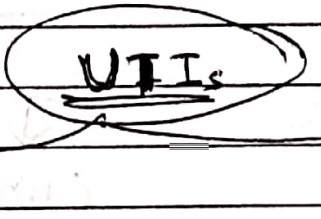
Urinary Tract Anti-Infective Agents

Urinary Tract Infections' (Also called UTIs)

microbial infection of any part of urinary system such as

→ Bladder : Pelvic pain, Pain in urination.
→ Ureter :
→ Urethra :
→ kidney : back pain, nausea, vomiting & fever
↳ More serious



Lower Tract UTI

Upper Tract UTI

(1) Infection in bladder called : Cystitis

Symptoms :- Cloudy / Bloody urine
→ pain in Urination
→ low abdominal pain

(2) Infection in kidney :- Pyelonephritis

fever, Chill, nausea, Vomiting

(3) Urethra infection : Urethritis
- discharg & burning during micturation (Urination)

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Causative agents for UTI

Gram ⊕ (5%)	Gram ⊖ (95%)
Enterococci	E. Coli (Mostly 80%)
Streptococci	~~Proteus~~ Proteus
Staphylococci	Klebsiella
	pseudomonas

Types of UTI:

Acute Infection

→ Very common
→ Urethritis & Cystitis
Acute pyelonephritic

Chronic Infection

→ less common
polyuria
→ Chronic pyelonephritis
Causes hypertension & Chronic renal failure

Treatment of UTI involves

1. Symptomatic relief by altering pH of urine
2. By killing the microbes
3. By prevention & treatment of recurrence
4. By Blocking predisposing factors.

Classification of UTI Anti-infective Agent.

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(1) Bacteriostatic Agents :- Sulphonamides
Tetracyclines.
Nitrofurantoin

(2) Bactericidal agents :- Cotrimoxazole
Ampicillin
Extended spectrum penicillins
Aminoglycosides
Fluoroquinolones
Cephalosporins.

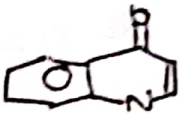
(3) Urinary antiseptics :- Nalidixic Acid
Methenamine mandelate

Quinolones as UTI anti-infectives

→ These are ideal agents against pyelonephritis & complicated UTIs. They are highly effective as oral treatment of UTI.

→ They are active against bacteria resistant to ~~beta~~-lactam & aminoglycosides.

Ex



Classification of Quinolones

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1st generation Quinolones :- Effective against G⊖ but not pseudomonas species
Short half life

Ex Nalidixic Acid, Cinoxacin

IInd generation :- Effective against G⊖ including pseudomonas
Some G⊕ bacteria such as S. aureus

Ex. Norfloxacin, Ciprofloxacin, Ofloxacin enoxacin

IIIrd generation :- Same as IInd generation with extended G⊕ bacteria & atypical Coverage

Ex Levofloxacin, Sparfloxacin, [redacted] Gatifloxacin

IVth generation :- Mainly G⊖ Spetrum, ↑mproved G⊕ coverages Anaerobes coverages

ex Trovafloxacin, Gemifloxacin, Moxifloxacin

Mode of action of Quinolones

Block DNA (bacterial) synthesis

↓

By inhibiting

↓

Topoisomerase-II (G⊖ bacteria)
(Also called DNA gyrase)

↓

Prevent relaxation of positively supercoiled DNA

↓

Required for normal replication & transcription

↓

Stop DNA synthesis & RNA & protein synthesis

Topoisomerase-IV in G⊖ bacteria

↓

Inhibition of this enzyme interfere seperation of replicated Chromosomal DNA into respective daughter cell

↓

During Cell division

↓

Stop cell division or growth

↓

Ultimately Bacterial Cell death

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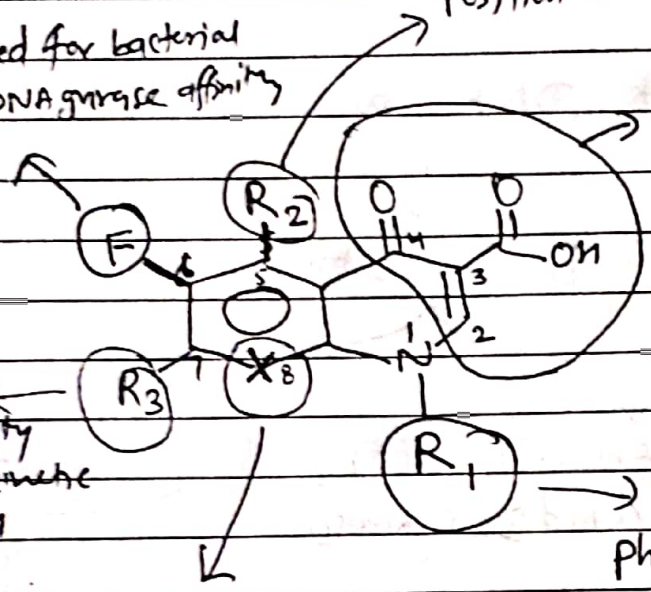
SAR of Quinolones / Fluoroquinolones

