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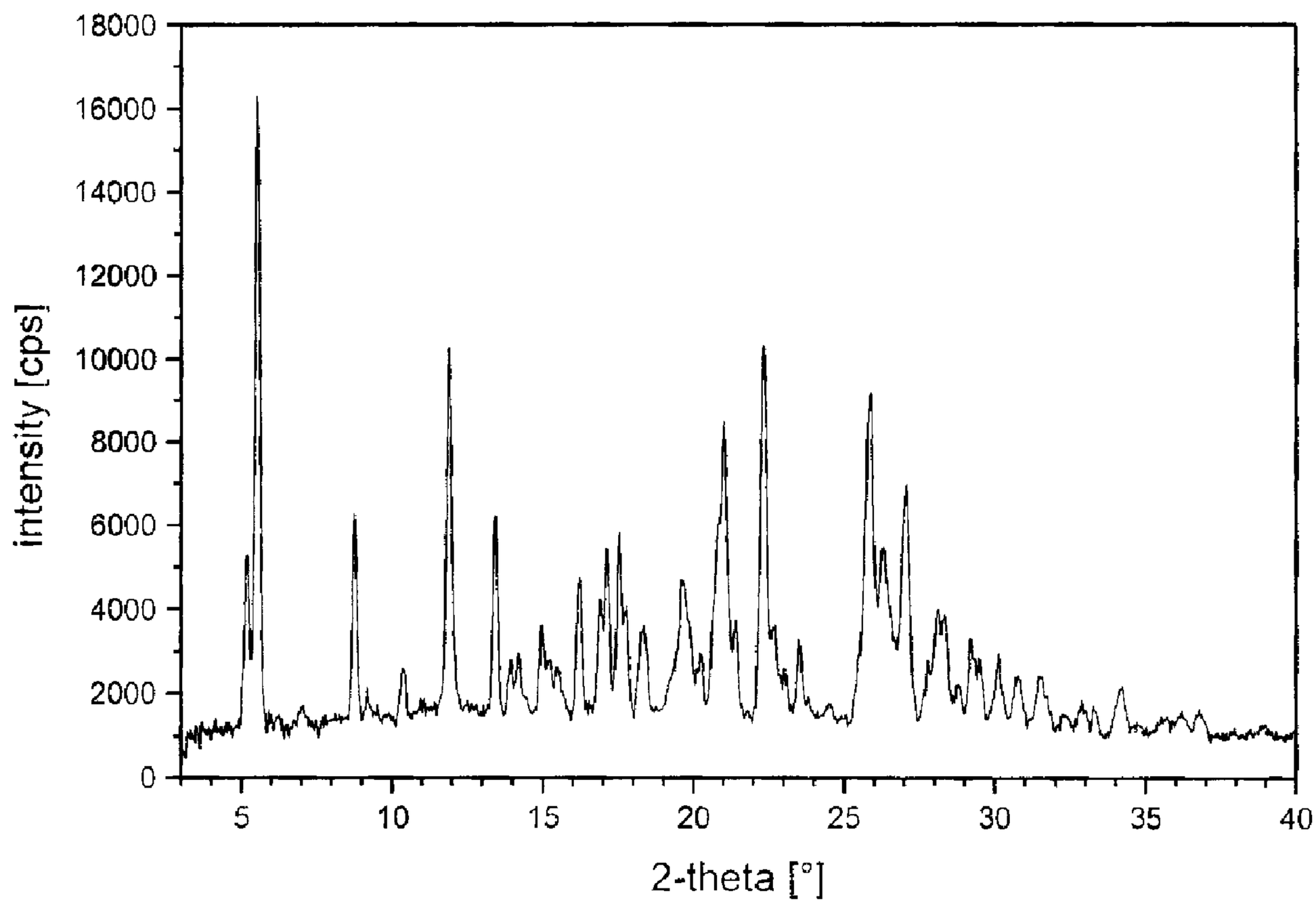


(57) Abrégé/Abstract:
The present invention relates to new crystalline salt forms of flibanserine which have valuable pharmacological properties, to a process for their manufacture, to pharmaceutical formulations containing them and to their use as medicament.

Abstract

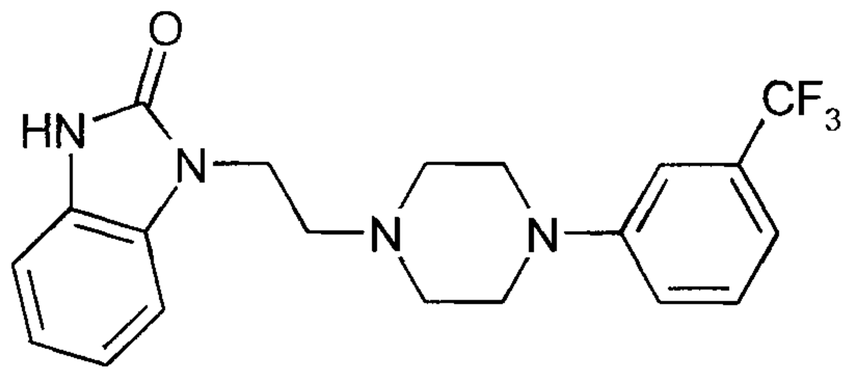
The present invention relates to new crystalline salt forms of flibanserine which have valuable pharmacological properties, to a process for their manufacture, to pharmaceutical formulations containing them and to their use as medicament.

NEW SALTS

The present invention relates to crystalline salts of flibanserin, 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one, to a process for their manufacture, to pharmaceutical formulations containing them and to their use as medicament.

Background to the invention

The compound 1-[2-(4-(3-trifluoromethyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one is known from EP 0 526 434 B1 and has the following chemical structure, depicted below as Formula (I)



(I)

Furthermore, the free base of this compound is known from EP 1 414 816 B1 in its polymorph B form, as well as a process for its manufacture.

The above mentioned patents further disclose the use of this compound for the treatment of different diseases inter alia for the treatment of HSDD (Hypoactive Sexual Desire Disorder).

Summary of the invention

The aim of the invention is to provide new forms of flibanserin with advantageous properties for pharmaceutical use.

The above mentioned pharmacologically valuable properties of flibanserin disclosed in the prior art constitutes the basic prerequisite for effective use of the compound as pharmaceutical compositions. However, to be permitted for use as a medicament, an active substance must also satisfy further requirements, besides actually being effective for the desired indication. These parameters are largely to do with the physicochemical nature of the active substance.

Without being restrictive, examples of these parameters are the stability of effect of the starting substance under various environmental conditions, the stability during production of the pharmaceutical formulation and stability in the final compositions of the drug. The pharmaceutically active substance used to prepare the pharmaceutical compositions should therefore have great stability which is ensured even under different environmental conditions. This is absolutely essential to prevent pharmaceutical compositions being used which contain breakdown products, for example, in addition to the active substance itself. In such a case the content of active substance present in the pharmaceutical formulation might be lower than specified.

The absorption of moisture reduces the content of pharmaceutically active substance as a result of the increased weight caused by the uptake of water. Pharmaceutical compositions with a tendency to absorb moisture have to be protected from moisture during storage, e.g. by the addition of suitable drying agents or by storing the drug in an environment where it is protected from moisture. In addition, the uptake of moisture may reduce the content of pharmaceutically active substance during manufacture if the pharmaceutical substance is exposed to the environment without being protected from moisture in any way. Preferably, therefore, a pharmaceutically active substance should be, if at all, only slightly hygroscopic.

Another criterion which may be of exceptional importance under certain

circumstances depending on the choice of formulation or the choice of manufacturing process is the solubility of the active substance. If for example pharmaceutical solutions are prepared (e.g. for infusions) it is essential that the active substance should be sufficiently soluble in physiologically acceptable solvents. It is also very important for drugs which are to be taken orally that the active substance should be sufficiently soluble.

The problem of the present invention is to provide a pharmaceutically active substance which not only is characterised by high pharmacological potency but also satisfies the above-mentioned physicochemical requirements as far as possible.

Accordingly, the aim of the present invention is to provide new crystalline salt forms of flibanserin, 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one, which are characterized by advantageous physicochemical properties, especially improved solubility in water and minimized hygroscopicity

Another embodiment of the present invention relates to the process for manufacture of new crystalline salt forms of 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one.

Another embodiment of the present invention relates to pharmaceutical compositions containing the new crystalline salt forms of 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one and to their use as medicament.

Detailed description of the invention

In a first aspect, the present invention relates to the following salts and/or crystalline forms and/or crystalline salt forms of the compound 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one:

I. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one chloride (form I) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 215 ± 5°C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that two further weakly endothermic signals can be observed at approx. 122 °C and 186 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 15.99 ± 0.05 Å, d = 7.44 ± 0.05 Å, d = 3.98 ± 0.05 Å and d = 3.44 ± 0.05 Å;

II. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one chloride (form III) (= solvate form), characterized by a melting point of T_{fus} (onset) = 217 ± 5°C which occurs during thermal analysis using DSC. The DSC is characterised in that two further weakly endothermic signals can be observed at approx. 56 °C and 121 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 16.43 ± 0.05 Å, d = 5.08 ± 0.05 Å, d = 4.35 ± 0.05 Å, d = 3.47 ± 0.05 Å and d = 7.66 ± 0.05 Å;

III. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one bromide (form I) (= solvate form), characterized by a melting point of T_{fus} (onset) = 252 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that two further weakly endothermic signals can be observed at approx. 104 °C and 222 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 3.48 ± 0.05

Å, d = 3.33 ± 0.05 Å, d = 4.28 ± 0.05 Å, d = 3.43 ± 0.05 Å and d = 16.03 ± 0.05 Å;

IV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one bromide (form III) (= solvate form), characterized by a melting point of T_{fus} (onset) = 252 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that two further weakly endothermic signals can be observed at approx. 89 °C and 218 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 15.52 ± 0.05 Å, d = 5.15 ± 0.05 Å, d = 4.60 ± 0.05 Å, d = 4.36 ± 0.05 Å and d = 3.94 ± 0.05 Å;

V. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one edisylate (form I) (= solvate form), characterized by a melting point of T_{fus} (onset) = 144 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 14.34 ± 0.05 Å, d = 3.95 ± 0.05 Å, d = 4.64 ± 0.05 Å, d = 3.75 ± 0.05 Å and d = 9.50 ± 0.05 Å;

VI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one tosylate (form I) (hydrated form), characterized by a melting point of T_{fus} (onset) = 238 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 5.11 ± 0.05 Å, d = 4.84 ± 0.05 Å, d = 3.93 ± 0.05 Å and d = 3.48 ± 0.05 Å;

VII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one mesylate (form I) (= monohydrate form, characterized by a melting point of T_{fus} (onset) = 207 ± 5 °C which occurs

during thermal analysis using DSC. The DSC diagram is additionally characterised in that one further weakly endothermic signal can be observed at approx. 60 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 15.25 ± 0.05 Å, d = 4.18 ± 0.05 Å, d = 3.47 ± 0.05 Å, d = 4.95 ± 0.05 Å and d = 4.24 ± 0.05 Å; Its solubility in water at room temperature is 1.1 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 3.4 %.

VIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one besylate (form I) (= monohydrate form), characterized by a melting point of T_{fus} (onset) = 247 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that one further weakly endothermic signal can be observed at approx. 111 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 3.99 ± 0.05 Å, d = 4.69 ± 0.05 Å, d = 4.85 ± 0.05 Å and d = 6.42 ± 0.05 Å; Its solubility in water at room temperature is 0.1 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.15 %.

IX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one oxalate (form I) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 209 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 7.09 ± 0.05 Å, d = 6.01 ± 0.05 Å, d = 4.92 ± 0.05 Å, d = 4.24 ± 0.05 Å and d = 4.08 ± 0.05 Å; Its solubility in water at room temperature is 1.7 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.7 %.

X. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one oxalate (form V) (= dihydrate form), characterized by a melting point of T_{fus} (onset) = 254 ± 5 °C which occurs during thermal analysis using DSC.The DSC diagram is additionally characterised in that two further weakly endothermic signals can be observed at approx. 112 °C and 198 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 7.09 ± 0.05 Å, d = 5.67 ± 0.05 Å, d = 5.04 ± 0.05 Å, d = 4.87 ± 0.05 Å and d = 3.76 ± 0.05 Å;

XI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one sacharinate (form I) (= 1.5 hydrated form), characterized by a melting point of T_{fus} (onset) = 90 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 7.86 ± 0.05 Å, d = 5.90 ± 0.05 Å, d = 5.30 ± 0.05 Å, d = 5.14 ± 0.05 Å and d = 4.62 ± 0.05 Å; Its solubility in water at room temperature is 0.3 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.24 %.

XII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one phosphate (form I) (= hemihydrate form), characterized by a melting point of T_{fus} (onset) = 182 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that three further weakly endothermic signals can be observed at approx. 81 °C, 141 °C and 164 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 15.79 ± 0.05 Å, d = 5.06 ± 0.05 Å, d = 7.90 ± 0.05 Å and d = 3.75 ± 0.05 Å;

XIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one maleate (form I) (= THF solvate), characterized by a melting point of T_{fus} (onset) = 98 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that a further weakly endothermic signal can be observed at approx. 78 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 9.58 ± 0.05 Å, d = 7.71 ± 0.05 Å, d = 6.13 ± 0.05 Å, d = 5.93 ± 0.05 Å and d = 4.62 ± 0.05 Å;

XIV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one maleate (form III) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 172 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 6.07 ± 0.05 Å, d = 5.16 ± 0.05 Å, d = 4.52 ± 0.05 Å, d = 4.10 ± 0.05 Å and d = 3.20 ± 0.05 Å;

XV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one ethansulfonate (form I) (= monohydrate form), characterized by a melting point of T_{fus} (onset) = 207 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that two further weakly endothermic signals can be observed at approx. 105 °C and 189 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 15.30 ± 0.05 Å, d = 7.25 ± 0.05 Å, d = 5.00 ± 0.05 Å, d = 4.34 ± 0.05 Å and d = 4.23 ± 0.05 Å; Its solubility in water at room temperature is 1.3 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.32 %.

XVI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one camphorsulfonate (form I) (= anhydrous

form), characterized by a melting point of T_{fus} (onset) = 217 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that a further weakly endothermic signal can be observed at approx. 177 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 16.32 ± 0.05 Å, d = 5.69 ± 0.05 Å, d = 5.45 ± 0.05 Å, d = 5.50 ± 0.05 Å and d = 3.62 ± 0.05 Å;

XVII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one malonate (form I) (= dihydrate form), characterized by a melting point of T_{fus} (onset) = 103 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that a further weakly endothermic signal can be observed at approx. 79 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 23.23 ± 0.05 Å, d = 8.56 ± 0.05 Å, d = 4.62 ± 0.05 Å, d = 4.19 ± 0.05 Å and d = 3.72 ± 0.05 Å;

XVIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one malonate (form II) (= solvate form), characterized by the data listed in table 2.9;

XIX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one malonate (form VI) (= dihydrate form), characterized characterized by the data listed in table 2.10;

XX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one salicylate (form I) (= anhydrous form), characterized by the data listed in table 2.11;

XXI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one L-tartrate (= dihydrate form),

characterized by a melting point of T_{fus} (onset) = 151 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 5.46 ± 0.05 Å, d = 4.94 ± 0.05 Å, d = 4.30 ± 0.05 Å, d = 4.08 ± 0.05 Å and d = 3.74 ± 0.05 Å;

XXII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one hemifumarate (form I) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 195 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 6.38 ± 0.05 Å, d = 5.19 ± 0.05 Å, d = 4.87 ± 0.05 Å, d = 3.72 ± 0.05 Å and d = 3.45 ± 0.05 Å;

XXIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one fumarate (form II) (= dihydrate form), characterized by a melting point of T_{fus} (onset) = 193 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that a further weakly endothermic signal can be observed at approx. 157 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 5.42 ± 0.05 Å, d = 4.73 ± 0.05 Å, d = 4.25 ± 0.05 Å, d = 4.06 ± 0.05 Å and d = 3.72 ± 0.05 Å;

XXIV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one glycolate (form I) (=hydrate form), characterized by a melting point of T_{fus} (onset) = 139 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that two further weakly endothermic signals can be observed at approx. 30 °C and 115 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 3.96 ± 0.05

Å, d =4.48 ± 0.05 Å, d = 3.93 ± 0.05 Å, d = 8.43 ± 0.05 Å and d = 3.74 ± 0.05 Å;

XXV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one citrate (form I) (=solvate form), characterized by a melting point of T_{fus} (onset) = 176 ± 5 °C which occurs during thermal analysis using DSC.The DSC diagram is additionally characterised in that a further weakly endothermic signal can be observed at approx. 123 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 15.61 ± 0.05 Å, d = 7.81 ± 0.05 Å, d = 7.47 ± 0.05 Å, d = 5.34 ± 0.05 Å and d = 4.87 ± 0.05 Å;

XXVI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one mandelate (form I) (=anhydrous form), characterized by a melting point of T_{fus} (onset) = 148 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 4.87 ± 0.05 Å, d = 4.66 ± 0.05 Å, d = 4.10 ± 0.05 Å, d = 3.88 ± 0.05 Å and d = 3.73 ± 0.05 Å;

XXVII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one L-malate (form I) (= monohydrate form), characterized by a melting point of T_{fus} (onset) = 176 ± 5 °C which occurs during thermal analysis using DSC. The DSC diagram is additionally characterised in that a further weakly endothermic signal can be observed at approx. 106 °C. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 7.82 ± 0.05 Å, d = 6.10 ± 0.05 Å, d = 5.22 ± 0.05 Å, d = 4.95 ± 0.05 Å and d = 3.79 ± 0.05 Å;

XXVIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one succinate (form I) (= dihydrate form), characterized by the data listed in table 2.18;

XXIX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one naphthalenesulfonate (form I) (= hemihydrate form), characterized by peaks in the X-ray powder diffractogram which occur at d = 4.92 ± 0.05 Å, d = 3.43 ± 0.05 Å, d = 4.00 ± 0.05 Å and d = 3.96 ± 0.05 Å;

XXX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one tosylate (form II) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 241 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 4.94 ± 0.05 Å, d = 4.57 ± 0.05 Å, d = 4.32 ± 0.05 Å, d = 3.53 ± 0.05 Å and d = 3.35 ± 0.05 Å; Its solubility in water at room temperature is 0.09 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.25 %.

XXXI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one fumarate (form III) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 202 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 5.33 ± 0.05 Å, d = 5.21 ± 0.05 Å, d = 4.53 ± 0.05 Å, d = 4.12 ± 0.05 Å and d = 3.69 ± 0.05 Å; Its solubility in water at room temperature is 0.5 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.28 %.

XXXII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one camphorsulfonate (form II) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 231 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 5.47 ± 0.05 Å, d = 5.44 ± 0.05 Å, d = 4.76 ± 0.05 Å, d = 4.46 ± 0.05 Å and d = 3.70 ± 0.05 Å; Its solubility in water at room temperature is 0.7 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.13 %.

XXXIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one glycolate (form II) (= hydrate form), characterized by a melting point of T_{fus} (onset) = 231 ± 5 °C which occurs during thermal analysis using DSC. Particularly characteristic peaks in the X-ray powder diffractogram of this compound are d = 5.75 ± 0.05 Å, d = 4.64 ± 0.05 Å, d = 4.43 ± 0.05 Å, d = 4.02 ± 0.05 Å and d = 3.97 ± 0.05 Å; Its solubility in water at room temperature is 0.5 mg/ml. The hygroscopiycity expressed in the uptake of water in the range of 10-90 % relative humidity is 0.20 %.

In another embodiment the invention relates to a process for the preparation of the new crystalline salt forms of flibanserin as specified above under I) to XXIX).

According to the invention the compounds specified above can be obtained by

i) dissolving the free base of flibanserin and the acid providing the anion for salt formation in a suitable solvent (preferably TFE/water (80:20))

ii) mixing the free base of flibanserin with the acid at a predetermined base/acid molar ratio, which is selected from 1:1 or 2:1 depending on the acid

iii) removing the solvent (e.g. evaporation under reduced pressure)

iv) adding a suitable crystallization solvent to the residue obtained by step iii), and heating the reaction mixture slowly up (e.g. at a heating rate of about 5 °C/min) to about 50°C; leaving it to stand for a further period of time (e.g. about 30 min)

v) slowly cooling down (e.g. at a cooling rate of about 5°C/h) the reaction mixture to a suitable crystallization temperature, (e.g. between 20°C or 3°C) and leaving it to stand until enough crystals are formed

vi) isolating the precipitated crystals.

In the process according to the invention the free base of the compound of formula (I) is dissolved in a suitable solvent, such as TFE/water (80:20). The acid used for the crystallization is dissolved as well in a suitable solvent, such as TFE/water (80:20) (depending on the acid). The free base of the compound of formula (I) is then mixed with the acid at a predetermined base /acid molar ratio, which is selected from 1:1 or 2:1 depending on the acid. Then, the solvent is evaporated under reduced pressure. After evaporation of the solvent has occurred, a suitable crystallization solvent is added to the reaction mixture, and the reaction mixture is slowly heated up to 50°C (e.g. a heating rate of about 5 °C/min). Without being limited, suitable solvents for the crystallization are ethanol, tetrahydrofuran, dichloromethane, n-mthylpyrrolidone, propyl acetate, methyl tert-butyl ether, 1,4 dioxane, 1,2-dimetoxyethane, water, 2,2,2,-trifloroethanol, chloroform, methanol, nitrobenzene, nitromethane, cyclohexanone, propionitrile, ethyl phenyl ether, diisobutyl keton, isophorone, water/ethanol (20/80), water/n-methylpyrrolidone (80/20), water/2,2,2-trifluoroethanol (20/80), water/acteone (20/80) and water/DMSO (80/20). After staying for about 30 minutes at 50°C, the reaction mixture is slowly cooled down (e.g. at a cooling rate of 5°C/h) to a suitable crystallization temperature, which is for example between 20°C or 3°C. The reaction mixture stays at this temperature until enough crystals are formed, which can then be collected, for example by filtration.

The salt forms of flibanserin as specified above under I) to XXIX) were investigated more thoroughly by X-ray powder diffraction and thermal analysis (DSC). The diagrams obtained are shown in Figures 1.1 to 1.23. Tables 1.1 to 1.23 contain the data obtained in the analysis.

Tables 2.1 to 2.18 contain the single crystal data obtained in the analysis.

Table 1: Thermal analysis, stoichiometry and single crystal data of the different salts of 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one

salt form	**salt form** full name	**ratio base/acid**	**thermal analysis** T_{fus} **(onset)**	**single cyrstal data**	**XRPD data**
HCl 1	chloride, form I (= anhydrous form)	1:1	**T = 215°C** add. endotherm. signals: T = 122°C (following by an exotherm. signal) T = 186°C (following by an exotherm. signal)	n.d.	See Table 1.1a
HCl 3	chloride, form III (= solvate form)	1:1	**T = 217°C** add. endotherm. signals: T= 56°C T = 121°C (following by an exotherm. signal)	n.d.	See Table 1.1b
HBr 1	bromide from I (= solvate form)	1:1	**T = 252°C** add. endotherm. signals: T = 104°C T = 222°C following by an exotherm. signal)	n.d.	See Table 1.2a
HBr 3	bromide from III (= solvate form)	1:1	**T = 252°C** add. endotherm. signals: T = 89°C	see Table 2.1	See Table 1.2b

			T = 218°C (following by an exotherm. signal)		
Eds1	edisylate form I (= solvate form)	1:1	**T= 144°C**	n.d.	See Table 1.3
Tos 1	tosylate form I (hydrated form)	1:1	**T= 238°C**	n.d.	See Table 1.4
Mes 1	mesylate form I (= monohydrate form)	1:1	**T = 207°C** add. endotherm . signal: T_1= 60°C	n.d.	See Table 1.5
Bes 1	besylate form I (= monohydrate form)	1:1	**T = 247°C** add. endotherm. signal: T= 111°C	n.d.	See Table 1.6
Oxa 1	oxalate form I (= anhydrous form)	1:1	**T= 209°C**	see Table 2.2	See Table 1.7a
Oxa 5	oxalate form V (= dihydrate form)	1:1	**T = 254°C** add. endotherm. signal: T= 112°C T = 198°C	see Table 2.3	See Table 1.7b
Sac1	sacharinate form I (1,5 hydrated form)	1:1	**T= 90°C**	see Table 2.4	See Table 1.8
Pho	phosphate form I (= hemihydrate form)	1:1	**T = 182 °C** add. endotherm. signals T= 81 °C T = 141°C T = 164°C	n.d.	See Table 1.9
Mae1	maleate form I (=THF solvate)	1:1	**T = 98°C** add. endotherm. signal T= 78°C	see Table 2.5	See Table 1.10a
Mae3	maleate form III (= anhydrous form)	1:1	**T = 172°C**	see Table 2.6	See Table 1.10b
Ets	ethanesulfonate (= monhydrate form)	1:1	**T = 207°C** add. endotherm. signals: T = 105°C T = 189°C (following by an	see Table 2.7	See Table 1.11

			exotherm. signal)		
Cas1	camphorsulfonate form I (= anhydrous form)	1:1	**T = 217 °C** add. endotherm. signal: T = 177°C	n.d.	See Table 1.12
Mao 1	malonate form I (= dihydrate form)	1:1	**T = 103°C** add. endotherm. signal: T= 79°C	see Table 2.8	See Table 1.13
Mao 2	malonate form II (= solvate form)	1:1	n.d.	see Table 2.9	n.d.
Mao 6	malonate form VI (= dihydrate form)	1:1	n.d.	see Table 2.10	n.d.
Sal 1	salicylate form I (= anhydrous form)	1:1	n.d.	see Table 2.11	n.d.
L-Tart 1	L-tartate form (= dihydrate form)	1:1	**T = 151 °C**	see Table 2.12	See Table 1.14
Fum 1	fumarate form I (= anhydrous form) (co-crystal)	2:1	**T = 195 °C**	see Table 2.13	See Table 1.15a
Fum 2	fumarate form II (= dihydrate form)	2:1	**T = 193 °C** add. endotherm. signal: T = 157 °C	see Table 2.14	See Table 1.15b
Gly 1	glycolate form I (= hydrate form)	1:1	**T = 139°C** add. endotherm. signals: T= 30°C T = 115°C (following by an exotherm. signal)	n.d.	See Table 1.16
Cit1	citrate form I (= solvate form)	1:1	**T = 176 °C** add. endotherm. signal: T = 123 °C	see Table 2.15	See Table 1.17
Man 1	mandelate form I (= anhydrous form)	1:1	**T = 148 °C**	see Table 2.16	See Table 1.18
L-Mal 1	L-malate form I (= monohydrate	1:1	**T = 176 °C** add. endotherm. signal:	see Table	See Table

	form)		T = 106 °C	2.17	1.19
Suc 1	succinate form I (= dihydrate form)	1:1	n.d.	see Table 2.18	n.d.
Nas1	naphtalene-sulfonate form I (= hemihydrate form)	1:1	n.d.	n.d.	See Table 1.20
Tos 2	tosylate form II (= anhydrous form)	1:1	**T = 241°C**	n.d.	See Table 1.21
Fum 3	fumarate, form III (= anhydrous form)	1:1	**T = 202°C**	n.d.	See Table 1.22
Cas 2	camphorsulfonate form II (= anhydrous form)	1:1	**T = 231°C**	n.d.	See Table 1.23
Gly 2	glycolate form II (= hydrate form)	1:1	**T = 145 °C**	n.d.	See Table 1.24

* T_{fus} (onset) = melting point; n.d. = not determined

The values of the X-ray powder reflections and intensities (normalized) as recorded for the crystalline salt forms in accordance with the present invention are displayed In the preceding tables 1.1 to 1.23. For each crystalline salt form, the values (d [Å]) of the reflection peaks with the highest relative intensities the highest values of din the corresponding table characterizes this crystalline salt form. The value “2-theta [°]” denotes the angle of diffraction in degrees and the value “d [Å] spacing” denotes the specified distances in Å between the lattice planes.

