Quinolones

Introduction

- Synthetic.
- ↑ active against gram(-ve) bacteria.
- Newer — (-) g(+) bacteria.

1st member → Nalidixic acid.

Fluoroquinolones

- flourination of quinolone.

Classification

1st generation (1F)

Norfloxacin.
Ciprofloxacin
Ofloxacin
Pefloxacin
N-COP

IInd generation (>1F) (stability ↑)

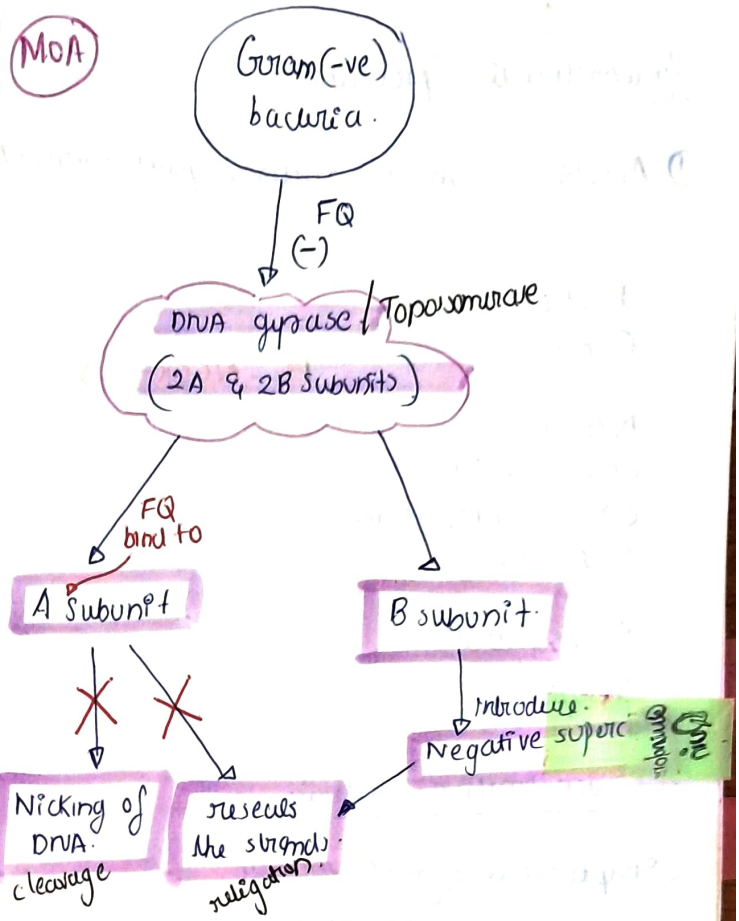
Levofloxacin
Gemifloxacin
Sparfloxacin.
Lomefloxacin
Moxifloxacin
Pradofloxacin

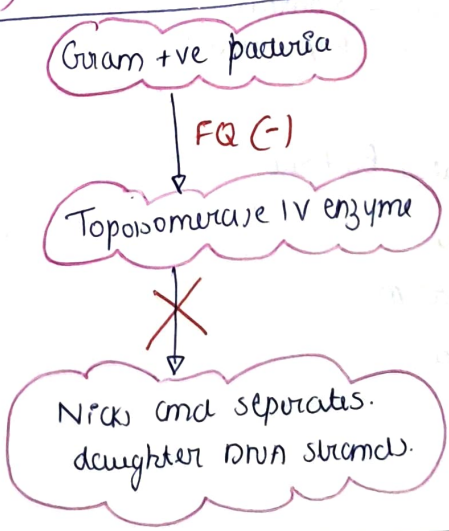
LG's Imp.

Mechanism of Action Resistance.

- mutation of DNA gyrase / topoisomerase IV producing ∈ having low FQ affinity.
- ↓ permeability of cm
- ↑ action of efflux pumps.

MoA





Bactericidal action → due to degestion of damaged DNA by exonuclease.

- mammalian cells → topoisomerase II
  - less affinity to FQ
  - low toxicity to host cells.

Antibacterial Spectrum

① Aerobic gram (-ve) bacteria - potent bactericidal

Proteus
E. coli

PE - NECK - SS

Neisseria.
Enterobacteria.
Campylobacter jejuni
Klebsiella.

Salmonella
Shigella.

② Gram positive bacteria

- Streptococcus → pneumonicae
  → pyogenes.
- staphylococcus → aureus.
  → epidermidis.

③ Intracellular Bacteria

Mycoplasma.
Mycobacterium.
Chlamydia.

④ Anaerobes

Ofloxacin
Moxifloxacin
Gemifloxacin
Gatifloxacin.

Therapeutic Uses.

① Urinary tract infections

- Nalidixic acid
- Norfloxacin

② Prostatitis

C - ciprofloxacin
O - ofloxacin
N - Norfloxacin
L - Levofloxacin

③ Sexually transmitted infections

Chlamydial urethritis & cervicitis } Levofloxacin / ofloxacin (7 day)

Gonorrhoea → ciprofloxacin. (no longer 1st line)

Chancroid → 3 day course. ciprofloxacin.

④ GI and Abdominal Infections

① Travellers Diarrhoea → C ciprofloxacin
O ofloxacin
N norfloxacin
L levofloxacin.

② Enteric fever → ofloxacin. / Ciprofloxacin

HIV.

(5) Respiratory tract infections

- Community acquired pneumonia

L levofloxacin
M moxifloxacin
G gemifloxacin.

- cystic fibrosis

O ofloxacin
C ciprofloxacin.

(6) Bone, joint, soft tissue infections

- chronic Osteomyelitis
- Diabetic foot

→ prophylaxis and treatment of Anthrax and Tularemia.

→ mycobacterial infections (moxiflo).

→ conjunctivitis, g(-ve) meningitis & septicemia.

→ Pt with granulocytosis & neutropenia.

Adverse effects

- GI → nausea, vomitting, [illegible] C. difficile colitis.
- CNS → headache, seizures, dizziness
- Musculoskeletal effects → Achilles tendon rupture.
- Metabolic effect → hypoglycemia
- CVS → QT prolonged. Torsades de pointes
- Skin → photosensitivity.

Drug Interactions

- divalent, trivalent cations, Antacids, Sucralfate ↓ iron, Zn, dairy.] reduce systemic bioavailability of FQ. due to chelation.

Enzyme (-)

- [ciprofloxacin] → Inhibit metabolism → leads to

→ theophylline, warfarin, caffeine toxicity.

- NSAIDS → enhance CNS toxicity of FQ.

Q) Why Norfloxacin in UTI?

→ High urinary concentration
- metabolized & excreted unchanged in urine

→ low systemic absorption, tissue penetration [illegible]

→ Broad spectrum activity against g(-) bacteria.

→ shorter T½ & lower resistance potential.

C/I → pregnancy ? — cartilage, tendon toxicity

ofloxacin – high B.A, D/I – warfarin, A/E – insomnia.] chlamydia, mycoplasma, TB/leprosy.

levofloxacin – 100% BA, no DrugInter.] Str. pneumoniae, anaerobes.

Exclusive – kidney elimination.

Cipro → C/I children ? cartilage tendon toxicity. growth plate abnormalities