PHARM.D • YEAR 3

Medicinal Chemistry

CHAPTER 2.4

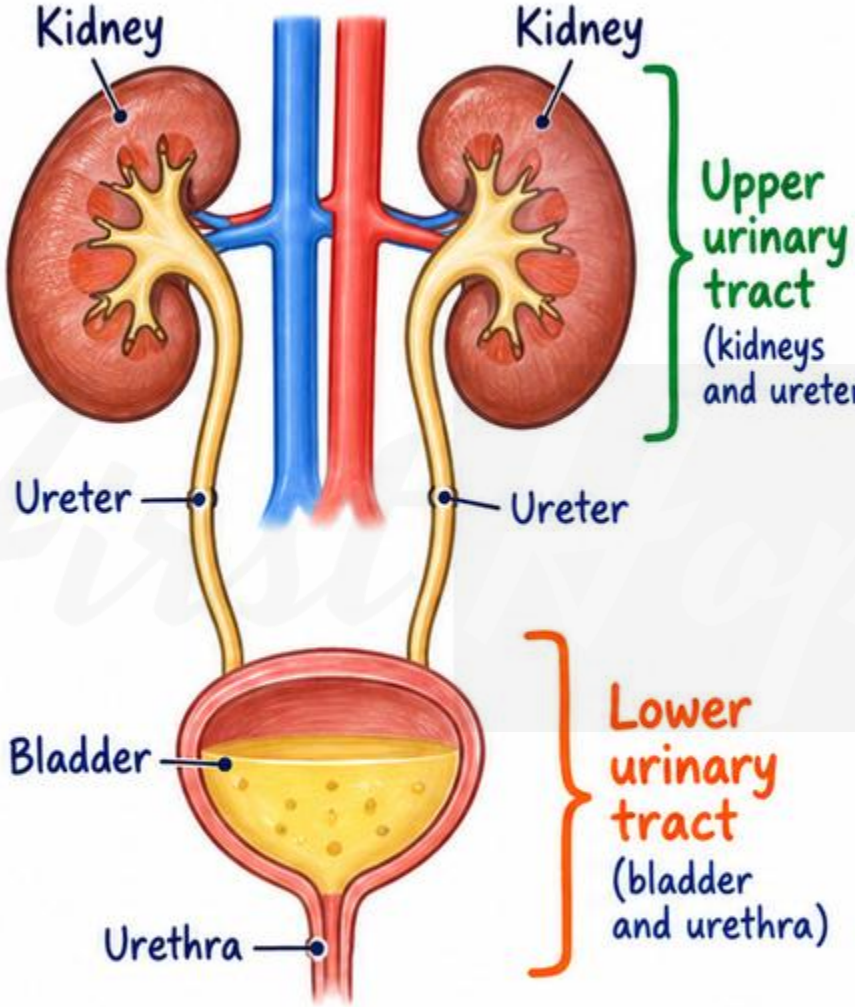
Urinary Tract Anti-Infectives

PPT CHAPTER COVER



Urinary infection: site matters

Urinary tract infection usually involves bacteria in the bladder, urethra or upper urinary tract. The infection site determines the exposure a medicine must achieve.



Cystitis

Cystitis commonly causes dysuria, urgency, frequency and lower abdominal discomfort.



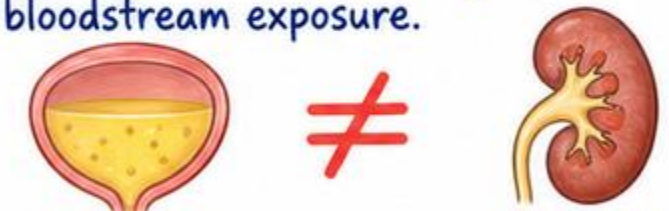
Features suggesting upper-tract involvement



Fever, flank pain, chills or vomiting suggest possible upper-tract involvement and require clinical assessment.

Drug exposure

A drug concentrated in urine may still provide inadequate kidney-tissue or bloodstream exposure.