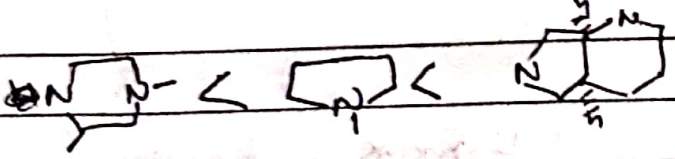


Position – 1 isopropyl > phenyl > allyl

potency increases

Position 5 :- $-NH_2 > -OH > -CH_3$ ↑ G⊕ activity

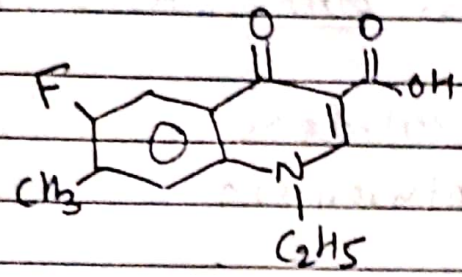
Position 6 :- -F ✓ require for DNA gyrase affinity

Position – 7 :-  for G⊕ activity

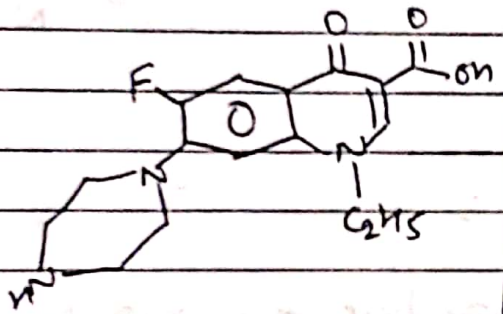
 for G⊖

Fluoroquinolones

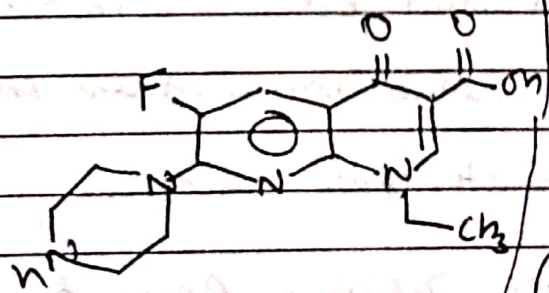
(1) Nalidixic Acid :-



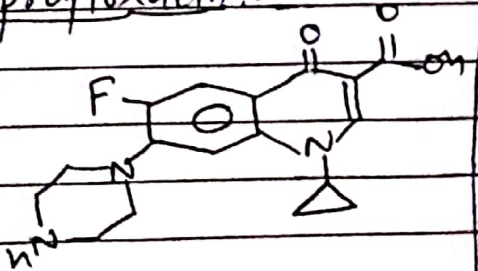
(2) Norfloxacin :-



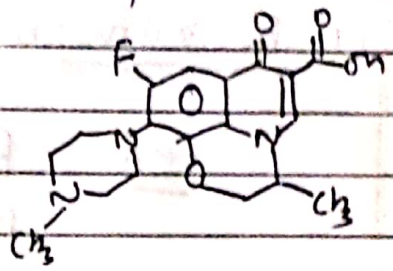
(3) Enoxacin



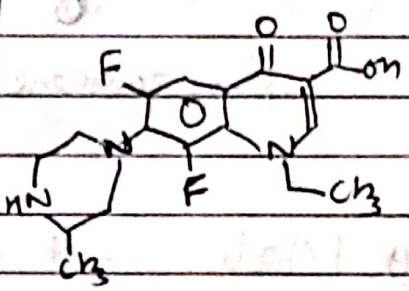
(4) Ciprofloxacin :-



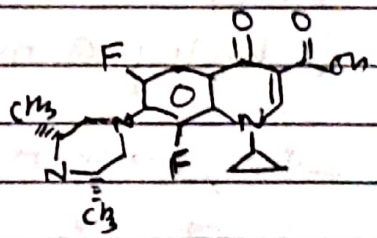
(5) Ofloxacin



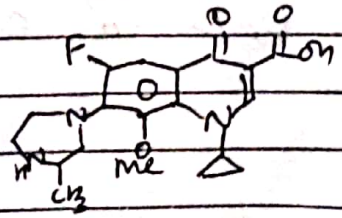
(6) Lomefloxacin



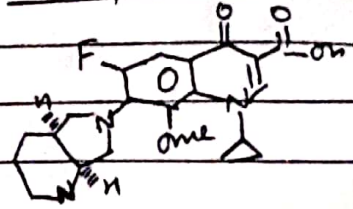
(7) Sparfloxacin



(8) Gatifloxacin :-



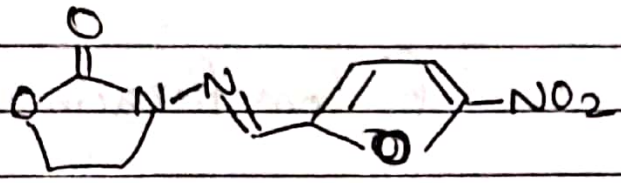