Table 1.1a X-ray powder reflections and intensity (normalized) of HCl1 = chloride, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5,18	17.05	32	18,33	4,83	21
5,52	15,99	100	19,64	4,52	27
6,23	14,20	8	20,22	4,39	17
7,01	12,59	10	21,00	4,23	48
8,75	10,10	38	21,38	4,15	22
9,18	9,62	13	22,32	3,98	62
9,50	9,30	11	22,64	3,92	21
10,36	8,53	15	23,00	3,86	16
10,94	8,08	11	23,52	3,78	19
11,06	7,99	11	24,51	3,63	11
11,88	7,44	63	25,85	3,44	54
13,41	6,59	38	26,30	3,38	33
13,93	6,35	17	27,04	3,29	41
14,18	6,24	18	27,66	3,22	13
14,97	5,91	22	27,78	3,21	17
15,18	5,83	17	28,11	3,17	24
15,49	5,71	16	28,31	3,15	23
16,22	5,46	28	28,80	3,10	13
16,94	5,23	25	29,23	3,05	19
17,14	5,17	32	29,48	3,02	16
17,55	5,05	34	30,13	2,96	17

Table 1.1b X-ray powder reflections and intensity (normalized) of HCl3 = chloride, form III

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5,37	16,43	100	20,40	4,35	96
6,90	12,79	24	20,92	4,24	66

8,70	10,16	58	21,22	4.18	37
9,10	9,71	46	21,34	4,16	35
10,21	8,66	47	22,00	4,04	63
11,54	7,66	80	22,21	4,00	54
11,84	7,47	45	22,33	3,98	47
12,13	7,29	30	22,87	3,88	56
13,32	6,64	57	23,47	3,79	44
14,03	6,30	47	24,06	3,69	24
14,82	5,97	38	24,25	3,67	24
14,90	5,94	38	25,18	3,53	33
15,30	5,78	46	25,63	3,47	82
15,38	5,75	48	26,11	3,41	42
15,50	5,71	48	26,68	3,34	53
16,23	5,45	38	26,98	3,30	40
16,61	5,33	38	27,05	3,29	38
16,86	5,25	48	27,64	3,22	44
17,02	5.20	46	27,91	3,19	39
17,44	5,08	99	28,44	3,13	33
18,20	4,87	32	29,03	3,07	33
18,93	4,68	42	29,92	2,98	34
19,23	4,61	54	30,73	2,91	30
19,73	4,50	42			

Table 1.2a X-ray powder reflections and intensity (normalized) of HBr1 = hydrobromide, form I

2-theta [°]	**d [Å] spacing**	**I/I_0 [%]**	**2-theta [°]**	**d [Å] spacing**	**I/I_0 [%]**
5,51	16,03	58	21,97	4,04	49
10,21	8,65	13	22,60	3,93	32
11,86	7,45	50	23,10	3.85	24
12,92	6,84	22	23,92	3,71	15

13,16	6,72	18	25,55	3,48	100
13,82	6,40	17	25,96	3,43	66
14,02	6,31	28	26,70	3,33	84
14,49	6,12	24	27,79	3,21	38
15,34	5,77	28	28,14	3,17	32
16,01	5,53	22	28,95	3,08	35
16,94	5,23	31	29,40	3,03	20
17,16	5,16	32	29,82	2,99	22
17,98	4,93	23	31,21	2,86	21
18,21	4,87	18	31,89	2,80	14
19,02	4,66	22	32,33	2,77	18
19,53	4,54	42	32,84	2,72	16
19,91	4,45	25	33,83	2,65	16
20,25	4,38	53	35,81	2,50	16
20,75	4,28	70	38,55	2,33	15
21,16	4,19	29			

Table 1.2b X-ray powder reflections and intensity (normalized) of HBr3 = hydrobromide, form III

2-theta [°]	**d [Å] spacing**	**I/I_0 [%]**	**2-theta [°]**	**d [Å] spacing**	**I/I_0 [%]**
5.69	15.52	100	23.58	3.77	21
7.13	12.38	24	24.04	3.70	26
12.20	7.25	54	25.38	3.50	29
13.24	6.68	31	25.74	3.46	56
14.13	6.26	35	26.26	3.39	35
14.85	5.96	27	26.50	3.36	31
16.24	5.45	24	26.92	3.30	32
17.21	5.15	56	27.89	3.19	37
18.05	4.91	26	28.31	3.15	26
19.29	4.60	63	30.21	2.95	33

19.93	4.45	28	30.76	2.90	18
20.37	4.36	71	31.36	2.85	21
20.97	4.23	43	32.31	2.77	17
21.54	4.12	24	32.91	2.72	21
22.13	4.01	36	35.08	2.56	16
22.54	3.94	64	35.99	2.49	17
23.25	3.82	24			

Table 1.3 X-ray powder reflections and intensity (normalized) of Eds1 = edisylate, form I

2-theta [°]	**d [Å] spacing**	**I/I_0 [%]**	**2-theta [°]**	**d [Å] spacing**	**I/I_0 [%]**
6,15	14,34	100	21,06	4,21	32
7,01	12,59	19	21,43	4,14	55
7,70	11,47	23	22,06	4,03	23
8,73	10,11	21	22,48	3,95	99
9,29	9,50	56	22,84	3,89	29
9,69	9,12	26	23,34	3,81	27
10,30	8,58	21	23,69	3,75	87
11,03	8,01	5	24,28	3,66	43
11,34	7,79	38	24,76	3,59	28
12,10	7,31	27	25,15	3,54	23
13,15	6,72	31	25,89	3,44	22
13,78	6,42	40	25,98	3,43	24
14,30	6,19	36	26,56	3,35	31
15,32	5,78	37	27,10	3,29	20
16,13	5,49	21	27,18	3,28	20
17,15	5,17	49	27,81	3,20	24
17,85	4,96	43	28,16	3,17	28
18,64	4,75	45	28,70	3,11	20
19,11	4,64	86	28,78	3,10	19

20,04	4,43	24	29,62	3,01	19
20,58	4,31	57	29,70	3,00	18
20,88	4,25	37	30,64	2,91	19

Table 1.4 X-ray powder reflections and intensity (normalized) of Tos1 = tosylate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
3,29	26,82	20	19,52	4,54	31
11,03	8,01	17	21,16	4,19	13
12,99	6,80	17	22,59	3,93	84
13,76	6,43	39	23,07	3,85	15
14,02	6,31	52	23,61	3,76	14
14,24	6,21	36	25,36	3,51	35
14,61	6,06	20	25,59	3,48	55
14,99	5,90	16	26,22	3,40	19
16,26	5,45	15	27,27	3,27	25
17,34	5,11	100	27,76	3,21	26
18,31	4,84	90	28,59	3,12	13
18,71	4,74	44	29,26	3,05	18
19,21	4,62	50	30,10	2,97	11

Table 1.5 X-ray powder reflections and intensity (normalized) of Mes1 = mesylate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5,79	15,25	100	20,22	4,39	52
7,02	12,58	24	20,66	4,29	64
7,89	11,19	21	20,91	4,24	73
9,42	9,38	14	21,21	4,18	97
9,80	9,02	16	22,54	3,94	13
11,58	7,63	34	23,05	3,85	28

12,23	7,23	47	23,60	3,76	31
13,17	6,71	25	24,33	3,65	20
14,10	6,27	39	25,60	3,47	95
14,56	6,07	29	26,15	3,40	20
15,78	5,61	23	26,50	3,36	20
16,12	5,49	59	26,98	3,30	16
16,60	5,33	15	27,66	3,22	56
17,36	5,10	15	28,23	3,16	16
17,89	4,95	92	29,22	3,05	12
19,13	4,63	23	29,68	3,01	23
19,62	4,52	20	30,19	2,96	11

Table 1.6 X-ray powder reflections and intensity (normalized) of Bes1 = besylate, form I

2-theta [°]	**d [Å] spacing**	**I/I_0 [%]**	**2-theta [°]**	**d [Å] spacing**	**I/I_0 [%]**
3,45	25,61	33	22,54	3,94	33
8,71	10,14	9	22,90	3,88	32
9,65	9,16	9	23,91	3,72	15
11,23	7,87	10	24,18	3,68	18
11,70	7,56	11	24,63	3,61	14
12,42	7,12	10	24,97	3,56	11
13,77	6,42	60	25,58	3,48	54
14,28	6,19	45	26,06	3,41	32
15,28	5,79	14	26,94	3,31	28
15,89	5,57	11	27,25	3,27	21
17,42	5,08	55	27,64	3,22	15
18,27	4,85	62	27,99	3,18	11
18,90	4,69	72	28,35	3,14	16
19,77	4,48	15	28,95	3,08	11
20,49	4,33	41	29,96	2,98	14

21,77	4,08	12	30,76	2,90	10
22,26	3,99	100			

Table 1.7a X-ray powder reflections and intensity (normalized) of Oxa 1, oxalate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
9.04	9.77	43	20.00	4.43	36
9.65	9.15	24	20.92	4.24	76
12.03	7.35	19	21.75	4.08	100
12.48	7.09	76	23.36	3.80	46
14.71	6.01	69	23.66	3.76	32
15.80	5.60	18	23.94	3.71	38
16.22	5.46	56	25.04	3.55	24
17.04	5.20	33	25.78	3.45	46
18.00	4.92	83	27.33	3.26	29
18.30	4.84	56	28.49	3.13	21
19.30	4.59	61	29.22	3.05	16

Table 1.7b X-ray powder reflections and intensity (normalized) of Oxa 5, oxalate, form V

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
6.26	14.11	9	19.26	4.60	13
9.03	9.78	11	20.60	4.31	12
9.49	9.31	15	20.92	4.24	10
11.00	8.04	12	21.72	4.09	11
12.48	7.09	34	22.45	3.95	16
12.66	6.98	22	23.35	3.80	27
14.17	6.24	15	23.66	3.76	34
14.73	6.01	11	25.09	3.54	13
15.25	5.80	13	25.62	3.47	20

15.60	5.67	27	26.19	3.40	24
16.26	5.45	11	26.46	3.36	21
17.24	5.14	16	27.73	3.21	16
17.58	5.04	28	28.64	3.11	9
18.21	4.87	100	30.86	2.89	8
18.70	4.74	19			

Table 1.8 X-ray powder reflections and intensity (normalized) of Sac 1, sacharinate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5.77	15.31	17	19.18	4.62	64
7.80	11.32	11	20.04	4.43	44
8.09	10.91	13	20.77	4.27	24
8.65	10.21	20	21.15	4.20	28
8.95	9.87	13	21.66	4.10	15
9.35	9.45	17	22.41	3.96	22
9.97	8.86	17	22.73	3.91	26
11.24	7.86	64	23.29	3.81	28
11.58	7.63	21	23.72	3.75	52
12.04	7.34	36	24.40	3.64	62
12.27	7.20	25	25.15	3.54	37
12.81	6.90	52	25.46	3.49	24
13.34	6.63	58	25.77	3.45	23
14.41	6.14	23	26.26	3.39	22
14.99	5.90	85	26.77	3.33	55
15.61	5.67	64	27.43	3.25	18
16.24	5.45	20	28.14	3.17	21
16.72	5.30	85	28.37	3.14	29
17.22	5.14	100	28.68	3.11	24
17.84	4.97	22	29.37	3.04	16

18.20	4.87	18	29.79	3.00	18
18.75	4.73	30	29.97	2.98	18

Table 1.9 X-ray powder reflections and intensity (normalized) of Pho1 = phosphate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5,59	15,79	100	19,50	4,55	27
6,12	14,42	18	19,79	4,48	29
6,77	13,04	36	20,57	4,31	37
7,30	12,10	17	21,00	4,23	27
7,65	11,54	15	21,77	4,08	6
8,35	10,58	16	22,15	4,01	32
9,25	9,55	24	22,38	3,97	38
10,00	8,83	24	23,30	3,81	36
10,47	8,44	17	23,68	3,75	54
10,86	8,14	20	23,89	3,72	35
11,19	7,90	60	24,54	3,62	26
11,90	7,43	28	25,03	3,55	16
11,98	7,38	22	25,36	3,51	27
12,10	7,30	35	25,88	3,44	20
13,90	6,37	28	26,84	3,32	14
14,70	6,02	28	27,36	3,26	15
15,86	5,58	22	27,89	3,19	18
16,34	5,42	23	28,16	3,17	22
16,77	5,28	27	28,50	3,13	20
17,10	5,18	40	29,18	3,06	13
17,50	5,06	89	30,37	2,93	14
18,65	4,75	26			

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Table 1.10a X-ray powder reflections and intensity (normalized) of Mae 1, maleate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
8.51	10.38	10	20.54	4.32	10
9.22	9.58	84	21.12	4.20	20
11.47	7.71	84	22.65	3.92	13
13.83	6.40	12	23.08	3.85	21
14.44	6.13	100	23.54	3.78	45
14.92	5.93	94	24.67	3.61	58
15.60	5.68	17	25.95	3.43	18
15.87	5.58	26	26.77	3.33	11
16.22	5.46	63	27.83	3.20	21
16.84	5.26	47	28.81	3.10	10
17.36	5.10	38	29.39	3.04	17
17.77	4.99	21	29.76	3.00	24
18.51	4.79	27	30.64	2.92	14
18.68	4.75	48	31.48	2.84	27
19.19	4.62	70			

Table 1.10b X-ray powder reflections and intensity (normalized) of Mae 3, maleate, form III

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
6.56	13.46	39	21.65	4.10	58
8.56	10.32	13	22.23	4.00	42
9.99	8.84	24	22.73	3.91	21
11.28	7.84	13	22.90	3.88	22
12.22	7.23	32	23.27	3.82	40
13.10	6.75	26	23.90	3.72	39
13.85	6.38	44	24.28	3.66	40
14.58	6.07	52	24.86	3.58	10

16.20	5.47	16	25.30	3.52	41
16.76	5.28	45	25.66	3.47	27
17.16	5.16	100	26.57	3.35	23
17.46	5.07	31	27.14	3.28	38
18.50	4.79	18	27.82	3.20	64
19.24	4.61	18	28.55	3.12	17
19.62	4.52	91	29.14	3.06	14
20.08	4.42	43	29.48	3.03	19
20.41	4.35	27	29.70	3.00	13
21.00	4.22	9	30.73	2.91	35

Table 1.11 X-ray powder reflections and intensity (normalized) of Ets 1, ethanesulfonate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5.77	15.30	62	18.97	4.67	21
6.97	12.66	14	19.45	4.56	15
7.82	11.29	15	20.06	4.42	32
9.70	9.11	10	20.46	4.34	52
11.55	7.65	29	20.98	4.23	100
12.19	7.25	40	21.54	4.12	15
13.04	6.78	17	22.83	3.89	12
14.16	6.25	31	23.38	3.80	26
14.42	6.14	14	24.06	3.69	18
15.69	5.64	21	25.18	3.53	27
15.97	5.54	33	25.61	3.47	37
16.46	5.38	9	26.00	3.42	21
16.80	5.27	9	26.34	3.38	12
17.18	5.16	13	26.85	3.31	11
17.70	5.00	56	27.78	3.21	37
17.94	4.94	20	28.34	3.15	9

Table 1.12 X-ray powder reflections and intensity (normalized) of Cas1 = camphorsulfonate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5,41	16,32	100	17,79	4,98	20
9,60	9,20	9	18,65	4,75	18
10,07	8,77	10	19,32	4,59	19
10,79	8,19	14	20,21	4,39	19
11,38	7,77	7	20,96	4,23	10
12,26	7,21	11	21,49	4,13	18
12,34	7,17	12	21,73	4,08	17
13,15	6,72	8	22,50	3,95	17
13,86	6,38	12	23,06	3,85	17
14,10	6,27	21	23,58	3,78	17
15,55	5,69	30	23,95	3,71	16
16,10	5,50	45	24,55	3,62	24
16,25	5,45	52	25,07	3,55	13
16,62	5,33	11	28,65	3,11	9
16,79	5,29	11	29,10	3,07	7
17,59	5,04	15	29,18	3,06	6

Table 1.13 X-ray powder reflections and intensity (normalized) of Mao 1, malonate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
3.80	23.23	99	21.69	4.09	31
7.63	11.57	37	22.27	3.99	45
7.93	11.13	45	22.86	3.89	47
10.32	8.56	60	23.34	3.81	47
13.06	6.77	61	23.90	3.72	68
13.36	6.62	43	24.71	3.60	65
13.91	6.36	35	25.65	3.47	50

14.49	6.1	57	26.35	3.38	26
15.21	5.82	37	26.84	3.32	28
15.89	5.57	42	26.94	3.31	27
16.78	5.28	57	27.86	3.20	24
17.96	4.93	39	28.38	3.14	23
19.18	4.62	60	28.94	3.08	21
20.34	4.36	49	29.10	3.06	22
20.74	4.28	32	29.18	3.06	21
21.20	4.19	100	30.30	2.95	28

Table 1.14 X-ray powder reflections and intensity (normalized) of L-Tar 1, L-tartrate, form I

2-theta [°]	**d [Å] spacing**	**I/I_0 [%]**	**2-theta [°]**	**d [Å] spacing**	**I/I_0 [%]**
10.04	8.80	15	21.74	4.08	99
10.55	8.37	23	23.08	3.85	17
11.82	7.48	13	23.76	3.74	100
13.10	6.75	12	24.31	3.66	9
15.32	5.77	34,	25.23	3.53	28
15.94	5.55	20	25.88	3.44	17
16.22	5.46	59	26.46	3.36	11
17.17	5.16	11	27.27	3.27	42
17.92	4.94	67	27.55	3.23	23
18.55	4.78	44	28.29	3.15	12
19.05	4.65	30	28.76	3.10	9
19.61	4.52	17	29.08	3.07	11
20.18	4.40	14	30.46	2.93	13
20.64	4.30	73	30.87	2.89	15
21.23	4.18	45			

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Table 1.15a X-ray powder reflections and intensity (normalized) of Fum 1, fumarate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
8.51	10.38	18	18.76	4.72	28
9.13	9.68	31	19.78	4.48	2
10.35	8.54	37	20.77	4.27	34
11.11	7.95	12	21.44	4.14	13
11.39	7.76	13	21.92	4.05	23
12.07	7.32	20	22.92	3.88	24
13.87	6.38	39	23.91	3.72	100
14.54	6.08	23	24.27	3.66	33
15.30	5.79	35	24.69	3.60	21
15.57	5.68	28	25.24	3.52	14
16.15	5.48	23	25.77	3.45	45
17.07	5.19	42	26.24	3.39	14
17.75	4.99	22	27.17	3.28	18
18.19	4.87	61	27.71	3.22	10
18.53	4.78	20			

Table 1.15b X-ray powder reflections and intensity (normalized) of Fum 2, fumerate, form II

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
10.20	8.66	30	21.54	4.12	40
10.84	8.15	18	21.85	4.06	85
11.89	7.43	25	23.07	3.85	14
13.29	6.66	16	23.92	3.72	100
15.19	5.83	40	25.39	3.50	36
15.81	5.60	14	27.41	3.25	39
16.32	5.42	64	27.78	3.21	17
18.07	4.90	36	28.76	3.10	12

18.74	4.73	87	29.23	3.05	14
19.17	4.63	18	30.99	2.88	12
19.41	4.57	15	32.95	2.72	15
19.94	4.45	15	33.80	2.65	11
20.13	4.41	15	36.61	2.45	12
20.53	4.32	25	39.21	2.29	10
20.90	4.25	49			

Table 1.16 X-ray powder reflections and intensity (normalized) of Gly1 = glycolate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
4,75	18,58	13	21,90	4,05	34
5,26	16,79	13	22,41	3,96	100
5,98	14,76	35	22,59	3,93	91
7,42	11,91	20	23,21	3,83	18
10,49	8,43	87	23,76	3,74	71
11,55	7,65	23	24,18	3,68	24
12,02	7,35	27	24,26	3,66	24
13,17	6,71	14	24,53	3,62	28
13,72	6,45	26	24,90	3,57	19
14,62	6,05	19	25,40	3,50	21
15,38	5,75	20	25,83	3,45	17
16,12	5,49	25	26,64	3,34	17
17,11	5,18	36	27,27	3,27	14
17,62	5,03	54	27,71	3,22	22
17,92	4,94	31	28,06	3,18	15
18,44	4,81	29	28,34	3,15	17
19,07	4,65	25	28,69	3,11	14
19,38	4,57	23	29,48	3,03	8
19,78	4,48	93	29,98	2,98	16

20,82	4,26	22	30,36	2,94	20
21,09	4,21	27			

Table 1.17 X-ray powder reflections and intensity (normalized) of Cit 1, citrate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5.66	15.61	100	21.70	4.09	19
6.64	13.29	18	22.75	3.90	7
8.93	9.89	8	23.06	3.85	6
11.31	7.81	26	23.88	3.72	8
11.83	7.47	25	24.28	3.66	10
13.50	6.55	6	24.61	3.61	13
13.86	6.38	7	25.07	3.54	7
14.65	6.04	9	25.82	3.45	5
16.58	5.34	27	26.26	3.39	6
16.95	5.22	10	27.00	3.30	13
17.61	5.03	9	27.75	3.21	8
18.21	4.87	52	28.05	3.18	7
18.95	4.68	18	28.55	3.12	7
19.26	4.60	7	29.38	3.04	6
20.87	4.25	15			

Table 1.18 X-ray powder reflections and intensity (normalized) of Man 1, mandelate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
7.42	11.90	9	19.69	4.50	23
8.35	10.57	29	20.08	4.42	31
10.57	8.36	26	21.05	4.22	12
12.00	7.36	16	21.41	4.14	26
12.32	7.17	10	21.66	4.10	36

14.08	6.28	30	22.08	4.02	21
14.74	6.00	15	22.89	3.88	37
15.29	5.79	11	23.54	3.77	28
15.69	5.64	32	23.86	3.73	41
16.34	5.42	14	24.41	3.64	23
16.67	5.31	11	24.81	3.58	10
17.34	5.11	13	25.23	3.53	14
18.19	4.87	100	26.09	3.41	4
18.56	4.78	18	26.47	3.36	12
19.01	4.66	63			

Table 1.19 X-ray powder reflections and intensity (normalized) of L-Mal 1, malate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
8.40	10.51	9	19.63	4.52	38
11.30	7.82	71	20.48	4.33	9
11.69	7.56	12	21.36	4.15	24
12.49	7.08	11	21.98	4.04	11
12.75	6.94	10	22.69	3.91	32
13.38	6.61	10	23.46	3.79	100
13.68	6.47	10	23.91	3.72	62
14.49	6.10	59	24.19	3.68	24
14.80	5.98	16	24.23	3.67	26
15.09	5.87	32	24.91	3.57	35
15.78	5.61	28	25.38	3.50	19
16.96	5.22	47	26.14	3.41	12
17.89	4.95	48	26.64	3.34	27
18.27	4.85	36	27.33	3.26	9
18.90	4.69	12			

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Table 1.20 X-ray powder reflections and intensity (normalized) of Nas1 = naphtalene-sulfonate, form I

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
3,17	27,83	17	23,22	3,83	25
12,71	6,95	11	23,99	3,70	9
12,93	6,84	9	25,58	3,48	13
13,97	6,33	25	25,88	3,43	63
14,14	6,26	24	26,57	3,35	11
14,44	6,13	20	26,80	3,32	12
14,83	5,96	20	27,07	3,29	25
15,06	5,88	11	27,37	3,25	27
15,89	5,57	40	28,18	3,16	16
17,64	5,02	46	29,01	3,07	7
18,02	4,92	100	29,64	3,01	10
18,33	4,83	29	29,95	2,98	10
19,05	4,65	43	30,47	2,93	8
19,43	4,56	31	31,57	2,83	10
20,51	4,32	14	33,33	2,69	8
21,69	4,09	11	35,92	2,50	10
22,17	4,00	59	36,96	2,43	8
22,41	3,96	53			

Table 1.21 X-ray powder reflections and intensity (normalized) of Tos 2, tosylate, form II

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
4.89	18.04	20	19.39	4.57	24
6.29	14.03	6	19.97	4.44	11
7.91	11.16	5	20.53	4.32	47
10.59	8.35	13	20.85	4.26	10
12.64	7.00	8	21.27	4.17	4

12.89	6.86	10	21.77	4.08	6
13.78	6.42	4	22.10	4.02	6
14.75	6.00	4	22.76	3.90	3
15.43	5.74	20	23.07	3.85	3
15.76	5.62	4	23.97	3.71	11
16.79	5.28	5	24.48	3.63	6
17.21	5.15	7	24.91	3.57	4
17.96	4.94	100	25.19	3.53	21
18.73	4.73	10	25.95	3.43	4
19.01	4.67	4	26.61	3.35	43

Table 1.22 X-ray powder reflections and intensity (normalized) of Tos 2, fumarate, form III

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
9.64	9.17	68	20.79	4.27	14
10.65	8.30	3	21.55	4.12	86
11.53	7.67	5	21.97	4.04	19
12.41	7.13	3	22.82	3.89	7
14.39	6.15	19	23.55	3.78	26
15.15	5.84	30	24.07	3.69	100
15.87	5.58	26	24.49	3.63	17
16.61	5.33	92	25.03	3.55	28
17.01	5.21	96	27.40	3.25	14
17.83	4.97	44	28.11	3.17	18
18.84	4.71	66	28.37	3.14	11
19.37	4.58	18			
19.59	4.53	80			
19.89	4.46	77			
20.33	4.36	33			

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Table 1.23 X-ray powder reflections and intensity (normalized) of Cas 2, camphorsulfonate,, form II

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
5.27	16.75	29	17.62	5.03	14
6.69	13.20	10	17.74	4.99	10
7.01	12.61	12	18.63	4.76	53
8.09	10.92	9	19.21	4.62	12
9.63	9.18	15	19.48	4.55	12
10.03	8.81	6	19.88	4.46	45
10.57	8.36	8	20.05	4.42	28
12.27	7.21	19	20.44	4.34	22
14.08	6.29	28	20.56	4.32	20
14.48	6.11	26	21.27	4.17	37
15.04	5.89	11	22.12	4.01	17
15.55	5.69	15	23.32	3.81	22
16.18	5.47	100	24.03	3.70	35
16.29	5.44	99	24.63	3.61	30
17.23	5.14	16	25.25	3.52	11

Table 1.24 X-ray powder reflections and intensity (normalized) of Gly 2, glycolate,, form II

2-theta [°]	d [Å] spacing	I/I_0 [%]	2-theta [°]	d [Å] spacing	I/I_0 [%]
9.98	8.86	12	17.30	5.12	18
10.47	8.44	13	17.73	5.00	13
10.98	8.05	7	18.11	4.89	8
11.25	7.86	5	18.38	4.82	15
11.62	7.61	15	18.67	4.75	13
12.65	7.00	14	19.10	4.64	34
13.05	6.78	30	19.77	4.49	21
13.85	6.39	9	20.02	4.43	31
14.18	6.24	4	20.34	4.36	22
14.57	6.07	4	21.12	4.20	15
15.40	5.75	40	21.61	4.11	18
15.59	5.68	24	22.09	4.02	100
16.03	5.53	11	22.38	3.97	78
16.19	5.47	13	23.21	3.83	15
16.61	5.33	5	23.56	3.77	13

The single crystal data and structure refinement for the crystalline salt forms in accordance with the present invention are displayed In the preceding tables 2.1 to 2.18. The abbreviations used in those tables have the following meanings:

Fw = formula weight;

T = Temperature of data collection;

λ = wavelength of X-ray source;

D_m = calculated density;

θ range = Theta range of data collection;

S = Goodness-o- fit on F^2;

R [I>2σ(I)] = Final R indices [I>2sigma(I)]

Table 2.1 Single crystal data and structure refinement of bromide form III

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet Br^- \bullet 0.5\ H_2O \bullet 0.5\ CH_3OH$
Fw	496,35
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	
a [Å]	6.9150(3)
b [Å]	30.801(2)
c [Å]	20.4990(8)
α [°]	90
β [°]	95.728(2)
γ [°]	90
V [$Å^3$]	4344.3 (3)(1)
Z	4
D_m [g/cm^3]	1.518
F(000)	2032
Crystal size [mm^3]	0.30 x 0.20 x 0.06
θ range [°]	2 → 27.5
Reflections collected	9029
Independent reflections	6180 [R_{int} = 0.0424]
S	1.15
R [I>2σ(I)]	R1 = 0.0605, wR2 = 0.1329
R indices (all data)	R1 = 0.0766, wR2 = 0.1423

Table 2.2 Single crystal data and structure refinement of oxalate form I

Empirical formula	$C_{20}H_{22}F_3N_4O \bullet C_2HO_4$
Fw	480.44
T [K]	293(2)
λ[Å]	0.71073 Å

Crystal system	Orthorhombic
Space group	P $2_12_12_1$
Unit cell dimensions	
a [Å]	10.3900(4)
b [Å]	11.3420(4)
c [Å]	19.3230(6)
α [°]	90
β [°]	90
γ [°]	90
V [$Å^3$]	2277.1(2)
Z	4
D_m [g/cm^3]	1.401
F(000)	1000
Crystal size [mm^3]	0.3 x 0.25 x 0.2
θ range [°]	3 → 27.5
Reflections collected	14241
Independent reflections	5179 [R_{int} = 0.0243]
S	1.058
R [I>2σ(I)]	R1 = 0.0379, wR2 = 0.0808
R indices (all data)	R1 = 0.0465, wR2 = 0.0856

Table 2.3 Single crystal data and structure refinement of oxalate form V

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet 0.5\ C_2O_4^{2-} \bullet H_2O$
Fw	453.44
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P $2_1/c$
Unit cell dimensions	
a [Å]	7.6030(3)
b [Å]	28.5050(10)
c [Å]	10.6200(4)
α [°]	90

β [°]	113.346(2)
γ [°]	90
V [Å^3]	2113.17(14)
Z	4
D_m [g/cm^3]	1.425
F(000)	948
Crystal size [mm^3]	0.2 x 0.15 x 0.1
θ range [°]	1.5 → 24.
Reflections collected	10041
Independent reflections	3302 [R_{int} = 0.0791]
S	4.655
R [I>2σ(I)]	R1 = 0.2415, wR2 = 0.5590
R indices (all data)	R1 = 0.2468, wR2 = 0.5629

Table 2.4 Single crystal data and structure refinement of sacharinate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_7H_4NSO_3^- \bullet 1.5\ H_2O$
Fw	600.61
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Triclinic
Space group	P –1
Unit cell dimensions	
a [Å]	8.1930(2)
b [Å]	11.7200(2)
c [Å]	30.7140(7)
α [°]	93.206(1)
β [°]	92.430(1)
γ [°]	103.257(1)
V [Å^3]	2861.5(2)
Z	4
D_m [g/cm^3]	1.394
F(000)	1252

Crystal size [mm^3]	0.4 x 0.35 x 0.2
θ range [°]	2 → 25.5
Reflections collected	15887
Independent reflections	10288 [R_{int} = 0.0372]
S	1.078
R [I>2σ(I)]	R1 = 0.0686, wR2 = 0.1316
R indices (all data)	R1 = 0.1218, wR2 = 0.1551

Table 2.5 Single crystal data and structure refinement of maleate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^- \bullet C_4H_3O_4^- \bullet C_4H_8O$
Fw	578.58
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	
a [Å]	19.9300(1)
b [Å]	12.2540(2)
c [Å]	24.2320(3)
α [°]	90
β [°]	90
γ [°]	90
V [$Å^3$]	5917.99(12)
Z	8
D_m [g/cm^3]	1.299
F(000)	2432
Crystal size [mm^3]	0.3 x 0.2 x 0.1
θ range [°]	1.7 → 25
Reflections collected	35074
Independent reflections	5199 [R_{int} = 0.0461]
S	1.107
R [I>2σ(I)]	R1 = 0.0625, wR2 = 0.1701
R indices (all data)	R1 = 0.0808, wR2 = 0.1901

Table 2.6 Single crystal data and structure refinement of maleate form III

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_4H_3O_4$
Fw	506.48
T [K]	293(2) K
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	C 2/c
Unit cell dimensions	
a [Å]	27.2820(5)
b [Å]	8.1960(2)
c [Å]	20.8440(4)
α [°]	90
β [°]	98.295(1)
γ [°]	90
V [$Å^3$]	4612.03(13)
Z	8
D_m [g/cm^3]	1.459
F(000)	2112
Crystal size [mm^3]	0.35 x 0.2 x 0.1
θ range [°]	2.5 → 30
Reflections collected	11604
Independent reflections	6688 [R_{int} = 0.0242]
S	1.023
R [I>2σ(I)]	R1 = 0.0504, wR2 = 0.1108
R indices (all data)	R1 = 0.0680, wR2 = 0.1219

Table 2.7 Single crystal data and structure refinement of ethanesulfonate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_2H_5SO_3^- \bullet H_2O$
Fw	518.55
T [K]	293(2) K
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell dimensions	
a [Å]	15.3580(2)
b [Å]	22.6680(7)
c [Å]	7.0870(6)
α [°]	90
β [°]	91.595(2)
γ [°]	90
V [$Å^3$]	2466.3(2)
Z	4
D_m [g/cm^3]	1.397 Mg/m^3
F(000)	1088
Crystal size [mm^3]	0.3 x 0.2 x 0.2
θ range [°]	2 → 26
Reflections collected	11237
Independent reflections	4736 [R_{int} = 0.0409]
S	1.033
R [I>2σ(I)]	R1 = 0.0598, wR2 = 0.1222
R indices (all data)	R1 = 0.0935, wR2 = 0.1389

Table 2.8 Single crystal data and structure refinement of malonate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_3H_3O_4^- \bullet 2H_2O$
Fw	530.50
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell dimensions	
a [Å]	23.2150(2)

b [Å]	12.7050(2)
c [Å]	8.3990(4)
α [°]	90
β [°]	92.422(1)
γ [°]	90
V [Å^3]	2475.0(2)
Z	4
D_m [g/cm^3]	1.424 Mg/m^3
F(000)	1112
Crystal size [mm^3]	0.45 x 0.4 x 0.3
θ range [°]	2 → 26
Reflections collected	8896
Independent reflections	4849 [R_{int} = 0.0207]
S	1.033
R [I>2σ(I)]	R1 = 0.0456, wR2 = 0.1076
R indices (all data)	R1 = 0.0595, wR2 = 0.1165

