

(19) DANMARK

(10) DK/EP 3119198 T3



(12)

Oversættelse af
europæisk patentskrift

Patent- og
Varemærkestyrelsen

(51) Int.Cl.: **A 01 N 37/06 (2006.01)** **A 61 K 31/215 (2006.01)** **A 61 K 31/225 (2006.01)**
A 61 K 31/231 (2006.01) **A 61 K 45/06 (2006.01)**

(45) Oversættelsen bekendtgjort den: **2020-07-13**

(80) Dato for Den Europæiske Patentmyndigheds
bekendtgørelse om meddelelse af patentet: **2020-04-08**

(86) Europæisk ansøgning nr.: **15733524.1**

(86) Europæisk indleveringsdag: **2015-03-17**

(87) Den europæiske ansøgnings publiceringsdag: **2017-01-25**

(86) International ansøgning nr.: **IB2015000633**

(87) Internationalt publikationsnr.: **WO2015140637**

(30) Prioritet: **2014-03-18 US 201461954785 P**

(84) Designerede stater: **AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR**

(73) Patenthaver: **Institut de Recherche en Semiochimie et Ethologie Appliquée, Quartier Salignan, 84400 Apt, Frankrig**

(72) Opfinder: **PAGEAT, Patrick, Le Fénier du Plan - Route de Saint-Saturnin, F-84400 Apt, Frankrig**

(74) Fuldmægtig i Danmark: **Patrade A/S, Ceresbyen 75, 8000 Århus C, Danmark**

(54) Benævnelse: **SEMIOKEMISKE SAMMENSÆTNINGER TIL AT REDUCERE SOCIALE KONFLIKTER MED KATTE**

(56) Fremdragne publikationer:
WO-A1-96/23414
WO-A1-99/37297
WO-A1-2014/001836
US-A- 6 054 481

DK/EP 3119198 T3

DESCRIPTION

FIELD OF THE INVENTION

[0001] The present disclosure discloses a semiochemical composition comprising methyl laurate, methyl myristate, methyl palmitate, methyl linoleate, methyl oleate, methyl stearate, dimethyl pimelate, dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities and mixtures thereof. The invention relates to a semiochemical composition as defined in claim 1, or a solution comprising it as defined in claim 7. The invention also relates to methods to reduce social conflicts in multi-cat households or in catteries or kennels boarding cats, as well as methods for inducing social facilitation in cats, as defined in claim 9.

BACKGROUND AND PRIOR ART

[0002] Felidae are known to be solitary predators and they generally do not live in socially structural groups, with the exception of lions. Cats travel alone, hunt alone and only associate with other adult cats for mating. Domestic cats tend to be solitary and do not form large complex social groups. Cats are also very territorial by nature and mark their territory using scent derived from facial glands, feces, urine and anal glands. This territorial marking helps the cat to communicate with other cats and to minimize direct conflict. If another cat encroaches its marked territory an aggressive interaction is maintained by the cat to chase the invading cat off its territory by staring, hissing and growling and if this does not happen to work, through a short noisy violent physical attack. Cats do not invest energy in maintaining social bonds nor do they reconcile after a conflict (Van den Bos (1998) Post-conflict stress-response in confined group-living cats (*Felis sylvestris catus*). *Applied Animal Behaviour Science* 59:323-330).

[0003] Cats are not aggressive for any reason. There are in fact causes for the aggressiveness, as well as different type of aggression such as intercat aggression caused when two or more cats have a hostile relationship with each other; redirected aggression caused when the cat hears or sees something that it cannot have access to; petting-induced aggression caused by petting beyond the cats tolerance; fear aggression caused when the cat feels backed in a corner with no way out; play-related aggression caused while the cats plays; territorial aggression caused when another animal invades the cats territory; pain-induced aggression caused when one touches a hurting or injured spot on the cat; maternal aggression caused when a cat's kitten is threatened; and unprovoked aggression caused for no reason whatsoever.

[0004] Aggressive behavior in cats is often encountered when there are several cats in a sole household that are unfamiliar with each other or when the cats are at a cattery or kennel boarding cats with other unfamiliar cats. Thus it is well known that when a new cat is brought into a household having other cats friction between these felines very often occurs. This is especially true when cats live indoors and are forced to live in close proximity to each other which is foreign to the cat's nature and forces cats into an unnatural social arrangement. Behavioral problems often arise such as territorial urine marking and infighting to establish a dominance controlled hierarchy. In many cases the less dominant cat can develop chronic stress which can result in idiopathic cystitis. In some cases the cat can become a social outcast and won't come out of hiding for meals or to eliminate.

[0005] The critical period for a cat's socialization to conspecifics and humans is between two to eight weeks postpartum (Jongman, EC (2007) Adaptation of domestic cats to confinement. *Journal of Veterinary*

Behavior 2;1920196). Cats that do not have adequate interactions during this period with conspecifics become socially dysfunctional and have inappropriate behavior towards other cats. Poorly socialized cats are more stressed than socialized cats in multi-cat households and have a negative affect on the rest of the group by increasing the other cats stress levels (Kessler MR and Turner DC (1999a) Effects of density and cage size on stress in domestic cats (*Felis sylvestris catus*) housed singly, in pairs and in groups in boarding catteries. Animal Welfare 6:243-254).

