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X-ray powder diffraction data for alaptide, 8(S)-methyl-6,9-diazaspiro/4,5/decane-7,10-dione (Cyclo(L-Alanyl-1-amino-1-cyclopentan carbonyl), cyclo(L-Ala-Acp)

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X-ray powder diffraction data, unit cells parameters and space group for alaptide are presented [a=21.136(4)Å, b=7.212(4)Å, c=6.126(3)Å], space group $P2_12_12_1$, cell volume=933.8(8) Å^3, Z=4]. All measured lines were indexed and are consistent with the $P2_12_12_1$ space group. No detectable impurities were observed.

Key words: X-ray powder diffraction, crystal structure, alaptide

I. INTRODUCTION

Alaptide, 8(S)-methyl-6,9-diazaspiro/4,5/decane-7,10-dione or Cyclo(L-Alanyl-1-amino-1-cyclopentancarbonyl) [cyclo(L-Ala-Acp), see Figure 1] is an original substance discovered by E.Kasafírek in the eighties at Prague. Substance preparation, production procedures and therapeutic application are protected by a number of patents in the Czech Republic and abroad .

The positive effect of alaptide on the central dopaminergnic system was documented on behaviour and memory of animals by testing. The positive influence on proliferative multiplying of the healthy cells was demonstrated in the tissue culture (e.g. in reducing the number of experimental gastro-intestinal ulcers in rats, in the healing of burns).

In 1990s alaptide was ready for the 3rd stage of the clinical testing for healing of burns and crura ulcers (gels, oinments), Alaptide is today manfactured mostly for veterinary and cosmetic purposes.

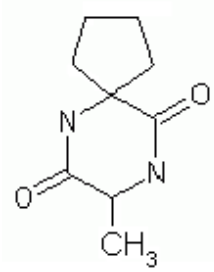

Figure 1. Structural formula of alaptide.

II. SAMPLE PREPARATION

Chemically pure alaptide is usually crystallized by a cyclization reaction from the methanol in the last step of production. It can be easily recrystallized from alcohols on cooling concentrated hot solutions .

Alaptide exists as one solid form only. The test consisting in mixing it in more than ten solvents did not reveal any polymorphism (as checked by IR and XRPD). The isolated crystals are plate-like, so care must be taken to produce a non-textured sample.

The microcrystalline sample was carefully ground by agate mortar and pestle. The size of crystallites was initially checked by optical microscopy and later by collecting a diffraction

image of the Debye-Scherrer rings on a capilary sample. The rings were continuous and no graininess was observed. The ground sample was then loaded into a glass cavity holder and measured in Bragg-Brentano parafocusing geometry.

TABLE I. Indexed X-ray powder diffraction data for alaptide. Only the peaks with Irel of 1 or greater are given. Lattice parameters: *a*=21.136(4)Å, *b*=7.212(4)Å, *c*=6.126(3)Å, V = 933.8(8) $Å^3$ and *Z*=4. All lines were indexed and are consistent with the $P2_12_12_1$ space group.

$2\theta_{obs}$[°]	d_{obs} [Å]	I_{rel}	h	k	l	$2\theta_{cal}$ [°]	d_{cal}[Å]	Δ2θ[°]
8,414	10,501	100	2	0	0	8,356	10,568	0,058
14,909	5,937	81	2	1	0	14,859	5,957	0,050
16,735	5,293	1	2	0	1	16,714	5,300	0,021
17,634	5,026	1	3	1	0	17,584	5,040	0,050
20,875	4,252	2	4	1	0	20,823	4,2625	0,052
22,222	3,9972	1	4	0	1	22,200	4,0012	0,022
22,841	3,8902	2	3	1	1	22,831	3,8919	0,010
24,699	3,6016	24	0	2	0	24,668	3,6061	0,031
25,609	3,4757	4	5	0	1	25,582	3,4793	0,027
26,118	3,4091	24	2	2	0	26,089	3,4129	0,021
27,803	3,2062	2	3	2	0	27,769	3,2101	0,034
28,227	3,1589	1	6	1	0	28,170	3,1653	0,057
30,008	2,9754	2	4	2	0	29,976	2,9786	0,032
31,441	2,8430	1	3	2	1	31,438	2,8433	0,003
32,655	2,7401	4	5	2	0	32,613	2,7435	0,042
33,897	2,6424	1	8	0	0	33,902	2,6420	-0,005
35,646	2,5167	2	6	2	0	35,600	2,5200	0,046
36,162	2,4820	2	8	1	0	36,179	2,4808	-0,017
36,241	2,4767	1	5	0	2	36,187	2,4803	0,054
37,059	2,4239	1	8	0	1	37,026	2,4260	0,033
38,909	2,3128	1	6	0	2	38,934	2,3114	-0,025

