Innovation, Sciences et Développement économique Canada
Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 2978366 C 2023/03/21

(11)(21) **2 978 366**

(12) **BREVET CANADIEN**
CANADIAN PATENT

(13) **C**

(86) Date de dépôt PCT/PCT Filing Date: 2016/03/01
(87) Date publication PCT/PCT Publication Date: 2016/09/09
(45) Date de délivrance/Issue Date: 2023/03/21
(85) Entrée phase nationale/National Entry: 2017/08/31
(86) N° demande PCT/PCT Application No.: EP 2016/054272
(87) N° publication PCT/PCT Publication No.: 2016/139188
(30) Priorité/Priority: 2015/03/02 (NL2014381)

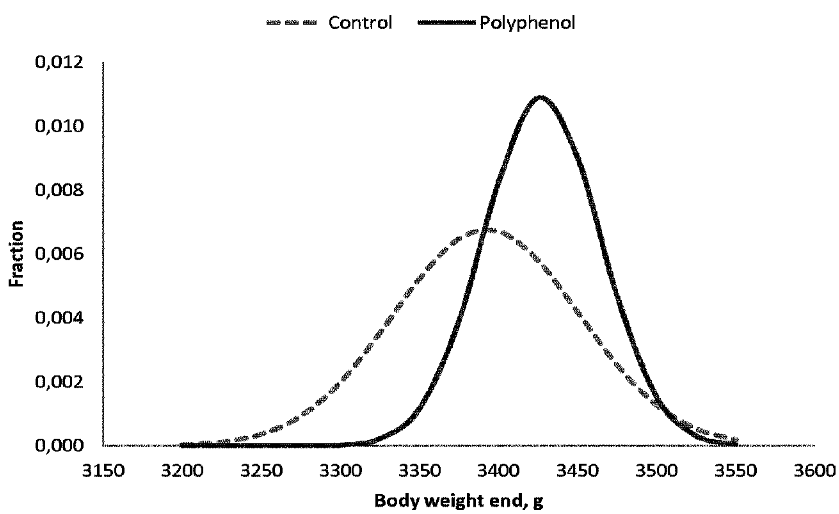
(51) Cl.Int./Int.Cl. *A23K 50/30* (2016.01), *A23K 20/111* (2016.01), *A23K 50/75* (2016.01)

(72) Inventeurs/Inventors:
ESCOBAR, SANDRA PATRICIA PAREDES, NL;
VAN KEMPEN, THEO A.T.G., NL

(73) Propriétaire/Owner:
NUTRECO NEDERLAND B.V., NL

(74) Agent: GOWLING WLG (CANADA) LLP

(54) Titre : UTILISATION DE POLYPHENOL POUR DIMINUER UN RETARD DE CROISSANCE
(54) Title: USE OF A POLYPHENOL FOR DECREASING GROWTH RETARDATION



(57) Abrégé/Abstract:
The present invention pertains to the use of a polyphenol as an additive in food for decreasing a growth retardation of an animal by feeding the animal with the said food. The invention also pertains to the use of a polyphenol as an additive in food for decreasing the weight variation in a herd of healthy animals by feeding these animals with the said food.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 September 2016 (09.09.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/139188 A1

(51) International Patent Classification:
A23K 50/30 (2016.01) *A23K 50/75* (2016.01) *A23K 20/111* (2016.01)

(21) International Application Number: PCT/EP2016/054272

(22) International Filing Date: 1 March 2016 (01.03.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2014381 2 March 2015 (02.03.2015) NL

(71) Applicant: **NUTRECO NEDERLAND B.V.** [NL/NL]; Veerstraat 38, 5831 JN Boxmeer (NL).

(72) Inventors: **ESCOBAR, Sandra Patricia Paredes**; Petuniastraat 24, 6663 DR Lent (NL). **VAN KEMPEN, Theo A.T.G.**; Alaertslaan 5, 5801 DC Venray (NL).

