

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
11 December 2008 (11.12.2008)

PCT

(10) International Publication Number
WO 2008/148552 A2

(51) International Patent Classification:
A23K 1/18 (2006.01) A23K 1/16 (2006.01)

(21) International Application Number:
PCT/EP2008/004490

(22) International Filing Date: 5 June 2008 (05.06.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/942,066 5 June 2007 (05.06.2007) US

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(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, BR, BW, BY, BZ, CA, CH, 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, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, 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))
- of inventorship (Rule 4.17(iv))

Published:

- without international search report and to be republished upon receipt of that report

(54) Title: METHODS AND COMPOSITIONS RELATING TO ADMINISTRATION OF L-CARNITINE

(57) Abstract: Methods and compositions for treating animal disorders characterized by a negative protein or energy balance and limited feed intake include providing a mixture prepared from a mixture of water containing L-carnitine and a potable acidifier, and delivering to an animal the water mixture as its water supply for free consumption. Another animal treatment method involves preparing a first and second media having L-carnitine, where the second media is different from the first media, and delivering to an animal the first and second media having L-carnitine. Such media may include drinking water, capsules, supplements, feed, injections, e.g., intramuscular, intraperitoneal, intravenous and subcutaneous, pastes, gels and tablets or any other media suitable for delivering L-carnitine to an animal or animal population.



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METHODS AND COMPOSITIONS RELATING TO ADMINISTRATION OF L-CARNITINE

Field of the Invention

[001] The present invention relates to compositions of L-carnitine and methods
5 of using L-carnitine to improve the mortality and morbidity of animals experiencing
periods of negative protein and/or energy balance. The present invention further relates
to the use of L-carnitine in combination with other supplemental or therapeutic
compositions in order to facilitate improvement of the health status of unhealthy
animals.

Background of the Invention

[002] A major function of lipids as understood in modern nutrition is to serve as
a substrate for production of metabolic energy. Mechanisms regulating the production
of metabolic energy under a wide variety of physiological conditions are required for
survival of the species, and have a critical role in the production of energy from long-
15 chain fatty acids. Carnitine facilitates the transport of fatty acids into the mitochondria.
Carnitine is a naturally occurring B vitamin-like compound found in humans and other
mammals, aquatic life forms and birds.

[003] Unlike most vitamins and vitamin-like substances, carnitine was identified
and synthesized long before the discovery of its nutritional role. Carnitine was first
20 found in muscle extracts by two Russian scientists in 1905, identified as β -hydroxy- α -
butyrobetaine, and named from the latin carnis, meaning flesh or meat. In the late
1940's, Fraenkel discovered that carnitine was a necessary substance for the
mealworm *Tenebrio molitor*, and named it vitamin B_r, although it was later established
that carnitine is not a vitamin for higher organisms. Early research literature also calls
25 carnitine vitamin B₁₁. In 1959, Fritz found that carnitine stimulated the rate of fat burning
(called "beta-oxidation"). Subsequent investigations revealed the mechanism of
carnitine's action: fats are transported by a carnitine-dependent mechanism into the
mitochondria where they are burned for energy.

[004] Carnitine is chemically termed 3-hydroxy-4-N-trimethylamino butyric acid;
30 it is similar to choline and a close cousin to amino acids. Unlike amino acids, carnitine

is not used for protein synthesis. Carnitine is not a vitamin, because part of the animal requirement is fulfilled by biosynthesis. Carnitine, like many other biological molecules, comes in two forms: L-carnitine and D-carnitine. These isomers are mirror images of each other, much like the left hand is a mirror image of the right. Only the L-isomer is biologically active, however. The D-form is completely inactive, and may even inhibit the utilization of L-carnitine.

[005] Whether supplied by the diet or from endogenous synthesis, carnitine is essential in the metabolism and movement of fatty acids within and between cells. An enzyme, carnitine acyltransferase, has been found to be part of the mechanism for releasing CoA (co-enzyme A) and acyl-CoA. The effect of carnitine on fatty acid metabolism seems to be limited to fatty acids with chain lengths greater than C₈. Palmitylcarnitine also stimulates fat synthesis in livers, so another vitamin role of carnitine may be in the regulation of lipogenesis.

[006] Most organisms have the ability to produce their own carnitine. In 1980, Rebouche and Engel first demonstrated carnitine biosynthesis in humans. The endogenous production of carnitine appears to occur mainly in the liver, and requires two amino acids, lysine and methionine, three vitamins, vitamin B₃ (niacin), vitamin B₆ and vitamin C (ascorbic acid), and iron. Trimethyl-lysine is produced by methylation of lysine using a methyl group from methionine. The trimethyl-lysine is converted to an aldehyde using PALP as a co-factor, which is oxidized to a butyrate by an NAD-linked dehydrogenase. The butyrate is then hydroxylated by a ketoglutarate-ferrous ascorbate compound to form carnitine.

[007] The role of carnitine in nutrition received little attention until 1973, when the first carnitine-deficient human patient was described. Since then, many clinical investigations have focused on biomedical aspects of carnitine deficiency, as well as on the effects of supplementary dietary carnitine on disease processes. No deficiency problems in normal vertebrates have yet been found under practical conditions.

