

## M.SC-Sem-IV, Elective Course – 1c , Organic Chemistry Special UNIT – IV Drugs Antineoplastic agents

Antineoplastic agents are used to treat the cancer. Cancer is a group of disease involving an abnormal and uncontrolled cell division in most of the normal body cells. This new cell growth invade the surrounding structures. The cancer may be benign and malignant.

Benign tumors do not metastasize (spread of cancer to other locations in the body) but malignant do metastasize. Cancer is classified according to the type of cell in which new growth occurs as.

**1. Carcinoma** : This type of cancer derived from epithelial cells. This group represents nearly all those in breast, lung, prostate, colon and pancreas cancer.

**2. Sarcoma** : This type of malignant tumor arises from transformed cells of connective tissue. This tumor is made of cartilage, fat, vascular, cancellous bone and hematopoietic tissues.

**3. Leukemia and Lymphoma** : These two malignant tumors derived from haematopoietic (blood cell forming). This tumor mature in lymph nodes and blood respectively. Lymphomas are Hodgkin Lymphoma and the non-Hodgkin Lymphomas. The enlarged Lymph nodes are usually painless.

**4. Germ cell tumor** : It is derived from germ cells. It may be malignant or benign. Germ cells normally found in the ovary and testis.

**5. Blastoma** : It is common in children. It is a tumor that resembles an immature or embryonic tissue. Examples are neuroblastoma, me

Antineoplastic agents are used to treat the cancer. Cancer is a group of disease involving an abnormal and uncontrolled cell division in most of the normal body cells. This new cell growth invade the surrounding structures. The cancer may be benign and malignant. Benign tumors do not metastasize (spread of cancer to other locations in the body) but malignant do metastasize. Cancer is classified according to the type of cell in which new growth occurs as.

1. Carcinoma : This type of cancer derived from epithelial cells. This group represents nearly all those in breast, lung, prostate, colon and pancreas cancer.

2. Sarcoma : This type of malignant tumor arises from transformed cells of connective tissue. This tumor is made of cartilage, fat, vascular, cancellous bone and hematopoietic tissues.

3. Leukemia and Lymphoma : These two malignant tumors derived from Haematopoietic (blood cell forming). This tumor mature in lymph nodes and blood respectively. Lymphomas are Hodgkin Lymphoma and the non-Hodgkin Lymphomas. The enlarged Lymph nodes are usually painless.

4. Germ cell tumor : It is derived from germ cells. It may be malignant or benign. Germ cells normally found in the ovary and testis.

5. Blastoma : It is common in children. It is a tumor that resembles an immature or embryonic tissue. Examples are neuroblastoma, medulloblastoma and retinoblastoma. Cancer can be treated by many ways including chemotherapy, surgery, radiation therapy and neoplastic agents. The antineoplastic agents are the specialized drugs used primarily to treat cancer. The first antineoplastic agents were used in 1940s, which were made naturally or synthetically.

Antineoplastic agents can be used alone or in combination with other

antineoplastic drugs. These drugs destroy the cancer cells but have some side effects like nausea, hair loss, mouth ulcer and lowering of the blood cells.

Antineoplastic agents have different mode of action and their effect depends upon cytotoxic action which is selective for benign cells i.e. rapidly dividing cells.

**Antineoplastic agents**, also known as **anticancer drugs** or **antineoplastic drugs**, are medications used to treat malignant tumors. These drugs work through various mechanisms to kill or inhibit cancer cells to achieve the goal of treating malignant tumors. Based on their pharmacological actions, antineoplastic drugs can be divided into cytotoxic drugs and non-cytotoxic drugs, with the former primarily consisting of DNA-toxic drugs and the latter mainly comprising molecularly targeted antineoplastic drugs. Commonly used antineoplastic drugs include cisplatin, doxorubicin, paclitaxel, and imatinib.

Traditional cytotoxic drugs, due to their lack of sufficient selectivity for cancer cells, cause varying degrees of damage to normal tissue cells while targeting cancer cells. However, with advancements in tumor molecular biology and translational medicine, antineoplastic drugs have evolved from traditional cytotoxic drugs to non-cytotoxic drugs. Non-cytotoxic drugs are characterized by high selectivity and a high therapeutic index, offering significant clinical advantages.

## Uses

Antineoplastic drugs are primarily used in medical settings to treat cancer.<sup>[4]</sup> Because some antineoplastic drugs also exhibit antiviral activity, they are used to treat certain viral infectious diseases. Certain steroid hormone drugs (used in endocrine therapy), although lacking direct antineoplastic activity, can regulate hormonal balance in the body and suppress certain functional adenocarcinomas, making them commonly used in combination therapies with antineoplastic drugs. Additionally, antineoplastic drugs are employed in scientific research to further understand the molecular biology of cancer through studies of their pharmacological effects.

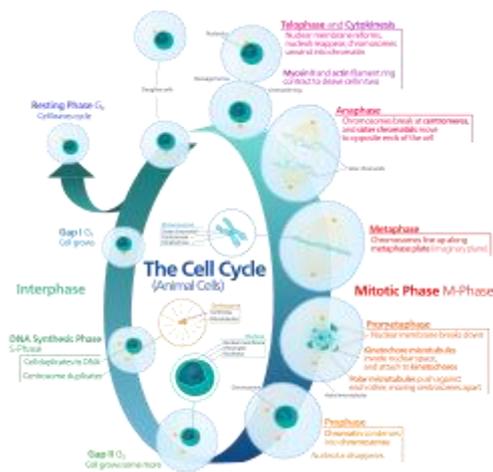
## Classification

The variety of antineoplastic drugs used in clinical practice is extensive and rapidly evolving, with classification not yet fully standardized. Generally, they are categorized based on their pharmacological actions and targets.