(74) Agent: **JANSSEN, Paulus J. P.**; Saltshof 1504, 6604 EJ Wijchen (NL).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:
— *with international search report (Art. 21(3))*

(54) Title: USE OF A POLYPHENOL FOR DECREASING GROWTH RETARDATION

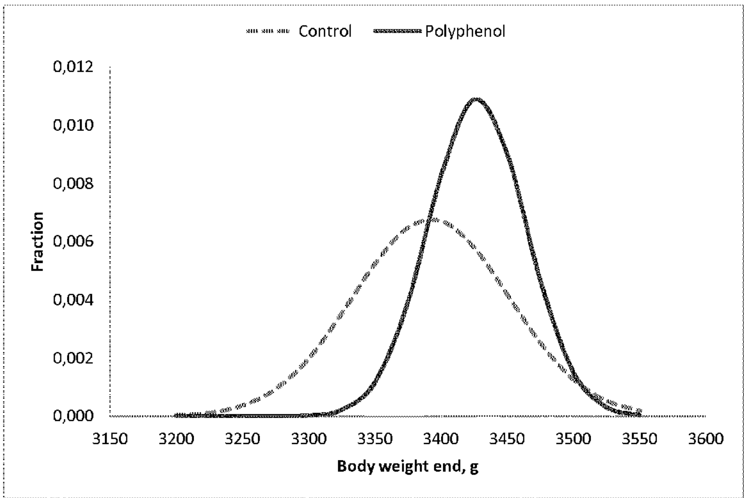


FIGURE 1

(57) Abstract: The present invention pertains to the use of a polyphenol as an additive in food for decreasing a growth retardation of an animal by feeding the animal with the said food. The invention also pertains to the use of a polyphenol as an additive in food for decreasing the weight variation in a herd of healthy animals by feeding these animals with the said food.

WO 2016/139188 A1

USE OF A POLYPHENOL FOR DECREASING GROWTH RETARDATION

GENERAL FIELD OF THE INVENTION

The present invention pertains to a method for decreasing a growth retardation of an animal. The invention also pertains to a method to arrive at a nutritional complete animal food for use in this method and the food itself.

BACKGROUND

Growth retardation (including intra uterine growth retardation) is a major concern in domestic animal production. Growth retardation appears to have a permanent stunting effect on growth during life. Often, an early small growth retardation even worsens during the lifespan of the animal, leading to a large variation of the end weight of the animals at their adult stage (in particular at slaughter). Fetal growth restriction may not only reduce neonatal survival, but may have an effect on the efficiency of feed/forage utilization. As such, even very early small growth retardation (in absolute weight) negatively affects postnatal growth throughout the life span of the animal, may negatively affect whole body composition and meat quality, and may impair long-term health and performance. Growth retardation is not the same as overall decreased growth performance for example due to ongoing infections with bacteria or parasites. Overall decreased growth performance in principle affects all animals in a herd, whereas growth retardation per definition does not affect the best growing animals in a herd. Decreased growth performance during infections can be easily treated by treating (optionally prophylactically) the underlying infection, for example using antibiotics or antiparasiticides. In contrast, since the underlying mechanisms of growth retardation are not yet well understood, treatment thereof is not straightforward. For example, animals may show a growth retardation due to an earlier infection. Although the infection is long gone, some animals still show less growth (weight increase) than other animals. The reason for this is not clear. Knowledge of the underlying mechanisms has important implications for the complete prevention of growth retardation and is crucial for enhancing the efficiency of livestock production and animal health by such prevention. This may ultimately provide a molecular mechanism for the role of maternal nutrition on fetal programming and genomic imprinting to prevent even the earliest growth retardation and its negative effects. Innovative interdisciplinary research in the areas of nutrition, reproductive physiology, and vascular biology will play an important role in designing the next generation of nutrient-balanced diets and developing new tools for livestock management that will enhance the efficiency of animal production and improve animal wellbeing. However, thus far no methods are available to completely prevent growth retardation in an animal.

