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<p>(54) Title: USE OF CREATINE AS ^{Feed additive} A FAT SUBSTITUTE As printed (54) Bezeichnung: VERWENDUNG VON KREATIN ALS FETTERZUSATZ (57) Abstract The invention relates to the use of creatine or creatine salts as a fat substitute to be given to breeding animals and feeder animals. The creatine or creatine salts are used as a substitute for flesh meal, fish meal and/or antimicrobial performance enhancers, growth hormones as well as anabolic agents. (57) Zusammenfassung Verwendung von Kreatin (Creatine) oder von Kreatinsalzen als Futterzusatz für Zucht- und Masttiere als Ersatz für Fleischmehl, Fischmehl und/oder antimikrobielle Leistungsförderer, Wachstumshormone, sowie Anabolika.</p>		

Use of creatine as feed additive

For decades, the use of meat and bonemeal, which consists of sanitized dried slaughtering waste, and also of dead animals including cattle and other ruminants, has been a general practice in feed rations for farm animals. After the occurrence of BSEs (bovine spongiform encephalopathies) in cattle, however, meat and bonemeal was banned as feed for ruminants. In pigs and other animals, comparable disease symptoms are known as TSEs (transmissible spongiform encephalopathies). Nevertheless, meat and bonemeal is considered harmless for pigs and poultry. However, the fear that these animals could be hosts and symptomless carriers of BSE- or TSE-specific structures, and the foods originating from them could have unwanted consequences on humans, had led to a widespread exclusion of meat and bonemeal from feed rations for pigs and poultry also.

However, for purely plant-based feeding, there are references according to which in the case of breeding animals and fatstock, as a result of deficiencies in constituents present in animal tissues, disadvantages must be expected.

Even in the case of usually prepared, for example boiled, slaughtering wastes and processed animal feed, the relatively low to absent creatine content, compared with fresh meat, is disadvantageous. In particular in the case of canned food, for example for cats and dogs, cooking the ingredients during food manufacture destroys the creatine content present in the fresh meat.

Creatine is a substance which has been known for more than a hundred years which is endogenous both in humans and animals, and is partly synthesized by the body itself or is taken up via the diet.

The importance of creatine in metabolism is at a cellular level, in that it forms a short-term energy

reserve and participates in energy transport (Wallimann et al., Biochem. J. 281, 21-40, 1992). The intake of creatine, in humans, leads to improved muscle performance with appropriate training. In the case of dogs also, in particular racing dogs, hunting dogs, etc., this effect has already been observed, as is described, for instance, in GB 2 300 103.

In addition, fewer and fewer antimicrobial growth promoters ("antibiotics") are being added as a feed additive to the feed of breeding animals and fatstock, but because of their absence in addition a greater sensitization of the animals to stresses of the digestive tract and the immune system are occurring.

Unexpectedly, it has now been found that not only does creatine lead to improved muscle performance in humans and animals, but the use of creatine in farm animals, in particular hens, pigs and salmon, can improve the performance of the animals, especially in the absence of feedstuffs of animal origin, such as meat and bonemeal or fishmeal.

The invention therefore relates to the use of creatine or creatine salts as feed additive for breeding animals and fatstock as a substitute for meat and bonemeal, fishmeal and/or antimicrobial growth promoters, growth hormones and anabolics.

Creatine is a substance which has long been known (The Merck Index, Eleventh Edition, No. 2570, 1989) and is commercially available or can easily be synthesized, for example, as described in Ullmann's Encyclopedia of Industrial Chemistry, 5th edition, volume A 12, 552, VCH-Verlagsgesellschaft, Weinheim (1987) or in US 2 654 779 by reacting cyanamide with sarcosine.

Other preparation variants are disclosed, for example, by EP-A-0754 679, which describes the reaction of cyanamide with sarcosinate.

The term creatine thus comprises the isolated form of naturally occurring creatine and chemically synthesized forms.

Creatine can be used as such or in the form of a salt. Suitable salts are, for example, creatine pyruvates of the general formula $(\text{creatine})_x(\text{pyruvate})_y(\text{H}_2\text{O})_n$, where $x = 1$ to 100 , $y = 1$ to 10 and $n = 0$ to 10 , which are described in WO 98/28263. Other suitable salts are the creatine salts disclosed by EP-A-0775 108, that is to say creatine citrate, creatine maleate, creatine fumarate, creatine tartrate or creatine malate, or the creatine ascorbates described in WO 98/38183 of the formula $(\text{creatine})_x(\text{ascorbate})_y(\text{H}_2\text{O})_n$, where $x = 1$ to 100 , $y = 1$ to 100 and $n = 0$ to 20 . Other suitable salts for the inventive use are also, for instance, creatine phosphorenylpyruvate, creatine succinates, creatine formates and creatine gluconates, potassium creatine, calcium creatine or sodium creatine, or creatine phosphate which is commercially available. In addition, cyclocreatine and other creatine analogs known from the literature also come into consideration. Mixtures of creatine with one or more of the abovementioned salts or mixtures of one or more of the abovementioned salts can also be used.

