X-ray powder diffraction data for gemcitabine, $C_9H_{11}F_2N_3O_4$

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X-ray powder diffraction data, unit-cell parameters and space group for gemcitabine, $C_9H_{11}F_2N_3O_4$, are reported [$a = 17.641(8)$ Å, $b = 6.985(1)$ Å, $c = 18.653(2)$ Å, $\alpha = \beta = \gamma = 90°$, unit-cell volume $V = 2298.61$ Å^3, $Z = 8$ and space group *Pmna*]. All measured lines were indexed and are consistent with the *Pmna* space group. No detectable impurities were observed. © *2015 International Centre for Diffraction Data*. [doi:10.1017/S0885715614001055]

Key words: X-ray powder diffraction, gemcitabine

I. INTRODUCTION

As a deoxycytidine analog that interferes with DNA synthesis, gemcitabine (Figure 1), systematic name 4-amino-1-[3,3-difluoro-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl] pyrimidin-2-one, is currently one of the most widely used and efficacious anticancer drugs. (Mini *et al.*, 2006). Gemcitabine combined with cytotoxins or molecularly targeted agents has been used in various carcinomas, including lung, pancreatic, bladder, and breast cancer (Plunkett *et al.*, 1995; Moysan *et al.*, 2013).

The crystal structure of gemcitabine has not been reported so far.

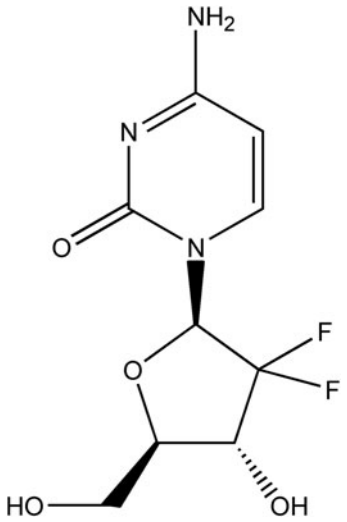

Figure 1. Structural formula of gemcitabine.

II. EXPERIMENTAL

A. Sample preparation

The title compound was purchased from J&K Chemical Co., Ltd., China. It was re-crystallized in methanol, dried, and ground into powder. The structure of gemcitabine was characterized by high-performance liquid chromatography (HPLC), ultraviolet (UV), and infrared (IR).

B. Diffraction data collection and reduction

The diffraction pattern for the title compound was collected at room temperature using an X'Pert PRO diffractometer (PANalytical Co., Ltd., Netherlands) with an X'celerator detector and Cu$K\alpha_1$ radiation ($\lambda = 1.540\,56$ Å, generator setting: 40 kV and 40 mA). The diffraction data were collected over the angular range from 5° to 50° 2θ with a step size of 0.013 13° 2θ and a counting time of 30 ms step^{-1}.

All the structure solution work was performed using the software package Material Studio 4.2 (Accelrys Co., Ltd. USA) and the powder diffraction pattern was pre-treated (Wu *et al.*, 2014). Indexing was carried out using peak positions obtained from the powder diffraction profiles by the X-Cell method. Then the best indexing results with 1074 for the value of figure of merit were refined using Pawley

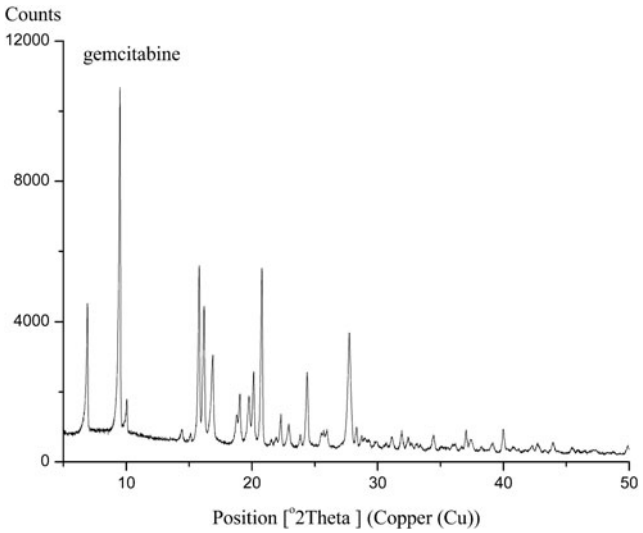

Figure 2. X-ray powder diffraction pattern of the gemcitabine, using Cu$K\alpha_1$ radiation ($\lambda = 1.540\,56$ Å).