OBJECT OF THE INVENTION

It is an object of the present invention to find a method for decreasing growth retardation in an animal such that the negative effects thereof are diminished instead of increased. In other words, it is an object to find a method that counteracts the normal physiological consequences of growth retardation, these normal consequences being at least an increase of the initial growth retardation.

SUMMARY OF THE INVENTION

In order to meet the object of the invention, a method as presented in the GENERAL FIELD OF THE INVENTION section here above has been devised, in which method a polyphenol is used as an additive in food for decreasing the growth retardation of the animal by feeding the animal with the said food. This invention can lead to a new nutritional complete animal food comprising a polyphenol, or a mixture of different polyphenols at a dose of 0.001 (one thousandth) -100,000 (one hundred thousand) mg polyphenol per kg of the food.

It was surprisingly found that by using a polyphenol as a feed additive, growth retardation, in particular a decreased growth that is not the direct result of an ongoing infection with a micro-organism or parasite, can be decreased. It is noted that this differs from the use of polyphenols as a general growth performance enhancer, since this would lead to an increase of growth of the whole population, *i.e.* even in animals that do not suffer from growth retardation. The effect of decreasing growth retardation has been established by feeding the test animals a nutritional over-complete food, to make sure that the animals can use their maximum growth capabilities without any nutritional restrictions. It was found that under such circumstances, a polyphenol cannot provide any general growth enhancing performance, but on the other hand, is capable of decreasing any existing growth retardation. Apparently, the physiological processes responsible for decreasing growth retardation differ from those responsible for normal growth. Still, the result of application of the present invention for any herd of healthy animals under circumstances of complete (not mal-) nutrition, is that, since the best growing animals under these circumstances do not show a weight increase, the weight variation within the herd decreases.

The use of a polyphenol to produce a nutritional complete animal food comprising the polyphenol at a dose of 0.001 -100,000 mg polyphenol per kg of the food, by mixing the polyphenol with an amount of carbohydrates, proteins and fats corresponding to the daily requirements hereof for the animal, can for example be practiced in a factory where nutritional complete animal food is produced. Here, the carbohydrates, proteins and fat are mixed in the right proportions with the polyphenol, forming a total amount that is at least enough to feed one animal for a day. Alternatively, the method can be practiced at a local food mixers', by mixing a pre-manufactured pre-mix containing the polyphenol (and optionally other constituents such as vitamins, minerals, anti-oxidants etc) with components that contain the required proteins, carbohydrates and fat. In another embodiment, a polyphenol premix is used as a top-dress for animal food at the site where the animals are actually fed. The present invention could also be used by providing the polyphenol as a separate supplement next to the food, for example in the form of a pill, via injection etc.

It is noted that the use of certain diets or feed additives in order to influence growth retardation is known from the prior art. For example, Tummaruk et al. describe in "*The use of herbal medicine as an alternative antimicrobial in the feed of post-weaning piglets: A field trial*", *Journal of Applied Animal Science*, Vol. 2, No. 3, September-December 2009, pp 25-31, that the use of the polyol compound colistin or the phenoxy compound berberine lead to lower retarded growth when compared with the use of the phenol compound halquinol. Lima et al. in the *FASEB Journal*, Vol. 28, No. 1, Supplement 1033.8 ("Effects of methylating vitamins and docosahexaenoic acid supplementation on intra-uterine growth retardation in a feed-restricted swine model") propose to use vitamins and docosahexanoic acid as feed additive to reduce growth retardation in mal-nourished piglets.

It is also noted that the anti-infective activity of polyphenols is known in the art. WO 2008/155393 and US2008/0160000 described the use of polyphenols to treat an infection with coccids in chickens. As a result, the overall growth performance of the chickens increases. The effect on growth retardation, in particular a decreased growth not due to an infection, is not known from these documents.

