Available online at www.elixirpublishers.com (Elixir International Journal)

Applied Botany

Elixir Appl. Botany 92 (2016) 39047-39050

ISSN: 2229-712X

Plant Derived Drugs and Use in Cancer Treatment

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ARTICLE INFO

Article history:

Received: 13 January 2016;

Received in revised form:

9 March 2015;

Accepted: 14 March 2015;

Keywords

Taxol,
Etoposide,
Camptothecin,
Topotican,
Vinblastine,
Anti-Cancer Activity.

ABSTRACT

Plant derived components have a great significance and act as potent alternatives for the treatment of cancer without having harmful after effects on human body. There are about 250,000 plant species out of which more than one thousand plants possess significant anticancer properties which has been proven by scientists. Plant derived components such as Taxol, podophyllotoxin, etoposide, camptothecin, topotican, vinblastine, etc are of great contribution towards anti-cancer activity by plants.

Introduction

Abnormal growth of cells that have potential to invade or spread to other parts of the body is termed as cancer or malignant tumor [1] [2]. Cancers are mainly caused due to various environmental factors with 90-95% cases attributed to environmental factors and 5-10% due to genetic disorder. The major cancer causing environmental factors are consumption of tobacco (25-30%), diet and obesity (30-35%), infections (15-25%), ionizing and non ionizing radiations (up to 10%), stress, lack of physical activity, and environmental pollutants. Approximately 18% of deaths all over the world due to cancer are because of infectious diseases. This percentage may be as high as 25% in Africa to as low as 10% in developed countries[3].All environmental factors cannot be controlled such as exposure to naturally occurring radiations or genetic factors but many of other factors such as diet, amount of physical activity, obesity, consumption of tobacco or alcohol, sexually transmitted infections can be controlled[4].Cancer deaths were 5.8 million in 1990 and this death rate is increasing by each passing year due to change in lifestyle and aging population. As per world health organization on cancer database on cancer incidence and mortality indicates occurrence of cancer cases more in less developed countries in accordance to year 2000, (Table 1. [5]), In 2008, diagnosis of approximately 12.7million cancer patients was done [6] and about 7.98 million people died in 2010, (Fig:1,[7]), [8].

There are a number of therapies and treatments that are available for cancer patients of all ages like surgery, chemotherapy, radiotherapy, etc. Different types of chemotherapeutic agents such as alkylating agents, antimetabolites, anti-tumor antibiotics like anthracyclines, topoisomerase inhibitors, mitotic inhibitors, corticosteroids, targeted therapies, differentiating agents, hormone therapy, immunotherapy, etc are available [9]. Due to harmful and life threatening hazards including cytotoxicity of these synthetic therapies and treatments people are moving towards natural and plant derived medicines and drugs against cancer treatment.

Plant derived compounds such as vinblastine, vincristine, the camptothecin derivatives, topotecan, and irinotecan, etoposide, derived from epipodophyllotoxin, and paclitaxel are a few potential compounds derived from plants that show anti-cancer properties.

Harmful Effects of Synthetic Chemotherapy and Radiotherapy

According to American Cancer Society, alkylating agents that are included in chemotherapy, target DNA and disrupt cell functioning thus blocking cell reproducing capacity. Since these agents directly affect the DNA, they may lead to bone marrow malfunctioning and its permanent damage. Anthracyclins such as Daunorubicin, Doxorubicin, Epirubicin, Idarubicin may lead to permanent cardiac damage if given at high dose. Mitoxantrone, an anti-tumor antibiotic is a potent drug for permanent cardiac damage and an inhibitor of topoisomerase II that can cause treatment related leukemia. Mitotic inhibitors such as Taxanes, Epothilones, Vinca alkaloids, Estramustine, etc that are known to work against various cancers including breast, lung, myelomas, lymphomas, and leukemias may lead to peripheral nerve damage, that is a dose limiting side effect[9]. Corticosteroids used in chemotherapy also has multiple hazards such as steroid psychosis[10], cardiovascular disorders like fluid retention and hypertension, muscle wasting[11], hyperglycemia[11], insulin resistance, diabetes mellitus[11], by inhibiting sex steroids action ,erectile dysfunction, hypogonadism and amenorrhea may be caused. Steroid -induced osteoporosis, colitis, Crohn's disease, peptic ulceration [12].Cataract and retinopathy may also be caused due to prolonged use of corticosteroids.

