Appendix

A.1 Physical Form Screening Results of Olanzapine (OZPN)

Table A.1 Solvent evaporation of olanzapine at room temperature (RT) and 277 K

Solvent	Evaporation at RT	Evaporation at 277 K
1,2-propanediol	Solvate hydrate	Solvate hydrate
1,2-dichloroethane	Form I	Form I
1,2-dimethoxyethane	Solvate hydrate	Solvate hydrate
1,4-butanediol	Solvate hydrate	Solvate hydrate
1,4-dioxane	Solvate hydrate	Solvate hydrate
1,5-pentanediol	No crystallisation	No crystallisation
1-butanol	Solvate hydrate	Solvate hydrate
1-methylnaphthalene	No crystallisation	No crystallisation
1-propanol	Solvate hydrate	Solvate hydrate
2-butanol	Solvate hydrate	Solvate hydrate
2-butanone	No crystallisation	Form I and solvate hydrate
2-butoxyethanol	Solvate	Solvate
2-methoxyethanol	Solvate hydrate	Solvate hydrate
2-methyl-1-butane	Insoluble	–
2-pentanol	Solvate hydrate	Solvate hydrate
3-methyl-1-butanol	Solvate hydrate	Solvate hydrate
4-fluoro toluene	Form1	Form1
Acetic acid + acetone	Solvate	Solvate
Acetone	Form I+ solvate hydrate	Form I and solvate hydrate
Acetonitrile	Solvate hydrate+ form I	Solvate hydrate and form I
Anhydrous acetonitrile	Form I	Form I
Butyl acetate	Form I	Form I and dihydrate B
Dichloromethane (DCM) + acetonitrile + water (1:1:1)	n.a.	Acetonitrile solvate hydrate
Chloroform	Form I	Solvate hydrate
Cyclohexane	Insoluble	–

(continued)

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Table A.1 (continued)

Solvent	Evaporation at RT	Evaporation at 277 K
DCM	No crystallisation	Mixture of DCM solvate and DCM solvate hydrate
DCM + cyclohexane (1:1)	Solvate hydrate	Solvate hydrate
Diethyl carbonate	Form1	Form I
Diethylether	Form I	Form I
Diisopropyl ether	Form I	Form I
Dodecane + water (1:1)	Dihydrate B and D	n.a.
Ethanol	Solvate	Solvate
Ethyl acetate + water (1:1)	Dihydrate B	n.a.
Ethyl acetate	Form I	Form I
Ethyl acetate + water + acetone (1:1:1)	Dihydrate B	n.a.
Ethylene glycol	Solvate	Solvate
Formamide	Insoluble	–
Formic acid	Salt/solvate	Salt/solvate
Hexane	Insoluble	–
Isobutyl acetate	Form I	Form I and dihydrate E
Isopropyl acetate	Form I	Form I
Methanol	Solvate	Solvate
Methyl acetate	Solvate hydrate + form I	Solvate hydrate and form I, unidentified peaks
m-xylene	Form I	Form I
N,N-dimethylacetamide	Form I	Form I
N,N-dimethylformamide	Solvate hydrate	Solvate hydrate
Nitrobenzene	No crystallisation	No crystallisation
Nitromethane	Solvate hydrate	Solvate hydrate and form I
N-methyl-2-pyrrolidone (NMP)	No crystallisation	No crystallisation
Pentyl acetate	Form I	Form I
Piperidine	No crystallisation	–
Pyridine	Solvate hydrate	Solvate hydrate
t-butanol	Solvate hydrate	n.a.
t-butyl methyl ether (TBMe)	Form I + solvate hydrate	Form I and solvate hydrate
Tetrahydrofuran (THF)	No crystallisation	Solvate hydrate
Toluene	Form I	Form I
Toluene + water (1:1)	Dihydrate D + E	n.a.
Trichloroethylene	Form I + solvate hydrate	Solvate hydrate
2,2,2-trifluoroethanol	No crystallisation	Solvate

n.a. not attempted

Table A.2 Fast solvent evaporation (on watch glass) of olanzapine at room temperature

Solvent	Results
1,4-dioxane	No sample
1-butanol	Solvate hydrate
1-propanol	Solvate hydrate
2-butanone	Solvate hydrate
Acetic acid	Solvate
Acetone	Solvate hydrate
Acetonitrile	Solvate hydrate
Butyl acetate	Dihydrate B
Chloroform	Solvate hydrate and form I
Ethanol	Solvate
Ethyl acetate	Dihydrate B and dihydrate E
Isopropyl acetate	Dihydrate B
Isoamyl alcohol	Solvate hydrate and dihydrate B
Methanol	Solvate
Nitromethane	Solvate hydrate
NMP	No sample
Pyridine	Solvate hydrate
TBMe	Solvate hydrate
THF	Solvate hydrate
Trichloroethylene	Solvate hydrate and form I
2,2,2-trifluoroethanol	Solvate hydrate

Table A.3 Cooling/evaporative crystallisation of olanzapine on Automated Platform Crystalliser

Solvent	Solvent dose (ml)	Crystallisation method	T sat (K)	T cool (K)	Vortex (rpm)	Vacuum (mbar)	Result
1-bromo-2-chloroethane	3	Cooling	343	298	850	NA	Solvate and form I
1-bromo-2-chloroethane	3	Cooling	343	298	850	NA	Solvate
1-bromobutane	3	Cooling	343	298	850	NA	No sample
1-bromobutane	3	Cooling	343	298	850	NA	No sample
1-methylnaphthalene	3	Cooling/solvent evaporation	343	298	850	NA	Solvate hydrate
1-methylnaphthalene	3	Cooling/solvent evaporation	343	298	850	NA	Form I
1-octanol	3	Cooling	343	298	850	NA/50	Solvate
1-octanol	3	Cooling	343	298	850	NA/50	Solvate
2-butanone	3	Cooling	343	298	850	NA	Form I and solvate hydrate
2-butanone	3	Cooling	343	298	850	NA	Solvate hydrate
2-methoxyethylether	3	Cooling	343	298	850	NA/50	Form I
2-methoxyethylether	3	Cooling	343	298	850	NA/50	Solvate hydrate
Benzene	3	Cooling	343	298	850	NA	Form I
Benzene	3	cooling	343	298	850	NA	Solvate hydrate
Bromoform	3	Cooling	343	298	850	NA/50	Form I
Bromoform	3	Cooling	343	298	850	NA/50	Solvate hydrate
Butyl ether	3	Cooling	343	298	850	NA/50	Solvate hydrate
Butyl ether	3	Cooling	343	298	850	NA/50	Solvate hydrate
Cyclohexane	3	Cooling	343	298	850	NA	Solvate hydrate and form I
Cyclohexane	3	Cooling	343	298	850	NA	Solvate hydrate
N,N-dimethylacetamide	3	Cooling	343	298	850	NA/50	Solvate hydrate
N,N-dimethylacetamide	3	Cooling	343	298	850	NA/50	Solvate hydrate
Dimethyl sulphoxide	3	Cooling	343	298	850	NA/50	Solvate hydrate