[0006] Semiochemicals are chemicals emitted by a plant or an animal that evokes a behavioral or physiological response in another organism. When the semiochemical affects an individual of the same species, it is called a pheromone. When the semiochemical affects an individual of a different species, it is called an allelochemical.

[0007] Pheromones are substances released by the body of particular species that cause a predictable reaction by another individual of the same species, which may serve, for example, as a specific attractant, social communicator, sexual stimulant, appeasement and effects basic animal behavior. There are different types of pheromones such as aggregation pheromones that function in defense against predators, mate selection and overcoming host resistance by massive attack; alarm pheromones, which are released when attacked by a predator; epideictic pheromones, which are recognized by insects for signaling other insect that they should clutch elsewhere; releaser pheromones, which are attractant pheromones that some organisms use to attract mates from a distant of two miles or more; signal pheromones, which cause short term changes such as releasing a neurotransmitter which activates a response; primer pheromones, which trigger a change of developmental events; territorial pheromones, which mark the boundary of an animal's territory; trail pheromones, prevalent in insects, such as ants that lay down pheromones as they return to their nest with food; information pheromones, which are indicative of an animal's identity or territory; sex pheromones, which indicate the availability of the female for breeding; cats' facial pheromones that prevents cats from urinating on a marked spot or to prevents anxiety in cats or to familiarize cats in a new environment; and appeasement pheromones, which decrease stress, anxiety and aggressiveness in animals.

[0008] U.S. Patent 5,709,863 discloses a composition comprising an emulsion comprising a mixture of oleic acid, azelaic acid, pimelic acid, and palmitic acid, said mixture capable of preventing cats from urinating in a marked spot; and a compound of vegetal origin that has an attractive effect on cats. It does not describe a semiochemical to reduce social conflicts in cats and/or to improve social facilitation in multi-cat households or catteries or in kennels boarding multiple cats. WO 96/23414 A1 also describes such a composition containing an emulsion comprising a mixture of fatty acids of oleic acid, azelaic acid, pimelic acid and palmitic acid for treating a cat's anxiety or preventing cats from urinating in a marked spot.

[0009] U.S. Patents 6,054,481, 6,077,867, 6,169,113, 6,384,252 and 7,723,388 all describe various mammalian and avian appeasing pheromones. However none of these patents describe the management of social conflicts and/or to improve social facilitation in multi-cat households or catteries or kennels that board cats.

[0010] It is also known from US 6 054 481 A a particular pig appeasing pheromone for enhancing weight gain in a mammal, and from WO 99/37297 A1 particular pig appeasing pheromone compositions, containing palmitic acid, oleic acid and linoleic acid, to decrease stress, anxiety and aggressiveness in mammals.

[0011] WO 2014/001836 A1 describes a particular semiochemical composition comprising a feline cat scratch marking pheromone including valeric acid, lactic acid and linoleic acid, to prevent cats from

scratching in particular places and on multiple objects.

[0012] Conversely, it is an object of the present invention to provide semiochemical compositions for the management of social conflicts in multi-cat households or catteries or kennels that board cats.

[0013] Yet another object of the present invention is to provide a method to reduce social conflicts in multi-cat households or catteries or kennels that board cats.

[0014] In yet another object is to provide a method to induce social facilitation of cats in multi-cat households or catteries or kennels that board cats.

[0015] These and other objects are achieved by the present invention as evidenced by the summary of the invention, the description of the preferred embodiments and the claims.

SUMMARY OF THE INVENTION

[0016] The present description discloses a semiochemical composition comprising methyl laurate, methyl myristate, methyl palmitate, methyl linoleate, methyl oleate, methyl stearate, dimethyl pimelate, dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities.

[0017] A semiochemical composition comprising a mixture of methyl laurate, methyl myristate, methyl palmitate, methyl linoleate, methyl oleate, methyl stearate, dimethyl pimelate, dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities is also encompassed by the present disclosure.

[0018] In another aspect a semiochemical composition is provided comprising between about 1% to 8% (w%/w%) methyl laurate, between about 1% to 8% (w%/w%) methyl myristate, between about 10% to 18% (w%/w%) methyl palmitate, between about 3% to 10% (w%/w%) methyl linoleate, between about 40% to 55% (w%/w%) methyl oleate, between about 1% to 8% (w%/w%) methyl stearate, between about 5% to 15% (w%/w%) dimethyl pimelate, between about 4% to 15% (w%/w%) dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities.