Table 2.9 a) Single crystal data and structure refinement of malonate form II

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_3H_3O_4^{-2} \bullet 2\ C_4H_{10}O$
Fw	642.71
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell dimensions	
a [Å]	9.2650(3)
b [Å]	24.2380(2)
c [Å]	30.128(8)
α [°]	90
β [°]	101.620(2)
γ [°]	90
V [Å^3]	6627.0 (4)

Z	8
D_m [g/cm^3]	1.288
F(000)	2736
Crystal size [mm^3]	0.25 x 0.1 x 0.08
θ range [°]	1.5 → 24
Reflections collected	22364
Independent reflections	10286 [R_{int} = 0.1143]
S	1.093
R [I>2σ(I)]	R1 = 0.1070, wR2 = 0.1271
R indices (all data)	R1 = 0.2167, wR2 = 0.1563

Table 2.9 b) Atomic coordinates and temperature factor (Uiso) of malonate form II

(hydrogen atoms were calculated according to well-established geometrical criteria)

atom	x	y	z	U iso
O1	0.06149(5)	0.95243(10)	0.12162(17)	0.0575(4)
C2	0.06563(7)	1.04882(15)	0.1421(2)	0.0460(4)
N3	0.02959(7)	1.12484(13)	0.0841(2)	0.0534(4)
H3	0.0000	11.075	0.013	0.05
C4	0.05036(8)	1.22360(15)	0.1289(2)	0.0483(4)
C5	0.03015(10)	1.32383(17)	0.0973(3)	0.0630(5)
H5	-0.0037	13.353	0.0364	0.05
C6	0.06249(11)	1.40672(17)	0.1605(3)	0.0694(6)
H6	0.0501	14.753	0.1412	0.05
C7	0.11273(10)	1.39022(17)	0.2513(3)	0.0653(6)
H7	0.1334	14.478	0.2912	0.05
C8	0.13280(9)	1.28983(16)	0.2841(2)	0.0546(5)
H8	0.1665	12.785	0.3453	0.05
C9	0.10068(7)	1.20725(14)	0.22200(19)	0.0428(4)
N10	0.10868(6)	1.09832(11)	0.23008(17)	0.0429(3)
C11	0.15342(7)	1.04136(15)	0.3200(2)	0.0433(4)
H11A	0.1395	0.9719	0.3469	0.05
H11B	0.1632	10.785	0.4183	0.05
C12	0.20654(7)	1.03133(14)	0.22173(18)	0.0389(4)
H12A	0.1957	10.007	0.119	0.05

H12B	0.2223	11.008	0.2033	0.05
N13	0.25191(5)	0.96389(10)	0.30396(15)	0.0334(3)
H13	0.2547	0.9800	0.411	0.05
C14	0.23667(7)	0.84980(13)	0.2895(2)	0.0397(4)
H14A	0.2288	0.833	0.1781	0.05
H14B	0.2017	0.8368	0.3457	0.05
C15	0.28364(7)	0.77827(14)	0.3555(2)	0.0420(4)
H15A	0.2891	0.7896	0.4694	0.05
H15B	0.2725	0.7054	0.3384	0.05
N16	0.33750(6)	0.79918(10)	0.27768(16)	0.0380(3)
C17	0.35469(7)	0.90831(13)	0.3045(2)	0.0416(4)
H17A	0.391	0.9214	0.2552	0.05
H17B	0.3602	0.921	0.4181	0.05
C18	0.30930(7)	0.98259(13)	0.2356(2)	0.0395(4)
H18A	0.3212	10.546	0.257	0.05
H18B	0.306	0.9734	0.1209	0.05
C19	0.38090(7)	0.72145(13)	0.28732(18)	0.0372(4)
C20	0.43295(7)	0.73712(14)	0.2127(2)	0.0437(4)
H20	0.4394	0.8002	0.1602	0.05
C21	0.47493(8)	0.65993(15)	0.2160(2)	0.0491(4)
C22	0.52955(9)	0.67841(19)	0.1321(3)	0.0676(6)
F23	0.54009(8)	0.77815(16)	0.0996(3)	0.1027(7)
F24	0.57558(6)	0.64307(19)	0.2129(3)	0.1119(7)
F25	0.52921(11)	0.6298(3)	-0.0085(3)	0.1296(9)
F1	0.5567(8)	0.5924(14)	0.126(2)	0.089(5)
F2	0.5243(8)	0.6933(16)	-0.003(2)	0.083(5)
F3	0.5524(8)	0.7631(16)	0.188(2)	0.081(5)
C26	0.46634(9)	0.56455(15)	0.2925(2)	0.0573(5)
H26	0.4947	0.5128	0.2949	0.05
C27	0.41504(9)	0.54833(15)	0.3645(2)	0.0571(5)
H27	0.4086	0.4847	0.4154	0.05
C28	0.37289(8)	0.62526(14)	0.3624(2)	0.0462(4)
H28	0.3385	0.6125	0.4121	0.05
O31	0.25950(6)	0.98586(10)	0.62415(13)	0.0515(3)
C32	0.28074(7)	1.05416(13)	0.71758(18)	0.0390(4)
O33	0.26985(6)	1.05918(9)	0.86187(13)	0.0486(3)
C34	0.32323(7)	1.13283(13)	0.65329(19)	0.0417(4)
H34A	0.3411	11.716	0.7417	0.05
H34B	0.3534	10.949	0.6009	0.05

C35	0.29546(8)	1.20947(13)	0.53724(19)	0.0425(4)
O36	0.2674(4)	1.1813(6)	0.4212(7)	0.0620(17)
O36	0.2496(4)	1.1918(7)	0.4706(10)	0.120(3)
O37	0.31592(7)	1.30312(10)	0.54566(16)	0.0606(4)
H37	0.2947	1.352	0.464	0.05
O40	0.13507(9)	0.68241(17)	0.4657(2)	0.0836(5)
H40A	0.1390	0.744	0.528	0.05
H40B	0.1122	0.639	0.520	0.05
O41	0.16352(9)	0.85416(13)	0.6539(2)	0.0708(4)
H41A	0.1533	0.848	0.747	0.05
H41B	0.1949	0.906	0.666	0.05

Table 2.10 a) Single crystal data and structure refinement of malonate form VI

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_3H_3O_4^{-2} \bullet H_2O$
Fw	530.50
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	
a [Å]	7.8050(2)
b [Å]	8.0730(2)
c [Å]	20.1470(4)
α [°]	80.0090(8)
β [°]	87.4660(8)
γ [°]	74.5320(9)
V [$Å^3$]	1204.92(3)
Z	2
D_m [g/cm^3]	1.462
F(000)	556
Crystal size [mm^3]	0.3 x 0.25 x 0.1
θ range [°]	2 → 37
Reflections collected	14593
Independent reflections	12114 [R_{int} = 0.0408]

S	1.062
R [I>2σ(I)]	R1 = 0.0742, wR2 = 0.1389
R indices (all data)	R1 = 0.1184, wR2 = 0.1594

Table 2.10 b) Atomic coordinates and temperature factor (Uiso) of malonate form VI

(hydrogen atoms were calculated according to well-established geometrical criteria)

atom	x	y	z	U (iso)
O1A	0.6256(4)	0.27887(16)	0.17045(13)	0.0277(11)
C2A	0.5192(7)	0.2652(3)	0.1409(2)	0.0212(15)
N3A	0.4241(5)	0.29908(19)	0.11247(15)	0.0212(12)
H3A	0.4286	0.3353	0.1127	0.02
C4A	0.3190(6)	0.2679(2)	0.0831(2)	0.0179(14)
C5A	0.2037(6)	0.2833(3)	0.04897(19)	0.0242(16)
H5A	0.1833	0.3211	0.0418	0.02
C6A	0.1185(6)	0.2416(3)	0.0255(2)	0.0294(17)
H6A	0.0385	0.2508	0.0016	0.02
C7A	0.1483(6)	0.1864(3)	0.0364(2)	0.0294(17)
H7A	0.0876	0.1587	0.0199	0.02
C8A	0.2654(6)	0.1710(3)	0.07092(19)	0.0262(16)
H8A	0.2868	0.1334	0.078	0.02
C9A	0.3485(6)	0.2127(2)	0.09428(19)	0.0190(15)
N10A	0.4703(5)	0.21199(19)	0.13030(15)	0.0204(12)
C11A	0.5469(5)	0.1621(2)	0.14896(18)	0.0172(14)
H11A	0.6436	0.1728	0.1675	0.02
H11B	0.5659	0.1392	0.1236	0.02
C12A	0.4662(6)	0.1273(2)	0.17793(18)	0.0172(14)
H12A	0.3589	0.1304	0.1659	0.02
H12B	0.494	0.0882	0.1753	0.02
N13A	0.4970(4)	0.14286(18)	0.22701(14)	0.0165(11)
H13A	0.5969	0.1372	0.2383	0.02
C14A	0.4135(6)	0.1054(2)	0.25244(19)	0.0238(15)
H14A	0.4441	0.0668	0.2488	0.02
H14B	0.3069	0.1083	0.2392	0.02

C15A	0.4389(6)	0.1192(2)	0.30237(19)	0.0226(15)
H15A	0.3777	0.0948	0.3175	0.02
H15B	0.5436	0.1128	0.3165	0.02
N16A	0.4004(5)	0.17688(19)	0.30840(15)	0.0199(12)
C17A	0.4908(6)	0.2133(2)	0.28613(19)	0.0223(15)
H17A	0.5963	0.2075	0.2996	0.02
H17B	0.4664	0.2523	0.2912	0.02
C18A	0.4638(6)	0.2019(2)	0.23563(18)	0.0184(14)
H18A	0.3598	0.21	0.2218	0.02
H18B	0.5272	0.2262	0.2214	0.02
C19A	0.3798(5)	0.1932(2)	0.35192(19)	0.0182(14)
C20A	0.3480(5)	0.2486(2)	0.3594(2)	0.0200(15)
H20A	0.3438	0.2749	0.3358	0.02
C21A	0.3225(6)	0.2651(2)	0.40129(19)	0.0187(14)
C22A	0.2861(7)	0.3240(3)	0.4078(2)	0.0254(16)
F23A	0.3146(4)	0.35757(15)	0.37532(12)	0.0509(11)
F24A	0.1446(4)	0.33182(15)	0.40826(14)	0.0566(12)
F25A	0.3606(4)	0.34482(15)	0.44665(12)	0.0541(12)
C26A	0.3277(6)	0.2278(3)	0.4358(2)	0.0262(16)
H26A	0.3117	0.2395	0.4646	0.02
C27A	0.3561(7)	0.1734(3)	0.4284(2)	0.0358(18)
H27A	0.3561	0.1472	0.4519	0.02
C28A	0.3849(6)	0.1560(2)	0.3871(2)	0.0284(16)
H28A	0.4082	0.1185	0.383	0.02
O31A	0.7669(4)	0.04516(16)	0.26795(14)	0.0319(11)
C32A	0.8398(6)	0.0894(3)	0.27126(19)	0.0209(15)
O33A	0.7893(4)	0.13579(16)	0.25753(13)	0.0282(11)
C34A	1.0035(5)	0.0870(2)	0.29359(19)	0.0203(15)
H34A	1.061	0.0976	0.2706	0.02
H34B	1.0222	0.1154	0.3177	0.02
C35A	1.0641(7)	0.0322(2)	0.3144(2)	0.0245(16)
O36A	0.9790(4)	-0.01052(16)	0.30492(15)	0.0352(12)
H36A	0.8956	-0.0003	0.2908	0.02
O37A	1.1868(4)	0.02969(16)	0.33793(14)	0.0333(12)
O41A	1.2576(4)	-0.05443(17)	0.40344(13)	0.0288(11)
H41A	1.2167	-0.0332	0.3826	0.02

C42A	1.2321(6)	-0.0346(3)	0.4464(2)	0.0277(16)
C43A	1.2648(7)	0.0266(3)	0.4509(2)	0.047(2)
H43A	1.3679	0.0332	0.4492	0.02
H43B	1.2471	0.0399	0.4801	0.02
H43C	1.2004	0.0465	0.4262	0.02
C44A	1.3404(7)	-0.0664(3)	0.4820(2)	0.045(2)
H44A	1.4413	-0.0583	0.4787	0.02
H44B	1.3216	-0.1061	0.478	0.02
H44C	1.328	-0.0554	0.5123	0.02
C45A	1.0738(7)	-0.0465(3)	0.4494(2)	0.058(2)
H45A	1.0073	-0.0258	0.4258	0.02
H45B	1.0573	-0.0353	0.4793	0.02
H45C	1.0544	-0.0861	0.4452	0.02
O51A	1.5312(4)	-0.08854(17)	0.39215(14)	0.0309(11)
H51A	1.4456	-0.0785	0.3938	0.02
C52A	1.5851(6)	-0.0545(3)	0.3599(2)	0.0286(16)
C53A	1.6192(7)	0.0023(2)	0.3799(2)	0.051(2)
H53A	1.5276	0.0201	0.3838	0.02
H53B	1.6655	0.0245	0.3595	0.02
H53C	1.6864	-0.0009	0.4094	0.02
C54A	1.7245(6)	-0.0836(3)	0.3520(2)	0.0405(19)
H54A	1.6987	-0.1202	0.339	0.02
H54B	1.7946	-0.0875	0.3809	0.02
H54C	1.7695	-0.0617	0.331	0.02
C55A	1.4715(7)	-0.0522(3)	0.3158(2)	0.049(2)
H55A	1.3826	-0.0334	0.321	0.02
H55B	1.4464	-0.0897	0.3049	0.02
H55C	1.5123	-0.0318	0.2931	0.02
O1B	0.1417(4)	0.19068(16)	0.17087(13)	0.0252(10)
C2B	0.0323(6)	0.2013(2)	0.1414(2)	0.0198(15)
N3B	-0.0561(5)	0.16559(19)	0.11321(15)	0.0209(12)
H3B	-0.0436	0.1296	0.1133	0.02
C4B	-0.1687(6)	0.1934(2)	0.08423(18)	0.0188(15)
C5B	-0.2809(6)	0.1751(3)	0.05088(18)	0.0236(15)
H5B	-0.2934	0.137	0.0434	0.02
C6B	-0.3765(6)	0.2155(3)	0.02831(19)	0.0258(16)

H6B	-0.4561	0.2045	0.0049	0.02
C7B	-0.3584(6)	0.2715(3)	0.03916(19)	0.0241(16)
H7B	-0.425	0.2977	0.0229	0.02
C8B	-0.2446(6)	0.2893(2)	0.07324(18)	0.0193(14)
H8B	-0.2318	0.3272	0.0808	0.02
C9B	-0.1505(6)	0.2498(2)	0.09576(18)	0.0146(14)
N10B	-0.0273(5)	0.25355(18)	0.13118(15)	0.0172(12)
C11B	0.0424(6)	0.3050(2)	0.14887(18)	0.0216(15)
H11C	0.0595	0.3277	0.1231	0.02
H11D	0.1399	0.2964	0.168	0.02
C12B	-0.0455(6)	0.3390(2)	0.17676(17)	0.0180(14)
H12C	-0.0201	0.3784	0.1744	0.02
H12D	-0.1518	0.3347	0.1636	0.02
N13B	-0.0190(5)	0.32326(18)	0.22561(15)	0.0171(12)
H13B	0.0805	0.3287	0.2378	0.02
C14B	-0.1054(6)	0.3604(2)	0.25018(18)	0.0216(15)
H14C	-0.2115	0.3571	0.2365	0.02
H14D	-0.0755	0.3992	0.2467	0.02
C15B	-0.0812(6)	0.3463(2)	0.29995(19)	0.0237(16)
H15C	0.0236	0.3521	0.3142	0.02
H15D	-0.1418	0.3708	0.315	0.02
N16B	-0.1215(4)	0.28845(19)	0.30597(15)	0.0187(12)
C17B	-0.0337(6)	0.2518(2)	0.28316(17)	0.0192(14)
H17C	-0.0624	0.2131	0.2872	0.02
H17D	0.0718	0.2559	0.2974	0.02
C18B	-0.0546(6)	0.2643(2)	0.23363(18)	0.0169(14)
H18C	-0.158	0.2566	0.2188	0.02
H18D	0.0099	0.2399	0.2198	0.02
C19B	-0.1474(6)	0.2726(2)	0.34842(19)	0.0190(15)
C20B	-0.1114(6)	0.2197(2)	0.36562(19)	0.0224(15)
H20B	-0.0582	0.1955	0.35	0.02
C21B	-0.1516(6)	0.2022(3)	0.4048(2)	0.0267(16)
C22B	-0.1134(9)	0.1451(3)	0.4220(2)	0.0395(19)
F23B	-0.0087(9)	0.1436(3)	0.4596(3)	0.083(3)
F24B	-0.2331(9)	0.1182(3)	0.4324(3)	0.084(3)
F25B	0.0721(10)	0.1111(2)	0.39188(19)	0.072(2)

F23B	0.0097(19)	0.1262(8)	0.4107(7)	0.045(6)
F24B	-0.083(2)	0.1414(10)	0.4649(9)	0.042(7)
F25B	-0.211(3)	0.1131(12)	0.4113(8)	0.068(9)
C26B	-0.2274(6)	0.2364(3)	0.4293(2)	0.0284(16)
H26B	-0.2571	0.2236	0.4559	0.02
C27B	-0.2578(6)	0.2894(3)	0.4136(2)	0.0293(16)
H27B	-0.3057	0.3141	0.4305	0.02
C28B	-0.2202(5)	0.3075(2)	0.37391(19)	0.0223(15)
H28C	-0.244	0.3441	0.3637	0.02
O31B	0.6664(4)	0.43895(16)	0.33478(13)	0.0302(11)
C32B	0.5421(7)	0.4349(2)	0.3115(2)	0.0221(15)
O33B	0.4540(4)	0.47697(16)	0.30146(13)	0.0276(11)
C34B	0.4840(6)	0.3795(2)	0.29294(19)	0.0213(15)
H34C	0.5031	0.3526	0.3182	0.02
H34D	0.5424	0.3677	0.2705	0.02
C35B	0.3212(6)	0.3755(3)	0.27050(19)	0.0196(15)
O36B	0.2732(4)	0.32836(16)	0.25941(13)	0.0249(10)
O37B	0.2453(4)	0.41894(16)	0.26514(14)	0.0278(11)
H37B	0.2978	0.4458	0.2761	0.02
O41B	0.7322(4)	0.51862(16)	0.40487(12)	0.0286(11)
H41B	0.7136	0.497	0.3827	0.02
C42B	0.7157(7)	0.4897(3)	0.4455(2)	0.0312(17)
C43B	0.7507(8)	0.5326(3)	0.4831(2)	0.062(2)
H43C	0.6785	0.5626	0.4771	0.02
H43D	0.8497	0.5474	0.4842	0.02
H43E	0.7466	0.5153	0.5122	0.02
C44B	0.5603(7)	0.4701(4)	0.4409(2)	0.089(3)
H44C	0.5383	0.443	0.4163	0.02
H44D	0.4928	0.5015	0.434	0.02
H44E	0.5479	0.4529	0.4694	0.02
C45B	0.8230(8)	0.4422(3)	0.4545(3)	0.073(3)
H45C	0.8004	0.4156	0.4296	0.02
H45D	0.8146	0.4241	0.483	0.02
H45E	0.9236	0.4561	0.4568	0.02
O51B	1.0131(4)	0.55326(16)	0.39488(13)	0.0263(10)
H51B	0.9303	0.5415	0.3979	0.02

C52B	1.0615(6)	0.5226(2)	0.3591(2)	0.0261(16)
C53B	1.0829(7)	0.4625(2)	0.3718(2)	0.0386(18)
H53C	0.9879	0.4462	0.3741	0.02
H53D	1.1514	0.4593	0.4011	0.02
H53E	1.1233	0.443	0.3486	0.02
C54B	1.2073(6)	0.5495(3)	0.3542(2)	0.046(2)
H54C	1.1901	0.5884	0.3458	0.02
H54D	1.2467	0.5304	0.3306	0.02
H54E	1.2781	0.547	0.383	0.02
C55B	0.9471(7)	0.5300(3)	0.3152(2)	0.0400(18)
H55C	0.8535	0.5135	0.3188	0.02
H55D	0.9818	0.5118	0.2903	0.02
H55E	0.9329	0.5694	0.3086	0.02

Table 2.11 a) Single crystal data and structure refinement of salicylate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_7H_5O_3^-$
Fw	528.53
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell dimensions	
a [Å]	16.3790(2)
b [Å]	15.4410(4)
c [Å]	10.1810(4)
α [°]	90
β [°]	98.1820(12)
γ [°]	90
V [$Å^3$]	2548.6(2)
Z	4
D_m [g/cm^3]	1.377
F(000)	1104
Crystal size [mm^3]	0.4 x 0.3 x 0.2

θ range [°]	2.5 → 26
Reflections collected	12472
Independent reflections	4948 [R_{int} = 0.0289]
S	0.949
R [I>2σ(I)]	R1 = 0.0565, wR2 = 0.1471
R indices (all data)	R1 = 0.0753, wR2 = 0.1647

Table 2.11 b) Atomic coordinates and temperature factor (Uiso) of salicylate, form I

(hydrogen atoms were calculated according to well-established geometrical criteria)

atom	x	y	z	U (iso)
O1	0.91497(11)	0.00803(11)	0.86442(19)	0.0872(6)
C2	0.92301(13)	0.08333(15)	0.9039(2)	0.0671(6)
N3	0.97769(12)	0.11514(13)	1.0059(2)	0.0722(6)
H3	1.0131(17)	0.0818(18)	1.054(3)	0.084(8)
C4	0.96828(12)	0.20377(15)	1.0166(2)	0.0624(5)
C5	1.00965(14)	0.26490(17)	1.0998(3)	0.0744(7)
H5	10.514	0.2491	11.672	0.08
C6	0.98680(16)	0.35012(18)	1.0790(3)	0.0828(7)
H6	1.014	0.3928	11.329	0.08
C7	0.92424(17)	0.37350(17)	0.9796(3)	0.0824(7)
H7	0.9107	0.4317	0.9676	0.08
C8	0.88124(15)	0.31250(15)	0.8975(3)	0.0709(6)
H8	0.8385	0.3283	0.8317	0.08
C9	0.90464(12)	0.22768(14)	0.9177(2)	0.0590(5)
N10	0.87721(10)	0.15220(12)	0.85117(18)	0.0616(5)
C11	0.81040(12)	0.14457(15)	0.7420(2)	0.0611(5)
H11A	0.8186	0.0935	0.6899	0.08
H11B	0.8098	0.1949	0.6848	0.08
C12	0.72893(12)	0.13770(14)	0.7952(2)	0.0567(5)
H12A	0.7233	0.0798	0.8296	0.08
H12B	0.7288	0.1781	0.8681	0.08
N13	0.65689(9)	0.15639(10)	0.69194(15)	0.0456(4)
H13	0.6660	0.2124	0.660	0.08
C14	0.65126(12)	0.09592(12)	0.57744(19)	0.0521(5)
H14A	0.646	0.0371	0.6084	0.08
H14B	0.7015	0.0995	0.5375	0.08
C15	0.57810(12)	0.11730(13)	0.47439(19)	0.0530(5)

H15A	0.5866	0.1736	0.4363	0.08
H15B	0.5742	0.0748	0.4036	0.08
N16	0.50127(9)	0.11822(9)	0.53024(14)	0.0463(4)
C17	0.50607(12)	0.17499(14)	0.6462(2)	0.0553(5)
H17A	0.4555	0.1702	0.685	0.08
H17B	0.5116	0.2346	0.6187	0.08
C18	0.57805(12)	0.15162(14)	0.7483(2)	0.0581(5)
H18A	0.5804	0.1909	0.8231	0.08
H18B	0.5707	0.0934	0.7804	0.08
C19	0.42806(11)	0.12442(11)	0.43852(18)	0.0460(4)
C20	0.35149(12)	0.12890(11)	0.48298(19)	0.0499(4)
H20	0.3489	0.1313	0.5736	0.08
C21	0.27903(12)	0.12987(12)	0.3938(2)	0.0539(5)
C22	0.19946(14)	0.13183(16)	0.4478(3)	0.0684(6)
F23	0.19854(9)	0.19130(12)	0.54236(17)	0.0973(5)
F24	0.18397(11)	0.05872(12)	0.5046(3)	0.1286(8)
F25	0.13575(9)	0.15083(16)	0.35812(18)	0.1216(7)
C26	0.28037(14)	0.12594(15)	0.2590(2)	0.0663(6)
H26	0.2316	0.1253	0.1997	0.08
C27	0.35586(16)	0.12292(16)	0.2143(2)	0.0702(6)
H27	0.3578	0.1212	0.1235	0.08
C28	0.42895(14)	0.12245(14)	0.3015(2)	0.0591(5)
H28	0.4791	0.1208	0.2686	0.08
O31	0.70266(9)	0.30926(9)	0.62125(18)	0.0738(5)
C32	0.66099(13)	0.37670(12)	0.62665(19)	0.0527(5)
O33	0.58513(11)	0.37610(11)	0.6255(2)	0.0935(6)
C34	0.70438(14)	0.46195(12)	0.63243(18)	0.0562(5)
C35	0.6612(2)	0.53938(14)	0.6406(2)	0.0754(7)
O36	0.57910(18)	0.53960(15)	0.6404(3)	0.1133(8)
H36	0.559	0.486	0.612	0.08
C37	0.7032(3)	0.61784(17)	0.6487(3)	0.1008(11)
H37	0.6747	0.6694	0.6551	0.08
C38	0.7862(3)	0.6191(2)	0.6473(3)	0.1212(15)
H38	0.8138	0.6719	0.6518	0.08
C39	0.8304(2)	0.5434(2)	0.6394(3)	0.1079(11)
H39	0.8872	0.5451	0.6395	0.08
C40	0.78916(17)	0.46572(17)	0.6314(2)	0.0780(7)
H40	0.8185	0.4146	0.6251	0.08

Table 2.12 Single crystal data and structure refinement of L-tartate form I

Empirical formula	$2\ C_{20}H_{22}F_3N_4O^+ \bullet C_4H_4O_6^{2-} \bullet 2\ H_2O$
Fw	966.94
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Triclinic
Space group	P 1
Unit cell dimensions	
a [Å]	9.4030(2)
b [Å]	10.7370(3)
c [Å]	11.7620(3)
α [°]	98.355(1)
β [°]	93.917(1)
γ [°]	109.172(1)
V [$Å^3$]	1101.14(5)
Z	1
D_m [g/cm^3]	1.458
F(000)	506
Crystal size [mm^3]	0.4 x 0.25 x 0.17
θ range [°]	2.5 → 27.5
Reflections collected	7358
Independent reflections	7358 [R_{int} = 0.0000]
S	1.028
R [I>2σ(I)]	R1 = 0.0444, wR2 = 0.1196
R indices (all data)	R1 = 0.0491, wR2 = 0.1257

Table 2.13 Single crystal data and structure refinement of fumarate form I

Empirical formula	$2\ (C_{20}H_{22}F_3N_4O^+) \bullet C_4H_2O_4^{2-} \bullet C_4H_4O_4$
Fw	1012.96
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Triclinic

Space group	P –1
Unit cell dimensions	
a [Å]	9.5900(2)
b [Å]	11.6620(2)
c [Å]	12.2070(3)
α [°]	67.0130(11)
β [°]	68.8250(10)
γ [°]	88.8640(12)
V [$Å^3$]	1160.20(4)
Z	1
D_m [g/cm^3]	1.450
F(000)	528
Crystal size [mm^3]	0.35 x 0.35 x 0.2
θ range [°]	3 → 26
Reflections collected	7642
Independent reflections	4536 [R_{int} = 0.0199]
S	1.058
R [I>2σ(I)]	R1 = 0.0452, wR2 = 0.0999
R indices (all data)	R1 = 0.0594, wR2 = 0.1091

Table 2.14 Single crystal data and structure refinement of fumarate form II

Empirical formula	$C_{20}H_{22}F_3N_4O^- \bullet 0.5\ C_4H_2O_4^{2-}H_2O \bullet\ H_2O$
Fw	466,46
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	
a [Å]	9.0720(3)
b [Å]	10.7140(2)
c [Å]	11.7530(8)
α [°]	96.708(2)
β [°]	95.355(2)

γ [°]	109.214(2)
V [Å^3]	1060.71 (11)
Z	2
D_m [g/cm^3]	1.460
F(000)	488
Crystal size [mm^3]	0.20 x 0.15 x 0.1
θ range [°]	2.5 → 26
Reflections collected	6160
Independent reflections	4054 [R_{int} = 0.0662]
S	1.061
R [I>2σ(I)]	R1 = 0.0618, wR2 = 0.1331
R indices (all data)	R1 = 0.0825, wR2 = 0.1465

Table 2.15 Single crystal data and structure refinement of citrate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_6H_9O_8^- \bullet C_2H_6O$
Fw	628.60
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Orthorhombic
Space group	$Pca2_1$
Unit cell dimensions	
a [Å]	25.4880(4)
b [Å]	15.6530(8)
c [Å]	7.6090(16)
α [°]	90
β [°]	90
γ [°]	90
V [Å^3]	3035.7(7)
Z	4
D_m [g/cm^3]	1.375
F(000)	1320
Crystal size [mm^3]	0.25 x 0.25 x 0.18
θ range [°]	2.5 → 25

Reflections collected	17271
Independent reflections	5321 [R_{int} = 0.0483]
S	1.073
R [I>2σ(I)]	R1 = 0.0493, wR2 = 0.1044
R indices (all data)	R1 = 0.0675, wR2 = 0.1126

Table 2.16 Single crystal data and structure refinement of mandelate form I

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_8H_7O_3^-$
Fw	542.55
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Orthorhombic
Space group	$P\ 2_12_12_1$
Unit cell dimensions	
a [Å]	9.7220(2)
b [Å]	22.5720(3)
c [Å]	23.9740(4)
α [°]	90
β [°]	90
γ [°]	90
V [$Å^3$]	5261.0(2)
Z	8
D_m [g/cm^3]	1.370
F(000)	2272
Crystal size [mm^3]	0.35 x 0.3 x 0.25
θ range [°]	1 → 26
Reflections collected	28800
Independent reflections	10298 [R(int) = 0.0760]
S	1.040
R [I>2σ(I)]	R1 = 0.0732, wR2 = 0.1539
R indices (all data)	R1 = 0.1163, wR2 = 0.1765

Table 2.17 Single crystal data and structure refinement of L-malate form I

Empirical formula	$C_{24}H_{22}F_3N_4O^- \bullet C_4H_5O_5^- \bullet H_2O$
Fw	542.51
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Triclinic
Space group	P 1
Unit cell dimensions	
a [Å]	7.8000(2)
b [Å]	8.0610(2)
c [Å]	21.1650(3)
α [°]	82.578(1)
β [°]	82.526(1)
γ [°]	77.692(1)
V [$Å^3$]	1282.05(3) $Å^3$
Z	2
D_m [g/cm^3]	1.405
F(000)	568
Crystal size [mm^3]	0.25 x 0.25 x 0.2
θ range [°]	2 → 26
Reflections collected	8379
Independent reflections	8379 [R_{int} = 0.0000]
S	1.026
R [I>2σ(I)]	R1 = 0.0350, wR2 = 0.0815
R indices (all data)	R1 = 0.0384, wR2 = 0.0844

