

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to pomegranate/pomegranate juice and maintenance of normal blood cholesterol concentrations (ID 1162, 1320, 2107, 2167), maintenance of normal erectile function (ID 1163), protection of lipids from oxidative damage (ID 1201, 1319, 2123), “antioxidant and anti-aging properties” (ID 1901), increase in appetite after unintentional weight loss leading to an increase in energy intake (ID 2122) and maintenance of normal blood glucose concentrations (ID 4471) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2, 3}

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to pomegranate/pomegranate juice and maintenance of normal blood cholesterol concentrations, maintenance of normal erectile function, protection of lipids from oxidative damage, “antioxidant and anti-aging properties”, increase in appetite after unintentional weight loss leading to an increase in energy intake and maintenance of normal blood glucose concentrations. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

¹ On request from the European Commission, Question No EFSA-Q-2008-1901, EFSA-Q-2008-1902, EFSA-Q-2008-1940, EFSA-Q-2008-2056, EFSA-Q-2008-2057, EFSA-Q-2008-2634, EFSA-Q-2008-2840, EFSA-Q-2008-2855, EFSA-Q-2008-2856, EFSA-Q-2008-2900, EFSA-Q-2010-00424, adopted on 09 July 2010.

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The Panel considers that, whereas pomegranate/pomegranate juice and polyphenols in pomegranate/pomegranate juice are not sufficiently characterised, the food constituents, punicalagin and ellagic acid in pomegranate/pomegranate juice, which the Panel assumes to be the subject of the health claims, are sufficiently characterised.

Maintenance of normal blood cholesterol concentrations

The claimed effects are “heart health”, “cardiovascular health” and “maintaining cholesterol”. The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed effects relate to the maintenance of normal blood cholesterol concentrations. The Panel considers that maintenance of normal blood cholesterol concentrations is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and the maintenance of normal blood cholesterol concentrations.

Maintenance of normal erectile function

The claimed effect is “sexual health in men”. The target population is assumed to be the general male population. In the context of the proposed wordings and the clarifications provided by Member States, the Panel assumes that the claimed effect refers to the maintenance of a normal erectile function. The Panel considers that maintenance of normal erectile function is a beneficial physiological effect.

Four references were provided in relation to this claim, including three references from which no conclusions could be drawn for the scientific substantiation of the claimed effect. The fourth reference reported on a randomised, double-blind, placebo-controlled, crossover intervention study in male subjects with erectile dysfunction. The Panel notes that pomegranate juice has not been sufficiently characterised with respect to polyphenols (i.e., punicalagin and/or ellagic acid content not specified) and that there was no significant effect of pomegranate juice on erectile function measured using either the Global Assessment Questionnaires (GAQ) score or the International Index of Erectile Function (IIEF).

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and maintenance of normal erectile function.

Protection of lipids from oxidative damage

The claimed effects are “antioxidative function”, “antioxidant properties”, and “antioxidants and immunity”. The target population is assumed to be the general population. In the context of the proposed wordings and conditions of use, the Panel assumes that the claimed effects relate to the protection of lipids from oxidative damage caused by free radicals. The Panel considers that protection of lipids from oxidative damage may be a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and the protection of lipids from oxidative damage.

“Antioxidant and anti-aging properties”

The claimed effect is “antioxidant and anti-aging properties”. The target population is assumed to be the general population.

The Panel considers that no evidence has been provided to establish that having antioxidant properties is a beneficial physiological effect. In addition, no definition has been provided of having “anti-aging properties” in relation to the antioxidant properties of foods.

The Panel considers that this claimed effect is general and non-specific and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

Increase in appetite after unintentional weight loss leading to an increase in energy intake

The claimed effect is “digestion”. The target population is assumed to be underweight individuals willing to increase their energy intake. In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the increase in appetite after unintentional weight loss. The Panel considers that increase in appetite after unintentional weight loss leading to an increase in energy intake, if sustained, might be a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and a sustained increase in appetite after unintentional weight loss leading to an increase in energy intake.

Maintenance of normal blood glucose concentrations

The claimed effect is “glucose metabolism”. The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the maintenance of normal blood glucose concentrations. The Panel considers that long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claimed effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and maintenance of normal blood glucose concentrations.

