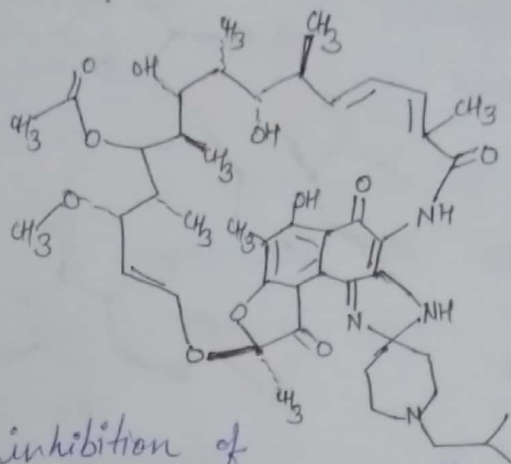


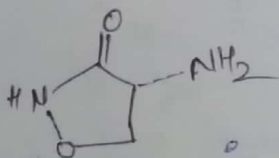
Antitubercular Antibiotics:—① Rifabutin:—

MOA:— It causes inhibition of DNA-dependent RNA polymerase in both gram +ve and some gram -ve bacteria and leads to suppression of RNA synthesis and cell death.

Uses:— ① It is used as an antibacterial and tuberculostatic.

② It is used to treat AIDS patients having Mycobacterium infections and inhibits replication of HIV-I.

③ It is also used to treat Mycobacterium avium complex.

② Cycloserine:

MOA:— It causes interference in bacterial cell wall synthesis in the cytoplasm by competitively inhibiting two enzymes, L-alanine racemase, which forms D-~~alanine~~ alanine from L-alanine and D-alanylanine synthetase, which incorporates D-alanine into the pentapeptide which is required for peptidoglycan formation and bacterial cell wall synthesis.

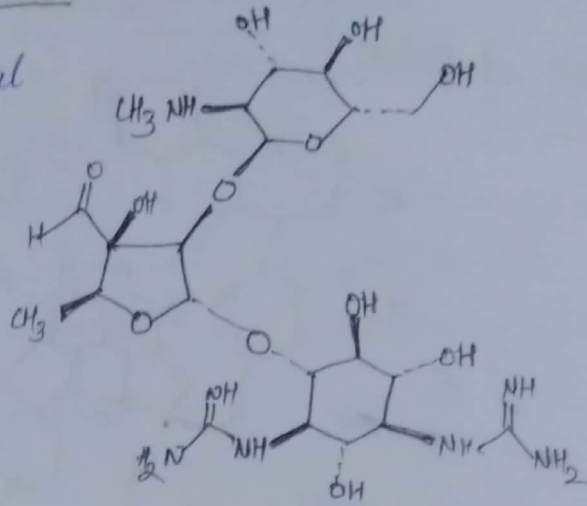
Uses:— ① It is used in combination with other antitubercular drugs in the treatment of tuberculosis.

② It is also used as an anti-infective agent, an antibiotic and as an antimetabolite.

③ It is also used to treat Mycobacterium avium complex.

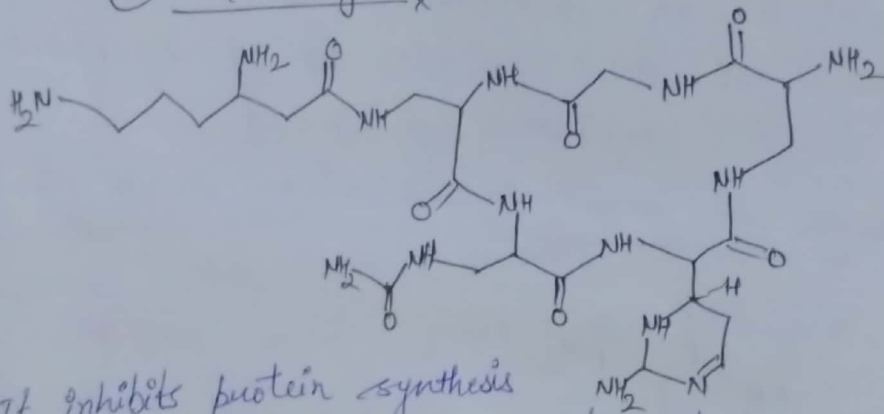
③ Streptomycin

MOA → It binds to the bacterial 30S ribosomal subunit and causes misreading of t-RNA, hence the bacterium becomes unable to synthesize proteins essential for its growth.



