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(73) Patenthaver: **Hill's Pet Nutrition, Inc., 400 Southwest 8th Street, Topeka, KS 66603, USA**

(72) Opfinder: **Wedekind, Karen, Joy, 197 North Palmberg, Meriden, KS Kansas 66512, USA**
Fritsch, Dale, Allen, 3800 Southwest King Forest Road, Topeka, KS Kansas 66610, USA
Dodd, Chadwick, Everett, 4609 Woodridge Drive, Lawrence, KS Kansas 66049, USA
Allen, Timothy, Arthur, 4604 Royal Birkdale Court, Lawrence, KS Kansas 66049, USA

(74) Fuldmægtig i Danmark: **Zacco Denmark A/S, Arne Jacobsens Allé 15, 2300 København S, Danmark**

(54) Benævnelse: **FREMGANGSMÅDER OG SAMMENSÆTNINGER TIL BEHANDLING AF FELIN HYPERTHYROIDISME**

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Description

Field of the Invention

[0001] The invention relates generally to food compositions for treating hyperthyroidism and particularly to food compositions for treating feline hyperthyroidism.

Description of the Prior Art

[0002] Hyperthyroidism is a relatively common endocrine disorder, particularly in older cats. Typical hyperthyroidism treatments include chronic administration of an anti-thyroid medication, surgical removal of the thyroid glands, and/or radioactive iodine therapy. These treatments are expensive and have their limitations and side effects. For example, as most anti-thyroid medications are administered orally, compliance is often compromised. Surgery requires anesthesia and is not necessarily an option for older felines, particularly felines that suffer from other diseases as well. Radioactive iodine therapy is available only in facilities licensed to use radioactive materials, and requires hospitalization of the felines until their body levels of radioactivity are safe. There is, therefore, a need for alternative compositions and methods for treating hyperthyroidism which provide partial or complete relief. The invention provides compositions and methods of treatment that generally address such a need.

SUMMARY OF THE INVENTION

[0003] It is an object of the invention to provide compositions suitable for treating feline hyperthyroidism.

[0004] It is another object of the invention to provide articles of manufacture comprising a composition of the invention or two or more ingredients that, when combined together and optionally with additional ingredients that are or are not a part of the article of manufacture, yield a composition of the invention.

[0005] Accordingly, the present invention provides a food composition comprising from 0.1 to less than 1 mg/kg selenium on a dry matter basis in conjunction with an antithyroid agent as a combined preparation for use in treating hyperthyroidism in a feline. The present invention also provides a kit for treating hyperthyroidism in a feline comprising in separate containers in a single package food: a food composition comprising from 0.1 to less than 1 mg/kg selenium on a dry matter basis, and an antithyroid agent, or two or more ingredients, that, when combined together and optionally with additional ingredients that are or are not a part of the kit, yield a food composition comprising from 0.1 to less than about 1 mg/kg selenium on a dry matter basis, and an antithyroid agent, and one or more of (1) instructions for feeding the food composition to the feline, (2) instructions for

preparing the food composition by combining the two or more ingredients, (3) instructions for treating hyperthyroidism by feeding the feline the food composition, (4) one or more antithyroid agents, (5) instructions for administering an antithyroid agent to the feline in conjunction with feeding the feline the food composition, and (6) instructions for treating hyperthyroidism by administering to the feline an antithyroid agent in conjunction with feeding the feline the food composition.

[0006] The scope of the invention is defined by the claims. Subject matter outside the scope of the claims is provided for information only.

[0007] Additional and further objects, features, and advantages of the present invention will be readily apparent to those skilled in the art.

DETAILED DESCRIPTION OF THE INVENTION

[0008] In one aspect, the invention provides compositions for treating hyperthyroidism in a feline. Hyperthyroidism is characterized by hypermetabolism of the thyroid gland and excessive production of the thyroid hormones triiodothyronine (T_3) and tetraiodothyronine (thyroxine or T_4). Most of T_3 and T_4 are bound to serum proteins. The portion of T_3 and T_4 partitioned into serum, and not associated with protein, is called free T_3 (fT_3) and T_4 (fT_4). One skilled in the art can accurately diagnose hyperthyroidism in a feline utilizing thyroid function tests, examining clinical signs, and/or observing the animal's response to trial thyroid hormone administration. Thyroid function tests are known to those skilled in the art and include, for example, tests for determining the concentrations of total and free serum T_3 and T_4, tests for determining the concentration of thyroid stimulating hormone (TSH), and the sodium pertechnetate and T_3 suppression tests. See, for example, Small Animal Clinical Nutrition (Michael Hand ed., Mark Morris Institute 4th ed. 2000), pages 863 - 868. Treating hyperthyroidism as described herein includes ameliorating, suppressing, and/or eradicating hyperthyroidism.

[0009] In some embodiments, the feline is a companion feline. A companion feline can be a feline kept as a pet. A companion feline can also be a feline from a widely domesticated species, for example, cats (*Felis domesticus*) regardless of whether or not it is kept as a pet. In some embodiments, the feline is an adult feline. An adult feline is a feline of any age after juvenile growth and development has been completed, including senior and geriatric felines. For example, an adult cat typically is one that is from about one year old through the remainder of its life. A senior feline is one of an age at which it is at a risk for suffering from an age-related disease regardless of whether or not the feline shows obvious physical or behavioral signs of aging. For example, a senior cat typically is a cat from about seven to about eleven years old. A geriatric feline is a feline showing signs of aging. For example, a geriatric cat typically is a cat of about twelve years of age and beyond.