(continued)

Table A.3 (continued)

Solvent	Solvent dose (ml)	Crystallisation method	T sat (K)	T cool (K)	Vortex (rpm)	Vacuum (mbar)	Result
Dimethyl sulphoxide	3	Cooling	343	298	850	NA/50	Solvate hydrate
Dodecane	3	Cooling/solvent evaporation	343	298	850	NA	Solvate hydrate
Dodecane	3	Cooling/solvent evaporation	343	298	850	NA	Form I
Formamide	3	Cooling/solvent evaporation	343	298	850	NA	No crystallisation
Formamide	3	Cooling/solvent evaporation	343	298	850	NA	No crystallisation
Furfural	3	Cooling	343	298	850	NA/50	Solvate hydrate
Furfural	3	Cooling	343	298	850	NA/50	Solvate hydrate
Methanoic acid	3	Cooling	343	298	850	NA	No sample
Methanoic acid	3	Cooling	343	298	850	NA	No sample
Nitromethane	3	Cooling	343	298	850	NA	Form I
Nitromethane	3	Cooling	343	298	850	NA	Form I
NMP	3	Cooling/solvent evaporation	343	298	850	NA	Solvate hydrate
NMP	3	Cooling/solvent evaporation	343	298	850	NA	Solvate hydrate
Pentyl acetate	3	Cooling	343	298	850	NA/50	Solvate hydrate
Pentyl acetate	3	Cooling	343	298	850	NA/50	Form I and solvate hydrate
Tetrahydrothiophene	3	Cooling	343	298	850	NA	No sample
Tetrahydrothiophene	3	Cooling	343	298	850	NA	No sample
Thioacetic acid	3	Cooling	343	298	850	NA	No sample
Thioacetic acid	3	Cooling	343	298	850	NA	No sample
Trichloroethylene	3	Cooling	343	298	850	NA	Form I

(continued)

Table A.3 (continued)

Solvent	Solvent dose (ml)	Crystallisation method	T sat (K)	T cool (K)	Vortex (rpm)	Vacuum (mbar)	Result
Trichloroethylene	3	Cooling	343	298	850	NA	Solvate hydrate
N,N,N-triethylamine	3	Cooling	343	298	850	NA	Solvate hydrate
N,N,N-triethylamine	3	Cooling	343	298	850	NA	Solvate hydrate
Water	3	Cooling	343	298	850	NA	No sample
Water	3	Cooling	343	298	850	NA	No sample
Acetonitrile	3	Evaporative	303	303	850	NA	Solvate hydrate and unidentified phase
Acetonitrile	3	Evaporative	303	303	850	NA	Solvate hydrate
Chloroform	3	Evaporative	303	303	850	NA	Solvate hydrate
Chloroform	3	Evaporative	303	303	850	NA	Solvate hydrate
DCM	3	Evaporative	303	303	850	NA	Form I
DCM	3	Evaporative	303	303	850	NA	DCM solvate and DCM solvate hydrate
Iodomethane	3	Evaporative	303	303	850	NA	No sample
Iodomethane	3	Evaporative	303	303	850	NA	No sample
1-butanol	3	Evaporative	323	323	850	50	Solvate hydrate
1-butanol	3	Evaporative	323	323	850	50	Solvate hydrate
Acetonitrile	3	Evaporative	323	323	850	50	Form I
Acetonitrile	3	Evaporative	323	323	850	50+RT[a]	Solvate hydrate
Bromoform	3	Evaporative	323	323	850	50	Form I
Carbon tetrachloride	3	Evaporative	323	323	850	50	Form I
Carbon tetrachloride	3	Evaporative	323	323	850	50/RT[a]	Solvate hydrate
Ethanol	3	Evaporative	323	323	850	50	Solvate
Ethanol	3	Evaporative	323	323	850	50	Solvate
Methanol	3	Evaporative	323	323	850	50	Form I and solvate hydrate

(continued)

Table A.3 (continued)

Solvent	Solvent dose (ml)	Crystallisation method	T sat (K)	T cool (K)	Vortex (rpm)	Vacuum (mbar)	Result
Methanol	3	Evaporative	323	323	850	50+RT[a]	Solvate hydrate
Nitromethane	3	Evaporative	323	323	850	50	Form I
Nitromethane	3	Evaporative	323	323	850	50+RT[a]	Solvate hydrate
Pyridine	3	Evaporative	323	323	850	50	Form I
Tetrachloroethylene	3	Evaporative	323	323	850	50	Form I
Tetrachloroethylene	3	Evaporative	323	323	850	50/RT[a]	Solvate hydrate
2,2,2-trifluoroethanol	3	Evaporative	323	323	850	50	No sample
2,2,2-trifluoroethanol	3	Evaporative	323	323	850	50/ RT[a]	Solvate hydrate
Water	3	Evaporative	323	323	850	50	No sample

NA not applicable

[a]after 9 h at 323 K, the temperature was decreased to room temperature

Table A.4 Antisolvent crystallisation of olanzapine

Solvent	Antisolvent	Result
1-butanol	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
2-butanone	Cyclohexane	Form I and solvate hydrate
	Diisopropylether	Form I and solvate hydrate
	Heptane	Form I and solvate hydrate
1,4-dioxane	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
1-propanol	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
Acetonitrile	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
Acetic acid	Cyclohexane	Solvate and unidentified phase
	Diisopropylether	Solvate and unidentified phase
	Heptane	Solvate and unidentified phase
Acetone	Cyclohexane	Form I and solvate hydrate
	Diisopropylether	Form I and solvate hydrate
	Heptane	Solvate hydrate+ form I
Butyl acetate	Cyclohexane	Form I and dihydrate B
	Diisopropylether	Dihydrate B
	Heptane	Form I and dihydrate B
Chloroform	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
Ethanol	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
Ethyl acetate	Cyclohexane	Dihydrate B
	Diisopropylether	Dihydrate B
	Heptane	Form I and dihydrate B
Isoamyl alcohol	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
Isopropyl acetate	Cyclohexane	Form I and dihydrate B
	Diisopropylether	Form I
	Heptane	Form I

(continued)

Table A.4 (continued)

Solvent	Antisolvent	Result
Methanol	Cyclohexane	Solvate
	Diisopropylether	Solvate
	Heptane	Solvate
Nitromethane	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
NMP	Cyclohexane	No sample
	Diisopropylether	No sample
	Heptane	No sample
Pyridine	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
TBMe	Cyclohexane	Form 1 and solvate hydrate
	Diisopropylether	Form 1 and + solvate hydrate
	Heptane	Dihydrate B
2,2,2-trifluoroethanol	Cyclohexane	Solvate hydrate (isostructural to $C2_1/c$ group)
	Diisopropylether	Solvate hydrate (isostructural to $C2_1/c$ group) and trifluoroethanol solvate
	Heptane	Solvate hydrate (isostructural to $C2_1/c$ group)
THF	Cyclohexane	Solvate hydrate
	Diisopropylether	Solvate hydrate
	Heptane	Solvate hydrate
Trichloroethylene	Cyclohexane	Form I
	Diisopropylether	No sample
	Heptane	Dihydrate E and B