[0019] A semiochemical composition is provided comprising a mixture of between about 1% to 8% (w%/w%) methyl laurate, between about 1% to 8% (w%/w%) methyl myristate, between about 10% to 18% (w%/w%) methyl palmitate, between about 3% to 10% (w%/w%) methyl linoleate, between about 40% to 55% (w%/w%) methyl oleate, between about 1% to 8% (w%/w%) methyl stearate, between about 5% to 15% (w%/w%) dimethyl pimelate, between about 4% to 15% (w%/w%) dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities.

[0020] A semiochemical composition comprising between about 2% to 6% (w%/w%) methyl laurate, between about 2% to 6% (w%/w%) methyl myristate, between about 11% to 15% (w%/w%) methyl palmitate, between about 4% to 8% (w%/w%) methyl linoleate, between about 42% to 50% (w%/w%) methyl oleate, between about 2% to 6% (w%/w%) methyl stearate, between about 7% to 13% (w%/w%) dimethyl pimelate, between about 6% to 11% (w%/w%) dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities is yet

another aspect disclosed herein.

[0021] A semiochemical composition comprising a mixture of between about 2% to 6% (w%/w%) methyl laurate, between about 2% to 6% (w%/w%) methyl myristate, between about 11% to 15% (w%/w%) methyl palmitate, between about 4% to 8% (w%/w%) methyl linoleate, between about 42% to 50% (w%/w%) methyl oleate, between about 2% to 6% (w%/w%) methyl stearate, between about 7% to 13% (w%/w%) dimethyl pimelate, between about 6% to 11% (w%/w%) dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities is yet another aspect disclosed herein.

[0022] The invention more particularly relates to a semiochemical composition as defined in any one of claims 1 to 3.

[0023] The semiochemical compositions, as described herein, can further comprise an acceptable vehicle. This acceptable vehicle is a pharmaceutically acceptable vehicle or a veterinarian acceptable vehicle, as defined in claim 4.

[0024] The semiochemical compositions, as described herein, can further comprise a nontoxic filler or an enhancer composition. The nontoxic filler is selected from the group of fatty acids, alcohols, amines, squalene, glycerol and mixtures thereof, while the enhancer composition contains amines and fatty acids from indolic derivatives, esters of these amines and fatty acids, ketones, acetone, alcohols or sterols, as defined in claims 5 and 6.

[0025] In yet another aspect of the present disclosure, the semiochemical compositions, can be an ester, an alcohol, a ketone, an amide, an ether, an aldehyde or a sterol derivative of methyl laurate, methyl oleate, methyl myristate, methyl palmitate, methyl linolate, methyl linoleate, methyl stearate, dimethyl pimelate, dimethyl azelate, salts thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities and mixtures thereof.

[0026] A solution comprising the semiochemical composition, as described herein, and a solvent is yet another aspect of the invention, as defined in claim 7. The solution is in the form of a spray, an aerosol, is administered in diffuser, is microencapsulated or is a slow release matrix, as defined in claim 8.

[0027] A method to reduce social conflicts in multi-cat households or in catteries or kennels or for inducing social facilitation in cats said method comprising releasing said semiochemical composition of the invention, or the solution of the invention, in an environment surrounding cats is another aspect of the invention, as defined in claim 9. In this embodiment, the semiochemical composition or said solution can be released slowly. This release occurs between 3 to 5 weeks, as defined in claim 11, or 4 to 6 weeks and is generally in an indoor environment or an enclosed environment, as defined in claim 12.

[0028] A semiochemical composition, as described herein, for use in reducing social conflicts in catteries or kennels containing cats or in multi-cat households is another aspect of present disclosure.

[0029] A semiochemical composition, as described herein, for use in inducing social facilitation in cats is yet another aspect of present disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030]

Fig. 1 is a copy of the analogical visual scales that were filled out by the multi-cat owners and submitted at day 0, day 10, day 20 and day 30, which were presented in the analysis in the examples.

Fig. 2 is a graph showing the final results from the aggressiveness analysis from the study over 30 days. The scale 0 means that the cats never stop fighting when they are together since they threaten, scratch and bite one another. The scale 10 means that the cats do not ever fight. There was no significant difference between the two groups of treatment at day 0 (AVS aggression $z=0.868$; $p=0.385$; Mann Whitney test), but there was a significant improvement between the scores day 0 and day 30 $df=3$; $F=4.24$; $p=0.01$; ANOVA).

Fig. 3 is a graph showing the final results from the affiliation analysis from the study over 30 days. The scale 0 means that the cat's owners were not confident to let their cats together in the same room. The scale 10 means that the cat's owners were confident to let their cats together in the same room. There was no significant difference between the two groups of treatment at day 0 (AVS affiliation $z=-0.172$; $p=0.862$; Mann Whitney test), but there was a significant improvement between the scores day 0 and day 30 $df=3$; $F=5.49$; $p=0.003$; ANOVA).