III.POWDER DIFFRACTION DATA

The diffraction data for alaptide are presented in Table I; the diffraction pattern, shown in Figure 2, was collected at room temperature with an X'Pert PRO θ-θ powder diffractometer with parafocusing Bragg-Brentano geometry using CuK_α radiation (λ = 1.5418 Å, generátor setting: 40kV, 30mA). An ultrafast X'Celerator detektor was employed over the angular range 7-70° (2θ) with a step size of 0.017° (2θ) and a counting time of 81.28 s $step^{-1}$. Data evaluation were performed in the software package HighScore Plus.

The data collected are consistent with the orthorombic cell parameters *a*=21.136(4), *b*=7.212(4) and *c*=6.126(3) Å, space group $P2_12_12_1$, cell volume=933.8(8) $Å^3$, *Z*=4. These parameters were derived using the DICVOL04 with the results all being within the errors indicated. The following figures of merits were achieved F_{20} = 19.6(0.0192,53) and M_{20} = 13.6.

ACKNOWLEDGMENTS

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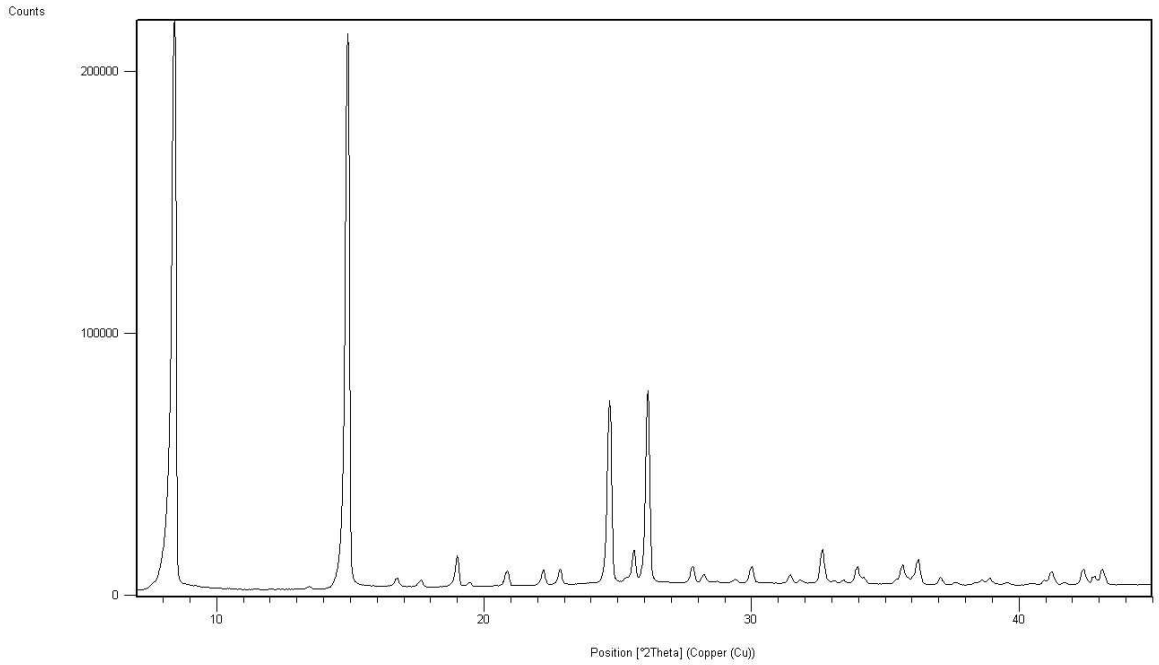

Figure 2. X-ray powder diffraction pattern of alaptide using CuK_{α} radiation (λ = 1.5418 Å).

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HighScore Plus, Full Powder Pattern Analysis Software, V2.2, PANALYTICAL, Almelo, Netherlands.