[008] Previous research has shown that carnitine supplementation of diets increases the lean to fat ratio of swine (U.S. Pat. Nos. 5,124,357 and 5,192,804), enhances reproductive performance in sows (U.S. Patent No. 7,169,770), and provides benefits for gestating and lactating swine (U.S. Patent No. 6,242,487). Its beneficial effects of increasing carcass leanness and improving the lean to fat ratio were also

shown in fish (U.S. Pat. No. 5,030,657). In addition, carnitine has been shown to improve the hatchability of eggs when fed to laying hens (U.S. Pat. No. 5,362,753).

[009] However, the above studies focus on carnitine supplementation in the diets of healthy animals. Carnitine supplementation has not been targeted towards health-challenged animals, such as animals that are losing muscle mass or that are experiencing a protein imbalance.

[010] Accordingly, there is an absence of information on how carnitine-supplemented diets might be used for aiding unhealthy animals in order to improve their health and performance.

Brief Summary of the Invention

[011] Various embodiments of the invention address the issues described above by providing L-carnitine supplemented media for delivery to health challenged animals or animal populations.

[012] According to one embodiment, a method for treating animal disorders characterized by a negative protein or energy balance and limited feed intake includes preparing a mixture of water containing L-carnitine and a potable or ingestible acidifier; and delivering to an animal said water mixture as its water supply for free consumption.

[013] In another embodiment, a method for treating animal disorders characterized by a negative protein or energy balance and limited feed intake includes preparing first media having L-carnitine; preparing a second media having L-carnitine different from the first media; and delivering to an animal said first and second media having L-carnitine.

[014] In another embodiment, a method for treating animal disorders characterized by a negative protein or energy balance and limited feed intake includes preparing a mixture of water containing L-carnitine, an ingestible acidifier and animal feed.

[015] In yet another embodiment, a composition for treating animal disorders characterized by a negative protein or energy balance and little solid food intake includes L-carnitine; and one or more vitamins selected from the group consisting of pantothenic acid (Vitamin B₅), thiamin (Vitamin B₁), pyridoxine (Vitamin B₆), niacin (Vitamin B₃), folic acid (Vitamin B₉), riboflavin (Vitamin B₂), biotin (Vitamin B₇), vitamin

B₁₂, ascorbic acid (Vitamin C), choline, Vitamin A, Vitamin D, Vitamin E, Vitamin K and/or selenium.

[016] These and other features and advantages of aspects of the present invention will become apparent to those skilled in the art from the following detailed description, where it is shown and described in illustrative embodiments, including best modes contemplated for carrying out the invention. As it will be realized, the various aspects of the invention are capable of modifications in various respects, all without departing from the spirit and scope of the present invention. Accordingly, the drawings and detailed description are to be regarded as illustrative in nature and not restrictive.

Detailed Description

[017] Overview. Achieving good health and performance of animals is a primary focus of animal production. It has been found that improving mortality and morbidity for unhealthy animals, such as those experiencing a period of negative protein or energy balance, may be accomplished by providing animals with L-carnitine delivered in certain ways, for example via a supplemented diet, e.g., water and/or food containing L-carnitine, or other delivery mechanisms described further below. In particular, L-carnitine provided to a health challenged animal may positively impact feed conversion and average daily gain, resulting in improved mortality and morbidity.

[018] Health challenged animals may lose appetite and energy and have reduced or no feed intake. They may also have gastrointestinal disturbances that cause such feed as is ingested not to be used efficiently. Thus, such animals are at a disadvantage in relation to normal or medication-assisted healing processes, because such situations require a high amount of energy to heal, and without an adequate amount of feed, expendable energy sources are not readily available for healing. In these instances mortality and morbidity may be high. While desiring not to be bound to any particular scientific theory, it is believed that because L-carnitine increases metabolic processes by helping conversion of lipids into energy, providing L-carnitine to the diet of a health challenged animal may increase its reduced metabolic activity and, in turn, support and improve healing processes.

[019] Periods of negative protein and energy balance may occur in animals due to disease, infection, or from poor management practices or environment; resulting in

poor daily gain, morbidity, and in some cases, mortality. For swine, such periods of negative protein and energy balance may be the result of a variety of health challenges, for example, porcine circovirus associated disease, post-weaning multisystemic wasting syndrome, circovirus, salmonellosis, transmissible gastroenteritis virus, ileitis, colibacillosis, dysentery, actinobacillus pleuropneumoniae, porcine respiratory disease complex (mycoplasma), hemolytic E. coli, hog cholera or influenza. In cattle or calves, such periods may be the result of bovine respiratory syncytial virus, infectious bovine rhinotracheitis, corona virus, bovine viral diarrhea or Johnes disease. In equine species, such periods may be the result of, for example, equine infectious anemia. Such periods are commonly marked by an animal's reduction of or cessation of food intake. As a result, diets for such unhealthy animals need to be engineered to ensure that, even with a reduced or nonexistent feed intake, a sufficient amount of energy is available. The present method addresses this by providing ways in which an effective amount of L-carnitine may be delivered.