Table A.5 Solution crystallisation of olanzapine on functionalised surfaces

Surface	Results
(3-Aminopropyl)triethoxysilane (APTES)	Form I
(3-Aminopropyl)triethoxysilane (APTES)	Form I
(3-glycidoxypropyl) trimethoxysilane (GPTMS)	Form I
(3-glycidoxypropyl) trimethoxysilane (GPTMS)	Form I
(3-Mercaptopropyl)trimethoxysilane (MPTMS)	Form I
(3-Mercaptopropyl)trimethoxysilane (MPTMS)	Form I
Mica	Form I
Mica	Form I
Silicon wafer	Form I
Silicon wafer	Form I
Trimethoxy(propyl)silane (TPS)	Form I
Trimethoxy(propyl)silane (TPS)	Form I

Table A.6 Crystallisation of olanzapine by pH swing

(a)			
	pH	Base	Results
OZPN and acetic acid	9	15 % Ammonium hydroxide	Dihydrate B
OZPN and acetic acid	10	30 % Ammonium hydroxide	Dihydrate B
OZPN and acetic acid	9	50 % Aq NaOH	Dihydrate B
OZPN and acetic acid	8	10 % Methanolic NaOH	Methanol solvate
OZPN and acetic acid	10	50 % Aq NaOH	Dihydrate B
(b)			
Salt	pH	Base	Results
Adipate	12	50 % Aq NaOH	Dihydrate B
Citrate	12	50 % Aq NaOH	Dihydrate B
Formate	12	50 % Aq NaOH	Dihydrate B
Fumarate	12	50 % Aq NaOH	Dihydrate B
Glutarate	12	50 % Aq NaOH	Dihydrate B
Glycolate	12	50 % Aq NaOH	Dihydrate B
Hydrochloride	8	50 % Aq NaOH	Dihydrate B + D
Hydrochloride	12	50 % Aq NaOH	Dihydrate B
L-Tartrate	12	50 % Aq NaOH	Dihydrate B
L-malate	12	50 % Aq NaOH	Dihydrate B
Maleate	12	50 % Aq NaOH	Dihydrate B
Tosylate	12	50 % Aq NaOH	Dihydrate B
Succinate	12	50 % Aq NaOH	Dihydrate B

Table A.7 X-ray crystallographic crystal data, data collection and refinement details for olanzapine and its solvates

	Form I	Form II	2-butoxyethanol	2,2,2-trifluoroethanol
Chemical formula	$C_{17}H_{20}N_4S$	$C_{17}H_{20}N_4S$	$C_{17}H_{20}N_4S{\cdot}(C_6H_{14}O_2)$	$C_{17}H_{20}N_4S{\cdot}2(C_2F_3H_3O)$
M_r	312.43	312.43	430.60	512.52
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	123	123	123	123
a, b, c (Å)	10.3411 (13), 14.521 (2), 10.5314 (14)	9.8544 (14), 16.314 (2), 9.9754 (12)	10.442 (1), 17.7328 (15), 15.5165 (13)	12.7244 (9), 11.7538 (8), 16.0067 (11)
α, β, γ (°)	90, 100.291 (4), 90	90, 98.304 (8), 90	90, 126.279 (5), 90	90, 94.782 (2), 90
V (Å^3)	1555.9 (4)	1586.9 (4)	2316.2 (4)	2385.6 (3)
Z	4	4	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.21	0.21	0.17	0.21
Crystal size (mm)	0.20 × 0.18 × 0.09	0.34 × 0.14 × 0.03	0.12 × 0.10 × 0.04	0.39 × 0.23 × 0.21
Data collection				
Diffractometer	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.648, 0.745	0.537, 0.745	0.672, 0.746	0.648, 0.745
No. of measured, independent and observed [$I > 2s(I)$] reflections	12077, 3194, 2735	11000, 3115, 1892	47912, 6074, 4445	16124, 4689, 3190
R_{int}	0.028	0.085	0.048	0.039
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.033, 0.087, 1.03	0.054, 0.142, 1.00	0.039, 0.101, 1.02	0.058, 0.156, 1.06
No. of reflections	3194	3115	6074	4689
No. of parameters	205	205	282	321
No. of restraints	0	1	0	1
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.34, −0.22	0.47, −0.43	0.29, −0.32	0.49, −0.44

(continued)

Table A.7 (continued)

	Acetic acid	Ethylene glycol	Ethanol	TBMe hydrate
Chemical formula	$C_{17}H_{20}N_4S \cdot (C_2H_4O_2)$	$C_{17}H_{20}N_4S \cdot (C_2H_6O_2)$	$C_{17}H_{20}N_4S \cdot (C_2H_6O)$	$C_{17}H_{20}N_4S \cdot (C_5H_{12}O) \cdot 2(H_2O)$
M_r	372.48	375.51	358.50	436.61
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Temperature (K)	123	123	123	123
a, b, c (Å)	10.0427(11),12.7430(13), 14.3886(15)	9.8393(16), 13.278(2), 14.588(2)	10.3489(18), 13.003(2), 13.870(2)	14.2070(1), 12.2211(9), 14.550(1)
α, β, γ (°)	90, 92.436 (4), 90	90, 96.328 (7), 90	90, 92.496 (6), 90	90, 109.239(3), 90
V (Å^3)	1839.7 (3)	1894.4 (5)	1864.7 (5)	2385.2(2)
Z	4	4	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.2	0.19	0.19	0.17
Crystal size (mm)	0.60 × 0.30 × 0.15	0.12 × 0.08 × 0.04	0.15 × 0.07 × 0.04	0.51 × 0.32 × 0.12
Data collection				
Diffractometer	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.701, 0.746	0.540, 0.745	0.656, 0.745	0.643, 0.745
No. of measured, independent and observed [$I > 2s(I)$] reflections	19550, 4040, 3686	14389, 3718, 2441	14895, 3746, 2596	44786, 4915, 3962
R_{int}	0.014	0.093	0.047	0.040
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.031, 0.100, 1.14	0.064, 0.172, 1.01	0.041, 0.094, 1.03	0.049, 0.143, 1.02
No. of reflections	4040	3718	3746	4915
No. of parameters	246	249	237	326
No. of restraints	1	0	0	5
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.40, −0.31	0.87, −0.37	0.35, −0.25	1.37, −0.51

(continued)

Table A.7 (continued)

