Anticancer drugs

1) Cisplatin

- Platinum coordination compounds

MOA

- Enters cells → hydrolysed intracellularly → produces a highly reactive moiety
  - also react with SH groups of cytoplasmic & nuclear proteins
  - cross linking of DNA (Cite: N^7 of guanine residue)

PK

- Slowly excreted unchanged in urine

Therapeutic uses:

* Metastatic testicular & ovarian carcinoma
* Solid tumors – eg. lungs, stomach, liver

AOR

* Highly emetogenic
* Renal impairment – ∴ Normal saline is infused IV before cisplatin to reduce toxicity.

2) Alkylating agents

- Nitrogen mustards – Cyclophosphamide
- Ethylenimine
- Alkylsulfonate
- Nitrosoureas
- Triazine
- Methyl hydrazine

MOA:

- Produce highly reactive carbonium ion intermediates
  - ↓
  - transfers alkyl groups to cellular macromolecules by forming covalent bonds
- Alkylating agents may react with carboxyl, hydroxyl, amino, sulfhydryl
- Alkylation results in cross linking / abnormal base pairing

3) Methotrexate

- Folic acid analogue
- Dihydrofolic acid
  - ↓ DHF reductase
- Tetrahydrofolate acid ← essential for denovo purine synthesis

→ * Also it enters into cells & is transformed to more active polyglutamate form by the enzyme FPGS

* kills cells in S-phase

- inhibits thymidylate synthase ∴ DNA synthesis affected

ADR

- BM depression → megaloblastic anemia, pancytopenia
- diarrhea
- Alopecia

PK

- orally.
- excreted unchanged in urine

MTX toxicity → Antidote : Folinic acid

Uses :

- Choriocarcinoma
- ALL
- NHL
- Breast, bladder, osteogenic sarcoma
- RA, psoriasis, AI disorders.

4) Azathioprine

acts by getting converted to 6-mercaptopurine (6-MP)

Antineoplastic action : of 6-MP

Inosine monophosphate

↓

guanine & adenine } same MOA for mercaptopurine.

building blocks of RNA & DNA

Immunosuppressant actions :

Selective uptake into immune cells & intracellular conversion to 6-MP, inhibits denova & DNA synthesis

Uses :- Suppress cell

AI

6) Vinca alkaloids

- mitotic inhibitors

MOA:

Vinca + tubulin → microtubulous protein

↓

prevent polymerization & assembly of microtubules

↓

cause disruption of mitotic spindle

↓

interfere with cytoskeletal function

- chromosomes fail to move apart during mitosis → metaphase arrest
- cell cycle specific
- Acts in mitotic phase

VINCRISTINE

- Rapidly acting

Uses:

- Induce remission in child hood ALL
- AML
- Hodgkin's HL
- Wilms
- Ewing's
- neuroblastoma
- Ca lung

ADR

- Peripheral neuropathy, alopecia
- Ataxia, nerve palsies
- Autonomic dysfunction
- Seizures
- Bm depression - minimal

VINBLASTINE

- Hodgkin's
- Non-Hodgkins
- Kaposi
- Neuroblastoma
- Breast & testicular carcinoma.

ADR.: Bm depression - prominent, neurotoxicity & alopecia less marked.