[020] L-carnitine may be provided as a supplement in the form of L-carnitine or an acceptable salt thereof, e.g., acetylated L-carnitine, L-tartrate carnitine, L-carnitine fumarate, L-carnitine chloride, L-carnitine magnesium citrate, L-carnitine acetyl-HCl, L-carnitine propionyl-HCl, and L-carnitine palmitoyl-HCl, in either a protected or unprotected form. For example, L-carnitine may be encapsulated in one or more materials capable of passing through the stomach without significantly dissolving and then dissolving in the small intestine so that L-carnitine is not absorbed until it reaches the small intestine. In addition or alternatively, gamma-butyrobetaine, a precursor of L-carnitine, may be provided as a supplement. Various media for delivering L-carnitine may include drinking water, capsules, supplements, feed, injections (e.g., intramuscular, intraperitoneal, intravenous and subcutaneous), pastes, gels and tablets or any other media suitable for delivering L-carnitine to an animal or animal population.

[021] Water As Delivery Medium. In accordance with a particular embodiment, L-carnitine is provided in an animal's drinking water. Previously, providing L-carnitine in water was disfavored because it led to bacterial growth in the water. However, it has been determined that combining a suitable potable acidifier with L-carnitine in the water prevents bacterial flourishing because the acidifier serves as an antibacterial agent.

Accordingly, for example, L-carnitine may be combined with a suitable amount of an acidifier and introduced into an unhealthy animal's water supply.

[022] L-carnitine ingested via the water supply may, as discussed above, facilitate improvement of an animal's body energy reserves during times of limited or restricted feed intake, thereby improving feed conversion and average daily gain.

[023] Typically, swine consume between 0.5 to 2.0 gallons of water per day (1890 to 7570 ml/day). In swine populations experiencing health disorders, 0.0001 to 4 g of L-carnitine may be provided to each animal per day. Accordingly, when providing swine with the L-carnitine in drinking water, the amount of L-carnitine in the water supply may range from 0.000013 to 2.116 mg L-carnitine per ml of water. In another implementation about 0.01 to 2 grams of L-carnitine may be provided to an animal per day, which equates to from 0.00132 to 1.0582 mg L-carnitine per ml of water. In yet another implementation, 0.5 grams of L-carnitine is provided per day per animal, resulting in between 0.06605 to 0.2646 mg L-carnitine per ml of water.

[024] With water consumption by a health challenged animal falling in the range from half to full normal amount, L-carnitine may be provided in the water in an amount sufficient to deliver to an animal 0.001 to 4 grams per day of L-carnitine. In one embodiment where water consumption falls in the range from half to full normal amount, L-carnitine may be provided in the water in an amount sufficient to deliver to an animal 0.01 to 2 grams per day of L-carnitine. In another embodiment where water consumption falls in the range from half to full normal amount, L-carnitine may be provided in the water in an amount sufficient to deliver to an animal 0.5 grams per day of L-carnitine.

[025] The amount of acidifier added to the water supply may vary depending on the acidifier type. Various potable or ingestible acidifiers may be used in accordance with the present invention and may include, for example, citric acid, formic acid, butyric acid, lactic acid, phosphoric acid and/or propionic acid. Generally, the amount of acidifier used is determined by identifying the amount of acidifier required to prevent bacteria from degrading L-carnitine and from building bacterial populations that may foul water lines. In a particular embodiment, the mixture of L-carnitine to citric acid is about 80 parts L-carnitine to about 20 parts citric acid, and may be provided as a premix for addition to water supplies. In another embodiment, citric acid in an amount of 120

mg/ml of water may be included in the L-carnitine supplemented water supply of animal populations experiencing health disorders characterized by increased body protein catabolism and/or negative energy balance. In further embodiments, citric acid in a range of 50-300 mg/ml of water may be included in the L-carnitine supplemented water supply. The pH of the water, L-carnitine and acid mixture may vary, for example, depending on the acidifier(s) selected and on the quality of the water supply, e.g., hard water generally has a starting pH of 8.0. When citric acid is used as the acidifier, the pH may be adjusted so that it falls below a pH of 7.0 such that an acidic environment unfriendly to bacterial growth is created. It should be understood that other acids have known antibacterial and/or bacteriocidal effectiveness at a different pH than citric acid, and the pH of the mixture may be adjusted according to the selected acidifier.

[026] The above-mentioned embodiment may provide advantages over supplementing L-carnitine in the feed of animal populations experiencing health disorders. This is because a typical unhealthy animal eats less food or no food, resulting in periods of increased body protein catabolism and/or negative energy balance. As a result, providing L-carnitine in water supplies may ensure that the unhealthy animal population, which in most instances continues to drink water, still receives the intended amount of L-carnitine. Because it is believed that L-carnitine supplements may improve the health status of such animal populations, its consistent delivery via the water supply may increase the probability that the animal populations will have improved mortality and morbidity.

[027] While it is desirable to recognize individual animals as health challenged and treat them, this can be difficult and requires investment in instrumentation and/or personnel. Accordingly, the delivery of L-carnitine in the water supply of an entire population in which there is some statistical level of health challenges may be a cost effective way of reaching the group of health challenged animals. Although all receive the L-carnitine, there appears to be no adverse effect on the healthy animals.

