Crystal structure of choline fenofibrate (Trilipix®), ($C_5H_{14}NO$) ($C_{17}H_{14}ClO_4$)

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The crystal structure of choline fenofibrate has been solved and refined using synchrotron X-ray powder diffraction data, and optimized using density functional techniques. Choline fenofibrate crystallizes in space group *Pbca* (#61) with $a = 12.341\,03(2)$, $b = 28.568\,70(6)$, $c = 12.025\,62(2)$ Å, $V = 4239.84(1)$ Å^3, and $Z = 8$. The hydroxyl group of the choline anion makes a strong hydrogen bond to the ionized carboxylate group of the fenofibrate anion. Together with C–H···O hydrogen bonds, these link the cations and anions into layers parallel to the *ac*-plane. The powder pattern has been submitted to ICDD for inclusion in the Powder Diffraction File™. © *2016 International Centre for Diffraction Data*. [doi:10.1017/S0885715616000099]

Key words: choline fenofibrate, Trilipix, powder diffraction, Rietveld refinement, density functional theory

I. INTRODUCTION

Choline fenofibrate (the choline salt of fenofibric acid), marketed as Trilipix®, is a lipid regulating agent available as delayed release capsules for oral administration. It is generally used for the management of low-density lipoprotein cholesterol to reduce triglycerides and increase the quantity of high-density lipoprotein cholesterol in the blood. Trilipix can be used alone or in conjunction with statins in the treatment of hypercholesterolemia and hypertriglyceridemia. The choline salt of fenofibric acid was first disclosed in US Patent 7,259,186 (Clink *et al.*, 2007; Abbott Laboratories), and a crystalline form A was claimed in US Patent 2011/0288331 (Ponnaiah *et al.*, 2011; Alembic Pharmaceuticals, Ltd.). The systematic name (CAS Registry Number 856676-23-8) is 2-hydroxy-*N,N,N*-trimethylethanaminium 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate. A two-dimensional molecular diagram is shown in Figure 1. After this work was completed, the morphology of choline fenofibrate was described by Bordawekar *et al.* (2014), and the crystal structure included in the Cambridge Structural Database (Groom and Allen, 2014) as Refcode KUKYUM.

The presence of high-quality reference powder patterns in the PDF™ (Powder Diffraction File; ICDD, 2014) is important for phase identification, particularly by pharmaceutical, forensic, and law enforcement scientists. The crystal structures of a significant fraction of the largest dollar volume pharmaceuticals have not been published, and thus calculated powder patterns are not present in the PDF-4 databases. Sometimes experimental patterns are reported, but they are generally of low quality. This structure is a result of a collaboration among ICDD, Illinois Institute of Technology (IIT), Poly Crystallography Inc., and Argonne National Laboratory to measure high-quality synchrotron powder patterns of commercial pharmaceutical ingredients, include these reference patterns in the PDF, and determine the crystal structures of these Active Pharmaceutical Ingredients (APIs).

Even when the crystal structure of an API is reported, the single-crystal structure was often determined at low temperature. Most powder diffraction measurements are performed at ambient conditions. Thermal expansion (generally anisotropic) means that the peak positions calculated from a low-temperature single-crystal structure often differ significantly from those measured at ambient conditions. These peak shifts can result in failure of default search/match algorithms to identify a phase, even when it is present in the sample. High-quality reference patterns measured at ambient conditions are thus critical for easy identification of APIs using standard powder diffraction practices.

II. EXPERIMENTAL

Choline fenofibrate was commercial reagent (M.P. 206–212 °C), purchased from Toronto Research Chemicals (lot# 1-GUY-9-1), and was used as-received. The white powder was packed into a 1.5 mm diameter Kapton capillary, and rotated during the measurement at ~50 cycles s^{-1}. The powder pattern was measured at 295 K at beam line 11-BM (Lee *et al.*, 2008; Wang *et al.*, 2008) of the Advanced Photon Source at Argonne National Laboratory using a wavelength of 0.413 685 Å from 0.5 to 50°2θ with a step size of 0.001° and a counting time of 0.1 s step^{-1}. The pattern was indexed on a primitive orthorhombic unit cell having $a = 12.337$, $b = 28.561$, $c =$

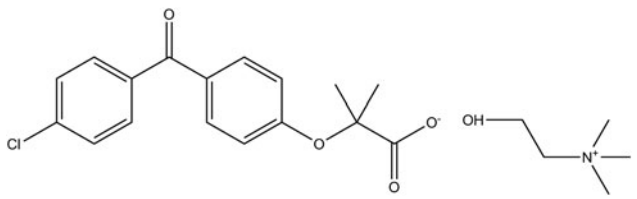

Figure 1. The molecular structure of choline fenofibrate.