	2-pentanol hydrate	N,N,N-triethylamine hydrate	t-butanol hydrate	3-methyl-1-butanol hydrate
Chemical formula	$C_{17}H_{20}N_4S \cdot (C_5H_{12}O) \cdot (H_2O)$	$C_{17}H_{20}N_4S, \cdot 0.5 (C_6H_{15}N) \cdot 2(H_2O)$	$2(C_{17}H_{20}N_4S) \cdot 2(C_4H_{10}O) \cdot 5(H_2O)$	$2(C_{17}H_{20}N_4S) \cdot 2(C_5H_{12}O) \cdot 2(H_2O)$
M_r	418.59	399.06	863.18	837.18
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Triclinic, P-1
Temperature (K)	123	123	123	123
a, b, c (Å)	13.4466 (10), 12.3833 (9), 14.5522 (9)	14.817(1), 12.623(1), 14.461(1)	14.2491 (9), 12.3838 (8), 27.1418 (17)	12.3420 (17), 13.3559 (18), 14.630 (2)
α, β, γ (°)	90, 104.839 (2), 90	90, 113.36 (2), 90	90, 99.052 (2), 90	105.883 (6), 90.290 (6), 92.005 (6)
V (Å^3)	2342.3 (3)	2483.0 (3)	4729.7 (5)	2317.9 (5)
Z	4	4	12	2
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.16	0.15	0.17	0.16
Crystal size (mm)	0.53 × 0.19 × 0.08	0.55 × 0.25 × 0.12	0.21 × 0.19 × 0.05	0.51 × 0.21 × 0.12
Data collection				
Diffractometer	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX-II* CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.688, 0.746	0.651, 0.745	0.449, 0.745	0.608, 0.745
No. of measured, independent and observed [$I > 2s(I)$] reflections	33467, 4604, 3805	23283, 5090, 3419	35550, 9701, 7175	30830, 8815, 7345
R_{int}	0.028	0.042	0.046	0.039
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.044, 0.126, 1.03	0.092, 0.331, 1.28	0.047, 0.142, 1.02	0.082, 0.240, 1.03
No. of reflections	4604	5090	9701	8815
No. of parameters	290	364	598	560

(continued)

Table A.7 (continued)

	2-pentanol hydrate	N,N,N-triethylamine hydrate	t-butanol hydrate	3-methyl-1-butanol hydrate
No. of restraints	8	322	6	0
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.59, −0.33	1.04, −0.67	0.46, −0.26	1.93, −0.52

	1,4-butanediol hydrate	DMF hydrate	Pyridine hydrate	THF hydrate
Chemical formula	$2(C_{17}H_{20}N_4S) \cdot (C_4O_2H_{10}) \cdot 2(H_2O)$	$2(C_{17}H_{20}N_4S) \cdot (C_3H_7NO) \cdot 2(H_2O)$	$2(C_{17}H_{20}N_4S) \cdot (C_5H_5O) \cdot 2(H_2O)$	$C_{17}H_{20}N_4S{\cdot}0.5(C_4H_8O) \cdot (H_2O)$
M_r	751.01	733.99	739.99	366.50
Crystal system, space group	Triclinic, *P*-1	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Monoclinic, $C2/c$
Temperature (K)	123	123	123	123
a, *b*, *c* (Å)	12.2637 (11), 14.1146 (10), 14.1783 (12)	14.9885 (9), 12.7558 (7), 19.8567 (12)	14.8824 (7), 12.7289 (7), 20.3218 (11)	24.2355 (10), 12.5913 (5), 15.0767 (6)
α, β, γ (°)	63.985 (3), 65.649 (4), 65.437 (4)	90, 93.348 (2), 90	90, 93.465 (2), 90	90, 124.999 (1), 90
V (Å^3)	1924.9 (3)	3789.9 (4)	3842.7 (3)	3768.8 (3)
Z	2	4	4	8
Radiation type	Mo *K*α	Mo *K*α	Mo *K*α	Mo *K*α
μ (mm^{-1})	0.19	0.19	0.19	0.19
Crystal size (mm)	0.10 × 0.07 × 0.05	0.41 × 0.34 × 0.12	0.15 × 0.08 × 0.03	0.35 × 0.24 × 0.05
Data collection				
Diffractometer	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.670, 0.745	0.539, 0.745	0.662, 0.746	0.634, 0.745
No. of measured, independent and observed [$I > 2s(I)$] reflections	35551, 7560, 6322	29202, 7753, 5522	63158, 7558, 5873	15067, 3637, 3219
R_{int}	0.03	0.045	0.034	0.026

(continued)

Table A.7 (continued)

	1,4-butanediol hydrate	DMF hydrate	Pyridine hydrate	THF hydrate
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.035, 0.092, 1.02	0.040, 0.114, 1.01	0.035, 0.103, 1.03	0.042, 0.115, 1.03
No. of reflections	7560	7753	7558	3637
No. of parameters	505	494	497	267
No. of restraints	4	0	0	34
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.29, −0.26	0.35, −0.26	0.40, −0.25	0.54, −0.56

	1,4-dioxane hydrate	Acetone hydrate	1-butanol hydrate[a]	Acetonitrile[b]
Chemical formula	$C_{17}H_{20}N_4S \cdot 0.5(C_4H_8O_2) \cdot (H_2O)$	$C_{17}H_{20}N_4S \cdot 0.5(C_3H_6O) \cdot H_2O$	$C_{17}H_{20}N_4S \cdot 0.5(C_4H_{10}O) \cdot H_2O$	$(C_{17}H_{20}N_4S) \cdot (C_2H_3N) \cdot (H_2O)$
M_r	372.48	359.48	367.50	368.48
Crystal system, space group	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*
Temperature (K)	123	123	123	123
a, *b*, *c* (Å)	24.447 (3), 12.5660 (16), 14.9591 (19)	24.226 (2), 12.5269 (12), 15.0737 (15)	24.575 (6), 12.429 (3), 15.006 (3)	24.381 (2), 12.3856 (9), 15.0565 (14)
α, β, γ (°)	90, 125.421 (5), 90	90, 124.976 (4), 90	90, 125.255 (7), 90	90, 125.321 (7), 90
V (Å^3)	3744.9 (8)	3748.3 (6)	3743.1 (15)	3709.8 (6)
Z	8	8	8	8
Radiation type	Mo *K*α	Mo *K*α	Mo *K*α	Mo *K*α
μ (mm^{-1})	0.19	0.19	0.18	0.19
Crystal size (mm)	0.35 × 0.24 × 0.05	0.24 × 0.18 × 0.05	0.40 × 0.35 × 0.10	0.40 × 0.20 × 0.10
Data collection				
Diffractometer	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*

(continued)

Table A.7 (continued)