[028] Other Delivery Media. The L-carnitine and acidifier composition, provided in accordance with further embodiments, may also be useful when delivering L-carnitine to health challenged animal populations via pastes and gels. Due to the aqueous environment present in many pastes and gels, L-carnitine introduced into such media creates a suitable environment for bacterial growth. Accordingly, including a suitable

acidifier in pastes or gels may result in providing the pastes or gels with antibacterial properties that may enable the safe delivery of L-carnitine to the subject population.

[029] In accordance with another embodiment, L-carnitine may be provided in food supplies of animal populations experiencing health disorders, but still consuming animal feed. In this embodiment, an amount of L-carnitine used to supplement daily intake may be from 0.0001 to 4.0 grams (0.1 mg to 4000 mg) of L-carnitine, and the amount added to each kg. of feed depends on the food intake per animal per day. The feed may be corn, oats or other feeds traditionally fed to various species.

[030] Furthermore, L-carnitine and an acidifier composition may be provided in wet feed supplies or water/feed mixtures of an animal population. Due to the wet environment in the feed, providing an acidifier with L-carnitine may provide the wet media with antibacterial properties that may allow for the safe delivery of L-carnitine to the animal population.

[031] In another embodiment, L-carnitine may be provided as a supplement to health challenged animal populations and delivered in pill or capsule form. According to further embodiments, L-carnitine may be a component of a base mix, a premix, a concentrate, in a vitamin micromineral (trace mineral) and/or macromineral mix fed to health challenged animal populations. In yet another embodiment, L-carnitine may be provided via injection to health challenged animal populations.

[032] Additional Ingredients and Compositions. In each of the above-described embodiments, L-carnitine may be used alone or combined with a feed supplement. For example, L-carnitine may be provided with vitamins and minerals such as pantothenic acid (Vitamin B₅), thiamin (Vitamin B₁), pyridoxine (Vitamin B₆), niacin (Vitamin B₃), folic acid (Vitamin B₉), riboflavin (Vitamin B₂), biotin (Vitamin B₇), vitamin B₁₂, ascorbic acid (Vitamin C), choline, Vitamin A, Vitamin D, Vitamin E, Vitamin K, iron, selenium, cobalt, chromium, copper, iodine, manganese, zinc, and/or molybdenum. Combining L-carnitine with one or more vitamins or minerals may provide greater benefits than L-carnitine alone, because when L-carnitine causes metabolic processes to increase, vitamins and minerals in the body are consumed and need replenishing to meet the metabolic need. By combining L-carnitine with one or more suitable vitamins and/or minerals, the consumed vitamins and/or minerals may be replenished and/or may be provided at therapeutic amounts. For example, any of the vitamins may be used alone

or in combination in an amount between 0.2-2 mg/day or 50-500 IU/day. Alternatively, vitamins and minerals combined with L-carnitine may be provided to each head of swine in a range from the table listed below in Table 1.

	unit	Low Range	Middle Range	High Range
Vitamin A	IU	275	7996	21000
Vitamin D	IU	27.5	922	2100
Vitamin E	IU	2	68	462
Vitamin K	IU	0.065	3.08	5.2
Biotin	mg	0.01	0.3	2.2
Choline	g	0.075	1.84	10.6
Folacin	mg	0.04	1.84	13.6
Niacin	mg	2.5	43.06	106
Pantothenic	mg	1.5	43.06	126
Ribovlavin	mg	0.5	12.3	39.4
Thiamin	mg	0.19	6.16	10.6
Pyridoxine	mg	0.25	6.16	10.6
Vitamin B12	ug	2.5	30.76	158
Vitamin C	mg/day	10	500	500
Selenium	mg/day	0.2	2	2

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Table 1

[033] In market swine populations, the range of vitamins and minerals provided may fall in the low to middle range of values provided in Table 1. For example, piglets may be provided an amount of vitamins and minerals falling near the low range, and full-grown swine may be provided the same vitamins and minerals in an amount falling near the middle range. For swine with special needs, e.g., pregnant or lactating swine, the vitamins and minerals may be provided in an amount falling between the low and high range.

[034] Further components or other feed supplements may in addition or alternatively be added to an L-carnitine supplemented media. For example, therapeutic

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agents for treating a particular disorder in the animal population may be provided. In another embodiment of the present invention, Tylan® (tylosin antibiotic), Denaguard® (tiamulin), neomycin, penicillin or other substances for use as a therapeutic management tool may be added in order to facilitate control and/or treatment of disease and/or to improve feed efficiency in animal populations.

[035] In another example, specialty proteins that deliver antibody-type products, mannon oligosaccharides, fructooligosaccharides and/or arabinogalactan may be delivered at 0.25-5 grams per head per day and/or sodium butyrate may be included in an L-carnitine supplemented media in order to prevent the animal populations from experiencing further health disorders.