Lippens et al in Arch.Geflügelk., **69**(6). S.261-266, 2005 ("*Effect of the use of coated plant extracts and organic acids as alternatives for antimicrobial growth promoters on the performance of broiler chickens*"), described the use of essential oils as antimicrobials as an alternative for regular antibiotics that are commonly used as overall growth promotors, also known as AGP's (antimicrobial growth promoters). In such cases, the treatment inherently also affects the heaviest animals in the herd, showing as an increased overall growth. Moreover, as indicated here above, Lippens uses essential oils in his research. None of the used compounds listed in the Lippens publication fall within the commonly accepted definition of polyphenols (see below).

DEFINITIONS

A *polyphenol*, also known as a polyhydroxyphenol, is a compound that belongs to the structural class of natural organic chemicals, typically derived from the shikimate/phenylpropanoid and/or the polyketide pathway, featuring one or more phenolic units and deprived of nitrogen-based functions (see Quideau S "Why bother with polyphenols?", a short article published online in 2011 by the Groupe Polyphenols of the Université Bordeaux; http://www.groupepolyphenols.com/the-society/why-bother-with-polyphenols/), and its synthethic functional equivalents. By definition, the group of polyphenols exclusively consist of compounds that belong to either the flavonoids (isoflavones, flavones, flavonols, anthocyanins, flavanols, flavanones), or the non-flavonoid phenolic acids, stilbenes and lignans. For this see Spencer et al. in *British Journal of Nutrition* (2008), 99, 12-22 (in particular Fig. 1) as confirmed i.a. by Scalbert et al. in *Critical Reviews in Food Science and Nutrition*, 45:287-306 (2005).

A *plant polyphenol* is a natural polyphenol obtained from a plant.

The term *animal* includes non human animals such as animals belonging to the suidae, equidae, bovidae, aves (including chickens, ducks, quail and turkeys), fish and crustaceans (including crabs, lobsters, crayfish and shrimps).

A *feed additive* is a component added to the regular nutrients (i.e. the food) of an animal, in particular to its solid food or drinking water.

Growth retardation (also denoted as growth restriction) is the failure of an individual animal to develop a normal weight for his age under optimal growing conditions (i.e. without ongoing infections). Per definition, animals having a weight below average in a herd of healthy animals having a corresponding age, have a growth retardation.

A *dose of X ppm* of component Y in food means that the component Y is present at a level of X mg per kg of the food.

A *start up phase* of an animal is the phase wherein the animal reaches at maximum 20% of its final weight, i.e. the regular (mean) weight of a grown up animal, in particular at slaughter.

A *grower phase* of an animal is the phase wherein the animal weighs between 20% and 100% of its final weight.

A *nutritional complete animal food* is a blend of various food components comprising the total daily requirements of carbohydrates, proteins and fats for this animal, i.e. the carbohydrates, proteins and fats are present in proportions and amounts such that at a regular intake the food meets the said total daily requirements.

EMBODIMENTS OF THE INVENTION

In a first embodiment the polyphenol is a, preferably naturally derived, plant polyphenol. More than 8,000 polyphenolic compounds have been identified in various plant species.

All plant phenolic compounds arise from a common intermediate, phenylalanine, or a close precursor, shikimic acid. Primarily they occur in conjugated forms, with one or more sugar residues linked to hydroxyl groups, although direct linkages of the sugar (polysaccharide or monosaccharide) to an aromatic carbon also exist. Association with other compounds, like carboxylic and organic acids, amines, lipids and linkage with other phenol is also common.

A polyphenol according to the invention is chosen from the group that consists of phenolic acids, flavonoids, stilbenes and lignans (having different numbers of phenol rings that they contain and/or different structural elements that bind these rings to one another). Phenolic acids are further divided into hydroxyl benzoic and hydroxyl cinnamic acids. Phenolic acids account for about a third of the polyphenolic compounds in our diet and are found in all plant material, but are particularly abundant in acidic-tasting fruits. Caffeic acid, gallic acid, ferulic acid are some common phenolic acids. Flavonoids are the most abundant polyphenols in human diet and share a common basic structure consisting of two aromatic rings, which are bound together by three carbon atoms that form an oxygenated heterocycle. Biogenetically, one ring usually arises from a molecule of resorcinol, and other ring is usually derived from the shikimate pathway. Stilbenes contain two phenyl moieties connected by a two carbon methylene bridge. Most stilbenes in plants act as antifungal phytoalexins, compounds that are synthesized only in response to infection or injury. The most extensively studied stilbene is resveratrol. Lignans are diphenolic compounds that contain a 2,3-dibenzylbutane structure that is formed by the dimerization of two cinnamic acid residues.