[0010] In some embodiments, the compositions of the invention further comprise from about 0.1 to less than about 1 or from about 0.1 to about 0.27 mg/kg iodine on a dry matter basis. In some such embodiments, the composition further comprises from about 0.1 to

about 0.5 mg/kg iodine on a dry matter basis. In other such embodiments, the composition further comprises from about 0.1 to about 0.3 mg/kg iodine on a dry matter basis. In yet other such embodiments, the composition further comprises from about 0.15 to about 0.25 mg/kg iodine on a dry matter basis. And in further such embodiments, the composition further comprises from about 0.1 to about 0.2 or 0.27 mg/kg iodine on a dry matter basis. As discussed above, iodine is a constituent of T_3 and T_4. The thyroid glands actively trap iodine to ensure an adequate supply of thyroid hormones. Iodine as used herein refers to the iodine atom without reference to its molecular or ionic form, and includes iodine present in one or more chemical forms such as, for example, iodide, iodate, and periodate. Preferably, iodine is endogenous to an ingredient.

[0011] The compositions of the invention comprise from 0.1 to less than 1, 0.2 - 0.66, or about 0.4 to about 0.7 mg/kg selenium on a dry matter basis. In some such embodiments, the composition comprises from about 0.1 to about 0.8 mg/kg selenium on a dry matter basis. In other such embodiments, the composition comprises from about 0.15 to about 0.65 mg/kg selenium on a dry matter basis. In yet other such embodiments, the composition comprises from about 0.4 to about 0.7 mg/kg selenium on a dry matter basis. In further such embodiments, the composition comprises from about 0.3 to about 0.65 mg/kg selenium on a dry matter basis. Selenium has a role in maintaining normal thyroid and iodine metabolism, particularly through the control of the deiodinase enzymes that regulate the conversion of T_4 to T_3. Selenium as used herein refers to the selenium atom without reference to its molecular or ionic form, and includes selenium present in one or more chemical forms such as, for example, selenide, selenite, and selenate.

[0012] In some embodiments, the compositions of the invention comprise from about 0.1 to less than about 1 or from about 0.1 to about 0.27 mg/kg iodine on a dry matter basis and from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis. The composition comprises from about 0.1 to about 0.5 mg/kg iodine on a dry matter basis and from about 0.1 to about 0.8 mg/kg selenium on a dry matter basis. In other such embodiments, the composition comprises from about 0.1 to about 0.3 mg/kg iodine on a dry matter basis and from about 0.15 to about 0.65 mg/kg selenium on a dry matter basis. In further such embodiments, the composition comprises (1) from about 0.1, about 0.15, or about 0.2 to about 0.25, about 0.3, or about 0.5 mg/kg iodine on a dry matter basis, and (2) from about 0.1, about 0.15, about 0.3, or about 0.4 to about 0.65, about 0.7, or about 0.8 mg/kg selenium on a dry matter basis. The composition of the invention comprises a food composition (*i.e.*, the composition comprises one or more food compositions). In some such embodiments, the composition meets the AAFCO's minimum nutrient level requirements for reproduction or maintenance. See AAFCO Official Publication, pages 137-140 (2005). In other such embodiments, the composition comprises less than the AAFCO's minimum requirements for reproduction or maintenance (*e.g.*, the composition comprises less iodine and/or selenium than the amount recommended by the AAFCO). In some embodiments, the food composition comprises a dry food. In some embodiments, the food composition comprises a semi-moist food. In some embodiments, the food composition comprises a moist food. As familiar to one of skill in the art, "wet" food refers to food which is sold in cans or foil bags and has a moisture content of about 70 to about a 90%; "semi-moist" refers to a food that has a moisture content of about 15% to about 40% and "dry" food refers to compositions with about 5 to about 15% moisture content and is often manufactured in the form of small

bits or kibbles. In some embodiments, the food composition comprises a supplement, treat, snack, or partially or fully edible toy. In some embodiments, the composition comprises a mixture of two or more foods.

[0013] In some embodiments, a composition of the invention as described above further comprises an antithyroid agent (*i.e.*, the composition comprises one or more antithyroid agents). An antithyroid agent is a compound, a derivative thereof (*e.g.*, a salt, solvate, or hydrate of the compound), or a composition comprising such compounds and/or derivatives that is used to treat hyperthyroidism. Suitable antithyroid agents include, for example, thioureylenes (*e.g.*, methimazole, propylthiouracil, and carbimazole), aniline derivatives (*e.g.*, sulfonamides), polyhydric phenols (*e.g.*, resorcinol), and lithium salts. In some embodiments, the antithyroid agent comprises a thioureylene. Thioureylenes are five- or six-member thiourea derivatives that block production of thyroid hormones. In some such embodiments, the antithyroid agent comprises the thioureylene methimazole. In other such embodiments, the antithyroid agent comprises the thioureylene propylthiouracil. In further such embodiments, the antithyroid agent comprises the thioureylene carbimazole.

[0014] In some embodiments, a composition of the invention comprises a therapeutically-effective amount of an antithyroid agent (*i.e.*, the composition comprises one or more antithyroid agents, and the total amount of the antithyroid agents is a therapeutically-effective amount). A therapeutically-effective or effective amount is an amount that will achieve the goal of treating the targeted condition. Those skilled in the art either know or can determine by routine experimentation how much of an agent or combination of agents to administer to a feline to treat hypothyroidism. For example, one skilled in the art can prepare a composition that, when fed to the feline in a maintenance-sufficient amount, typically will deliver a therapeutically-effective amount of the agent(s) present in the composition. In some cases, the amount of the antithyroid agent may vary with the stage of treatment. For example, higher doses of an antithyroid agent may be used in the initial stage of treatment (*i.e.*, the therapeutically-effective amount of the particular agent may vary with the stage of the disease). One skilled in the art can prepare compositions of the invention with varying amounts of an antithyroid agent, and then feed those compositions sequentially to deliver the desired amount of antithyroid agent(s) to the feline.

