

# Anticancer drugs

## 1) Cisplatin

- Platinum coordination compounds

MOA:

- enters cells  $\rightarrow$  hydrolysed intracellularly  $\rightarrow$  produces a highly reactive moiety

also react with SH groups  
of cytoplasmic & nuclear  
proteins

cross linking of DNA  
(site is N<sup>7</sup> of guanine residue)

PK

- slowly excreted unchanged in urine

Therapeutic uses:

\* metastatic testicular & ovarian carcinoma

\* Solid tumors - e.g. lungs, stomach, liver

ADR

\* Highly emetogenic

\* Renal impairment -  $\therefore$  Normal saline is infused IV before cisplatin to reduce toxicity.

## 2) Alkylating agents

- Nitrogen mustard - Cyclophosphamide

- Ethylenimine

- Alkylsulfonate

- Nitrosoureas

- Thiazine

- Methyl hydrazine

MOA:

- Produce highly reactive carbonium ion intermediates

$\downarrow$   
transfers alkyl groups  $\rightarrow$  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

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Dihydrofolic acid

$\downarrow$  DHF ~~inhibitor~~

Tetrahydrofolic acid  $\leftarrow$  essential for de novo purine synthesis

- \* Also it enters into cells & is transformed to more active polyglutamate form by the enzyme FPCs

- \* Kills cells in S-phase

- inhibits thymidylate synthase  $\therefore$  DNA synthesis affected

ADR

- BM depression  $\rightarrow$  megaloblastic anemia, pancytopenia

- Anorexia

- Alopecia

PK

- orally

- Excreted unchanged in urine

MTX toxicity  $\rightarrow$  Antidote: Folic acid

Uses

- Chemoprevention

- ALL

- NHL

- Breast, bladder, osteogenic sarcoma

- RA, psoriasis, AI disorders

4) Azathioprine

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

Antineoplastic action  $\approx$  of 6-MP

Inosine monophosphate

$\times$

guanine & adenine

building blocks of RNA & DNA

} some may lose mercaptopurine

Immunosuppressant actions:

Selective uptake into tumour cells & intracellular conversion to 6-MP,  
inhibits de novo & DNA synthesis

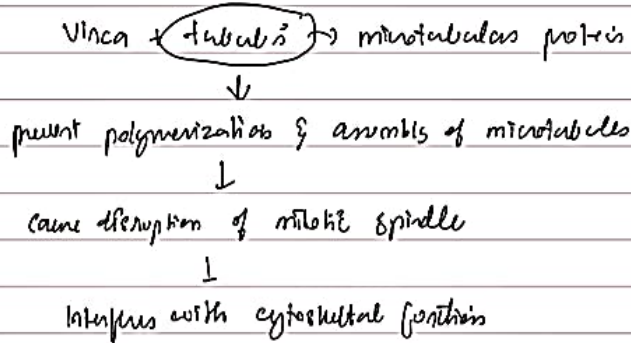
Uses - suppress (ms)

AI

## 6) Vinca alkaloids

- mitotic inhibitors

mechanism:



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

### VINCERISTINE

- rapidly acting

uses:

- Induces remission in childhood ALL
- AML
- Hodgkin's HL
- Wilms
- Ewing's
- neuroblastoma
- Ca lung

ADR:

- peripheral neuropathy & alopecia
- Ataxia, nerve paresthesias
- Autonomic dysfunction
- seizures
- 80% depression - minimal

### VINBLASTINE

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

ADR: 80% depression - prominent; neurotoxicity & alopecia less marked.