In yet another embodiment the polyphenol is chosen from the group of flavan-3-ol, flavanone, flavonolignan, stilbene and caffeic ester.

In still another embodiment the polyphenol is used at a dose between 1 ppb and 100,000 ppm. This means that the animal food contains between 0.001 and 100,000 mg per kg of the food, in particular any value between 0.001 and 100,000 ppm, such as 0.001, 0.002, 0.003 ……0.999, 1, 2, 3, 4, 5, 6, 7, 9, ……. 99993, 99994, 99995, 99996, 99997, 99998 and 99999 ppm (any intermediate integer in this range being explicitly disclosed herewith). The lower limit, in particular when being at the level of at least 0.1 ppm, is in the range found to have a significant effect according to the invention, while the upper limit (i.e. up to 10% in mass) is the level found in some rich-in-polyphenol content materials such as concentrated grape juice.

In again another embodiment the polyphenol is used at a dose between 0.1 and 5000 ppm, in particular between 0.1 and 400 ppm, in particular between 1 and 300 ppm, in particular between 1 and 250 ppm.

The polyphenol can be used during the start up and/or grower phase of the animal. In an embodiment the polyphenol is used during at least seven days. In particular, the polyphenol is used during the entire start up and/or grower phase of the animal.

Instead of one single polyphenol, multiple different polyphenols can be used in the feed additive. In particular when the polyphenol is derived from a natural plant, often a mixture of polyphenols is derived from this plant. Although each polyphenol may be purified and used as such, also the mixture derived from the plant, or any other mixture of polyphenols, may be used according to the invention.

The invention will now be explained in more detail using the following examples.

EXAMPLES

Example 1 describes a first experiment with a polyphenol as feed additive, in this case in chickens.
Example 2 describes a next experiment in chickens.
Example 3 describes an experiment in piglets early in the start up phase.
Example 4 describes an experiment in piglets late in the start up phase.
Example 5 describes an experiment with piglets in the grower phase.

Example 1

Example 1 describes a first experiment with a polyphenol as feed additive, in this case in chickens. A polyphenol was added to the diet (i.e. the food) of broilers for a period of 7 days starting at the age of 37 days. The animals were present in 33 pens divided over two rooms with 30 (room A) or 36 (room B) birds per pen. 22 of these pens were used as a control, 11 were used for the treatment divided over both rooms. The starting

weight of the animals was approximately 2700g.
The control animals received a commercial diet, 10% over formulated to assure that the animals could express their full genetic growth potential. The test group animals received the same diet supplemented with 175 ppm of flavan-3-ol.

Feed intake was approximately 210g per animal per day. The animals fed with the food containing the polyphenol blend were slightly heavier (3427 vs. 3392g) although this did not represent a significant increase. There was however a significant interaction between starting body weight and treatment: birds fed with the polyphenol blend responded strongly to the treatment when they suffered from a growth retardation (low starting body weight), while effectively no response was seen when the starting body weight was high. As a consequence, a narrower weight distribution (a smaller variation) was seen in the polyphenol treated group. The results are indicated below in Table 1 and presented graphically in Figure 1.

Table 1 Weight range covering 95% of the population, mean and standard deviation in g

	Mean	Stdev	Mean -2 stdev	Mean +2 stdev
Control	3392	59	3274	3510
Polyphenol	3427	37	3354	3500

In this trial the variation was notably decreased from 59 grams to 37 grams. This was mainly due to the growth retarded animals showing a decrease in growth retardation during the treatment (the heaviest animals in the control and treatment group ending at about the same weight).