[0015] Tables 2 and 3 of U.S. Patent Application Publication No. US 2005/0058691 A1 list the iodine and selenium content of commercially available canned and dry cat foods. The average amounts of selenium in the 28 tested canned foods and 14 tested dry foods were 1.77 and 0.69 mg/kg on a dry matter basis, respectively, with many foods having more than 2 mg/kg. The average amounts of iodine in those foods were 7.83 mg/kg and 2.77 mg/kg on a dry matter basis, respectively, with some foods having more than 30 mg/kg. Thus, the compositions of the invention comprise amounts of iodine and/or selenium that are lower (and in some embodiments, much lower) than the amounts of iodine and selenium in many commercially available foods. Thus, in some embodiments, feeding a composition of the invention to a feline results in restricting the feline's intake of iodine. In other embodiments, feeding a composition of the invention to a feline results in restricting the feline's intake of selenium. In further embodiments, feeding a composition of the invention to a feline results in restricting the feline's intake of both iodine and selenium.

[0016] Also described is a method for preparing a composition of the invention. Such a composition can be prepared, for example, by combining two or more compositions (including food compositions) or one or more food compositions and additional ingredient(s) such as, for example, an antithyroid agent. A composition of the invention can also be prepared by one or more of the methods discussed in, for example, Small Animal Clinical Nutrition (Michael Hand ed., Mark Morris Institute 4th ed. 2000), pages 127 - 146.. To prepare a low selenium-comprising composition of the invention, one can use, for example, a selenium-free mineral mix and ingredients that contain small amounts of selenium such as, for example, potato concentrate, soy concentrate, and soy protein isolate. To prepare a low iodine-comprising composition, one can, for example, avoid food colorings rich in iodine and can use an iodine-free mineral mix, non-iodized salt, or ingredients that contain small amounts of iodine such as, for example, potato concentrate, soy concentrate, and soy protein isolate.

[0017] Iodine and selenium-containing ingredients suitable for preparing a composition of the invention are listed in, for example, table 3 of U.S. Patent Application Publication No. US 2005/0058691 A1. Protein sources low in iodine are particularly useful, e.g., vegetable protein sources low in iodine, with regard to the compositions of the present invention. Plant ingredients suitable for preparing a composition of the invention include, for example, soybean meal, corn gluten meal, rice protein isolate, pea protein concentrate, wheat protein concentrate, and wheat protein isolate. Eggs can be used for preparing a composition of the invention as well. Meat (including fish) ingredients suitable for preparing a composition of the invention include, for example, pork liver, beef spleen, beef tongue, pork lung lobes, beef lung, meat protein isolate, deboned turkey, chicken backs, mackerel, oceanfish, and poultry by-product meal.

[0018] Crude protein content in the compositions of the present invention can be in an amount of from about 10%, from about 15%, from about 20%, from about 25%, from about 30%, from about 35% up to about 40%, up to about 45%, up to about 50%, up to about 55%, up to about 60%, up to about 70%, up to about 80%, up to about 90% or greater on a dry matter basis. Preferably the crude protein content is from 30 to 34%. Preferably composition comprises 1 - 10% animal protein as formulated.

[0019] Carbohydrate can be supplied from grain ingredients. Such grain ingredients can comprise vegetable materials, typically farinaceous materials, which can supply primarily, dietary digestible carbohydrate and indigestible carbohydrate (fiber) and less than about 15% protein on a dry matter basis. Examples include without limitation brewers rice, yellow corn, corn flour, soybean mill run, rice bran, cellulose, gums, and the like. Typically, carbohydrate can be present in the compositions of the present invention in amounts of from about 5%, from about 10%, from about 15%, from about 20%, from about 25%, from about 30%, up to about 35%, up to about 40%, up to about 45%, up to about 50%, up to about 55%, up to about 60%, up to about 70%, up to about 80%, up to about 90% or greater, on a dry matter basis. Preferably carbohydrate is present in an amount from 35 - 55%. Preferably 35 - 50% of the composition is grain.

[0020] Fats used include animal fats and oils, such as choice white grease, chicken fat, and the like; vegetable fats and oils; and fish oils. Fats can be present in the compositions

of the present invention in concentrations of from about 5%, from about 10%, from about 15%, up to about 20%, up to about 25%, up to about 30% up to about 35%, up to about 40% or greater on a dry matter basis. Preferably fat is present in an amount from 10 - 20% as analyzed. The composition may comprise 8 - 12% animal fat as formulated.

[0021] Vitamins and minerals may can be included into the food compositions of the present invention, and are known by those of skill in the art. Sources of vitamins can include complex natural sources such as brewers yeast, engivita yeast, and the like, and synthetic and purified sources such as choline chloride and the like. Minerals in the food compositions of the present invention can include dicalcium phosphate, calcium carbonate, calcium sulfate, potassium chloride, potassium citrate, iodized and non-iodized salt as required to achieve a desired iodine content, and other conventional forms of the mineral nutrients known in the art. Preferably, potassium iodide is not added to the compositions of the present invention, as potassium iodide may provide levels that are undesirably high with regard to the compositions of the present invention (data not shown).

[0022] As discussed above, commercially available cat foods typically contain higher amounts of iodine and selenium than the amounts of iodine and/or selenium in a composition of the invention. Thus, to minimize iodine and/or selenium carryover, before preparing a composition of the invention, it may be desirable to clean the equipment that will be used. For example, to minimize iodine or selenium carryover from an earlier retort or extrusion run, the equipment can be appropriately flushed before a low iodine- and/or low selenium-comprising composition of the invention will be made. In some cases, it may also be desirable to discard the initial portion of a batch to obtain a composition with a consistent concentration of iodine and/or selenium throughout the entire batch.

