Mechanisms of Action of Anticancer Drugs

Cancer is a group of diseases characterized by uncontrolled cell division, loss of normal growth regulation, and potential to invade and metastasize. Anticancer drugs (chemotherapeutic agents) aim to selectively destroy or inhibit the proliferation of malignant cells while minimizing damage to normal tissues.

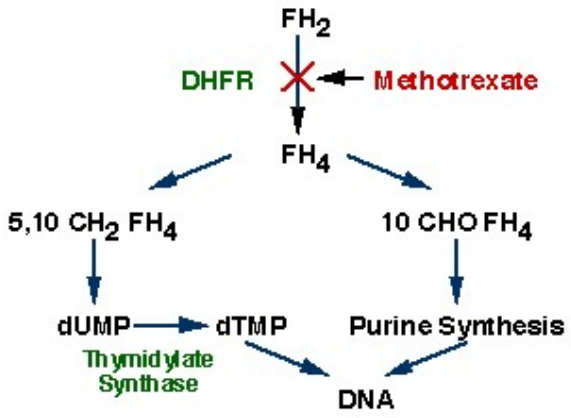
These agents act through various **molecular mechanisms** targeting DNA synthesis, mitotic processes, cell signaling, or specific oncogenic pathways. Understanding their mechanisms is essential for rational drug design, clinical application, and management of drug resistance.

Mechanisms of Anticancer Drugs

There are variety of drug that is being used to treat the disease. Based on their similary in action it can be categoried in following ways-

Inhibition of DNA Synthesis and Function

Certain anticancer drugs act by directly interfering with the genetic material of cells, disrupting DNA replication and transcription. This interference halts the cell cycle and often triggers programmed cell death, or apoptosis. Cyclophosphamid, Cisplatin, Methotrexate, 5-Fluorouracil.



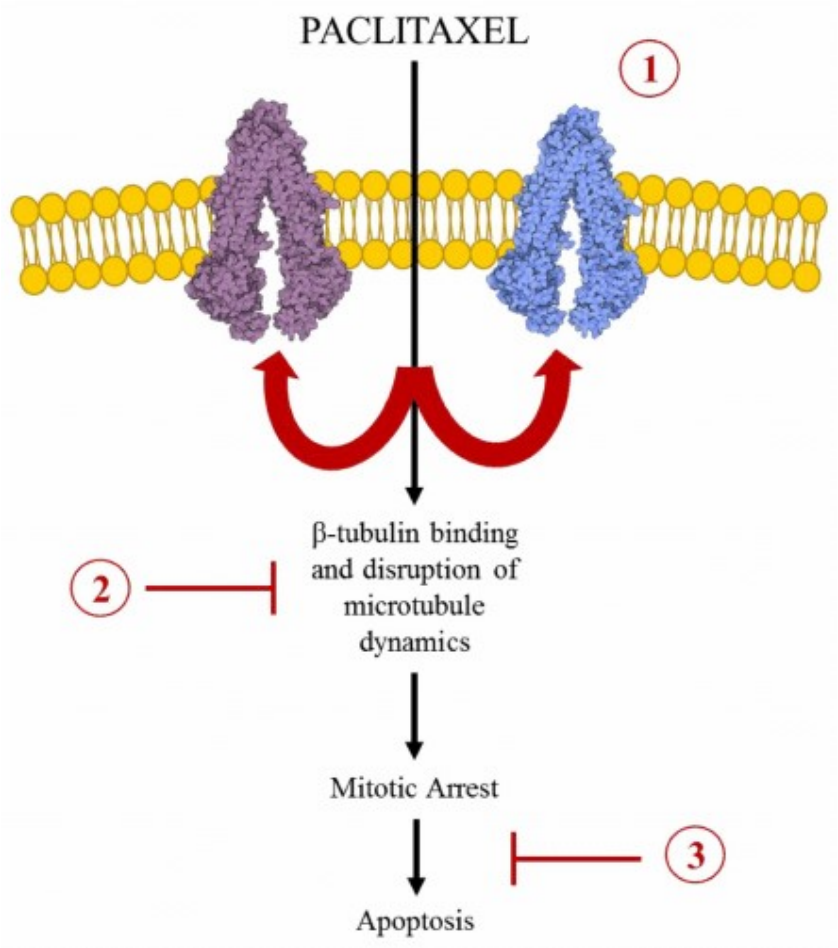
Within the cell, folic acid undergoes a series of transformations to become active forms such as tetrahydrofolate (FH4). Tetrahydrofolate plays a vital role in transferring one-carbon units necessary for the synthesis of nucleotides— the building blocks of DNA.