Creatine or its salts are used in animal feed as feed additive for the most varied animals and are thus used for the most varied types of feed.

The invention therefore also relates to the use of creatine or creatine salts as feed additive in predominantly plant-origin feed as a substitute for meat and bonemeal or fishmeal and/or antimicrobial growth promoters for improving meat quality, improving weight gain and percent muscle meat, improving the lean body mass index and embryo development, for increasing fertility of the mother animals, male fertility and survival rate of young animals, increasing the laying performance in poultry and lowering the infection rate. By using creatine as a feed additive, in poultry species, such as hens, ducks, geese and turkeys, a higher growth rate at the weight with decreased feed expenditure is achieved, in which case the time in

which the corresponding increase in weight is achieved is reduced in comparison with previously used feeding methods using meat and bonemeal and antimicrobial growth promoters. The increase in growth is produced
5 here by an increased percent protein ("increase in meat") and not by increased fattening of the animals, which produces an improvement in the lean body mass index. In addition, the addition of creatine makes the addition of growth hormones, other growth factors or
10 hormones or of hormone-like substances and also anabolics, which have previously been used to achieve an improved increase in meat, superfluous.

Other advantages in poultry feed supplementation by creatine or its salts are increased
15 egg laying performance of the hens, increase in fertility and in sperm production and sperm quality of the cocks, and a decreased infection rate due to an improved immune system.

The invention therefore relates to the use of
20 creatine or creatine salts as feed additive for poultry as a substitute for meat and bonemeal and/or antimicrobial growth promoters for increasing meat quality, improving weight gain and percent muscle meat, improving the lean body mass index, for increasing egg
25 laying performance of the hens, for increasing sperm production and sperm quality of the cocks and for lowering the infection rate.

In the case of pigs, the use of meat and bonemeal in feeding can also be entirely dispensed
30 with. Secondly, the addition of antimicrobial growth promoters, such as antibiotics, can also be avoided, since creatine also has growth-promoting properties in pigs. In addition, the inventive use of creatine or creatine salts achieves improved fertility of the
35 female animals, which is shown in an increase in cycles on heat and receptivity to pregnancy, as a result of which, inter alia, the number of piglets per litter is increased. Other advantages are improved embryo development by feeding the mother animals with creatine

or creatine salts, improved spermatogenesis in male breeding animals, and improved weight gain. The survival rates and thriving of the piglets during lactation as a result of creatine uptake via the milk
5 from the mother animal which is optimally supplied by creatine-supplemented feed and later by creatine supplementation of the young animals are increased. In addition, decrease in infection rate is achieved by an improved immune system.

10 The invention therefore also relates to the use of creatine or creatine salts as feed additive for pigs as substitute for meat and bonemeal and/or antimicrobial growth promoters for improving meat quality, improving weight gain and percent muscle meat,
15 improving the lean body mass index and embryo development, increasing the fertility of the mother animals and survival rate of the young animals, improving spermatogenesis, and lowering the infection rate.

In the case of breeding salmon, by using
20 creatine or creatine salts as feed additive, feeding can be performed on a predominantly plant-origin basis, as a result of which the consumption of fish meal, which is generally produced from small Pacific fish is substantially decreased. A further advantage is lowering
25 the infection rates due to an improved immune system.

The invention therefore further relates to the use of creatine or creatine salts as feed additive for breeding salmon as substitute for fishmeal and/or antimicrobial growth promoters.

30 Creatine or creatine salts can, however, also be added to the powdered milk replacer for growing calves, as a result of which milk constituents can be economized and an improved weight gain, improved meat quality, increase in lean body mass and a reduction in
35 the fat content of the calves is achieved, and also a lowering of the infection rate due to an improved immune system and improved feed utilization.

The use of creatine or creatine salts as additive for powdered milk replacer for growing calves

to improve the weight gain, to improve meat quality, to increase the lean body mass and to reduce the fat content of the calves, and to lower the infection rate and improve feed utilization is thus also a subject-matter of the invention.

5 A further possible use of creatine and creatine salts as feed additive is wet or canned food for dogs and cats, in which in the production process the creatine content originally present in the starting material is reduced.

10 In this case, firstly lowering of the infection rate due to an improved immune system is again achieved, and, in addition to the fact that the animals are livelier and stronger, the animals secondly have a significantly glossier coat.

15 Creatine or its salts can thus be added to the most varied types of feed. The following types of feed are suitable for the inventive addition: Feed meal administered dry or wet, pelleted feed, expanded feed, 20 extruded feed, feed flakes, powdered milk replacement, wet or canned food.

Creatine or its salts are added as dietary supplements to the feed mixture during production, that is to say before filling and packing in cans etc. 25 Another possibility is the addition after expansion or extrusion of the feed, and in pellet production. Creatine is added either in powdered form or in the case of water-soluble salts in the form of an aqueous solution.