Table 2.18 a) Single crystal data and structure refinement of succinate form I

Empirical formula	$2\ C_{20}H_{22}F_3N_4O^+ \bullet C_4H_4O_4^{2-} \bullet 2\ H_2O$
Fw	934.94
T [K]	293(2)
λ[Å]	0.71073

Crystal system	Triclinic
Space group	P –1
Unit cell dimensions	
a [Å]	9.5450(4)
b [Å]	10.7120(5)
c [Å]	11.7330(7)
α [°]	97.597(2)
β [°]	93.690(2)
γ [°]	110.663(3)
V [$Å^3$]	1104.6(1)
Z	1
D_m [g/cm^3]	1.405
F(000)	490
Crystal size [mm^3]	0.3 x 0.3 x 0.2
θ range [°]	3.5 → 26
Reflections collected	6382
Independent reflections	4176 [R_{int} = 0.0194]
S	1.036
R [I>2σ(I)]	R1 = 0.0555, wR2 = 0.1386
R indices (all data)	R1 = 0.0649, wR2 = 0.1484

Table 2.18 b) Atomic coordinates and temperature factor (Uiso) of succinate, form I

(hydrogen atoms were calculated according to well-established geometrical criteria)

atom	x	y	z	U (iso)
O1	0.11215(14)	-0.33344(13)	0.08086(12)	0.0588(4)
C2	0.20693(19)	-0.36147(17)	0.02653(15)	0.0473(4)
N3	0.18520(18)	-0.47601(15)	-0.04935(14)	0.0510(4)
H3	0.097	-0.541	-0.0650	0.07
C4	0.3180(2)	-0.46756(17)	-0.09559(14)	0.0471(4)
C5	0.3527(2)	-0.5538(2)	-0.17731(17)	0.0582(5)
H5	0.2808	-0.6367	-0.2123	0.07
C6	0.4993(3)	-0.5117(2)	-0.20481(18)	0.0655(5)
H6	0.5258	-0.5667	-0.2606	0.07
C7	0.6070(3)	-0.3898(2)	-0.15142(19)	0.0659(5)

H7	0.7047	-0.3653	-0.1712	0.07
C8	0.5727(2)	-0.3037(2)	-0.06925(17)	0.0575(5)
H8	0.6455	-0.222	-0.0328	0.07
C9	0.42669(19)	-0.34370(17)	-0.04361(14)	0.0461(4)
N10	0.35550(16)	-0.28081(14)	0.03201(12)	0.0471(3)
C11	0.4200(2)	-0.14335(17)	0.09490(15)	0.0486(4)
H11A	0.3413	-0.106	0.1011	0.07
H11B	0.495	-0.0883	0.052	0.07
C12	0.49289(19)	-0.13732(16)	0.21523(14)	0.0438(4)
H12A	0.4149	-0.1742	0.2638	0.07
H12B	0.5543	-0.1928	0.2106	0.07
N13	0.58818(14)	0.00287(13)	0.26891(11)	0.0378(3)
H13	0.687(3)	0.048(3)	0.204(3)	0.109(9)
C14	0.6605(2)	0.00347(17)	0.38462(14)	0.0457(4)
H14A	0.7202	-0.0534	0.3767	0.07
H14B	0.5831	-0.0343	0.4333	0.07
C15	0.7605(2)	0.14425(18)	0.44207(15)	0.0489(4)
H15A	0.7997	0.141	0.5196	0.07
H15B	0.8455	0.1773	0.3987	0.07
N16	0.68001(16)	0.23859(14)	0.44916(12)	0.0452(3)
C17	0.6059(2)	0.23599(17)	0.33567(16)	0.0501(4)
H17A	0.6818	0.2708	0.2849	0.07
H17B	0.5479	0.2942	0.3435	0.07
C18	0.50283(19)	0.09428(17)	0.28235(15)	0.0460(4)
H18A	0.4242	0.0608	0.3312	0.07
H18B	0.4552	0.0956	0.2072	0.07
C19	0.75610(19)	0.36736(17)	0.51691(14)	0.0452(4)
C20	0.7328(2)	0.48246(18)	0.49104(16)	0.0505(4)
H20	0.6692	0.4758	0.4252	0.07
C21	0.8033(2)	0.60673(18)	0.56230(16)	0.0517(4)
C22	0.7781(3)	0.7274(2)	0.5290(2)	0.0703(6)
F23	0.8472(13)	0.7647(11)	0.4342(8)	0.100(3)
F24	0.6390(9)	0.7062(9)	0.5010(11)	0.132(4)
F25	0.8386(14)	0.8364(12)	0.6034(12)	0.126(4)
F23	0.7798(13)	0.8151(14)	0.6255(14)	0.122(4)
F24	0.6396(8)	0.6996(6)	0.4736(8)	0.087(2)
F25	0.8708(10)	0.7912(12)	0.4664(10)	0.130(4)
C26	0.8986(2)	0.6210(2)	0.66037(17)	0.0588(5)
H26	0.9447	0.7044	0.7082	0.07
C27	0.9232(3)	0.5083(2)	0.68525(18)	0.0701(6)
H27	0.9883	0.5162	0.7506	0.07
C28	0.8541(2)	0.3836(2)	0.61586(17)	0.0625(5)
H28	0.8732	0.3092	0.6354	0.07
O31	0.78415(16)	0.08581(15)	0.12641(13)	0.0662(4)
C32	0.8705(2)	0.0184(2)	0.11696(17)	0.0535(4)

O33	0.8627(2)	-0.0710(2)	0.17358(17)	0.0949(6)
C34	0.9814(3)	0.0534(3)	0.0300(3)	0.0867(8)
H34A	0.9416	0.0936	-0.0273	0.07
H34B	10.741	0.1224	0.0697	0.07
O35	1.1282(2)	-0.1195(2)	0.26152(16)	0.0836(5)
H35A	1.023(5)	-0.114(4)	0.246(4)	0.165(16)
H35B	1.107(4)	-0.204(4)	0.196(3)	0.135(12)

A further object of the present invention is the use of the above salts and crystalline salt forms for the manufacture of a medicament for the treatment or prevention of the following diseases.

The indication of the above salts and crystalline salt forms of the present invention may include all known indications for flibanserin, e.g. in the treatment of patients suffering from central nervous system disorders, in particular in affective disorders (e.g. depression like major depressive disorder, childhood depression, dysthymia, seasonal affective disorder, dysthymic disorder and minor depressive disorder; bipolar disorders), anxiety (incl. panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobia (simple phobia), social phobia (social anxiety disorder), obsessive-compulsive disorder (OCD), post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder and anxiety disorder not otherwise specified), sleep and sexual disorders (e.g. Hypoactive Sexual Desire Disorder, premenstrual disorders like premenstrual dysphoria, premenstrual syndrome, premenstrual dysphoric disorder; sexual aversion disorder, sexual arousal disorder, orgasmic disorder, sexual pain disorders like dyspareunia, vaginismus, noncoital sexual pain disorder; sexual dysfunction due to a general medical condition and substance-induced sexual dysfunction), psychosis, schizophrenia (including the disorganized type, the catatonic type, the paranoid type, the undifferentiated type, the residual type of schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, substance-induced psychotic disorder, and psychotic disorder not otherwise specified), personality disorders, mental organic disorders, mental disorders in childhood, aggressiveness, age associated memory impairment, for neuroprotection, the treatment and/or prevention of neurodegenerative diseases as well as cerebral ischaemia of various origins

(e.g. epilepsy, hypoglycaemia, hypoxia, anoxia, brain trauma, brain oedema, amyotropic lateral sclerosis, Huntington's disease, Alzheimer's disease, hypotension, cardiac infarct, brain pressure (elevated intracranial pressure), ischaemic and haemorrhagic stroke (stroke), global cerebral ischaemia during stoppage of the heart, diabetic polyneuropathy, tinnitus, perinatal asphyxia, cardiac hypertrophia (thickening of the heart muscle) and cardiac insufficiency (weakness of the heart muscle); anorexia nervosa (incl. binge-eating/purging type of anorexia nervosa and the restricting type of anorexia nervosa), Attention Deficit Hyperactivity Disorder (ADHD) (incl. ADHD predominantly combined type, ADHD predominantly inattentive type, and ADHD predominantly hyperactive-impulsive type), obesity (incl. exogenic obesity, hyperinsulinaemic obesity, hyperplasmic obesity, hyperphyseal adiposity, hypoplasmic obesity, hypothyroid obesity, hypothalamic obesity, symptomatic obesity, infantile obesity, upper body obesity, alimentary obesity, hypogonadal obesity and central obesity), urinary incontinence (incl. overactive bladder syndrome, urgency, urge urinary incontinence, stress urinary incontinence, mixed urinary incontinence), chronic pain (incl. neuropathic pain, diabetic neuropathy, post-herpetic neuralgia (PHN), carpal tunnel syndrome (CTS), HIV neuropathy, phantom limb pain, complex regional pain syndrome (CPRS), trigeminal neuralgia / trigeminus neuralgia / tic douloureux, surgical intervention (e.g. post-operative analgesics), diabetic vasculopathy, capillary resistance or diabetic symptoms associated with insulitis, pain associated with angina, pain associated with menstruation, pain associated with cancer, dental pain, headache, migraine, trigeminal neuralgia, temporomandibular joint syndrome, myofascial pain muscular injury, fibromyalgia syndrome, bone and joint pain (osteoarthritis), rheumatoid arthritis, rheumatoid arthritis and edema resulting from trauma associated with burns, sprains or fracture bone pain due to osteoarthritis, osteoporosis, bone metastases or unknown reasons, gout, fibrositis, myofascial pain, thoracic outlet syndromes, upper back pain or lower back pain (wherein the back pain results from systematic, regional, or primary spine disease (radiculopathy), pelvic pain, cardiac chest pain, non-cardiac chest pain, spinal cord injury (SCI)-associated pain, central post-stroke pain, cancer neuropathy, AIDS pain, sickle cell pain and geriatric pain), Valvular Heart Disease (incl. valvular stenosis, valvular regurgitation, atresia of one of the valves, mitral valve prolapse), insomnia (including primary and secondary Insomnia), and vasomotor symptoms.

Preferably, salts and crystalline salt forms can be used for the treatment of disorders of sexual desire, more preferably for HSDD (Hypoactive Sexual Desire Disorder).

The present invention also relates to pharmaceutical compositions comprising the above-mentioned salts or crystalline salt forms of the present invention.

The above salts and crystalline salt forms of the present invention, may be incorporated into the conventional pharmaceutical preparation in solid, liquid or spray form. The composition may, for example, be presented in a form suitable for oral, rectal, parenteral administration or for nasal inhalation: preferred forms includes for example, capsules, tablets, coated tablets, ampoules, suppositories and nasal spray.

The active ingredient may be incorporated in excipients or carriers conventionally used in pharmaceutical compositions such as, for example, talc, arabic gum, lactose, gelatine, magnesium stearate, corn starch, acqueous or non acqueous vehicles, polyvynil pyrrolidone, semisynthetic glicerides of fatty acids, benzalconium chloride, sodium phosphate , EDTA, polysorbate 80. The compositions are advantageously formulated in dosage units, each dosage unit being adapted to supply a single dose of the active ingredient. The dosis range applicable per day is between 0.1 to 400, preferably between 1.0 to 300, more preferably between 2 to 200 mg.
Each dosage unit may conveniently contain from 0,01 mg to 100 mg, preferably from 0,1 to 50 mg.

Suitable tablets may be obtained, for example, by mixing the active substance(s) with known excipients, for example inert diluents such as calcium carbonate, calcium phosphate or lactose, disintegrants such as corn starch or alginic acid, binders such as starch or gelatine, lubricants such as magnesium stearate or talc and/or agents for delaying release, such as carboxymethyl cellulose, cellulose acetate phthalate, or polyvinyl acetate. The tablets may also comprise several layers.

Coated tablets may be prepared accordingly by coating cores produced analogously to the tablets with substances normally used for tablet coatings, for example collidone or shellac, gum arabic, talc, titanium dioxide or sugar. To achieve delayed release or prevent incompatibilities the core may also consist of a number of layers. Similarly the tablet coating may consist of a number or layers to achieve delayed release, possibly using the excipients mentioned above for the tablets.

Syrups or elixirs containing the active substances or combinations thereof according to the invention may additionally contain a sweetener such as saccharine, cyclamate, glycerol or sugar and a flavour enhancer, e.g of. a flavouring such as vanilline or orange extract. They may also contain suspension adjuvants or thickeners such as sodium carboxymethyl cellulose, wetting agents such as, for example, condensation products of fatty alcohols with ethylene oxide, or preservatives such as p-hydroxybenzoates.

Solutions for injection are prepared in the usual way, e.g of. with the addition of preservatives such as p-hydroxybenzoates, or stabilisers such as alkali metal salts of ethylenediamine tetraacetic acid, and transferred into injection vials or ampoules.

Capsules containing one or more active substances or combinations of active substances may for example be prepared by mixing the active substances with inert carriers such as lactose or sorbitol and packing them into gelatine capsules.

Suitable suppositories may be made for example by mixing with carriers provided for this purpose, such as neutral fats or polyethyleneglycol or the derivatives thereof.

Brief description of the Figures

Figure 1.1a: X-ray powder diffraction diagram of HCl 1 = chloride, form I;

Figure 1.1b: X-ray powder diffraction diagram of HCl 3 = chloride, form III;

Figure 1.2a: X-ray powder diffraction diagram of HBr 1 = hydrobromid, form I;

Figure 1.2b: X-ray powder diffraction diagram of HBr 3 = hydrobromid, form III;

Figure 1.3: X-ray powder diffraction diagram of Eds 1 = edisylate, form I;

Figure 1.4: X-ray powder diffraction diagram of Tos 1 = tosylate, form I;

Figure 1.5: X-ray powder diffraction diagram of Mes 1 = mesylate, form I;

Figure 1.6: X-ray powder diffraction diagram of Bes 1 = besylate, form I;

Figure 1.7a: X-ray powder diffraction diagram of Oxa 1 = oxalate, form I;

Figure 1.7b: X-ray powder diffraction diagram of Oxa 5 = oxalate, form V;

Figure 1.8: X-ray powder diffraction diagram of Sac 1 = saccharinate, form I;

Figure 1.9: X-ray powder diffraction diagram of Pho 1 = phosphate, form I;

Figure 1.10a: X-ray powder diffraction diagram of Mae 1 = maleate, form I;

Figure 1.10b: X-ray powder diffraction diagram of Mae 3 = maleate, form III;

Figure 1.11: X-ray powder diffraction diagram of Ets 1 = ethanesulfonate, form I;

Figure 1.12 X-ray powder diffraction diagram of Cas 1 = camphorsulfonate, form I;

Figure 1.13: X-ray powder diffraction diagram of Mao 1 = malonate, form I;

Figure 1.14: X-ray powder diffraction diagram of L-Tar 1 = L-tartrate, form I;

Figure 1.15a: X-ray powder diffraction diagram of Fum 1 = fumarate, form I;

Figure 1.15b: X-ray powder diffraction diagram of Fum 2 = fumarate, form II;

Figure 1.16 X-ray powder diffraction diagram of Gly 1 = glycolate, form I;

Figure 1.17: X-ray powder diffraction diagram of Cit 1 = citrate, form I;

Figure 1.18: X-ray powder diffraction diagram of Man 1 = mandelate, form I;

Figure 1.19: X-ray powder diffraction diagram of L-Mal 1 = L-malate, form I;

Figure 1.20 X-ray powder diffraction diagram of Nas 1 = naphtalene-sulfonate, form I;

Figure 1.21 X-ray powder diffraction diagram of TOS 2 = tosylate, form II;

Figure 1.22 X-ray powder diffraction diagram of Fum 3 = fumarate, form III;

Figure 1.23 X-ray powder diffraction diagram of Cas 2 = camphorsulfonate, form II;

Figure 1.24 X-ray powder diffraction diagram of Gly 3 = glycolate, form II.

Examples

Analytical methods for the characterization of the salts

The harvested crystals may be characterized by X-ray powder diffraction and thermal analysis (DSC). If suitable single crystals grow, single crystal X-ray structure analysis may be performed. The following equipment was used to characterize the crystalline salts forms.

X-ray powder diffraction (= XRPD)

XRPD patterns were obtained using a high throughput XRPD set-up. The plates were mounted on a Bruker GADDS diffractometer equipped with a Hi-Star area detector. The diffractometer was calibrated using Silver Behenate for the long d-spacings and corundum for the short d-spacings.

The data collection was carried out at room temperature using monochromatic CuKα radiation in the region of 2Θ between 1.5 and 41.5 °. The diffraction pattern of each well was collected with an exposure time of 3 – 4 minutes.

Single crystal X-ray structure analysis

Suitable single crystals were selected and glued to a glass fibre, which is mounted on a X-ray diffraction goniometer. X-ray diffraction data were collected for the mounted crystals at a temperature of 233 K using a KappaCCD system and MoKα radiation generated by a FR590 X-ray generator (Bruker Nonius Delft, The Netherlands).

Unit-cell parameters and crystal structure were determined and refined using the software package maXus (Mackay et al., 1997).

Thermal analysis (DSC)

Melting properties were obtained from differential scanning calorimetry (= DSC) thermograms recorded on a DSC822e (Mettler-Toledo GmbH, Switzerland). The DSC822e was calibrated for temperature and enthalpy with a small piece of indium (T_{fus} = 156.6 °C, ΔH_{fus} = 28.45 J/g). Samples were sealed in standard 40 µl aluminium pans and heated in the DSC from 25 to 300 °C with a heating rate of 20 °C/min. Dry nitrogen gas was used to purge the DSC equipment during measurements at a flow rate of 50 ml/min.The melting temperature used was the T_{fus} (onset) temperature of the corresponding melting peak in the DSC diagram. The accuracy of the melting points specified is about ± 5°C.

Hygroscopicity

IGAsorp water sorption monitor from Hiden Isochema was used for the analysis of the hygroscopical behaviour at room temperature.

humidity profile: from 10 – 90 % r.h. in steps of 10 %, sorption as well as desorption profiles were registered

weight-in quantity: 10 – 20 mg

Solubility

Solubility of the different crystalline salt forms in water was determined by adding approx. 5 mg of compound into 5 ml of water at room temperature. The mixture was vigorously shaken for 2 hours at room temperature. Afterwards the undissolved solid was removed by filtering through a 0.45 µm PTFE filter, in the filtrate the dissolved amount of compound was determined by UV-spectroscopy.

Synthesis of the salt forms

The process is illustrated by the following example of manufacturing process of the salts and crystalline salt forms, as can be done in parallel in 96 well assay plates (maximum volume of each well is about 200 µl).

Approximately 1 g of the free base of flibanserin were dissolved in 10 ml TFE/water 80:20. The acids used to prepare the salts were dissolved in different solvents such that the molar ratio of the flibanserin to the respective acid was set according to the information given in Table 3 under “ratio base/acid”. Fumaric acid was dissolved in THF/water 80:20, HCl in water and all other acids used were dissolved in TFE/water 80:20. However it is to mention that all other solvents which are able to dissolve the acid used could have been used. The 96 well plates were then placed in a vacuum chamber (1 kPa) at room temperature for 24 h in order to evaporate the solvent. Afterwards, different solvents were added in each well according to the information given in Table 3 under “crystallization solvent”, and the well plates were sealed and heated up to 50 °C at a heating rate of approx. 5 °C/min. The plate stayed then for an additional 30 minutes at 50 °C. Afterwards, the plate was cooled at a cooling rate of 5°C/h to a final temperature of 3 or 20 °C according to the information given in Table 3 under “T_{final}[°C]”. At this temperature, the plates remained for a holding time of 24 h. The plates were then opened and the solids were collected by filtration. All salts specified in table 3 were synthesized according to the above specification.

Table 3: Conditions for the preparation of the different salts of 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one

salt form	salt form full name	used acid	ratio base/a	crystallization solvent	T_{final} [°C]
HCl	chloride, form I	hydrochloric acid	1:1	ethanol/water (80:20)	3
HCl3	chloride, form III	hydrochloric acid	1:1	water/NMP* (80:20)	20

salt form	salt form full name	used acid	ratio base/a	crystallization solvent	T_{final} [°C]
HBr 1	bromide from I	hydrobromic acid	1:1	dichlormethane	20
HBr 3	bromide from III	hydrobromic acid	1:1	methanol	20
Eds1	edisylate form I	ethane-1,2 disulfonic acid	1:1	methanol	20
Tos 1	tosylate form I	p-toluenesulfonic acid	1:1	THF*	20
Mes 1	mesylate form I	methanesulfonic acid	1:1	TBME*	20
Bes 1	besylate form I	benzenesulfonic acid	1:1	TBME*	20
Oxa 1	oxalate form I	oxalic acid	1:1	1,2 Dimethoxyethane	20
Oxa 5	oxalate form V	oxalic acid	1:1	water/acetone (20:80)	3
Sac1	sacharinate form I	sacharine	1:1	dichloromethane	3
Pho	phosphate form I	phsophoric acid	1:1	cyclohexanone	20
Mae1	maleate form I	maleaic acid	1:1	THF*	3
Mae3	maleate form III	maleaic acid	1:1	propyl acetate	20
Ets	ethanesulfonate	ethanesulfonic acid	1:1	1,2 Dimethoxyethane	20
Cas1	camphorsulfonate form I	campher-10 sulfonic acid	1:1	cyclohexane	20
Mao 1	malonate form I	malonic acid	1:1	acetone/water (80:20)	3
Mao 2	malonate form II	malonic acid	1:1	tert-Butanol	3
Mao 6	malonic form VI	malonic acid	1:1	Nitromethane	3
Sal 1	salicylate form I	salicylic acid	1:1	DMSO*/water (20:80)	3
L-Tart 1	L-tartate form	L-tartaric acid	1:1	ethanol	20
Fum 1	fumerate form I	fumaric acid	2:1	chloroform	20
Fum 2	fumerate form II	fumaric acid	2:1	nitromethane	20
Gly 1	glycolate form I	glycolic acid	1:1	TBME*	20

salt form	salt form full name	used acid	ratio base/a	crystallization solvent	T_{final} [°C]
Cit1	citrate form I	citric acid	2:1	ethanol/water (80:20)	20
Man 1	mandelate form I	L-mandelic acid	1:1	ethanol	20
L-Mal 1	L-malate form I	L-malic acid	1:1	ethanol	3
Suc 1	succinate form I	succinic acid	1:1	H_2O	20
Nas1	naphtalene-sulfonate form I	naphtalene-2-sulfonic acid	1:1	2-butanone	3
Tos 2	tosylate form II (= anhydrous form)	p-toluenesulfonic acid	1:1	ethanol	20
Fum 3	fumarate, form III (= anhydrous form)	fumaric acid	1:1	chloroform	20
Cas 2	camphorsulfonate form II (= anhydrous form)	campher-10 sulfonic acid	1:1	ethanol	20
Gly 2	glycolate form II (= hydrate form)	glycolic acid	1:1	TBME*	20

* THF = tetrahydrofurane

* DMSO = dimethylsulfoxide

* NMP = 1-methyl-2-pyrrolidinone

* TBME = tert-butyl methyl ether

* TFE = 2,2,2,-Trifuoroethanol

Examples of formulations:

The Examples which follow illustrate the present invention without restricting its scope:

Examples of pharmaceutical formulations

A)	Tablets	per tablet
	active substance	100 mg
	lactose	240 mg
	corn starch	340 mg
	polyvinylpyrrolidone	45 mg
	magnesium stearate	15 mg
		740 mg

The finely ground active substance, lactose and some of the corn starch are mixed together. The mixture is screened, then moistened with a solution of polyvinylpyrrolidone in water, kneaded, wet-granulated and dried. The granules, the remaining corn starch and the magnesium stearate are screened and mixed together. The mixture is compressed to produce tablets of suitable shape and size.

B)	Tablets	per tablet
	active substance	80 mg
	corn starch	190 mg
	lactose	55 mg
	microcrystalline cellulose	35 mg
	polyvinylpyrrolidone	15 mg
	sodium-carboxymethyl starch	23 mg
	magnesium stearate	2 mg
		400 mg

The finely ground active substance, some of the corn starch, lactose, microcrystalline cellulose and polyvinylpyrrolidone are mixed together, the mixture is screened and worked with the remaining corn starch and water to form a granulate which is dried and screened. The sodium-carboxymethyl starch and the magnesium stearate are added and mixed in and the mixture is compressed to form tablets of a suitable size.

C) Coated tablets per coated tablet

active substance	5 mg
corn starch	41.5 mg
lactose	30 mg
polyvinylpyrrolidone	3 mg
magnesium stearate	0.5 mg
	80 mg

The active substance, corn starch, lactose and polyvinylpyrrolidone are thoroughly mixed and moistened with water. The moist mass is pushed through a screen with a 1 mm mesh size, dried at about 45°C and the granules are then passed through the same screen. After the magnesium stearate has been mixed in, convex tablet cores with a diameter of 6 mm are compressed in a tablet-making machine . The tablet cores thus produced are coated in known manner with a covering consisting essentially of sugar and talc. The finished coated tablets are polished with wax.

D) Capsules per capsule

active substance	1 50 mg
Corn starch	268.5 mg
Magnesium stearate	1.5 mg
	420 mg

The substance and corn starch are mixed and moistened with water. The moist mass is screened and dried. The dry granules are screened and mixed with magnesium stearate. The finished mixture is packed into size 1 hard gelatine capsules.

E) Ampoule solution

active substance	50 mg
sodium chloride	50 mg

water for inj.	5 ml

The active substance is dissolved in water at its own pH or optionally at pH 5.5 to 6.5 and sodium chloride is added to make it isotonic. The solution obtained is filtered free from pyrogens and the filtrate is transferred under aseptic conditions into ampoules which are then sterilised and sealed by fusion.

F) Suppositories

active substance	50 mg
solid fat	1650 mg
	1700 mg

The hard fat is melted. At 40°C the ground active substance is homogeneously dispersed. It is cooled to 38°C and poured into slightly chilled suppository moulds.

Patent Claims

1. Salt of the compound 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one, which is selected from the group consisting of:

I. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one chloride, characterized by a melting point of T_{fus} (onset) = 215 ± 5°C which occurs during thermal analysis using DSC;

II. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one chloride, characterized by a melting point of T_{fus} (onset) = 217 ± 5°C which occurs during thermal analysis using DSC;

III. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one bromide, characterized by a melting point of T_{fus} (onset) = 252 ± 5 °C which occurs during thermal analysis using DSC and by the peaks in the X-ray powder diffractogram which occur at d = 3.48 ± 0.05 Å, d = 3.33 ± 0.05 Å, d = 4.28 ± 0.05 Å, d = 3.43 ± 0.05 Å and d = 16.03 ± 0.05 Å;

IV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one bromide, characterized by a melting point of T_{fus} (onset) = 252 ± 5 °C which occurs during thermal analysis using DSC and by the peaks in the X-ray powder diffractogram which occur at d = 15.52 ± 0.05 Å, d = 5.15 ± 0.05 Å, d = 4.60 ± 0.05 Å, d = 4.36 ± 0.05 Å and d = 3.94 ± 0.05 Å;

V. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one edisylate, characterized by a melting point

of T_{fus} (onset) = 144 ± 5 °C which occurs during thermal analysis using DSC;

VI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one tosylate, characterized by a melting point of T_{fus} (onset) = 238 ± 5 °C which occurs during thermal analysis using DSC;

VII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one mesylate, characterized by a melting point of T_{fus} (onset) = 207 ± 5 °C which occurs during thermal analysis using DSC;

VIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one besylate, characterized by a melting point of T_{fus} (onset) = 247 ± 5 °C which occurs during thermal analysis using DSC;

IX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one oxalate, characterized by a melting point of T_{fus} (onset) = 209 ± 5 °C which occurs during thermal analysis using DSC;

X. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one oxalate, characterized by a melting point of T_{fus} (onset) = 254 ± 5 °C which occurs during thermal analysis using DSC;

XI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one sacharinate, characterized by a melting point of T_{fus} (onset) = 90 ± 5 °C which occurs during thermal analysis using DSC;

XII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one phosphate, characterized by a melting point of T_{fus} (onset) = 182 ± 5 °C which occurs during thermal analysis using DSC;

XIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one maleate, characterized by a melting point of T_{fus} (onset) = 98 ± 5 °C which occurs during thermal analysis using DSC;

XIV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one maleate, characterized by a melting point of T_{fus} (onset) = 172 ± 5 °C which occurs during thermal analysis using DSC;

XV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one ethansulfonate, characterized by a melting point of T_{fus} (onset) = 207 ± 5 °C which occurs during thermal analysis using DSC;

XVI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one camphorsulfonate, characterized by a melting point of T_{fus} (onset) = 217 ± 5 °C which occurs during thermal analysis using DSC:

XVII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one malonate, characterized by a melting point of T_{fus} (onset) = 103 ± 5 °C which occurs during thermal analysis using DSC;

XVIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one malonate, characterized by the following data:

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_3H_3O_4^{-2} \bullet 2\ C_4H_{10}O$
Fw	642.71
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell dimensions	
a [Å]	9.2650(3)
b [Å]	24.2380(2)
c [Å]	30.128(8)
α [°]	90
β [°]	101.620(2)
γ [°]	90
V [Å^3]	6627.0 (4)
Z	**8**
D_m [g/cm^3]	1.288
F(000)	2736
Crystal size [mm^3]	0.25 x 0.1 x 0.08
θ range [°]	1.5 → 24
Reflections collected	22364
Independent reflections	10286 [R_{int} = 0.1143]
S	1.093
R [I>2σ(I)]	R1 = 0.1070, wR2 = 0.1271
R indices (all data)	R1 = 0.2167, wR2 = 0.1563

XIX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one malonate, characterized characterized by the following data:

Empirical formula	$C_{20}H_{22}F_3N_4O^+ \bullet C_3H_3O_4^{-2} \bullet H_2O$
Fw	530.50
T [K]	120(2)
λ[Å]	0.71073
Crystal system	Triclinic

Space group	P -1
Unit cell dimensions	
a [Å]	7.8050(2)
b [Å]	8.0730(2)
c [Å]	20.1470(4)
α [°]	80.0090(8)
β [°]	87.4660(8)
γ [°]	74.5320(9)
V [$Å^3$]	1204.92(3)
Z	2
D_m [g/cm^3]	1.462
F(000)	556
Crystal size [mm^3]	0.3 x 0.25 x 0.1
θ range [°]	2 → 37
Reflections collected	14593
Independent reflections	12114 [R_{int} = 0.0408]
S	1.062
R [I>2σ(I)]	R1 = 0.0742, wR2 = 0.1389
R indices (all data)	R1 = 0.1184, wR2 = 0.1594

XX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one salicylate, characterized by the following data:

Empirical formula	$C_{20}H_{22}F_3N_4O^- \bullet C_7H_5O_3^-$
Fw	528.53
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell dimensions	
a [Å]	16.3790(2)
b [Å]	15.4410(4)
c [Å]	10.1810(4)

α [°]	90
β [°]	98.1820(12)
γ [°]	90
V [Å^3]	2548.6(2)
Z	4
D_m [g/cm^3]	1.377
F(000)	1104
Crystal size [mm^3]	0.4 x 0.3 x 0.2
θ range [°]	2.5 → 26
Reflections collected	12472
Independent reflections	4948 [R_{int} = 0.0289]
S	0.949
R [I>2σ(I)]	R1 = 0.0565, wR2 = 0.1471
R indices (all data)	R1 = 0.0753, wR2 = 0.1647

XXI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one L-tartrate, characterized by a melting point of T_{fus} (onset) = 151 ± 5 °C which occurs during thermal analysis using DSC;

XXII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one hemifumarate, characterized by a melting point of T_{fus} (onset) = 195 ± 5 °C which occurs during thermal analysis using DSC;

XXIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one fumarate, characterized by a melting point of T_{fus} (onset) = 193 ± 5 °C which occurs during thermal analysis using DSC;

XXIV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one glycolate (form I) (=hydrate form), characterized by a melting point of T_{fus} (onset) = 139 ± 5 °C which occurs during thermal analysis using DSC;

XXV. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one citrate, characterized by a melting point of T_{fus} (onset) = 176 ± 5 °C which occurs during thermal analysis using DSC;

XXVI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one mandelate, characterized by a melting point of T_{fus} (onset) = 148 ± 5 °C which occurs during thermal analysis using DSC;

XXVII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one L-malate, characterized by a melting point of T_{fus} (onset) = 176 ± 5 °C which occurs during thermal analysis using DSC;

XXVIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one succinate, characterized by the following data:

Empirical formula	$2\ C_{20}H_{22}F_3N_4O^{1+} \bullet C_4H_4O_4^{2-} \bullet 2\ H_2O$
Fw	934.94
T [K]	293(2)
λ[Å]	0.71073
Crystal system	Triclinic
Space group	P –1
Unit cell dimensions	
a [Å]	9.5450(4)

b [Å]	10.7120(5)
c [Å]	11.7330(7)
α [°]	97.597(2)
β [°]	93.690(2)
γ [°]	110.663(3)
V [Å^3]	1104.6(1)
Z	1
D_m [g/cm^3]	1.405
F(000)	490
Crystal size [mm^3]	0.3 x 0.3 x 0.2
θ range [°]	3.5 → 26
Reflections collected	6382
Independent reflections	4176 [R_{int} = 0.0194]
S	1.036
R [I>2σ(I)]	R1 = 0.0555, wR2 = 0.1386
R indices (all data)	R1 = 0.0649, wR2 = 0.1484

XXIX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one naphthalenesulfonate, characterized by peaks in the X-ray powder diffractogram which occur at d = 4.92 ± 0.05 Å, d = 3.43 ± 0.05 Å, d = 4.00 ± 0.05 Å and d = 3.96 ± 0.05 Å;

XXX. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one tosylate (form II) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 241 ± 5 °C which occurs during thermal analysis using DSC;

XXXI. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one fumarate (form III) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 202 ± 5 °C which occurs during thermal analysis using DSC;

XXXII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one camphorsulfonate (form II) (= anhydrous form), characterized by a melting point of T_{fus} (onset) = 231 ± 5 °C which occurs during thermal analysis using DSC;

XXXIII. Crystalline 1-[2-(4-(3-trifluoro-methyl-phenyl)piperazin-1-yl)ethyl]-2,3-dihydro-1H-benzimidazol-2-one glycolate (form II) (= hydrate form), characterized by a melting point of T_{fus} (onset) = 231 ± 5 °C which occurs during thermal analysis using DSC;

2. Crystalline salt form of claim 1 for its use as medicament.

3. Pharmaceutical composition containing one or more crystalline salt forms according to claim 1 optionally together with one or more pharmaceutically acceptable excipients.

