

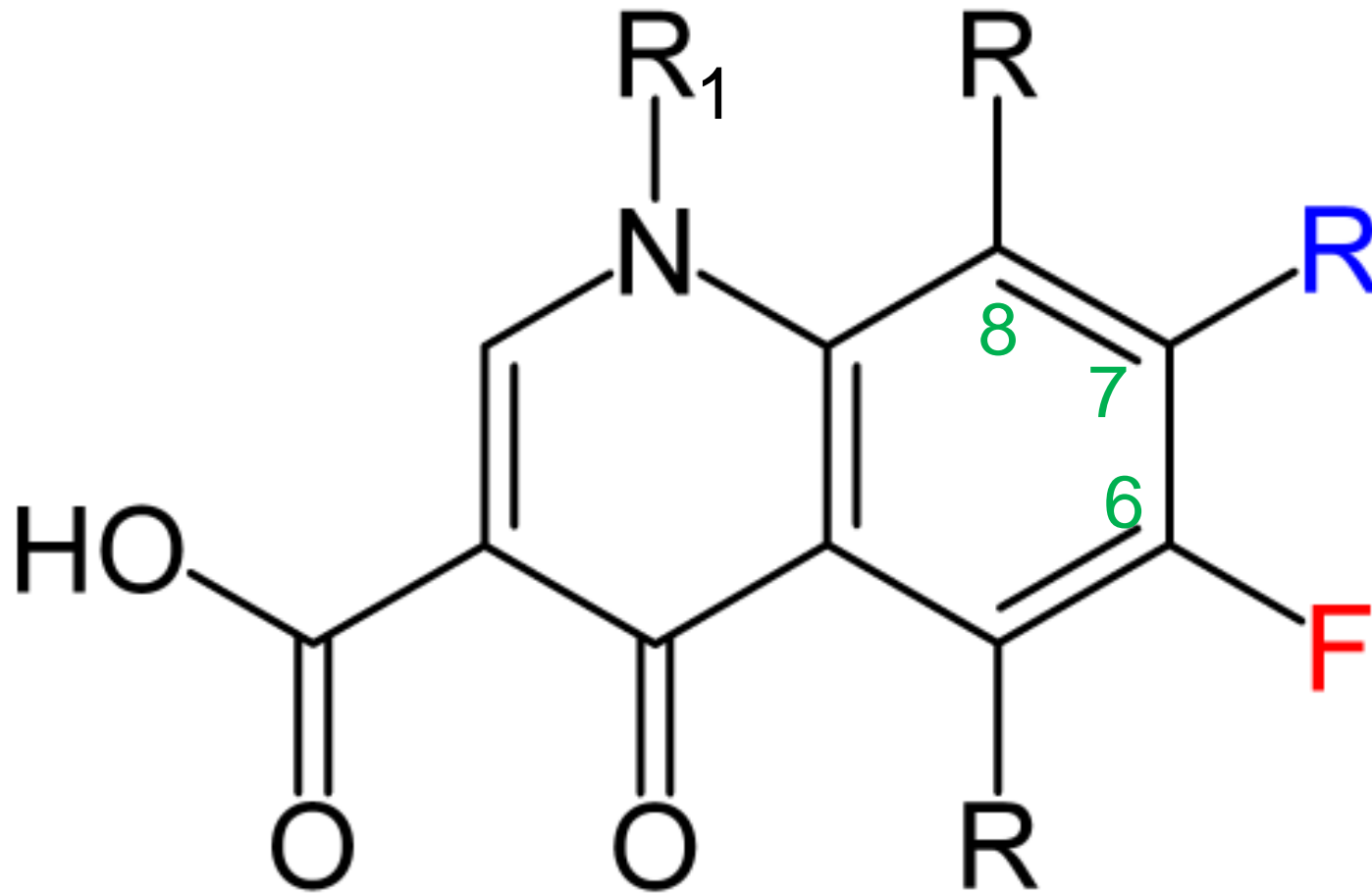
Fluoroquinolones Cross reaction

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Quinolones

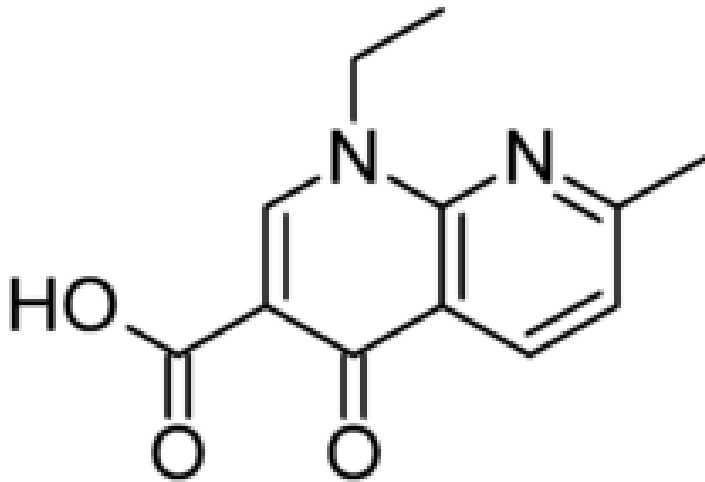
generation	drug
First	Non-fluorinated drug; nalidixic acid
Second	Norfloxacin, Ofloxacin, Ciprofloxacin
Third	Levofloxacin
Fourth	Moxifloxacin

