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**Datasheet for the decision
of 26 March 2019**

Case Number: T 2534/16 - 3.3.09
Application Number: 10839868.6
Publication Number: 2508084
IPC: A23L1/30, A23L1/076, A61K35/64,
A61K36/734
Language of the proceedings: EN

Title of invention:

BIOLOGICALLY ACTIVE FOOD ADDITIVE FOR PREVENTING CARDIOVASCULAR
DISEASES AND ENHANCING THE CARDIOVASCULAR SYSTEM

Applicant:

Obshestvo S Ogranichennoj Otvetstvennostju
"PARAFARM"

Headword:

Relevant legal provisions:

EPC Art. 54(5), 56, 123(2)

Keyword:

Inventive step: main request and auxiliary request 4 (no);
auxiliary request 7 (yes)
Added matter: auxiliary request 1 (yes)

Decisions cited:

Catchword:



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Case Number: T 2534/16 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 26 March 2019

Appellant: Obshestvo S Ogranichennoj Otvetstvennostju
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 24 May 2016
refusing European patent application No.
10839868.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman N. Perakis
Members: A. Veronese
E. Kossonakou

Summary of Facts and Submissions

- I. This decision concerns the appeal filed by the applicant against the examining division's decision refusing European patent application No. 10839868.6.
- II. The examining division decided that the subject-matter of the main request, filed by letter dated 1 April 2015, and of auxiliary request 3, filed during the oral proceedings before the examining division did not involve an inventive step. Auxiliary requests 1 and 2, also filed during the oral proceedings, were not admitted into the proceedings.

Claim 1 of the main request reads:

"1. A biologically active food additive for use in the prevention of cardiovascular diseases and for use in the enhancement of the cardiovascular system, characterized in that it comprises hawthorn flowers and/or berries and/or leaves, royal jelly and excipient in a following ratio of ingredients:

- *hawthorn flowers and/or berries and/or leaves: from 61 to 90 wt. %,*
- *royal jelly: from 10 to 24 wt.%,*
- *excipients: from 0 to 29 wt.%."*

- III. The examining division referred to the following documents:

D1: Federalny Reestr Biologocheski Aktivnykh Dobakov K Pische (Federal Register of Biologically Active Food Compounds), 2005, pp. 400, 401, 406 and 407 (a document in Russian)

D2: V.N. Krylov *et al.*, "Experimental Study of Bee Royal Jelly Cardioprotective Characteristics", *Mellifera*, 2006, vol.6 no. 10-12, pp. 28-32

D3: A.L. Miller, "Botanical Influences on Cardiovascular Disease", *Alternative Medicine Review*, 1998, vol.3, no.6, pp. 421-431

D4: S.R. Long *et al.*, "Effect of hawthorn (*Crataegus oxycantha*) crude extract and chromatographic fractions on multiple activities in a cultured cardiomyocyte assay", *Phytomedicine*, 2006, vol.13, pp. 643-650

E1: Report of a research no.2 (filed by letter dated 23 September 2015)

IV. The examining division considered that any of D2, D3 or D4, which disclosed the use of either hawthorn material or royal jelly for strengthening the cardiovascular system, could be selected as the closest prior art for the assessment of inventive step. The claimed subject-matter differed from the teaching of these documents in that it related to a composition which combined the two aforementioned ingredients in specific amounts. There was, however, no evidence that this combination resulted in any unexpected technical effect. The experimental results presented by the appellant with its letter dated 23 September 2015 were not statistically relevant. There was also no evidence that the claimed composition promoted regeneration and cicatrisation of tissues damaged by myocarditis. Even if such evidence had been provided, it would not have been sufficient to render the alleged therapeutic effect plausible across the entire scope claimed. Thus, the problem underlying the claimed invention in view of

the closest prior art was the provision of an alternative composition for strengthening the cardiovascular system. The claimed solution was obvious in the light of a combination of the teaching of D2 with D3 or D4. The skilled person would not have had any reason not to combine hawthorn material with royal jelly because D1 described a composition comprising these ingredients and its use for promoting cardiovascular health.

- V. In the statement setting out the grounds for appeal, the applicant ("appellant") requested that the examining division's decision be set aside and that a patent be granted on the basis of the main request or, alternatively, any of auxiliary requests 1 to 3 on which the contested decision was based. The appellant also filed the following experimental report:

E2: Experimental Data by the Medical Center "Secrety dolgoletia" (in Russian accompanied by an English translation)

- VI. On 30 January 2019, the board issued a communication in preparation for the oral proceedings and gave its preliminary non-binding opinion on the outstanding issue of inventive step. The board noted that the technical evidence at hand appeared unsuitable to substantiate any unexpected technical effect, in particular in regard to claims relating to a generic "prevention of cardiovascular diseases" or "enhancement of the cardiovascular system".