Fig. 4 is a graph showing the final results at day 20 and day 30 for the treated group and the placebo group. At day 30 there was a higher score in the treated group than the placebo group for AVS 1 for aggressiveness and AVS 2 for Affiliation. The mean AVS 1 for aggression the treated group was 6.4, while the placebo was 5.5. For the AVS 2 Affiliation group, the mean for the treated was 7.02 and for the placebo was 4.93. At follow up 30 days after the treatment or placebo was discontinued, the owners confirmed that the situation was stable in the treated and placebo groups.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0031] As used herein the word "cat" encompasses any member of the family Felidae including the common domestic cats as well as feral cats, tigers, lions, leopards, mountain lions, lynx, bobcats, cheetahs, ocelots and the like.

[0032] As used herein "semiochemical" means a chemical emitted by a plant or an animal that evokes a behavioral or physiological response in another organism. When the semiochemical affects an individual of the same species, it is called a pheromone. When the semiochemical affects an individual of a different species, it is called an allelochemical.

[0033] "That maintain their semiochemical capabilities" means that the semiochemical composition reduces social conflicts in cats in multi-cat households, in catteries or in kennels containing cats. This is evidenced by the cats behavior which shows less aggressiveness to other cats and/or can be left together in the same room. It also includes inducing social facilitation in cats such that cats, for example eat together.

[0034] As used herein "aggressiveness in cats is when cats bite, scratch or threaten another cat by stalking, staring, yowling, howling and/or puffing up their fur.

[0035] By "social facilitation" is meant that cats that live together in a household are familiar, affiliated and friendly with one another and share a group scent.

[0036] By "stress-associated disease," as used herein, is meant any disease whose symptoms increase due to stress.

[0037] As used herein by "structural analogues" is meant any compound that has a structure similar to that of another but differs in one or more functional groups, atoms, or substructures which are replaced with other functional groups, atoms, or substructures. For instance, replacement of methyl groups with heteroatoms in the methyl fatty acids, described herein.

[0038] "Derivatives" as used herein include esters, alcohols, ketones, amides, ethers, aldehydes and sterols of the methyl esters of the fatty acids of methyl laurate, methyl myristate, methyl palmitate, methyl linolate, methyl linoleate, methyl stearate, methyl oleate, dimethyl pimelate, dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof and mixtures of methyl esters of the fatty acids of palmitate, linoleate, oleate, stearate, laurate, myristate, as well as structural analogs thereof and/or salts thereof. These methylated fatty acid derivatives can replace one or more of the fatty acids in the composition, as described herein, and have the same effects.

[0039] "Isomers" includes structural isomerism and spatial isomerism and refers to the methyl esters of the fatty acids of palmitate, linoleate, oleate, stearate, laurate, myristate, dimethyl pimelate, dimethyl azelate as well as salts thereof, derivatives thereof and/or structural analogs that maintain the pheromonal appeasement activity and/or social facilitation activity thereof and mixtures of methyl esters of the fatty acids of palmitate, linoleate, oleate, stearate, laurate, myristate, as well as structural analogs thereof that maintain the semiochemical activity and/or social facilitation activity, salts thereof and/or derivatives thereof.

[0040] As used herein the term "mixtures" encompasses the methyl esters of the fatty acids of palmitate, linoleate, oleate, stearate, laurate, myristate, dimethyl pimelate, dimethyl azelate as well as salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain the semiochemical activity and/or social facilitation activity in which the methyl esters of the fatty acids, as described herein, can be replaced with their salts and/or derivatives and/or isomers and/or structural analogs thereof that maintain the semiochemical activity and/or social facilitation activity. For example, the mixture can comprise the methyl ester of palmitate and the methyl ester of linoleate, derivatives of oleate and stearate, isomers of methyl laurate dimethyl pimelate and dimethyl azelate and a structural analogue of myristate.

[0041] The term "solution" is meant a solid or oil that is dispersed in a liquid either by being dissolved or in suspension.

[0042] The term "releasing" means to deliver the semiochemical composition, as described herein, or the solution, as described herein.

[0043] By "environments surrounding cats" is meant any surroundings in which the cats are present including houses, apartments, rooms, cages, enclosed porches and the like.

[0044] As used herein "reduce social conflicts in cats" means to lower the aggressiveness of cats for other cats.

[0045] "Released slowly" means that the semiochemical composition, as described herein, or the solution, as described herein, is released over a period of time and not at once. The time period may vary from 3 to 5 weeks or 4 to 6 weeks.

[0046] By "acceptable vehicle" is meant any pharmaceutically acceptable vehicle or veterinary vehicle that does not interfere with the activity of the cat appeasing pheromone composition and is not toxic to the cats to which it is administered. It includes solvents, dispersion media, absorption delaying agents and the like. These pharmaceutically acceptable vehicles are described in Remington's Pharmaceutical Sciences 21st edition 2005. An acceptable vehicle can be, for example, glycol ethers. It can be added to the cat appeasing pheromone during formulation.

[0047] By "enhancer composition" is meant an active semiochemical composition or analogues thereof that is species-specific in cats and which can be used to enhance or act synergistically with the basic semiochemical composition, as described herein, salts and/or analogues thereof to increase the effectiveness in felines of the basic semiochemical composition or analogues thereof.

