrol (red grapes, peanuts and berries), genistein (soybean), diallyl sulfide (allium), S-allyl cysteine (allium), allicin (garlic), lycopene (tomato),

capsaicin (red chilli), diosgenin (fenugreek), 6-gingerol (ginger), ellagic acid (pomegranate), ursolic acid (apple, pears, prunes), silymarin (milk thistle), anethol (anise, camphor, and fennel), catechins (green tea), eugenol (cloves), indole-3-carbinol (cruciferous vegetables), limonene (citrus fruits), beta carotene (carrots), and dietary fiber [13]. Some naturally occurring drugs being used are vinca alkaloids (vincristine, vinblastine, vindesine, vinorelbine), taxanes (paclitaxel, docetaxel), podophyllotoxin and its derivative (etoposide, teniposide), camptothecin and its derivatives (topotecan, irinotecan), anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin) and others [14,15].

Vinca alkaloid family is the most significant and is secluded from *Catharanthus roseus* [16]. Etoposide is another highly active compound which is used to treat testicular cancer, used in combination with bleomycin and cisplatin [17]. It is derived from *Podophyllum peltatum* [18]. It also shows remarkable exercise towards small cell lung carcinoma [19,20,21]. Parsley, celery, chamomile consists of a flavone apigenin which demonstrates cytotoxic activities against breast cancer linings [22]. Saffron obtained from Saffron crocus flower is listed as potent agent for novel anticancer drug [23]. Its ethanolic extracts are being studied for human lung cancer, pancreatic cancer linings, skin carcinoma, colorectal cancer cells and breast cancer [24]. Epigallocatechin gallate are most copious catechin compounds found in green tea, evidences show that they're beneficial in treating brain, prostate, cervical and bladder cancers. Yang *et al* reviewed tea and cancer prevention on molecular mechanisms, molecular targets and human relevance of tea constituents [25,26,27]. Similarly various alkaloids, flavonoids and terpenoids are isolated and studied for cancer. Many herbs, dietary sources, medicinal plants, micro organisms are studied for the same.

Glycoalkaloids, found in eggplants, potatoes and tomatoes, and its hydrolysis derivatives inhibit growth of cells in culture and inhibits tumor growth [28]. Taxol from *Taxus brevifolia* is found to be effective in arresting the cell cycle (Fig. 2). Its active substances are being tested for application against breast and ovarian cancer [29].

Alkaloids from *Catharanthus roseus* or *Vinca rosea* (vincristine and vinblastine) are also found efficient in breast cancer treatment (Fig. 3) [31].