	1,4-dioxane hydrate	Acetone hydrate	1-butanol hydrate[a]	Acetonitrile[b]
T_{min}, T_{max}	0.680, 0.745	0.691, 0.745	0.701, 0.745	0.693, 0.746
No. of measured, independent and observed [$I > 2s(I)$] reflections	25185, 3686, 2615	25336, 3850, 2421	20876, 3827, 3457	64953, 5672, 4818
R_{int}	0.046	0.076	0.017	0.024
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.081, 0.237, 1.03	0.046, 0.118, 1.03	0.047, 0.121, 1.07	0.058, 0.195, 1.14
No. of reflections	3686	3850	3827	5672
No. of parameters	238	267	219	247
No. of restraints	0	15	3	216
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	2.32, −0.51	0.31, −0.46	0.49, −0.55	1.85, −1.07
	Nitromethane hydrate[a]	1,2-dimethoxyethane hydrate[c]	2-methoxyethanol hydrate	Methyl acetate hydrate
Chemical formula	$C_{17}H_{20}N_4S \cdot 0.5(CH_3NO_2) \cdot H_2O$	$(C_{17}H_{20}N4s) \cdot (C_4H_{10}O_2) \cdot (H_2O)$	$C_{17}H_{20}N_4S \cdot 0.5(C_3H_8O_2) \cdot (H_2O)$	$C_{17}H_{20}N_4S \cdot 0.5(C_3H_6O_2) \cdot H_2O$
M_r	361.95	330.45	368.49	367.48
Crystal system, space group	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*
Temperature (K)	123	123	123	123
a, *b*, *c* (Å)	24.352 (3), 12.3706 (13), 15.0182 (18)	24.4675 (13), 12.2298 (8), 15.1073 (8)	25.0869 (8), 12.3821 (4), 15.1983 (5)	24.899 (4), 12.5316 (19), 15.243 (2)
α, β, γ (°)	90, 125.531 (5), 90	90, 125.675 (2), 90	90, 126.872 (1), 90	90, 126.990 (5), 90
V (Å^3)	3681.9 (7)	3672.3 (4)	3776.7 (2)	3798.9 (10)
Z	8	8	8	8
Radiation type	Mo *K*α	Mo *K*α	Mo *K*α	Mo *K*α
μ (mm^{-1})	0.19	0.19	0.19	0.19
Crystal size (mm)	0.39 × 0.25 × 0.07	0.44 × 0.28 × 0.10	0.24 × 0.18 × 0.05	0.42 × 0.39 × 0.07

(continued)

Table A.7 (continued)

	Nitromethane hydrate[a]	1,2-dimethoxyethane hydrate[c]	2-methoxyethanol hydrate	Methyl acetate hydrate
Data collection				
Diffractometer	Bruker *APEX-II* CCD diffractometer	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD
Absorption correction	Multi-scan *SADABDS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.673, 0.745	0.663, 0.745	0.697, 0.746	0.680, 0.746
No. of measured, independent and observed [$I > 2s(I)$] reflections	32496, 3620, 3219	13280, 3598, 2382	26974, 3722, 3105	26450, 3751, 3148
R_{int}	0.033	0.042	0.029	0.030
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.033, 0.101, 1.12	0.053, 0.133, 1.02	0.068, 0.191, 1.04	0.045, 0.129, 1.07
No. of reflections	3620	3598	3722	3751
No. of parameters	222	220	236	257
No. of restraints	2	3	13	6
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.32, −0.24	0.28, −0.24	1.43, −1.12	0.96, −0.44

	1,2-propanediol hydrate[d]	1-propanol hydrate	Methanol	Dichloromethane
Chemical formula	$C_{17}H_{20}N_4S \cdot (C_3H_8O_2) \cdot (H_2O)$	$C_{17}H_{20}N_4S \cdot 0.5(C_3H_8O) \cdot (H_2O)$	$C_{17}H_{20}N_4S(CH_4O)$	$2(C_{17}H_{20}N_4S) \cdot (CH_2Cl_2)$
M_r	369.47	360.49	344.47	709.79
Crystal system, space group	Monoclinic, *C*2/*c*	Monoclinic, *C*2/*c*	Monoclinic, $P2_1/c$	Triclinic, *P*-1
Temperature (K)	123	123	123	123
a, *b*, *c* (Å)	24.704 (2), 12.1883 (10), 15.1242 (12)	24.4748 (13), 12.3515 (6), 15.1109 (8)	10.1493 (9), 12.2895 (10), 14.0944 (13)	9.6671 (15), 11.5070 (17), 16.697 (2)
α, β, γ (°)	90, 125.206 (3), 90	90, 125.649 (1), 90	90, 91.905 (5), 90	103.991 (6), 96.989 (6), 99.825 (6)

(continued)

Table A.7 (continued)

	1,2-propanediol hydrate[d]	1-propanol hydrate	Methanol	Dichloromethane
V (Å^3)	3721.0 (5)	3712.0 (3)	1757.0 (3)	1749.8 (4)
Z	8	8	4	2
Radiation type	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.20	0.19	0.2	0.34
Crystal size (mm)	0.28 × 0.22 × 0.08	0.39 × 0.36 × 0.07	0.14 × 0.07 × 0.04	0.60 × 0.30 × 0.15
Data collection				
Diffractometer	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.699, 0.746	0.674, 0.745	0.665, 0.746	0.680, 0.745
No. of measured, independent and observed [$I > 2s(I)$] reflections	26423, 3649, 2911	15925, 3775, 3337	18613, 4068, 2964	22706, 6166, 5615
R_{int}	0.034	0.019	0.033	0.016
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.053, 0.154, 1.06	0.034, 0.091, 1.04	0.039, 0.100, 1.03	0.028, 0.073, 1.05
No. of reflections	3649	3775	4068	6166
No. of parameters	258	266	225	436
No. of restraints	13	4	0	0
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	1.26, −0.62	0.43, −0.21	029 −0.24	0.28, −0.24

	Dihydrate B	Higher hydrate
Chemical formula	$C_{17}H_{20}N_4S{\cdot}2(H_2O)$	$C_{17}H_{20}N_4S{\cdot}2.5(H_2O)$
M_r	348.46	357.47
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $C2/c$
Temperature (K)	123	123
a, b, c (Å)	9.846 (2), 12.672 (3), 14.384 (3)	24.940 (6), 12.156 (3), 14.867 (3)
α, β, γ (°)	90, 92.724 (9), 90	90, 124.928 (6), 90

(continued)

Table A.7 (continued)

	Dihydrate B	Higher hydrate
V (Å^3)	1792.7 (7)	3695.2 (14)
Z	4	8
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.20	0.20
Crystal size (mm)	0.27 × 0.26 × 0.02	0.24 × 0.21 × 0.10
Data collection		
Diffractometer	Bruker *APEX-II* CCD	Bruker *APEX-II* CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.688, 0.745	0.374, 0.745
No. of measured, independent and observed [$I > 2s(I)$] reflections	13492, 3655, 2881	12338, 3582, 2479
R_{int}	0.028	0.063
Refinement		
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.039, 0.098, 1.02	0.070, 0.210, 1.05
No. of reflections	3655	3582
No. of parameters	235	250
No. of restraints	4	10
H-atom treatment	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.57, −0.37	0.60, −0.48