[0023] Also described is a method for treating hyperthyroidism in a feline. The method may comprise feeding the feline a composition selected from the compositions of the invention discussed herein. One skilled in the art would understand that either a single composition of the invention can be fed to the feline or, alternatively, different compositions can be fed to the feline for varying time intervals.

[0024] The present invention requires feeding the feline a composition that comprises from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis. In some such methods, the method comprises feeding the feline a composition that comprises from about 0.1 to about 0.8 mg/kg selenium on a dry matter basis. In other such methods, the method comprises feeding the feline a composition that comprises from about 0.15 to about 0.65 mg/kg selenium on a dry matter basis. In further such methods, the method comprises feeding the feline a composition that comprises from about 0.4 to about 0.7 mg/kg selenium on a dry matter basis. In yet further such methods, the method comprises feeding the feline a composition that comprises from about 0.3 to about 0.65 mg/kg selenium on a dry matter basis.

[0025] In some described methods, the method comprises feeding the feline a composition that comprises from about 0.1 to less than about 1 or from about 0.1 to about 0.27 mg/kg iodine on a dry matter basis and from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis. In some such methods, the method comprises feeding the feline a composition that comprises from about 0.1 to about

0.5 mg/kg iodine on a dry matter basis and from about 0.1 to about 0.8 mg/kg selenium on a dry matter basis. In other such methods, the method comprises feeding the feline a composition that comprises from about 0.1 to about 0.3 mg/kg iodine on a dry matter basis and from about 0.15 to about 0.65 mg/kg selenium on a dry matter basis. In further such methods, the method comprises feeding the feline a composition that comprises (1) from about 0.1, about 0.15, or about 0.2 to about 0.25, about 0.3, or about 0.5 mg/kg iodine on a dry matter basis, and (2) from about 0.1, about 0.15, about 0.3, or about 0.4 to about 0.65, about 0.7, or about 0.8 mg/kg selenium on a dry matter basis.

[0026] In some described methods, the method for treating hyperthyroidism of the invention comprises administering to the feline an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.1 to less than about 1 or from about 0.1 to about 0.27 mg/kg iodine on a dry matter basis. "Administering" means that the antithyroid agent is introduced in a suitable dosage form into the feline by a suitable administration route, for example, orally, topically, or parenterally. The term "in conjunction" means that the antithyroid agent is administered to the feline either together with a composition of the invention or separately from the composition at the same or different frequency via the same or different administration route and either at about the same time as the composition or periodically. "About at the same time" generally means that an agent is administered when a composition of the invention is fed to the feline or within about 72 hours of feeding the composition to the feline. "Periodically" generally means that an agent is administered to a feline following a dosage schedule suitable for administering the agent while a composition of the invention is fed to the feline routinely as appropriate for that feline. Thus, the term "in conjunction" specifically includes situations when an agent is administered to a feline for a prescribed period of time while a composition of the invention is fed to the feline for a much longer period of time (e.g., for life). If more than one agent is administered to a feline, the dosage form and route of administration for each agent may vary. In addition, as discussed above, one composition of the invention may be substituted with another composition of the invention while a specific agent is administered to the feline.

[0027] The method for treating hyperthyroidism of the invention comprises administering to the feline an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.1 to less than about 1, or 0.2 - 0.66 mg/kg selenium on a dry matter basis. In some such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.1 to about 0.8 mg/kg selenium on a dry matter basis. In other such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.15 to about 0.65 mg/kg selenium on a dry matter basis. In further such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.4 to about 0.7 mg/kg selenium on a dry matter basis. In yet further such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.3 to about 0.65 mg/kg selenium on a dry matter basis.

[0028] In some methods, the method for treating hyperthyroidism of the invention comprises administering to the feline an antithyroid agent in conjunction with feeding the

feline a composition that comprises from about 0.1 to less than about 1 or from about 0.1 to about 0.27 mg/kg iodine on a dry matter basis and from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis. In some such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.1 to about 0.5 mg/kg iodine on a dry matter basis and from about 0.1 to about 0.8 mg/kg selenium on a dry matter basis. In other such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises from about 0.1 to about 0.3 mg/kg iodine on a dry matter basis and from about 0.15 to about 0.65 mg/kg selenium on a dry matter basis. In further such methods, the method comprises administering an antithyroid agent in conjunction with feeding the feline a composition that comprises (1) from about 0.1, about 0.15, or about 0.2 to about 0.25, about 0.3, or about 0.5 mg/kg iodine on a dry matter basis, and (2) from about 0.1, about 0.15, about 0.3, or about 0.4 to about 0.65, about 0.7, or about 0.8 mg/kg selenium on a dry matter basis.

[0029] As discussed in the context of the food compositions for use of the invention, the antithyroid agents suitable for the methods of treatment discussed above include, for example, thioureylenes, aniline derivatives, polyhydric phenols, and lithium salts. In some methods, the method comprises administering to the feline an antithyroid agent that comprises a thioureylene. In some methods, the method comprises administering an antithyroid agent comprising methimazole. In some methods, the method comprises administering to a feline an antithyroid agent comprising propylthiouracil. In some methods, the method comprises administering an antithyroid agent comprising carbimazole. In some methods, the method comprises administering a therapeutically-effective amount of an antithyroid agent in conjunction with feeding the feline a composition of the invention. The composition fed to a feline comprises the antithyroid agent administered to the feline. In some such methods, the method comprises feeding the feline a composition of the invention that comprises a therapeutically-effective amount of an antithyroid agent. Antithyroid agents can be administered, for example, in the form of salts derived from inorganic or organic acids. Depending on the particular compound, a salt of the compound may be advantageous due to one or more of the salt's physical properties, for example, enhanced pharmaceutical stability in differing temperatures and humidities, or a desirable solubility in water or oil. The salt preferably is a pharmaceutically-acceptable salt.