Methotrexate exerts its effect by inhibiting the enzyme dihydrofolate reductase (DHFR). Normally, DHFR converts dihydrofolate (FH2) into tetrahydrofolate (FH4). When methotrexate binds to DHFR, it blocks this conversion. As a result, the cell's supply of tetrahydrofolate decreases.

Without sufficient tetrahydrofolate, the cell cannot produce thymidylate (dTMP) or purine nucleotides, both of which are essential for DNA synthesis. This shortage causes a disruption in DNA replication and repair, especially in rapidly dividing cells such as cancer cells. Consequently, methotrexate treatment leads to cell cycle arrest and eventually cell death.

Inhibition of Microtubule Function (Mitotic Inhibitors)

During cell division, microtubules form the mitotic spindle, which ensures proper chromosome separation. Some drugs target these structures to block mitosis. E.g. **Vincristine, Vinblastine**, **Paclitaxel and Docetaxel**



Paclitaxel works by binding to β-tubulin, a protein that is a key component of microtubules within the cell. Microtubules are essential for the process of mitosis, as they form the mitotic spindle required to separate chromosomes during cell division. By attaching to β-tubulin, paclitaxel stabilizes the microtubules and prevents their normal dynamic breakdown, which is crucial for proper mitotic progression. This disruption of microtubule dynamics causes the cell to become arrested during

mitosis, unable to complete division. As a result of this prolonged mitotic arrest, the affected cells trigger apoptotic pathways, leading to programmed cell death.

Inhibition of Topoisomerase Enzymes

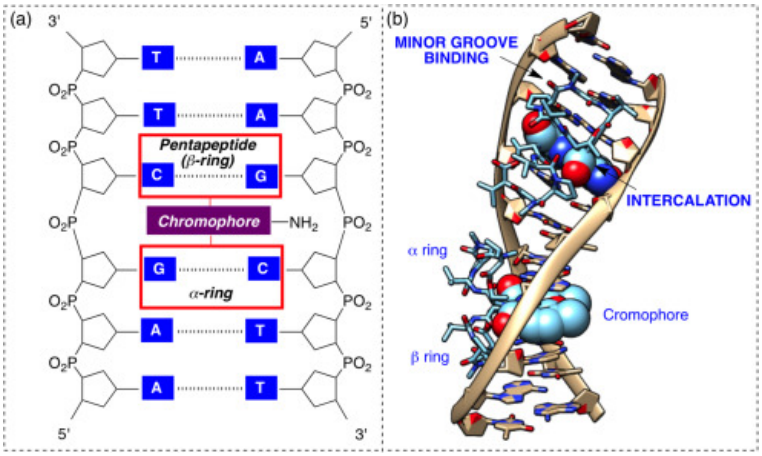
Topoisomerases are enzymes that relieve DNA supercoiling during replication and transcription. Inhibiting these enzymes causes DNA strand breaks.