30 The amount of creatine added to the feed preferably corresponds to the amount determined in dose-effect experiments or the amount determined on the basis of the creatine content present in fresh meat. If appropriate, twice to four times the amount can also be added.

35 The amounts of added creatine are dependent here on the animals to be fed, so that they can then be within a broad range. Preferred amounts of creatine are in the range of 1 to 50 g/kg, particularly preferably

from 1 to 5 g/kg of air-dry feed. The amount of feed administered should in this case preferably ensure a supply with 0.2 to 0.5 g of creatine per kg of metabolic body weight ($G^{0.75}$).

5 Creatine and its salts can if appropriate be added together with customary feed additives, such as fats, amino acids, minerals, trace elements, vitamins and flavorings.

10 Example 1:

The effect of addition of creatine in the feed for growing hens was studied.

15 It was found here that by adding 0.2% creatine (0.2 g/kg) to the air-dried feed for a growing period of 41 days, an increase in the final weight of 4% compared with previous feeding methods (without creatine addition) was achieved. This increase in weight was achieved only by increase in meat, but not
20 by increase in fat (improvement of lean body mass index), in which case the meat also had an improved quality.

The feed consumption decreased here by about 2-3% in comparison with previous feeding methods.

It is to be understood that a reference herein to a prior art document does not constitute an admission that the document forms part of the common general knowledge in the art in Australia.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. The use of creatine or creatine salts as feed additive for breeding animals and fatstock as a substitute for meat and bonemeal, fishmeal and/or antimicrobial growth promoters, growth hormones, and anabolics.

2. The use of creatine and/or creatine salts as claimed in claim 1 in predominantly plant-origin feed for improving meat quality, improving weight gain and percent muscle meat and/or improving the lean body mass index and/or embryo development and/or for increasing fertility of the mother animals and/or male fertility and/or survival rate of the young animals and/or increasing the laying performance in the case of poultry and/or lowering the infection rate.

3. The use of creatine and/or creatine salts as claimed in claim 1 for poultry for increasing meat quality, improving weight gain and percent muscle meat and/or improving the lean body mass index and/or for increasing the egg laying performance of the hens and/or for increasing sperm production and sperm quality of the cocks and/or for lowering the infection rate.

4. The use of creatine and/or creatine salts as claimed in claim 1 for pigs for improving the meat quality, improving weight gain and percent muscle meat and/or improving the lean body mass index and/or embryo development and/or increasing the fertility of the mother animals and/or survival rate of the young animals and/or improving the spermatogenesis of the male animals and/or for lowering the infection rate.

5. The use of creatine and/or creatine salts as feed additive for breeding salmon as substitute for fishmeal and/or antimicrobial growth promoters.

6. The use of creatine and/or creatine salts as additive for powdered milk replacer for growing calves

to improve the weight gain and/or improve meat quality and/or to increase the lean body mass and to reduce the fat content and/or to lower the infection rate and/or improve feed utilization.

5 7. The use of creatine and/or creatine salts as feed additive for wet or canned food for dogs and cats, to lower the infection rate, improve the immune system and/or achieve a glossy coat.

8. The use of creatine and/or creatine salts as
10 feed additive for breeding animals and fatstock as a substitute for meat and bonemeal, fishmeal and/or antimicrobial growth promoters, growth hormones, and anabolics, characterized in that naturally occurring creatine or chemically synthesized forms, creatine

15 pyruvates of the general formula $(\text{creatine})_x(\text{pyruvate})_y(\text{H}_2\text{O})_n$, where $x = 1$ to 100, $y = 1$ to 10 and $n = 0$ to 10, that is to say creatine citrate, creatine maleate, creatine fumarate, creatine tartrate or creatine malate, or creatine ascorbate of the
20 formula $(\text{creatine})_x(\text{ascorbate})_y(\text{H}_2\text{O})_n$, where $x = 1$ to 100, $y = 1$ to 100 and $n = 0$ to 20, creatine phosphorenylpyruvate, creatine succinates, creatine formates and creatine gluconates, potassium creatine, calcium creatine or sodium creatine or creatine
25 phosphate, cyclocreatine or other creatine analogs or mixtures thereof are used.

9. The use of creatine and/or creatine salts as feed additive as claimed in one of claims 1 to 8, characterized in that creatine and/or creatine salts
30 are added to the feed as food supplement in powder form or in the case of water soluble salts in the form of an aqueous solution.

10. The use of creatine and/or creatine salts as feed additive as claimed in one of claims 1 to 9,
35 characterized in that creatine and/or creatine salts are added in an amount of 1 to 50 g/kg of air-dry feed.

11. The use of creatine and/or creatine salts as feed additive as claimed in claim 1, 7 or 8, substantially as herein described with reference to Example 1.

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Dated this 21st day of October 2003

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By their Patent Attorneys

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