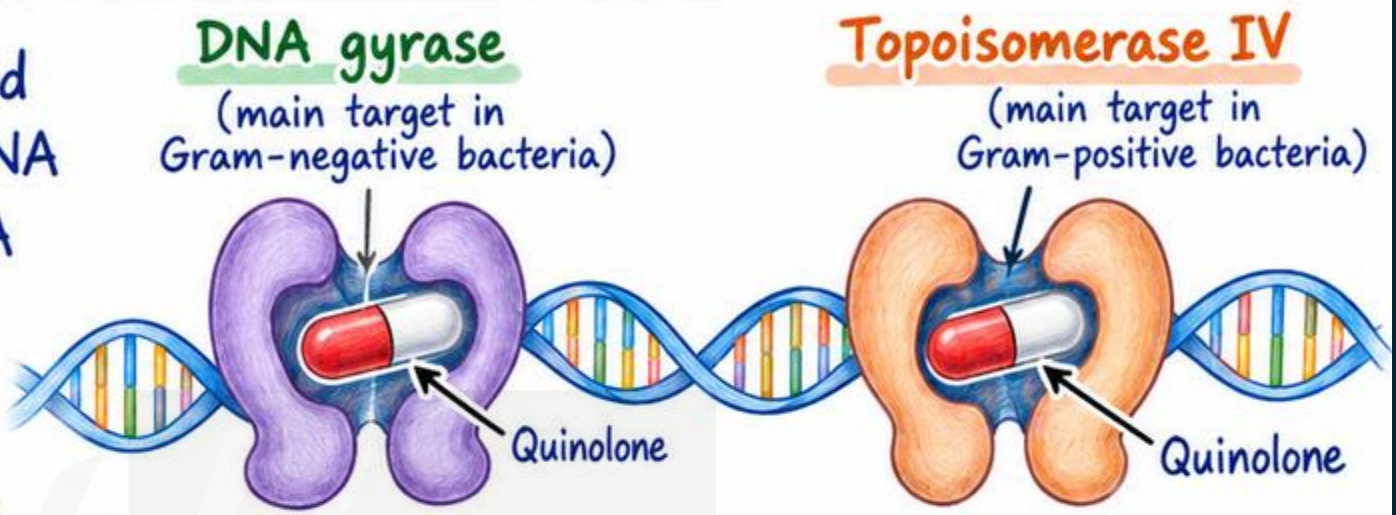


Diagnosis and treatment

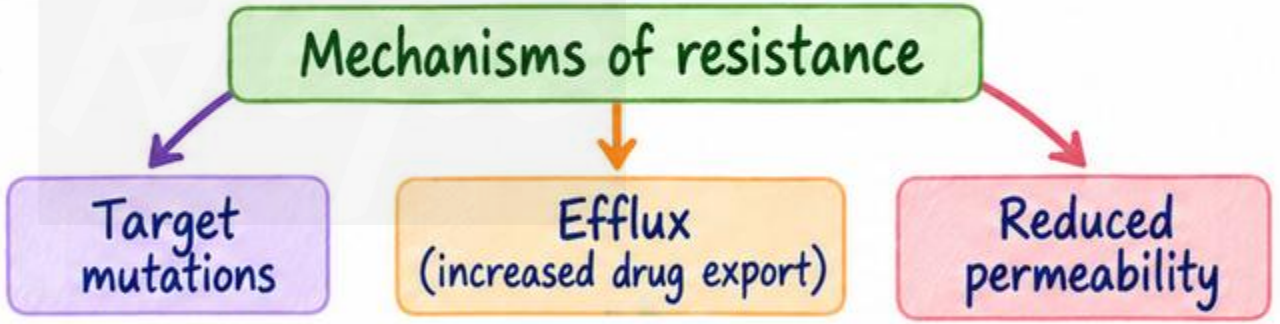
Symptoms alone do not identify the organism or its susceptibility. Diagnosis, severity, culture when appropriate and patient factors guide treatment rather than a generic list of urinary antibiotics.

Quinolones: DNA targets

Quinolones inhibit bacterial DNA gyrase and topoisomerase IV. They stabilize enzyme–DNA cleavage complexes and interfere with DNA processing, producing bactericidal effects.



The relative importance of the two targets differs among organisms. Target mutations, efflux and reduced permeability can cause resistance.



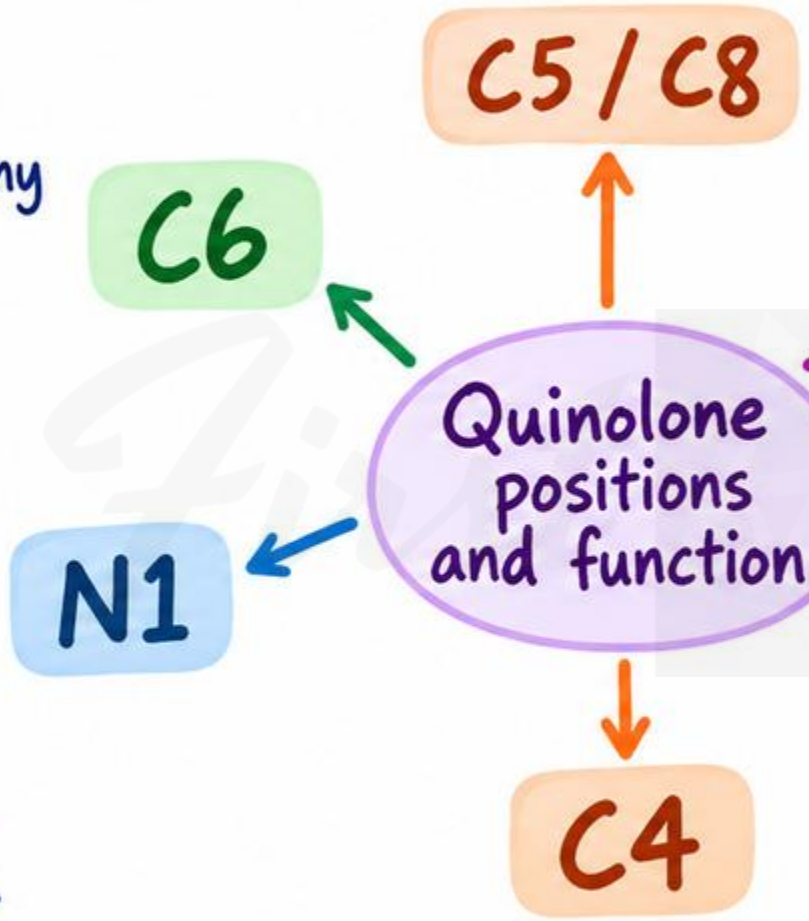
Nalidixic acid is an older nonfluorinated quinolone. Many later agents contain fluorine, but not every active quinolone requires it.