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TABLE I. Indexed X-ray powder diffraction data of gemcitabine, $C_9H_{11}F_2N_3O_4$. Only the peaks with I_{rel} of 1 or greater are reported [$a = 17.641(8)$ Å, $b = 6.985(1)$ Å, $c = 18.653(2)$ Å, $\alpha = \beta = \gamma = 90°$, unit-cell volume $V = 2298.61$ Å^3, $Z = 8$, and space group *Pmna*]. All measured lines were indexed and are consistent with the *Pmna* space group. The *d*-values were calculated using Cu$K\ \alpha_1$ radiation ($\lambda = 1.540\ 56$ Å).

$2\theta_{obs}$ (°)	d_{obs} (Å)	I_{obs}	h	k	l	$2\theta_{cal}$ (°)	d_{cal} (Å)	$\Delta 2\theta$
6.9134	12.7754	41	1	0	1	6.8908	12.8173	0.0226
9.5000	9.3020	100	0	0	2	9.4749	9.3266	0.0252
10.0384	8.8043	15	2	0	0	10.0194	8.8209	0.0190
14.4501	6.1246	7	1	1	1	14.4294	6.1334	0.0207
15.1067	5.8599	6	1	0	3	15.0956	5.8642	0.0110
15.8026	5.6034	51	3	0	1	15.7881	5.6085	0.0145
16.1965	5.4680	41	2	1	0	16.1725	5.4760	0.0240
16.8924	5.2443	27	2	1	1	16.8599	5.2543	0.0325
18.7831	4.7204	11	2	1	2	18.7758	4.7222	0.0074
19.0457	4.6559	17	0	0	4	19.0153	4.6633	0.0304
19.7548	4.4904	16	1	1	3	19.7508	4.4913	0.0039
20.7921	4.2686	51	3	0	3	20.7734	4.2724	0.0187
21.9081	4.0536	5	3	1	2	21.9176	4.0519	−0.0095
22.3020	3.9829	11	4	0	2	22.2783	3.9871	0.0238
22.9323	3.8749	8	0	1	4	22.9111	3.8784	0.0212
23.8514	3.7276	6	4	1	0	23.8405	3.7293	0.0109
24.3766	3.6484	23	1	0	5	24.3666	3.6499	0.0100
25.7028	3.4631	7	4	1	2	25.7059	3.4627	−0.0031
25.9654	3.4287	7	0	2	1	25.9333	3.4329	0.0321
27.7249	3.2150	33	1	2	2	27.7165	3.2159	0.0083
28.3157	3.1492	8	3	0	5	28.3067	3.1502	0.0090
28.7359	3.1041	5	5	1	1	28.7235	3.1054	0.0123
28.9460	3.0821	5	2	1	5	28.9356	3.0831	0.0104
29.0773	3.0684	4	5	0	3	29.0748	3.0687	0.0025
29.3005	3.0456	4	0	2	3	29.3058	3.0450	−0.0053
29.7469	3.0009	4	1	2	3	29.7491	3.0007	−0.0022
30.6792	2.9118	3	4	1	4	30.6715	2.9125	0.0076
31.1125	2.8722	5	3	1	5	31.1185	2.8717	−0.0060
31.9134	2.8019	7	1	1	6	31.8875	2.8041	0.0259
32.4124	2.7599	5	1	2	4	32.3994	2.7610	0.0129
32.6881	2.7373	3	4	2	0	32.6789	2.7380	0.0092
33.1083	2.7035	3	3	2	3	33.1073	2.7036	0.0009
33.3840	2.6818	3	6	1	1	33.3833	2.6818	0.0007
34.4344	2.6023	5	6	1	2	34.4341	2.6024	0.0003
35.0516	2.5579	2	3	1	6	35.0566	2.5576	−0.0051
35.9444	2.4964	3	7	0	1	35.9271	2.4976	0.0173
36.1151	2.4850	3	6	1	3	36.1258	2.4843	−0.0107
36.6666	2.4489	2	2	2	5	36.6593	2.4493	0.0073
37.0342	2.4254	7	3	0	7	37.0063	2.4272	0.0279
37.4675	2.3983	4	5	2	2	37.4624	2.3987	0.0052
38.2291	2.3523	2	7	1	1	38.2384	2.3518	−0.0093
39.0563	2.3044	3	5	2	3	39.0406	2.3053	0.0157
39.9754	2.2535	7	2	0	8	39.9616	2.2542	0.0138
40.3168	2.2352	2	2	3	1	40.3197	2.2350	−0.0029
40.6976	2.2151	2	7	1	3	40.6979	2.2151	−0.0003
40.8945	2.2049	2	8	0	0	40.8887	2.2052	0.0058
41.1703	2.1908	2	5	2	4	41.1642	2.1911	0.0061
41.7086	2.1638	1	1	3	3	41.7033	2.1640	0.0053
42.2732	2.1361	3	6	0	6	42.2719	2.1362	0.0013
42.6540	2.1180	3	0	2	7	42.6422	2.1185	0.0118
42.7196	2.1149	3	6	2	3	42.7131	2.1152	0.0066
43.9408	2.0589	4	1	0	9	43.9509	2.0584	−0.0101
44.2428	2.0455	1	3	3	3	44.2668	2.0445	−0.0240
45.3982	1.9961	2	7	2	2	45.3925	1.9963	0.0057
45.9366	1.9740	2	1	1	9	45.9239	1.9745	0.0127
46.4486	1.9534	1	3	0	9	46.4148	1.9547	0.0339
47.1445	1.9262	1	2	3	5	47.1100	1.9275	0.0345
47.3546	1.9181	2	8	1	4	47.3831	1.9170	−0.0285
48.7858	1.8651	1	0	0	10	48.7803	1.8653	0.0055
49.8888	1.8264	3	6	0	8	49.8743	1.8269	0.0145

