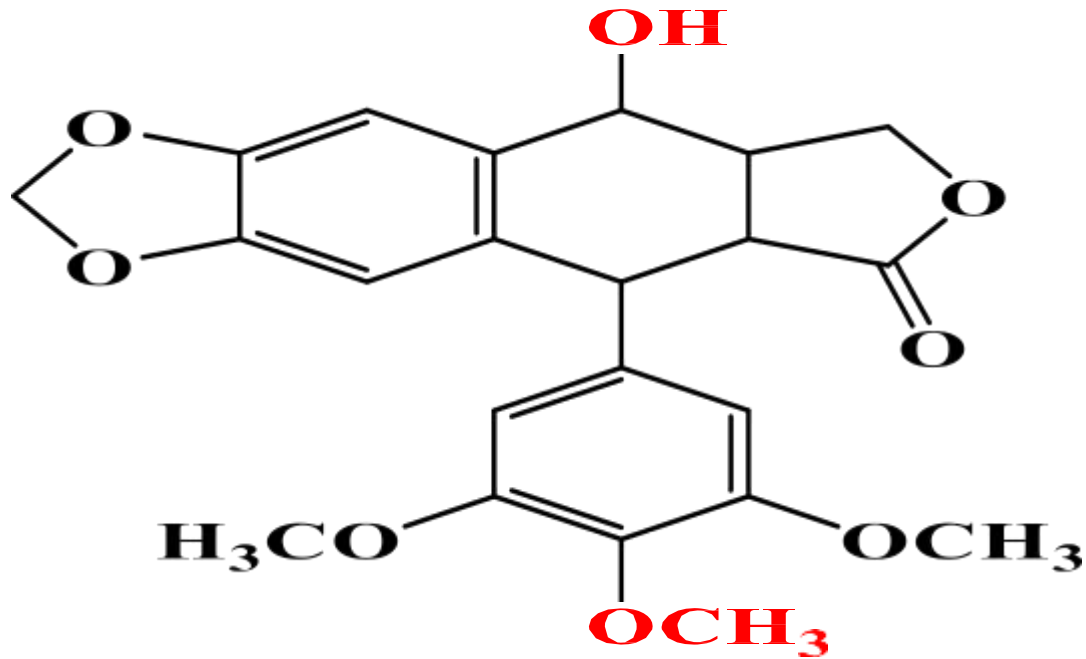


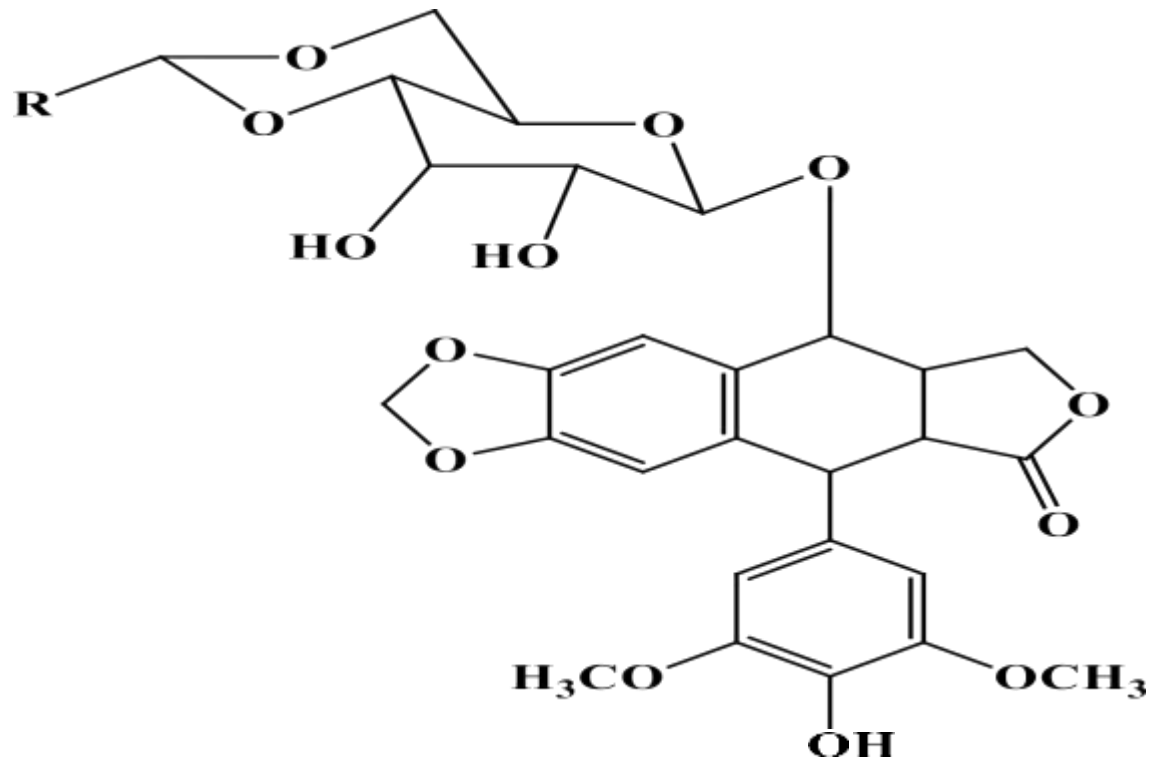
Plant products(Natural products)