Fluoroquinolones structure



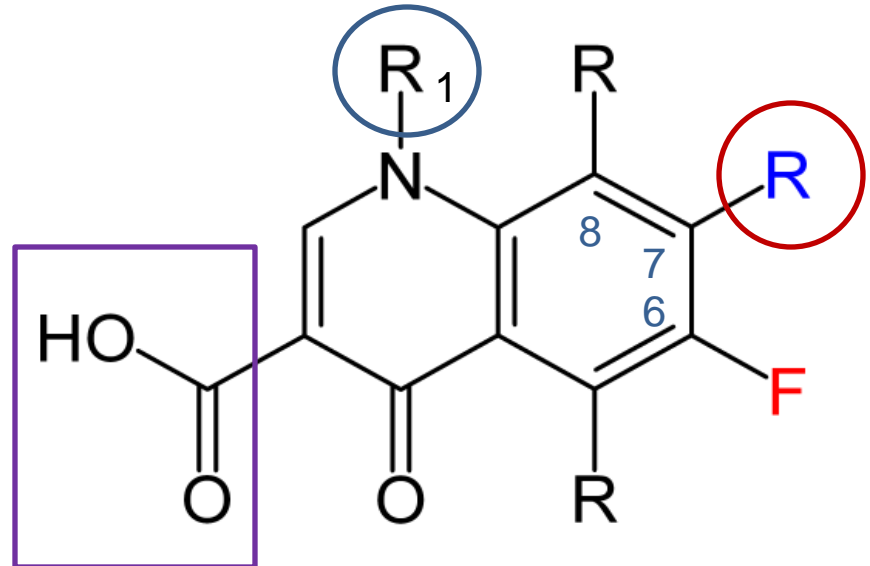
Structure

Quinolones



Nalidixic acid

Floroquinolones

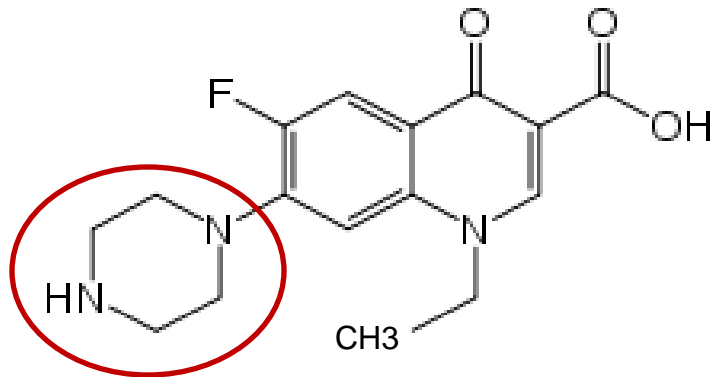


R side chain = covalent bond of protein to “**Adduct**”

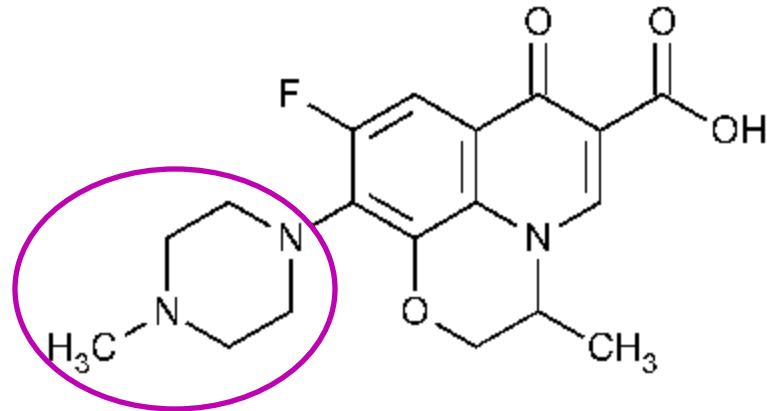
carboxylic group = Drug Interaction position