4. Process for preparing a crystalline salt form according to claim 1, comprising the steps:

i) dissolving the free base of flibanserin and the acid providing the anion for salt formation in a suitable solvent

ii) mixing the free base of flibanserin with the acid at a predetermined base/acid molar ratio, which is selected from 1:1 or 2:1 depending on the acid

iii) removing the solvent

iv) adding a suitable crystallization solvent to the residue obtained by step iii), and heating the reaction mixture slowly up to about 50°C; leaving it to stand for a further period of time

v) slowly cooling down the reaction mixture to a suitable crystallization temperature and leaving it to stand until enough crystals are formed

vi) isolating the precipitated crystals.

5. Use of a compound according to claim 1 for the preparation of a pharmaceutical composition for the treatment of central nervous system disorders, in particular in affective disorders (e.g. depression like major depressive disorder, childhood depression, dysthymia, seasonal affective disorder, dysthymic disorder and minor depressive disorder; bipolar disorders), anxiety (incl. panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobia (simple phobia), social phobia (social anxiety disorder), obsessive-compulsive disorder (OCD), post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder and anxiety disorder not otherwise specified), sleep and sexual disorders (e.g. Hypoactive Sexual Desire Disorder, premenstrual disorders like premenstrual dysphoria, premenstrual syndrome, premenstrual dysphoric disorder; sexual aversion disorder, sexual arousal disorder, orgasmic disorder, sexual pain disorders like dyspareunia, vaginismus, noncoital sexual pain disorder; sexual dysfunction due to a general medical condition and substance-induced sexual dysfunction), psychosis, schizophrenia (including the disorganized type, the catatonic type, the paranoid type, the undifferentiated type, the residual type of schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, substance-induced psychotic disorder, and psychotic disorder not otherwise specified), personality disorders, mental organic disorders, mental disorders in childhood, aggressiveness, age associated memory impairment, for neuroprotection, the treatment and/or prevention of neurodegenerative

diseases as well as cerebral ischaemia of various origins (e.g. epilepsy, hypoglycaemia, hypoxia, anoxia, brain trauma, brain oedema, amyotropic lateral sclerosis, Huntington's disease, Alzheimer's disease, hypotension, cardiac infarct, brain pressure (elevated intracranial pressure), ischaemic and haemorrhagic stroke (stroke), global cerebral ischaemia during stoppage of the heart, diabetic polyneuropathy, tinnitus, perinatal asphyxia, cardiac hypertrophia (thickening of the heart muscle) and cardiac insufficiency (weakness of the heart muscle); anorexia nervosa (incl. binge-eating/purging type of anorexia nervosa and the restricting type of anorexia nervosa), Attention Deficit Hyperactivity Disorder (ADHD) (incl. ADHD predominantly combined type, ADHD predominantly inattentive type, and ADHD predominantly hyperactive-impulsive type), obesity (incl. exogenic obesity, hyperinsulinaemic obesity, hyperplasmic obesity, hyperphyseal adiposity, hypoplasmic obesity, hypothyroid obesity, hypothalamic obesity, symptomatic obesity, infantile obesity, upper body obesity, alimentary obesity, hypogonadal obesity and central obesity), urinary incontinence (incl. overactive bladder syndrome, urgency, urge urinary incontinence, stress urinary incontinence, mixed urinary incontinence), chronic pain (incl. neuropathic pain, diabetic neuropathy, post-herpetic neuralgia (PHN), carpal tunnel syndrome (CTS), HIV neuropathy, phantom limb pain, complex regional pain syndrome (CPRS), trigeminal neuralgia / trigeminus neuralgia / tic douloureux, surgical intervention (e.g. post-operative analgesics), diabetic vasculopathy, capillary resistance or diabetic symptoms associated with insulitis, pain associated with angina, pain associated with menstruation, pain associated with cancer, dental pain, headache, migraine, trigeminal neuralgia, temporomandibular joint syndrome, myofascial pain muscular injury, fibromyalgia syndrome, bone and joint pain (osteoarthritis), rheumatoid arthritis, rheumatoid arthritis and edema resulting from trauma associated with burns, sprains or fracture bone pain due to osteoarthritis, osteoporosis, bone metastases or unknown

reasons, gout, fibrositis, myofascial pain, thoracic outlet syndromes, upper back pain or lower back pain (wherein the back pain results from systematic, regional, or primary spine disease (radiculopathy), pelvic pain, cardiac chest pain, non-cardiac chest pain, spinal cord injury (SCI)-associated pain, central post-stroke pain, cancer neuropathy, AIDS pain, sickle cell pain and geriatric pain), Valvular Heart Disease (incl. valvular stenosis, valvular regurgitation, atresia of one of the valves, mitral valve prolapse), insomnia (including primary and secondary Insomnia), and vasomotor symptoms..