- VII. By letter dated 6 February 2019, the appellant filed:

D1': an English translation of D1

VIII. By letter dated 25 February 2019, the appellant submitted new auxiliary requests 1 to 3, replacing the previous auxiliary requests and a further experimental report:

E3: V.N. Trifonov *et al.*, "Research of KARDIOTON influence on the heart muscle in acute myocardial infarction", Sekreti dolgoletiya Medical Center, 2013, Russia

IX. On 26 March 2019 oral proceedings took place before the board. The discussion concerned the issues of inventive step of the main request and the amendments of the subject-matter of the auxiliary requests. In the course of the hearing, the appellant filed auxiliary requests 4, 5, 6 and 7. The discussion then focused on the issues of the amendments, clarity and inventive step of the subject-matter of the auxiliary requests. Before the closure of the debate the appellant withdrew auxiliary requests 2, 3, 5 and 6.

X. Claim 1 of auxiliary requests 1, 4 and 7 differs from claim 1 of the main request (see point II above), in that the intended use specified therein

"..for use in the prevention of cardiovascular diseases and for use in the enhancement of the cardiovascular system.."

was replaced

- in auxiliary request 1 by: *"..for use in the reduction [of] the incidence and severity of cardiovascular diseases and for use in the enhancement of the cardiovascular system after incidence of cardiac infarction.."*,

- in auxiliary request 4 by: "*..for use in the reduction [of] the incidence and severity of heart diseases..*",
- in auxiliary request 7 by: "*..for use in the treatment of myocardial ischemia..*".

XI. The appellant's arguments relevant for the present decision may be summarised as follows:

Main request

- The subject-matter of claim 1 involved an inventive step. D1/D1' was the closest prior-art document because it disclosed a food additive composition comprising both a hawthorn extract and royal jelly as well as the use of that additive composition for maintaining the function of the cardiovascular system. D2, D3 and D4 disclosed the beneficial effects of either a hawthorn extract or royal jelly on the cardiovascular system. However, since they neither mentioned nor hinted at a combination of these agents, they were more remote than D1/D1' from the claimed subject-matter.
- The experimental reports showed that the specific amounts of the ingredients of the claimed composition prevented and promoted the repair of damages to the heart. After heart infarction the necrotic volume and the size of scars decreased, the heart haemodynamic parameters were improved and recurrences were prevented. The appellant considered these effects surprising, but it also conceded that there was no evidence that they could

be relevant for all conditions encompassed by the claims.

- According to the appellant, the underlying technical problem concerned the provision of an improved food additive for use in the prevention of the recurrence of cardiovascular diseases, in particular after an acute heart infarct, the additive promoting the regeneration and the performance of the heart muscle damaged by a heart infarct.
- The skilled person would not have found in D1/D1' any reason to adapt the amounts of the ingredients of the additive composition in accordance with claim 1. Furthermore, neither D2, D3 nor D4 suggested combining the claimed ingredients.

Auxiliary request 1

- Although the application as filed did not literally mention the intended use specified in claim 1, this use was implicitly disclosed by the application as a whole. Thus, auxiliary request 1 did not infringe Article 123(2) EPC.

Auxiliary request 4

- Since the intended use specified in claim 1 of auxiliary request 4 was explicitly disclosed in the application as filed, this request fulfilled the requirements of Article 123(2) EPC.
- The claimed subject-matter also involved an inventive step starting from D1/D1' and considering the unexpected technical effect shown by the

submitted technical evidence. The skilled person seeking to reduce the incidence and severity of heart diseases would not have been prompted by D1/D1' to adapt the amounts of the ingredients in the food additive composition in accordance with claim 1. Neither did D2, D3 nor D4 suggest combining these ingredients.

Auxiliary request 7

- The intended use specified in claim 1 of auxiliary request 7 was explicitly disclosed in the application as filed.

- The subject-matter of claim 1 was limited to the treatment of myocardial ischemia. The results of the clinical studies described in E2 and E3 proved that the claimed composition induced unexpected therapeutic effects in patients affected by myocardial infarction, a condition characterised by myocardial ischemia. Starting from D1/D1' (or from D3) as the closest prior art and confronted with the problem of providing an improved food additive for treating myocardial ischemia, the skilled person would not have considered combining the relevant agents in the claimed amounts. Thus, the claimed subject-matter involved an inventive step.