Example 2

Example 2 describes a next experiment in chickens. Introduction: A polyphenol was added to the diet of broilers for a period of 9 days starting at the age of 27 days. The animals were divided over 29 pens with 66 birds each. 16 of these pens were control pens, 13 were used for the treatment. The starting weigh of the animals was approximately 1600 g. The animals were treated with the polyphenol enriched food for 9 days. The control food was a commercial diet, over formulated by 10% to assure that birds could express their full genetic potential. The test group received the same diet supplemented with 22, 45, 68 or 90 ppm of flavan-3-ol (equally divided over the pens).

The feed intake averaged 101 g per animal per day. Animals fed the polyphenol blend were marginally heavier (2502 vs. 2488g) on day 36. There was an interaction between starting body weight and treatment: birds fed with the polyphenol blend responded strongly to the treatment when the starting body weight was low, while only a modest response was seen when the starting body weight was high. As a consequence, a narrower weight distribution and slightly shifted to the right was seen in the polyphenol group. See Table 2 below (data of the four polyphenol groups are combined).

Table 2 Weight range covering 95% of the population, mean and standard deviation in g

	Mean	Stdev	Mean -2 stdev	Mean +2 stdev
Control	2488	34	2420	2556
Polyphenol	2502	26	2450	2555

In this trial the variation was notably decreased from 34 grams to 26 grams. This was mainly due to the growth retarded animals showing a decrease in growth retardation during the treatment (the heaviest animals in the control and treatment group, i.e. the “mean + 2 stdev” animals, ending at about the same weight).

Example 3

Example 3 describes an experiment with piglets early in the start up phase. A polyphenol blend was added to the diet of nursery piglets having an age of 20 days for a period of 40 days as a partial substitute for Vit. E (kept at least at a level meeting the 2012 NRC recommendations for Vit. E in each instance). The animals were kept in 28 pens with 12 piglets each of equal age but sorted based on body weight. The starting weight was approximately 5.7 kg.

The control group received a nutritional complete food (a so called three-phase diet formulated to exceed the nutritional requirements) comprising 65 ppm Vit. E during the first 18 days, and 40 ppm Vit. E from days 19-40. The test group received the same nutritional complete food supplemented with 16 ppm Vit. E and 0.7 ppm of a polyphenol blend during the first 18 days, and 11 ppm Vit. E plus 0.4 ppm of the polyphenol blend from days 19-40 (test diets are thus formulated to meet at least the 2012 NRC recommendations for Vit. E. As is commonly known, high levels of Vitamine E are good for decreasing weight variation in the herd (see Van Enckevort et al. in *Tijdschrift voor Diergeneeskunde*, Deel 128, Februari, Aflevering 3, 2003), it was expected that lowering the amount in the control group would lead to a natural increase of weight variation. The polyphenol blend contained 38.9% flavanone, 39.9% flavonolignan, 5.2% stilbene and 16% caffeinic ester.

The daily feed intake was approximately 34 g/kg body weight. The animals fed with the polyphenol blend were numerically 0.65 kg heavier on day 40. Notably, despite receiving less Vit. E, this group was substantially more homogeneous with a coefficient of variation (CV) of 7.6% vs. 11.6% for the controls. This shift appeared to be caused mainly by more rapid growth of the growth retarded animals without a significant impact on the growth of the heavier animals, completely in line with the results seen in chickens. The results are given in table 3.

Table 3 Weight range and standard deviation in kg

	Mean	Stdev	Mean -2 stdev	Mean +2 stdev
Control	14.6	1.7	11.2	18.0
Polyphenol	15.2	1.2	12.9	17.6

Example 4

Example 4 describes an experiment in piglets late in the start-up phase. A polyphenol blend was added to the diet of nursery piglets for a period of 9 days as a substitute for Vit. E. Seven days into the supplementation the piglets were heat-stressed for one day to try and induce (additional) growth retardation. 26 piglets (half barrows, half gilts) of equal age, having a weight of approximately 12 kg at 46 days at the start of the test period were used.
The control group received a single phase diet formulated to exceed the nutritional requirements, supplemented with 80 ppm Vit. E (common level, well above the 2012 NRC recommendations). The test group animals received the same diet supplemented

with 11 ppm Vit. E (at the NRC requirements for Vit. E) plus 2 ppm of the same polyphenol blend used in example 3.