6. Use according to claim 6, wherein the disease is Hypoactive sexual Desire disorder.

Figure 1.1a X-ray powder diffraction diagram of HCl1 = chloride, form I

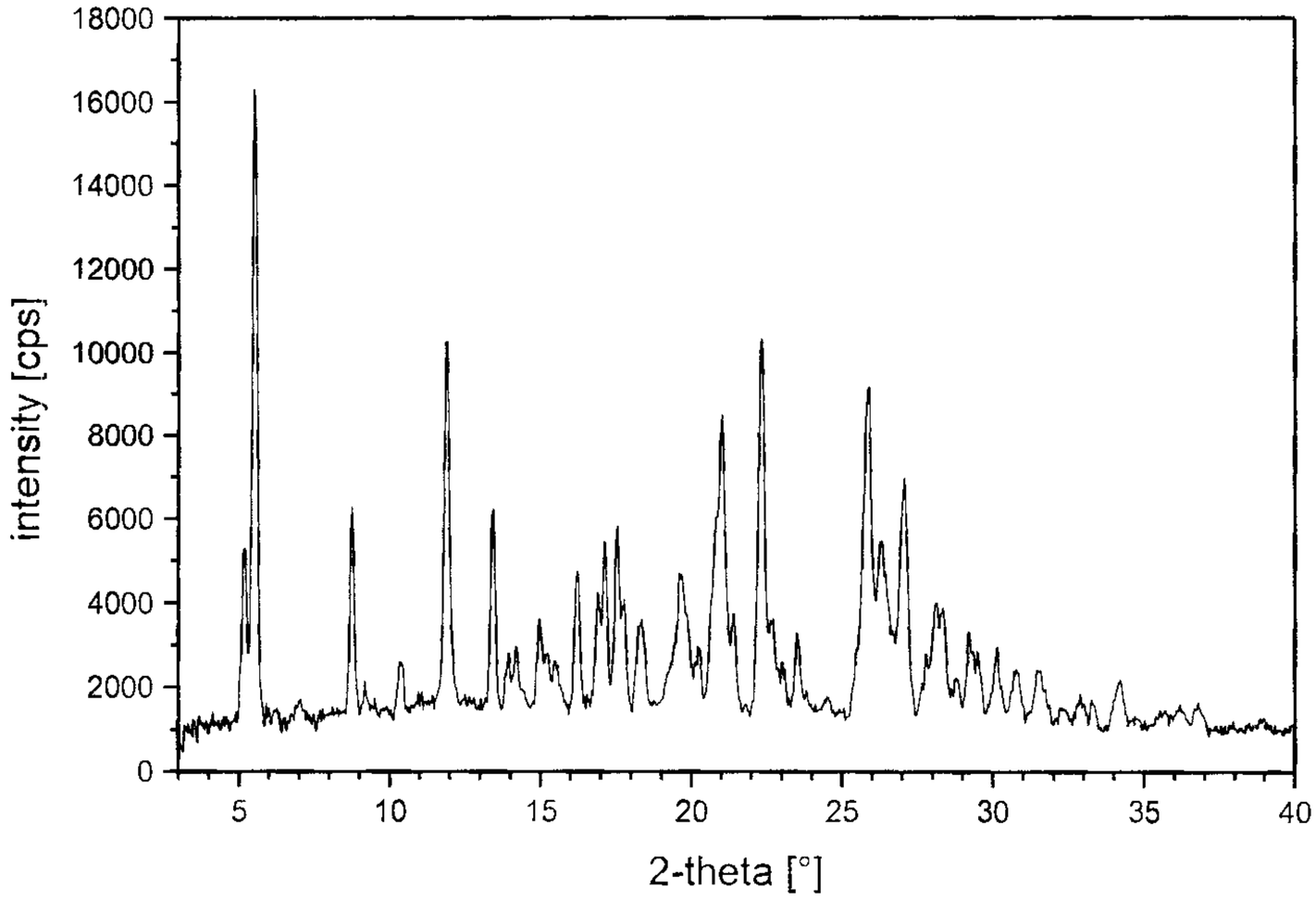


Figure 1.1b X-ray powder diffraction diagram of HCl3 = chloride, form III

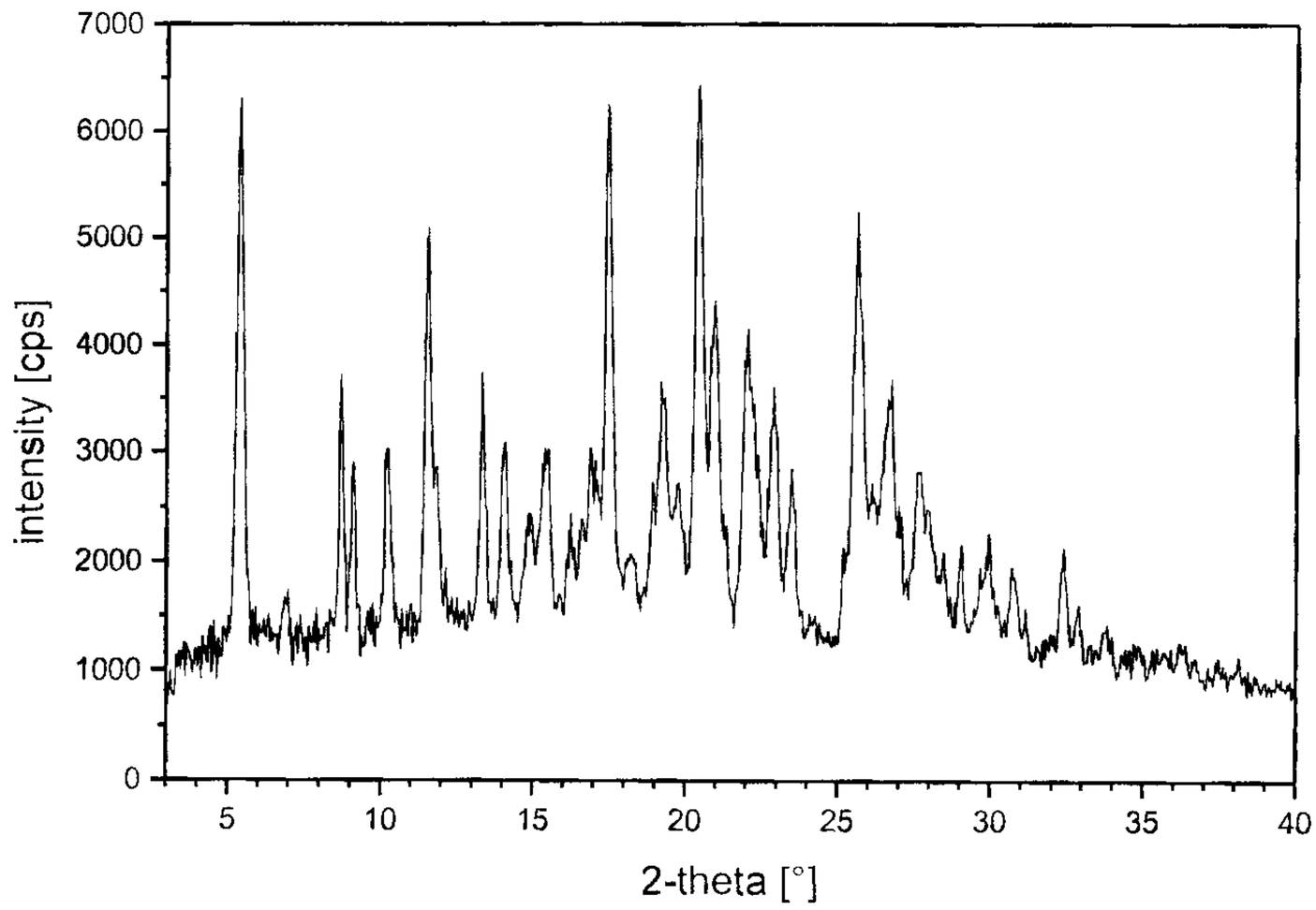


Figure 1.2a X-ray powder diffraction diagram of HBr1 = hydrobromid, form I

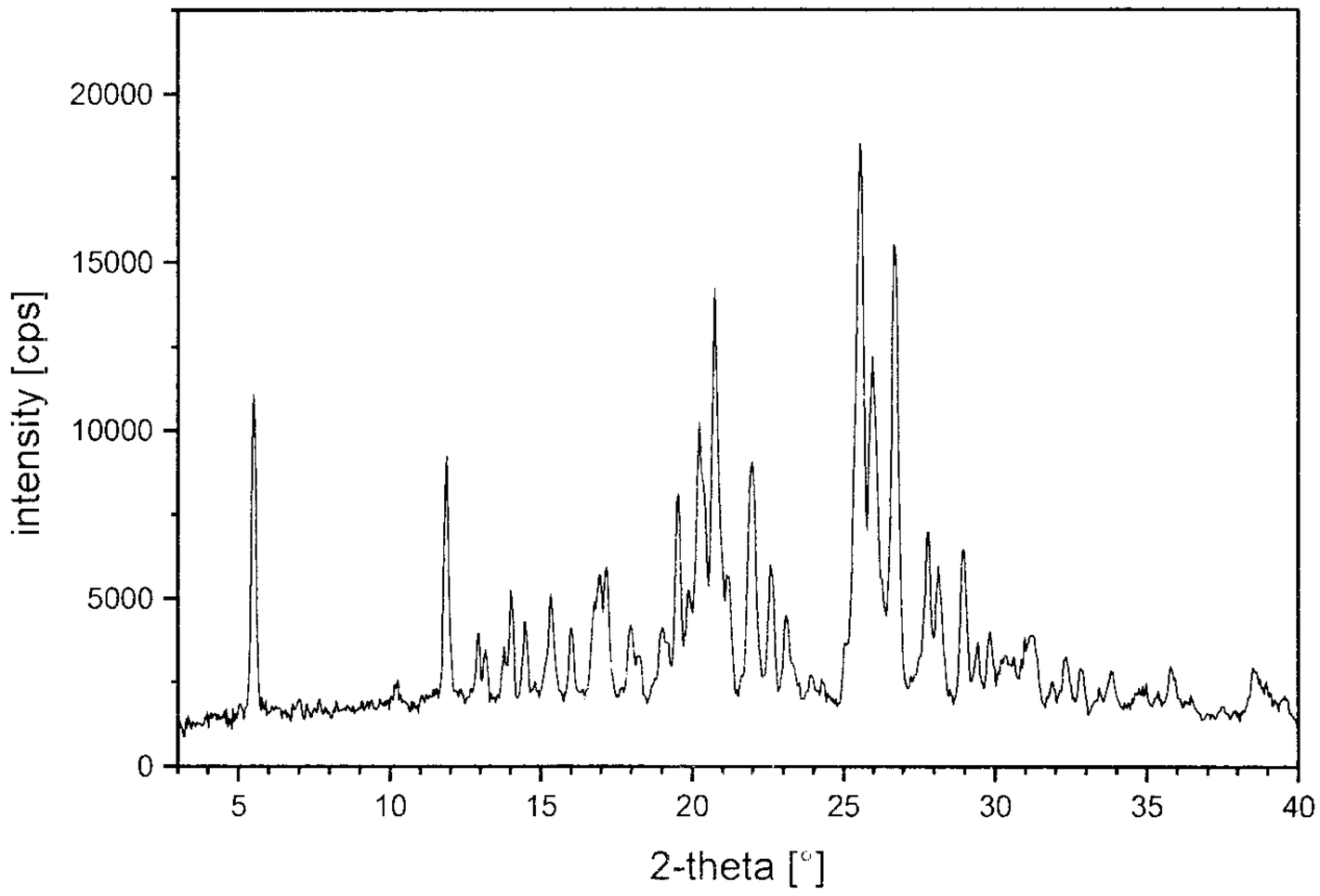


Figure 1.2b X-ray powder diffraction diagram of HBr3 = hydrobromid, form III

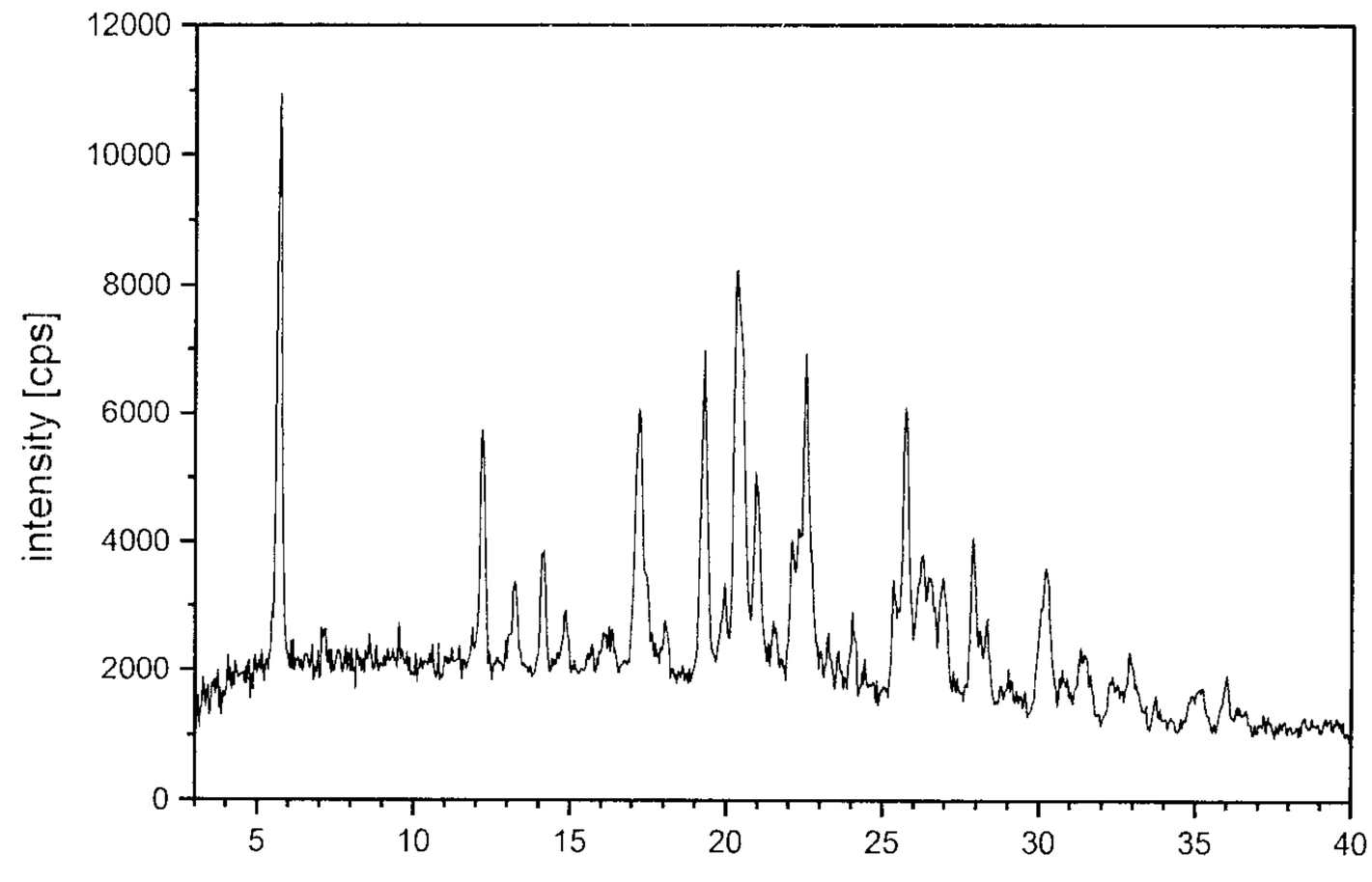


Figure 1.3 X-ray powder diffraction diagram of Eds1 = edisylate, form I

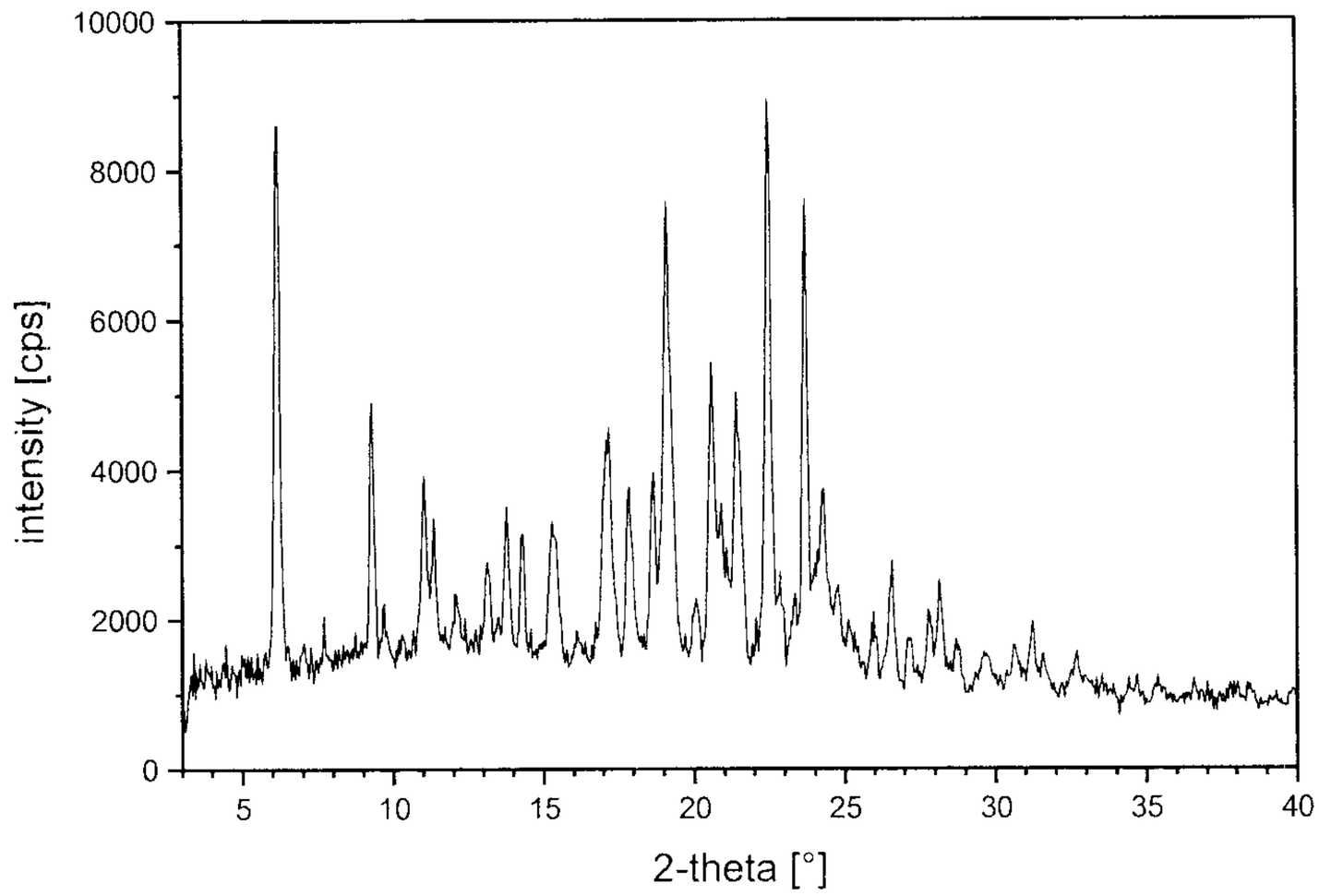


Figure 1.4 X-ray powder diffraction diagram of Tos1 = tosylate, form I

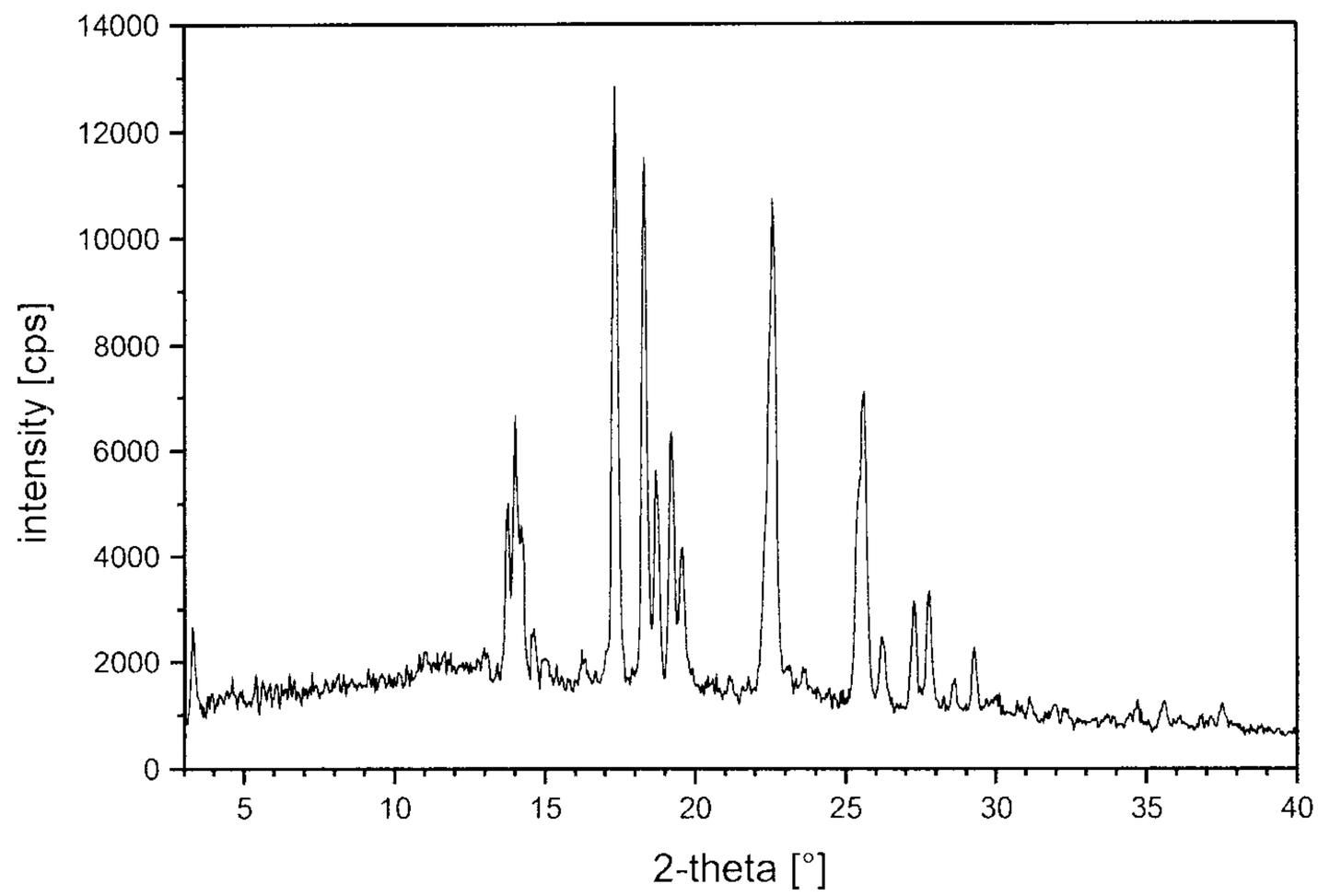


Figure 1.5 X-ray powder diffraction diagram of Mes1 = mesylate, form I

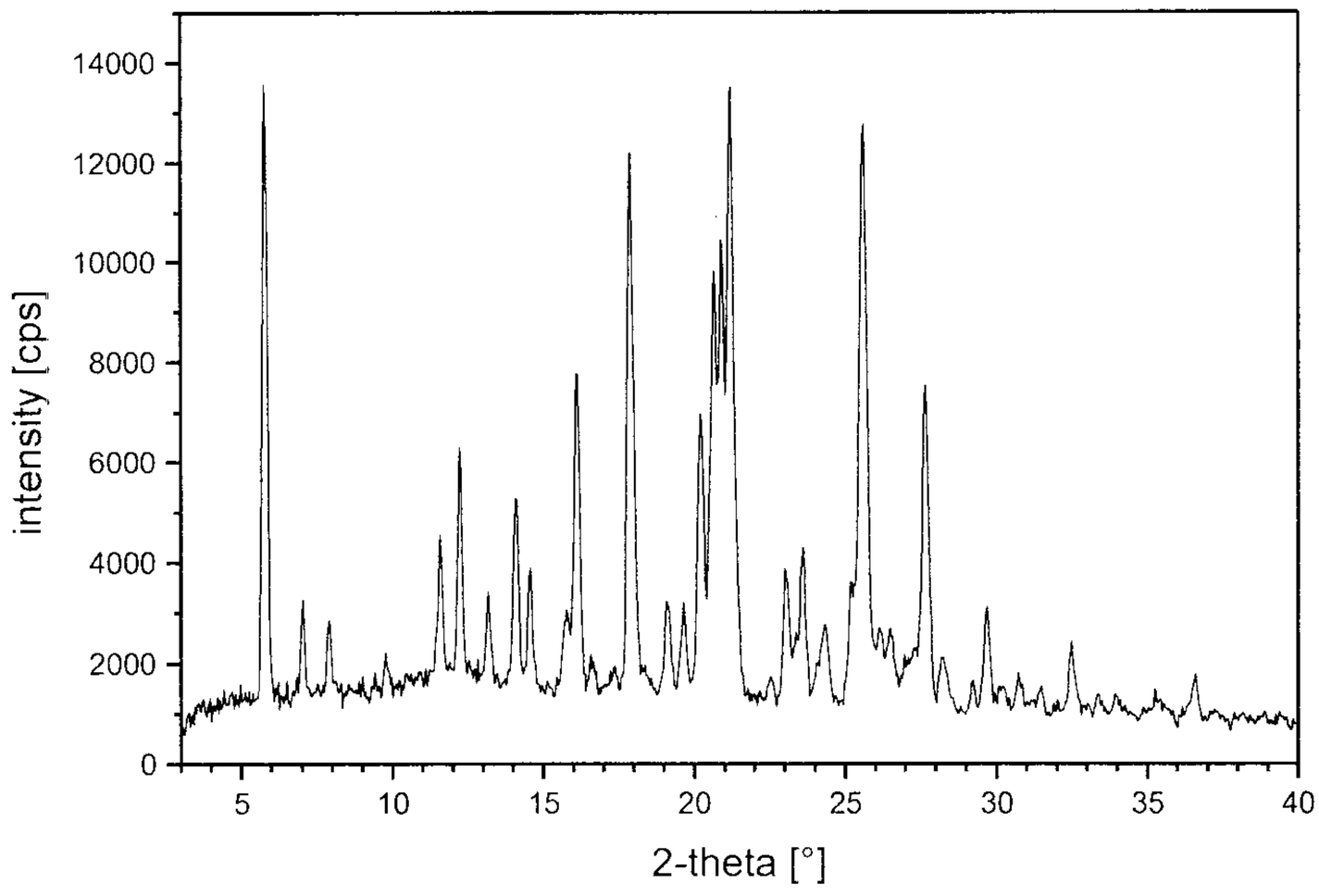


Figure 1.6 X-ray powder diffraction diagram of Bes1 = besylate, form I

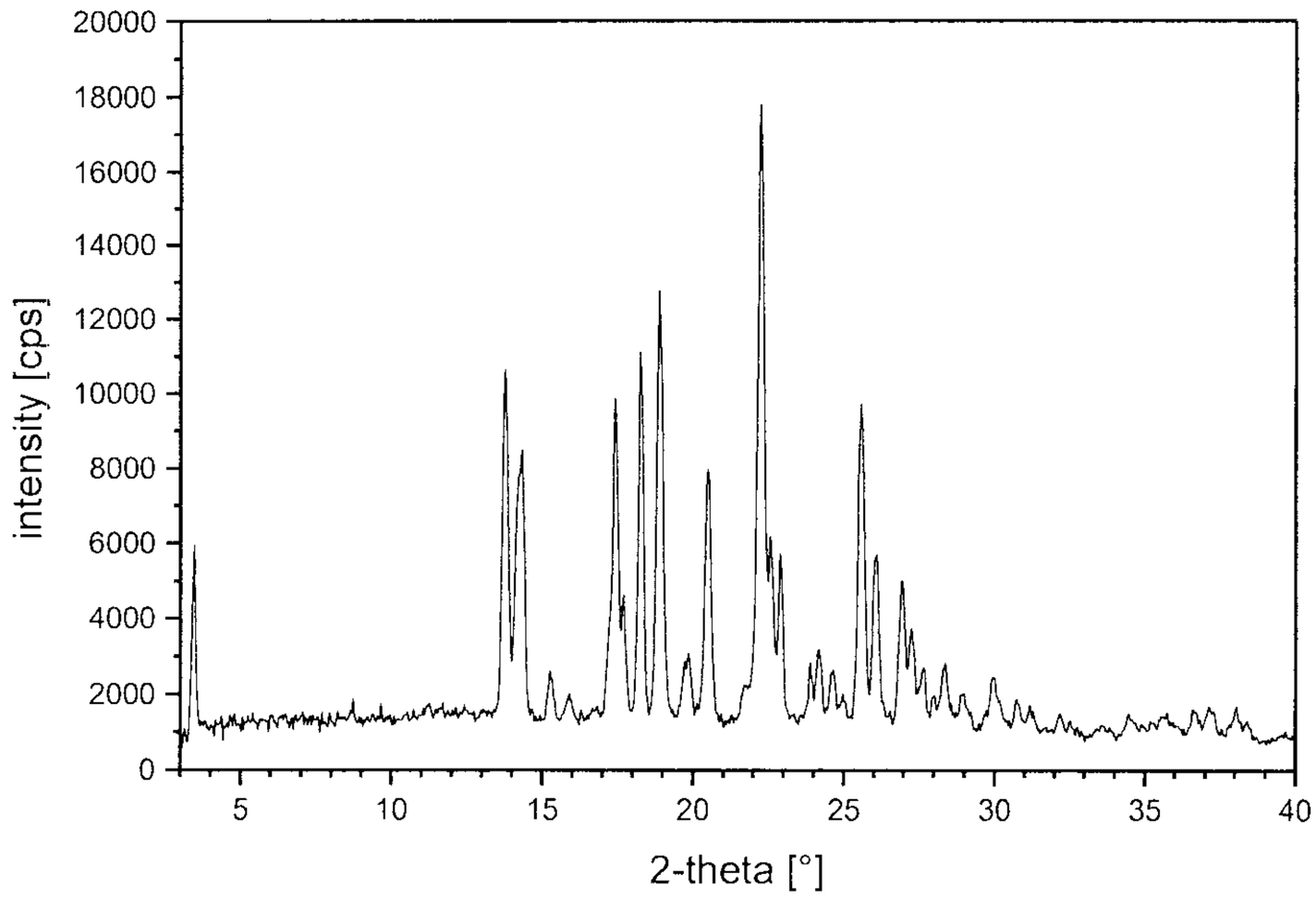


Figure 1.7a X-ray powder diffraction diagram of Oxa 1 = oxalate, form I

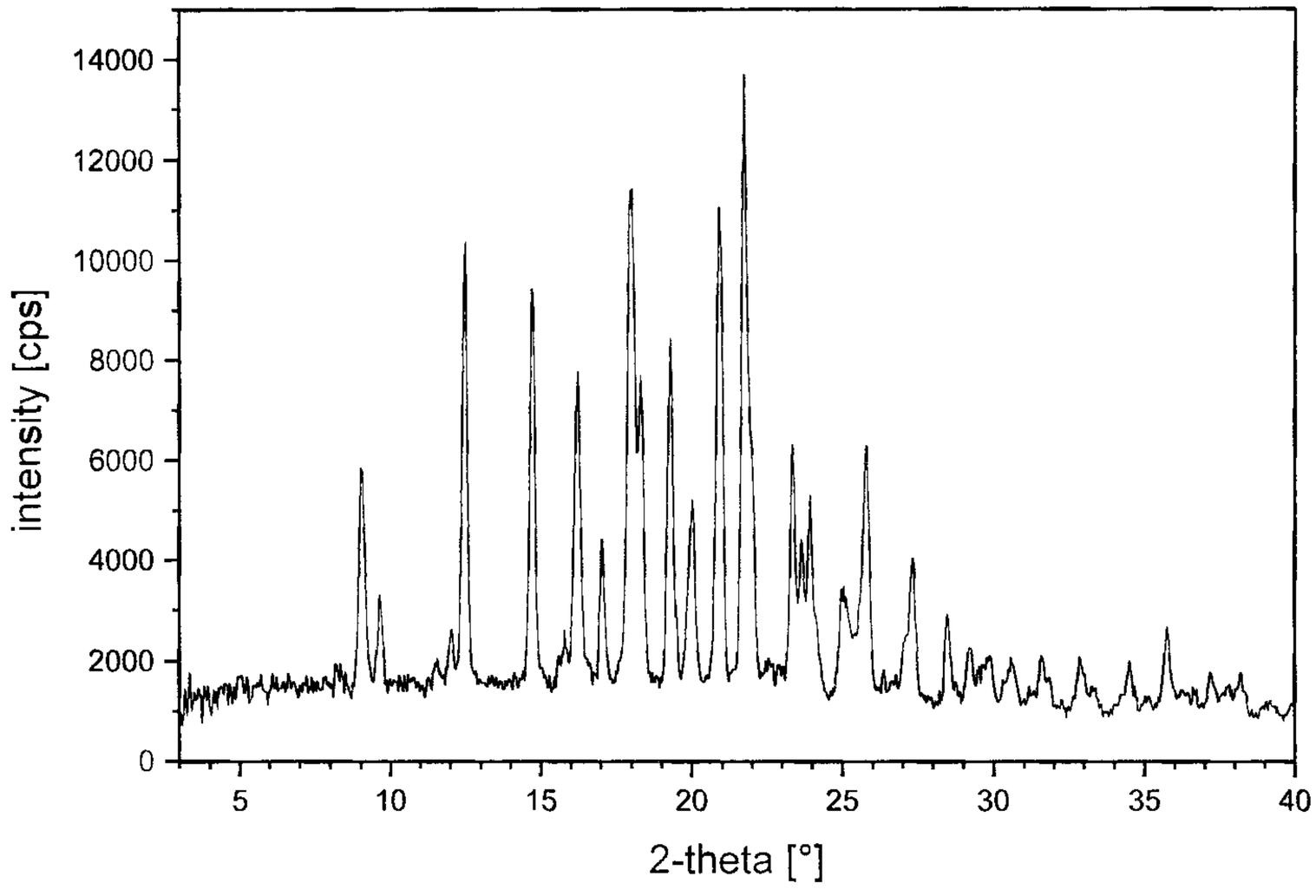


Figure 1.7b X-ray powder diffraction diagram of Oxa 5 = oxalate, form V