[036] Other components such as essential oils may also be included in an L-carnitine supplemented media. For example, essential oils may include anise, cardamom, chamomile, cinnamon, citronella, clove, cumin, eucalyptus, fennel seed, fenugreek, geranium, ginger, henna, juniper berry, lavender, lemon and other citrus extracts, mentha arvensis, menthol (mint and/or peppermint), onion, oregano, orris, rosehip, rosemary, rosewood, sage, sandalwood, terragon, tea tree, thyme, thymol and/or yarrow. One or more of the aforementioned essential oils may provide antibacterial or bacteriocidal properties and may be provided in a range of 10-200 ppm, or at 50 ppm, for example. Further, one or more of the aforementioned essential oils may provide flavoring to water or feed, making the delivery material more palatable and/or desirable for an animal.

[037] For the water supply or aqueous forms of delivery discussed above, the aforementioned additional ingredients are used in their water-soluble forms or may be made water soluble, along with L-carnitine, for example using a coating or an encapsulation technology.

[038] Exemplary compositions that may be prepared for treatment of the condition of negative protein or energy balance are the following:

[039] **Embodiment 1: L-carnitine, potable acidifier, Vitamin E and selenium**

[040] L-carnitine may be provided in an amount between 0.000013 and 2.116 mg per ml of water, a potable acidifier provided in an amount between 0.001 and 6.00 mg per ml of water, Vitamin E provided in an amount between 0.00026 and 0.244 IU per

ml of water, and selenium provided in an amount between 0.000026 and 0.00106 mg per ml of water.

[041] In another embodiment it may be preferable to provide L-carnitine in an amount between 0.06605 and 2.626 mg per ml of water, an acidifier in an amount
5 between 0.05 and 3.00 mg per ml of water, Vitamin E in an amount between 0.013 and 0.053 IU per ml of water, and selenium in an amount between 0.00026 and 0.00106 mg per ml of water.

[042] **Embodiment 2: L-carnitine, potable acidifier, Vitamin E, selenium and essential oils**

10 [043] In a second embodiment, L-carnitine may be provided in an amount between 0.000013 and 2.116 mg per ml of water, a potable acidifier provided in an amount between 0.001 and 6.00 mg per ml of water, Vitamin E provided in an amount between 0.00026 and 0.244 IU per ml of water, selenium provided in an amount between 0.000026 and 0.00106 mg per ml of water, and essential oils provided in an
15 amount between 0.00132 and 0.21164 mg per ml of water.

[044] In another embodiment it may be preferable to provide L-carnitine in an amount between 0.06605 and 2.626 mg per ml of water, an acidifier in an amount between 0.05 and 3.00 mg per ml of water, Vitamin E in an amount between 0.013 and 0.053 IU per ml of water, selenium in an amount between 0.00026 and 0.00106 mg per
20 ml of water, and essential oils in an amount between 0.0132 and 0.053 mg per ml of water.

[045] **Embodiment 3: L-carnitine, potable acidifier, Vitamin E, selenium, essential oils and arabinogalactan**

[046] In a third embodiment, L-carnitine may be provided in an amount between
25 0.000013 and 2.116 mg per ml of water, a potable acidifier provided in an amount between 0.001 and 6.00 mg per ml of water, Vitamin E provided in an amount between 0.00026 and 0.244 IU per ml of water, selenium provided in an amount between 0.000026 and 0.00106 mg per ml of water, essential oils provided in an amount between 0.00132 and 0.21164 mg per ml of water, and arabinogalactan provided in an
30 amount between 0.000032 and 0.00265 mg per ml of water.

[047] In another embodiment it may be preferable to provide L-carnitine in an amount between 0.06605 and 2.626 mg per ml of water, an acidifier in an amount

between 0.05 and 3.00 mg per ml of water, Vitamin E in an amount between 0.013 and 0.053 IU per ml of water, selenium in an amount between 0.00026 and 0.00106 mg per ml of water, essential oils in an amount between 0.0132 and 0.053 mg per ml of water, and arabinogalactan in an amount between 0.00026 and 0.00106 mg per ml.

5 **[048] Embodiment 4: L-carnitine, potable acidifier, Vitamin E, selenium, essential oils, arabinogalactan and Vitamin C**

[049] In a fourth embodiment, L-carnitine may be provided in an amount between 0.000013 and 2.116 mg per ml of water, a potable acidifier provided in an amount between 0.001 and 6.00 mg per ml of water, Vitamin E provided in an amount
10 between 0.00026 and 0.244 IU per ml of water, selenium provided in an amount between 0.000026 and 0.00106 mg per ml of water, essential oils are provided in an amount between 0.00132 and 0.21164 mg per ml of water, arabinogalactan provided in an amount between 0.000032 and 0.00265 mg per ml of water, and Vitamin C provided in an amount between 0.00132 and 0.26455 mg per ml of water.

15 [050] In another embodiment it may be preferable to provide L-carnitine in an amount between 0.06605 and 2.626 mg per ml of water, an acidifier in an amount between 0.05 and 3.00 mg per ml of water, Vitamin E in an amount between 0.013 and 0.053 IU per ml of water, selenium in an amount between 0.00026 and 0.00106 mg per ml of water, essential oils in an amount between 0.0132 and 0.053 mg per ml of water,
20 arabinogalactan in an amount between 0.00026 and 0.00106 mg per ml, and Vitamin C in an amount between 0.06605 and 0.26455 mg per ml of water.