KEY WORDS

Pomegranate/pomegranate juice, polyphenols, punicalagin and ellagic acid, blood cholesterol, erectile function, lipids, antioxidant, anti-aging, skin, appetite, energy intake, weight loss, blood glucose, health claims.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

See Appendix A

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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EFSA DISCLAIMER

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006⁴ submitted by Member States contains main entry claims with corresponding conditions of use and literature for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out⁵. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. The information provided in the consolidated list for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food that is the subject of the health claims is pomegranate/pomegranate juice and polyphenols in pomegranate/pomegranate juice.

The information provided (e.g. food, conditions of use) for the majority of the health claims on pomegranate and pomegranate juice refers to the type and/or amount of polyphenols in pomegranate/pomegranate juice that should be consumed daily in order to achieve the claimed effect. The Panel assumes that such phenolic compounds are also mentioned (and occasionally quantified) to allow standardisation of pomegranate juice, for which information on composition and on the manufacturing process has not been provided. In the remaining health claims, reference is made to dried fruit or herb powders for which the information on composition and on the manufacturing process has not been provided.

Polyphenols comprise a very wide group (several thousands of compounds) of plant secondary metabolites including flavonoids, isoflavonoids, phenolic acids, proanthocyanidins and other tannins, and lignans with different biological activities. Polyphenol content in foods is usually expressed as gallic acid equivalents (GAE), but also other phenolic compounds such as catechin/epicatechin or caffeic acid which are used for standardisation. This standardisation refers to traditional spectrophotometrical measurement of total polyphenols using the Folin-Ciocalteu method (Singleton and Rossi, 1965), which is based on reducing capacity. The method is not specific for polyphenols because other reducing compounds such as ascorbic acid, sugars and proteins will also be included in the quantification, thus leading to an overestimation of the actual polyphenol content. The total polyphenol content assessed with this method is not suitable for characterisation of polyphenols in foods.

Regarding the nature of specific polyphenols in pomegranate (*Prunus granatum*), punicalagin and ellagic acid have been specified in the conditions of use. Punicalagins are tannins that are known to be hydrolysed *in vivo* into smaller polyphenols such as ellagic acid. Punicalagin and ellagic acid can be measured in foods by established methods. Pomegranate polyphenols are bioavailable (Mertens-Talcott et al., 2006; Seeram et al., 2006).

⁴ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

⁵ Briefing document for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims: <http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf>

The Panel considers that, whereas pomegranate/pomegranate juice and polyphenols in pomegranate/pomegranate juice are not sufficiently characterised, the food constituents, punicalagin and ellagic acid in pomegranate/pomegranate juice, which the Panel assumes to be the subject of the health claims, are sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Maintenance of normal blood cholesterol concentrations (ID 1162, 1320, 2107, 2167)

The claimed effects are “heart health”, “cardiovascular health” and “maintaining cholesterol”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effects relate to the maintenance of normal blood cholesterol concentrations.

Low-density lipoproteins (LDL) carry cholesterol from the liver to peripheral tissues, including the arteries. Elevated LDL-cholesterol, by convention >160 mg/dL (>4.14 mmol/L), may compromise the normal structure and function of the arteries. High-density lipoproteins (HDL) act as cholesterol scavengers and are involved in the reverse transport of cholesterol in the body (from peripheral tissues back to the liver).

The Panel considers that maintenance of normal blood cholesterol concentrations is a beneficial physiological effect.

2.2. Maintenance of normal erectile function (ID 1163)

The claimed effect is “sexual health in men”. The Panel assumes that the target population is the general male population.

In the context of the proposed wordings and the clarifications provided by Member States, the Panel assumes that the claimed effect refers to the maintenance of normal erectile function.

The Panel considers that maintenance of normal erectile function is a beneficial physiological effect.

2.3. Protection of lipids from oxidative damage (ID 1201, 1319, 2123)

The claimed effects are “antioxidative function”, “antioxidant properties”, and “antioxidants and immunity”. The Panel assumes that the target population is the general population.

The Panel considers that “immunity” is not sufficiently defined for a scientific evaluation and the proposed wordings or scientific references submitted for this claim (ID 2123) do not provide further information. The Panel also considers that no evidence has been provided to establish that having antioxidant properties is a beneficial physiological effect.