[1]H atoms treated by a mixture of independent and constrained refinement
[a]Stoichiometric information was obtained from TGA analysis
[b]Stoichiometric information reported in Chap. 6 was obtained from multiple TGA analysis. Refinement of the structure with stoichiometric information from TGA was not stable
[c]No stoichiometric information
[d]Stoichiometric information reported in Chap. 6 was obtained from multiple TGA analysis. Refinement of the structure with stoichiometric information from TGA was not stable and provide high ADP for solvent

Table A.8 Grinding experiments of olanzapine

Solvent	XRPD	Solvent	XRPD
Neat	Form II	DCM, acetonitrile and water (1:1:1)	Solvate hydrate
Neat, cryogenic	Form I	N,N-dimethylformamide	Solvate hydrate
1,4-butanediol	Solvate hydrate	Ethanol	Solvate hydrate
1-butanol	Solvate hydrate + form I	Ethylacetate	Form I
2-butoxyethanol	Solvate	Ethylene glycol	Solvate
2-methxoyethanol	Solvate hydrate + form I	Isoamylalcohol	Solvate hydrate + form I
2-pentanol	Form I	Methanol	Solvate
1,2-dimethoxyethane	Form I	Methanol, cryogenic grinding	Solvate
1,4-dioxane	Solvate hydrate + form I	Methanol:water (1:1)	Solvate hydrate
1,2-propanediol	Solvate hydrate	Methyl acetate	Form I
2,2,2-trifluoroethanol	Solvate	Nitromethane	Form I
Acetic acid	Acetic acid solvate	Pyridine	Solvate hydrate + form I
Acetonitrile	Form I	TBMe	Form I
Acetone	Form I	N,N,N-triethylamine	Form I
Chloroform	Form I	Toluene	Form I
1,2-dichloroethane	Form I	THF	Form I + solvate hydrate
DCM and water (1:1)	Solvate hydrate	Water	Higher hydrate transforms to dihydrate E and B within minutes
DCM	Solvate / form I		

Table A.9 Desolvation results of various olanzapine solvates

Solvate	At 318 K	At 333 K
1-butanol hydrate	Form I +II + III	Form 1 + II +III
2-butoxyethanol solvate	Form I+ II + III	Form 1
2-methoxyethanol hydrate	Form 1	Form I
2 pentanol hydrate	Form I	Form I
1,2-dimethoxyethane hydrate	Form 1	Form 1
1,2-propanediol hydrate	Form I	Form I
1,4-butanediol dihydrate	Form I	Form I
1,4-dioxane hydrate	Form I	Form I
2,2,2-trifluoroethanol solvate	Form 1 + II + III	Form 1 + II + III
3-methyl 1-butanol hydrate	Form I	Form I
Acetone hydrate	Form 1	Form 1

(continued)

Table A.9 (continued)

Solvate	At 318 K	At 333 K
Acetic acid solvate	Form I	Form I
Acetonitrile hydrate	Form 1	Form 1
Chloroform hydrate	Form I + II + III	form I
DCM solvate	Form II +III	Form I
Dihydrate B	Form II + III	Form I + II + III
Dihydrate E	Form I	Form I
Ethanol solvate	Form I+II + III	Form I + II + III
Ethylene glycol solvate	Form I	Form I
Methanol solvate	Form 1	Form 1
Methyl acetate solvate hydrate	Form 1	Form 1
N,N-dimethylformamide solvate hydrate	Form 1	Form 1
Nitromethane solvate hydrate	Form 1	Form 1
Pyridine solvate hydrate	Form 1	Form 1
TBMe solvate hydrate	Form 1	Form 1
THF hydrate	Form 1	Form

2-butoxyethanol solvate, DCM solvate, 1-butanol hydrate, 2,2,2-trifluoroethanol solvate, ethanol solvate, dihydrate B and chloroform hydrate were further subjected to desolvation in vacuum at RT and at 313 K at ambient pressure. Mixtures of form II and III were obtained in varying proportions

Table A.10 Recrystallisation of amorphous olanzapine under various conditions

S. No	Sample	Temperature	Results
1	Undisturbed on slide	RT	Amorphous
2	Undisturbed invial	RT	Form I + II + III
3	Boro silicate capillary_*in-situ*	RT	Form II + III
4	Boro silicate capillary_*in-situ*	−50 °C	Amorphous
5	Boro silicate capillary_*in-situ*	−25 °C	Amorphous
6	Boro silicate capillary_*in-situ*	−10 °C	Amorphous
7	Boro silicate capillary_*in-situ*	0 °C	Amorphous
8	Boro silicate capillary_*in-situ*	40 °C	Form I + II + III
9	Boro silicate capillary_*in-situ*	100 °C	Form I
10	Boro silicate capillary_*in-situ*	100 °C	Form I
11	Boro silicate capillary_fridge	−80 °C	Amorphous
12	Boro silicate capillary_ fridge	4 °C	Form I +II + III

A.2 Physical Form Screening Results of Clozapine (CZPN)

Table A.11 Solvent evaporation of clozapine at room temperature

Solvent	Evaporation at RT
1,2-dichloroethane	Form I
1,4-butanediol	No crystallisation
1,4-dioxane	Form I
1,5-pentanediol	No crystallisation
1-butanol	Form I
1-chlorobutane	Form I
1-propanol	Form I
2,2,2-trifluoroethanol	Form I
2-butanol	Form I
2-butanone	Form I
2-butoxyethanol	Form I
2-methoxyethanol	Form I
Acetic acid + acetone	Form I
Acetic acid + Isobutyl acetate	Form I
Aceticacid + cyclohexane	Form I
Acetone	Form I
Acetonitrile	Form I
Benzyl alcohol	Form I
Butyl acetate	Form I
Cyclohexanol	Non-crystalline
DCM	Form I
Diethylether	Form I
Dimethyl sulphoxide	Form I
Ethanol	Monohydrate
Ethanol + water	Monohydrate
Ethyl acetate	Form I
Ethylene glycol	Solvate
Isoamyl alcohol	Form I
Isobutyl acetate	Monohydrate
Methanol	Form I
Methanol + water	Monohydrate
Methyl acetate	Form I
N,N-dimethylacetamide	Solvate
N,N-dimethylformamide	Form I
Nitromethane	Form I

(continued)

Table A.11 (continued)

Solvent	Evaporation at RT
NMP	Non-crystalline
Propyl acetate	Form I
Propyleneglycol	No crystallisation
Pyridine	Form I
Toluene	Form I
Water	Form I

Table A.12 Fast solvent evaporation (on watch glass) of clozapine at room temperature