Uses → ① It is used as an antibacterial and tuberculostatic.
② It is also used as a fungicide.

④ Capreomycin Sulphate



MOA → It inhibits protein synthesis by binding to the 70S ribosomal unit.

⇒ It also binds to the components in the bacterial cell which results in the production of abnormal proteins.

Uses → It is used as an antibacterial and tuberculostatic.

② It is used in combination with other antitubercular drugs in the treatment of tuberculosis.

Urinary Tract Anti-infective Agents

(2)

- Urinary Tract infections are mainly caused by Escherichia coli, and Staphylococcus saprophyticus.
- It is common in young women.
- UTI are less common in men. and if occur is due to prostatic hypertrophy i.e abnormality of genitourinary tract.
- Generally this infection involves the bladder and urethra.

Symptoms of UTI are:-

- * Burning sensation during micturition
- * Strong and continuous urge to urinate.
- * Pain in pelvic area
- * Red or pink coloured urine.

⇒ Bacteria like E. coli from the large intestine enter the urethra by escaping through the anus and then travel to the bladder and later to the kidney.

⇒ After entering into the bladder E. coli gets attached to the wall of bladder and form a bio-film which resists the body.

⇒ In men the main causative agent for urethritis is Neisseria gonorrhoeae along with Chlamydia trachomatis.

Classification of Urinary tract anti-infective agents:-

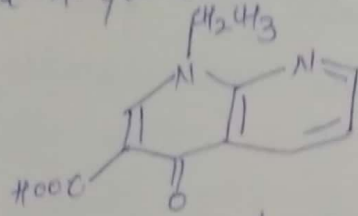
(1) Quinolones:- Nalidixic acid, ciprofloxacin, Norfloxacin, ofloxacin, oxolinic acid, Sparfloxacin, Gatifloxacin, Moxifloxacin, Enoxacin.

(2) Other agents:- Nitrofurantoin, Methanamine, Furazolidone

SAR of Quinolones

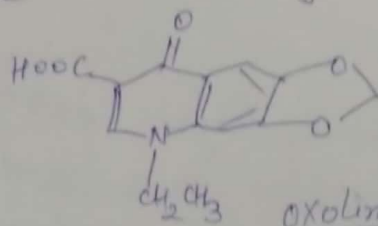
① 1,4-dihydro-4-oxo-3-pyridine carboxylic acid moiety is essential for antibacterial activity.

② Nalidixic acid is the prototype drug in this category. It is an 8-aza-4-quinoline.



Nalidixic acid

③ Side chain of Nalidixic acid to quinoline can be modified to give oxolinic acid having similar actions to Nalidixic acid.

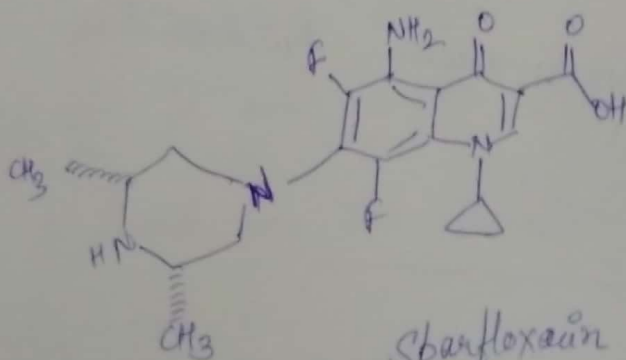


Oxolinic acid

④ Presence of $-COOH$ gp. at C-3 is essential for gyrase binding and bacterial transport. Modification or removal of this gp. abolishes the activity.

⑤ Introduction of fluoro at C-6 and piperazine ring at C-7 gives highly potent drugs. for eg → Iprofloxacin and Norfloxacin

⑥ Subst. at C-7 and C-8 controls potency and Pharmacokinetic of the drug. Introduction of fluoro at C-6 and C-8 gives Sparfloxacin, which has broad spectrum of activity.