[051] Such mixtures may preferably be handled at micropremix facilities in order to accurately measure the supplemented materials. Mixing facilities that meet good manufacturing practices (GMPs), e.g., for blending and manufacturing, in general are
25 preferred.

[052] The compositions described may be used for the manufacture of a medicament for therapeutic application to animals suffering from a period of negative protein or energy balance. Accordingly, the invention also includes use of a fatty acid metabolism increasing effective amount of L-carnitine in the manufacture of a diet or
30 medicament for oral administration, the diet or medicament comprising a bacteria growth preventing or bacteriocidal amount of an ingestible acidifier, for the treatment of periods of negative protein or energy balance in animals. In certain embodiments, the ingestible

acidifier is selected from the group consisting of citric acid, formic acid, butyric acid, lactic acid, phosphoric acid, propionic acid, and any combination of the foregoing acids. From 0.001 to 4 grams of L-carnitine may be administered per day; from 0.01 to 2 grams of L-carnitine may be administered per day; or 0.5 grams of L-carnitine may be administered per day.

[053] Alternatively, and according to Embodiment 1 above, from 0.000013 and 2.116 mg of L-carnitine per ml of water and between 0.001 and 6.00 mg of a potable acidifier per ml of water may be administered. Further, Vitamin E and selenium may be used in combination with L-carnitine and a potable acidifier, Vitamin E provided in an amount between 0.00026 and 0.244 IU per ml of water and selenium provided in an amount between 0.000026 and 0.00106 mg per ml of water. Other substances may be included with the above-described mixture, and may include those described in Embodiments 2-4 above. Further, the amount of L-carnitine, potable acidifier, Vitamin E, selenium and other substances may vary, and may be present in ranges such as those described in Embodiments 1-4 above.

[054] Furthermore, a fatty acid metabolism increasing effective amount of L-carnitine may be combined with vitamins and minerals in the manufacture of a diet or medicament for oral administration for the treatment of periods of negative protein or energy balance in animals. Moreover, essential oils may be in addition or alternatively combined with L-carnitine in order to achieve increased fatty acid metabolism.

[055] The fatty acid metabolism increasing effective amount of L-carnitine with an ingestible acidifier provided orally may treat porcine circovirus associated disease, post-weaning multisystemic wasting syndrome, circovirus, salmonellosis, transmissible gastroenteritis virus, ileitis, colibacillosis, dysentery, actinobacillus pleuropneumoniae, porcine respiratory disease complex (mycoplasma), hemolytic E. coli, hog cholera and/or influenza, bovine respiratory syncytial virus, infectious bovine rhinotracheitis, corona virus, bovine viral diarrhea or Johnes disease, and equine infectious anemia.

[056] Treatment Modes. L-carnitine, used alone or in combination with the above-mentioned substances may be provided as a supplement to animal populations having compromised health daily for a period of 1 to 45 days, for a duration of about 1 day to 28 days, or for a duration of 7 to 14 days. L-carnitine may also be used alone or in combination for a duration of greater than 45 days. Alternatively, L-carnitine may be

provided intermittently over a period of time, e.g., every 2, 3, 4, 5 or 6 days, once a week, twice a month, once a month, or once every 45 days.

[057] In certain treatment modes, high levels of L-carnitine may be flooded in an animal's system over a short period of time, e.g., for 7-14 days, during a time of need.

5 However, it is contemplated that providing low or smaller levels of L-carnitine to an animal's system over an extended period of time, e.g., for at least 45 days, or even over essentially its full lifetime (i.e., a continuing maintenance dose) may prevent or lessen mortality or morbidity.

[058] Treatment modes may also have a variable time frame. For example, a
10 treatment period may begin once a period of negative energy or protein imbalance is detected; and upon an animal or animal population positively responding to treatment with L-carnitine, the treatment period may reach an end point. Positive responses in an animal or animal population may include the animal or animal population ceasing weight loss, beginning weight gain, eating feed, eating a targeted amount of feed, or having an
15 appearance or behavior indicative of adequate health. Alternatively, L-carnitine treatment may be modified upon identifying such health markers.

[059] Furthermore, L-carnitine may be provided to a population in various forms during a treatment period. For example, L-carnitine may be provided in an animal population's water supply for a first portion of a treatment period and then may be
20 provided in feed alone (e.g., mixed with corn, oats or other feeds traditionally provided to various species) or in combination with L-carnitine supplemented water. In a particular example, a preferred amount of L-carnitine may be provided in the water supply, while additional L-carnitine may be provided in animal feed (e.g., mixed with corn, oats or other feeds traditionally provided to various species). This may ensure
25 that the population is receiving at least an intended amount of L-carnitine, even when some animals ingest only water and no feed.

[060] In another embodiment, each of L-carnitine and other therapeutic or metabolic substances may be delivered to an animal population via separate media. For example, L-carnitine may be provided to an animal population via its water supply,
30 and vitamin supplements may be provided in tablet form or may be injected. This may be useful in situations where vitamins or other substances do not easily flow or disperse in water supplies.

[061] In yet another embodiment, the amount of L-carnitine provided to an animal population may vary during a treatment period. For example, more or less L-carnitine may be provided to a population at the beginning of a treatment regimen compared to the end of the treatment period.