- **Podophyllotoxin (Tubulin inhibitor) :-**



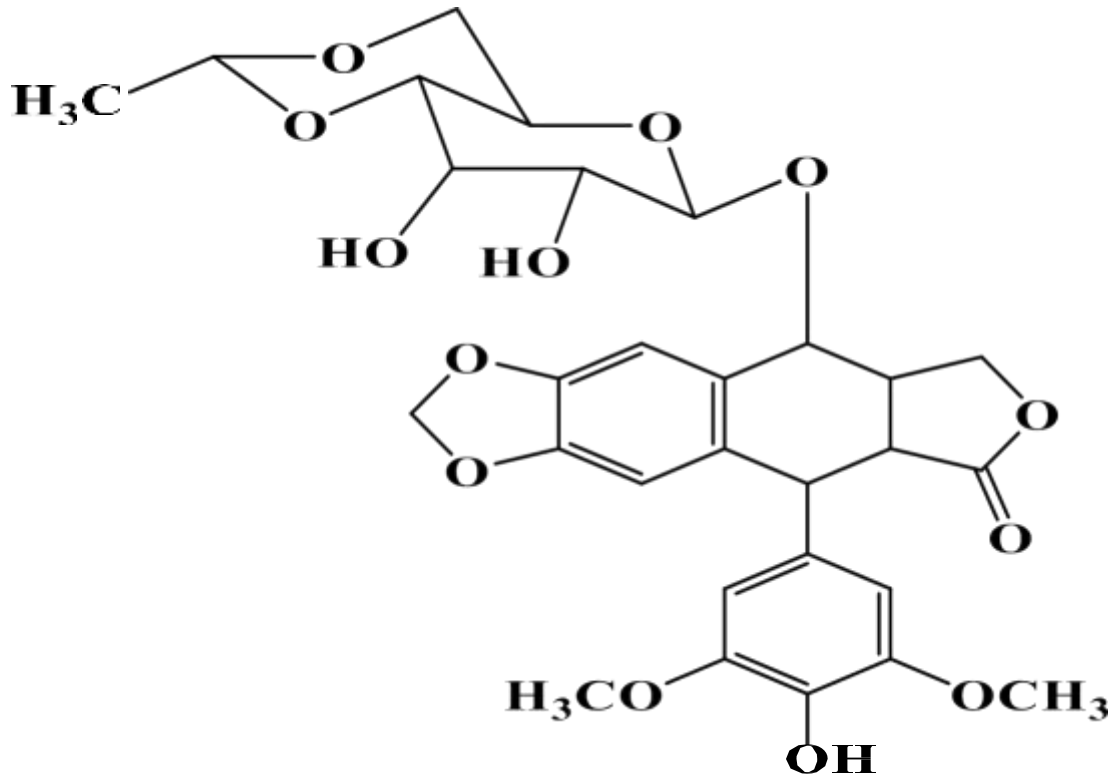
Podophyllotoxin

The epipodophyllotoxins:- are semisynthetic derivatives of podophyllotoxin :-



Epipodophyllotoxin

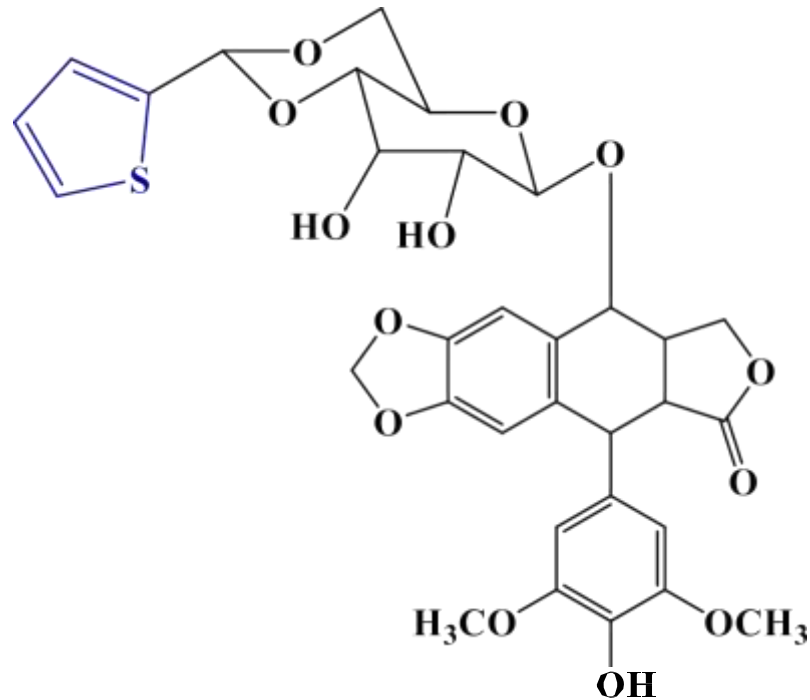
Etoposide



Etoposide

Uses:- The agent is approved for use in testicular cancer and small cell lung cancer. It has also been used in a wide variety of cancers including NSCLC, Hodgkin's and non-Hodgkin's disease, Kaposi sarcoma, acute lymphocytic leukemia, neuroblastoma, choriocarcinoma, and epithelial, ovarian, gastric, endometrial, and breast cancers