Solvent	XRPD results
1,2-dichloroethane	Form I
1,2-dimethoxyethane	Form I
1,4-dioxane	Non-crystalline
1-chlorobutane	Form I
1-methyl naphthalene	Form I
1-propanol	Form I
2,2,2-trifluoroethanol	Form I + monohydrate
2-butoxy ethanol	Form I
Acetic acid	Form I + amorphous
Acetone	Form I + monohydrate
Acetonitrile	Form I
Carbon tetrachloride	Form I
DCM	Form I
Dimethyl sulphoxide	Form I
Dodecane	Form I
Ethanol	Monohydrate
Ethyl acetate	Form I
Ethyl methyl ketone	Form I
Formic acid	Non-crystalline
Isobutyl acetate	Form I
Methanol	Form I + monohydrate
N,N-dimethylacetamide	Form I
N,N-dimethylformamide	Form I
1-butanol	Form I
Nitromethane	Form I
Pentyl acetate	Form I
Pyridine	Form I + monohydrate
TBMe	Form I
THF	Form I
Toluene	Form I
Trichloroethylene	Form I
Water	Form I

Table A.13 Cooling crystallisation of clozapine on React Array

Solvent	XRPD results
1,2-dichloroethane	Form I
1,2-dimethoxyethane	Form I
1,4-dioxane	Monohydrate + form I
1-chlorobutane	Form I
1-methyl naphthalene	Form I
2,2,2-trifluoroethanol	Form I
2-butoxy ethanol	Form I
Acetic acid	No diffraction
Acetone	Form I
Acetonitrile	Form I
Carbon tetrachloride	Form I
DCM	Monohydrate + form I
Dimethyl sulphoxide	Form I
Dodecane	Form I
Ethanol	Form I
Ethyl acetate	Monohydrate
Ethyl methyl ketone	Form I
Formic acid	Form I
Isoamyl alcohol	Form I
Isobutyl acetate	Form I
Methanol	Form I
N,N-dimethylacetamide	Solvate
N,N-dimethylformamide	Form I
n-butanol	Form I
Nitromethane	Form I
Pentyl acetate	Form I
Pyridine	Form I
TBMe	Form I
THF	Form I
Toluene	Form I
Trichloroethylene	Form I
Water	Form I

Table A.14 Grinding results of clozapine

Solvent	XRPD results
1,2-dichloroethane	Form I
1,2-dimethoxyethane	Form I
1,4-dioxane	Form I
1-butanol	Form I
1-chlorobutane	Form I
1-methyl naphthalene	Form I
1-propanol	Form I
2,2,2-trifluoroethanol	Form I
2-butoxy ethanol	Form I
Acetic acid	Form I
Acetone	Form I
Acetonitrile	Form I
Carbon tetrachloride	Form I
DCM	Form I
N,N-dimethylacetamide	Form I
N,N-dimethylformamide	Form I
DMSO	Form I
Dodecane	Form I
Ethanol	Form I
Ethyl acetate	Form I
Ethyl methyl ketone	Form I
Formic acid	Form I
Isobutyl acetate	Form I
Methanol	Form I
Methanol_cryo grinding	Form I
Neat cryo grinding	Form I
Nitromethane	Form I
Pentyl acetate	Form I
Pyridine	Form I
TBMe	Form I
THF	Form I
Toluene	Form I
Trichloroethylene	Form I
Water	Monohydrate

Table A.15 X-ray crystallographic crystal data, data collection and refinement details for clozapine and its solvates

	Clozapine	Clozapine monohydrate	Clozapine_DMA	Clozapine_EG
Chemical formula	$C_{18}H_{19}ClN_4$	$C_{18}H_{21}ClN_4O$	$C_{22}H_{28}ClN_5O$	$C_{20}H_{25}ClN_4O_2$
M_r	326.82	344.84	413.94	370.83
Crystal system, space group	Orthorhombic, $P2_12_12_1$	Monoclinic, $P2_1/c$	Orthorhombic, *Pbca*	Monoclinic, $P2_1/c$
Temperature (K)	123	123	123	123
a, *b*, *c* (Å)	9.328 (7), 9.632 (7), 17.836 (13)	9.9149 (3), 16.3646 (4), 10.9198 (3)	8.8660 (4), 17.5418 (7), 28.1238 (12)	20.6282 (9), 10.8488 (5), 17.5021 (8)
β (°)	90	102.229 (1)	90	93.134 (2)
V (Å^3)	1603 (2)	1731.57 (8)	4374.0 (3)	3911.0 (3)
Z	4	4	8	8
Radiation type	Mo Kα	Mo Kα	Mo Kα	Mo Kα
m (mm^{-1})	0.24	0.23	0.20	0.22
Crystal size (mm)	0.24 × 0.20 × 0.08	0.30 × 0.25 × 0.05	0.20 × 0.19 × 0.06	0.250 × 0.22 × 0.09
Data collection				
Diffractometer	Bruker APEX-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.4329 0.7454	0.6856 0.7454	0.6856 0.7454	0.4596 0.7454
No. of measured, independent and observed [$I > 2s(I)$] reflections	12686, 3146, 1771	15541, 3510, 3301	18417, 4460, 3730	29562, 8005, 7122
R_{int}	0.187	0.013	0.018	0.039
Refinement				
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.062, 0.148, 0.99	0.029, 0.076, 1.04	0.083, 0.239, 1.04	0.079, 0.232, 1.02
No. of reflections	3146	3510	4460	8005

(continued)

Table A.15 (continued)

	Clozapine	Clozapine monohydrate	Clozapine_DMA	Clozapine_EG
No. of parameters	213	230	270	513
No. of restraints	1	0	4	15
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.32, −0.38	0.33, −0.22	2.35, −1.59	1.69, −1.26

Cif files will be dealt with publication

[1]H atoms treated by a mixture of independent and constrained refinement

A.3 Physical Form Screening Results of Loxapine (LXPN)

Table A.16 Solvent evaporation of loxapine at room temperature

Solvent	Results
1,2-dichloroethane	Form I
1,2-dimethoxyethane	Form I
1,4-dioxane	Form I
1-butanol	No crystallisation
1-chlorobutane	Form I
1-methyl naphthalene	No crystallisation
2,2,2-trichloroethylene	Form I
2,2,2-trifluoroethanol	New
2-butoxy ethanol	No crystallisation
3-methyl-1-butanol	No crystallisation
Acetic acid	Non-crystalline
Acetone	Form I
Acetonitrile	Form I
Carbon tetrachloride	Form I
DCM	Form I
Dimethyl sulfoxide	No crystallisation
Dodecane	No crystallisation
Ethanol	Form I
Ethyl acetate	Form I
Ethyl methyl ketone	Form I
Formic acid	Flat
Isobutyl acetate	No crystallisation
Methanol	Form I
N,N-dimethyl acetamide	No crystallisation
N,N-dimethylformamide	No crystallisation
Nitromethane	Form I
Pentyl acetate	No crystallisation
Pyridine	No crystallisation
TBMe	Form I
THF	Form I
Toluene	Form I
Water	Not soluble, slurry same form