In the context of the proposed wordings and conditions of use, the Panel assumes that the claimed effects relate to the protection of lipids from oxidative damage caused by free radicals.

Reactive oxygen species (ROS) including several kinds of radicals are generated in biochemical processes (e.g. respiratory chain) and as a consequence of exposure to exogenous factors (e.g. radiation, pollutants). These reactive intermediates damage biologically relevant molecules such as DNA, proteins and lipids if they are not intercepted by the antioxidant network which includes free radical scavengers such as antioxidant nutrients.

The Panel considers that protection of lipids from oxidative damage may be a beneficial physiological effect.

2.4. “Antioxidant and anti-aging properties” (ID 1901)

The claimed effect is “antioxidant and anti-aging properties”. The Panel assumes that the target population is the general population.

The Panel considers that no evidence has been provided to establish that having “antioxidant properties” is a beneficial physiological effect. In addition, no definition has been provided of having “anti-aging properties” in relation to the antioxidant properties of foods.

The Panel considers that this claimed effect is general and non-specific and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006.

2.5. Increase in appetite after unintentional weight loss leading to an increase in energy intake (ID 2122)

The claimed effect is “digestion”. The Panel assumes that the target population is underweight individuals willing to increase their energy intake.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the increase in appetite after unintentional weight loss.

The Panel considers that an increase in appetite after unintentional weight loss leading to an increase in energy intake, if sustained, might be a beneficial physiological effect.

2.6. Maintenance of normal blood glucose concentrations (ID 4471)

The claimed effect is “glucose metabolism”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the maintenance of normal blood glucose concentrations.

The Panel considers that long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

3.1. Maintenance of normal blood cholesterol concentrations (ID 1162, 1320, 2107, 2167)

Most of the references provided in the list addressed topics other than polyphenols in pomegranate/pomegranate juice and the claimed effect. These include narrative reviews on polyphenols, food composition, and human studies investigating the effects of polyphenols on anti-angiogenic potential, angiotensin converting enzyme activity, blood pressure, lipid oxidation, oxidative stress, platelet aggregation, or in relation to cancer prevention. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

In a pilot, single arm, uncontrolled intervention study, the effects of consuming a concentrated pomegranate juice (40 g per day) for eight weeks on the blood lipid profile were investigated in 22

diabetic patients (Esmailzadeh et al., 2004, 2006). The Panel considers that no conclusions can be drawn from this small and uncontrolled study for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and the maintenance of normal blood cholesterol concentrations.

3.2. Maintenance of normal erectile function (ID 1163)

Four references were provided in relation to this claim, which included a human intervention study on the effects of pomegranate juice on prostate-specific antigen (PSA) progression. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claimed effect.

A randomised, double-blind, placebo-controlled, crossover intervention study (described as a pilot study) which investigated the ability of pomegranate juice to improve erections in 53 male subjects with mild to moderate erectile dysfunction (ED) was provided (Forest et al., 2007). Subjects consumed daily eight ounces of pomegranate juice (total dose of 1.5 mmol polyphenols per day) and eight ounces placebo juice for 28 days each with a two-week washout period in between. Efficacy was assessed using the International Index of Erectile Function (IIEF) and the Global Assessment Questionnaires (GAQ). The Panel notes that pomegranate juice has not been characterised with respect to polyphenols (i.e. punicalagin and/or ellagic acid) and that there was no significant effect of pomegranate juice on erectile function measured using either the Global Assessment Questionnaires (GAQ) score or the International Index of Erectile Function (IIEF).

The two remaining references (one full article and one letter to the editor) refer to a study on the effects of different fruit juices, including pomegranate juice, in a rabbit model of arteriogenic erectile dysfunction. The Panel considers that the evidence from this animal study is not sufficient to predict an occurrence of an effect of polyphenols (i.e. punicalagin and/or ellagic acid) in pomegranate/pomegranate juice on the maintenance of normal erectile function in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and maintenance of normal erectile function.