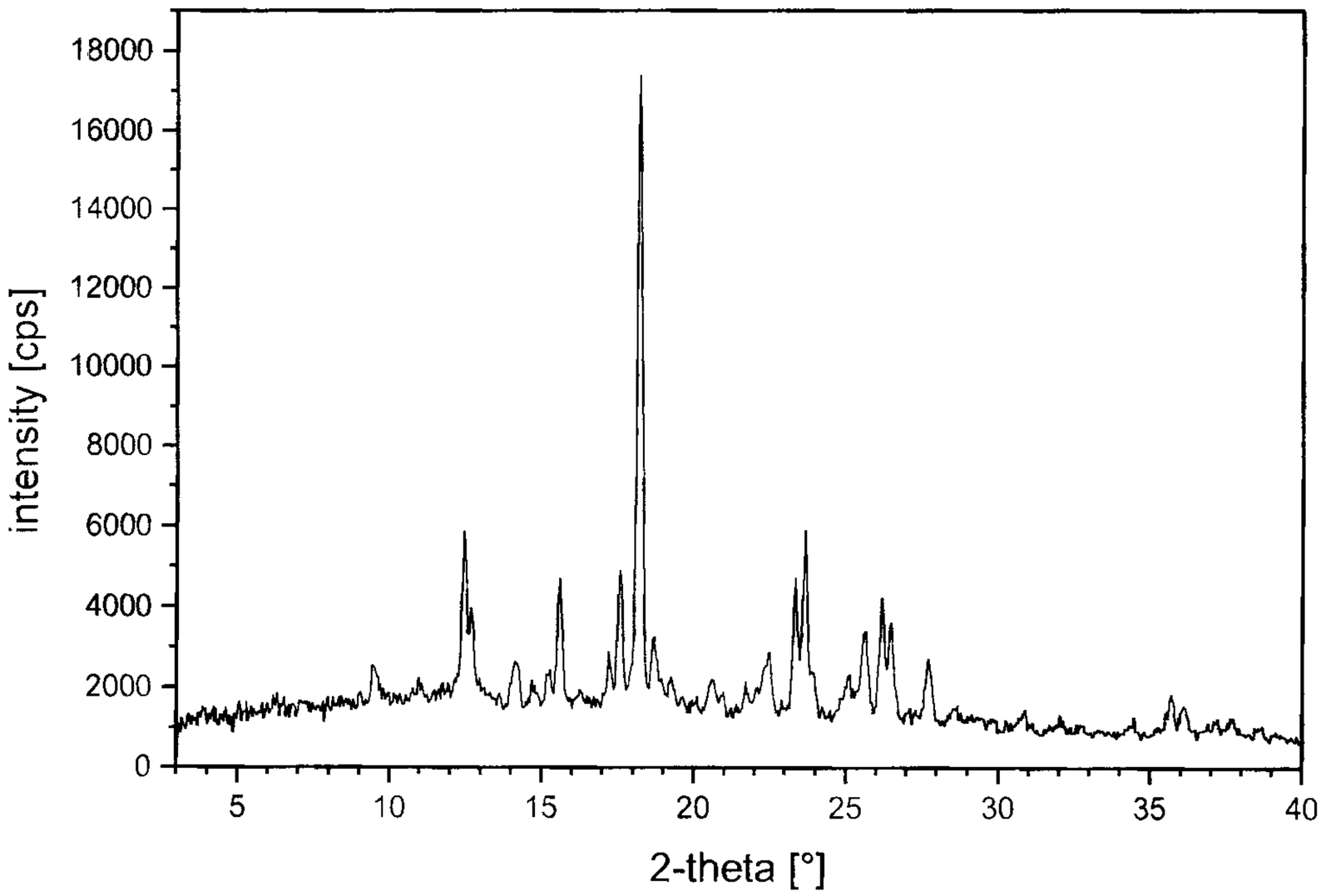


Figure 1.8 X-ray powder diffraction diagram of Sac 1 = sacharinate, form I

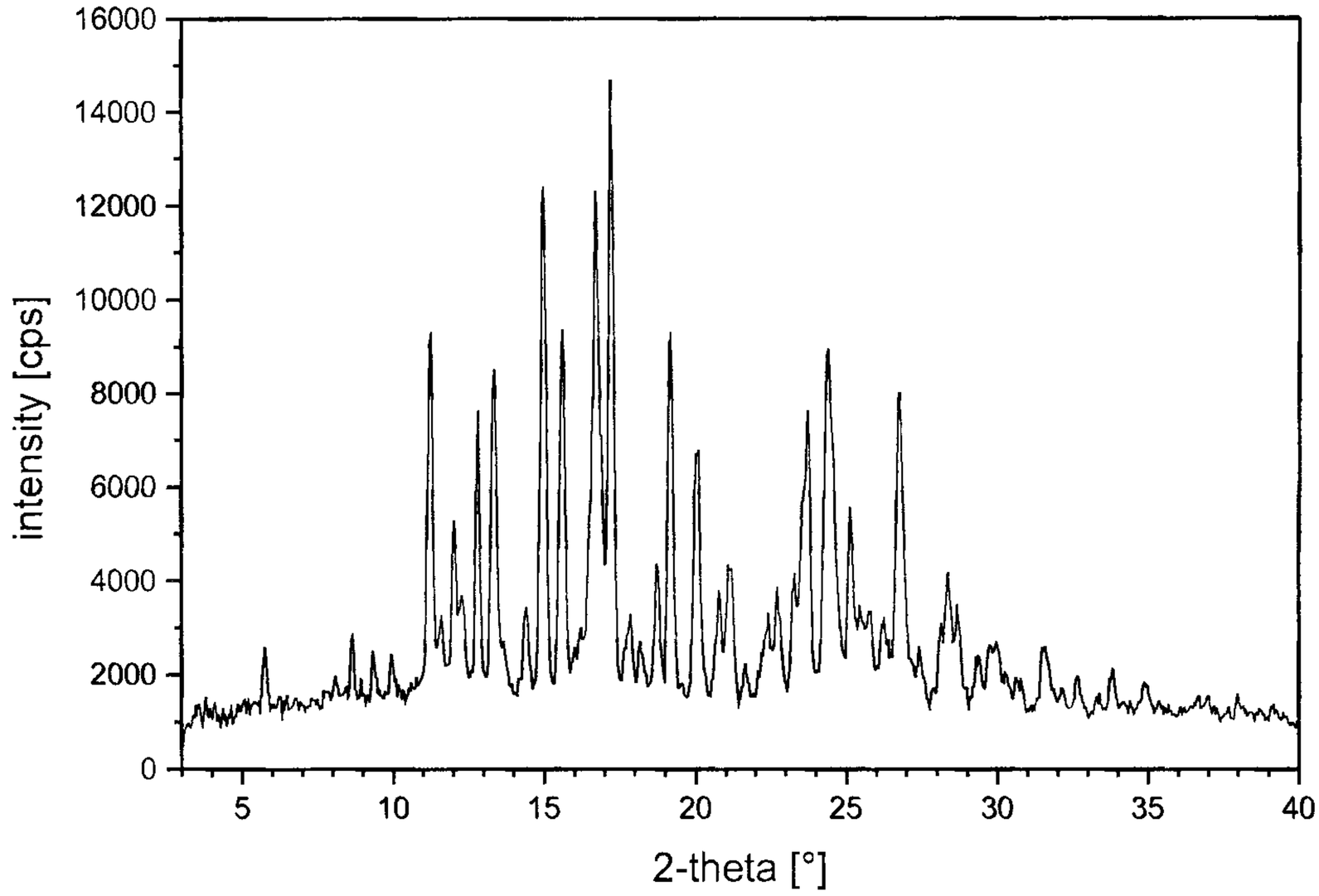


Figure 1.9 X-ray powder diffraction diagram of Pho1 = phosphate, form I

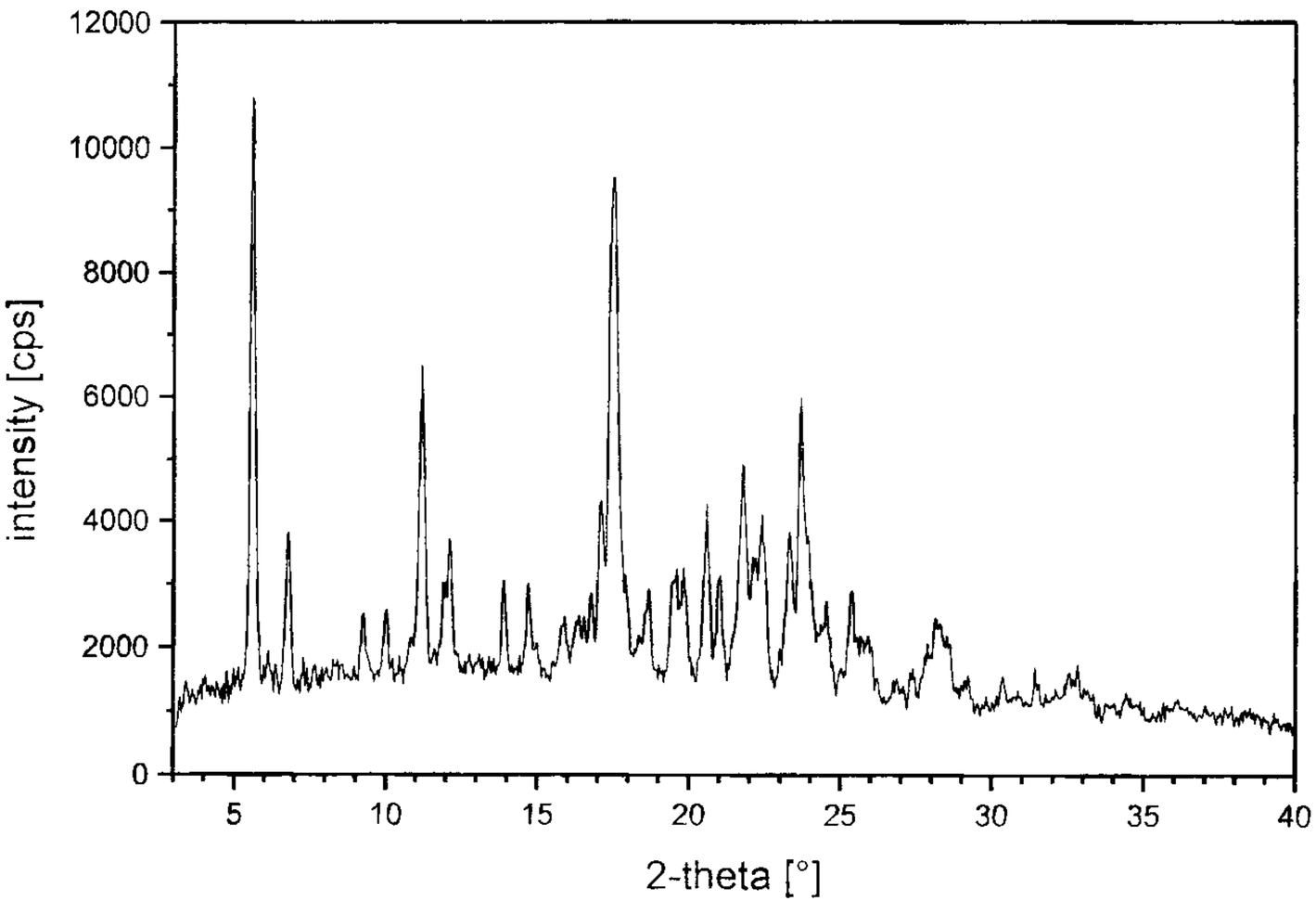


Figure 1.10a: X-ray powder diffraction diagram of Mae 1 = maleate, form I

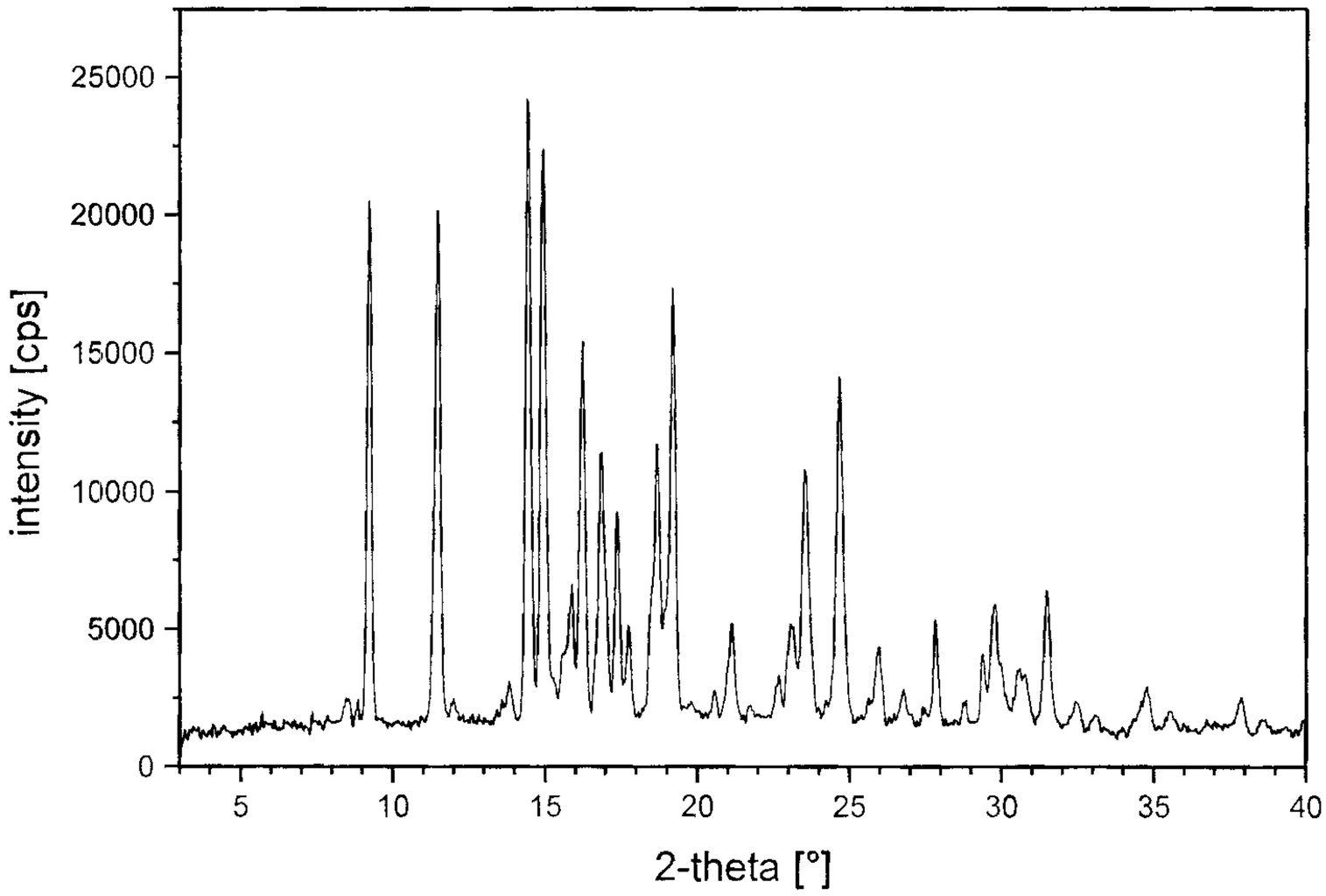


Figure 1.10b: X-ray powder diffraction diagram of Mae 3 = maleate, form III

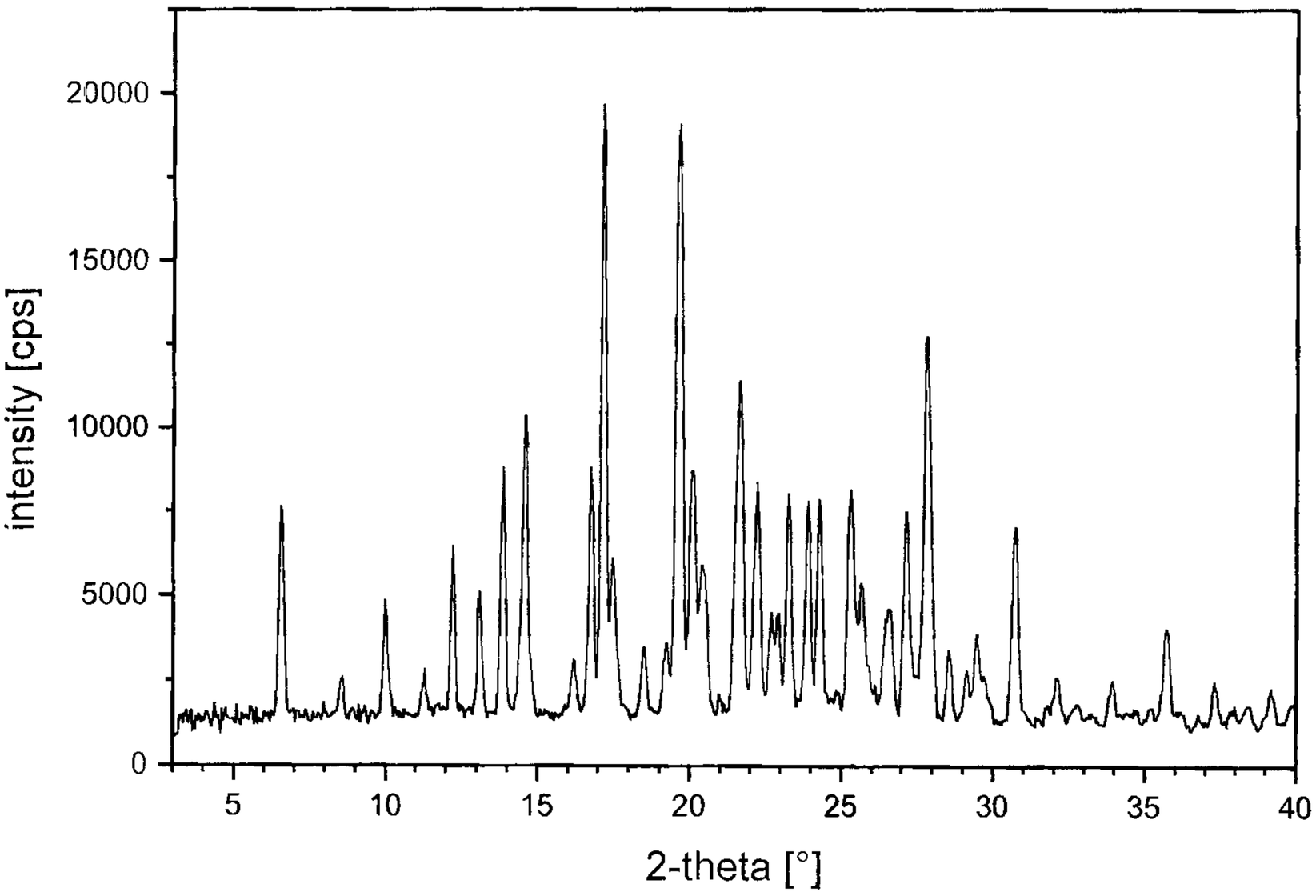


Figure 1.11: X-ray powder diffraction diagram of Ets 1 = ethanesulfonate, form I

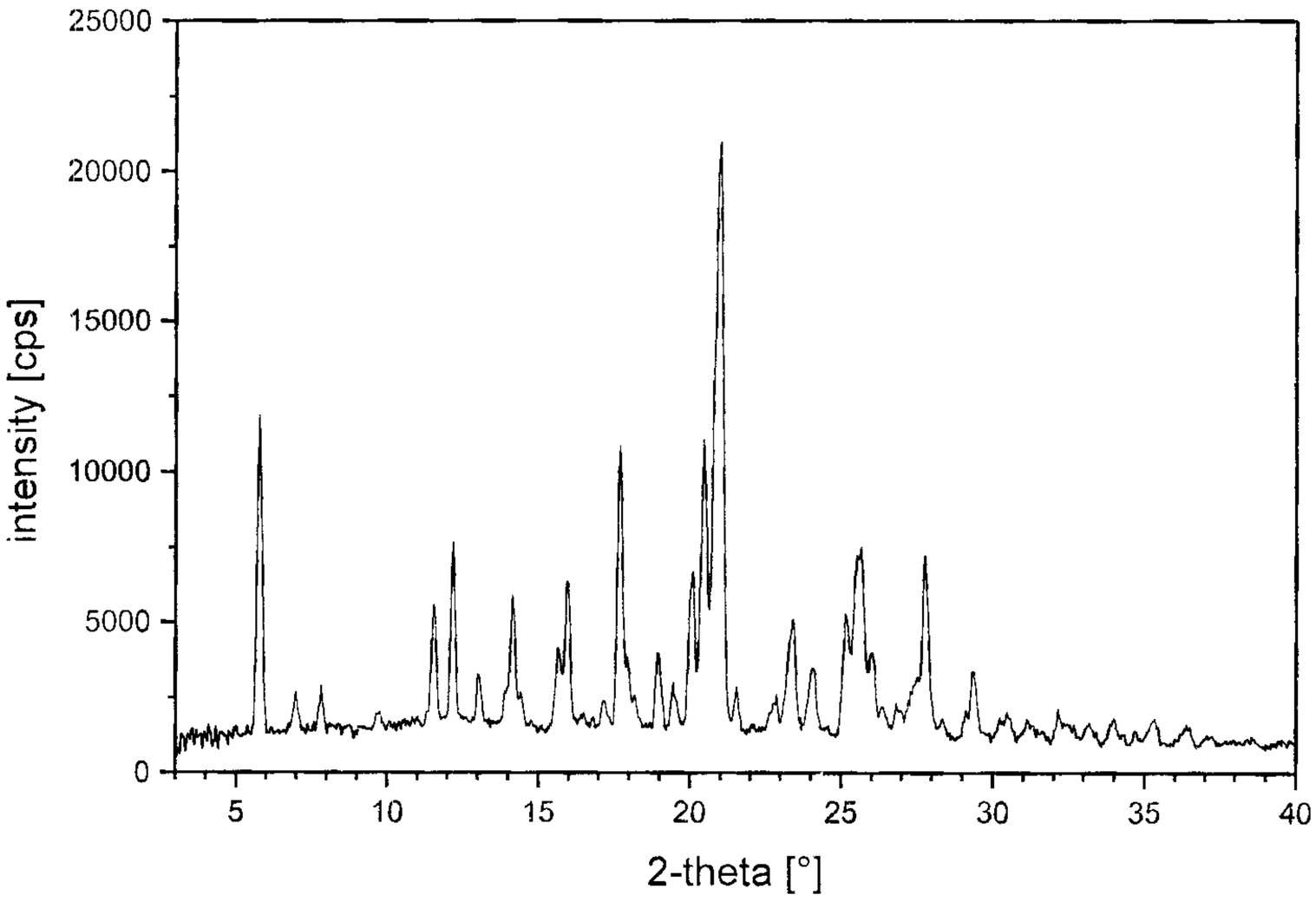


Figure 1.12 X-ray powder diffraction diagram of Cas1 = camphorsulfonate, form I

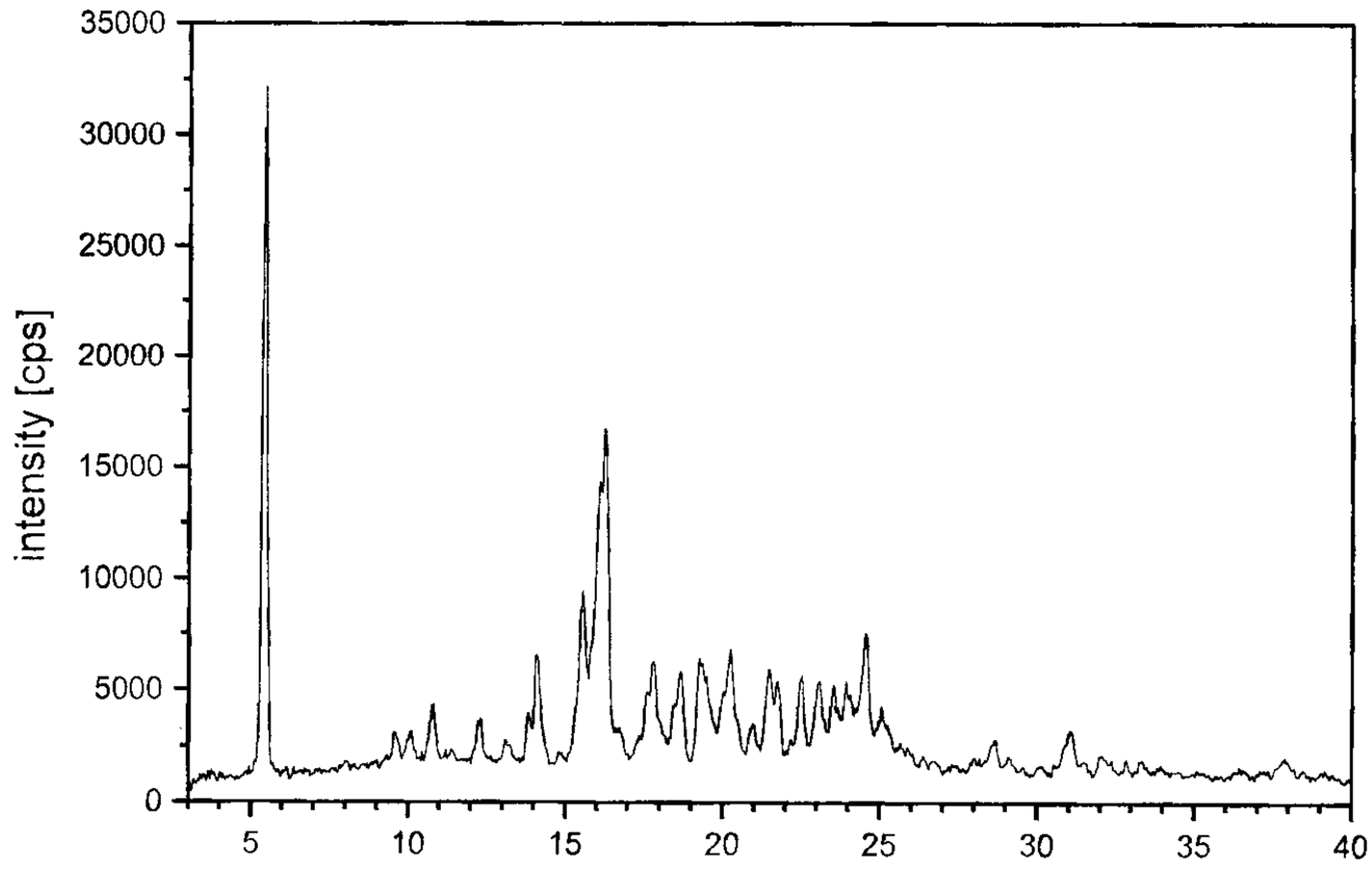


Figure 1.13: X-ray powder diffraction diagram of Mao 1 = malonate, form I

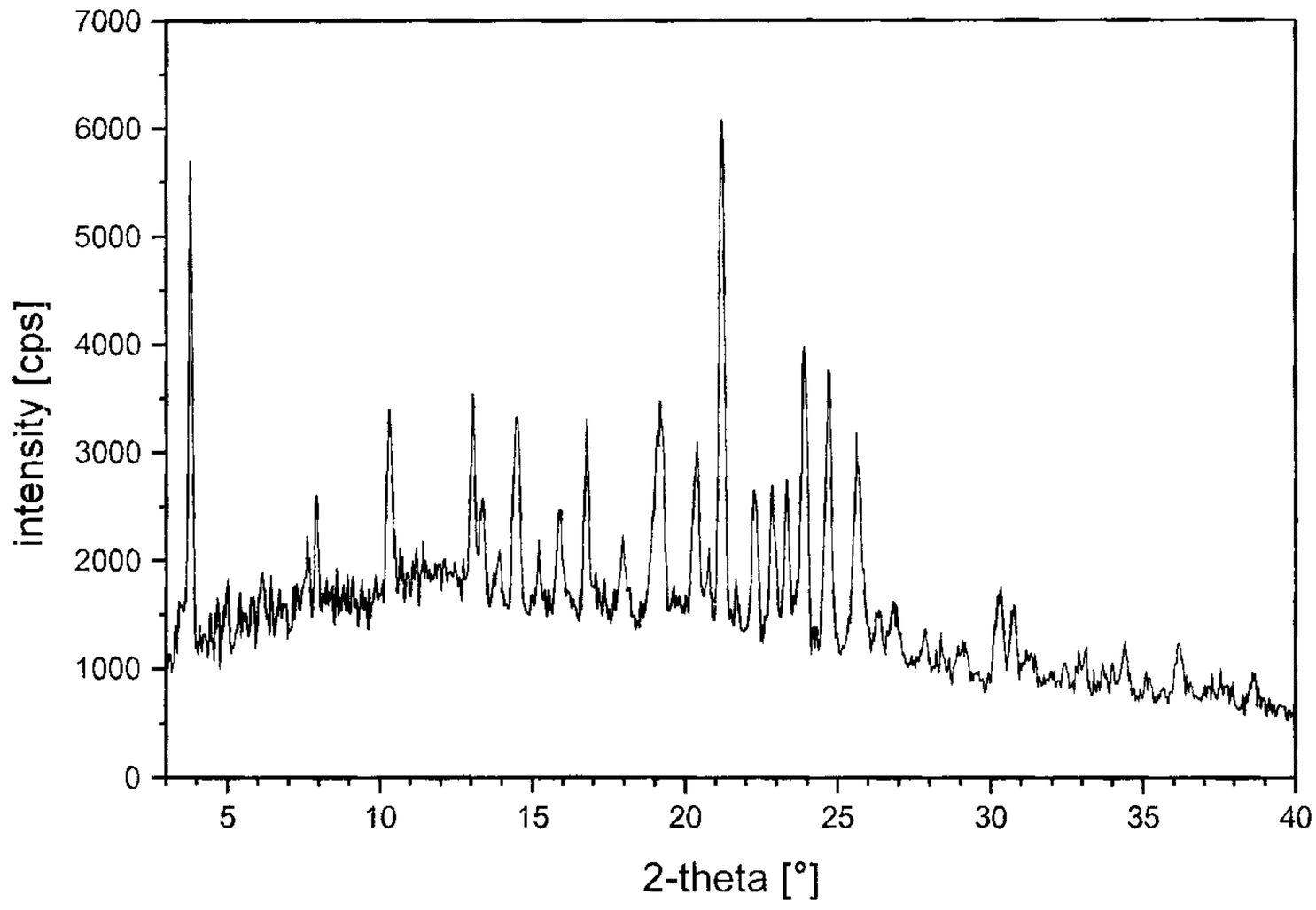


Figure 1.14: X-ray powder diffraction diagram of L-Tar 1 = L-tartrate, form I

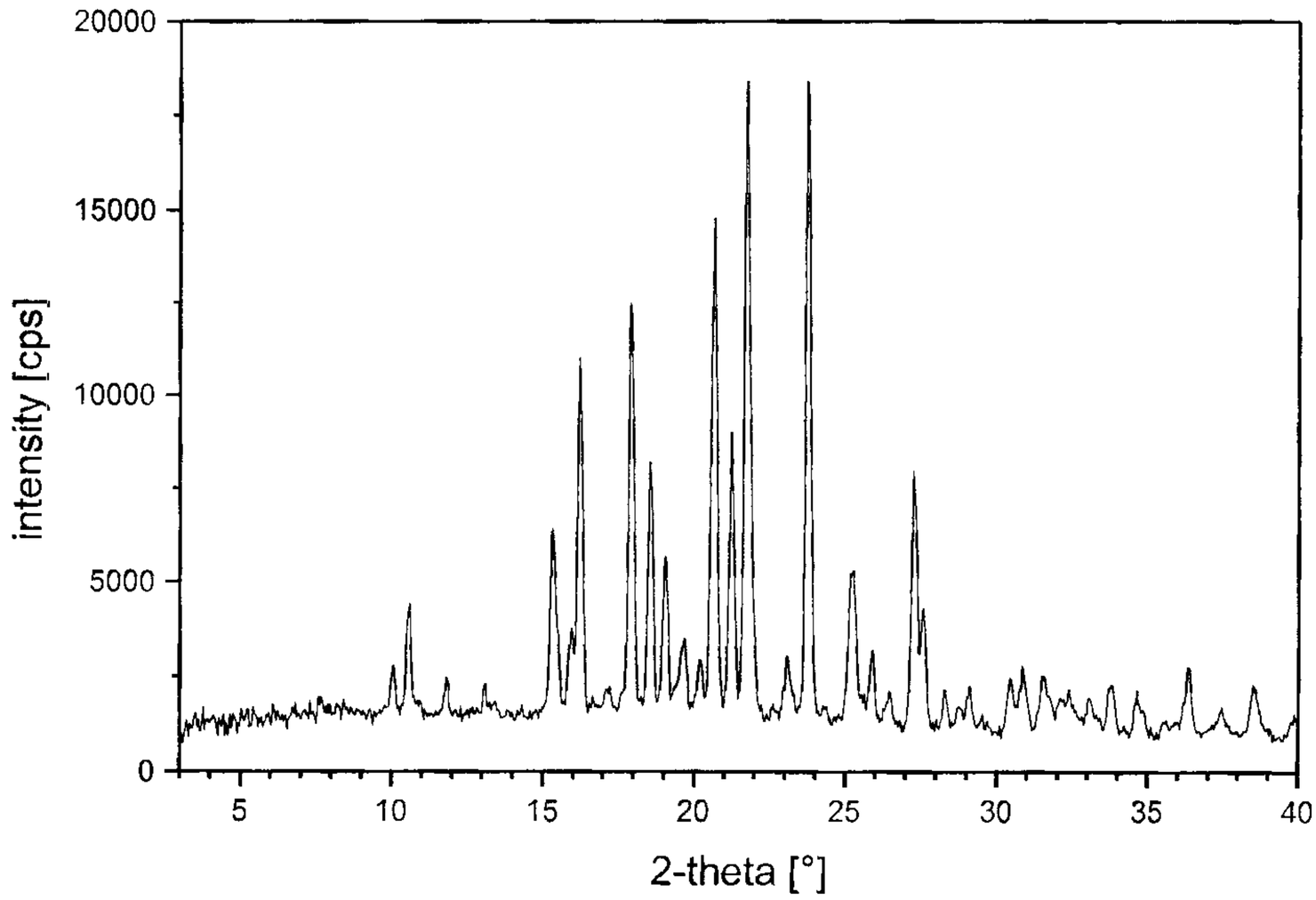


Figure 1.15a: X-ray powder diffraction diagram of Fum 1 = fumarate, form I

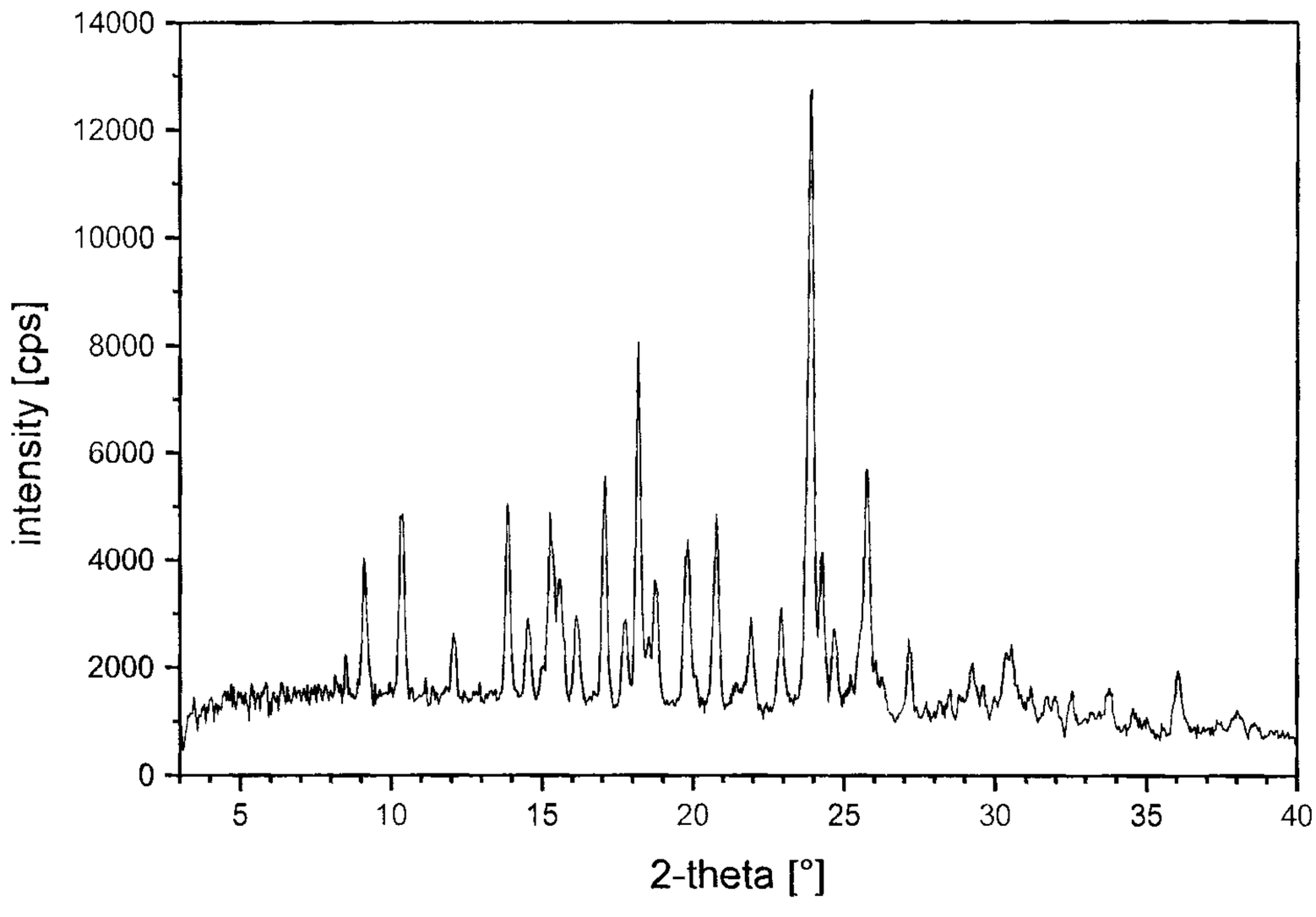


Figure 1.15b: X-ray powder diffraction diagram of Fum 2 = fumarate, form II