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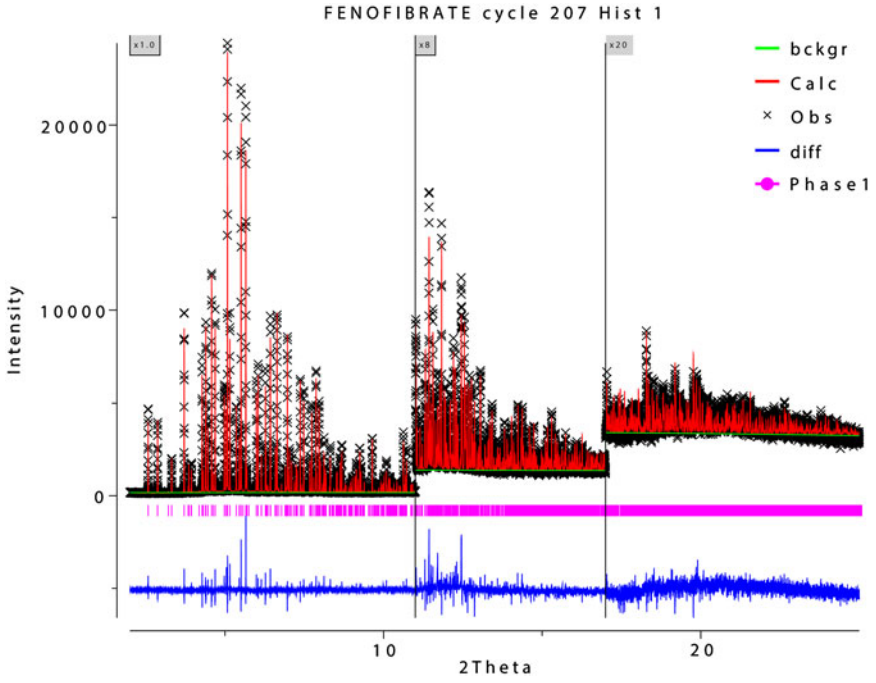

Figure 2. (Color online) The Rietveld plot for the refinement of choline fenofibrate. The black crosses represent the observed data points, and the red line is the calculated pattern. The blue curve is the difference pattern, plotted at the same vertical scale as the other patterns, and the green line is the background. The vertical scale has been multiplied by a factor of 8 for $2\theta > 11.0°$, and by a factor of 20 for $2\theta > 17.0°$.

TABLE I. Rietveld refined crystal structure of choline fenofibrate.

Crystal data	
$C_{22}H_{28}ClNO_5$	$V = 4239.84\ (1)$ Å^3
$M_w = 421.92$	$Z = 8$
Orthorhombic, *Pbca*	Synchrotron radiation, $\lambda = 0.413\,685$ Å
$a = 12.341\,03\ (2)$ Å	$T = 295$ K
$b = 28.568\,70\ (6)$ Å	Cylinder, 1.5×1.5 mm^2
$c = 12.025\,62\ (2)$ Å	
Data collection	
11-BM APS diffractometer	Scan method: step
Specimen mounting: Kapton capillary	$2\theta_{min} = 0.5°$, $2\theta_{max} = 50.0°$, $2\theta_{step} = 0.001°$
Data collection mode: transmission	
Refinement	
Least-squares matrix: full	23 002 data points
$R_p = 0.081$	Profile function: CW Profile function number 4 with 18 terms Pseudo-voigt profile coefficients as parameterized in Thompson *et al.* (1987). Asymmetry correction of Finger *et al.* (1994). Microstrain broadening by Stephens (1999). #1(GU) = 1.419 #2(GV) = −0.126 #3 (GW) = 0.063 #4(GP) = 0.000 #5(LX) = 0.173 #6(ptec) = 0.00 #7(trns) = 0.00 #8(shft) = 0.0000 #9(sfec) = 0.00 #10(S/L) = 0.0011 #11 (H/L) = 0.0011 #12(eta) = 0.3109 #13(S400) = 5.1×10^{-5} #14(S040) = 3.7×10^{-5} #15(S004) = 0.0E+00 #16(S220) = 6.4×10^{-6} #17 (S202) = 2.2×10^{-5} #18(S022) = -1.0×10^{-5} Peak tails are ignored where the intensity is below 0.0010 times the peak Aniso. broadening axis 0.0 1.0 0.0
$R_{wp} = 0.100$	85 parameters
$R_{exp} = 0.054$	43 restraints
$R(F^2) = 0.175\,67$	$(\Delta/\sigma)_{max} = 0.04$
$\chi^2 = 3.423$	Background function: GSAS Background function number 1 with 3 terms. Shifted Chebyshev function of 1st kind 1: 169.205 2: −3.557 31 3: −3.179 28

