REPÚBLICA PORTUGUESA

DEFINIÇÃO DE FRONTEIRAS ENTRE MEDICAMENTOS E SUPLEMENTOS ALIMENTARES

PARECER ARGININA

Divisão de Comunicação e Informação - 2017

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OIPM

Definição de fronteiras entre medicamentos e suplementos alimentares

Parecer Arginina

Enquadramento

A arginina (ácido 2-amino-5-guanidopentanoico – Fig. 1) é um aminoácido básico natural, tendo sido isolada, pela primeira vez, a partir de plântulas de tremoço em 1886 (Patel *et al*., 2017).

A sua ocorrência em proteínas de mamíferos foi descoberta 9 anos mais tarde, em 1895, por Hedin (Böger e Bode-Böger, 2001).

Estudos relativos às suas funções e estrutura bioquímica tiveram início por volta de 1930 e, desde essa altura, a L-arginina (forma fisiologicamente activa) tem sido descrita como estando envolvida em numerosos processos metabólicos e vias bioquímicas (Patel *et al*., 2017).

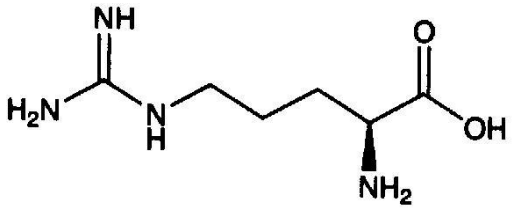

Figura 1

A arginina é um aminoácido "semi-essencial" ou "condicionalmente essencial", o que significa que, na maioria das circunstâncias, a síntese endógena pelo corpo humano é suficiente. O consumo médio alimentar de arginina é 5-7 g/dia (Patel *et al.*, 2016). Contudo, em certas condições (ex. períodos de stress traumático ou metabólico) podem ser produzidas quantidades insuficientes para satisfazer as necessidades fisiológicas (Patel *et al.*, 2016). Em condições normais, a produção diária endógena de 15-20 g ocorre via eixo intestinal-renal da citrulina (Barbul e Uliyargoli, 2007).

A bioquímica da arginina é complexa e envolve muitos processos metabólicos chave e sistemas de órgãos (Evoy *et al*., 1998). A arginina está envolvida na produção de uma variedade de enzimas, hormonas e proteínas estruturais e facilita a libertação da

hormona do crescimento, da insulina, do glucagon e da prolactina. É um componente da hormona vasopressina, produzida pela glândula pituitária e é o precursor fisiológico de diversos compostos biológicos tais como o óxido nítrico, poliaminas, prolina, glutamato, creatina, agmatina e ureia. Como estimulante imunitário, a arginina atua ao nível do timo, promovendo a produção de linfócitos. A arginina tem efeito positivo na circulação cerebral e na circulação sistémica (Gad, 2010).

As concentrações plasmáticas normais de arginina são, aproximadamente, 80 a 120μM; as concentrações intracelulares são ainda superiores, até 1 mM (Gad, 2010).

Segundo estudos publicados, a L-arginina tem sido bem tolerada quando administrada oralmente em doses ≤ 30 g, sendo os efeitos adversos mais relatados náuseas e vómitos, não tendo sido notificadas alterações da função renal, glicémia, ou de electrólitos no plasma (Gad, 2010).

De referir que, dado que a L-arginina poder baixar a pressão sanguínea, medicamentos antihipertensores podem interagir com a L-arginina, causando uma quebra brusca da pressão sanguínea. Medicamentos que aumentem o fluxo sanguíneo para o coração (nitratos) podem, também, interagir com a L-arginina causando tonturas. Medicamentos contendo sildenafil podem interagir com a L-arginina (VKM, 2016).

Em Portugal existem medicamentos autorizados contendo arginina na sua composição. As indicações terapêuticas para os quais foram autorizados são: Estados de astenia (fadiga) de causa identificada (física, psíquica ou sexual), Fadiga sexual primária; - Perturbações do sono; Fadiga física do desportista, da grávida, estados de convalescença médica e cirúrgica; Fadiga intelectual. São medicamentos que contêm, na sua composição, 500 mg de aspartato de arginina, sendo que a posologia proposta corresponde a uma dose diária de arginina de 1700 mg.