[0048] By "consisting essentially of" means that the compositions contain all of the methyl ester fatty acids, salts thereof, derivatives thereof and isomers thereof and/or structural analogues, as described herein, as well as other additives that do not affect the semiochemical nature of the compositions.

[0049] More specifically, the present invention relates to the identification and synthesis of cat semiochemicals that are used to reduce social conflicts or induce social facilitation in cats. These compositions are made up of volatile molecules, the essential components being fatty acid methyl esters comprising methyl laurate, methyl myristate, methyl palmitate, methyl linoleate, methyl oleate, methyl stearate, dimethyl pimelate, dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogues thereof that maintain their semiochemical capabilities.

[0050] In another aspect a semiochemical composition is disclosed comprising between about 1% to 8% (w%/w%) methyl laurate, between about 1% to 8% (w%/w%) methyl myristate, between about 10% to 18% (w%/w%) methyl palmitate, between about 3% to 10% (w%/w%) methyl linoleate, between about 40% to 55% (w%/w%) methyl oleate, between about 1% to 8% (w%/w%) methyl stearate, between about 5% to 15% (w%/w%) dimethyl pimelate, between about 4% to 15% (w%/w%) dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities. The invention more particularly relates to a semiochemical composition as defined in claim 1.

[0051] A semiochemical composition comprising between about 2% to 6% (w%/w%) methyl laurate, between about 2% to 6% (w%/w%) methyl myristate, between about 11% to 15% (w%/w%) methyl palmitate, between about 4% to 8% (w%/w%) methyl linoleate, between about 42% to 50% (w%/w%) methyl oleate, between about 2% to 6% (w%/w%) methyl stearate, between about 7% to 13% (w%/w%) dimethyl pimelate, between about 6% to 11% (w%/w%) dimethyl azelate, salts thereof, derivatives thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities is yet another embodiment of the present disclosure. A particular embodiment of the invention is more particularly as defined in claim 2.

[0052] The concentration of the semiochemical composition in the final product can range from about 0.1% (w%/w%) to about 10% (w%/w%). In another aspect the concentration of the semiochemical composition in the final product can range from about 0.3% (w%/w%) to about 4% (w%/w%). In another aspect the concentration of the semiochemical composition in the final product can range from about 0.4% (w%/w%) to about 1% (w%/w%).

[0053] More specifically the semiochemical compositions described herein comprises a mixture of methyl laurate, methyl myristate, methyl palmitate, methyl linoleate, methyl oleate, methyl stearate, dimethyl pimelate, dimethyl azelate, salts, derivatives and isomers as well as their structural analogues, which

represents between 65% to 95% (wt%/wt%) of the total composition, the remaining ingredients being nontoxic filler compounds such as fatty acids, alcohols, amines, squalene and glycerol; more particularly, aproic acid, azelaic acid, propanoic acid, geraniol, octadecatrianol, hexacosanol, trimethyl amine and methyl amine.

[0054] An enhancer composition comprising between 5% to 35% (w%/w%) can also be added to the semiochemical composition, if desired. This enhancer composition comprises volatile organic compounds and mixtures thereof. This enhancer may be species-species specific in nature. The compounds that can be used in the enhancer composition include, but are not limited to amines and fatty acids from indolic derivatives, esters of these amines and fatty acids, ketones such as acetone, alcohols, sterols and the like, as defined in claim 6.

[0055] The cat appeasing semiochemical composition can be attached to a chemical carrier provided that the bioactive structure of the fatty acid methyl esters is preserved. Such carrier molecules include crown compounds, liposomes and carrier proteins.

[0056] The pharmaceutically acceptable salts of the cat semiochemical compositions that are used in the compositions, described herein, include those that are organic or inorganic salts of the fatty acid esters of methyl palmitate, methyl linoleate, methyl oleate, methyl stearate, methyl laurate, methyl myristate, dimethyl pimelate and dimethyl azelate. These are well known and described in the Physician's Desk Reference, The Merck Index and Goodman and Gilman's The Pharmacological Basis of Therapeutics. The pharmaceutically acceptable salts are, for example, sodium, potassium, ammonium, calcium and magnesium and salts formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and the like or salts formed with organic acids such as oxalic acid, fumaric acid, tartaric acid, malonic acid, acetic acid, citric acid, benzoic acid and the like.

[0057] The semiochemical compositions can also comprise an acceptable vehicle, as defined in claim 4. This acceptable vehicle can be a pharmaceutically acceptable vehicle or a veterinarian acceptable vehicle. The pharmaceutically acceptable vehicle can be any acceptable carrier or vehicle that does not interfere with the pharmaceutical or veterinary activity of the composition and is not toxic to cats to it is administered. It includes solvents, dispersion media, coatings, absorption delaying agents and the like. These pharmaceutically acceptable vehicles are described in Remington's Pharmaceutical Sciences 22nd edition 2012. An acceptable vehicle can be, for example, saline, buffered saline and the like. It can be added to the composition after its formulation.

