

Development and properties of anticancer drug: A review

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Abstract

This review describes the development and properties of plant that have anticancer drugs. The natural products played a powerful role in human treatment disease. The classification of anticancer drugs, main steps in anticancer drugs development and plant Compound with their anticancer properties are described in this review. The main aim of this review provide a complete summary of the most known anticancer drugs with their mechanism of action, plant Compound with their anticancer properties, and cancer therapy. This review creates a solid base for further study of development and properties of anticancer drugs with additional research and study.

Keywords: anticancer, chemotherapy, polyphenol, cytotoxicity, diterpenoquinone, antineoplastic

Introduction

Cancer is an unlimited growth of cells which can be again malignant (develop to other part of body) cancer is the important global health problem accountable for a millions of died all over world. It is dependable for about 7.6 millions died world. That expected enhance to 13.1 million by 2030. Despite a advance in the area of research. There is requirement to discover and develop the anticancer therapeutic agent. Since longer it has identify that natural substance described the richest source of higher chemical diversity, supply the basis of identify of novel scaffold structure that the serves begin point for national drug design. Natural product contain some substance produce by a life organism.

These substance are little molecular mass (3000 Dalton's) and a significant structural diversity. Above 40 years natural product played important roll as begin cancer chemotherapeutic agents. Additionally in its naturally happen from or it synthetically modified form. For example antitumor antibiotics across microbe involve in the anthracyclines plant have been using in a traditional medicines for a centuries possess established application as a origin of material obtain highly biological activity. In one approach is achieve these substance using extraction form plant material. In a second approach is a using biotechnological tools to the provide plant- derived anticancer compound. The material of a natural origin (example: form plant and aquatic animal) that is show anti tumour properties be a component of many groups of compound like alkaloids, diterpens, purine - based compound, diterpenoquinone, proteins, etc. Occasionally the cost of extraction of these substance. Occurred natural material is greater than cost of its chemical synthesis. The work characterize the compound of plant source, their happening and variety of mechanism of action. Their are properties posses been trial on a various can cell lines, and human chemotherapy. It convey substance can using alone or combination along more antineoplastic agent of a natural origin. Cancer is the life- threatening disease. They are many cause of a cancer as smoking, family history, environment factor. The cancer first treatment is a surgical removal of solid tumors. The cancer are second leading cause of died. [2, 3, 4, 5, 6, 7]



Fig 1: Anticancer drug.

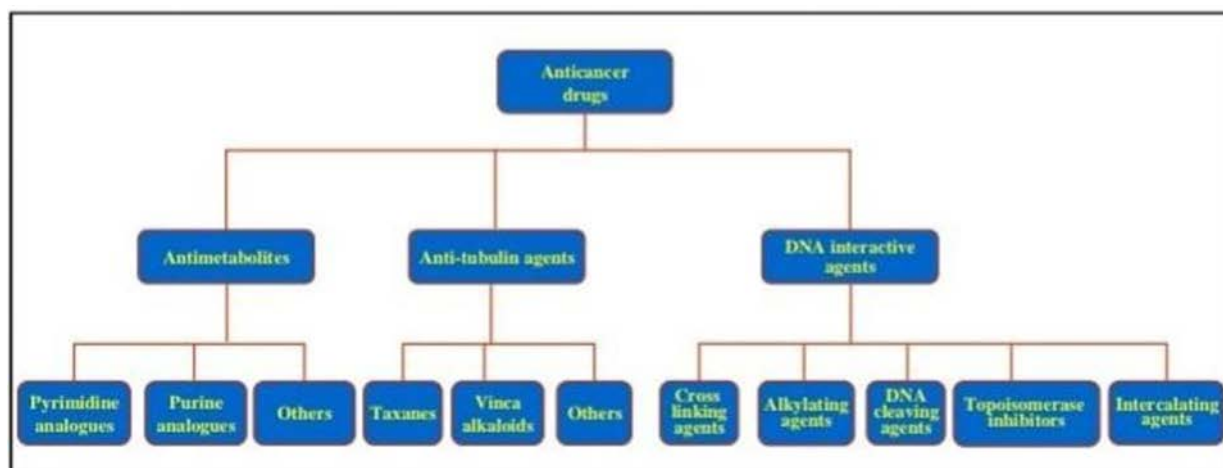
Classification of Anticancer drug ^[3]

Fig 2: Classification of anticancer drug on the basis of their mechanism of action.