Utilização de arginina em suplementos alimentares

As alegações de saúde relativas à arginina submetidas à EFSA para avaliação, ao abrigo do artigo 13(1) do Regulamento (CE) nº 1924/2006 relativo às alegações nutricionais e de saúde sobre os alimentos, de 30 de dezembro de 2006, foram alvo de avaliação

negativa por parte da EFSA (Anexo I), pelo que não há quaisquer alegações de saúde aprovadas para esta substância.

Da análise do exposto, considera-se que os suplementos alimentares não devem ter teores de arginina superiores a 1250 mg (toma diária).

Neste contexto, a DGAV só aceitará notificações de suplementos alimentares contendo arginina, com teores que correspondam a tomas diárias iguais ou inferiores a 1250 mg e não se destinem a crianças.

Suplementos alimentares que não obedeçam a estas características mas que tenham sido devidamente notificados até à data de publicação deste documento, podem ser comercializados até ao limite das suas existências, quer se encontrem já colocados no mercado, quer venham ser produzidos até dia 30 de junho.

A ASAE enquanto autoridade com competência para a fiscalização do cumprimento das normas do Decreto-Lei nº 136/2003, de 28 de junho e suas alterações, relativos aos suplementos alimentares, procederá em conformidade.

Data de Publicação

10-01-2017

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- Regulamento (UE) nº 536/2013, de 11 de Junho de 2013, que estabelece uma lista de alegações de saúde permitidas relativas a alimentos que não referem a redução de um risco de doença ou o desenvolvimento e a saúde das crianças.
- VKM. 2016. Risk assessment of other substances. – L-arginine and arginine alpha - ketoglutarate. Opinion of the panel of nutrition, dietetic products, Novel Food and Allergy of the Norwegian Scientific Committee for Food Safety, ISBN: 978-82-8259-197-3., Oslo, Norway.

Anexo I - Alegações de saúde

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference / Journal reference	Commission Regulation	Status	Entry Id
Art.13 (1)	Arginine	Acide aminé régulateur du cortisol, médiateur du stress.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food is not sufficiently defined to be able to be assessed and the claim could not therefore be substantiated	"Système nerveux"	2011;9(4) :2051		Non-authorised	608
Art.13 (1)	Arginine	Conditionally-essential amino acid that plays an important role in the growth and immune system. It supports tissue growth acceleration.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food is not sufficiently defined to be able to be assessed and the claim could not therefore be substantiated.	"Immune system functions"	2011;9(4) :2051		Non-authorised	455
Art.13 (1)	Arginine	Essential amino acid that plays an important role in the immune system.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food is not sufficiently defined to be able to be assessed and the claim could not therefore be substantiated.	"Immune system functions"	2011;9(4) :2051		Non-authorised	1713
Art.13 (1)	Arginine	It has positive effects on muscle integrity and on haematopoiesis (for red blood cells building)	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Normal red blood cell formation	2011;9(4) :2051		Non-authorised	456
Art.13 (1)	Arginine	It has positive effects on muscle integrity and on haematopoiesis (for red blood cells building)	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	growth or maintenance of muscle mass	2011;9(4) :2051		Non-authorised	456
Art.13 (1)	Arginine	It has positive effects on muscle integrity and on haematopoiesis (for red blood cells building).	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Normal red blood cell formation	2011;9(4) :2051		Non-authorised	1712
Art.13 (1)	Arginine	It has positive effects on muscle integrity and on haematopoiesis (for red blood cells building).	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	growth or maintenance of muscle mass	2011;9(4) :2051		Non-authorised	1712
Art.13 (1)	Arginine	Support of normal blood circulation	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Improvement of endothelium-dependent vasodilation	2011;9(4) :2051		Non-authorised	1443
Art.13 (1)	Arginine	Support of normal blood circulation	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this	Maintenance of normal blood pressure	2011;9(4) :2051		Non-authorised	1443

