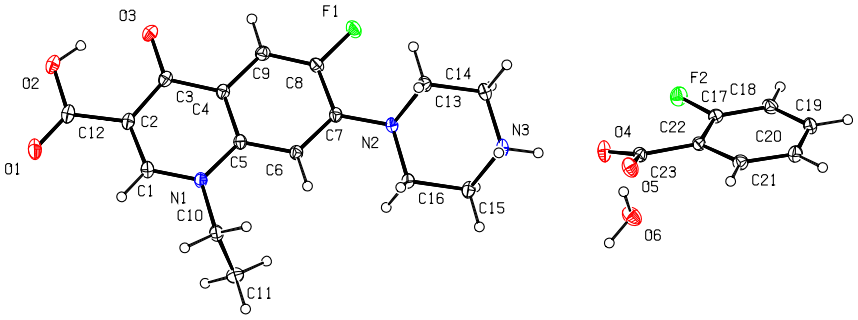
Shu-hui Wang, Cheng-Yu Yang, Jia-Shu He and Cheng-Jun Jiang*

The crystal structure of 4-(3-carboxy-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-ium 2-fluorobenzoate hydrate, $C_{23}H_{25}F_2N_3O_6$



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Abstract

$C_{23}H_{25}F_2N_3O_6$, triclinic, $P\bar{1}$, a = 7.3162(3) Å, b = 10.4107(5) Å, c = 15.4537(7) Å, α = 84.3830(10)°, β = 82.7090(10)°, γ = 70.1110(10)°, V = 1096.01(9) Å^3, Z = 2, $R_{gt}(F)$ = 0.0376, $wR_{ref}(F^2)$ = 0.1097, T = 170 K.

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The molecular structure is shown in the figure. Table 1 contains the crystallographic data and the list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.28 × 0.10 × 0.06 mm
Wavelength:	Ga $K\alpha$ radiation (1.34139 Å)
μ:	0.65 mm^{-1}
Diffractometer, scan mode:	Bruker APEX2, φ and ω scans
θ_{max}, completeness:	60.7°, 98 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	23440, 4977, 0.034
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 4,686
$N(param)_{refined}$:	312
Programs:	Bruker,[1] Olex2,[2] SHELX[3, 4]

1 Source of materials

Equimolar quantities of norfloxacin (0.032 g) and 2-fluorobenzoic acid (0.014 g) were given in a 10 mL glass vial. The solid mixture was subsequently treated with a binary solvent system consisting of deionized water (2 mL) and absolute ethanol (2 mL). The mixture was transferred to a temperature-controlled magnetic stirring apparatus and gradually heated to 60 °C under gentle agitation (200 rpm) until complete dissolution was achieved. Through controlled solvent evaporation, the system was maintained in a metastable supersaturated state for 24 h to facilitate crystal nucleation and growth. The resulting suspension was vacuum-filtered through a Büchner funnel to isolate the crystalline product. The obtained compound was characterized as 4-(3-carboxy-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-ium 2-fluorobenzoate hydrate.

2 Experimental details

Absorption corrections were applied by using multi-scan program.[1] Using Olex2,[2] the structure was solved with the ShelXT[3] structure solution program and refined with the ShelXL[4] refinement package. The H atoms were fixed, fixed U_{iso} were set to 1.2 times of All C(H) groups, C(H,H) groups and N(H,H) groups; 1.5 times of C(H,H,H,H) groups, O(H) groups and O(H,H) groups.

***Corresponding author: Cheng-Jun Jiang**, School of Biological and Chemical Engineering, Zhejiang University of Science and Technology, Liuhe Road 318#, Hangzhou, China, E-mail: jcj312@zust.edu.cn. https://orcid.org/0000-0001-9297-9399
Shu-hui Wang and Jia-Shu He, School of Biological and Chemical Engineering, Zhejiang University of Science and Technology, Liuhe Road 318#, Hangzhou, China
Cheng-Yu Yang, Zhejiang Lepu Pharmaceutical Co., Ltd., Binhai Road 29#, Taizhou, China

3 Comment

Norfloxacin, a broad-spectrum fluoroquinolone antibiotic, is widely used to treat bacterial infections. However, its therapeutic potential is limited by poor aqueous solubility and low bioavailability. To address these limitations, various salt forms of Norfloxacin have been explored,[5–8] including those with adipic acid, malonic acid, hydroxybenzoic acids, sulfonic acids, and non-steroidal anti-inflammatory drugs (NSAIDs). Some of us investigated the formation of norfloxacin cocrystals.[9] Additionally, ionic cocrystals,[10, 11] cocrystals with flavonoids such as naringenin and hesperetin have been reported to improve NOR's physicochemical properties.[12] Building upon these advancements in supramolecular crystal engineering, this study aims to develop novel pharmaceutical salts of Norfloxacin using 2-fluorobenzoic acid as counterions. These pharmaceutically acceptable phenolic acids were selected to modulate Norfloxacin's solubility and antibacterial activity.

The asymmetric unit of the title compound contains one target cation, one counter anion as well as one water molecule (see the figure). The title crystal was formed by connecting the raw materials norfloxacin, 2-fluorobenzoic acid and water molecules through intermolecular hydrogen bonds. N3H3A in the piperazine group participates in a classical N3–H3B···O4^{1}(^{1} = –1–x, –y, –z) hydrogen bond to the oxygen atom in 2-fluorobenzoic acid; N3H3A in the piperazine group is involved in a N3–H3A···O5^{2}(^{2} = 1+x, +y, +z) hydrogen bond with 2-fluorobenzoic acid molecule. 2-Fluorobenzoic acid form hydrogen bonds with water molecule O6–H6A···O4.

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