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D E C I S I O N
of 22 July 1997

Case Number: T 0509/92 - 3.3.4

Application Number: 84301763.3

Publication Number: 0119837

IPC: C07K 5/06

Language of the proceedings: EN

Title of invention:

Dipeptide crystals, a process for their production, tablets containing the dipeptide crystals and a process for the production thereof

Patentee:

AJINOMOTO CO., INC.

Opponent:

Holland Sweetener Company VoF

Headword:

Dipeptide crystals/AJINOMOTO

Relevant legal provisions:

EPC Art. 87, 88, 54, 56

Keyword:

"Priority (denied)"
"Prior use (no)"
"Novelty (yes)"
"Inventive step (yes)"

Decisions cited:

G 0002/88

Catchword:

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Case Number: T 0509/92 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 22 July 1997

Appellant: AJINOMOTO CO., INC.
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Decision under appeal: Interlocutory decision of the Opposition Division
of the European Patent Office posted 14 May 1992
concerning maintenance of European patent
No. 0 119 837 in amended form.

Composition of the Board:

Chairman: L. Galligani
Members: D. D. Harkness
W. Moser

Summary of Facts and Submissions

I. European patent application no. 84 301 763.3 was filed on 15 March 1984 claiming priority from JP 44447/83 of 18 March 1983. The main claim read as follows;

"1. α -L-aspartyl-L-phenylalanine methyl ester II crystals which have two forms, type II_A and type II_B, which interconvert from one to the other depending upon the equilibrium moisture content of the crystals, wherein type II_A exhibits X-ray diffraction peaks at angles of diffraction of at least 20.6°, 21.2°, 5.0° and 11.1°, and type II_B exhibits X-ray diffraction peaks at angles of diffraction of at least 15.2°, 11.1°, 19.6°, 4.5°, both as measured by X-ray diffractometry using CuK α radiation."

European patent no. 0 119 837 was granted on the basis of seven claims of which claim 1 read as follows;

"1. α -L-aspartyl-L-phenylalanine methyl ester II crystals which have two forms, type II_A and type II_B, which interconvert from one to the other depending upon the equilibrium moisture content of the crystals, wherein type II_A exhibits X-ray diffraction peaks at angles of diffraction of at least 20.6°, 21.2°, 5.0° and 11.1°, and type II_B exhibits X-ray diffraction peaks at angles of diffraction of at least 15.2°, 11.1°, 19.6°, 4.5°, both as measured by X-ray diffractometry using CuK α radiation."

- II. An opposition was filed against the patent by the other party (Opponent) based on Article 100 EPC on the grounds of lack of novelty and lack of inventive step. On 14 May 1992 the opposition division issued an interlocutory decision within the meaning of Article 106(3) EPC whereby the patent was maintained on the basis of amended claims 1 to 4 filed on 23 December 1991.
- III. Both parties lodged an appeal against this decision.
- IV. On 22 September 1992 the Appellant (Patentee) filed a main request and three auxiliary requests the last of which related to the same claims as were allowed by the opposition division. The other party withdrew both its opposition and its appeal in a letter filed on 15 January 1993.
- V. The Board issued a provisional opinion in a communication dated 27 January 1997. A letter dated 26 February 1997 was received from the Appellant and oral proceedings were appointed for 22 July 1997.
- VI. The following documents have been cited:
- (1) Code of Federal Regulations 21 CFR 170.1
§ 172.804, 01-04-81
 - (2) Low Calories and Special Dietary Foods, pages 77
to 78, ED Basant Editor, CRC Press, 1978
 - (3) AU-A-59 258

(4) Equa 200 brochure, 1974, G. D. Searle & Co.

(5) = (2), pages 79 and 112

(6) Textbook of Physical Chemistry, S. Gladstone
(1946)

(7) JP-A-59 95862 (English Translation)

The following declarations were referred to in the considerations relating to the alleged prior use by Pierrel of the claimed aspartame crystals;

Dr J A H Moonen filed on 21 August 1991,

Dr J Witt filed on 22 September 1992,

Mr S Franzese filed on 23 September 1992,

Dr T T Tjioe filed on 23 September 1992.