(9) Moxifloxacin



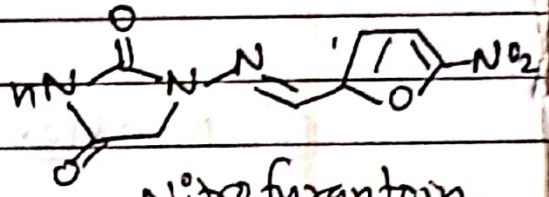
Miscellaneous Urinary tract anti infectants

(a) Nitrofuran Class antibacterial / antimicrobials

ex Furazolidone
Nitrofurantoin



Furazolidone



Nitrofurantoin

Mode of action :-

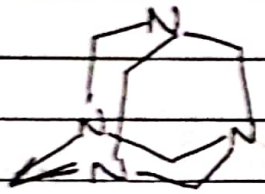
Bacterial cell → reduce the nitrofurantoin by nitrofuran reductase (a flavoprotein) enzyme. and this reduced nitrofuran product is highly active and bind to ribosomal protein, DNA, pyruvate metabolism & other macromolecules & show it bactericidal action.

→ So it inhibit DNA & RNA function of bacterial cell.

(B) Methenamine

→ It is a prodrug.

→ It is hexamethylene tetramine



→ After decomposition, it generate formaldehyde

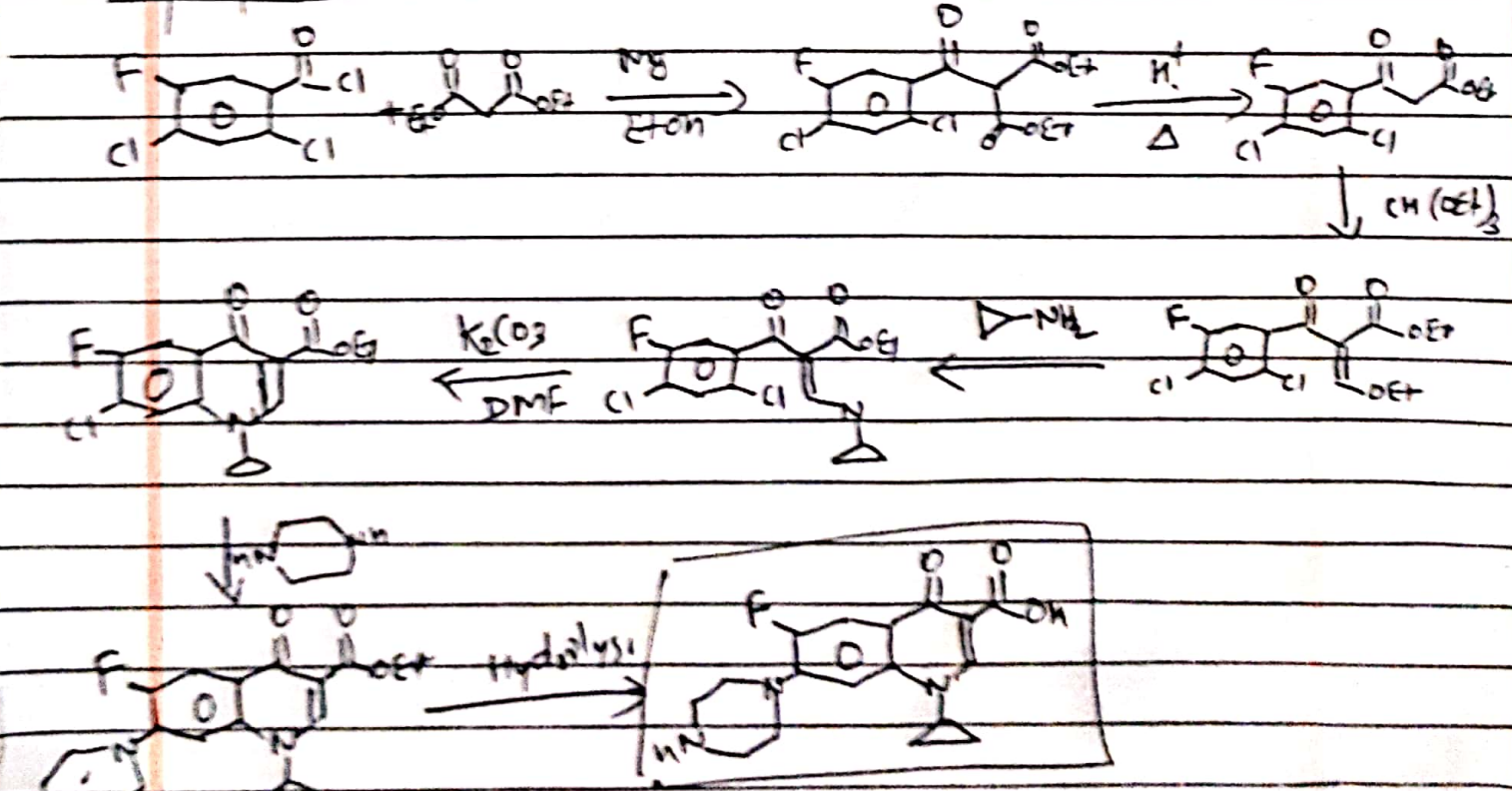
→ It is usually used in salt of ~~mandelic~~ mandelic acid or hippuric acid.