Fluoroquinolones Structure

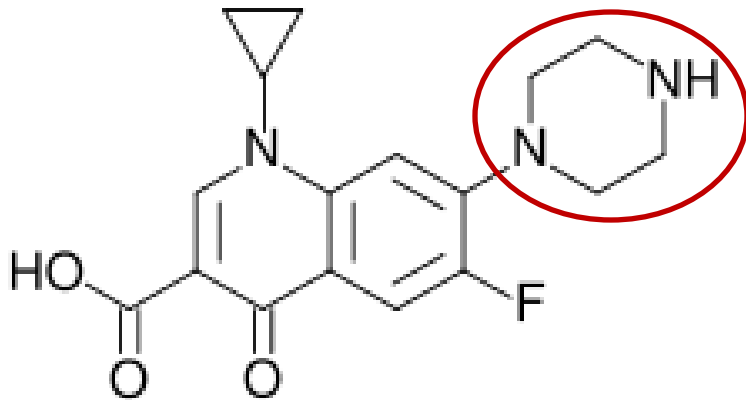
R = piperazine



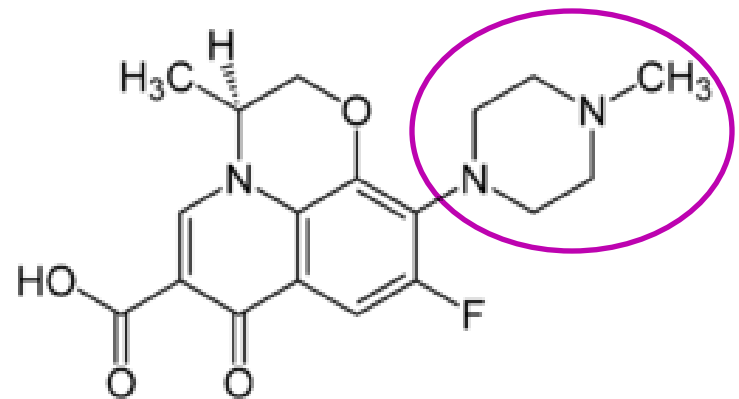
norfloxacin



ofloxacin



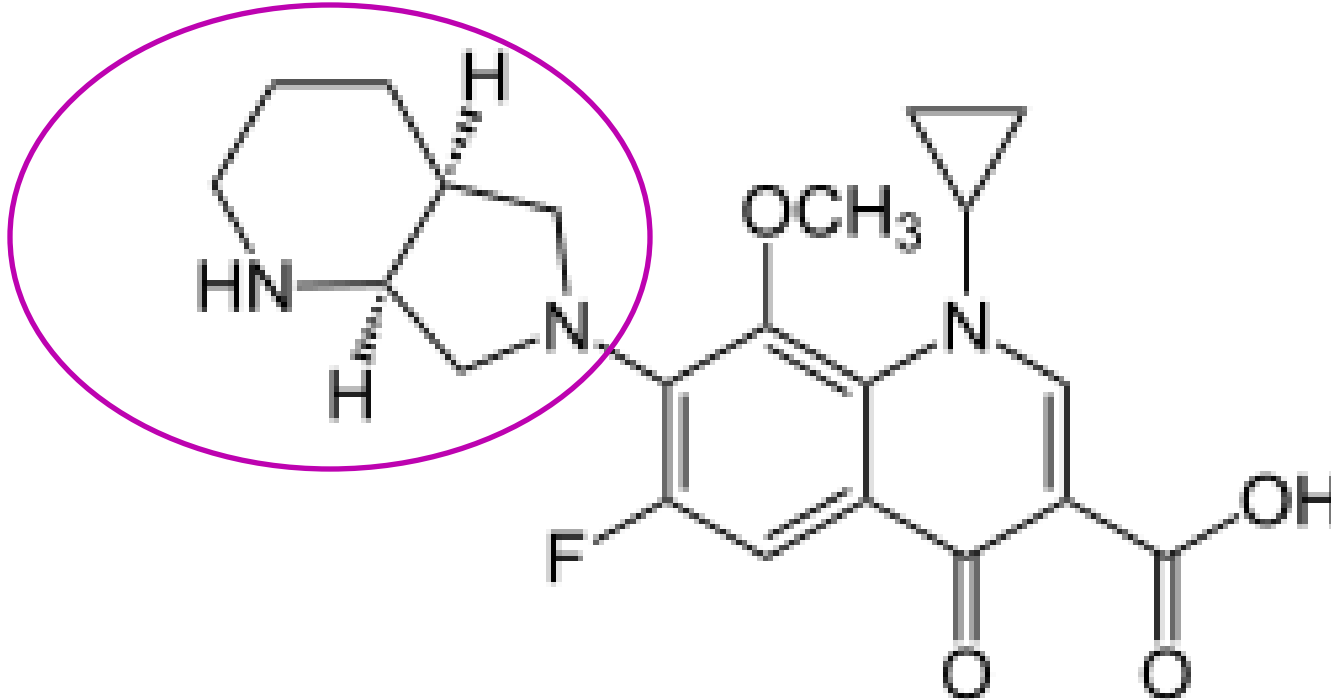
ciprofloxacin



levofloxacin

New fluoroquinolones

เช่น Moxifloxacin



Immediate hypersensitivity to quinolones: moxifloxacin cross-reactivity.

Gonzales, I, et al. J Invest Allergol Clin Immunol 2005; Vol.15(2):146-149

Patient	Years	Sex	Clinic	Culprit drug
1	39	female	urticaria	ciprofloxacin
2	50	female	urticaria	moxifloxacin
3	29	female	urticaria	ofloxacin ciprofloxacin
4	42	female	urticaria	ciprofloxacin
5	63	female	anaphylaxis	moxifloxacin
6	53	male	urticaria	moxifloxacin

High degree of cross-reactivity between different groups of quinolones

Pt	ยาที่ผู้ป่วยแพ้	ciprofloxacin		norfloxacin		levofloxacin		ofloxacin		moxifloxacin	
		Skin test	Oral challenge test	Skin test	Oral challenge test	Skin test	Oral challenge test	Skin test	Oral challenge test	Skin test	Oral challenge test
1	ciprofloxacin	+	NT	-	NT	+	NT	-	NT	+	+
2	moxifloxacin	+	+	-	NT	-	NT	+	+	+	+
3	ofloxacin ciprofloxacin	-	WT	-	NT	+	+	-	NT	+	+
4	ciprofloxacin	-	+	-	NT	+	WT	+	NT	+	+
5	moxifloxacin	-	WT	-	NT	-	WT	+	NT	+	+
6	moxifloxacin	+	WT	-	NT	-	NT	-	NT	-	+

WT=well tolerate, NT=not test, + = positive

AVOID !!!

Immediate reactions of fluoroquinolones

- ปัจจุบัน ถึงแม้ยังไม่สามารถอธิบาย pathomechanism ได้ แต่อย่างไรก็ตามดูเหมือนว่า ตำแหน่งที่ 7 ของ quinolone molecule จะเกิด covalent binding กับ IgE-molecule
- Some immediate-type reactions to fluoroquinolone may also be attributed to a nonspecific histamine release from mast cells and basophils
- Nonallergic histamine release may induce an anaphylactoid reaction