[0030] The preferred total daily dose of the antithyroid agent (administered in single or divided doses) is typically from about 0.001 to about 100 mg/kg body weight, more preferably from about 0.01 to about 30 mg/kg body weight, and even more preferably from about 0.01 to about 10 mg/kg body weight. Dosage unit compositions can contain such amounts and submultiples thereof to make up the daily dose. In many instances, the administration of the antithyroid agent will be repeated a plurality of times. Multiple doses per day typically may be used to increase the total daily dose, if desired. Factors affecting the preferred dosage regimen include, for example, the age, weight, and condition of the feline; the severity of the disease; the route of administration; pharmacological considerations, such as the activity, efficacy, pharmacokinetic, and toxicology profiles of the particular antithyroid agent used; whether a drug delivery system is utilized; and whether the antithyroid agent is administered as part of a drug combination. Thus, the

dosage regimen can vary widely, and therefore, can differ from the preferred dosage regimen discussed above.

[0031] The methods of treatment described are convenient and easy to practice. In some methods, it is sufficient to feed a composition of the invention to a feline diagnosed with hyperthyroidism. In some such methods, the composition does not contain any antithyroid agents nor are such agents administered to the feline in conjunction with feeding the feline the composition. Thus, such methods provide a cost-effective alternatives to treatment with antithyroid agents. In addition, such methods do not cause the side effects attributed to treatment with antithyroid agents, for example, kidney damage. Finally, such methods result in better compliance because one need only feed a feline a composition of the invention rather than administer, for example, an oral or topical antithyroid drug. As discussed above, in some methods, the methods of treatment comprise feeding the feline a composition comprising an antithyroid agent. Such methods of treatment are more convenient and easier to practice because they eliminate the need for, for example, oral or topical administration of antithyroid agents. In some methods, the methods of treatment allow for administering less antithyroid agent than would be administered in a drug only treatment because the administration of an antithyroid agent in conjunction with feeding the feline a composition of the invention results in a synergistic cooperation between the antithyroid agent administered to the feline and the composition of the invention fed to the feline. In addition, one skilled in the art would know that either a single composition of the invention can be fed to the feline or that different compositions of the invention can be fed to the feline for varying time intervals.

[0032] Also described is a use of a composition of the invention as discussed above to prepare a medicament for treating hyperthyroidism in a feline. The medicament may also comprise one or more conventional pharmaceutically acceptable carriers, adjuvants, and/or vehicles (together referred to as excipients).

[0033] Also described is a use of iodine and selenium to prepare a composition of the invention (as discussed above) to treat hyperthyroidism in a feline.

[0034] Described is a use of selenium to prepare a composition that comprises from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis and, optionally, an anti-thyroid agent. The composition is used to treat hyperthyroidism. Described is a use of selenium to prepare a composition to treat hyperthyroidism that comprises from about 0.1, about 0.15, about 0.3, or about 0.4 to about 0.65, about 0.7, or about 0.8 mg/kg selenium on a dry matter basis and, optionally, an antithyroid agent. The composition is a food composition.

[0035] Described is a use of iodine and selenium to prepare a composition that comprises from about 0.1 to less than about 1 or from about 0.1 to about 0.27 mg/kg iodine on a dry matter basis, from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis, and, optionally, an anti-thyroid agent. The composition is used to treat hyperthyroidism. Described is a use of iodine and selenium to prepare a composition to treat hyperthyroidism that comprises from about 0.1, about 0.15, or about 0.2 to about 0.25, about 0.3, or about 0.5 mg/kg iodine on a dry matter basis, from about 0.1, about 0.15, about 0.3, or about 0.4 to about 0.65, about 0.7, or about 0.8 mg/kg

selenium on a dry matter basis, and, optionally, an antithyroid agent. The composition is a food composition.

[0036] In a further aspect, the invention provides an article of manufacture, for example, a kit for treating hyperthyroidism in a feline that comprises a composition of the invention. The kit further comprises an antithyroid agent (*i.e.*, the kit comprises one or more antithyroid agents). In some embodiments, the kit can further comprise instructions for one or more of (1) feeding the food composition to a feline, (2) administering an antithyroid agent to a feline in conjunction with feeding the feline the composition, (3) treating hyperthyroidism in a feline by feeding the feline the composition, and (4) treating hyperthyroidism in a feline by administering to the feline an antithyroid agent in conjunction with feeding the feline the food composition.

[0037] In a further aspect, the invention provides an article of manufacture, for example, a kit for treating hyperthyroidism in a feline that comprises two or more ingredients that, when combined together and optionally with additional ingredients that are not a part of the kit, yield a food composition of the invention. One of the two or more ingredients that are to be combined can be, for example, iodine or a derivative thereof or a composition comprising iodine or the iodine derivative(s). Another one of the two or more ingredients that are to be combined can be, for example, selenium or a derivative thereof or a food composition comprising selenium or the selenium derivative(s). Yet another one of the two or more ingredients that are to be combined can be, for example, a food composition. If, to prepare a composition, additional ingredients that are not a part of the kit are needed, the kit provides instructions about those ingredients. The kit further comprises an antithyroid agent. In some embodiments, the kit further comprises instructions for one or more of (1) preparing a composition of the invention by combining the two or more ingredients and, optionally, additional ingredients that are not a part of the kit, (2) feeding the composition to a feline to, for example, treat hyperthyroidism, (3) administering an antithyroid agent to the feline in conjunction with feeding the feline the composition, (4) treating hyperthyroidism in a feline by feeding the feline a composition of the invention, and (5) treating hyperthyroidism in a feline by administering to the feline an antithyroid agent in conjunction with feeding the feline the composition.