Tenoposide•



Teniposide

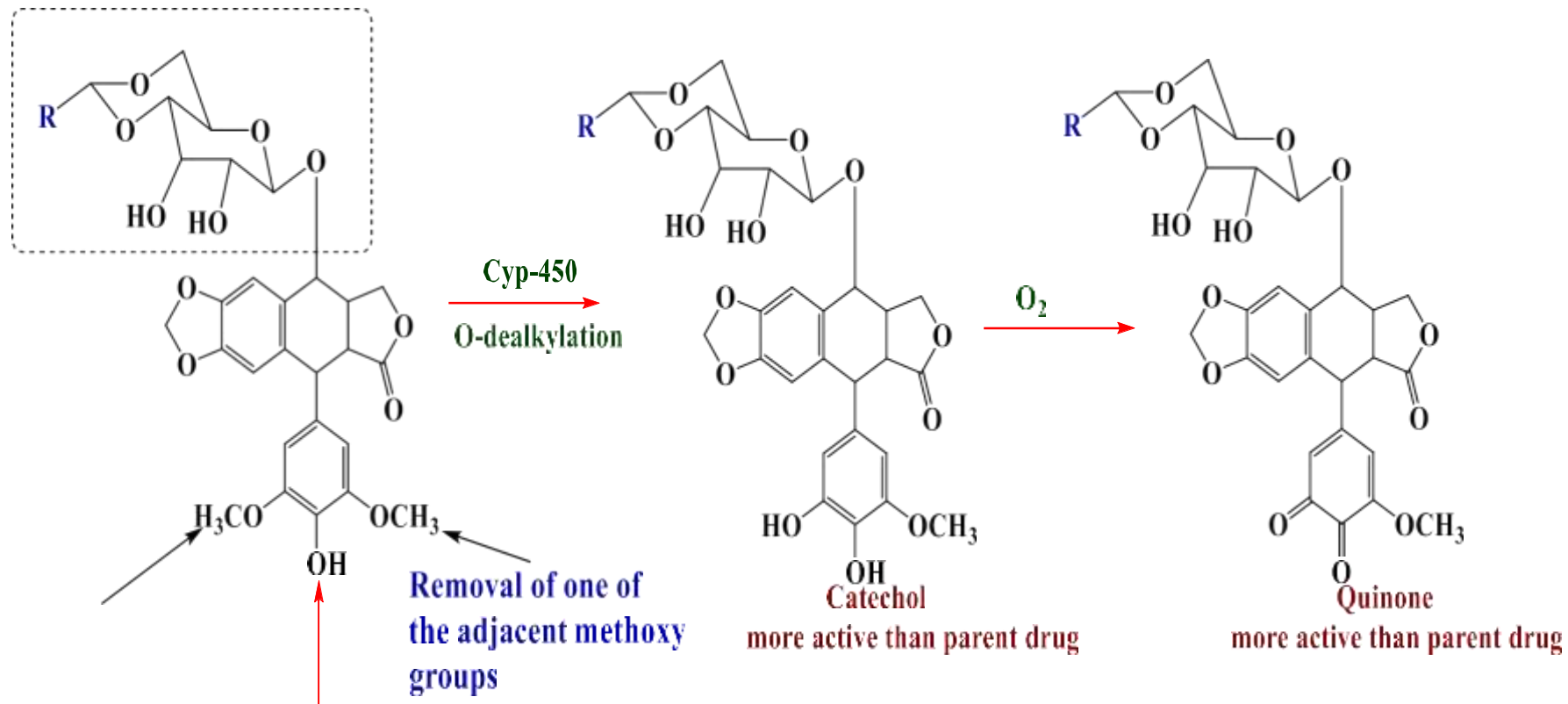
Replacement of the glycosidic 8-methyl group with thiophene gives teniposide, which is 10-fold more potent than etoposide

Uses:- treatment of acute lymphoplastic leukemia(ALL).

SAR

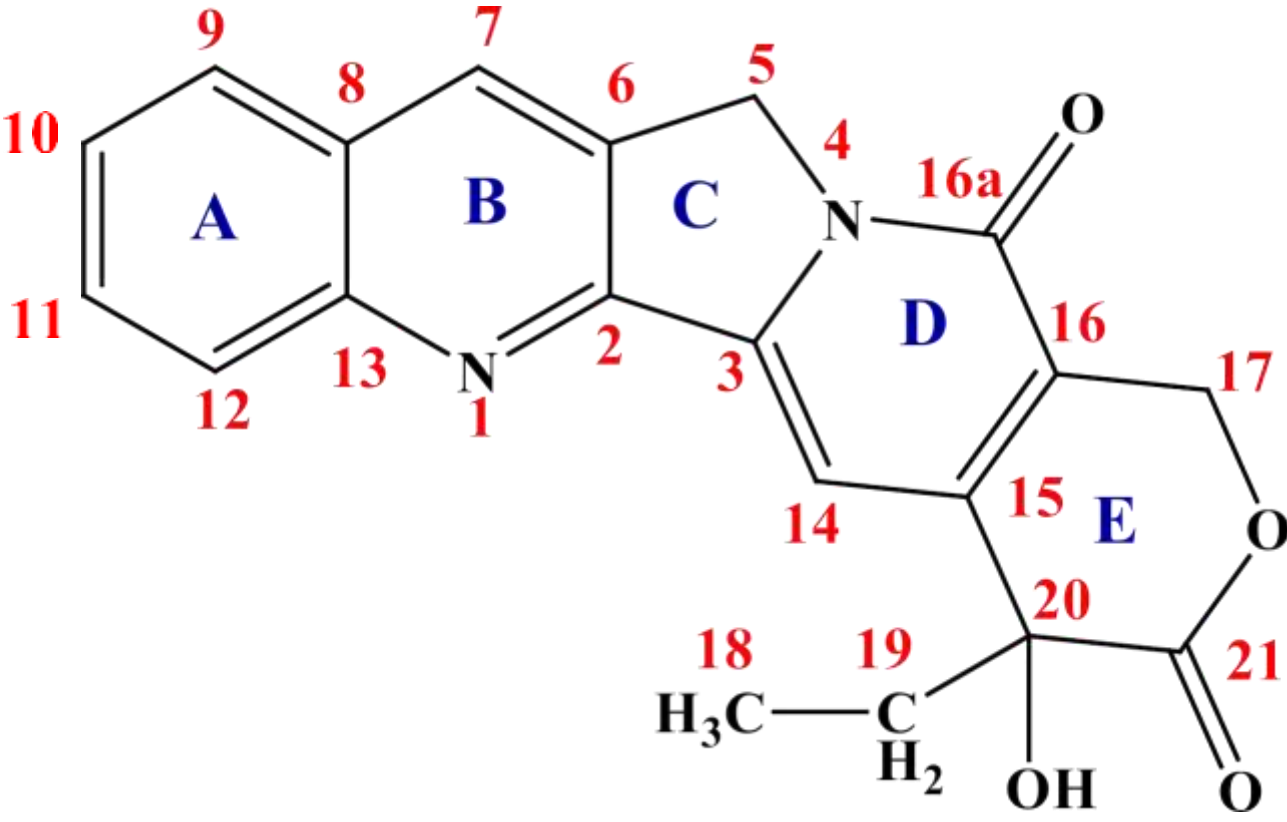
substitution the glycosidic moiety at 4-OH of podophyllotoxins