Fractional atomic coordinates and isotropic displacement parameters (Å2)

	x	*y*	*Z*	U_{iso}
C1	1.0521 (2)	0.427 80 (12)	−0.1448 (3)	0.0365 (7)
C2	1.0911 (3)	0.419 74 (10)	−0.2518 (3)	0.0365 (7)
C3	1.1764 (3)	0.446 47 (13)	−0.2931 (2)	0.0365 (7)
C4	1.2227 (2)	0.481 26 (12)	−0.2275 (3)	0.0365 (7)
C5	1.1838 (3)	0.489 32 (10)	−0.1205 (3)	0.0365 (7)
C6	1.0985 (3)	0.462 59 (13)	−0.0792 (2)	0.0365 (7)

Continued

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TABLE I. Continued

	x	y	Z	U_{iso}
H7	1.0591 (4)	0.395 75 (14)	−0.2970 (4)	0.0475 (8)
H8	1.2032 (4)	0.4409 (2)	−0.3668 (2)	0.0475 (8)
H9	1.2157 (4)	0.513 31 (14)	−0.0753 (4)	0.0475 (8)
H10	1.0716 (4)	0.4682 (2)	−0.0055 (3)	0.0475 (8)
Cl11	1.330 43 (16)	0.513 91 (7)	−0.277 08 (15)	0.0731 (7)
C12	0.9644 (4)	0.3970 (2)	−0.1056 (4)	0.0540 (14)
O13	0.9067 (3)	0.375 78 (15)	−0.1736 (3)	0.0540 (14)
C14	0.9376 (3)	0.393 20 (12)	0.0172 (2)	0.0365 (7)
C15	0.8294 (3)	0.384 81 (12)	0.0436 (3)	0.0365 (7)
C16	0.7987 (2)	0.378 64 (13)	0.1540 (3)	0.0365 (7)
C17	0.8761 (3)	0.380 85 (13)	0.2380 (2)	0.0365 (7)
C18	0.9842 (3)	0.389 23 (12)	0.2117 (3)	0.0365 (7)
C19	1.0149 (2)	0.395 41 (13)	0.1013 (4)	0.0365 (7)
H20	0.7761 (4)	0.383 29 (18)	−0.0144 (4)	0.0475 (8)
H21	0.7241 (2)	0.372 85 (19)	0.1721 (5)	0.0475 (8)
H22	1.0375 (4)	0.390 76 (18)	0.2697 (4)	0.0475 (8)
H23	1.0895 (2)	0.401 19 (19)	0.0832 (5)	0.0475 (8)
O24	0.8357 (3)	0.377 07 (15)	0.3414 (3)	0.0420 (7)
C25	0.9042 (4)	0.3834 (2)	0.4410 (4)	0.0420 (7)
C26	0.8308 (4)	0.3680 (2)	0.5378 (5)	0.0420 (7)
C27	0.9449 (4)	0.4349 (2)	0.4523 (5)	0.0420 (7)
C28	0.9983 (4)	0.3468 (2)	0.4447 (5)	0.0420 (7)
O29	1.0778 (3)	0.357 66 (13)	0.5005 (3)	0.0420 (7)
O30	0.9829 (3)	0.310 05 (16)	0.3921 (3)	0.0420 (7)
H31	0.778 61	0.4096	0.5638	0.0546 (9)
H32	0.750 48	0.352 83	0.526 65	0.0546 (9)
H33	0.857 33	0.365 21	0.617 92	0.05
H34	1.017 26	0.429 29	0.511 01	0.0546 (9)
H35	0.892 72	0.457 04	0.485	0.0546 (9)
H36	0.9792	0.441 53	0.372 51	0.0546 (9)
N37	0.2708 (4)	0.762 12 (19)	0.6831 (4)	0.0472 (8)
C38	0.3266 (5)	0.8056 (2)	0.7213 (5)	0.0472 (8)
C39	0.2084 (4)	0.7742 (2)	0.5831 (5)	0.0472 (8)
C40	0.1905 (5)	0.7477 (2)	0.7694 (5)	0.0472 (8)
C41	0.3512 (5)	0.7260 (2)	0.6613 (5)	0.0472 (8)
C42	0.4480 (5)	0.7352 (2)	0.5802 (5)	0.0472 (8)
O43	0.4113 (3)	0.737 59 (14)	0.4694 (3)	0.0472 (8)
H44	0.2591	0.832 96	0.744 62	0.0614 (10)
H45	0.3851	0.824 81	0.667 41	0.0614 (10)
H46	0.368 39	0.800 38	0.803 89	0.0614 (10)
H47	0.284 92	0.773 72	0.504 92	0.0614 (10)
H48	0.158 42	0.752 92	0.558 43	0.0614 (10)
H49	0.196 96	0.812 44	0.577 44	0.0614 (10)
H50	0.241 01	0.733 95	0.836 98	0.0614 (10)
H51	0.152 96	0.717 86	0.723 24	0.0614 (10)
H52	0.141	0.774 59	0.782 83	0.0614 (10)
H53	0.351 02	0.698 49	0.715 61	0.0614 (10)
H54	0.448 91	0.745 12	0.703 24	0.0614 (10)
H55	0.327 93	0.694 32	0.511 09	0.0614 (10)
H56	0.467 72	0.689 62	0.544 74	0.0614 (10)
H57	0.4569	0.7731	0.4467	0.0614 (10)