5 [062] In a further implementation, L-carnitine may be provided simultaneously via two or more media. For example, L-carnitine supplemented water and topical gel may be introduced in an animal population.

[063] In certain embodiments, L-carnitine may be provided to an animal population regardless of their current health status. L-carnitine may be provided in a
10 maintenance dose, for example. This may be useful for animal populations in general because it is typical for at least some animals in a large production population to have some sort of health challenge that could benefit from L-carnitine supplementation.

[064] It will be understood that an effective amount L-carnitine required for an animal may be dependent *inter alia* on its ailment, age, sex, species, breed, and feed
15 composition. As a result, if individual water or feed intake can be provided, L-carnitine may be provided among animals in the same population in different amounts depending a particular animal's makeup. However, it should be noted that delivery of L-carnitine in a common water supply for healthy and health challenged animals, is acceptable, as there appears to be no ill effect to providing healthy animals L-carnitine in the amounts
20 that are helpful for health challenged animals.

[065] Furthermore, the response of an L-carnitine supplemented diet in animals within a population may vary due to their makeup. Accordingly, growth rate, feed conversion, and carcass composition may differ within an animal population, even if each animal is receiving the same supplemental amount of L-carnitine.

25 [066] It is understood that the methods of the present invention can be practiced with respect to many kinds of health challenged animals having a metabolism that involves L-carnitine and who may suffer from periods of negative protein and/or energy balance, including non-ruminants, ruminants, avian, and aquaculture. Meat, milk and egg producing animals, livestock in general, production livestock animals, companion
30 animal, i.e., horses, cats, dogs, rabbits, may all be provided with L-carnitine supplemented media. It is further understood that the methods are practiced according

to one embodiment, with respect to swine. In a further alternative, the methods are practiced with livestock or any known animal.

[067] From the above description and drawings, it will be understood by those of ordinary skill in the art that the particular embodiments shown and described are for purposes of illustration only and are not intended to limit the scope of the present invention. Those of ordinary skill in the art will recognize that the present invention may be embodied in other specific forms without departing from its spirit or essential characteristics. References to details of particular embodiments are not intended to limit the scope of the invention.

The present invention will be described in the following, non-limiting examples.

[068]

[069] **Example 1**

[070] 2000 animals in a treatment group having health issues such as porcine circovirus associated disease, post-weaning multisystemic wasting syndrome and circovirus were provided a water supply supplemented with L-carnitine and citric acid. The targeted amount of L-carnitine and citric acid provided to each animal was 500 mg of L-carnitine per day and 125 mg citric acid per day. The supplemented water was provided to the animal population over a period of 14 days, and 50 died, resulting in a 2.5% mortality rate. In the control group, 1000 animals with comparable health issues were not provided the L-carnitine/citric acid water mixture and 58 died, resulting in a 5.8% mortality rate. Accordingly, the population provided with L-carnitine experienced a reduced mortality rate by over 55% compared to the control population.

[071] **Example 2**

[072] 199 total swine were fed complete diets formulated to meet or exceed National Research Council (NRC) nutrient recommendations such that 100 of the total were fed a control diet with no added L-carnitine, and 99 were fed a treatment diet that provided the same basal feed that was fed to the control swine but with an additional 100 mg of L-carnitine per Kg. of feed. L-carnitine intake for the treatment group

averaged 293 mg of L-carnitine per day. Swine in both groups had a comparable health status and were known to have health issues such as mycoplasma and hemolytic E. coli. Swine were fed their respective dietary treatments for a total of 83 days and from an initial average starting weight of 43 kg to an average final weight of 125 kg. For the control group of swine that did not receive L-carnitine, 15 swine were removed for a removal rate of 15%, compared to 8 swine and a corresponding removal rate of 8.1% for the L-carnitine supplemented swine. Accordingly, the population provided with L-carnitine experienced a reduced mortality rate of 46% compared to the control population.

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Claims

What is claimed is:

1. A method for treating animal disorders characterized by a negative protein or energy
5 balance and limited feed intake comprising:
 preparing a mixture of water containing L-carnitine and a potable acidifier; and
 delivering to an animal said water mixture as its water supply for free
consumption.
- 10 2. The method of claim 1, wherein the potable acidifier is one or more acidifiers
selected from the group consisting of citric acid, formic acid, butyric acid, lactic acid,
phosphoric acid and/or propionic acid.
3. The method of claim 1, wherein the L-carnitine is present in the water in a
15 concentration of between 0.000013 to 2.116 mg L-carnitine/ml of water.
4. The method of claim 1, wherein the L-carnitine is present in the water in a
concentration of between 0.00132 to 1.0582 mg L-carnitine/ml of water.
- 20 5. The method of claim 1, wherein the L-carnitine is present in the water in a
concentration of between 0.06605 to 0.2646 mg L-carnitine/ml of water.
6. The method of claim 1, wherein the L-carnitine is present in the water in an
amount sufficient to deliver to an animal 0.001 to 4 grams per day of L-carnitine with
25 water consumption of half to full normal amount.