[0038] In some embodiments, the kit comprises in separate containers in a single package, a food composition of the invention or two or more ingredients, that, when combined together and optionally with additional ingredients that are not a part of the kit, yield a food composition of the invention, and instructions for one or more of (1) feeding the food composition to a feline, (2) preparing a food composition of the invention by combining the two or more ingredients and, optionally, additional ingredients that are not a part of the kit, (3) treating hyperthyroidism in a feline by feeding the feline the food composition, (4) administering an antithyroid agent to the feline in conjunction with feeding the feline the food composition, and (5) treating hyperthyroidism in a feline by administering to the feline an antithyroid agent in conjunction with feeding the feline the food composition. The term "single package" generally means that the components of a kit are physically associated in or with one or more containers and considered as a unit of manufacture, distribution, sale, or use. Containers include, for example, bags, boxes, bottles, shrink wrap packages, stapled or otherwise fixed components, or combinations thereof. A single package can be, for example, containers or individual food compositions

physically associated such that they are considered a unit for manufacture, distribution, sale, or use.

[0039] Described is a kit comprising in separate containers in a single package a composition comprising from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis, and, optionally, an antithyroid agent, or two or more ingredients, that, when combined together and optionally with additional ingredients that are or are not a part of the kit, yield a composition comprising from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis, and an antithyroid agent, and one or more of (1) instructions for feeding the composition to the feline, (2) instructions for preparing the composition by combining the two or more ingredients, (3) instructions for treating hyperthyroidism in a feline by feeding the feline the composition, (4) one or more antithyroid agents, (5) instructions for administering an antithyroid agent to the feline in conjunction with feeding the feline the composition, and (6) instructions for treating hyperthyroidism in a feline by administering to the feline an antithyroid agent in conjunction with feeding the feline the composition. In some kits, the two or more ingredients combined to prepare a composition of the invention comprise one or more of a composition comprising selenium, a composition comprising iodine and selenium, and a composition suitable for consumption by a feline.

[0040] Also described is a means for communicating information about or instructions for one or more of (1) using a composition of the invention to treat hyperthyroidism in a feline, (2) treating hyperthyroidism in a feline by administering to the feline an antithyroid agent in conjunction with feeding the feline a composition of the invention, and (3) using a kit of the invention for treating hyperthyroidism in a feline. The means for communicating information comprises a document, digital storage media, optical storage media, audio presentation, or visual display containing the information or instructions. The communicating means may comprise a document, digital storage media, optical storage media, audio presentation, or visual display containing the information or instructions. Preferably, the communication means is a displayed web site or a brochure, product label, package insert, advertisement, or visual display containing such information or instructions. Useful information or instructions include, for example, (1) information and instructions how to use a composition, method, or kit of the invention and (2) contact information for animal caregivers if they have a question about the invention and its uses.

[0041] Also described is a means for communicating information about or instructions for one or more of (1) treating hyperthyroidism in a feline by feeding the feline a composition comprising from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis, and an antithyroid agent, (2) treating hyperthyroidism in a feline by administering to the feline an antithyroid agent in conjunction with feeding the feline a composition comprising from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis, (3) using a kit of the invention, and (4) using selenium to prepare a composition for treating hyperthyroidism in a feline that comprises from from about 0.1 to less than about 1, or from about 0.2 to about 0.66 mg/kg selenium on a dry matter basis, and, an antithyroid agent. The means for communicating information comprises a document, digital storage media, audio presentation, or visual display containing the information or instructions. In some such means, the means for

communicating information comprises a brochure, product label, package insert, advertisement, displayed web site, or visual display.

[0042] All percentages expressed herein are by weight of the composition on dry matter basis unless specifically stated otherwise. The term "dry matter basis" means that an ingredient's concentration in a composition is measured after any moisture in the composition is removed.

[0043] The invention is not limited to the particular methodology, protocols, and reagents described herein because they may vary. Further, the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the present invention. As used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Similarly, the words "comprise", "comprises", and "comprising" are to be interpreted inclusively rather than exclusively.

[0044] Unless defined otherwise, all technical and scientific terms and any acronyms used herein have the same meanings as commonly understood by one of ordinary skill in the art in the field of the invention.

EXAMPLES

[0045] The invention can be further illustrated by the following examples, although it will be understood that the examples are included merely for purposes of illustration and are not intended to limit the scope of the invention unless otherwise specifically indicated.

Example 1

[0046] Example 1 illustrates the effect of the compositions of the invention on treating hyperthyroidism in cats.

[0047] Food B1 is formulated as a dry cat food containing 0.6% selenium on a dry matter basis. Food B1 comprises soybean meal, corn gluten meal, poultry meal, and pork meat protein isolate as the protein ingredients, and is formulated with both iodized and non-iodized salt but no selenomethionine and selenium. The average moisture content is 6.6% on a dry matter basis, the average protein content is 33.7% on a dry matter basis, and the average iodine content is 0.38 mg/kg on a dry matter basis (ten samples are taken for iodine analysis, and the iodine content of those samples vary from 0.27 to 0.60 mg/kg on a dry matter basis).

[0048] Food B2 is formulated as a wet cat food containing 0.6% selenium on a dry matter basis. It comprises soybean meal, pork lungs, chicken, and pork liver as the protein ingredients. No source of iodine is intentionally added to Food B2. No selenomethionine or selenium salts are added to Food B1. The average moisture content for those samples is

78.2% on a dry matter basis, the average protein content is 33.2% on a dry matter basis, and the average iodine content is 0.21 mg/kg on a dry matter basis (ten samples are taken for iodine analysis, and the iodine content of those samples vary from 0.14 to 0.27 mg/kg on a dry matter basis).