12.022 Å, $V = 4236.0$ Å^3, and $Z = 8$ using Jade 9.5 (MDI, 2014). The space group was suggested to be *Pbca*, which was confirmed by successful solution and refinement of the structure. A reduced cell search in the Cambridge Structural Database (Groom and Allen, 2014) combined with the chemistry "C H N O Cl only" yielded two hits, but no structure for choline fenofibrate; the same search in the 2016 release of the CSD yields KUKYUM (Bordawekar *et al.*, 2014). A name search on "fenofibrate" yielded hits for ethyl fenofibrate (Yang and Wang, 2012; PAWFUQ) and isopropyl fenofibrate (Henry *et al.*, 2003, TADLIU; Balendiran *et al.*, 2012, TADLIU01 and TADLIU02). A connectivity search on the fenofibrate backbone yielded these two hits, plus the methyl ester (Zou *et al.*, 2012, PAVPUZ) and fenofibric acid (Rath *et al.*, 2005, QANHUJ).

A choline cation and a fenofibrate anion were built and their conformations optimized using Spartan '14 (Wavefunction, 2013), and saved as mol2 files. These files were converted into Fenske–Hall *Z*-matrix files using OpenBabel (O'Boyle *et al.*, 2011). Using these two fragments, the structure was solved with FOX (Favre-Nicolin and Černý, 2002). One of the solutions had a much lower cost factor than the other nine.

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TABLE II. DFT-optimized (CRYSTAL09) crystal structure of choline fenofibrate.

Crystal data

$(C_5H_{14}NO)(C_{17}H_{14}ClO_4)$	$V = 4239.84\ (1)$ Å^3
$M_w = 421.92$	$Z = 8$
Orthorhombic, *Pbca*	
$a = 12.341\ 03\ (2)$ Å	
$b = 28.568\ 70\ (6)$ Å	
$c = 12.025\ 62\ (2)$ Å	

