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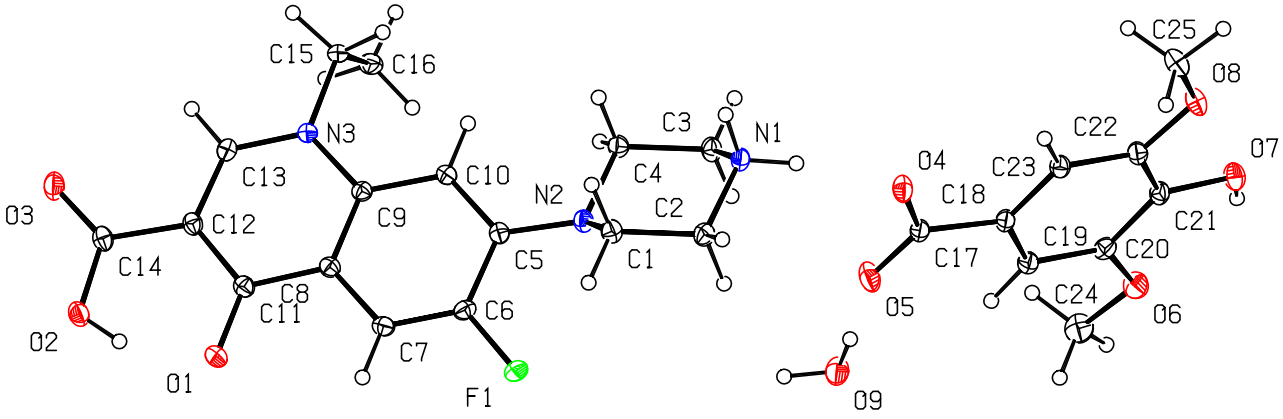
The crystal structure of 4-(3-carboxy-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-ium 4-hydroxy-3,5-dimethoxybenzoate monohydrate, $C_{25}H_{30}FN_3O_9$



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Abstract

$C_{25}H_{30}FN_3O_9$, monoclinic, $P2_1/n$, a = 16.3585(4) Å, b = 7.8763(2) Å, c = 18.7735(4) Å, β = 90.5690(10)°, V = 2418.74(10) Å^3, Z = 4, R_{gt} (F) = 0.0410, wR_{ref} (F^2) = 0.1055, T = 170 K.

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The molecular structure is shown in the figure. Table 1 contains the crystallographic data. 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	0.42 × 0.20 × 0.15 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.12 mm^{-1}
Diffractometer, scan mode:	Bruker D8 Venture, φ and ω scans
θ_{max}, completeness:	28.3°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	42,141, 5,967, 0.038
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 5094
$N(param)_{refined}$:	351
Programs:	Bruker,[1] Olex2,[2] SHELX[3,4]

1 Source of materials

Equimolar quantities of norfloxacin (0.032 g) and syringic acid (0.020 g) 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 30 °C under gentle agitation (200 rpm) until complete dissolution was achieved. Through controlled

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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 4-hydroxy-3,5-dimethoxybenzoate monohydrate.

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 using Intrinsic Phasing and refined with the ShelXL[4] refinement package using Least Squares minimisation. 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.

3 Comment

Norfloxacin, a fluoroquinolone antibacterial agent, is widely employed in treating infections caused by Gram-positive and Gram-negative bacteria.[5] Like other fluoroquinolones, its aqueous solubility exhibits a pronounced pH-dependent profile due to zwitterion formation *via* proton transfer between the carboxylic acid group and the basic piperazine ring.[6] At physiological pH, norfloxacin suffers from limited solubility and poor permeability, classifying it as a Biopharmaceutics Classification System (BCS) Class IV drug with inherently low bioavailability.[7] To address these limitations, pharmaceutical salt/cocrystal engineering has emerged as a strategic approach, wherein pairing the drug with a pharmaceutically acceptable counterion can modulate its physicochemical properties.[8] Previous studies have demonstrated the efficacy of salt formation with organic acids in enhancing norfloxacin's solubility and dissolution performance.[9–11] In this study, we successfully designed, synthesized, and structurally characterized a novel norfloxacin-syringic acid salt. The asymmetric unit of the crystal structure [norfloxacin···syringic acid···H_2O] comprises one norfloxacin cation, one syringic acid anion, and one water molecule. Key structural features include: A classical N–H···O hydro gen bond formed between the N1H1A moiety of the piperazine group and the O4 oxygen atom of syringic acid. Hydration-mediated interactions where the O9–H9A group of water forms hydrogen bonds with the O5 oxygen atom of syringic acid. The crystal packing exhibits a distinctive two-fold screw symmetry along the [0 1 0] axis, with screw components positioned at (¼, *y*, ¼). This symmetry element contributes to the three dimensional network formation through systematic molecular repetition.

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