XII. The appellant requested that a patent be granted on the basis of:

- the main request, filed by letter dated 1 April 2015 (main request in the appealed decision) or, alternatively,

- auxiliary request 1, filed by letter dated 25 February 2019, or
- auxiliary requests 4 or 7, filed during the oral proceedings before the board.

Reasons for the Decision

Main request

1. *Inventive step*

1.1 Claim 1 relates to a biologically active food additive comprising specific amounts of royal jelly and hawthorn flowers and/or berries and/or leaves, and optionally excipients to be used in:

- the "prevention of cardiovascular diseases", and
- the "enhancement of the cardiovascular system".

1.2 The term "cardiovascular diseases" encompasses a broad spectrum of disorders affecting the heart and/or the blood vessels. Diseases affecting the heart include, for example, myocardial infarction, valvular heart diseases, congestive heart failure and arrhythmia, whereas diseases affecting blood vessels include venous and arterial disease, vein thrombosis, hypertension and atherosclerosis.

1.3 The expression "enhancement of the cardiovascular system" is also broad and considered to encompass uses in both the prevention and treatment of cardiovascular diseases. The patent application as filed indeed confirms that the claimed food additive "is a long lasting agent for the prevention and systematic

comprehensive treatment" (page 8, lines 9-10), that it has "a wide spectrum of preventive and health improving systemic actions" (page 3, lines 14-15), that it can be used as anti-arrhythmic, cardiogenic, coronary dilatory, hypotensive and that it is also beneficial for treating atherosclerosis, stenocardia, myocardial ischemia (page 7, lines 15-19, 32-33).

The closest prior art

- 1.4 D3 is a review article focusing on the use of botanical agents for the treatment and prevention of cardiovascular diseases. As reported in D3, berries and flowers of hawthorn have been traditionally used as cardiac tonic and are still widely employed for treating conditions such as angina, hypertension, arrhythmia and congestive heart failure (page 422). D3 further summarises the results of preclinical and clinical investigations indicating that extracts from hawthorn (also known as Crataegus) induce beneficial inotropic and chronotropic effects on the heart, scavenge free radicals, induce vasodilatation and enhance blood vessel integrity (page 423). It also reports that hawthorn material can be used for treating myocardial ischemia (page 423) and arrhythmia (page 424, right-hand column) and to reduce congestive heart failure (page 425) and the deposition of cholesterol in the aorta (page 424, right-hand column).

- 1.5 Thus, D3 teaches that hawthorn material can be employed, in the same manner as the food additive defined in claim 1, for treating and preventing a broad range of diseases of the cardiovascular system. Since D3 provides a comprehensive picture of the therapeutic benefits of material from hawthorn, the main ingredient of the claimed food additive, and these benefits

overlap to a large extent with those mentioned in the description of the application in suit, it is considered the closest prior art.

- 1.6 The appellant argued that D1/D1' should be selected as the closest prior art. The board does not agree. D1/D1' may relate to a food additive comprising both royal jelly and hawthorn extract. However, beyond a generic mention of a use "for maintaining the function of the cardiovascular system", D1/D1' does not give the slightest hint as to which specific condition(s) can be prevented or treated using this additive. Furthermore, the food additive described in D1/D1' comprises a number of further ingredients beside hawthorn and royal jelly for the biological activity of which D1/D1' does not provide any information. Thus, it is not possible to establish from the concise disclosure of D1/D1' how and to what extent the royal jelly and hawthorn material have an effect on the cardiovascular system. For these reasons, D1/D1' cannot be considered the closest prior art.

Effects induced by the claimed additive and formulation of the objective technical problem

- 1.7 The appellant asserted that the claimed food additive was suitable for inducing heart muscle self-regeneration after myocardial infarction by:
- inducing the formation of new heart muscle cells from mature cardiac myocytes and stem cells and as a result, restoring heart damage;
 - inducing the production of enzymes splitting the collagen fibres of tissues and decreasing the mass of the scar in the myocardial tissue; and

- restoring heart muscle performance by increasing the heart ejection fraction.