Fractional atomic coordinates and isotropic displacement parameters (Å2)

	x	y	Z	U_{iso}
C1	1.052 13	0.426 59	−0.148 56	0.036 50
C2	1.090 84	0.420 19	−0.257 27	0.036 50
C3	1.175 43	0.447 34	−0.298 26	0.036 50
C4	1.220 21	0.481 38	−0.229 66	0.036 50
C5	1.181 34	0.490 06	−0.123 27	0.036 50
C6	1.096 82	0.462 44	−0.083 24	0.036 50
H7	1.055 49	0.393 77	−0.310 67	0.047 50
H8	1.205 37	0.441 82	−0.381 82	0.047 50
H9	1.215 50	0.517 89	−0.073 27	0.047 50
H10	1.065 86	0.469 42	−0.000 78	0.047 50
Cl11	1.333 06	0.515 34	−0.280 30	0.073 10
C12	0.961 50	0.395 87	−0.109 68	0.054 00
O13	0.906 80	0.374 48	−0.179 29	0.054 00
C14	0.935 74	0.391 49	0.010 68	0.036 50
C15	0.827 65	0.382 20	0.041 32	0.036 50
C16	0.798 19	0.377 51	0.151 81	0.036 50
C17	0.875 91	0.381 22	0.237 01	0.036 50
C18	0.984 64	0.388 69	0.207 37	0.036 50
C19	1.013 33	0.394 03	0.096 03	0.036 50
H20	0.765 56	0.378 21	−0.021 63	0.047 50
H21	0.714 35	0.370 89	0.173 27	0.047 50
H22	1.047 20	0.390 93	0.269 85	0.047 50
H23	1.098 45	0.398 94	0.076 92	0.047 50
O24	0.837 13	0.376 23	0.341 54	0.0420 0
C25	0.903 65	0.383 05	0.440 35	0.042 00
C26	0.825 93	0.372 23	0.536 56	0.042 00
C27	0.941 96	0.434 00	0.448 57	0.042 00
C28	0.997 89	0.346 74	0.447 02	0.042 00
O29	1.075 13	0.357 01	0.510 04	0.042 00
O30	0.985 73	0.308 70	0.393 25	0.042 00
H32	0.872 90	0.457 35	0.435 56	0.054 60
H33	1.004 27	0.442 73	0.387 74	0.050 00
N37	0.266 07	0.763 96	0.686 90	0.047 20
C38	0.325 08	0.807 06	0.725 81	0.047 20
C39	0.200 39	0.775 89	0.585 32	0.047 20
C40	0.188 91	0.748 46	0.776 10	0.047 20
C41	0.344 05	0.723 78	0.663 94	0.047 20
C42	0.435 00	0.733 17	0.581 13	0.047 20
O43	0.398 94	0.737 22	0.470 20	0.047 20
H44	0.263 89	0.833 27	0.745 28	0.061 40
H45	0.375 10	0.820 04	0.657 83	0.061 40
H46	0.372 12	0.798 41	0.799 85	0.061 40
H47	0.141 99	0.802 71	0.608 98	0.061 40
H48	0.255 44	0.788 98	0.522 25	0.061 40
H49	0.235 48	0.740 37	0.850 53	0.061 40
H50	0.143 52	0.718 40	0.745 25	0.061 40
H51	0.133 74	0.777 45	0.792 44	0.061 40
H52	0.437 12	0.764 60	0.436 90	0.061 40
H53	0.619 60	0.285 68	0.256 20	0.061 40
H54	0.706 37	0.305 36	0.363 95	0.061 40
H55	0.519 16	0.235 69	0.394 23	0.061 40
H57	0.841 00	0.255 79	0.441 84	0.061 40
H58	0.711 08	0.662 31	0.026 85	0.061 40
H59	0.738 63	0.601 62	0.040 19	0.061 40
H60	0.630 40	0.626 75	0.115 54	0.061 40
H56	0.510 11	0.296 90	0.409 28	0.061 40
H31	0.975 34	0.440 42	0.531 14	0.061 40

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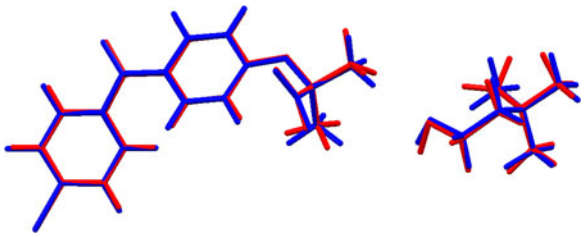

Figure 3. (Color online) Comparison of the refined and optimized structures of choline fenofibrate. The Rietveld refined structure is in red, and the DFT-optimized structure is in blue.