### General classification

Cytotoxic drugs	Drugs directly acting on DNA	<ul style="list-style-type: none"> <li>Alkylating agents (nitrogen mustards, aziridines, mesylate, nitrosourea, etc.)</li> <li>Metal platinum complexes</li> <li>Bleomycins</li> <li>DNA topoisomerase inhibitors (drugs acting on DNA topoisomerase 1, drugs acting on DNA topoisomerase 2-beta)</li> </ul>
	Drugs interfering with DNA Synthesis (Antimetabolites)	<ul style="list-style-type: none"> <li>Folic acid antagonists</li> <li>Pyrimidine antagonists (uracil derivatives, cytosine derivatives)</li> <li>Purine antagonists</li> <li>Multi-target antagonists</li> </ul>
	Drugs acting on structural proteins	<ul style="list-style-type: none"> <li>Drugs inhibiting tubulin polymerization (drugs with one binding site on tubulin, drugs with two binding sites on tubulin)</li> <li>Drugs inhibiting tubulin depolymerization</li> <li>Drugs interfering with ribonucleoprotein function</li> <li>Drugs affecting amino acid supply</li> </ul>
Non-Cytotoxic Drugs	Molecularly targeted drugs [zh]	<ul style="list-style-type: none"> <li>Small-molecule kinase inhibitors</li> <li>Proteasome inhibitors</li> <li>Histone deacetylase inhibitors</li> <li>Monoclonal antibody drugs</li> <li>Antisense oligonucleotide drugs</li> </ul>
	Other antineoplastic drugs	<ul style="list-style-type: none"> <li>Drugs regulating hormone balance</li> <li>Drugs with other antineoplastic mechanisms</li> </ul>

### Mechanism of action



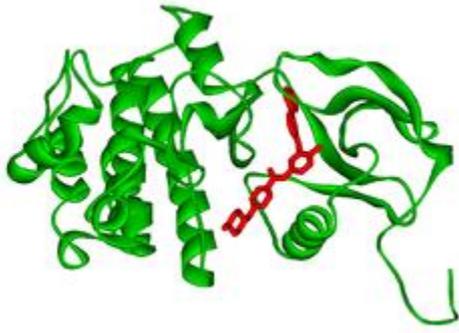
Cytotoxic drugs disrupt tumor cells by affecting one or more phases of the cell cycle but lack specificity, resulting in significant toxicity.

Tumor cell populations include proliferating cells, quiescent cells (G<sub>0</sub> phase), and non-proliferative cells. The ratio of proliferating tumor cells to the total tumor cell population is called the growth fraction (GF). The time from the end of one cell division to the end of the next is called the cell cycle, which consists of four phases: pre-DNA synthesis (G<sub>1</sub> phase), DNA synthesis (S phase), post-DNA synthesis (G<sub>2</sub> phase), and mitosis (M phase).

## Cytotoxic drugs

Cytotoxic drugs exert cytotoxic effects on tumor cells in different phases of the cell cycle and delay phase transitions by affecting biochemical events. Based on their sensitivity to tumor cells in specific phases, cytotoxic drugs are broadly divided into two categories:

1. **Cell cycle non-specific agents (CCNSA):** These drugs kill cells in various phases of the proliferative cycle, including G<sub>0</sub> phase cells, such as drugs that directly damage DNA structure or affect its replication or transcription functions (e.g., alkylating agents, antitumor antibiotics, and platinum complexes). These drugs often have a strong effect on malignant tumor cells, rapidly killing them in a dose-dependent manner, with effects increasing exponentially within the body's tolerable toxicity limits.
2. **Cell cycle (phase) specific agents (CCSA):** These drugs are sensitive only to specific phases of the proliferative cycle and not to G<sub>0</sub> phase cells, such as antimetabolites acting on S-phase cells and vinblastine drugs acting on M-phase cells. These drugs have a weaker effect on tumor cells, with time-dependent cytotoxicity, requiring a certain duration to take effect, and their efficacy does not increase beyond a certain dose.



Bcr-Abl kinase is one of the targets of protein tyrosine kinase inhibitors and was the first specific target identified.

### **Non-cytotoxic drugs**

Non-cytotoxic drugs primarily target key regulatory molecules in tumor molecular pathology processes. Examples include hormones or their antagonists that alter hormone imbalance; protein tyrosine kinase inhibitors, farnesyltransferase inhibitors, MAPK signaling pathway inhibitors, and cell cycle regulators targeting cell signal transduction molecules; monoclonal antibodies targeting proliferation-related cell signal transduction receptors; angiogenesis inhibitors that disrupt or inhibit new blood vessel formation, effectively preventing tumor growth and metastasis; anti-metastatic drugs that reduce cancer cell shedding, adhesion, and basement membrane degradation; and inhibitors targeting telomerase to promote differentiation of malignant tumor cells.