The feed intake was approximately 3% of body weight. No substantial difference in mean weight at termination of the experiment was seen between the two treatment groups (p=0.71). The variation in weight, however, was 17.7% in the control group and 11.5% in the test group (receiving food supplemented with polyphenols).
The relationship between starting and final weight was also significantly different between the two treatment groups. This resulted in lighter test animals at the start of the trial growing relatively faster than control, while the opposite was seen for animals that entered the trial with a heavy starting weight. Data are given in table 4.

Table 4. Weight range covering 95% of the population, mean and standard deviation in kg

	Mean	Stdev	Mean -2 stdev	Mean +2 stdev
Control	16.1	2.9	10.4	21.8
Polyphenol	15.8	1.8	12.1	19.4

Example 5

Example 5 describes an experiment with piglets in the grower phase. Flavan-3-ol was added to the diet of finisher pigs at levels of 25, 100, or 400 ppm and performance was tracked over a 2 week period. For this experiment 264 gilts and barrows were used having a starting weight of 50-55 kg, approximately at 100 days of age. The animals were treated for a period of 2 weeks.
The control animals received a single phase diet formulated to exceed the nutritional requirements. The test animals received the same diet supplemented with 25, 100 or 400 ppm of the polyphenol. Sex interactions were not observed and removed before the final analysis. The results are indicated in table 5.

The feed intake averaged 2.1 kg/day. It appeared that the polyphenol blend in the food increased final body weight as well as average daily gain by increasing the growth of the lightest animals in the group: pigs starting the trial at only 45 kg responded linearly to treatment; with 440 ppm polyphenols they were 1.77 kg heavier than the controls at 14 days. In contrast, pigs starting the trial at 60 kg showed no clear treatment effect. As a consequence, the variation in body weight within the herd at day 14 was reduced.

Table 5 Mean body weight in kg, standard deviation and weight range covering 95% of the population at various polyphenol levels in the food.

	0 ppm	25 ppm	100 ppm	400 ppm
Mean	64.6	65.5	65.6	65.8
STD	6.7	6.7	6.3	5.6
Mean - 2xSTD	51.3	52.0	52.9	54.5
Mean + 2xSTD	77.9	79.0	78.3	77.1

What is claimed is:

1. Use of a flavan-3-ol as an additive in food for decreasing a growth retardation of an animal by feeding the animal with said food.

2. Use according to claim 1, wherein the flavan-3-ol is used at a dose between 1 ppb and 100,000 ppm.

3. Use according to claim 2, wherein the flavan-3-ol is used at a dose between 0.1 and 5000 ppm.

4. Use according to any one of claims 1 to 3, wherein the flavan-3-ol is used at a dose between 0.1 and 400 ppm.

5. Use according to any one of claims 1 to 4, wherein the flavan-3-ol is used during the start-up and/or grower phase of the animal.

6. Use according to any one of claims 1 to 5, wherein the flavan-3-ol is used during at least seven days.

7. Use according to any one of claims 1 to 6, wherein the flavan-3-ol is used during the entire start up and/or grower phase of the animal.

8. Use of a flavan-3-ol as an additive in food for decreasing the weight variation in a herd of healthy animals by feeding these animals with the said food.