Rietveld refinement was carried out using GSAS (Toby, 2001; Larson and Von Dreele, 2004). Only the 1.0°–25.0° portion of the pattern was included in the refinement (d_{min} = 0.955 Å). All non-H bond distances and angles were subjected to restraints, based on a Mercury/Mogul Geometry Check (Bruno *et al.*, 2004; Sykes *et al.*, 2011) of the molecule. The Mogul average and standard deviation for each quantity were used as the restraint parameters. The restraints contributed 0.60% to the final χ^2. The C1–H10 and C14–H23 benzene rings were refined as rigid bodies. Isotropic displacement coefficients were refined, grouped by chemical similarity. The hydrogen atoms were included in calculated positions, which were recalculated during the refinement. The U_{iso} of each hydrogen atom was constrained to be 1.3× that of the heavy atom to which it is attached. The peak profiles were described using profile function #4 (Thompson *et al.*, 1987; Finger *et al.*, 1994), which includes the Stephens (1999) anisotropic strain broadening model. The background was modeled using a three-term shifted Chebyshev polynomial, with a four-term diffuse scattering function to model the Kapton capillary and any amorphous component. The final refinement of 85 variables using 23 045 observations (23 002 data points and 43 restraints) yielded the residuals R_{wp} = 0.100, R_p = 0.081, and χ^2 = 3.423. The largest peak (0.58 Å from Cl11) and hole (1.95 Å from Cl11) in the difference Fourier map were 0.84 and −0.70 e(Å)$^{-3}$, respectively. The Rietveld plot

TABLE III. Lattice parameters of choline fenofibrate at two temperatures. KUKYUM used a different choice of axes, but the space group in both cases is *Pbca*; the lattice transformation does not change the short Hermann-Mauguin symbol.

	KUKYUM single crystal	This work synchrotron powder	295/273 ratio
T (K)	273	295	
a (Å)	12.275(3)	12.341 03(2)	1.005 38
b (Å)	28.281(7)	28.568 70(6)	1.010 17
c (Å)	12.009(3)	12.025 62(2)	1.001 38
V (Å^3)	4168.91	4239.84(1)	1.017 01

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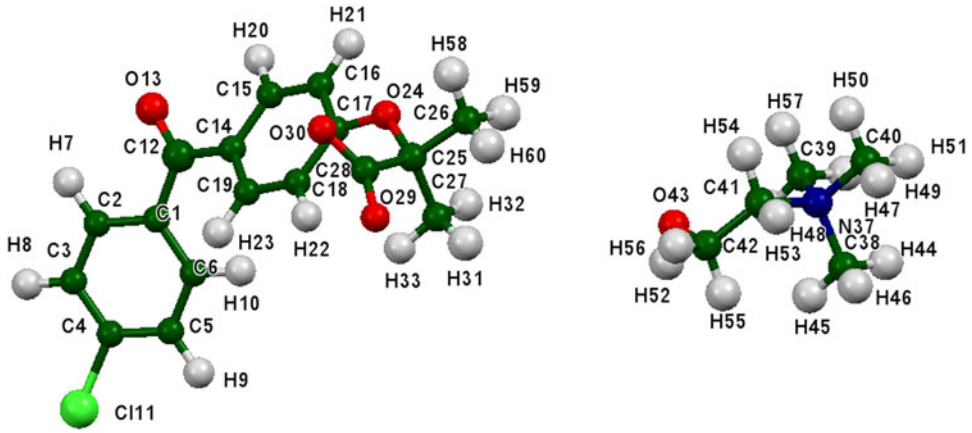

Figure 4. (Color online) The molecular structure of choline fenofibrate, with the atom numbering. All atoms are represented by 50% probability spheroids.