Anticancer drugs

Anticancer drugs are classified on the basis of mechanism of action as DNA interactive agents, hormones, antitubulin agents, antimetabolites, molecular targeting agents, biological agents and other monoclonal antibodies.

1. Antimetabolites

Antimetabolites interact with essential biosynthesis pathways and with mechanism of action and these are also known as one of the oldest families of anticancer drugs. They masquerade as a purine or pyrimidine and they become the building blocks of DNA that are incorporated into DNA during S phase and arresting the cell development and cell division.

Example of pyrimidine includes 5-fluorouracil while a typical example of purine includes 6-mercaptopurine. Methotrexate represents another example of antimetabolites which interferes with the essential enzymatic processes of metabolism.

2. Antitubulin agents

The important antitubulin agents are taxanes and vinca alkaloids; they cause cell death through connecting with microtubule dynamics and blocking the division of nucleus.

3. DNA interactive agents

DNA is the best molecular target of many anticancer drugs; they act through different mechanisms of action, summarized under.

- a. **Alkylating agents:** Alkylating agents cause the alkylation in either major or minor grooves of DNA, example: dacarbazine, temozolomide and procarbazine
- b. **Cross-linking agents:** Most of platinum complexes such as oxaliplatin, cisplatin, carboplatin, and nitrogen mustards such as cyclophosphamide (CP) and ifosfamide that cause the inter-strand or intra-strand cross linking of DNA.
- c. **Intercalating agents:** They bind between base pairs of DNA
- d. **Topoisomerase inhibitors:** Some anticancer drugs such as irinotecan and etoposide compounds that inhibit the topoisomerase enzyme which is responsible for cleavage, annealing, and topological state of DNA.
- e. **DNA-cleaving agents:** Anticancer drugs like bleomycin cause the strand scission of DNA.

Development of phase 1 trials ^[10]

Phase 1 trials show the leading administration of a new or a drug mixture of living being oncology phase 1 trials diverge from a non-oncology phase 1 trial. They are generally performed in cancer patients. The practice that obtains the narrow therapeutic index of cytotoxic agent. In phase 1 trials, successive patient cohorts collect developing doses of treatment. Preclinical toxicology studies are used to decide a relatively safe begin dose for a first-in-living study; also to anticipate potential toxicities and their reversibilities. In European guidelines, conditions estimate new drugs in two species: one rodent and one non-rodent (monkey and dogs) model. In non-rodent types, trials appear to be highly sensitive than rodent species. The option of a dose even to the tested is based on some factor including preclinical data, in present

standard treatment in tumor types which a mixture is calculated. Some strategies for a dose escalation are viable. The basic goal of a phase 1 trials is to congregate data on toxicity.