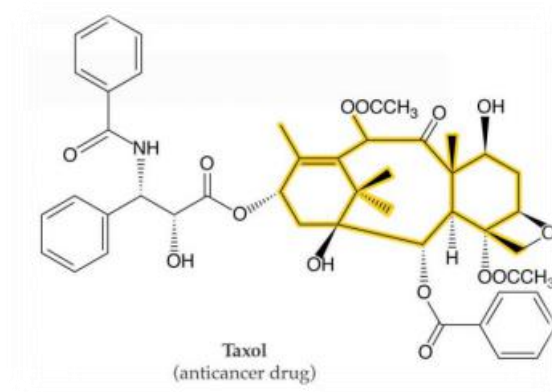


Fig 2. Molecular diagram of Taxol

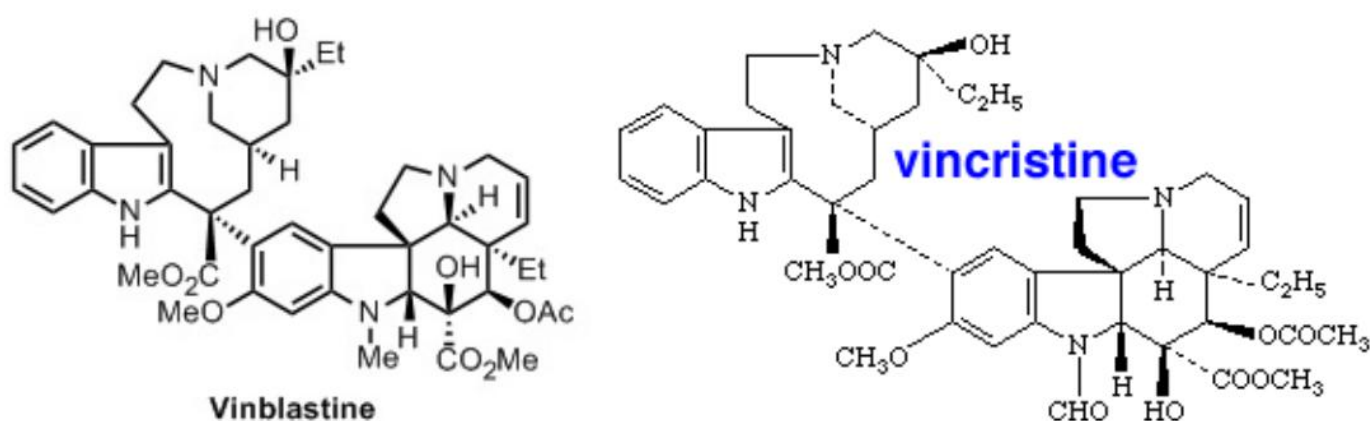


Fig 3. Molecular diagram of Vinblastine and Vincristine

V. amygdalina extracts was also found to inhibit proliferation of breast cancer [31]. *Saraca indica bark extract* (SIE) has been studied and is found to have antioxidant and antibreast cancer activity [32,55]. Taxol has been found to be the most outstanding compound for the treatment of refractory ovarian, breast and other cancers. *Jatropha curcas*, *Pyrenacantha staudtii*, *Picralima nitida* and *Jatropha gossypifolia* are the plants which have been found useful in the treatment of various cancers. Specially for the treatment of breast cancer [33]. Ukrain is an anticancer drug based on the extract of the plant *Chelidonium majus* L and is studied widely for treating various cancer including breast cancer (Fig. 4) [30].

Saraca indica belonging to family Caesalpiniaceae is the most ancient plant exhibiting various pharmacological effects such as Antioxidant, antibreast cancer activity etc [32]. *Trigonella foenum in graecum* (*Fenugreek*) are found to have anti cancerous properties but the mechanism is yet to be elucidated [34,35]. Some tea and herbal infusions are

found to be effective against treatment and prevention of cancer [36].

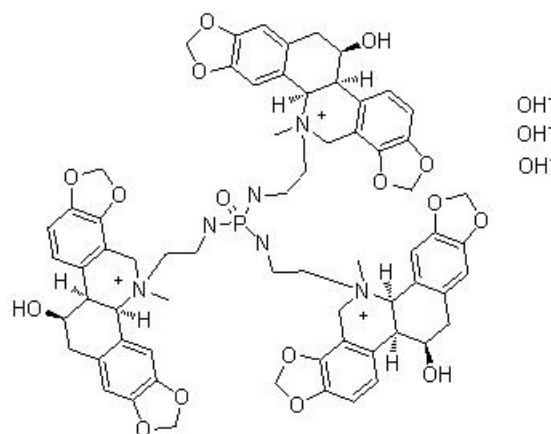


Fig 4. Molecular diagram of Ukrain

Antiproliferative properties of *Melissa officinalis* were investigated and is shown that its extracts are potential anti breast cancer agents [37].

Juglans regia L. (*Juglandaceae*) has medicinal applications to treat a wide range of diseases

such as cancer. Its chloroform fraction induces cell cycle arrest [38]. Three new dimeric indole alkaloids together with five known ones were isolated from the

whole plants of *Catharanthus roseus*. All these compounds were evaluated for their in vitro cytotoxic activities against human breast cancer cell line MDA-MB-231 (Fig. 5) [39].