[0058] In yet another aspect the semiochemical composition disclosed herein, is an ester, an alcohol, a ketone, an amide, an ether, an aldehyde or a sterol derivative of methyl laurate, methyl myristate, methyl palmitate, methyl linolate, methyl linoleate, methyl stearate, methyl oleate, dimethyl pimelate, dimethyl azelate, salts thereof, isomers thereof and/or structural analogs thereof that maintain their semiochemical capabilities and mixtures thereof.

[0059] A solution comprising the semiochemical composition, as described herein, and a solvent is yet another aspect of the invention, as defined in claim 7. Solvents such as propylene glycol, alcohol, ether, chloroform, ethanol benzene, carbon disulfide, propyl alcohol, isopropanol, 2-propanol, fixed and volatile oils, diethylene glycol monoethyl ether, diethylene glycol monomethyl ether, diethylene glycol monopropyl ether, diethylene glycol monoisopropyl ether, diethylene glycol monobutyl ether, diethylene glycol monophenyl ether, diethylene glycol monobenzyl ether, diethylene glycol dimethyl ether, ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, ethylene glycol monopropyl ether, ethylene glycol monoisopropyl ether, ethylene glycol monobutyl ether, ethylene glycol monophenyl ether, ethylene glycol

monobenzyl ether or ethylene glycol dimethyl ether and the like.

[0060] The solution can be in the form of a spray, an aerosol, is administered in a diffuser, is microencapsulated or is a slow release matrix or a spray, as defined in claim 8. It can also be in the form of a cat collar which releases the semiochemical at a slow rate.

[0061] A method to reduce social conflicts in multi-cat households by releasing said semiochemical composition, as described herein, or the solution containing the semiochemical composition, as described herein, in an environment surrounding cats, is encompassed by the present invention, as defined in claim 9. In this aspect, the multi-cat households have at least two cats, as defined in claim 10. The semiochemical composition, as described herein, or said solution, as described herein, is released slowly into the environment surrounding cats. This slow release occurs between 4 to 6 weeks. In another aspect the slow release occurs between 3 to 5 weeks, as defined in claim 11.

[0062] The environment is an indoor environment or an enclosed environment, as defined in claim 12. Some examples of enclosed environments include pet carriers, enclosed rooms, animal pens and enclosed porches.

[0063] A method to reduce social conflicts in catteries or kennels containing cats said method comprising releasing said semiochemical composition, as described herein or the solution containing the semiochemical composition, as described herein, in an environment surrounding cats, is encompassed by the present invention, as defined in claim 9. The semiochemical composition, as described herein, or said solution, as described herein is released slowly into the environment surrounding cats. This slow release occurs between 4 to 6 weeks. In another aspect the slow release occurs between 4 to 6 weeks or 3 to 5 weeks, as defined in claim 11.

[0064] The environment is an indoor environment or an enclosed environment, as defined in claim 12. Some examples of enclosed environments include pet carriers, enclosed rooms, animal pens and enclosed porches.

[0065] In another aspect the present invention provides a method for inducing social facilitation in cats said method comprising releasing said semiochemical composition, as described herein, or the solution containing the semiochemical composition, as described herein, in an environment surrounding cats, as defined in claim 9. In this embodiment, the semiochemical composition or said solution is released slowly. This slow release occurs between 4 to 6 weeks. In another aspect the slow release occurs between 3 to 5 weeks, as defined in claim 11.

[0066] Present disclosure also discloses the semiochemical compositions, as described herein, for use in reducing social conflicts in multi-cat households.

[0067] Present disclosure also discloses the semiochemical compositions, as described herein, for use in reducing social conflicts in catteries or kennels containing cats.

[0068] Present disclosure also discloses the semiochemical compositions, as described herein, for use in inducing social facilitation in cats.

[0069] The semiochemical compositions and solutions, as described herein contain fatty acids. Fatty acids are commercially available from various companies in solid form. However, since it is difficult to solubilize fatty acids, the fatty acid is generally added to the solvent under constant agitation and at a temperature of

between about 37°C to about 38°C more preferably about 38°C.

[0070] Once obtained, the compositions of the present invention can be tested for the efficacy to manage social conflicts in cats and/or to induce social facilitation in cats. The present semiochemical compositions were discovered after intense evaluation of the behavior of cats with different pheromones.

[0071] In order to further illustrate the present invention and advantages thereof the following specific examples are given it being understood that the same are intended only as illustrative and in nowise limitative.