9. Use according to any one of claims 1 to 8, wherein the animal belongs to the suidae family.

Date Reçue/Date Received 2022-05-09

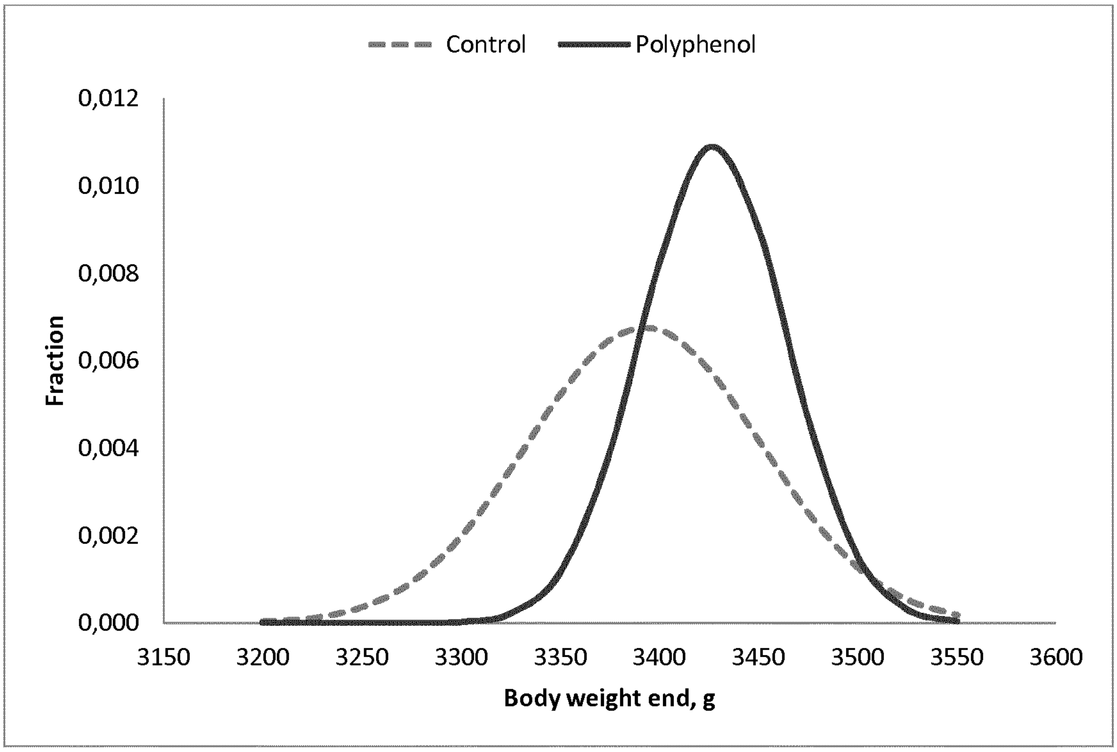
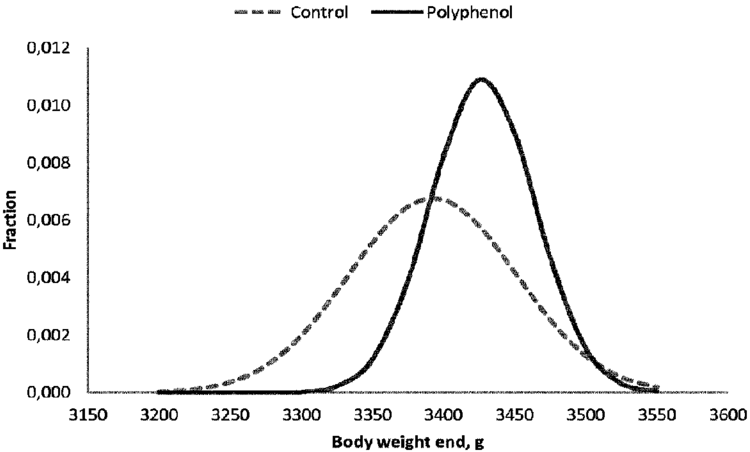

Control
Polyphenol
Fraction
0,012
0,010
0,008
0,006
0,004
0,002
0,000
3150
3200
3250
3300
3350
3400
3450
3500
3550
3600
Body weight end, g

FIGURE 1



Control
Polyphenol
0,012
0,010
0,008
0,006
0,004
0,002
0,000
Fraction
3150
3200
3250
3300
3350
3400
3450
3500
3550
3600
Body weight end, g