VII. During oral proceedings which took place on 22 July 1997 the Appellant filed as a new main request claims 1 to 7 of which claim 1 reads as follows:

"1. α -L-aspartyl-L-phenylalanine methyl ester crystals of type II_A form, which form has X-ray diffraction peaks at angles of diffraction of at least 20.6°, 21.2°, 5.0° and 11.1°, as measured by X-ray diffractometry using CuK α radiation, and an equilibrium moisture content of the crystals at a relative humidity of 78% of about 0.9 to 3.0%."

Claim 2 concerns crystals according to claim 1 in admixture with crystals of type IIB. Claims 3 and 4 are directed to tablets or granules containing crystals

according to claims 1 or 2. Process claims 5 to 7 are identical with claims 2 to 4 maintained by the opposition division.

Two auxiliary requests filed on 22 September 1992 were maintained as first and second auxiliary requests.

VIII The Appellant's arguments can be summarised as follows;

It was a requirement of Article 87(1) EPC when claiming a priority date that the priority document be the first document in which the invention was disclosed. Since document (7) (a Japanese patent application of 25 November 1982 by the same applicant) concerned granulation of aspartame, it did not relate to the same invention as was being claimed in the patent in suit, thus the cited document was not relevant and could not be used to negate the claimed priority date.

Although example 2 of document (7) did prepare type IIa (II') crystals as characterised by the given x-ray diffraction diagram which was the same as that disclosed in the patent in suit, document (7) did not relate to the same invention because it was the intention to prepare granulates which were bound by adhesive forces which increased when a transition took place from type II or II' to type I' crystals (see page 6 last 5 lines).

Whether or not the claimed subject-matter was entitled to the priority date, it was novel and inventive having regard to the cited prior art, including the alleged prior use between the priority and filing dates. The

prior use was in respect of a product which lacked any connection with what was claimed.

- IX. The Appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of (a) claims 1 to 7 submitted during the oral proceedings as main request, or (b) claims 1 to 8 filed on 22 September 1992 as first auxiliary request, or (c) claims 1 to 5 filed on 22 September 1992 as second auxiliary request.

Reasons for the Decision

Main request.

1. *Amendments*

1.1 Article 123(2) EPC.

The subject-matter of the new independent claim 1 which is recited above in paragraph VII represents type IIa crystals being one of the crystal forms originally claimed, (see claim 1 as filed paragraph I above) but limited by stating the specified equilibrium moisture content which was disclosed at line 6 on page 7 of the originally filed application. This claim and claims 2, 3 and 4 appendant to it do not therefore relate to any subject-matter which extends beyond the content of the application as filed.

Claims 5 and 7 are independent claims for which support

is found in claim 7, example 2 and the table on page 16 of the originally filed application. The subject-matter of claim 6, which is appendant to claim 5, corresponds with that of the originally filed claim 6 and therefore also complies with Article 123(2) EPC.

1.2 Article 123(3) EPC

Claim 1 has not been amended in such a way as to extend the protection conferred because the amendment made is by way of limitation in that the moisture content of the crystals has now been specified. Claim 1 and its appendant claims 2, 3 and 4 therefore comply with Article 123(3) EPC.

The amendments made to claims 5 and 7 do not give rise to an extension in scope of these claims because all the introduced temperature and time details fall within the ranges quoted in the corresponding claims as granted and therefore Article 123(3) EPC has been complied with. Claim 6 was not amended.

2. *Priority (Articles 87 and 88 EPC)*

According to Article 87(1) EPC, a prerequisite for claiming priority is that the application used as a basis therefor must be the "first application" for the **same** subject-matter. In accordance with Article 87(4) EPC, the definition of "first application" extends also to an application which is not truly the first, provided that at the date of its filing, the previous truly first application has been withdrawn, abandoned or refused without having become open to public

inspection and without having served as a basis for claiming a right of priority.

Article 88(4) EPC sets out the principle that in comparing the priority and subsequent applications, although the claims are to be considered, it suffices if the features claimed in the later application are disclosed by the earlier application taken as a whole.

In the present case, document (7), which is a laid-open Japanese patent application filed before the Japanese patent application on which the patent in suit relies for claiming priority, discloses the X-ray details of type II'(IIa) aspartame crystals in Figure 2 and their preparation and granulation to give type I' granules.