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Side effects of radiotherapy include nausea and vomiting[13],Epithelial surface damage[14],mouth, throat and stomach sores[15], discomfort in intestines, edema, infertility[16],heart problems[17], radiation proctitis, fibrosis, etc. All these synthetic treatments have such hazardous effects on animal body. Thus scientists are moving towards the application of non hazardous drugs and treatments that may cure the patients without damaging their body as an ideal drug is that disrupts the diseased cells without damaging other cells.

Plant Derived Drugs

There are about 250,000 plant species out of which more than one thousand plants have been proven to possess significant anticancer properties. One of the most beneficial agent that works against refractory ovarian, breast and other cancers is Taxol. Podophyllotoxin is found to be one more outstanding component derived from plants. Synthetic modification done on this component resulted in development of Etoposide which has been experimentally proven against small cell cancers of the lungs and testes. Camptothecin isolated from Camptotheca acuminate is also being widely studied [18].

One of the first clinically used agents derived from plants were vinca alkaloids, vinblastine (VLB) and vincristine (VCR), that were extracted from the Madagascar penwinkle[19], Recent discovery of semi synthetic derivatives of these agents are vinorelbine (VRLB) and vindesine (VDS) that are widely used along with other chemotherapy drugs for treatment of different types of cancers.VLB is utilized for the treatment against leukemias, lymphomas, advanced testicular cancer, lung and breast cancers, and Kaposi's sarcoma. VCR is utilized for treatment of lymphomas and leukemias, particularly acute lymphocytic leukemia in childhood.VRLB actively works against non-small-cell lung cancer and advanced breast cancer.

Sandoz Laboratories in Switzerland in 1960s and 1970s developed etoposide (VM 26) and teniposide (VP 16-213), semi synthetic derivatives of epipodophyllotoxin (isomer of podophyllotoxin) found in plants used for treatment against lymphomas and bronchial and testicular cancers [20]. Podophyllum species (Podophyllaceae), P.emodii Wallich found in Indian subcontinent and P.peltatum Linnaeus (American mandrake or mayapple) have been used medicinally against the treatment of skin cancers and warts since ancient times. Isolation of podophyllotoxin, the major active constituent took place in 1880 and its accurate structure was discovered in 1950s.Different parts of T. brevifolia and other Taxus species like T. canadensis Marshall, T. baccata L. has been consumed by several Native American tribes for cancer treatment and T.baccata that is included in traditional Asiatic Indian (Ayurvedic) medicine system has also been reported against cancer [20]. Breast, ovarian and small-cell lung cancer (NSCLC), Kaposi sarcoma can be treated by consumption of Paclitaxel .According to clinical trials conducted by NCI against 2069 cancers till July 2004, 258 or nearly 12% involve Taxane-derived drugs ,including 134 paclitaxel (Taxol®), 105 docetaxel (Taxotere®) , and 10 miscellaneous taxanes derived, either as single entity or as a mixture with other anti-cancer agents(fig 2,3).

Camptothecin isolated from Chinese ornamental tree, Camptotheca acuminata Decne (Nyssaceae) also known as tree of joy [21], discovered by U.S. Department of Agriculture which showed anti-tumor activity (Fig 4), on several pharmaceutical researches for a better and advanced derivative of camptothecin, and Topotican (Hycamtin®), developed by SmithKline Beecham (now Glaxo SmithKline), and Irinotican (CPT 11; Camptosar®), developed by Yakult Honsha, a Japanese company, are clinically used. Ovarian and small-cell lung cancers are treated by Topotican, whereas colorectal cancers are treated by Irinotecan. Homoharrigtonine (HHT) derived from Chinese tree, Cephalotaxus harringtonia var. drupacea (Sieb and Zucc.) (Cephalotaxaceae) [22], and elliptinium, derived from ellipticine, isolated from many genera of Apocynaceae family, including Bleekeria vitensis A. C.Sm., a medicinal plant from Fiji also have appreciable anti-cancer properties. Treatment of Breast cancer is conducted in France by Elliptinium.