EXAMPLES

Example 1-Evaluation of the Efficacy of Treatment with semiochemical vs. placebo

[0072] This example was to test for the aggressiveness of multi-cat households in which the cats were currently in a situation of conflict. The evaluation of the treatment which consisted of a mixture of 11.4% (wt%/wt%) of dimethyl pimelate, 7.8% (wt%/wt%) of dimethyl azelate, 35.6% (wt%/wt%) of methyl palmitate, 95.2% (wt%/wt%) methyl oleate, 11% (wt%/wt%)methyl laurate, 11% (wt%/wt%)methyl myristate, 17% (wt%/wt%)methyl linoleate and 11% methyl sterate. 0.5% (wt%/wt%) of this mixture was diluted in 99.5% isopar V as a social facilitator in multi-cat households was administered via a diffuser. Households having 2 or 3 cats for more than 1 year, were evaluated with the aid of two analogical visual scales(AVS) filled out by the cats owner at different times of the study. The two analogical visual scales(AVS) were for aggressiveness(AVS 1) and affiliation (AVS 2). The cats' owner filled out these two forms at day 0 (T0), day 10 (T1), day 20 (T2) and day 30 (T3)of the study. The control was evaluated at 60 days (T4) by telephone. T1, T2 and T3 were effectuated by telephone with the people conducting this study. The questioner containing the analogical visual scales (AVS) used in the experiment and given to the owners of multi-cat households are described in Figure 1.

[0073] All the questioners were returned to the people conducting the study after the evaluation at day 30 (T3). At 1 month (T4) later a post-treatment evaluation by telephone was undertaken.

[0074] Eighteen households having at least two or three cats for more than 1 year and no aggression towards the owner, no aggression with wounds of the other cats and no other treatments were used in this study. Seven veterinary clinics recruited the multiple cat households or participated in the study and discussed the study and their acceptance into it by filing an agreement. This started at day 0 (T0) and called the inclusion visit.

[0075] Each owner was then provided with an electric diffuser that had either only the excipient, which was the placebo or the treatment. Instructions were also given on how to use the diffuser. The study was a multicenter, blinded placebo-controlled study having 10 placebos and 8 treatments. The diffusers were labeled 1 and 2 and were given to the cat owners depending on the surface area of the home. The diffusers covered rooms that were 500 to 700 square feet. The following Table 1 shows the distribution of the diffusers and their content:

Table 1

house	Processing Code	Treatment	Diffuser content
1	1	A	placebo

house	Processing Code	Treatment	Diffuser content
2	2	B	treatment
3	3	B	treatment
4	4	A	placebo
5	5	B	treatment
6	6	A	placebo
7	13	B	treatment
8	14	A	placebo
9	17	A	placebo
10	23	B	treatment
11	24	A	placebo
<hr/>			
12	45/48	A	placebo
13	46	B	treatment
14	49	B	treatment
15	50	A	placebo
16	51/54	B	treatment
17	52	A	placebo
18	53	A	placebo

[0076] The data was collected from the 18 owners of the multi-cat household. In the case of household 13, the owner dropped out of the study after three days since the owner decided not to participate in the study. In consequence the results were excluded from the data analysis and only 17 results were analyzed.

[0077] The analysis was analyzed for 17 households as set forth in Tables 2 and 3 below.

Table 2-student T test

variable	Average group A	Average Group B	t value	df	p value	Number of actives A	Number of actives B	Standard Deviation A	Standard Deviation B
AVS 1 Day 0	4.000000	4.100000	- .086130	15	0.932503	10	7	2.835881	1.346601
AVS 1 Day 10	4.300000	4.985714	- .484836	15	0.634797	10	7	3.459608	1.624221
AVS 1 Day 20	5.500000	5.842857	- .229643	15	0.821472	10	7	3.470191	2.209719
AVS 1 Day 30	5.888889	6.414286	- .347797	14	0.733166	9	7	3.352031	2.446377
AVS 2 Day 0	3.490000	4.300000	- .489146	15	0.631814	10	7	3.519612	3.105908
AVS 2 Day 10	4.040000	5.157143	- .715854	15	0.485077	10	7	3.520164	2.546146

variable	Average group A	Average Group B	t value	dl	p value	Number of actives A	Number of actives B	Standard Deviation A	Standard Deviation B
AVS 2 Day 20	5.160000	6.371429	- .758726	15	0.459773	10	7	3.644539	2.513772
AVS 2 Day 30	5.366667	7.028571	- .942942	14	0.361699	9	7	3.744663	3.137257

[0078] The ratio of F variances and the p variances are set forth in Table 3 below based on the data from the student T test for Group A and Group B. The two analogical visual scales(AVS) were for aggressiveness(AVS 1) and affiliation (AVS 2).

Table 3

Variable	Ratio of the F variance	p variance
AVS 1 Day 0	4.435049	0.083689
AVS 1 Day 10	4.536943	0.079445
AVS 1 Day 20	2.466225	0.284188
AVS 1 Day 30	1.877453	0.458448
AVS 2 Day 0	1.284140	0.786508
AVS 2 Day 10	1.911434	0.443555
AVS 2 Day 20	2.102005	0.378261
AVS 2 Day 30	1.424706	0.685197

[0079] No significant difference was observed between Group A (placebo) and Group B (treated).