Nalidixic acid
(older nonfluorinated quinolone)

Fluorine
(present in many later agents, but not essential for activity)

This family includes compounds with different exposure and safety profiles. A common mechanism does not make every fluoroquinolone appropriate for a urinary infection.

Quinolone SAR: positions and function



C5 and C8 substitution can alter activity, phototoxicity and resistance behavior.

C6 fluorine is characteristic of many fluoroquinolones.

C7 heterocycles influence spectrum, disposition and adverse effects.

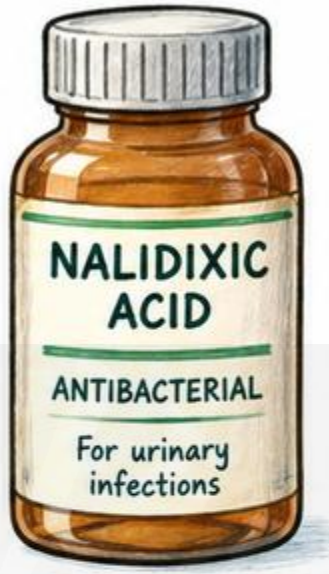
N1 substitution influences potency and spectrum; the position is a ring nitrogen, not C1. Ciprofloxacin has an N1 cyclopropyl group.

The C3 carboxylic acid and C4 keto groups support target-complex binding, including metal-mediated interactions.

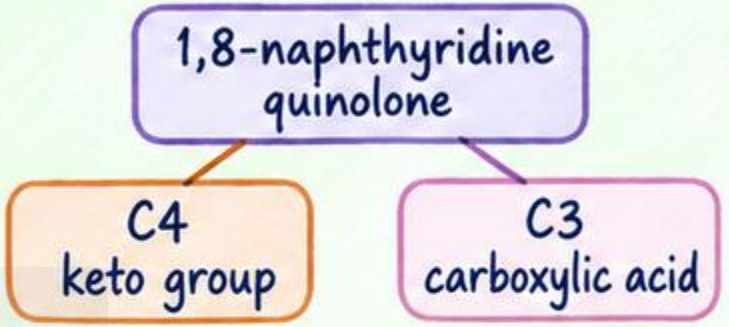
SAR trends apply within related series, not as unlimited rules. Structural modification can improve one property while worsening solubility, exposure or host safety.

Nalidixic acid

- Nalidixic acid is an older 1,8-naphthyridine quinolone with a C3 carboxylic acid and C4 keto group, formula $C_{12}H_{12}N_2O_3$.
- Its historical use focused on susceptible urinary pathogens. It lacks the C6 fluorine found in many later drugs.
- Target inhibition is bactericidal, but resistance and limited clinical utility reduce its modern role.
- Gastrointestinal symptoms, central nervous system effects and photosensitivity are relevant adverse effects; hemolysis can be a concern in susceptible patients.
- A historical urinary indication is not a recommendation for current empirical use.

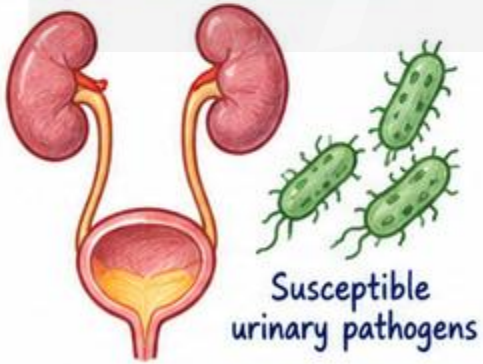


1,8-Naphthyridine quinolone



Formula: $C_{12}H_{12}N_2O_3$

Urinary pathogens



Susceptible urinary pathogens

Key points



No C6 fluorine



Bactericidal target inhibition



Resistance limits use

Adverse effects



Gastrointestinal symptoms



Central nervous system effects



Photosensitivity



Hemolysis (susceptible patients)

⚠ A historical urinary indication is not a recommendation for current empirical use.

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