			claimed effect for this food has not been substantiated.					
Art.13 (1)	Arginine	Support of normal blood circulation	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated	Normal red blood cell formation	2011;9(4) :2051		Non-authorised	1443
Art.13 (1)	Arginine	Arginine can contribute to the maintenance of the healthy blood circulation. Clarification provided Arginine can contribute to the maintenance of the healthy blood circulation. Arginine can contribute to the maintance of the normal blood circulation, such as the healthy blood pressure and the haematopoiesis.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Improvement of endothelium-dependent vasodilation	2011;9(4) :2051		Non-authorised	664
Art.13 (1)	Arginine	Arginine can contribute to the maintenance of the healthy blood circulation. Clarification provided Arginine can contribute to the maintenance of the healthy blood circulation. Arginine can contribute to the maintance of the normal blood circulation, such as the healthy blood pressure and the haematopoiesis.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Maintenance of normal blood pressure	2011;9(4) :2051		Non-authorised	664
Art.13 (1)	Arginine	Arginine can contribute to the maintenance of the healthy blood circulation. Clarification provided Arginine can contribute to the maintenance of the healthy blood circulation. Arginine can contribute to the maintance of the normal blood circulation, such as the healthy blood pressure and the haematopoiesis.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Normal red blood cell formation	2011;9(4) :2051		Non-authorised	664
Art.13 (1)	Arginine	L-arginine helps to induce and improve erection.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Maintenance of normal erectile function	2011;9(4) :2051		Non-authorised	649
Art.13 (1)	Arginine	L-arginine influence positively on spermatogenesis (sperms formation and mobility).	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Contribution to normal spermatogenesis	2011;9(4) :2051		Non-authorised	650
Art.13 (1)	Arginine	Power for muscles. Increases nitric oxide production.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food is not sufficiently defined to be able to be assessed and the claim could not therefore be substantiated.	"Physical performance and condition"	2011;9(4) :2051		Non-authorised	1820
Art.13 (1)	Arginine	Contributes to the synthesis of creatinine and nitric oxide, with important role in dilatation and relaxation of blood vessels.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Improvement of endothelium-dependent vasodilation	2011;9(4) :2051		Non-authorised	4680
Art.13 (1)	Arginine	Helps the organism to maintain and to recover after prolonged physical effort. / Helps in muscular atrophy. / Invigorator of the muscle mass. / Helps in the harmonious growth and development of the young organisms. / Helps to stimulate the production of Human Growth Hormone. / Helps in the	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	growth or maintenance of muscle mass	2011;9(4) :2051		Non-authorised	4681

		development of the muscle mass.						
Art.13 (1)	Arginine	Helps to improve blood circulation on pelvic level. / Helps protein synthesis and cellular replication with important role in the spermatogenesis process.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Contribution to normal spermatogenesis	2011;9(4):2051		Non-authorised	4682
Art.13 (1)	Arginine	Helps to improve blood circulation on pelvic level. / Helps protein synthesis and cellular replication with important role in the spermatogenesis process.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Maintenance of normal erectile function	2011;9(4):2051		Non-authorised	4682
Art.13 (1)	Arginine	Interferes in the ureogenesis, helping the elimination of ammonia.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, no conditions of use to accompany this claim could be defined.	Maintenance of normal ammonia clearance	2011;9(4):2051		Non-authorised	4683
Art.13 (1)	Vitamins, minerals, lysine and/or arginine and/or taurine (Pharmaton Kiddi)	It helps to support an adequate vitamins/minerals/lysine supplementation in children, in case of unbalanced or insufficient nutrition To support a healthy growth and development in children. When a child is recovering from illness, or has a loss of appetite.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this food is not sufficiently characterised for a scientific assessment of this claimed effect and the claim could not therefore be substantiated.	not validated	2011;9(4):2083		Non-authorised	6
Art.13 (1)	Vitamins, minerals, lysine and/or arginine and/or taurine (Pharmaton Kiddi)	When a child is recovering from illness, or has a loss of appetite, Pharmaton Kiddi provides important vitamins, minerals. These are important for developing and supporting proper immune system functions.	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this food is not sufficiently characterised for a scientific assessment of this claimed effect and the claim could not therefore be substantiated.	not validated	2011;9(4):2083		Non-authorised	1676
Art.13 (1)	Vitamins, minerals, lysine and/or arginine and/or taurine (Pharmaton Kiddi)	scientifically proven to support attention and mental performance	Non-compliance with the Regulation because on the basis of the scientific evidence assessed, this food is not sufficiently characterised for a scientific assessment of this claimed effect and the claim could not therefore be substantiated.	not validated	2011;9(4):2083		Non-authorised	1677