Table A.17 Cooling crystallisation of loxapine on React array

Solvent	Results
1,2-dichloroethane	Form I
1,2-dimethoxyethane	Form I
1,4-dioxane	Form I
1-butanol	Form I
1-chlorobutane	Form II (major) + I
1-methyl naphthalene	Flat spectra
2,2,2,-trifluoroethanol	New
2-butoxy ethanol	New
3-methyl-1-butanol	Form II
Acetic acid	New
Acetone	Form I
Acetonitrile	Form I
Carbon tetrachloride	Form I
DCM	Form I
Dimethyl sulphoxide	Form II
Dodecane	Form II
Ethanol	Form I
Ethyl acetate	Form I
Ethyl methyl ketone	Form I
Formic acid	New
Isobutyl acetate	Form I
Methanol	Form I
N,N-dimethylacetamide	Form I
N,N-dimethylformamide	Form I
Nitromethane	Form I
Pentyl acetate	Form I
Pyridine	Form I
TBMe	Form I
THF	Form I
Toluene	Form I
Trichloroethylene	Form I
Water	Form I

Table A.18 Fast solvent evaporation (on watch glass) of loxapine at room temperature

Solvent	Results
1,2-dichloroethane	Form II
1,2-dimethoxyethane	Form II
1,4-dioxane	No crystallisation
1-butanol	Form II
1-chlorobutane	Form II

(continued)

Table A.18 (continued)

Solvent	Results
1-methyl naphthalene	No crystallisation
1-propanol	Form II
2,2,2-trifluoroethanol	New
2-butoxy ethanol	No crystallisation
Acetic acid	New
Acetone	Form II
Acetonitrile	Form I + II
Carbon tetrachloride	Form II
DCM	Form II
Dimethyl sulphoxide	Form II
Dodecane	Form I
Ethanol	Form I
Ethyl acetate	Form II
Ethyl methyl ketone	Form II
Formic acid	no crystallisation
Isobutyl acetate	Form II
Methanol	Form I
N,N-dimethylacetamide	Form II
N,N-dimethylformamide	Form II
Nitromethane	Form I
Pentyl acetate	Form II
Pyridine	Form II
TBMe	Form II
THF	Form II
Toluene	Form II
Trichloroethylene	Form II
Water	Form I

Table A.19 X-ray crystallographic crystal data, data collection and refinement details for amoxapine and loxapine crystal structures

	Amoxapine	Loxapine_form I	Loxapine_form II
Chemical formula	$C_{17}H_{16}ClN_3O$	$C_{18}H_{18}ClN_3O$	$C_{18}H_{18}ClN_3O$
M_r	313.78	327.80	327.80
Crystal system, space group	Orthorhombic, *Pna*21	Orthorhombic, P*bca*	Monoclinic, $P2_1/c$
Temperature (K)	123	123	123
a, *b*, *c* (Å)	11.670 (8), 9.733 (7), 12.904 (9)	14.0245 (5), 12.8546 (5), 17.7500 (7)	12.8867 (7), 10.8108 (6), 12.3806 (6)

(continued)

Table A.19 (continued)

	Amoxapine	Loxapine_form I	Loxapine_form II
b (°)	90	90	109.484 (2)
V (Å^3)	1465.6 (18)	3200.0 (2)	1626.04 (15)
Z	4	8	4
Radiation type	Mo Kα	Mo Kα	Mo Kα
m (mm^{-1})	0.27	0.25	0.24
Crystal size (mm)	0.24 × 0.22 × 0.07	0.22 × 0.19 × 0.06	0.20 × 0.19 × 0.09
Data collection			
Diffractometer	Bruker APEX-II CCD	Bruker *APEX*-II CCD	Bruker *APEX*-II CCD
Absorption correction	Multi-scan *SADABS*	Multi-scan *SADABS*	Multi-scan *SADABS*
T_{min}, T_{max}	0.1299 0.7454	0.6392 0.7454	0.6129 0.7454
No. of measured, independent and observed [$I > 2s(I)$] reflections	5727, 2283, 1973	16853, 3243, 3044	20163, 3307, 2714
R_{int}	0.070	0.018	0.032
Refinement			
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.067, 0.185, 1.08	0.031, 0.079, 1.04	0.040, 0.115, 1.10
No. of reflections	2283	3243	3307
No. of parameters	203	209	209
No. of restraints	1	0	0
H-atom treatment	Mixed[1]	Mixed[1]	Mixed[1]
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.59, −1.25	0.31, −0.24	0.42, −0.31

All cif files will be dealt with the publication
[1]H atoms treated by a mixture of independent and constrained refinement

Table A.20 X-ray crystallographic crystal data, data collection and refinement details for loxapine succinate and its monohydrate

	Loxapine succinate	Loxapine succinate monohydrate
Chemical formula	$C_{18}H_{19}ClN_3O^+$. $C_4H_5O_4^-$	$2C_{18}H_{19}ClN_3O^+ \cdot C_4H_4O_4^{2-} \cdot C_4H_6O_4 \cdot 2H_2O$
M_r	445.89	927.82
Crystal system, space group	Monoclinic, C2/c	Triclinic, $P\bar{1}$
Temperature (K)	298	123
a, b, c (Å)	36.1824 (5), 7.08622 (14), 18.7690 (2)	9.4171 (6), 9.7604 (7), 13.7949 (9)
A, β, γ (°)	90, 113.8402 (10), 90	74.708 (2), 86.102 (2), 65.518 (2)
V (Å^3)	90, 113.8402 (10), 90	1111.86(13)

(continued)

Table A.20 (continued)

	Loxapine succinate	Loxapine succinate monohydrate
Z	8	1
Radiation type	Cu Kα1	Mo Kα
μ (mm^{-1})	1.87	0.22
Specimen shape, size (mm)	Cylinder, 12 × 0.7	0.33 × 0.18 × 0.06
Data collection		
Diffractometer	Bruker AXS D8 Advance diffractometer	Bruker *APEX*-II CCD
Specimen mounting	0.7 mm borosilicate capillary	–
Data collection mode	Transmission	–
Data collection method	Step	–
Absorption correction	–	Multi-scan *SADABS*
T_{min}, T_{max}	–	0.6392 0.7454
No. of measured, independent and observed [$I > 2s(I)$] reflections	–	15591, 4287, 3385
R_{int}	–	0.027
θ values (°)	2θmin = 3.5, 2θmax = 70.0, 2θstep = 0.014	θmax = 26.0, θmin = 2.4
Distance from source to specimen (mm)	–	0.617
Refinement		
R factors and goodness of fit	R_p = 0.030, R_{wp} = 0.033, R_{exp} = 0.015, R_{Bragg} = 0.025, χ^2 = 4.831	$R[F^2 > 2s(F^2)]$ = 0.038, $wR(F^2)$ = 0.100, S = 1.03
Profile function	Fundamental parameters with axial divergence correction	–
No. of reflections/data points	988	4287
No. of parameters	50	306
No. of restraints	–	3
H-atom treatment	–	Mixed[1]
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	–	0.25, −0.25
Preferred orientation correction	A spherical harmonics-based preferred orientation correction was applied with TOPAS during the Rietveld refinement	–

[1]H atoms treated by a mixture of independent and constrained refinement