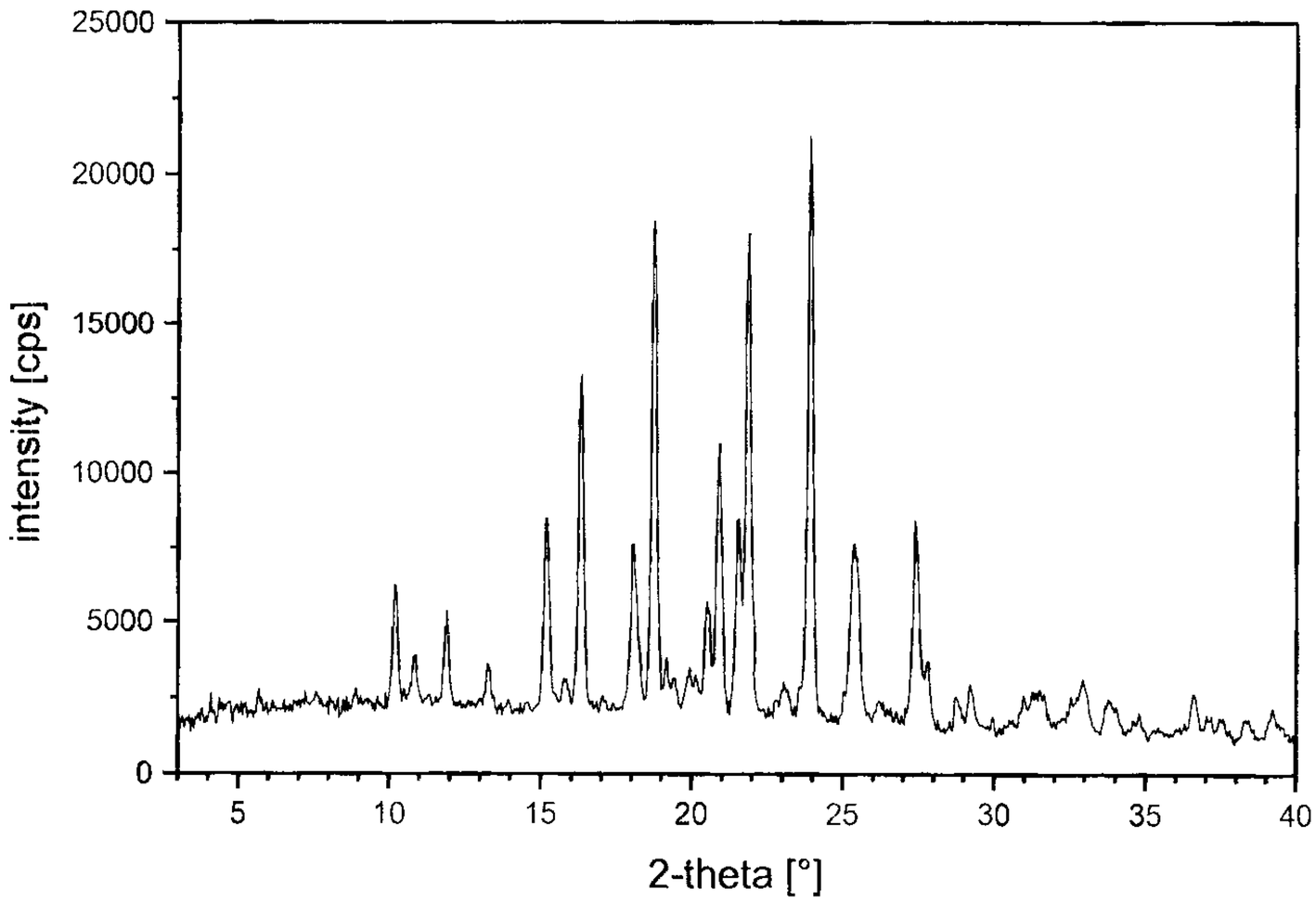


Figure 1.16 X-ray powder diffraction diagram of Gly1 = glycolate, form I

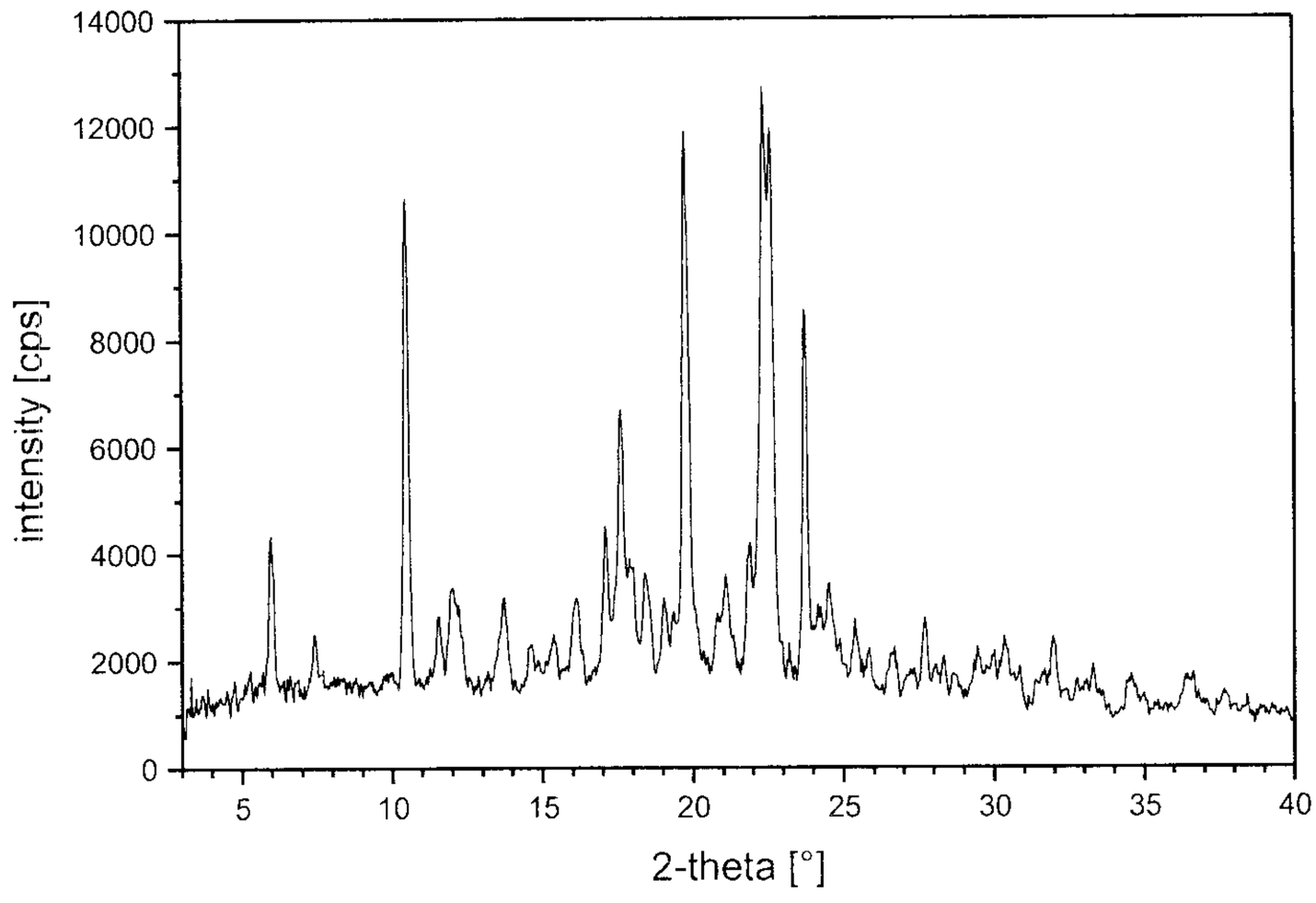


Figure 1.17: X-ray powder diffraction diagram of Cit 1 = citrate, form I

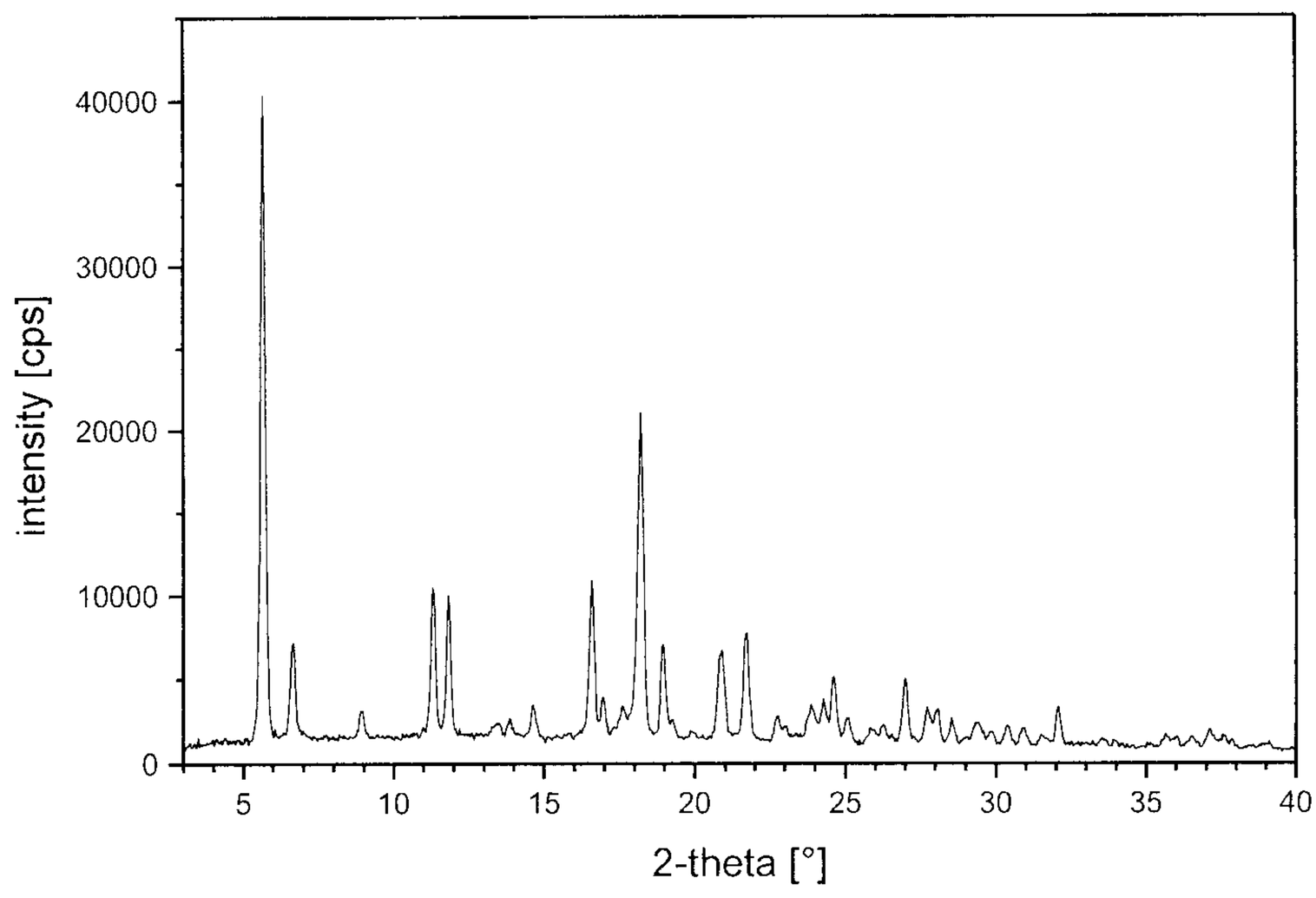


Figure 1.18: X-ray powder diffraction diagram of Man 1 = mandelate, form I

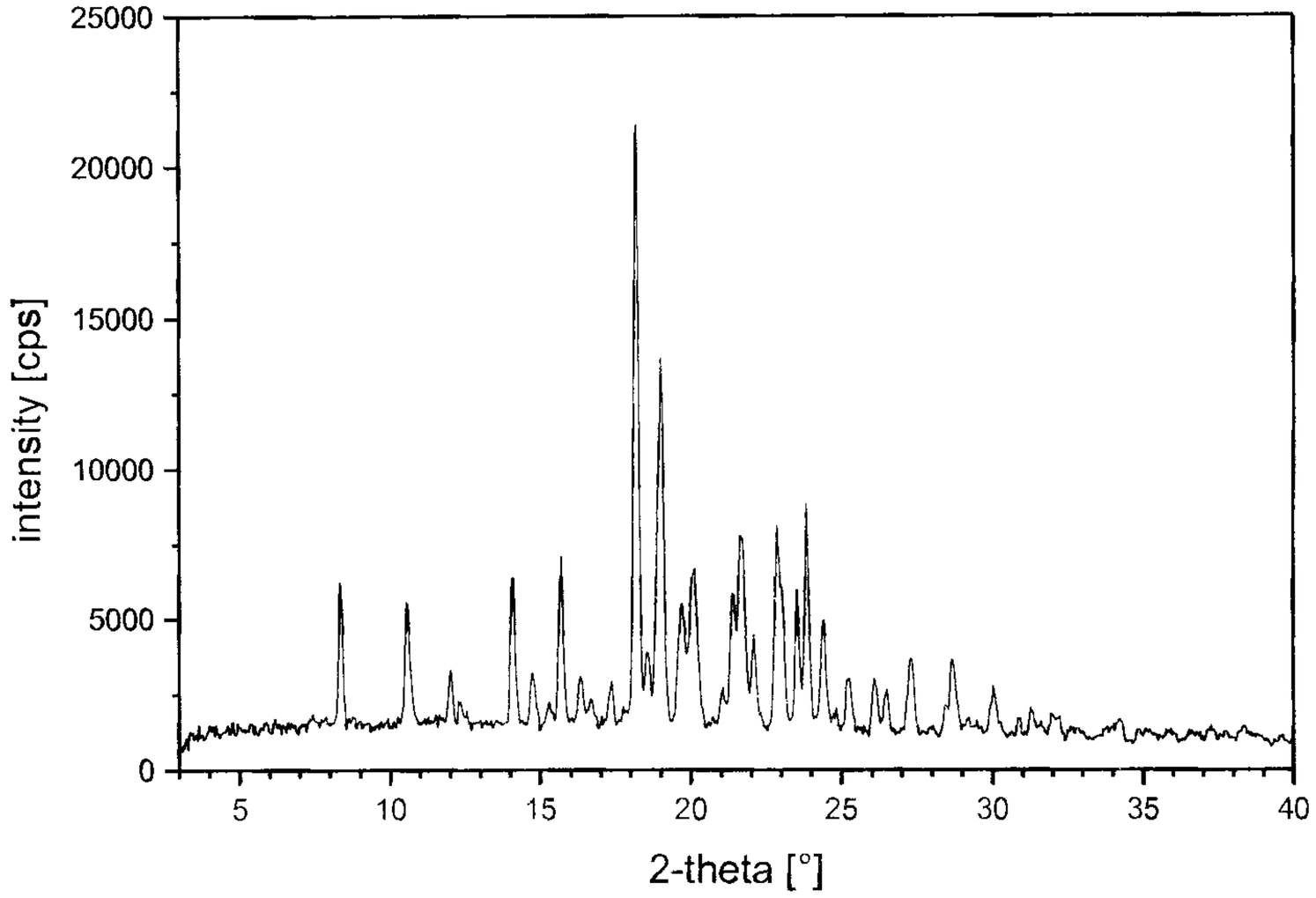


Figure 1.19: X-ray powder diffraction diagram of L-Mal 1 = L-malate, form I

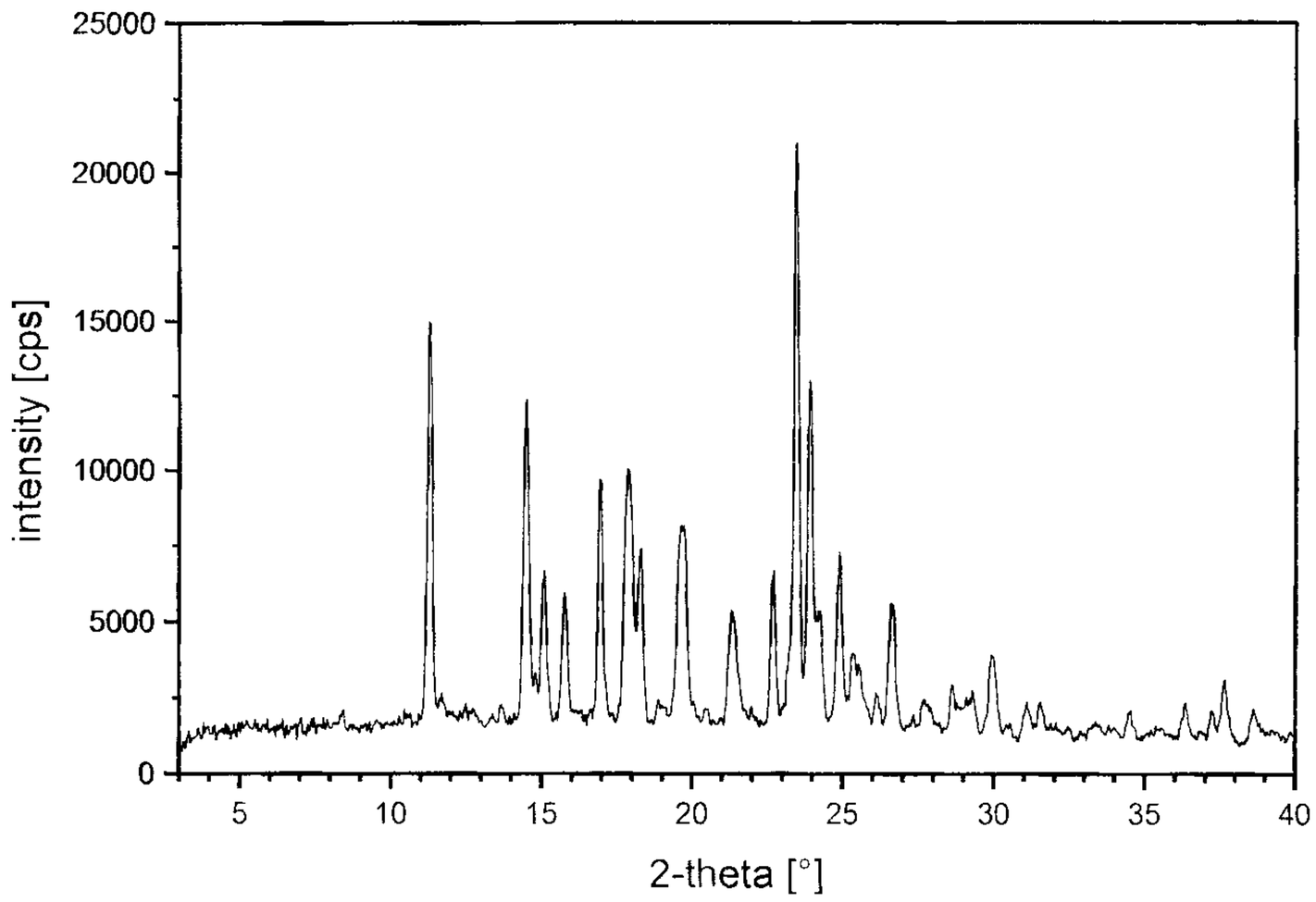


Figure 1.20 X-ray powder diffraction diagram of Nas1 = naphtalene-sulfonate, form I

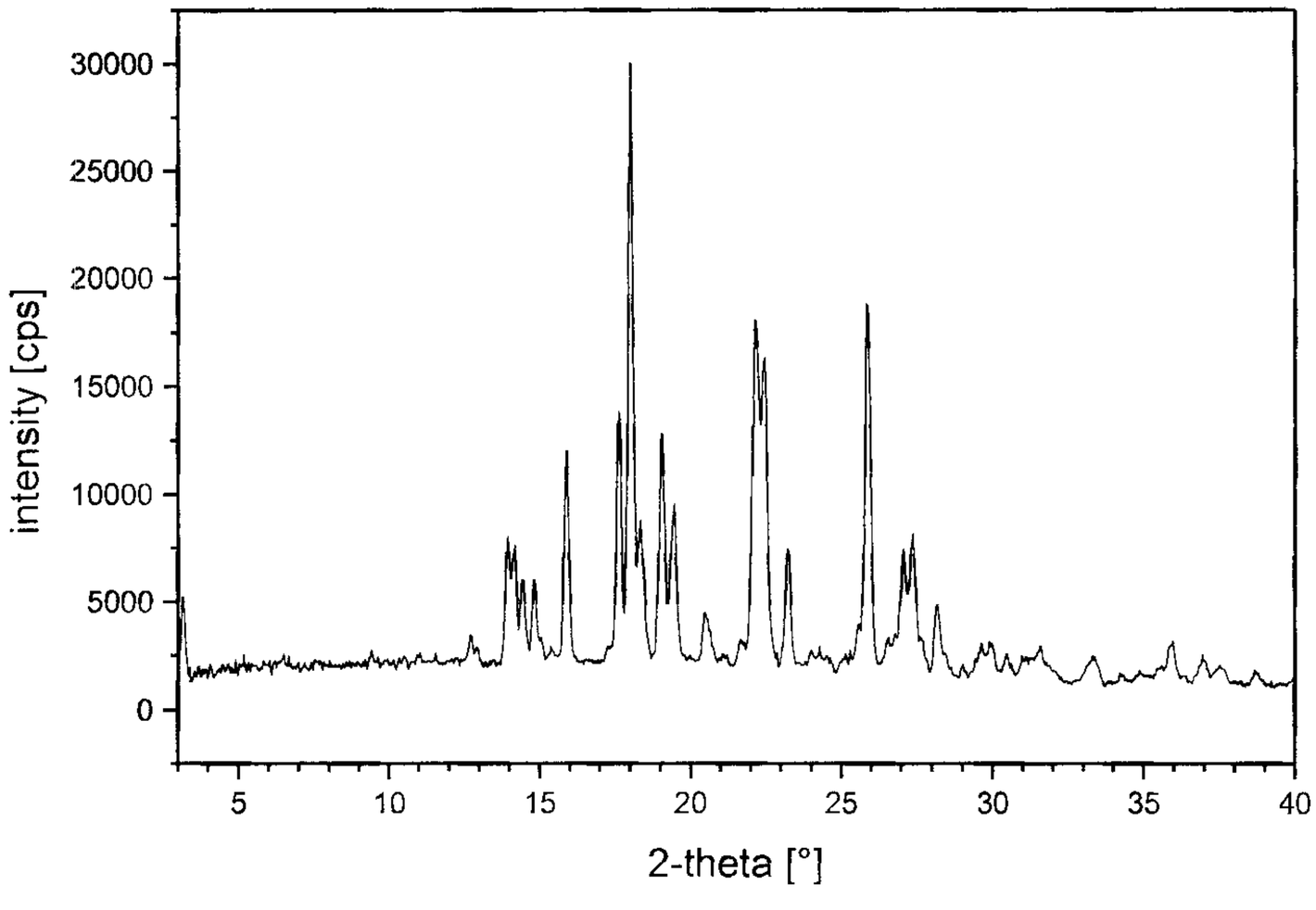


Figure 1.21: X-ray powder diffraction diagram of Fum 3 = fumarate, form III

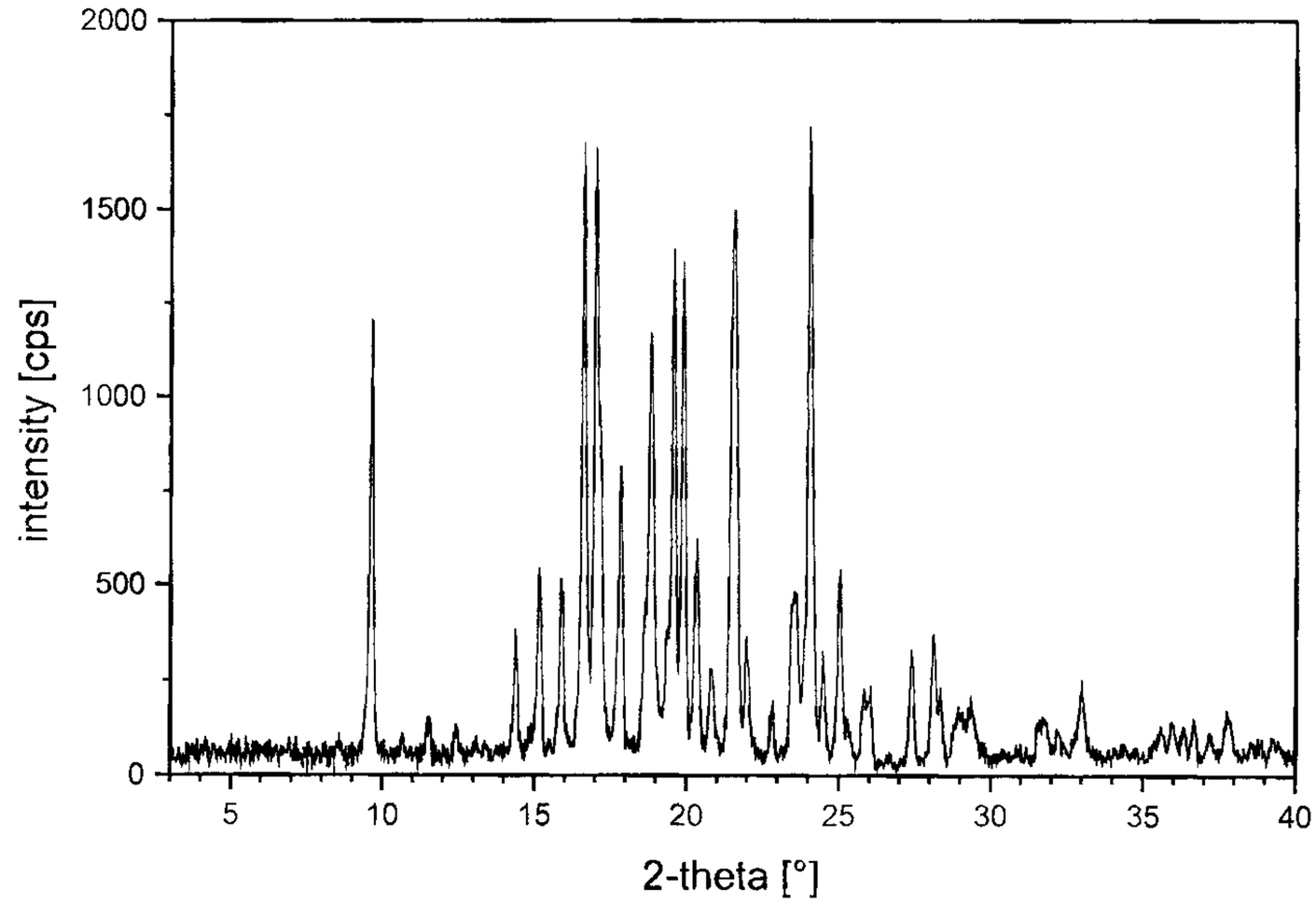


Figure 1.22: X-ray powder diffraction diagram of TOS 2 = tosylate, form II

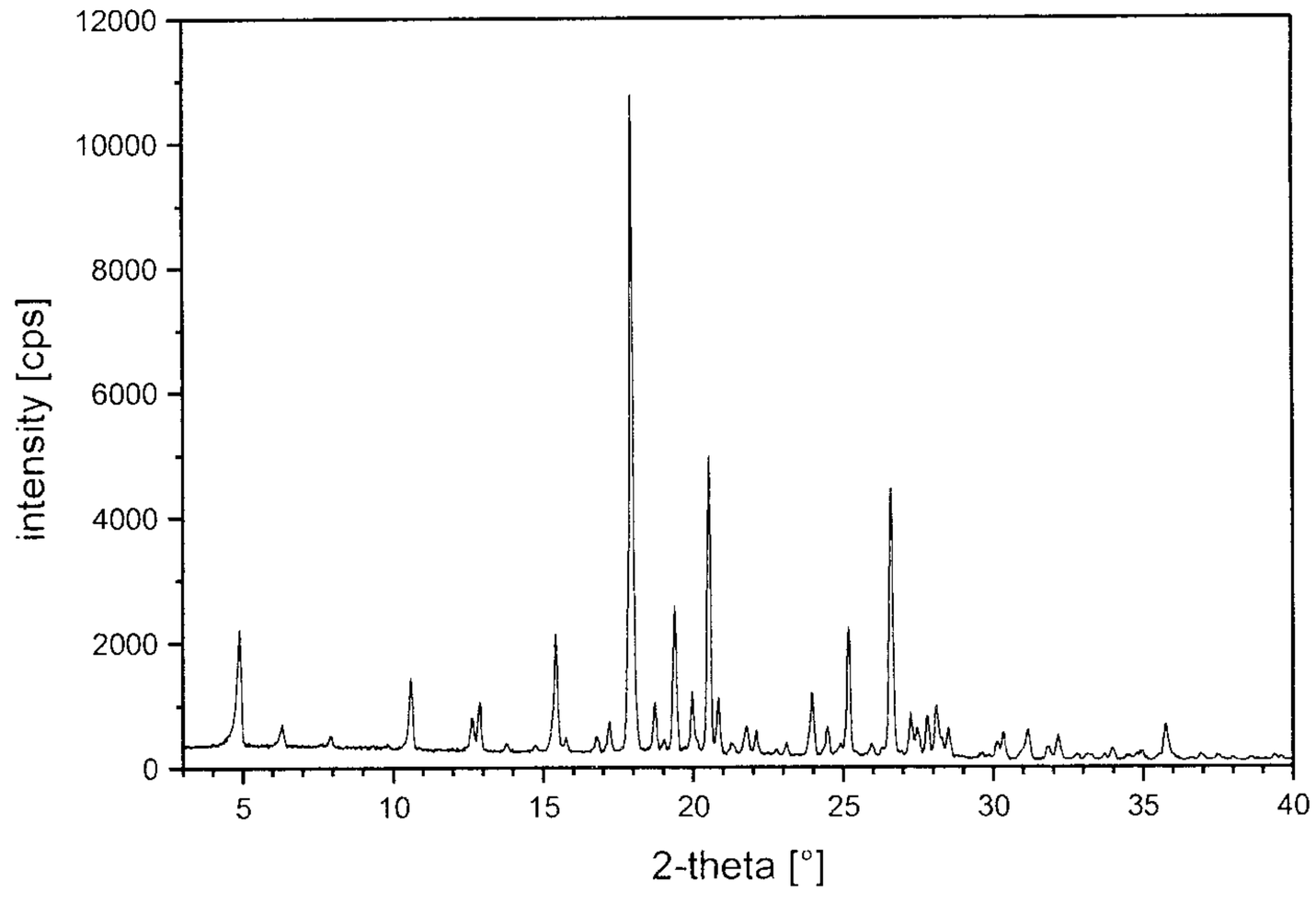


Figure 1.23: X-ray powder diffraction diagram of Cas 2 = camphorsulfonate, form II

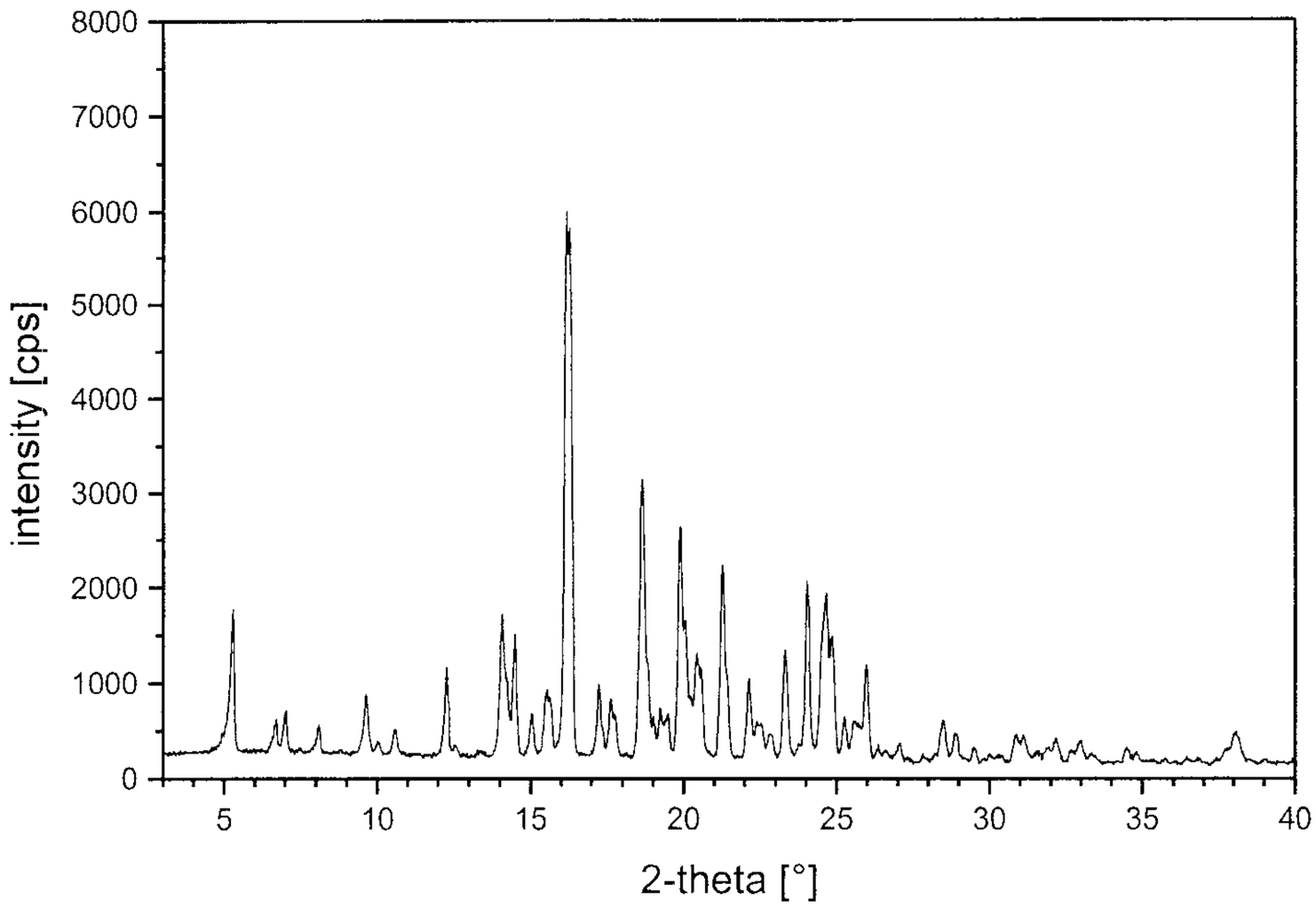
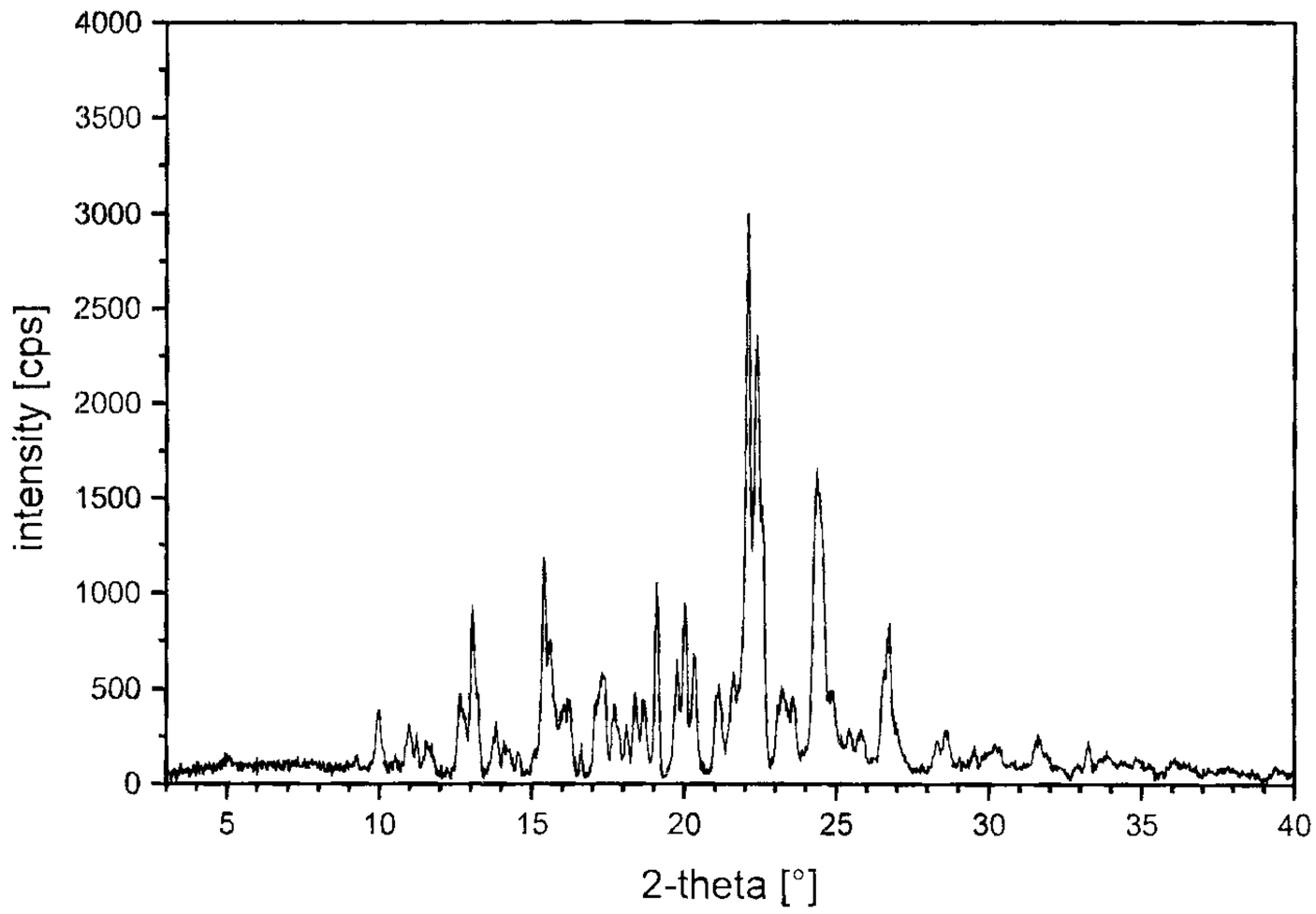
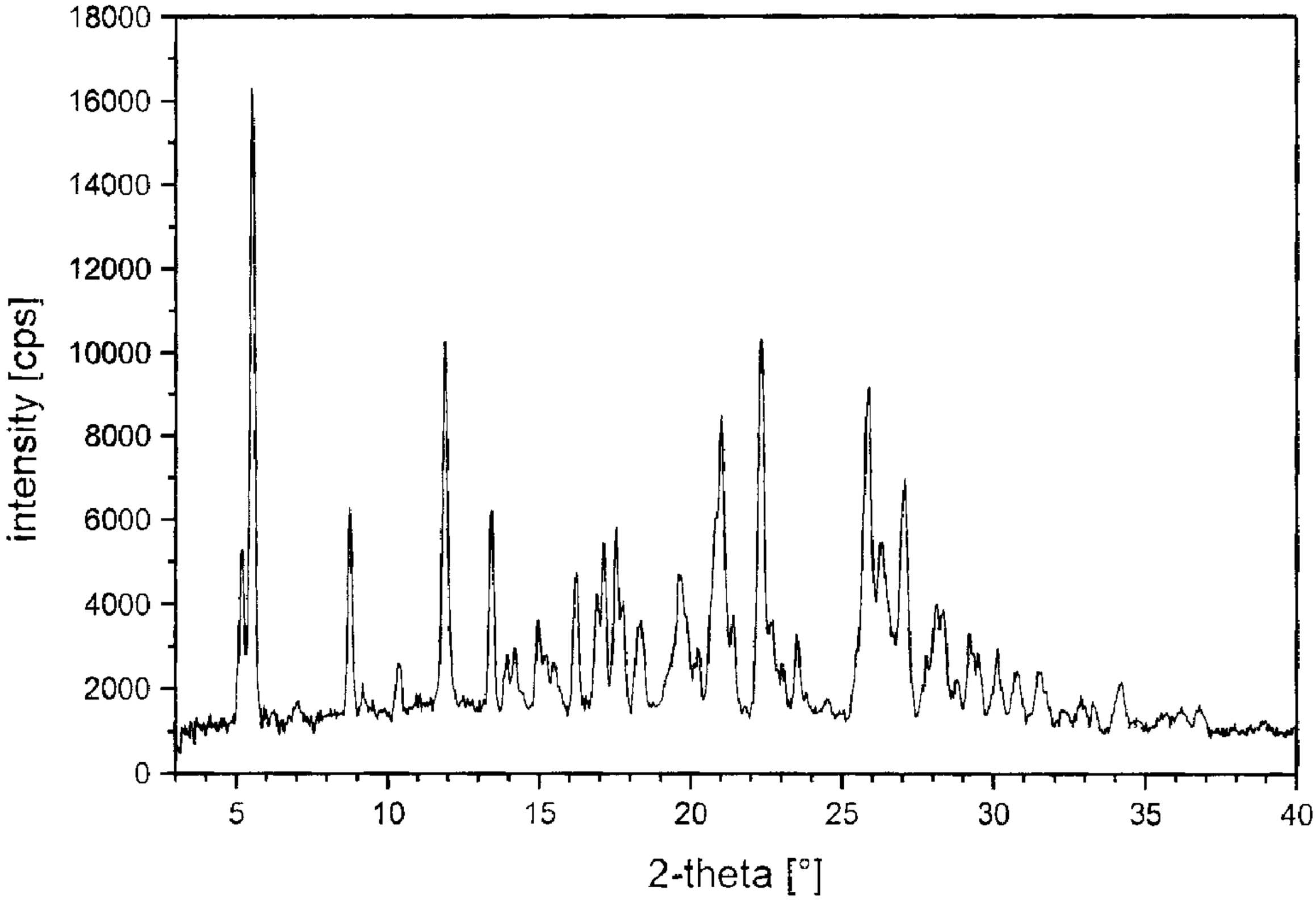


Figure 1.24: X-ray powder diffraction diagram of Gly 3 = glycolate, form II

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