The Appellant agreed that document (7) did disclose an X-ray diffraction pattern (figure 2) of type IIa (II') crystals, as confirmed by Moonen in a declaration filed on 21 August 1991, and that this was characterising for the crystals.

The Board considers that example 2 of document (7), which prepared and used type IIa crystals and disclosed the x-ray diffraction diagram figure 2, constituted a prior disclosure of the claimed subject-matter and therefore relates to the same invention as is now claimed. Accordingly, the priority application of the patent in suit was not the first application for the subject matter claimed which is therefore not entitled to the claimed priority date.

3. *Clarity (Article 84 EPC)*

As the crystal form and behaviour depends upon the moisture content, the claims needed to make reference to the equilibrium moisture content. This feature is now part of claim 1, thus no further clarity objection arises.

4. *Novelty (Article 54 EPC)*

4.1 Prior use

4.1.1 In the written submissions, the other party alleged that the manufacture and unrestricted sale of aspartame in 1982 by the Pierrel company constituted a prior use of the claimed type IIa aspartame crystals and that subsequent analysis had shown that type IIa crystals were present in the original product.

The Appellant has argued that "only that which was publicly available" before the relevant date can be taken into account when deciding novelty, and this did not include what may have been inherent in the disclosure, this being the opinion expressed in the Enlarged Board of Appeal Decision G 02/88 (OJ EPO 1991, 93). He submits that in the present case a particular crystal form IIa of aspartame has been invented and this has not been made available by the prior art.

4.1.2 There was filed during the written proceedings a great deal of evidence from both sides which was of a contradictory nature.

In particular for the Appellant, Dr Witt reported that the Pierrel process for aspartame production employed a three stage drying process at temperatures of 80°C or below and that no granulation took place. This indicated a crystal structure other than that of type IIa which was produced by drying at 90°C or above.

On the other hand, the 2nd Franzese affidavit at page 4 stated that Dr Witt was wrong in saying that the second stage drying was at 65°C, it was conducted at 85°C for 3 to 4 hours followed by granulation in the Viani granulator, there was no third stage drying step.

The affidavit of Dr Moonen for the Opponent filed on 21 August 1991 referred to an X-ray diffraction analysis carried out in 1990 on aspartame samples prepared in October-December of 1983 by Pierrel, and showed that type IIa crystals were present in all samples. The declaration of Dr Tjioe filed on 23 September 1992 stated in paragraphs 5 and 6 that the Pierrel aspartame samples analysed by DSM contained two crystal types, one being type IIa. The other was called I_c and was said to be very stable. Tests were carried out to show that the original manufactured sample must have contained type IIa crystals because type I_c was so stable that it could not have changed during the course of time into type IIa crystals.

In evidence filed on 16 July 1997, the Appellant stated that two of the five original Pierrel samples did not contain type IIa crystals because only one of the necessary four x-ray diffraction peaks necessary to

characterise type IIa crystals was found by Dr Moonen and therefore his evidence was misleading. The Appellant agreed with Dr Tjioe that type I_c crystals otherwise known as type III were present in the original Pierrel samples but disagreed that type IIa crystals were present in the manufactured product. This latter form of crystal was only present in the five Pierrel samples tested by DSM in 1990 in amounts of from 2 to 23% and hence the overwhelming majority was type III, furthermore the moisture content in all these samples was at least 4.9% which lay outside the range of 0,9 to 3,0% moisture content characteristic of the claimed type IIa crystals.

- 4.2 Having considered the above evidence, the Board is of the opinion that there is no proof that the Pierrel Company did manufacture and sell that form of aspartame identified as type IIa crystals and the prior use objection must fail.

This conclusion has been reached for the following reasons:

- (a) There was considerable divergence in the opinions of Dr Witt and Mr Franzese as to the exact nature of the aspartame manufacturing process and therefore the product may not have been what was expected, especially as the disputed drying and granulation stages were important in determining crystal structure.
- (b) The x-ray diffraction diagrams filed by Dr Moonen relating to five Pierrel original samples all

showed a strong peak at approximately 4°, yet this was not a peak said to characterise the type IIa aspartame crystal and must therefore cast doubt on the possibility of the products of the manufacturing process being predominantly type IIa crystals.

- (c) The evidence of the other party showed that there was a considerable proportion of type III crystals present in the analysed samples, only some of the aspartame being of type IIa in November of 1990.