→ In ~~acid~~ Acidic urin ph it decompose to (5.5 or less)

formaldehyde which kill bacteria.

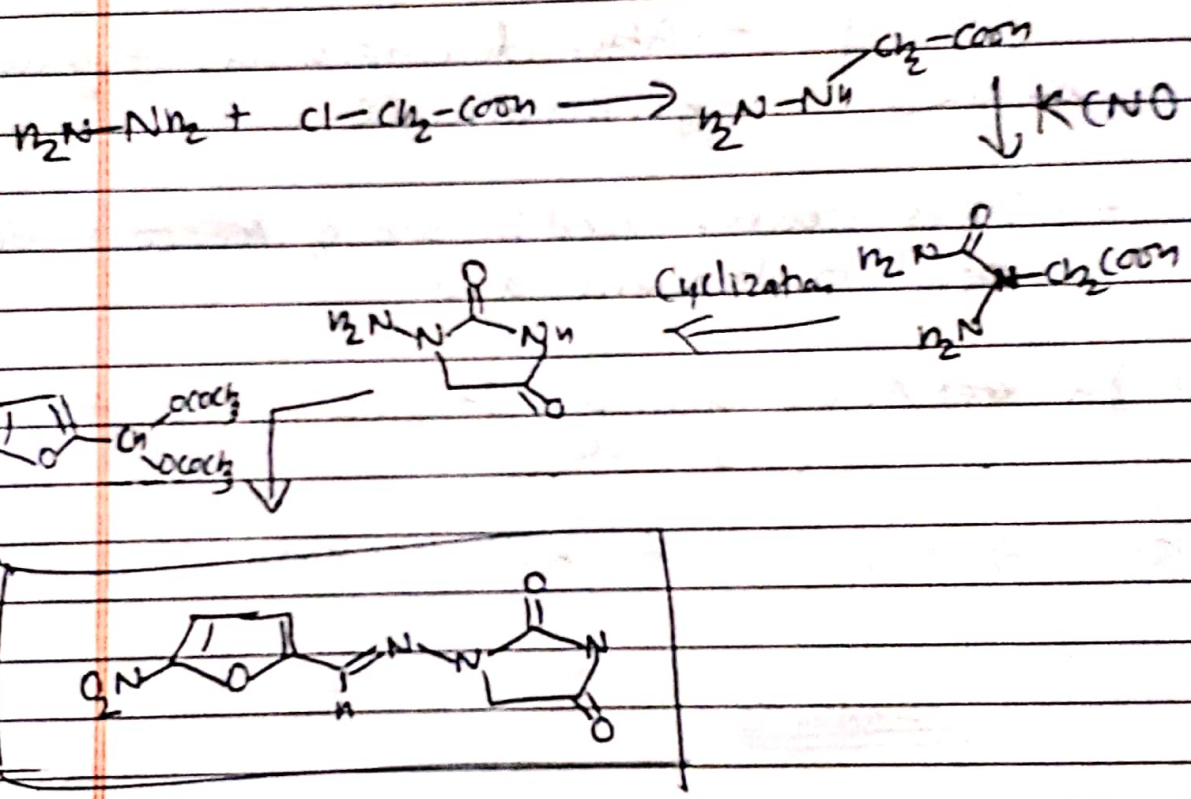
Synthesis

Ciprofloxacin:



Synthesis

Nitrofurantoin ⇒



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