[0049] Food B1 and Food B2 are mixed in a 1:1 ratio, thus resulting in Food B. A group of five cats diagnosed with hyperthyroidism is fed Food B for six weeks. Another five cats diagnosed with hyperthyroidism are given 2.5 mg methimazole orally once a day for six weeks while they are fed Food B. Eight cats diagnosed with hyperthyroidism are given 2.5 mg methimazole orally once a day for six weeks while they are fed a commercially available cat food. The thyroid hormone profiles and serum chemistries of all cats are measured at zero, two, four, and six weeks. All cats enrolled in the study have elevated total T_4 and/or free T_4, with the majority of the cats exhibiting one or more clinical signs associated with hyperthyroid disease (*e.g.*, weight loss, heart murmur/tachycardia, unkempt hair coat, thyroid gland enlargement, increased appetite, vomiting, increased activity, diarrhea, polyuria/polydipsia, aggressiveness, and panting).

[0050] Food intake is measured daily and body weight is measured weekly. Blood is drawn aseptically after overnight removal of food. Blood for complete blood counts and serum for thyroid hormone analyses is analyzed. Blood for other measurements is centrifuged at 5000 g and the serum harvested and frozen and stored at -70°C for serum chemistries and iodine and selenium concentration analysis.

[0051] T4 concentration is measured by radioimmunoassay for use in cats. Serum free T4 concentration is determined by use of equilibrium dialysis to separate the bound forms from the free forms; radioimmunoassay is used to measure the concentrations of the free forms in the dialysate. Serum creatinine levels is measured at the beginning and end of the study (Boehringer Mannheim automated serum chemistry analyzer).

[0052] Serum and dietary iodine levels are measured by epithermal instrumental neutron activation analysis using a boron nitride irradiation capsule (Spate et al., J Radioanalytical Nuclear Chem 195: 21-30, 1995).

[0053] The results from the study are presented in Tables 1 and 2.

Table 1

Change in Serum Total T_4 Levels	
Treatment	Change in Serum Total T_4 Levels (nmol/L)
Methimazole	-20.3
Food B	-31.5
Methimazole + Food B	-42.2

Table 2

Change in Serum Creatinine Levels	
Treatment	Change in Serum Creatinine Levels (mg/dL)
Methimazole	+0.46

Change in Serum Creatinine Levels	
Treatment	Change in Serum Creatinine Levels (mg/dL)
Food B	-0.08
Methimazole + Food B	-0.03

[0054] The results indicate treatment with 2.5 mg methimazole administered orally once daily for six weeks results in a decrease in serum total T_4 concentration and in an increase in serum creatinine concentration (serum creatinine is a bit higher than the 0.8-1.8mg/dL normal creatinine concentration range). Although this treatment is effective (the total T_4 concentration is lowered although it did not reach the normal total T_4 concentration range of 10-55 nmol/dL), it may cause or exacerbate kidney disease, and may therefore be unsuitable for treating hyperthyroidism in cats with renal insufficiency.

[0055] Feeding Food B results in a greater decrease in serum total T_4 concentration than treatment with 2.5 mg methimazole alone (although the total T_4 concentration is still a bit higher than the normal total T_4 concentration range). It also results in a decrease in serum creatinine concentration (with creatinine concentration falling within the normal creatinine range). Feeding Food B is a more effective treatment for hyperthyroidism than administering 2.5 mg methimazole alone. Feeding Food B does not result in the side effects associated with methimazole treatment. Food B is also suitable for felines suffering from or susceptible to developing renal insufficiency.

[0056] Administering 2.5 mg methimazole while feeding Food B results in the greatest decrease in serum total T_4 concentration. That decrease in serum total T_4 concentration is higher than the corresponding decrease for treatment with methimazole only with T_4 falling within the normal total T_4 concentration range, indicating that there is a synergism between the action of Food B and the antithyroid agent. Administering methimazole in conjunction with feeding Food B also results in a decrease in serum creatinine concentration (with serum creatinine concentration within the normal range), indicating that the combination is suitable for felines with or susceptible to developing renal insufficiency. Treating hyperthyroidism with methimazole typically involves administering a total of 5 mg methimazole orally (2.5 mg twice a day). The above results demonstrate that administering methimazole in conjunction with feeding Food B allows for lowering the amount of the antithyroid drug, thus improving compliance, lowering treatment cost, and/or minimizing side effects.

Example 2

[0057] Examples 2 illustrates the effect of the compositions of the invention on treating hyperthyroidism in cats.

[0058] Fifteen cats diagnosed with hyperthyroidism are fed Food B (from Example 1) for twelve weeks. Eleven cats diagnosed with hyperthyroidism are fed a commercially

available cat food (*i.e.,* control food) for twelve weeks. The thyroid hormone profiles and serum chemistries of all cats are measured at zero, two, four, six, and twelve weeks. All cats enrolled in the study have elevated total T_4 and/or free T_4, with the majority of the cats exhibiting one or more clinical signs associated with hyperthyroid disease. The results from this study are presented in Tables 3 and 4.

Table 3

Change in Serum Total T_4 Levels	
Treatment	Change in Serum Total T_4 Levels (nmol/L)
Control Food	+6.5
Food B	-50.4

Table 4

Change in Serum Creatinine Levels	
Treatment	Change in Serum Creatinine Levels (mg/dL)
Control Food	+0.282
Food B	-0.277

[0059] Feeding control food for twelve weeks results in an increase in both serum total T_4 and serum creatinine concentrations (with the total T_4 concentration above the normal range and the creatinine concentration within the normal range). Feeding Food B for twelve weeks results in a decrease in both serum total T_4 and serum creatinine concentrations (with both total T_4 and creatinine concentrations falling within the normal ranges).