Conclusion

Cancer is one of the most deadly diseases. Following is a list of common types of cancer and its estimated cases and deaths in 2013[23]. Cancer patients are at a dangerous position not just because of the sufferings of the disease but also due to the harmful hazards and sufferings of radiotherapy, chemotherapy and other synthetic treatments which although are competent enough to act against the cancer cells and cure a patient from this deadly disease but their side effects and hazardous outcomes may sometimes lead to development of secondary diseases like permanent cardiac damage, bone marrow disorder, fibrosis, renal damage, etc apart from the hair loss, vomiting, infertility and other troubles of chemotherapy and radiotherapy. A wide range of plant derived components like Taxol, podophyllotoxin, etoposide, camptothecin, topotican, vinblastine, etc are proven to have anticancer properties and many commercially available phyto-drugs are also available in market.

Thus, cancer treatment is possible with plant derived drugs that are now ready to compete with the chemotherapy and radiotherapy without any hazardous impact on human body and thus leading to a healthier and natural cure against cancer disease.

Figure and tables

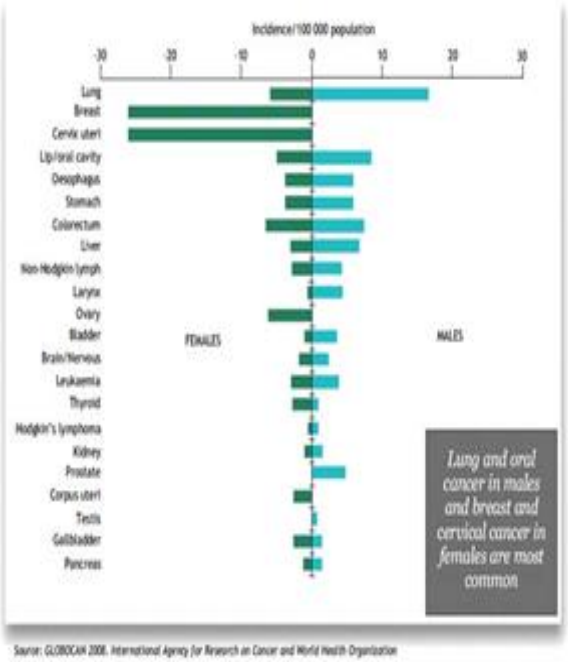


Figure 1. Cancer growth in males and females according to WHO

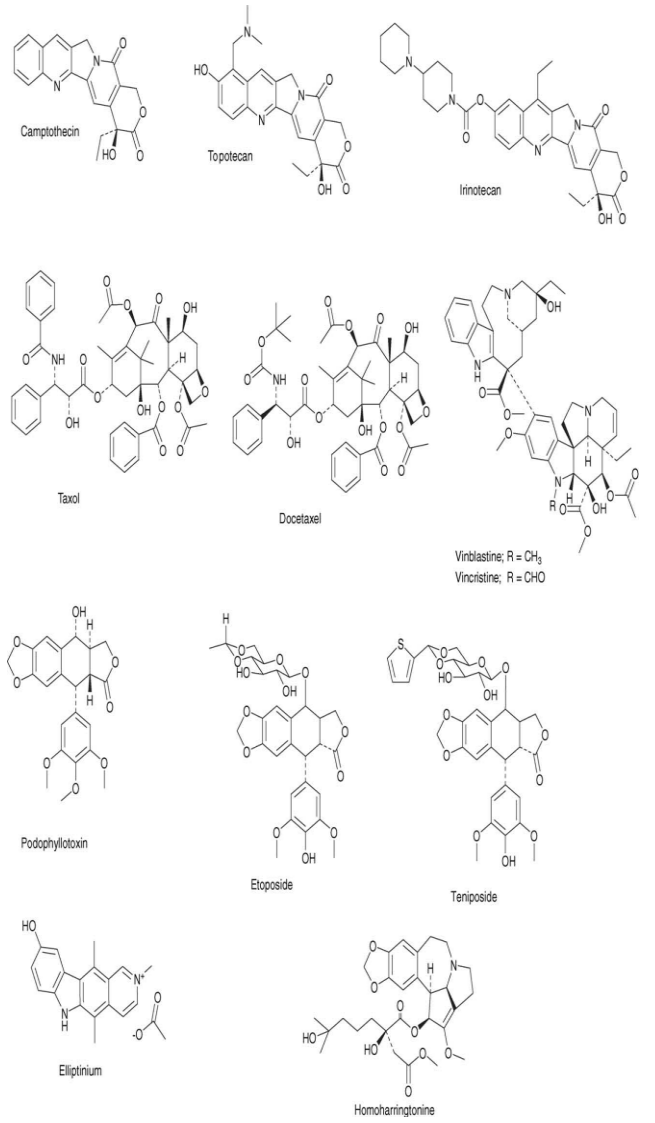


Figure 2. Plant derived anti-cancer agents in clinical use

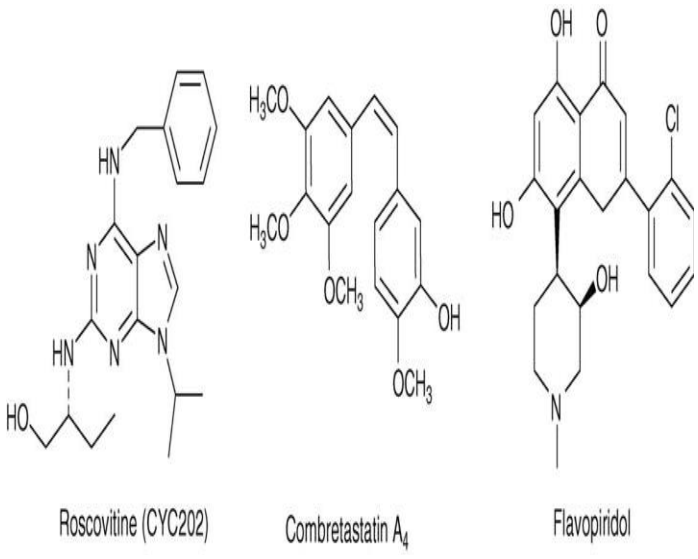


Figure 3. Anti-cancer agents in clinical development isolated from plants.

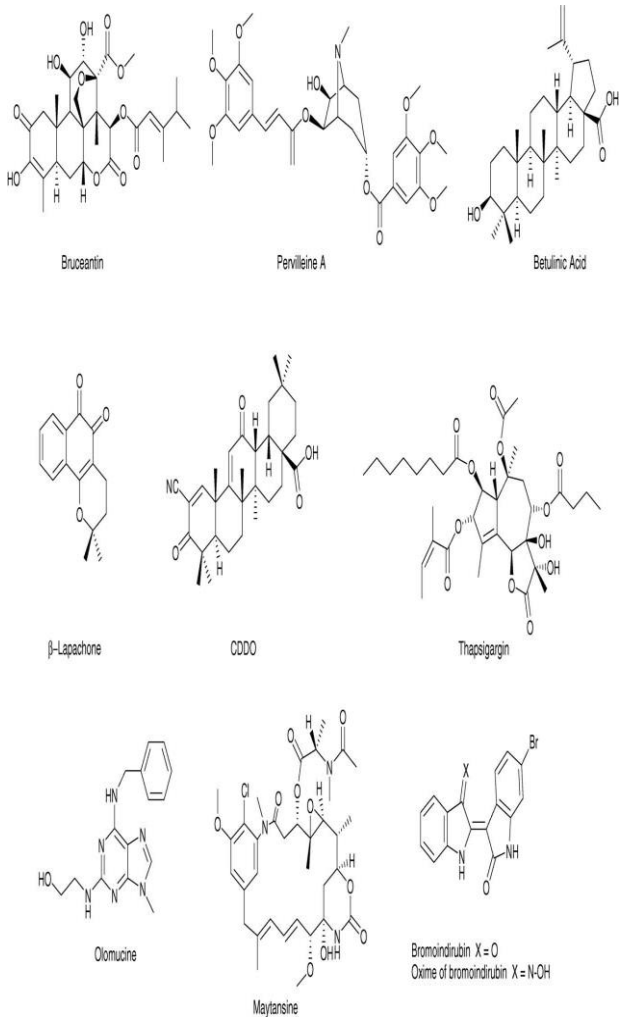


Figure 4. Anti-tumor agents in preclinical treatments isolated from plants.