Tubulin inhibitor
↓
Topoisomerase inhibitor



4'-OH group is important for the activity

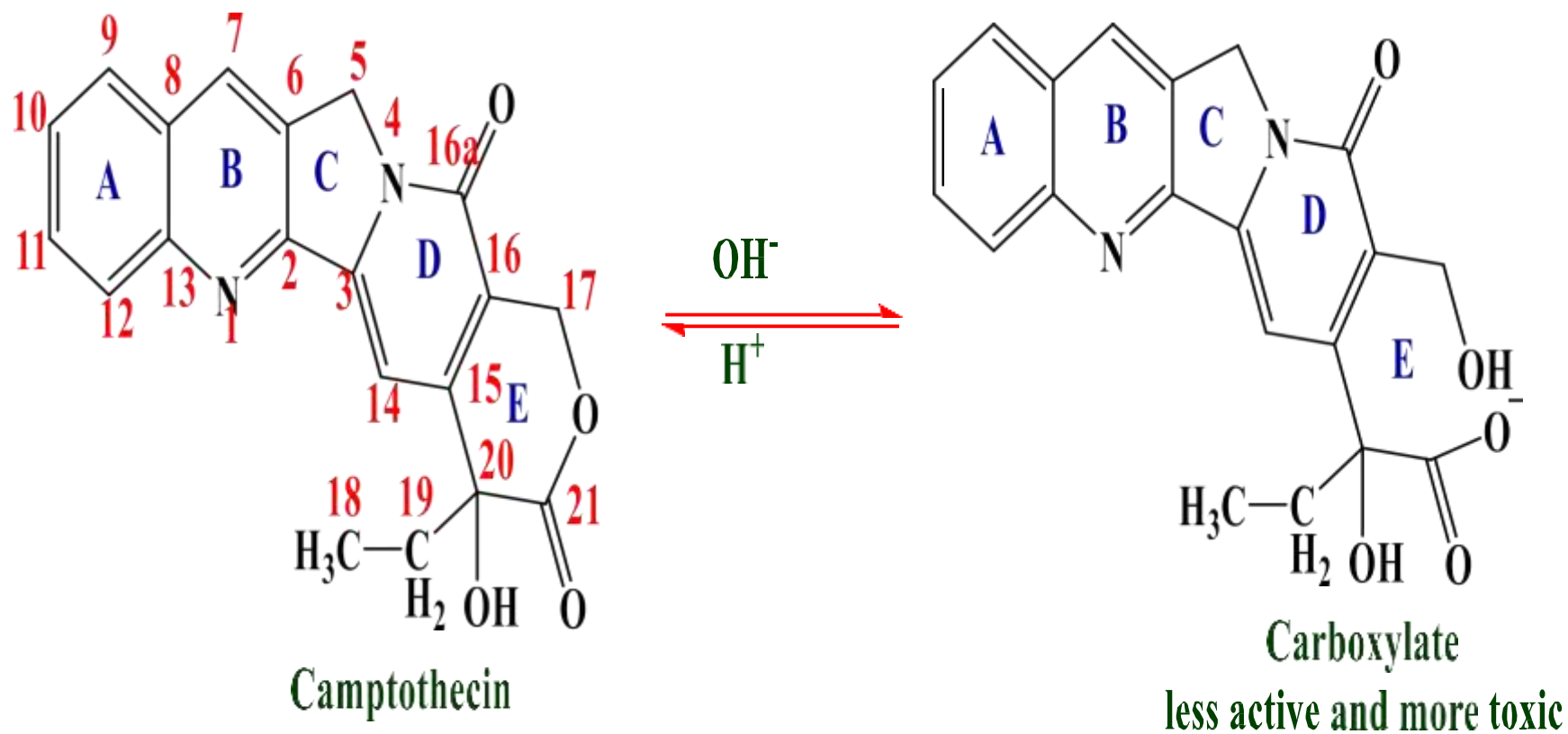
Camptothecins:- are inhibitors of topoisomerase I and •
are used clinically for the treatment of various cancers. •