- 1.8 The appellant referred to the experimental reports E1 to E3 to substantiate the aforementioned effects.
- 1.9 In E1, the myocardial tissue of rats was insulted by infusing adrenalin and the myocardial concentration of malondialdehyde (MDA), a marker of oxidative damage, was monitored. The results show that the concentration of MDA is reduced after administration of hawthorn material and royal jelly. The effect of their combination is stronger than that observed when using each ingredient alone at the same concentration. These results render it credible that the claimed combination induces a beneficial effect against oxidative damage to the heart tissue induced by adrenalin insult.
- 1.10 E2 and E3 describe studies in which compositions as defined in claim 1 were administered to patients after myocardial infarction. E3 compares the effects of the administration of a combination of hawthorn material and royal jelly with those observed after administering each ingredient alone. The results indicate that the combined treatment is more effective than that based on the individual ingredients in improving the haemodynamic parameters (e.g. ejection fraction) and in reducing the incidence of further episodes of myocardial infarction and heart failure. Notably, whereas no decrease in the necrosis area caused by infarct was noted after the administration of hawthorn material and royal jelly as single ingredients, their combination induced a reduction of necrosis. E2 confirms that the claimed combination improves certain haemodynamic parameters and reduces the necrotic area

in patients after infarction. However, it does not provide comparisons with compositions comprising the two ingredients alone. Furthermore, there is no evidence in E2 and E3, that these effects are mediated by a mechanism involving the formation of new heart muscle cells (e.g. from stem cells) and/or by the production of particular enzymes.

- 1.11 Furthermore, and most importantly, the appellant has not provided evidence that these effects have any relevance for the treatment or prevention of conditions which differ substantially in nature and aetiology from myocardial infarction. The appellant conceded that, as far as the claims cover conditions such as hypertension, atherosclerosis or heart arrhythmia, the results do not prove that the combined administration of hawthorn material and royal jelly induces any new technical effect beyond the effects induced by the single administration of hawthorn described in D3.
- 1.12 During the proceedings, the appellant formulated the technical problem as that of providing "an improved food additive for use in the prevention of the recurrence of cardiovascular diseases, in particular after an acute heart infarct, the additive promoting the regeneration and the performance of the heart muscle damaged by a heart infarct".
- 1.13 Taking into account the scope of claim 1, this is not an appropriate formulation of the underlying technical problem. Claim 1 is a purpose-limited product claim drafted under Article 54(5) EPC. Attaining the therapeutic effect specified in this claims is a functional feature characterising the claimed invention. From this it also follows that any new effect relied upon to prove that this invention

involves an inventive step must be achieved over the entire scope claimed. As noted above (points 1.2 and 1.3), claim 1 encompasses both the prevention and the treatment of a broad spectrum of diseases affecting the heart and the peripheral vascular system. However, as already explained, the available evidence does not prove that the effects presented in the aforementioned reports have any relevance for the treatment or prevention of conditions which differ substantially in nature and aetiology from myocardial infarction and that, as far as these conditions are concerned, the therapeutic effects of the claimed composition extend beyond those already disclosed in the prior art D3.

- 1.14 Thus, the objective technical problem in view of D3 has to be formulated in a less ambitious way, namely, as in the provision of an alternative biologically active agent with beneficial therapeutic properties on the cardiovascular system and in the formulation of that agent in a form suitable for administration to a patient.

Obviousness of the solution

- 1.15 The question which remains to be answered is whether the skilled person starting from D3 and seeking an alternative biologically active material would have been motivated by the prior art to combine a hawthorn material with royal jelly at the claimed ratio.
- 1.16 D2 discloses that royal jelly was known before the priority date to induce beneficial effects on the cardiovascular system. Positive effects on myocarditis and atherosclerosis are mentioned on page 28. Cardioprotective effects such as the limitation of damages induced by ischemia and reperfusion injury

after infarct and the correction of disturbances in the heart rhythm are also reported (page 28, abstract; page 31, "discussion"; page 32, "conclusion").

- 1.17 Thus, the skilled person would have taken into consideration the disclosure of D2 and would have combined hawthorn material with royal jelly. It is common practice in the relevant field to combine pharmacologically active compounds with similar activities for improving patient compliance, efficacy, and to reduce side-effects.
- 1.18 The ratio of hawthorn material and royal jelly in the composition is arbitrary since no evidence has been put forward showing that this ratio is associated with a technical effect. No tests are available comparing the effect of compositions comprising the two agents within and outside the claimed ratio. Thus, the claimed ratio would have been one of many obvious possibilities available to the skilled person when combining the two active ingredients.
- 1.19 Lastly, with regard to the formulation of the two active ingredients, when confronted with the underlying problem, the skilled person would have contemplated preparing a food additive, i.e. a formulation which can be incorporated in or administered together with a food (e.g. as a tablet or a capsule). The use of tablets and capsules for administering biologically active ingredients was part of the common general knowledge and was within the capabilities of the skilled person in this technical field. D1 discloses examples of such tablets which comprise both relevant agents and their administration as food additives.

1.20 For these reasons, the subject-matter of claim 1 of the main request does not involve an inventive step and this request is not allowable (Article 56 EPC).