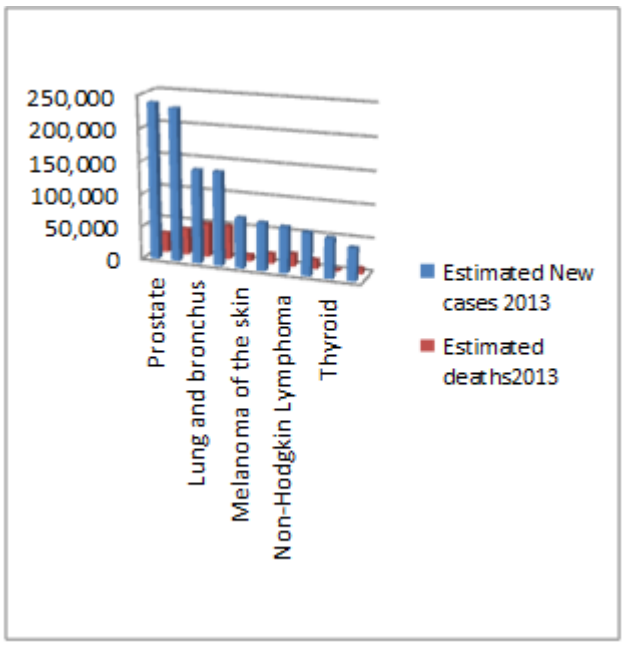
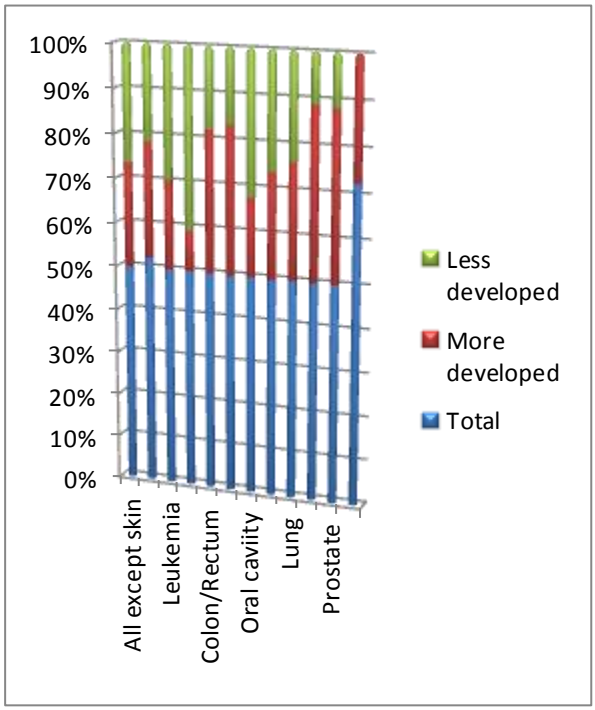


Figure 5. Current scenario of cancer cases and associated estimated deaths 2013

Table 1. As per world health organization on cancer database on cancer incidence and mortality indicates occurrence of cancer cases more in less developed countries in accordance to year 2000.



Acknowledgement

The research papers were collected from various sources like Elsevier, Willey, Pubmed, etc. This reviw paper was compiled and completed at National Botanical Research Institute CSIR Laboratory, under the guidance of our principal scientist Dr. Ch. V Rao .Under consatant guidance and support this paper was accomplished. Two of scholar Lubna azmi and Shyam sundar gupta make thanks to Department of science and technology , New delhi.

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