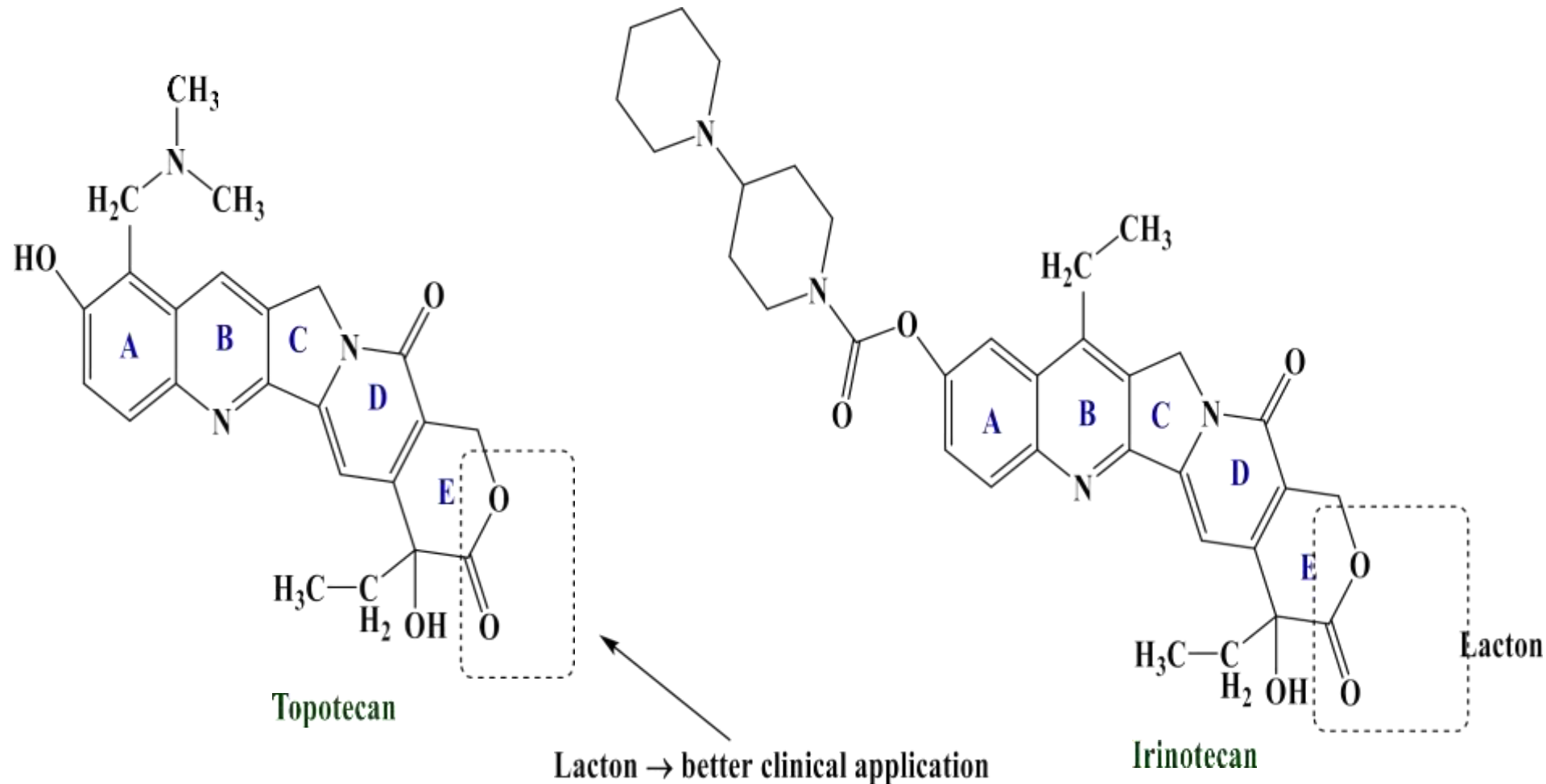
Camptothecin

Camptothecin had low water solubility

1- The sodium salt had been prepared.

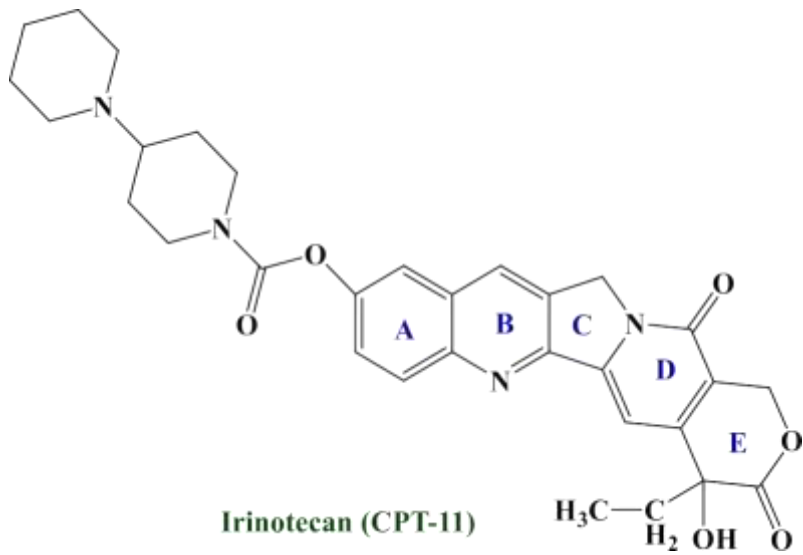


2- The incorporation of side chains containing basic amines

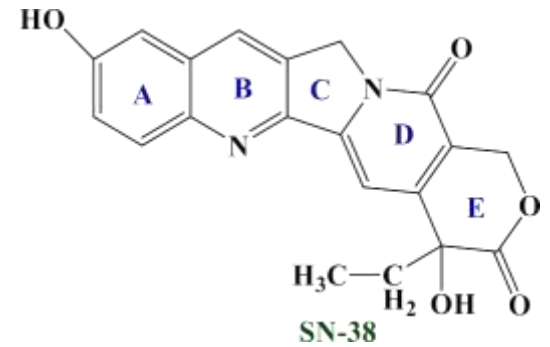


Several mechanisms of resistance to the camptothecin analogs are known.

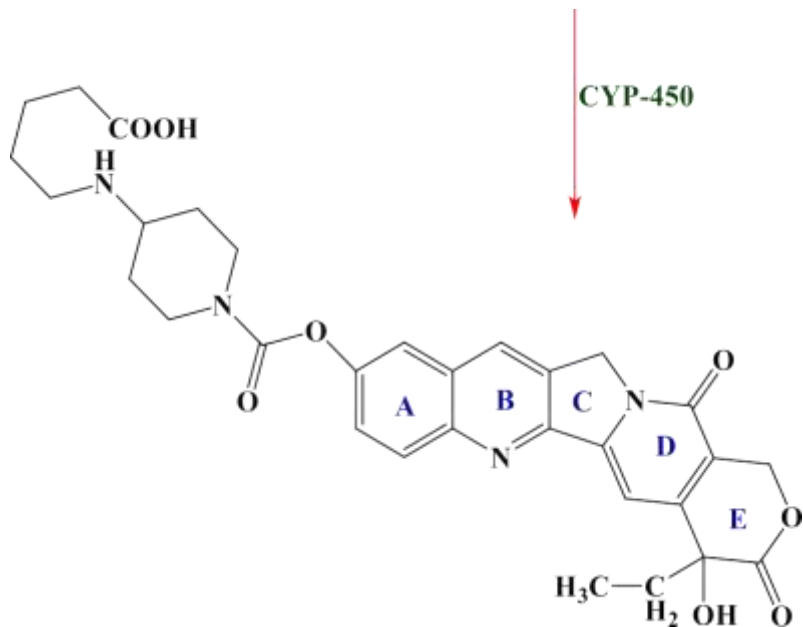
- 1- Decrease expression different levels of topoisomerase I.**
- 2- Increased DNA-repair enzymes may limit the damage to DNA.**



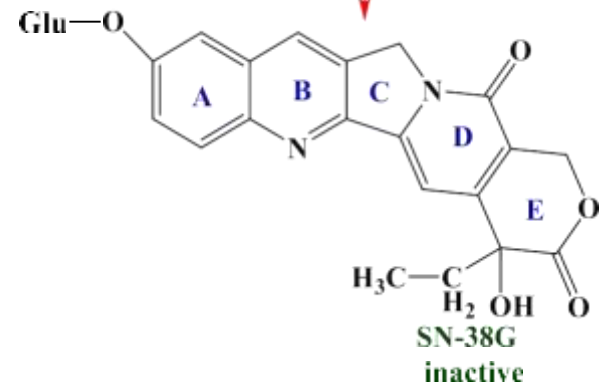
irinotecan carboxylesterase
converting enzyme