3.3. Protection of lipids from oxidative damage (ID 1201, 1319, 2123)

Most of the references provided in the list addressed topics other than polyphenols in pomegranate/pomegranate juice and the claimed effect. These references included narrative reviews on polyphenols, food composition tables, *in vitro* testing of antioxidant properties and human studies investigating the effects of polyphenols on anti-angiogenic potential or in relation to cancer prevention. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

A single arm, uncontrolled intervention study in 13 healthy male volunteers which assessed the effects of pomegranate juice consumption (50 mL per day containing 1.5 mmol total polyphenols) for two weeks on changes in the *ex vivo* activity of serum paraoxonase (an HDL-associated esterase), in plasma lipid peroxides (AAPH induced spectrophotometric method), and in the oxidation lag time of low-density lipoproteins (LDL) *ex vivo* was provided (Aviram et al., 2000). A second single arm (Rosenblat et al., 2006), uncontrolled intervention study in 10 healthy subjects and 10 non-insulin dependent diabetes mellitus (NIDDM) patients under pharmacological treatment was provided with the consolidated list. All subjects consumed 50 mL per day of pomegranate juice containing 1979 mg/L of tannins (1561 mg/L of punicalagin and 417 mg/L of hydrolysable tannins), 384 mg/L of

anthocyanins (delphinidin 3,5-diglucoside, cyanidin 3,5-diglucoside, delphinidin-3-glucoside, cyanidin 3-glucoside and pelargonidine 3-glucoside) and 121 mg/L of ellagic acid derivatives for three months. Serum concentrations of lipid peroxides, thiobarbituric acid reactive substances (TBARS), serum SH groups, serum paraoxonase 1 (PON1) activity, cellular peroxides and glutathione content in monocytes-derived macrophages (HMDM), and oxidised LDL uptake by HMDM were measured at the beginning and end of the intervention. The Panel considers that no conclusions can be drawn from these small and uncontrolled studies for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and the protection of lipids from oxidative damage.

3.4. Increase in appetite after unintentional weight loss leading to an increase in energy intake (ID 2122)

None of the references provided in relation to this claim provided scientific data on the effects of polyphenols (i.e. punicalagin and/or ellagic acid) in pomegranate/pomegranate juice on appetite in humans. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and a sustained increase in appetite after unintentional weight loss leading to an increase in energy intake.

3.5. Maintenance of normal blood glucose concentrations (ID 4471)

None of the references provided in relation to this claim provided scientific data on the effects of polyphenols (i.e. punicalagin and/or ellagic acid) in pomegranate/pomegranate juice on blood glucose concentrations in humans. The Panel considers that no conclusions can be drawn from these references for the scientific substantiation of the claimed effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and maintenance of normal blood glucose concentrations.

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituents, punicalagin and ellagic acid in pomegranate/pomegranate juice, which are the subject of the health claims are sufficiently characterised.

Maintenance of normal blood cholesterol concentrations (ID 1162, 1320, 2107, 2167)

- The claimed effects are “heart health”, “cardiovascular health” and “maintaining cholesterol”. The target population is assumed to be the general population. Maintenance of normal blood cholesterol concentrations is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and the maintenance of normal blood cholesterol concentrations.

Maintenance of normal erectile function (ID 1163)

- The claimed effect is “sexual health in men”. The target population is assumed to be the general male population. Maintenance of normal erectile function is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and maintenance of normal erectile function.

Protection of lipids from oxidative damage (ID 1201, 1319, 2123)

- The claimed effects are “antioxidative function”, “antioxidant properties”, and “antioxidants and immunity”. The target population is assumed to be the general population. Protection of lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and the protection of lipids from oxidative damage.

“Antioxidant and anti-aging properties” (ID 1901)

- The claimed effect is “antioxidant and anti-aging properties”. The target population is assumed to be the general population. No evidence has been provided to establish that having antioxidant properties is a beneficial physiological effect. In addition, no definition has been provided of having “anti-aging properties” in relation to the antioxidant properties of foods.
- The claimed effect is general and non-specific and does not refer to any specific health claim as required by Regulation (EC) No 1924/2006

Increase in appetite after unintentional weight loss leading to an increase in energy intake (ID 2122)

- The claimed effect is “digestion”. The target population is assumed to be underweight individuals willing to increase their energy intake. An increase in appetite after unintentional weight loss leading to an increase in energy intake, if sustained, might be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and a sustained increase in appetite after unintentional weight loss leading to an increase in energy intake.