Auxiliary request 1

2. Added subject-matter

2.1 Claim 1 of the first auxiliary request was amended to specify that the claimed composition is intended:

"..for use in the reduction [of] the incidence and severity of cardiovascular diseases and for use in the enhancement of the cardiovascular system after incidence of cardiac infarction.."

2.2 As basis for the amendment, the appellant referred to page 6, lines 11-27, and to page 7, lines 15-27, of the application as filed, which refer respectively to the treatment of "heart diseases" and "myocardial ischemia". In the appellant's opinion, although myocardial infarction is not mentioned in the application as filed, the skilled person would have derived the medical indication of claim 1 from the aforementioned passages, taking into account the teaching of the entire application as filed.

2.3 The board does not agree. Although cardiac ischemia is a causative factor of cardiac infarction, the two medical conditions are different, infarct being characterised by extensive cellular death. Thus, neither the specific disclosure of "myocardial ischemia" nor the generic disclosure of "heart diseases" directly and unambiguously discloses the treatment of patients "after incidence of cardiac infarct" as defined in claim 1.

2.4 Since no further basis for the amendments can be found in the application as filed, the subject-matter of claim 1 of auxiliary request 1 extends beyond the content of that application and this request is not allowable (Article 123(2) EPC).

Auxiliary request 4

3. *Inventive step*

3.1 Claim 1 of auxiliary request 4 was amended to specify the medical indication as follows:

"..for use in the reduction [of] the incidence and severity of heart diseases.."

3.2 It is acknowledged that this amendment limits the subject-matter of claim 1 of auxiliary request 4 over that of claim 1 of the main request. However, the generic definition "heart diseases" is still very broad and encompasses conditions differing substantially in nature and aetiology from myocardial infarction. The available evidence does not prove that, as far as claim 1 relates to the treatment of heart diseases such as arrhythmia, the combined administration of hawthorn material and royal jelly induces any new technical effect beyond that induced by the single administration of hawthorn described in D3. Thus, the arguments presented above when dealing with the main request apply also to auxiliary request 4.

3.3 Thus, the objective technical problem in view of the closest prior art D3 is the provision of an alternative biologically active material with beneficial therapeutic properties against heart diseases and its

formulation in a form suitable for administration to a patient.

3.4 As mentioned above (points 1.4 and 1.16) the beneficial effects of both hawthorn material and royal jelly against heart diseases, including disturbances of heart rhythm, were known before the relevant date from D2 and D3. Thus, for the same reasons discussed above when dealing with the main request, when confronted with the underlying technical problem, the skilled person would have considered providing a food additive as defined in claim 1.

3.5 Thus, the subject-matter of claim 1 of auxiliary request 4 does not involve an inventive step and this request is not allowable (Article 56 EPC).

Auxiliary request 7

4. Added subject-matter and inventive step

4.1 Claim 1 of auxiliary request 7 was amended to specify the medical indication as follows:

"..for use in the treatment of myocardial ischemia..".

4.2 This therapeutic application is disclosed on page 7, lines 15-18 of the application as filed. Thus, claim 1 fulfils the requirement of Article 123(2) EPC.

4.3 As mentioned above, the submitted evidence, in particular that presented in E3, indicates that the therapeutic treatment using the biologically active food additive of claim 1 improves the haemodynamic parameters and reduces the incidence of further episodes of infarction and heart failure after acute

myocardial infarction. Most surprisingly, the evidence shows that, whereas hawthorn material and royal jelly used alone do not have any effect on the necrosis caused by an infarct, a reduction of the necrotic area is observed when these compounds are administered in combination. Taking also into account the results shown in E1, it is reasonable to assume a reparative mechanism of damages induced by the ischemic and hypoxic state present during the infarct. This renders it credible that the combined treatment will not only induce unexpected effects after myocardial infarction, but also more generally in subjects suffering from a myocardial ischemia.

4.4 Thus, the objective technical problem in view of the closest prior art D3 consists in the provision of an improved combination for treating and in particular for recovering from damages induced by myocardial ischemia, and the formulation of this material in a form suitable for administration to a patient.

4.5 The results of the technical evidence submitted by the appellant prove that that underlying technical problem has been solved. Since the prior art would not have suggested the proposed solution to the skilled person, the subject-matter of claim 1 of auxiliary request 7 involves an inventive step and this request is allowable (Article 56 EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the examining division with the order to grant a patent on the basis of the following documents:
 - claim 1 of the seventh auxiliary request filed during the oral proceedings
 - description pages 1, 2, 2a, 3 and 6-8 filed during the oral proceedings
 - description pages 4 and 5 of the application as originally filed

The Registrar:

The Chairman:



M. Canueto Carbajo

N. Perakis

Decision electronically authenticated