Example 3 (illustrative)

[0060] 15 hyperthyroid cats, averaging 13.7 years of age, are allotted to one of three groups fed different foods (i.e., 5 cats per food). Diets are similar in composition, with the exception of iodine concentration indicated below. A majority of the iodine is from the ingredients. The foods generally comprise crude protein 30 - 34%, fat 10 - 20%, selenium 0.4 - 0.7 mg/kg selenium, grain 50 - 55%, animal fat 8 - 10 %, animal protein 1 - 10%, and 5 - 6% other ingredients. The foods are fed for 12 weeks. Material and methods for analysis of serum T_4 levels are as previously described. The results of the study are presented in Tables 5 and 5A

Table 5 - T_4 serum levels in cats.

Iodine concentration	Initial T_4 (nmol/L)	Week 3 T_4 (nmol/L)	Week 12 T_4 (nmol/L)
0.27 mg/kg	79.8	45	48
0.42 mg/kg	84.6	76	81.2
2.52 mg/kg	73.2	77.2	98.5

Table 5A - Analysis of change in T_4 serum levels

Iodine concentration	Week 0 to 3 T_4 change	Statistical signif. week 3	Week 0 - 12 T_4 change	Statistical signif. week 12
0.27 mg/kg	-34.8	(P < 0.05)	-31.8	(P<0.05)
0.42 mg/kg	-8.6	NS*	-3.4	NS*
2.52 mg/kg	4.0	NS*	25.3	(P<0.05)
* NS = Not signifigant				

[0061] The results show that diets containing 0.27 mg/kg iodine are efficacious in lowering T_4 serum levels, whereas 0.42 mg/kg iodine is not. While T_4 serum levels is not statistically decreased in cats consuming the 0.42 mg/kg iodine concentration, T_4 is also not increased. Hyperthyroid cats fed the control diet of 2.52 mg/kg iodine, which is a typical iodine concentration found in commercially available catfoods, have increased T_4 concentrations at the end of the 12 week study.

[0062] In the specification, there are disclosed typical preferred embodiments of the invention and, although specific terms are employed, they are used in a generic and descriptive sense only and not for purposes of limitation, the scope of the invention being set forth in the claims.

Patentkrav

1. Fodersammensætning, der omfatter fra 0,1 til mindre end 1 mg/kg selen på tørstofbasis, i forbindelse med et antithyroidt middel, som et kombinations-præparat til anvendelse til behandling af hyperthyroidisme hos et kattedyr.

2. Fodersammensætning ifølge krav 1, der endvidere omfatter fra 0,1 til 0,8 mg/kg selen på tørstofbasis.

3. Fodersammensætning ifølge et hvilket som helst af de foregående krav, der omfatter fra 0,15 til 0,65 mg/kg selen på tørstofbasis.

4. Fodersammensætning ifølge krav 1 eller krav 2, der omfatter fra 0,2 til 0,66 mg/kg selen på tørstofbasis.

5. Fodersammensætning ifølge et hvilket som helst af de foregående krav, der yderligere omfatter fra 0,1 til mindre end 1 mg/kg jod på tørstofbasis.

6. Fodersammensætning ifølge et hvilket som helst af de foregående krav, der omfatter fra 0,1 til 0,5 mg/kg jod på tørstofbasis.

7. Fodersammensætning ifølge et hvilket som helst af de foregående krav, der omfatter fra 0,1 til 0,3 mg/kg jod på tørstofbasis.

8. Fodersammensætning ifølge et hvilket som helst af de foregående krav, der omfatter fra 0,1 til 0,27 mg/kg jod.

9. Fodersammensætning ifølge et hvilket som helst af de foregående krav, der omfatter fra 0,1 til 0,5 mg/kg jod på tørstofbasis og fra 0,1 til 1,0 mg/kg selen på tørstofbasis.

10. Fodersammensætning ifølge det foregående krav, der omfatter fra 0,1 til 0,3 mg/kg jod på tørstofbasis og fra 0,15 til 0,65 mg/kg selen på tørstofbasis.

11. Fodersammensætning ifølge et hvilket som helst af de foregående krav, hvor kattedyret er en kat.

12. Fodersammensætning ifølge et hvilket som en helst af de foregående krav, hvor det antithyroide middel omfatter thioureylen, fortrinsvis udvalgt fra gruppen bestående af methimazol, propylthiouracil og carbimazol.

13. Kit til behandling af hyperthyreoidisme hos et kattedyr, der i separate beholdere i en enkeltpakning efter behov omfatter:
en fodersammensætning, der omfatter fra 0,1 til mindre end 1 mg/kg selen på tørstofbasis, og et antithyroidt middel, eller
to eller flere bestanddele, der, når de kombineres sammen og eventuelt med yderligere bestanddele, som er eller ikke er en del af kittet, giver en fodersammensætning, som omfatter fra 0,1 til mindre end 1 mg/kg selen på tørstofbasis, og et antithyroidt middel, og
én eller flere (1) instruktioner til fodring af kattedyret med fodersammensætningen, (2) instruktioner til tilberedning af fodersammensætningen ved kombinering af de to eller flere bestanddele, (3) instruktioner til behandling af hyperthyroidisme ved fodring af kattedyret med fodersammensætningen, (4) et eller flere antithyroide midler, (5) instruktioner til indgivelse af et antithyroidt middel til kattedyret i forbindelse med fodring af kattedyret med fodersammensætningen, og (6) instruktioner til behandling af hyper-thyroidisme ved indgivelse af et antithyroidt middel til kattedyret i forbindelse med fodring af kattedyret med fodersammensætningen.