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refinement (Pan *et al.*, 2012). MC/SA search algorithm in the Powder Solve package (Engel *et al.*, 1999) was used to constantly adjust the conformation, position, and orientation of the trial model in a unit cell of gemcitabine. The result of Powder Solve ($R_{wp} = 6.59\%$) was refined by Rietveld refinement techniques based on the experimental X-ray powder diffraction pattern. In the Rietveld refinement (Young, 1993; Li *et al.*, 2014), variables defining the structural model and the powder diffraction profiles were refined by the least-squares methods for obtaining an optimal fit between the experimental pattern and the calculated pattern. After the Rietveld refinement, the final R_{wp} was 8.34%.

III. RESULTS

The experimental powder diffraction pattern is depicted in Figure 2. Indexing results confirmed that gemcitabine is orthorthombic with space group *Pmna* and unit-cell parameters after Pawley refinement: $a = 17.641(8)$ Å, $b = 6.985(1)$ Å, $c = 18.653(2)$ Å, $\alpha = \beta = \gamma = 90°$, unit-cell volume $V = 2298.61$ Å^3, $Z = 8$. The values of $2\theta_{obs}$, d_{obs}, I_{obs}, h, k, l, $2\theta_{cal}$, d_{cal}, and $\Delta 2\theta$ are listed in Table I.

SUPPLEMENTARY MATERIALS AND METHODS

The supplementary material for this article can be found at http://www.journals.cambridge.org/PDJ

Engel, G. E., Wilke, S., König, O., Harris, K. D. M., and Leusen, F. J. J. (**1999**). "Powder Solve–a complete package for crystal structure solution from powder diffraction patterns," J. Appl. Crystalogr. **32**, 1169–1179.

Li, S. S., Wu, X. Q., Pan, Q. Q., Cheng, Q., and Li, H. (**2014**). "Comparison of the accuracy of powder and single crystal X-ray diffraction techniques in determining organic crystal structure," Chin. Sci. Bull. **59**, 497–501.

Mini, E., Nobili, S., Caciagli, B., Landini, I., and Mazzei, T. (**2006**). "Cellular pharmacology of gemcitabine," Ann. Oncol. **17**, v7–v12.

Moysan, E., Bastiat, G., and Benoit, J. P. (**2013**). "Gemcitabine versus modified gemcitabine: a review of several promising chemical Modifications," Mol. Pharm. **10**, 430–444.

Pan, Q. Q., Guo, P., Duan, J., Cheng, Q., and Li, H. (**2012**). "Comparative crystal structure determination of griseofulvin: powder X-ray diffraction versus Single-crystal X-ray diffraction," Chin. Sci. Bull. **57**, 3867–3871.

Plunkett, W., Huang, P., and Gandhi, V. (**1995**). "Preclinical characteristics of gemcitabine," Anti-cancer Drugs **6**, 7–13.

Wu, D., Li, S. S., Xu, K. L., Zhang, L. L., Wu, X. Q., and Li, H. (**2014**). "X-ray powder diffraction data for loratadine," Powder Diffr. **29**(2), 193–195.

Young, R. A. (**1993**). *The Rietveld Method, IUCr Monographies of Crystallography* (Wiley, Oxford).

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