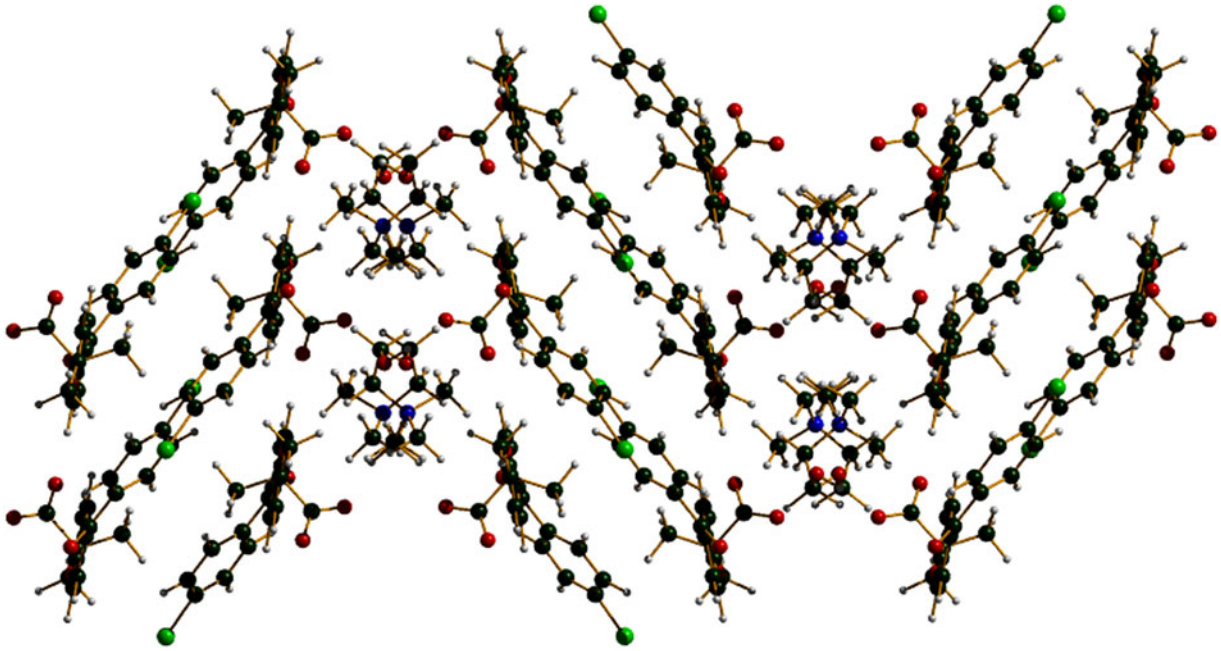

Figure 5. (Color online) The crystal structure of choline fenofibrate, viewed down the *c*-axis. The hydrogen bonds are shown as dashed lines.

is included as Figure 2. The largest errors are in the shapes of the low-angle peaks, and may indicate subtle changes in the sample during the measurement.

A density functional geometry optimization (fixed experimental unit cell) was carried out using CRYSTAL09 (Dovesi *et al.*, 2005). The basis sets for the H, C, N, and O atoms were those of Gatti *et al.* (1994), and the basis set for Cl was that of Apra *et al.* (1993). The calculation used 8 *k*-points and the B3LYP functional, and took ~37 days on a 2.4 GHz PC.

III. RESULTS AND DISCUSSION

The powder pattern does not correspond to the ones reported for choline fenofibrate polymorphs (Ponnaiah *et al.*, 2011). The refined atom coordinates of choline fenofibrate are reported in Table I, and the coordinates from the density functional theory (DFT) optimization in Table II. The root-mean-square (rms) deviation of the non-hydrogen atoms in the fenofibrate is 0.057 Å, and in the choline is 0.043 Å (Figure 3). This excellent agreement between the refined and optimized structures is strong evidence that the experimental structure is correct (van de Streek and Neumann, 2014). The major differences are in the orientations of the methyl hydrogen atoms, which are expected since they were included in the refinement in calculated positions. Compared with the single-crystal structure KUKYUM, the rms displacement of the fenofibrate is 0.052 Å and of the choline is 0.029 Å; the molecular structures are essentially identical. The unit cells and structures were determined at slightly different temperatures (Table III). The *c*-axes differ the most, but it is unclear whether the difference represents anisotropic thermal expansion or merely differences in samples. This discussion uses the DFT-optimized structure. The asymmetric unit (with atom numbering) is illustrated in Figure 4, and the crystal structure is presented in Figure 5.

All the bond distances, angles, and torsion angles fall within the normal ranges indicated by a Mercury Mogul Geometry

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TABLE IV. Hydrogen bonds in the DFT-optimized crystal structure of choline fenofibrate.