(d) In storage tests conducted using both plastic bags which allowed some access to the atmosphere and sealed glass bottles which did not, the Appellant showed that over a period of three months type III crystals of moisture content 3,55% in plastic bags changed to a mixture of crystal types III and IIa with a moisture content of 9,1%, whilst the same crystals in sealed glass bottles remained as type III and had only 4,1% moisture content after three months. In the Board's view this demonstrates the sensitivity of the type III crystals during storage and would explain why the x-ray diffraction results provided by Dr Moonen may have shown type IIa content in 1990 if the 1983 samples were type III aspartame crystals. Dr Tjioe did declare that type III crystals were present in the 1983 samples which was common ground for both parties. In the event that type III crystals were present, this explanation is accepted by the Board.

4.3 Discussion of the relevant prior art

Document (7) was filed on 25 November 1982 and published on 2 June 1984, thus it did predate the Appellant's application dated 15 March 1984, but did not prior disclose its subject-matter. Since it is a Japanese application document (7) is not relevant under Article 54(3) EPC.

Document (1) described the heating of aspartame at 105°C for 4 hours and no further details were given. There

was no recognition of any crystal form and granulation was not mentioned.

Document (2) published in 1978 discussed the stability of aspartame having different moisture contents 4,2 to 8,0% (IIa has 0,9% to 3,0%) when stored at room temperature, 40°C and 55°C for one year. No sign of decomposition below 8,0% moisture was seen. This document did not discuss any specific crystal forms of aspartame.

Document (3) related to soluble compositions dried at 100 °C or above, which contained more bulking agent than aspartame and no crystal forms were described.

The aspartame product known as EQUA 200 was disclosed in document (4) and the Appellant investigated its critical relative humidity (CRH) in the moisture equilibrium isotherm described in document (5) and found that this was about 80%, however there was no crystal type having the same CRH value using types Ib or III crystals. The nearest to that value that it was possible to achieve was obtained by starting with type III crystals and measuring the humidity after storing for four hours. This indicated that type III crystals were the starting crystals used in documents (4) and (5) and that conversion to type IIa did not occur during this test which produced a very similar moisture equilibrium isotherm.

Document (6) related to adsorption theory and techniques there being no disclosure of aspartame or

any specific form thereof.

The other party referred also to European patents Nos. 0 101 755 and 0 101 756 both filed on 31 August 1982 and published on 7 March 1984, ie, before the filing date of the patent in suit. From these, Dr Tjio (declaration filed on 23 September 1992) has repeated some examples. In particular aspartame was heated at 70°C for 5 hours, however according to the patent in suit at column 8 line 31 type II crystals cannot be obtained at by heating at 70°C. These citations were silent in respect of any particular crystal form and have not made available any crystal form of aspartame at all.

In summary, the Board is of the opinion that there was no disclosure in any of the said prior art documents of aspartame type IIa crystals having the given X-ray characteristics and moisture content. For these reasons novelty is acknowledged.

5. *Inventive step (Article 56 EPC)*

5.1 The closest prior art

The Board regards document (2) as the nearest prior art because this document discusses the dry stability of aspartame.

5.2 Having regard to this prior art the objective problem was to find a form of aspartame with improved dry storage stability.

5.3 The solution to the problem

This problem is solved by the provision of the particular crystal form of aspartame known as type IIa which are shown to have excellent storage stability and to be very stable in the presence of excipients, effervescent agents or neutralising agents.

5.4 Assessment of inventive step

The question to be answered is whether or not the prior art made such a type IIa aspartame crystal available in an obvious manner.

All the cited documents only refer to aspartame in general and do not give any evidence of the existence of any particular crystal form of it.

In the absence of any indication in document (2) or in any other of the cited documents of a type IIa aspartame crystal having the given moisture content and which had good dry stability, it is decided that the prior art did not make such a crystal obviously available to the skilled person and therefore the subject-matter of the main request is considered to involve an inventive step.

6. In view of the above finding it is not necessary to consider the auxiliary requests.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the first instance with the order to maintain the patent on the basis of claims 1 to 7 submitted during oral proceedings as main request and the description to be adapted thereto.

The Registrar: The Chairman:

D. Spigarelli L. Galligani