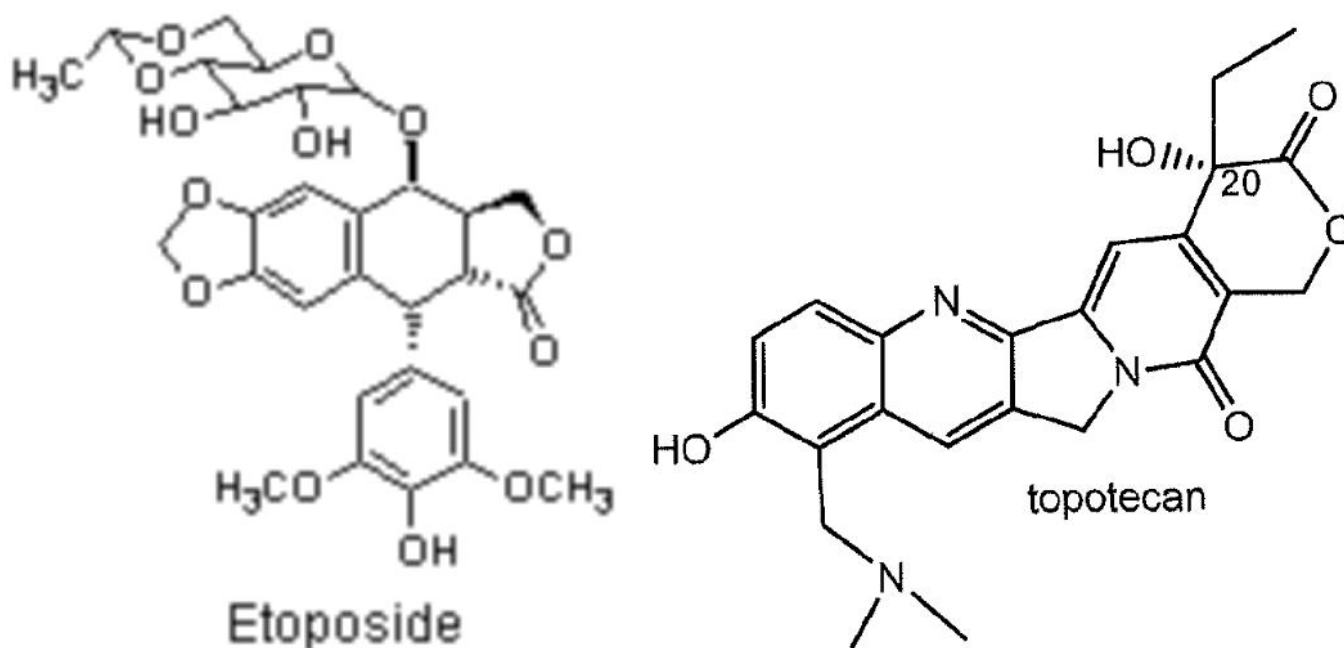


Fig 5. Molecular diagram of Etoposide and Topotecan

Ocimum tenuiflorum is a holy basil which is found to have antimicrobial, antioxidant, antidiabetic, anticancerous activity [40]. *Ocimum tenuiflorum* leaf powder also serves as a potent anticancerous agent [41]. *Beta Vulgaris* consists of chemical constituents such as Carotenoids, Glycine Betaine, Saponins, Betacyanines, Folate, Betanin, Polyphenols, Flavonoids due to which it shows various pharmacological activities such as antimicrobial activity, antiviral activity, antioxidant and specially it inhibits cancer [42].

Beetroot consists of betacyanins, which imparts red colour, whose structure resembles doxorubicin (an anti cancer drug [42]).

Traditional use of beetroot for antitumor, carminative, emmenagogue, and hemostatic properties, clinical trials are lacking to substantiate these claims [43]. Wheat Grass is a potent anticancer agent. Its various extracts are found to be pharmaceutical especially for cancer. But further studies are required to validate its pharmacological activities [44, 45]. Pomegranate shows marked effects in treating cancer such as prostate, Breast, colon and skin cancer [46, 47, 48]. Indian gooseberry is very effective against ovarian cancer liver cancer cells and breast cancer [49]. Various chemical constituents present in curry leaves

are, Catechin, Epicatechin, Rutin, Naringin, Myricetin, Quercetin, Gallic Acid, Cinnamic Acid, Ferulic acid, Vanillic acid. Due to the presence of these chemical constituents these serve as an extremely potent agents for treating cancer especially breast cancer [50].

Future Scope

Cancers in general can be treated by surgery or radiation therapy or chemotherapy [51]. The utilization of conventional chemotherapeutic agents which target the cancerous cells dividing rapidly are coupled with adverse side effects [52]. Cancer cells may also become resistant to chemotherapeutic drugs as of cellular changes such as increase in drug detoxifying enzymes and drug transporters, modified competence between drug and its target etc. The development of a novel class of anticancer drugs that lack lethal effects of traditional chemotherapeutic agents which remains non influential to common chemoresistance would prove to be a major advance in cancer treatment [53]. Revelation of various proteins/peptide receptors and cancer related peptides and proteins are expected to spawn a new wave in near future which may confiscate a large area of the salutary market [54].

Conclusion

Various active agents which have been derived from nature have changed the conventional history of human cancer. Green plants synthesize a variety of bioactive compounds which can be attributable and can be used for scientific investigation. Natural products extracted from medicinal plants play a vital role in generating leads for treatment of cancer. Various experimental agents have provided us an opportunity to figure out a new class of anticancer agents. Even though many studies are being carried out with alkaloids, flavonoids and terpenoids, still there are certain unexplored bioactive compounds which have anticancer properties with meagre side effects and maximum efficacy. Thus giving us an opportunity to explore more and find solutions to the unsolved questions.

Competing interests

The authors declare that they have no competing interests.

Acknowledgments

None

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