Maintenance of normal blood glucose concentrations (ID 4471)

- The claimed effect is “glucose metabolism”. The target population is assumed to be the general population. Long-term maintenance of normal blood glucose concentrations is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of punicalagin/ellagic acid in pomegranate/pomegranate juice and maintenance of normal blood glucose concentrations.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1901, EFSA-Q-2008-1902, EFSA-Q-2008-1940, EFSA-Q-2008-2056, EFSA-Q-2008-2057, EFSA-Q-2008-2634, EFSA-Q-2008-2840, EFSA-Q-2008-2855, EFSA-Q-2008-2856, EFSA-Q-2008-2900, EFSA-Q-2010-00424). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: <http://www.efsa.europa.eu/panels/nda/claims/article13.htm>.

REFERENCES

- Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Colemann R, Hayek T, Presser D and Fuhrman B, 2000. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice. *American Journal of Clinical Nutrition*, 71, 1062-1076.
- Esmailzadeh A, Tahbaz F, Gaieni I, Alavi-Majd H and Azadbakht L, 2004. Concentrated pomegranate juice improves lipid profiles in diabetic patients with hyperlipidemia. *Journal of Medicinal Food*, 7, 305-308.
- Esmailzadeh A, Tahbaz F, Gaieni I, Alavi-Majd H and Azadbakht L, 2006. Cholesterol-lowering effect of concentrated pomegranate juice consumption in type II diabetic patients with hyperlipidemia. *International Journal for Vitamin and Nutrition Research*, 76, 147-151.
- Forest CP, Padma-Nathan H and Liker HR, 2007. Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: a randomized, placebo-controlled, double-blind, crossover study. *International Journal of Impotence Research*, 19, 564-567.
- Mertens-Talcott SU, Jilma-Stohlawetz P, Rios J, Hingorani L and Derendorf H, 2006. Absorption, metabolism, and antioxidant effects of pomegranate (*Punica granatum L.*) polyphenols after ingestion of a standardized extract in healthy human volunteers. *Journal of Agricultural and Food Chemistry*, 54, 8956-8961.
- Rosenblat M, Hayek T and Aviram M, 2006. Anti-oxidative effects of pomegranate juice (PJ) consumption by diabetic patients on serum and on macrophages. *Atherosclerosis*, 187, 363-371.
- Seeram NP, Henning SM, Zhang YJ, Suchard M, Li ZP and Heber D, 2006. Pomegranate juice ellagitannin metabolites are present in human plasma and some persist in urine for up to 48 hours. *Journal of Nutrition*, 136, 2481-2485.
- Singleton and Rossi, 1965. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. *American Journal of Enology and Viticulture*, 16, 144-158.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods⁶ (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

- a) the role of a nutrient or other substance in growth, development and the functions of the body; or
- b) psychological and behavioural functions; or
- c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

- (i) based on generally accepted scientific evidence; and
- (ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD⁷

Foods are commonly involved in many different functions⁸ of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

⁶ OJ L12, 18/01/2007

⁷ The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

⁸ The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

- (a) the claimed effect of the food is beneficial for human health,
- (b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),
- (c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,
- (d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to

describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.
- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.
- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Main entry health claims related to pomegranate/pomegranate juice, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
1162	Pomegranate	Cardiovascular health	Contributes to a healthy cholesterol level and healthy blood vessels.
	<p>Conditions of use</p> <ul style="list-style-type: none"> - Früchte / Äquivalent von 50-240 mL Granatapfelsaft oder 78-330 mg Punicalagin. - 60 mL pro Tag; in In Vitro Studien 10-20 mL pro Tag. - Erwachsene Männer entspr. mind. 200 mL Granatapfelsaft. - > 50 ml Granatapfelsaft/Tag; > 100 mg Gesamt-Polyphenole/Tag. - The product must contain the equivalent of 50-240 mL pomegranate juice or 78-330 mg of punicalagin or 7-33 mg of ellagic acid. - 250 mg / day fruit extract with 200mg polyphenol content or 50 ml pomegranate fruit juice. - 300 mL daily - There are no documented limits for the effective ingredients. Due to inadequate data, pregnant women, nursing women, patients over antidepressant medicines (Mirtazapine), antipsychotic medicines (Risperidone, Ketiapine), statines medicines (Simvastatine, atorvastatine), antihypertensive medicines should take doctor's advice (relative contra-indication). There are no documented upper limits in the consumption of pomegranate juice. Time that a result is seen cannot be clarified yet. Interaction only with medicines referred (after doctor's advice) Process method cannot affect the effective ingredients. 		
ID	Food or Food constituent	Health Relationship	Proposed wording
1163	Pomegranate	Sexual health in men. <u>Clarification provided</u> Helps maintain erectile function. Antioxidant activity helps increase intracavernous blood flow, improve erectile response and smooth muscle relaxation.	Helps to maintain a healthy prostate. Contributes to healthy sexual function in men.
	<p>Conditions of use</p> <ul style="list-style-type: none"> - The product must contain at least the equivalent of 240 mL pomegranate juice or 330 mg of punicalagin or 33 mg of ellagic acid. - 300 ml daily - 300 ml ημερησίως There are no documented limits for the effective ingredients. Due to inadequate data, pregnant women, nursing women, patients over antidepressant medicines (Mirtazapine), antipsychotic medicines (Risperidone, Ketiapine), statines medicines (Simvastatine, atorvastatine), antihypertensive medicines should take doctor's advice (relative contra-indication). There are no documented upper limits in the consumption of pomegranate juice. Time that a result is seen cannot be clarified yet. Interaction only with medicines referred (after doctor's advice) Process method cannot affect the effective ingredients. 		

ID	Food or Food constituent	Health Relationship	Proposed wording
1201	Pomegranate juice	Oxidative stress control	Pomegranate juice: plays an important antioxidative function; supports the cardiovascular system.
	Conditions of use <ul style="list-style-type: none"> - 50 mL per day (over 14 days); increased antioxidative capacity in plasma; decreased LDL peroxidation. - 250 mg / day fruit extract with 200 mg polyphenol content or 50 mL pomegranate fruit juice. 		
ID	Food or Food constituent	Health Relationship	Proposed wording
1319	Pomegranate Juice - phenolic compounds (anthocyanins, tannines, ellagic acid)	Antioxidant activity. Target group: humans of all ages. Excluded group: due to inadequate data, pregnant women, nursing women, patients over antidepressant medicines (Mirtazapine), antipsychotic medicines (Risperidone, Ketiapine), statines medicines (Simvastatine, atorvastatine), antihypertensive medicines should take doctor's advice (relative contra-indication).	With powerful antioxidant properties.
	Conditions of use <ul style="list-style-type: none"> - 300 mL daily - There are no documented limits for the effective ingredients. Due to inadequate data, pregnant women, nursing women, patients over antidepressant medicines (Mirtazapine), antipsychotic medicines (Risperidone, Ketiapine), statines medicines (Simvastatine, atorvastatine), antihypertensive medicines should take doctor's advice (relative contra-indication). There are no documented upper limits in the consumption of pomegranate juice. Time that a result is seen cannot be clarified yet. Interaction only with medicines referred (after doctor's advice) Process method cannot affect the effective ingredients. 		
ID	Food or Food constituent	Health Relationship	Proposed wording
1320	Pomegranate Juice - phenolic compounds (anthocyanins, tannines, ellagic acid)	Fights factors which cause atherosclerosis. Target group: humans of high risk of vessel atheromatoses. Excluded group: due to inadequate data, pregnant women, nursing women,	Helps maintain the cholesterol and lipids levels.