1,000 times more potent than the parent compound



CYP-450

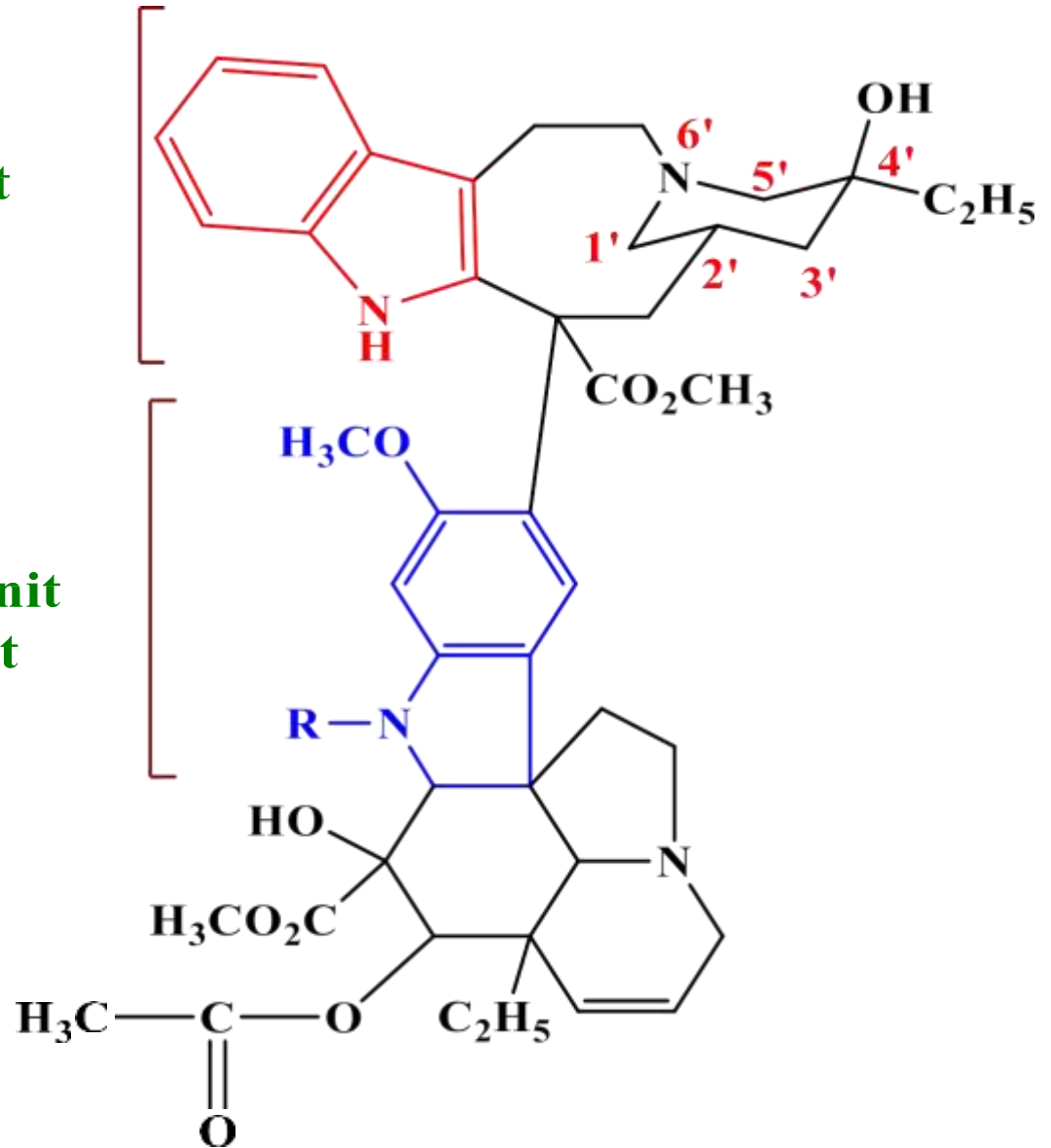


which is 100 times less active than SN-38

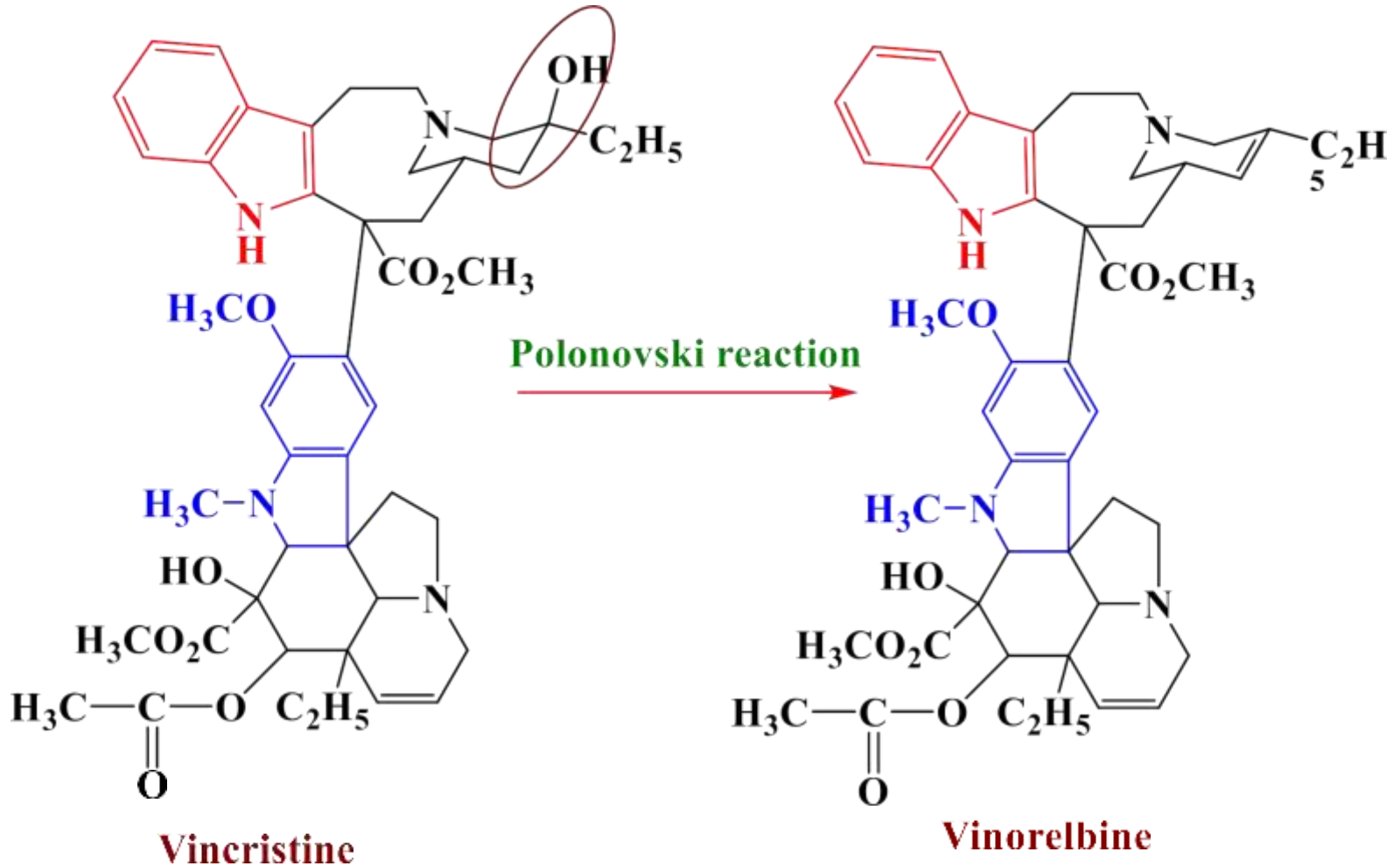
Vinca alkaloids:-

**Catharanthine subunit
indole subunit**

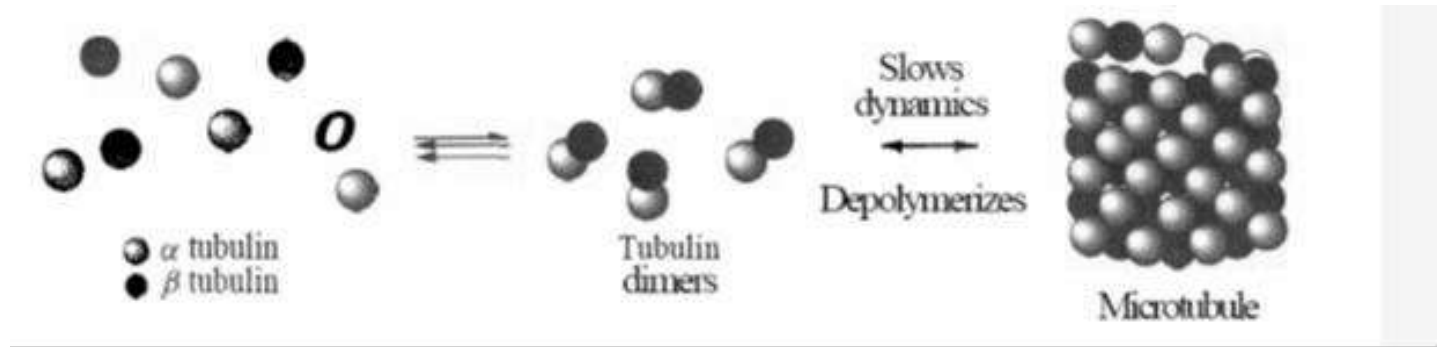
**Vindoline subunit
indoline subunit**



Vinorelbine is a semisynthetic material resulting from loss of water across the 3',4' bond



Mode of action (microtubuline inhibitor)



prevents proper chromosome formation ← preventing its polymerization into microtubules.

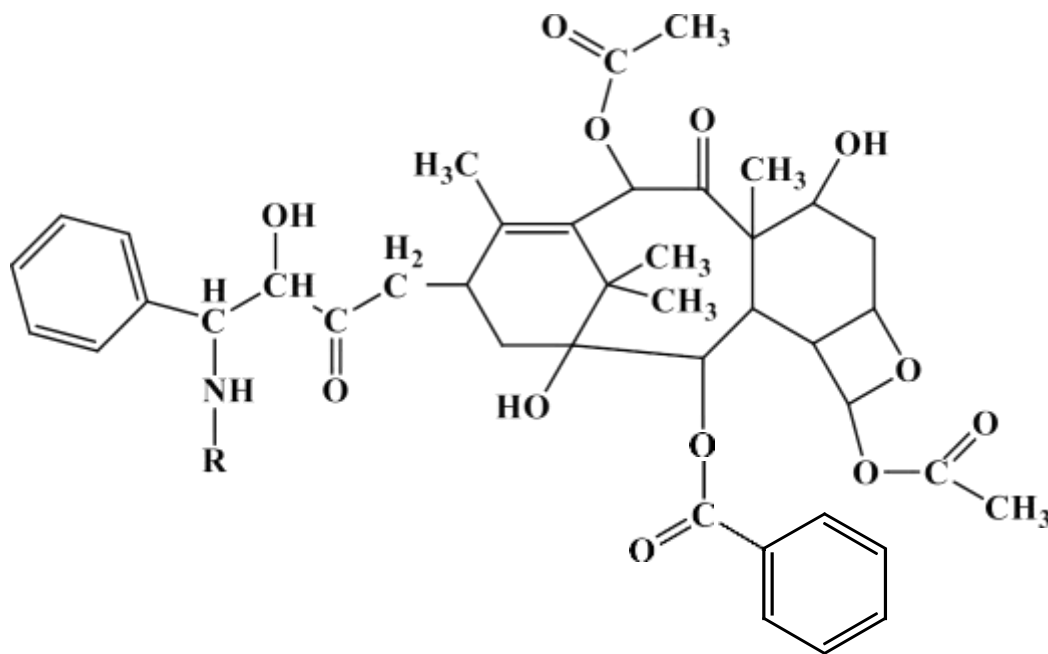
prevent cell division → The blocked cells then die (become apoptosis)

Uses of vinblastine sulfate:- Vinblastine is part of the ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) regimen used in the treatment of Hodgkin's lymphoma. This may be alternated with the MOPP regimen.

Uses of vincristine sulfate(Oncovin):- treatment of acute leukemia and as part of a multidrug regime for Hodgkin's and non-Hodgkin's lymphoma

Taxanes•

The taxanes, specifically, taxol (or paclitaxel) was discovered in the 1960s. proved to be active against various cancer models.