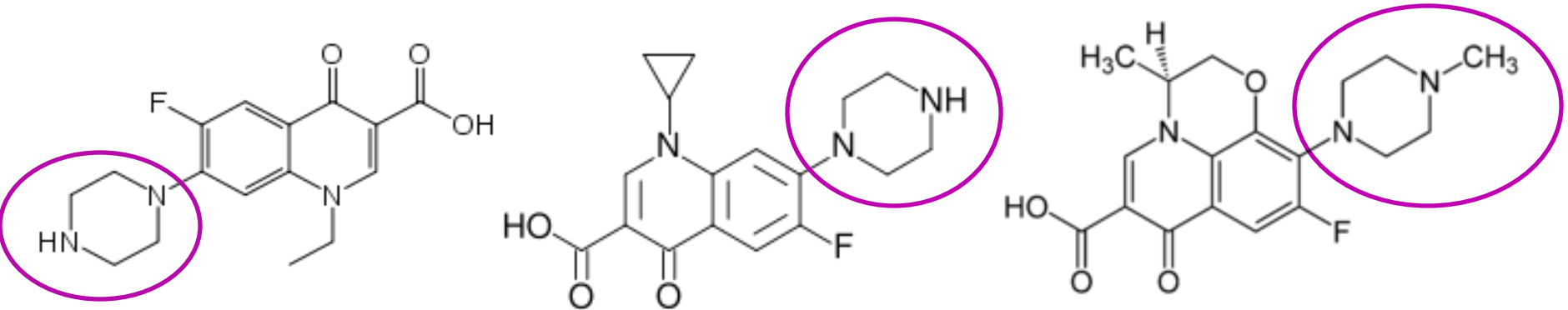
Immediate reactions of fluoroquinolones

- Most patients are sensitized to more than one fluoroquinolone, suggesting an extensive cross-reactivity between the different molecules
- This is probably due to the high structural similarity among fluoroquinolones, which all share a common core structure

Photosensitivity

- Formation of **quinolone-photoadducts** is thought to be the initial step for sensitization
- Cross-reactivity in the photoallergic response are differences in the potency to evoke photoallergic reactions for different molecules
- Substituent at position 8 of the structure
- **Protein-photobinding** site seems to be the **piperazinyl ring at position 7**, **photodegraded by UVA light**.
- dose-dependent phenomenon that requires exposure to direct or indirect ultraviolet A (UVA) light [Can J Infect Dis. 2002 Jan–Feb; 13(1): 54–61.]

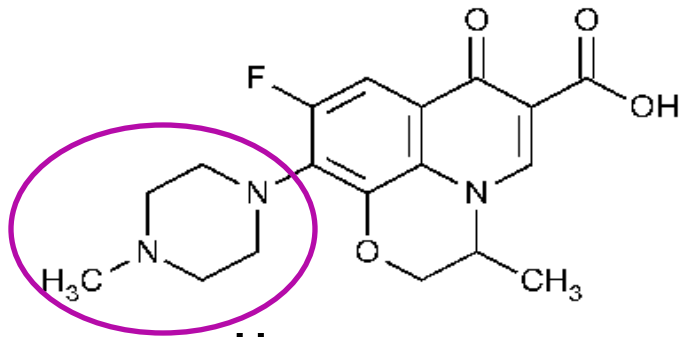
Fluoroquinolones Photosensitivity



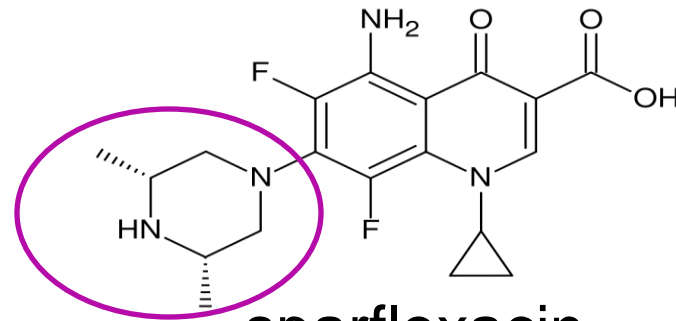
norfloxacin

ciprofloxacin

levofloxacin



ofloxacin



sparfloxacin

norfloxacin, ciprofloxacin, levofloxacin < ofloxacin < sparfloxacin

Photosensitivity

- Two types of photosensitivity reactions have been associated with fluoroquinolone therapy: photoallergic reactions and phototoxic responses. Photoallergic reactions are rare and require previous exposure to a drug in the class. In contrast, phototoxic responses are more common and can develop without previous exposure to a fluoroquinolone if the dose of the photo-labile drug and exposure to UVA light (around 350 to 360 nm) are sufficiently high, as demonstrated with the use of some fluoroquinolones in a murine model (Table III).^[33,34] Halogenation at position C8 is responsible for many of the photosensitivity reactions occurring during fluoroquinolone treatment.^[22] Some of the fluoroquinolones induce mild photosensitivity reactions, such as erythema of sun-exposed skin, with varying frequency; however, drugs such as lomefloxacin and sparfloxacin, with a C8-fluorine substituent, and cinafloxacin, with a C8-chlorine substituent, exhibit a greater incidence of phototoxic reactions than drugs without this substituent.

