

The examination is being carried out on the **following application documents**

Description, Pages

1-36 as published

Claims, Numbers

1-3 received on 22-07-2010 with letter of 22-07-2010

Basis of the opinion

The present application is the parent application of EP11150018.7 which claims resveratrol and/or grape leaf extract for energy metabolism activation/improving endurance/anti-fatigue and improving aging-induced reduction of energy metabolism. For the present application a non-unity objection had been raised in the PCT phase.

The present claim set is directed to the subject-matter of invention 5 (viz. as muscle strength improver).

subject-matter

Claim 1 use of a composition **comprising resveratrol and/or grape leaf extract for improving muscle strength**

d2 of claim 1 wherein the composition comprising resveratrol and/or grape leaf extract is **used for improving aging-induced reduction of muscle strength or muscle atrophy**

d3 of claim 1 wherein the composition comprising resveratrol and/or grape leaf extract is **used for inhibiting aging-induced reduction of muscle strength or muscle atrophy**

I. Amendments Art 123(2) EPC

Claim 1 is based on originally filed claim 19. New dependent claims 2 and 3 are more or less based on originally filed dependent claims 6 and 7 and cf. p.26/Test 4 of the description.

III. Patentability Art. 53c) and Art. 54 (4)/(5) EPC

Generally, from the wording of claims 1-3 it is not clear whether a medical use or a non-medical use is envisaged.

If the claims are envisaged to be used in a medical condition then it should be noted that a wording directed to a "method of treatment" falls under the exclusion of Art. 53 c) EPC in combination with Art. 54(4) EPC. Claims directed to a (further) medical use are only acceptable if they are in accordance with the wording set out in Art. 54(4) and (5) EPC.

IV. Prior art Art. 54 (2) EPC

The following documents were discussed regarding the aspect of invention 5 (viz. as muscle strength improver).

muscle strength improver

D4 **HU-A-163515** Chinoin Gyogyszer Vegyeszeti Termek Gyara Rt. [X]

AN - 1973:492007 HCAPLUS HU6072

Isoflavones as fodder additives with effective body weight and fodder utilization increasing effect, improving the quality of flesh, the **muscle strength** and performance of race horses, etc., when added in 0.0001 -0.1% amount to fodder, and without any estrogen effect, were prepared in several ways (cf. also for reference FR2236493 and/or AT340231).

D9 XP004727629 Porcu et al. [X/IS]

The emerging therapeutic potential of **sirtuin - interacting drugs**: from cell death to lifespan extension

Sirtuins have pathophysiological relevance to cancer, obesity, **muscle differentiation**, inflammation and neurodegeneration. In addition, experimental evidence unequivocally shows that sirtuin activity **extends the lifespan** of several organisms (p. 94/l-h col./last para).

Resveratrol is a sirtuin activator - cf. Fig 4(b).

IV. Novelty Art. 54 EPC

The specific concept to use isoflavones (which form part of a grape leaf extract as they fall under the definition of polyphenols/flavonoids) destroys the novelty of the more general disclosure, viz. the use of a grape leaf extract, for increasing muscular strength (as claimed) - cf. Guidelines C-IV, 9.5. Hence, the subject-matter of claim 1 is considered to be anticipated by D4.

Grape leaves contain a wide range of **polyphenol flavonoids** including flavon(ol)-glycosides and glucuronides, quercetin-3-O-beta-D-glucuronide (main flavonoid), isoquercitrin, anthocyanins, oligomeric proanthocyanidins, catechin, epicatechin monomers and dimers, gallic acid and astilbine. The **phytoalexin trans-resveratrol**, another **polyphenolic substance belonging to the stilbene group**, can **also be found** in grape vine. In grape vine leaves, also organic acids appear, mainly malic and oxalic acid but also tartaric acid; citric, fumaric and succinic acid can be detected in the leaves only in traces. Compared to the grape berries, grape leaves are richer in the content of carotenoids and vitamin C. According to the French Pharmacopeia, the **dried leaves of red vine should contain at least 4% of total polyphenols and 0.2% of anthocyanins** - cf. <http://www.florahealth.com/flora/home/Canada/HealthInformation/Encyclopedias/GrapeLeaf.htm>.