Taxol

Paclitaxel R= -(C=O)-ph

cancer. **Uses:** -Ovarian, breast, and non small lung

Mode of action (microtubule stabilizing agent)

Paclitaxel inhibits mitosis by acting as a spindle poison ; however, it acts by a unique mechanism in promoting the assembly of microtubules and stabilizing them against depolymerization. This mechanism is in contrast to that of compounds like vinca alkaloids, which prevent the assembly of microtubules.

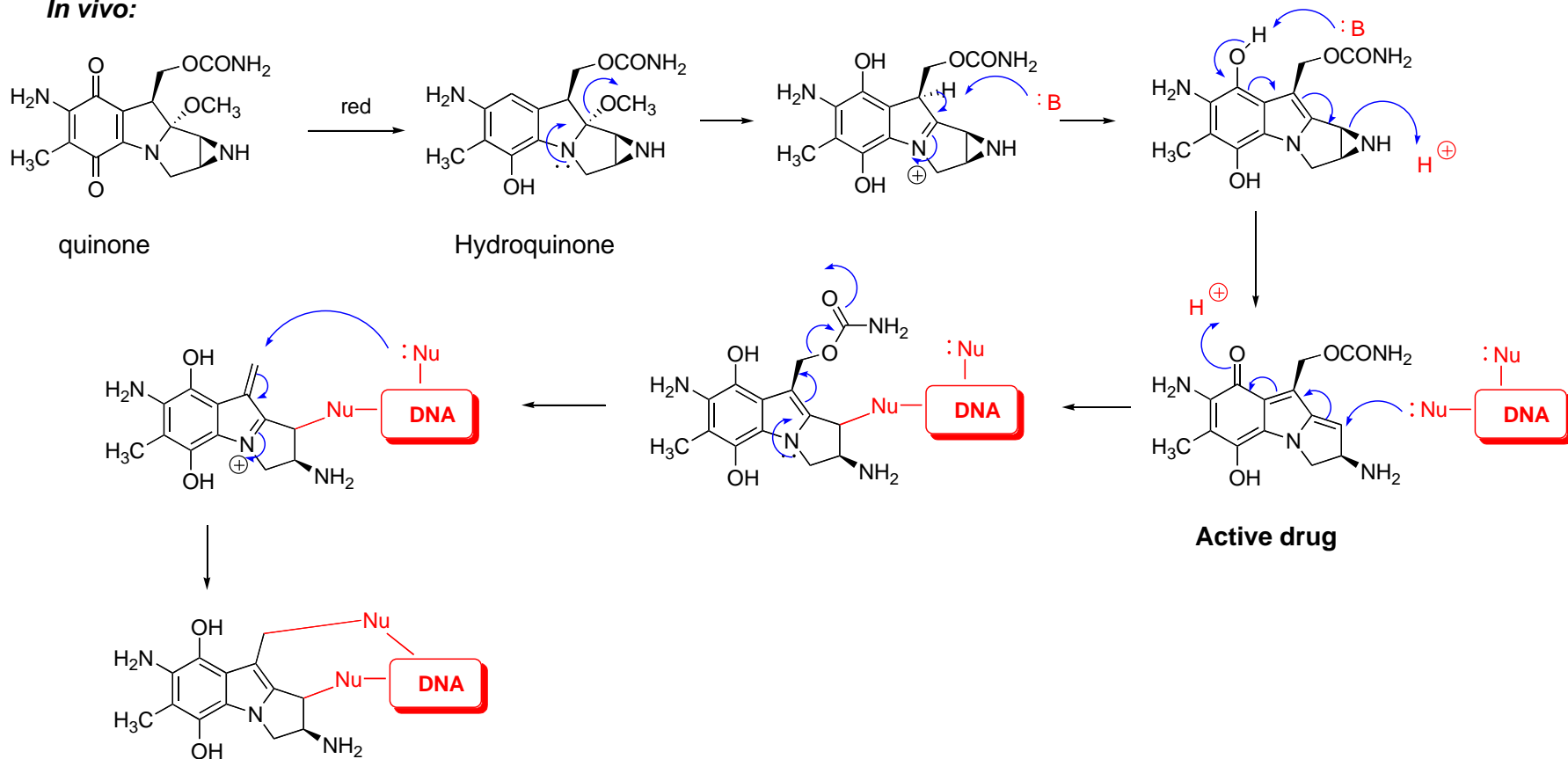
Mitomycins

Isolated *Streptomyces sp.*,

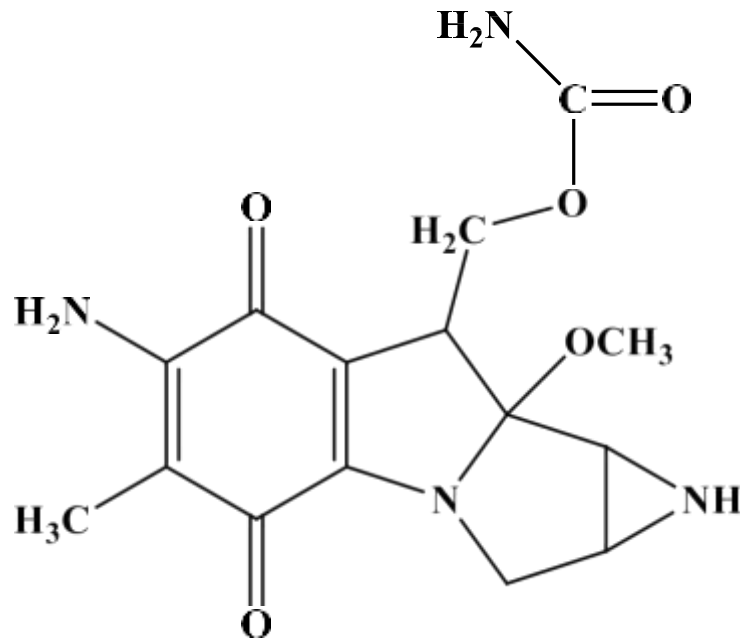
Mitomycin C

Mutamycin®

In vivo:



Mitomycin C



Uses:- IV administration in the treatment of cancers of the stomach and pancreas when other treatments have failed. Other uses have included breast, NSCLC, cervical, bladder, and head and neck cancers.