		patients over antidepressant medicines (Mirtazapine), antipsychotic medicines (Risperidone, Ketiapine), statines medicines (Simvastatine, atorvastatine), antihypertensive medicines should take doctor's advice (relative contra-indication).	
<p>Conditions of use</p> <p>- 300 mL daily - There are no documented limits for the effective ingredients. Due to inadequate data, pregnant women, nursing women, patients over antidepressant medicines (Mirtazapine), antipsychotic medicines (Risperidone, Ketiapine), statines medicines (Simvastatine, atorvastatine), antihypertensive medicines should take doctor's advice (relative contra-indication). There are no documented upper limits in the consumption of pomegranate juice. Time that a result is seen cannot be clarified yet. Interaction only with medicines referred (after doctor's advice) Process method cannot affect the effective ingredients.</p>			
ID	Food or Food constituent	Health Relationship	Proposed wording
1901	<p>Polyphenols and vitamins from pomegranate extract</p> <p><u>Clarification provided</u></p> <p>Pomegranate extract (amber liquid, pH 2.8) containing polyphenols and vitamins from pomegranate fruit, namely: vitamins B₁, B₂, C, niacin; tannins: hydrolysable tannins punicalagins and ellagitannins; ellagic acid.</p>	Antioxidant and anti - ageing properties	<p>Makes smoother and softer skin.</p> <p>Diminishes appearance of fine lines and wrinkles.</p> <p>Increases skin hydration and suppleness.</p> <p>Gives skin wellness and youthful appearance.</p> <p>Stimulates cell repair.</p>
<p>Conditions of use</p> <p>- 0,5 g/day.</p>			
ID	Food or Food constituent	Health Relationship	Proposed wording
2107	<p>Punica granatum</p> <p>(Common Name : Pomgranade)</p>	Cardiovascular health	<p>Contributes to a healthy cholesterol level and healthy blood vessels / antioxidants of pomegranate can be helpful for a healthy heart and arteries / antioxidants of pomegranate can help cells and arteries in their physiological function.</p>
<p>Conditions of use</p> <p>- owoc/ równowartość 50-240 mL soku z granatu lub 78-330 mg.</p> <p>- Fruit / The equivalent of 50-240 mL pomegranate; juice or 78-330 mg punicalagin.</p>			

ID	Food or Food constituent	Health Relationship	Proposed wording
2122	Punica granatum FRUIT & SEED	Digestion	Helps stimulate appetite. Helps stimulate appetite without problem for people with tendency to acid stomach. Helps maintain the integrity of the lining of stomach and intestines.
			<p>Conditions of use</p> <ul style="list-style-type: none"> - Fresh fruit ad libendum . Dried fruit powder 1.5-0.1 g/day.
ID	Food or Food constituent	Health Relationship	Proposed wording
2123	Punica granatum FRUIT & SEED	Antioxidant & immunity	Has significant antioxidant properties. Supports immunity.
			<p>Conditions of use</p> <ul style="list-style-type: none"> - Fresh fruit ad libendum. Dried fruit powder 1.5-0.1 g/day. - Fruit / Consommation traditionnelle dans le cadre d'une alimentation normale / 2 g de fruit par jour ou l'équivalent en jus.
ID	Food or Food constituent	Health Relationship	Proposed wording
2167	VitaGranate® Pomegranate Extract 40 % Ellagic Acid	<p>Excellent source of healthy fruit polyphenols known to help in the management of heart health.</p> <p><u>Clarification provided</u></p> <p>VitaGranate® Pomegranate Extract is an excellent source of ellagic acid that promotes healthy PSA (Prostate Specific Antigen) levels associated with prostate health.</p>	VitaGranate® Pomegranate Extract is an excellent source of pomegranate polyphenols, compounds that have been associated with the maintenance of cardiovascular health.
			<p>Conditions of use</p> <ul style="list-style-type: none"> - 100 to 600 mg daily recommended intake, which provides 40 to 240 mg polyphenols.
ID	Food or Food constituent	Health Relationship	Proposed wording
4471	Punica granatum-fruits-Punicaceae-Dadhima-Pomegranate	Glucose Metabolism	help to maintain a normal glucose level.
			<p>Conditions of use</p> <ul style="list-style-type: none"> - the equivalent of 4 g herb powder per day.

GLOSSARY AND ABBREVIATIONS

AAPH	2,2'-azobis-2-amidinopropane hydrochloride
DNA	Deoxyribonucleic acid
ED	Erectile dysfunction
Fe-NTA	Ferric nitrilotriacetate
GAE	Gallic acid equivalents
GAQ	Global Assessment Questionnaires
HDL	High-density lipoproteins
HMDM	Human Monocytes-derived macrophages
IIEF	International Index of Erectile Function
LDL	Low-density lipoproteins
NIDDM	Non-insulin dependent diabetes mellitus
PON1	Paraoxonase 1
PSA	Prostate-specific antigen
ROS	Reactive oxygen species
SH	Sulphydril group
TBARS	Thiobarbituric acid reactive substances