D–*H*···*A*	*D*–*H* (Å)	*H*···*A* (Å)	*D*···*A* (Å)	*D*–*H*···*A*(°)	Overlap (*e*)
O43–H52···O30	0.997	1.664	2.656	172.3	0.077
C2–H7···O29	1.083	2.410	3.336	142.5	0.023
C15–H20···O29	1.083	2.431	3.257	132.1	0.014
C38–H45···O29	1.089	2.157	3.207	161.2	0.033
C38–H46···O43	1.091	2.311	3.327	154.0	0.029
C39–H47···O13	1.090	2.298	3.311	153.7	0.023
C26–H60···O13	1.092	2.510	3.560	161.0	0.016

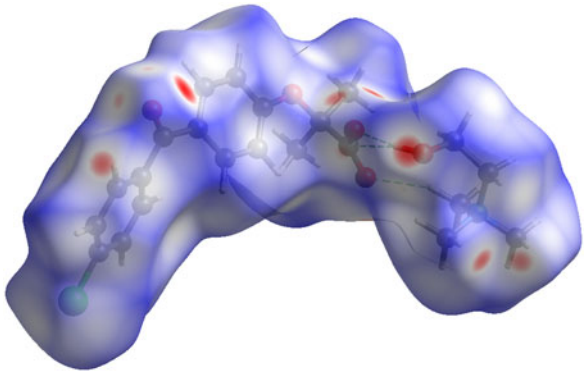

Figure 6. (Color online) The Hirshfeld surface of choline fenofibrate. Intermolecular contacts longer than the sums of the van der Waals radii are colored blue, and contacts shorter than the sums of the radii are colored red. Contacts equal to the sums of radii are white.

check (Macrae *et al.*, 2008). A quantum mechanical conformation examination (DFT/B3LYP/6-31G*/water) using Spartan '14 indicated that the observed conformation of the fenofibrate anion is ~2.4 kcal mole^{-1} higher in energy than a local minimum. A molecular mechanics (MMFF) sampling of conformational space indicated that the solid-state conformation is within 0.1 kcal mole^{-1} of the minimum energy conformation. The fenofibrate anion is in very close to its minimum-energy conformation in the solid state.

Analysis of the contributions to the total crystal energy using the Forcite module of Materials Studio (Accelrys, 2013) suggests that the intramolecular deformation energy contains significant contributions from bond, angle, and torsion angle distortion terms. The intermolecular energy is dominated by electrostatic contributions, which in this force-field-based analysis include hydrogen bonds, although van der Waals attraction is also significant. The hydrogen bonds are better analyzed using the results of the DFT calculation.

As might be expected, the hydroxyl group of the choline anion makes a strong hydrogen bond to the ionized carboxylate group of the fenofibrate anion (Table IV). This O–H···O hydrogen bond contributes ~15.2 kcal mole^{-1} to the crystal energy. These hydrogen bonds are discrete, having a graph set *D*1,1(2) (Etter, 1990; Bernstein *et al.*, 1995; Shields *et al.*, 2000). Together with the C–H···O hydrogen bonds, these link the cations and anions into layers parallel to the *ac*-plane. Between these layers there are layers of phenyl/chlorine contacts. Van der Waals attraction among the phenyl rings seems important to the crystal energy.

The volume enclosed by the Hirshfeld surface (Figure 6; Hirshfeld, 1977; McKinnon *et al.*, 2004; Spackman and Jayatilaka, 2009; Wolff *et al.*, 2012) is 520.90 Å^3, 98.3% of one-eighth the unit-cell volume. The molecules are thus not tightly packed. The only significant close contacts (red in Figure 6) involve the hydrogen bonds.

The Bravais–Friedel–Donnay–Harker (Bravais, 1866; Friedel, 1907; Donnay and Harker, 1937) morphology suggests that we might expect platy morphology for choline fenofibrate, with {010} as the principal faces. The more-sophisticated treatment of Bordawekar *et al.* also yields thick plates with {010} (our axes) as the principal faces. A fourth-order spherical harmonic preferred orientation model was included in the refinement; the texture index was only 1.019, indicating that preferred orientation was not significant in this rotated capillary specimen. The powder diffraction pattern of choline fenofibrate is included in the PDF as entry 00-065-1410.

SUPPLEMENTARY MATERIAL

The supplementary material for this article can be found at http://dx.doi.org/10.1017/S0885715616000099

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