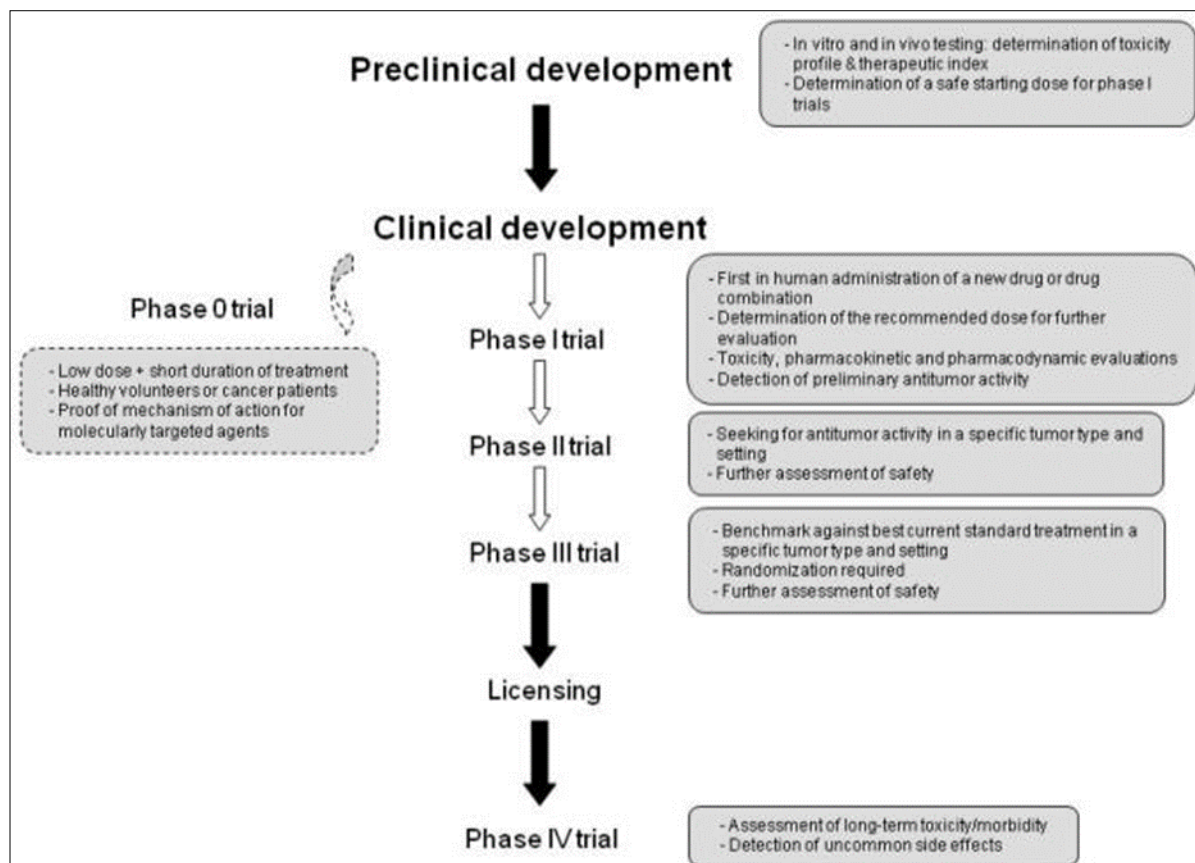


Fig 3: Main step of anticancer drug development.

Role on plant based drug ^[8]

Plant derived combine have the excellent significance to a cancer therapy. The medicinal appreciate of plant has know by most society on this planet. In nineteenth and earlier centuries of a natural substance are extract especially they are derived form botanical species. Require primary source of folk medicines. In a industrious nation at the present- day times. Few fifty percent of the all prscriptive drug are a derive form natural product. They widely applicable source are plant and microorganisms. It contemplate that is because of a structural and biological diversity terrestrial plant provide a individual resources for discovery of likely new drug and biological entities.

Development of Anticancer Drugs from Plants ^[8]

There are approximately concluded that there are roughly 500,000 higher flowering plants species covering terrestrial lands. A huge number of species of plants that only been almost examined for its pharmacological and the medical applications but out of that only less than 1% of species has thoroughly investigated therapeutic agents. For long time, cancer drugs were identified through big scale screening of man made chemical against animal tumor system, primarily murine leukemias. Those drugs which are discovered in the initial of two decades of cancer chemotherapy in years of 1950 to 1970 they are interacted with DNA or it's precursors, or stopping the action of new genetic material or causing irreparable damage to DNA itself in large amount. In the cancer treatment field, there are many applications have been created for the advantageous effects of plants. In the field of treatment of cancers the role of medicinal plants have very necessary role. The between years of 1940 to 2002 all of accessible drugs were 40% of natural products and rest of 8% natural products derived of that considered natural products mimics.

Drugs

1. Docetaxel

Docetaxel is trademarked as Taxotere by the Rhone- poulenc Rorer. Just like Paclitaxel, it also prevents the mitotic spindle from being break down by stabilizing the microtubules bundles, but it shows that in clinical trials that of Docetaxel is about twice effective as Paclitaxel in working so. If Docetaxel is being tested on cervix, lungs, ovaries, carcinomas of bladder then it can also given by intravenously.

2. Beta-lapachone and Lapachol

From Lapachol we can derived quinon tree which nothing but member of Catalpa family (Bignoniaceae). Just like camptothecin and topotecan and beta lapachone it also stopping the action of DNA topoisomerase I.

Plant compounds with anticancer properties: ^[9]

Medicinal plants have a used for thousands of years in a folk medicines in Asian and African populations and more plants are consumed for a their health benefits in the developed nations. Further compounds that possess found and an extracted from a terrestrial plants for its anticancer properties adding brassinosteroid ,taxols and polyphenols.