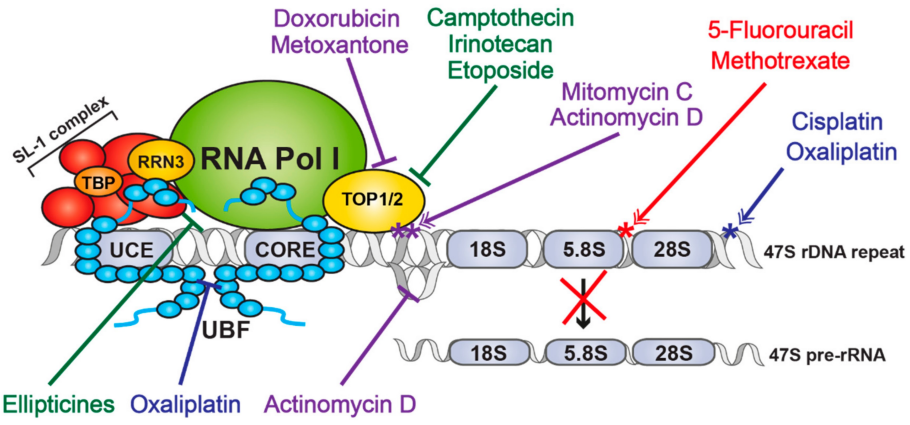
- **Topoisomerase I inhibitors** (e.g., Irinotecan, Topotecan) create single-strand breaks.
- **Topoisomerase II inhibitors** (e.g., Etoposide, Doxorubicin) induce double-strand breaks.

The accumulation of these DNA damages leads to cell death.

Intercalating Agents (Antitumor Antibiotics)

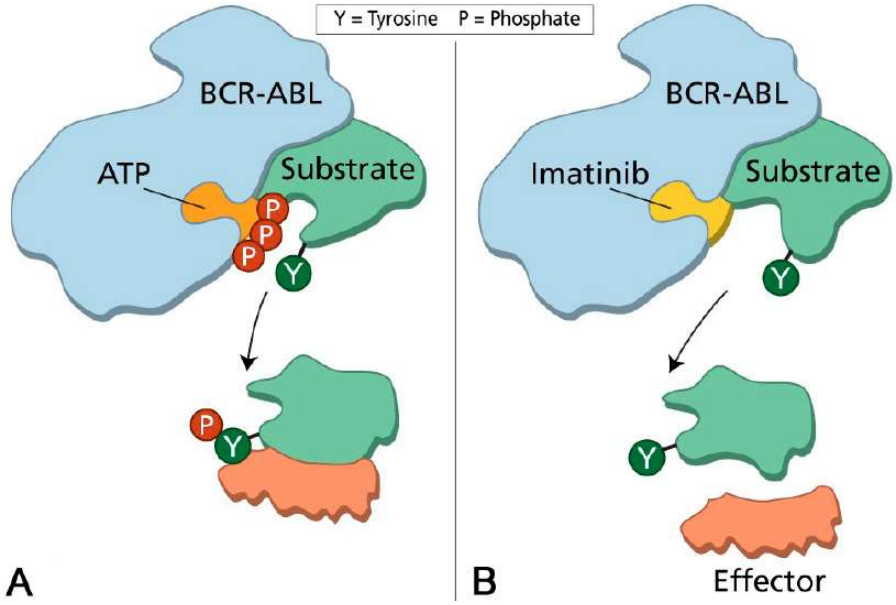
These drugs insert themselves between DNA base pairs, distorting the double helix and preventing DNA and RNA polymerases from working. Examples include **Doxorubicin, Daunorubicin, and Actinomycin D**. They can also generate free radicals that further damage DNA. This results in the inhibition of replication, transcription, and triggers apoptosis.





Targeted Therapy and Signal Transduction Inhibitors

Modern cancer treatments often aim at specific molecular targets or signaling pathways that drive tumor growth. For example, **Imatinib** targets the BCR-ABL kinase in chronic myeloid leukemia by blocking its ATP-binding site, stopping abnormal signaling that promotes cell growth



Hormone and Hormone Antagonists

Some tumors grow in response to hormones. Drugs in this category either reduce hormone production or block their receptors. e.g., Tamoxifen, block estrogen receptors in breast tissue. Or Anastrozole, prevent estrogen synthesis. The result is a reduction in hormone-driven tumor growth.

Immunotherapy

Cancer treatment now also includes therapies that boost the body's immune response against tumors.

- **Checkpoint inhibitors** such as **Pembrolizumab (anti-PD-1)** and **Ipilimumab (anti-CTLA-4)** remove the brakes on T cells, allowing them to recognize and destroy cancer cells.

The outcome is the reactivation of the immune system to attack the tumor