Sparfloxacin

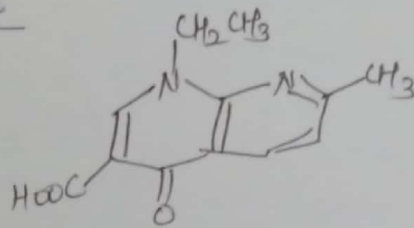
Mechanism of action of Quinalones: $\rightarrow$

Quinalones act as anti-infective agents and treat urinary tract infections by inhibiting the A-subunit of DNA gyrase enzyme (topoisomerase) which is required for reproduction of bacterial DNA. These agents inhibit DNA replication pathway.

$\Rightarrow$ DNA gyrase causes unwinding of DNA in the bacteria. Thus these inhibit this enzyme by binding to the A-subunit as a result of which bacteria is not able to replicate.

① Nalidixic acid

MOA $\rightarrow$ It inhibits bacterial replication by binding to the A-subunit of the enzyme DNA gyrase.

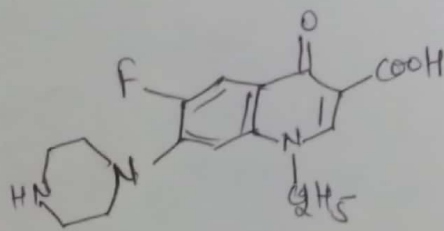


Uses: $\rightarrow$ It is mainly used in the treatment of lower urinary tract infections caused by *E. coli*.

② It is also used as a tool in studying the regulation of bacterial division.

② Norfloxacin

MOA $\rightarrow$ It inhibits enzymes topoisomerase II (DNA gyrase) and topoisomerase IV which are essential for replication, transcription, repair and recombination of bacterial DNA.

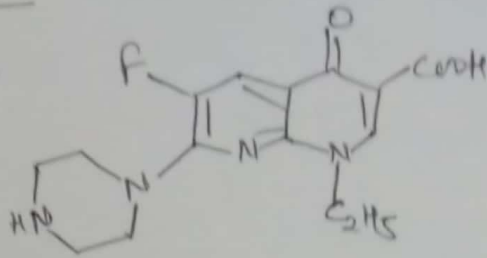


Uses: $\rightarrow$ ① It is used orally for the treatment of UTIs caused by *E. coli*.

② It is used in the treatment of prostatitis and gastro-enteritis.

③ Enoxacin

MOA → Same as Norfloxacin.



Uses → ① It is used in the treatment of UTIs caused by E. coli.

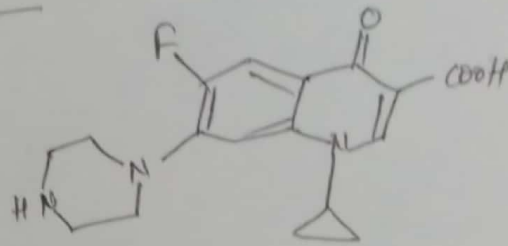
② It is also used in the treatment of diarrhea and respiratory tract infections.

④ Ciprofloxacin

MOA → Same as Norfloxacin.

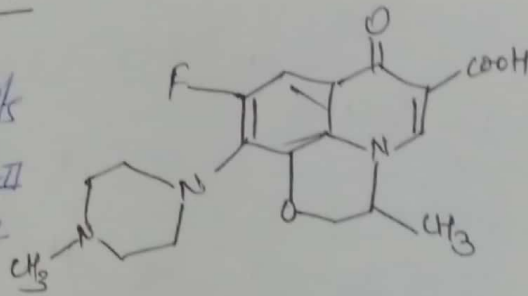
Uses → ① It is used in the treatment of recurrent urinary tract infections and chronic prostatitis caused by E. coli.

② It is also used in the treatment of pneumonia, skin infections and meningitis.



⑤ Ofloxacin

MOA → It binds and inhibits the bacterial topoisomerase-II and topoisomerase-IV enzyme which are involved in DNA replication and repair, resulting in cell death of bacteria.



Uses → ① It is used for the treatment of recurrent urinary tract infections caused by E. coli.

② It is also used in the treatment of acute pelvic inflammatory disease.

③ It is also used in the treatment of lower respiratory tract infections, diarrhea and chronic prostatitis.