X-ray powder diffraction data for levetiracetam

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Experimental X-ray powder diffraction data, unit-cell parameters, and space group for levetiracetam, $C_8H_{14}N_2O_2$, are reported [$a = 9.197(5)$ Å, $b = 8.006(0)$ Å, $c = 6.289(3)$ Å, $\beta = 108.457(3)°$, unit-cell volume $V = 439.261$ Å^3, $Z = 2$, and space group $P2_1$]. All measured lines were indexed and are consistent with the $P2_1$ space group. No detectable impurity was observed. © *2013 International Centre for Diffraction Data* [doi:10.1017/S0885715613000742]

Key words: X-ray powder diffraction, levetiracetam

I. INTRODUCTION

Levetiracetam (LEV, Figure 1), chemical name (*S*)-2-(2-oxopyrrolidin-1-yl) butanamide, an active single enantiomer (Haria *et al.*, 1997), is an ethyl analog of the nootropic drug piracetam and used to treat certain types of seizures in people with epilepsy. It works by decreasing abnormal excitement in the brain and has minimal interactions with other anticonvulsants (Gualtieri *et al.*, 2002). Compared with other antiepileptic drugs, levetiracetam has a unique mechanism for the treatment of epilepsy, satisfactory pharmacokinetic characteristics and efficiency with minimal side effects. Therefore, levetiracetam has been widely used in many countries at present.

The single-crystal structure of levetiracetam ($a = 9.199$ Å, $b = 7.993$ Å, $c = 6.272$ Å, $\beta = 108.65°$, unit-cell volume $V = 436.962$ Å^3, $Z = 2$ and space group $P2_1$) was first reported by Song *et al.* (2003). But detailed X-ray powder diffraction data for levetiracetam have not been reported in the literature. In this report, the X-ray powder diffraction data of levetiracetam were collected, analyzed, and evaluated using the software package Material Studio 4.2 (Accelrys Co., Ltd. USA).

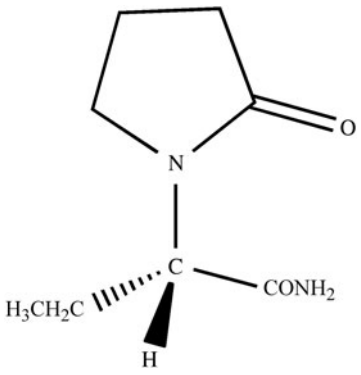

Figure 1. Structural formula of levetiracetam.

II. EXPERIMENTAL

A. Sample preparation

The title compound, levetiracetam (99% purity), in powder form was obtained from Zhejiang Jingxin Pharmaceutical Co., Ltd. The compound was re-crystallized in methanol (analytical grade) to obtain a single-crystal sample suiting for single-crystal measurement. The levetiracetam sample was also characterized by melting point and IR measurements.

B. Powder diffraction data collection and reduction

The diffraction pattern for the levetiracetam powder was collected at room temperature using an X'Pert PRO diffractometer (PANalytical) with an PIXcel 1D detector and Cu$K\alpha_1$ radiation ($\lambda = 1.540\,56$ Å, generator setting: 40 kV and 40 mA). The diffraction data were collected in the angular range from 5 to 50° 2θ with a step size of 0.013 13° 2θ and a counting time of 30 s/step. Data evaluation was performed using the software package Material Studio 4.2 (Accelrys Co., Ltd. USA).

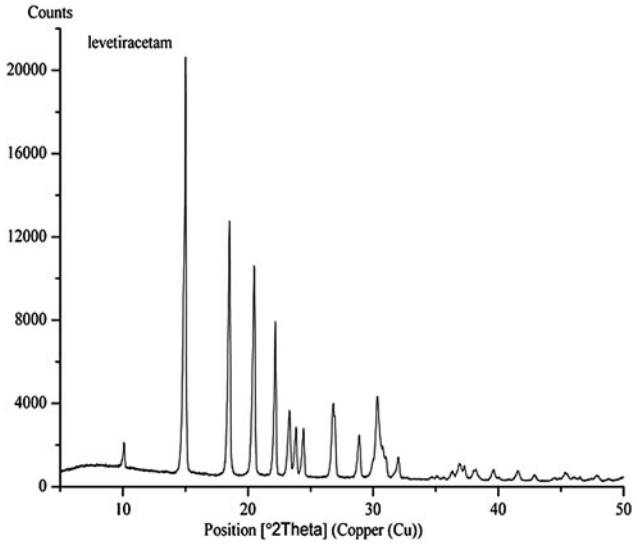

Figure 2. X-ray powder diffraction pattern of the levetiracetam, using Cu$K\alpha_1$ radiation ($\lambda = 1.540\,56$ Å).