7. The method of claim 1, wherein the L-carnitine is present in the water in an amount sufficient to deliver to an animal 0.01 to 2 grams per day of L-carnitine with water consumption of half to full normal amount.

5

8. The method of claim 1, wherein the L-carnitine is present in the water in an amount sufficient to deliver to an animal 0.5 grams per day of L-carnitine with water consumption of half to full normal amount.

10 9. The method of claim 1, wherein delivering said water mixture comprises delivering the water mixture for a period of 1 to 45 days.

10. The method of claim 1, wherein delivering said water mixture comprises delivering the water mixture for a period of 1 to 28 days.

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11. The method of claim 1, wherein delivering said water mixture comprises delivering the water mixture for a period of 7 to 14 days.

12. The method of claim 1, wherein delivering said water mixture comprises
20 delivering the water mixture for a period of greater than 45 days.

13. A method for treating animal disorders characterized by a negative protein or energy balance and limited feed intake comprising:

preparing first media having L-carnitine;

preparing a second media having L-carnitine different from the first media; and
delivering to an animal said first and second media having L-carnitine.

14. The method of claim 13, wherein the first and second media having L-carnitine
5 are delivered concurrently for a treatment period.

15. The method of claim 13, wherein the first and second media having L-carnitine
are delivered sequentially for a treatment period.

10 16. The method of claim 13, wherein at least one of the first or second media is
mixed with an ingestible acidifier.

17. The method of claim 13, wherein at least one of the first and second media is
water.

15

18. A method for treating animal disorders characterized by a negative protein or
energy balance and limited feed intake comprising:

preparing a mixture of water containing L-carnitine, an ingestible acidifier and
animal feed.

20

19. The method of claim 18, wherein the ingestible acidifier is one or more acidifiers
selected from the group consisting of citric acid, formic acid, butyric acid, lactic acid,
phosphoric acid and/or propionic acid.

20. The method of claim 18, further comprising adding one or more vitamins and minerals selected from the group consisting of pantothenic acid (Vitamin B₅), thiamin (Vitamin B₁), pyridoxine (Vitamin B₆), niacin (Vitamin B₃), folic acid (Vitamin B₉), riboflavin (Vitamin B₂), biotin (Vitamin B₇), vitamin B₁₂, ascorbic acid (Vitamin C),
5 choline, Vitamin A, Vitamin D, Vitamin E, Vitamin K and/or selenium.

21. The method of claim 18, further comprising adding one or more essential oils selected from the group consisting of anise oil, cardamom oil, chamomile oil, cinnamon oil, citronella oil, clove oil, cumin oil, eucalyptus oil, fennel seed oil, fenugreek oil,
10 geranium oil, ginger oil, henna oil, juniper berry oil, lavender oil, lemon and other citrus extract oil, mentha arvensis oil, menthol, mint oil, peppermint oil, onion oil, oregano oil, orris oil, rosehip oil, rosemary oil, rosewood oil, sage oil, sandalwood oil, terragon oil, tea tree oil, thyme oil, thymol oil and/or yarrow oil.

15 22. The method of claim 18, further comprising delivering the mixture in a maintenance dose for the lifetime of an animal.

23. A composition for treating animal disorders characterized by a negative protein or energy balance and inadequate solid food intake comprising:

20 L-carnitine; and

one or more vitamins or minerals selected from the group consisting of pantothenic acid (Vitamin B₅), thiamin (Vitamin B₁), pyridoxine (Vitamin B₆), niacin (Vitamin B₃), folic acid (Vitamin B₉), riboflavin (Vitamin B₂), biotin (Vitamin B₇), vitamin

B₁₂, ascorbic acid (Vitamin C), choline, Vitamin A, Vitamin D, Vitamin E, Vitamin K and/or selenium.

24. The composition of claim 23 further comprising essential oils selected from the group consisting of anise oil, cardamom oil, chamomile oil, cinnamon oil, citronella oil, clove oil, cumin oil, eucalyptus oil, fennel seed oil, fenugreek oil, geranium oil, ginger oil, henna oil, juniper berry oil, lavender oil, lemon and other citrus extract oil, mentha arvensis oil, menthol, mint oil, peppermint oil, onion oil, oregano oil, orris oil, rosehip oil, rosemary oil, rosewood oil, sage oil, sandalwood oil, tarragon oil, tea tree oil, thyme oil, thymol oil and/or yarrow oil.

25. The composition of claim 23 further comprising water mixed to provide to an animal with half to full normal water consumption:

about 0.5g/day L-carnitine;

15 about 0.1 g/day of vitamins or minerals selected from the group consisting of pantothenic acid (Vitamin B₅), thiamin (Vitamin B₁), pyridoxine (Vitamin B₆), niacin (Vitamin B₃), folic acid (Vitamin B₉), riboflavin (Vitamin B₂), biotin (Vitamin B₇), vitamin B₁₂, ascorbic acid (Vitamin C), choline, Vitamin A, Vitamin D, Vitamin E, Vitamin K and/or selenium; and

20 about 0.125 g/day ingestible acidifier selected from the group consisting of citric acid, formic acid, butyric acid, lactic acid, phosphoric acid and/or propionic acid.