A. Polyphenols

These compounds includes flavonoids, tannins, curcumin, resverasterol and are all considered to be anticancer compounds. Polyphenols are through to apoptosis actuate a properties showing the anticancer properties which can be utilized. Polyphenols are natural antioxidants and helps in persons diet can improve health and also reduce risk of cancers by being natural antioxidants.

Example .Curcumin treated cancer cells in various cell lines have shown suppression of Tumors Necrosis Factors (TNF) expression through interactions with various stimuli.

B. Flavonoids

Flavonoids are from the polyphenolic compounds and constitutes a large family of plants secondary metabolites with 10,000 known structures. There is a high content of flavonoids compounds such as anthocyanins, flavones, flavonols, chalcones which can be found in one structure of the plant like its seed. Flavonoids possess cytotoxicity on cancer cells and to have been more free radicals scavenging activity. Purified flavonoids possess also shown anticancer activities against further human cancers including. Hepatoma (Hep-G2), Cervical carcinoma (Hela), Breast cancer (MCF7).

Cancer therapy ^[3]:

The main purpose of cancer treatment is the complete removal of cancer or tumor without any single side effects or adverse effects to the body i.e also called as achieving cure with near zero adverse effects. Lists of cancer therapy:

1. Surgery
2. Radiation therapy
3. Chemotherapy
4. Targeted therapy

1. Surgery

It is the oldest kind of therapy and used for different types of cancer treatment. Aim of this i.e surgery helps to removal of only the tumor or entire organs such as mastectomy for breast cancer and prostatectomy for prostate cancer.

Types of surgeries

A. Diagnostic

A biopsy is the only way to make a definitive diagnosis for most of the types of cancer. There are two subclasses of a surgical biopsies:

1. **Incisional biopsy:** In this type removal of a piece of the suspicious area for examination.
2. **Excisional biopsy:** In this type removal of the entire suspicious area, such as unusual lumps.

B. Staging

It helps to find out the size of the tumor and its metastasis i.e where it has spread.

C. Primary or curative surgery

This surgery helps to remove the tumor along with surrounding healthy tissue for margin.

2. Radiation therapy

It is also called as radio therapy or x-ray therapy or irradiations. The aim of this therapy is to deprive cancer cells of their multiplication potential. Approximately, 50% of all cancers patients are receiving this therapy. In radiation therapy 2 types of radiations are used to treat cancer including photon radiation (x- ray and gamma rays) and particle radiation (electrons, photons and neurons beams).

3. Chemotherapy

The treatment of cancer or tumor with anticancer drugs is called chemotherapy. Chemotherapeutic drugs normally act by its cytotoxic action. They selectively arrest the growth of tumor cells. The side effects of many cytotoxic drugs include the hair loss (Alopecia), nausea, gastric lesions, bone marrow suppression. Nitrogen mustard was the 1st anticancer agent which heralded the chemotherapy in 1940s. Chemotherapeutic agents include strong alkylating agents and antimetabolites.

4. Targeted therapy

Agents of targeted therapy include specially designed anticancer drug which interacts with targeted molecules, mostly a protein. The identification of appropriate target of cancer cell therapy is based on detailed understanding of the molecule change in carcinogenesis.

Example - Imatinib, Gefitinib.

Medical plants demands ^[9]:

With successful clinical trials drugs developed from plant origin are popular for clinical development. There is a huge demand for medicinal plants in developing countries putting high pressure on the plants population. Attention is being drawn towards food with medicinal properties such as food includes cruciferous vegetables and fruits berries. Raw by-products retain industries should be used to extract anticancer agents from a source possessing these agents.

Example. One of the biggest crops grown globally are grapes (*Vitis vinifera*) and grape seeds extract they generally mix in ingredients of food products due to their health of human benefits. To growing the sustainability of medicinal plants in a large country utilization of all parts adding the stem, leaf, root and bark have been included in the treatment. Grape stem extracts possess demonstrated a possess antioxidant properties, stop DNA damage from a reactive oxygen species and displayed anti-carcinogenic potential contra an array of cancer cell line retained cervical cancer, thyroid cancer and many more.

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