V. Inventive Step/Insufficiency Art. 56 EPC/Art. 83 EPC

The grape leaf extract is known to be rich in flavonoids which include isoflavones (NB: The application itself does not disclose a detailed composition of the grape leaf extract). Thus the teaching of D4 which discusses the usefulness of isoflavones to induce body weight increase and muscular strength (cf. col.2/penultimate line and col. 10/l.29-25 "race horses") is considered to represent the closest prior art for the subject-matter of claim 1-3 and the aspect of "**grape leaf extract**" and **muscle strength improving**.

The difference in view of D4 is thus that D4 does not explicitly mention a "grape leaf extract".

The problem in view of D4 is thus to provide the same(?) and/or alternative ingredients for the same purpose of increasing muscle strength.

The solution to use a grape leaf extract which is known to be rich in flavonoids (which encompass isoflavones) is considered obvious at present.

Moreover, cf. infra, no data has been submitted for the purpose of using grape leaf extract for improvement of muscle strength, let alone for muscular atrophy.

The closest prior art for the subject-matter of claims 1-3 and the aspect of "**resveratrol**" and **muscle strength improving** is considered to be D9 (Porcu et al.).

D9 discusses the emerging therapeutic potential of sirtuin-interacting drugs (sirtuin activator = i.a. resveratrol). On the first page (viz. p.94)/last paragraph it is stated that "recent research indicates that sirtuins have pathophysiological relevance to cancer obesity, muscle differentiation" etc. Below Fig. 4 right-hand column last sentence bridging pages 100-101 it is said that "given the **ability of SIRT1 to block muscle differentiation**, chemical **regulators** of its deacetylating activity such as nicotinamide [19] might be harnessed **to promote muscle regeneration** and have a role in the **treatment of muscular diseases**" - [emphasis added].

The problem in view of this document is to provide a sirtuin modulating agent/extract that improves muscle strength/prevents muscular diseases (muscular atrophy).

The skilled person working in the field was undoubtedly guided to work into this direction also with resveratrol as preferred agent, particularly knowing the more complex effects of resveratrol on the cellular level, e.g. also its ATP influencing potential. In order to increase muscle strength the muscles need to be regenerated and the more muscle mass the better the muscle strength.

Besides, the application itself appears not to have credibly proven the claimed effect over the whole scope claimed. On page 26 - test example 4 - a disputable effect* of resveratrol on the muscle strength of the extensor digitorum longus muscle is shown (cf. tab 10/p.28), however no such an effect is shown for a grape leaf extract.

*A significant effect has only been shown in view elderly not exercising people. However, no significancy of the elderly exercising resveratrol treated group results if compared to the elderly exercising group.

Table 8 as indicated by the Applicant as support for inventiveness does not measure muscular strength but muscle weight (cf. in this context D4 supra!).

Moreover, no effect is shown for aging-induced muscle atrophy.

Hence, possibly an objection with regard to undue burden to carry out the invention could be raised in the further procedure.

Therefore, at present, claims 1-3 are considered to lack inventiveness.

VI. Third Party Observation Art. 115 EPC

The Third Party Observation of 1st June 2010 by V.K. Gupta has been taken into account. At present, however, the so far cited documents, viz. D4 and D9, appear to be more relevant to object on Novelty and Inventive Step. In order to be able to consider the teachings as a clear and unambiguous disclosure with regard to the now claimed muscle strength, a more detailed description thereof might be needed. The Applicant (cf. letter of 22nd July 2010) argues that "strength promoting" according to the understanding of the documents cited in the TKDL this effect is to be defined as to be one of overcoming weakness/fatigue or providing stamina rather than one of providing an increase in muscle strength in terms of muscle size. In support of this, the Applicant submitted short description of Ayurveda, Unani and Siddah. However, an indication is missing where exactly this information/interpretation can be found in the submitted documents. Hence very generally the strength promoting effect has to be considered to encompass promoting of muscle strength as well at present.

VII. Other Matter

When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims. Care should be taken during revision, especially of the introductory portion and any statements of problem or advantage, not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC).

In order to facilitate the examination, the Applicant should clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (GL E-II, 1). Preferably, these indications should be submitted in handwritten form on a copy of the relevant parts of the application as filed.