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TABLE I. Indexed X-ray powder diffraction data of levetiracetam, $C_8H_{14}N_2O_2$. Only the peaks with I_{obs} of 1 or greater are presented [$a = 9.19(7)$ Å, $b = 8.005(7)$ Å, $c = 6.289(4)$ Å, $\beta = 108.456(7)°$, unit-cell volume $V = 439.261$ Å^3, $Z = 2$, and space group $P2_1$]. All measured lines were indexed and are consistent with the $P2_1$ 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)	$\Delta 2\theta$
10.099	8.752	9	1	0	0	10.131	8.724	−0.0321
14.826	5.970	39	0	0	1	14.837	5.966	−0.0109
15.023	5.892	100	1	1	0	15.007	5.899	0.0156
18.529	4.785	61	0	1	1	18.532	4.784	−0.0037
20.485	4.332	51	1	0	1	20.507	4.327	−0.0215
22.179	4.005	37	0	2	0	22.189	4.003	−0.0104
23.321	3.811	16	1	1	1	23.348	3.807	−0.0268
23.846	3.728	12	2	1	−1	23.844	3.729	0.0022
24.437	3.64	12	1	2	0	24.446	3.638	−0.009
26.788	3.325	18	0	2	1	26.798	3.324	−0.0106
26.945	3.306	15	1	2	−1	26.944	3.306	0.0008
28.889	3.088	11	2	0	1	28.905	3.086	−0.0169
30.320	2.946	20	2	2	0	30.281	2.949	0.0392
30.451	2.933	15	1	2	1	30.393	2.939	0.0576
30.766	2.904	8	3	0	0	30.720	2.908	0.0461
30.792	2.901	8	2	2	−1	30.784	2.902	0.0083
31.016	2.881	5	2	1	1	31.030	2.880	−0.0139
32.014	2.793	5	0	1	2	31.992	2.795	0.0212
36.333	2.471	2	1	2	−2	36.307	2.472	0.0263
36.898	2.434	4	0	3	1	36.867	2.436	0.0305
36.977	2.429	4	1	3	−1	36.977	2.429	−0.0008
37.292	2.409	3	3	2	−1	37.289	2.409	0.0025
38.001	2.366	2	2	2	−2	38.006	2.366	−0.0051
38.172	2.356	2	3	2	0	38.222	2.353	−0.0508
39.550	2.277	2	2	3	0	39.556	2.276	−0.0057
39.642	2.272	2	1	3	1	39.647	2.271	−0.0045
41.560	2.171	2	1	2	2	41.573	2.171	−0.0137
42.912	2.106	1	4	0	−2	42.891	2.107	0.0206
45.314	1.100	2	3	3	−1	45.331	1.999	−0.0168
47.875	1.899	1	3	1	−3	47.855	1.899	0.0197

Through analyzing the peak positions in the powder XRD pattern by X-Cell method from "Powder Indexing", the preliminary unit-cell parameters were obtained. The indexing results were then refined with the type of Pawley (Zhang *et al.*, 2013), which involves assigning the Miller indices (*h, k, l*) to each observed peak in the experimental powder XRD pattern (Harris, 2012). The conformation, position, and orientation of the trial model in a unit cell of levetiracetam were continuously regulated by MC/SA search algorithm in the Powder Solve package (Engel *et al.*, 1999). In order to obtain an optimal structure, variables defining the structural model and the powder diffraction profiles from the results of Powder Solve were refined by Rietveld refinement (Young, 1993) techniques based on the least squares methods. After Rietveld refinement, the final R_{wp} of the structure was converged to 9.66%.

III. RESULTS

The experimental powder diffraction pattern is depicted in Figure 2. Indexing results confirmed that levetiracetam is monoclinic with space group $P2_1$ and unit-cell parameters: $a = 9.197(5)$ Å, $b = 8.006(0)$ Å, $c = 6.289(3)$ Å, $\beta = 108.457(3)°$, unit-cell volume $V = 439.261$ Å^3, $Z = 2$ and space group $P2_1$ (Table I). Using Rietveld refinement, the powder structure of levetiracetam was successfully determined.

Single-crystal data were also collected by Oxford Diffraction Xcalibur Nova system with Mo$K\alpha$ radiation ($\lambda = 0.710\,73$ Å) at room temperature and θ from 3.05 to 28.77°. The final results of the single-crystal levetiracetam were obtained and are in good agreement with those obtained by our X-ray powder diffraction analysis.

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. Crystal. **32**, 1169–1179.

Gualtieri, F., Manetti, D., Romanelli, M., and Ghelardini, C. (**2002**). "Design and study of piracetam-like nootropics, controversial members of the problematic of cognition-enhancing drugs," Curr. Pharm. Des. **8**, 125–138.

Haria, M., and Balfour, J. A. (**1997**). "Levetiracetam," CNS Drugs. **7**, 159–164.

Harris, K. D. M. (**2012**). "Powder diffraction crystallography of molecular solids," Top. Curr. Chem. **315**, 133–178.

Song, J., Lou, K. X., Li, X. J., Wu, X. P., and Feng, R. X. (**2003**). "2-(2-Oxopyrrolidin-1-yl) butyramide," Acta Crystallogr., Sect. E (structure Rep. Online). **59**, 1772.

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

Zhang, L. L., Pan, Q. Q., Xiao, D., Wu, X. Q., Wang, Q., and Li, H. (**2013**). "X-ray powder diffraction data for deoxyschisandrin," Powder Diffr. **28**, 231–233.

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