[0080] A Shapiro-Wilk test for normality was then performed on Group A and Group B. The results are shown in Table 4 below.

Table 4

Variable	Group A	Group B	Normality
AVS 1 day 0	0.06539	0.33781	Yes
AVS 1 day 10	0.01196	0.48727	No
AVS 1 day 20	0.25822	0.47791	Yes
AVS 1 day 30	0.49347	0.30573	Yes
AVS 2 day 0	0.07433	0.20306	Yes
AVS 2 day 10	0.02647	0.72960	No
AVS 2 day 20	0.25541	0.24576	Yes
AVS 2 day 30	0.18436	0.06120	Yes

[0081] Table 5 set forth below showed the results from a Mann-Whitney U test.

Table 5

Placebo				Treatment					
variable	average	median	Standard deviation	average	median	Standard deviation	U	Z	p value
AVS 1 Day 0	4.00	4.80	2.83	4.10	4.70	1.34	32.00	0.2439	0.807
AVS 1 Day10	4.30	4.40	3.45	4.98	4.70	1.62	33.0	-0.1463	0.883
AVS 1 Day 20	5.50	5.70	3.47	5.84	5.00	2.20	33.0	-0.1463	0.883
AVS 1 Day 30	5.88	7.00	3.35	6.41	6.40	2.44	29.0	-0.2117	0.832
AVS 2 Day 0	3.49	2.35	3.51	4.30	2.60	3.10	28.0	-0.6343	0.525
AVS 2 Day 10	4.04	2.15	3.52	5.15	5.20	2.54	25.0	-0.9271	0.353
AVS 2 Day 20	5.16	4.60	3.64	6.37	7.60	2.51	31.0	-0.3415	0.732
AVS2 Day 30	5.36	7.10	3.74	7.02	9.00	3.13	21.0	-1.0585	0.289

[0082] Tests significantly different at p<0.500

[0083] Another Mann Whitney U test was run and the results are shown in the Table below in Table 6.

Table 6

Variable	Total Regression A	Total Regression B	U	z	p value	Adjusted z	p value	Number active A
AVS 1 day 0	93.00000	60.00000	32.00000	0.24398	0.807250	0.2442	.806902	10
AVS 1 day 10	88.00000	65.00000	33.00000	-.14639	0.883618	-.14656	.883476	10
AVS 1 day 20	88.00000	65.00000	33.00000	-.14639	0.883618	-.14656	.883476	10
AVS 1 day 30	74.00000	62.00000	29.00000	-.21170	0.832339	-.21186	.832218	9
AVS 2 day 0	83.00000	70.00000	28.00000	-.63434	0.52863	-.63550	.525100	10
AVS 2 day 10	80.00000	73.00000	25.00000	-.92711	0.353873	-.92711	.353873	10
AVS 2 day 20	86.00000	67.00000	31.00000	-.34157	0.732678	-.34177	.732521	10
AVS day 30	66.00000	70.00000	21.00000	-1.05851	0.289823	-1.05851	.289823	9

[0084] A Mann Whitney U test was also performed for only the treated group B.

Table 7

variable	Number of active B	2*(1-p) p exact
AVS 1 day 0	7	0.812526
AVS 1 day 10	7	0.886775
AVS 1 day 20	7	0.886755
AVS 1 day 30	7	0.837063
AVS 2 day 0	7	0.536199
AVS 2 day 10	7	0.363842
AVS 2 day 20	7	0.739613
AVS 2 day 30	7	0.299126

[0085] There was no significant difference observed between group A and B in the treatment.

[0086] A Repeated Measures Anova statistical analysis was effectuated to evaluate the treatment factor for the four different times and the effect of time between day 0 (D0) and day 30 (D30), as well as the variations in the responses of the cats owner to the AVS and in function of time of the treatment. The results are shown in Table 8 for AVS1.

Table 8-AVS 1

Effect	Sum of Squares	Degree of liberty	Mean square	Degree of freedom F	p value
Ordinate of origin	1707.943	1	1707.943	69.33264	0.000001
treatment	1.048	1	1.048	0.04254	0.839568
error	344.877	14	24.634		
time	39.980	3	13.327	5.07375	0.004348
time of treatment	0.595	3	0.198	0.07555	0.972826
error	110.318	42	2.627		

[0087] A significant difference was observed regarding the time factor. In effect an augmentation was observed between D0 (day 0) and D30 (day 30).

[0088] A Tukey's HSD Post-hoc test was then utilized to calculate the data from the ANOVA statistical test set forth above in Table 8. The results are set forth in Table 9 below.

Table 9

Cell number	treatment	time	1 4.1111	2 4.6667	3 5.6444	4 5.8889	5 4.1000	6 4.9857
1	A	AVS 1 day 0		0.995681	0.489636	0.303788	1.000000	0.998438
2	A	AVS 1 day 10	0.995681		0.901241	0.747762	0.999910	0.999998
3	A	AVS 1 day 20	0.489636	0.901241		0.999981	0.956039	0.999756
4	A	AVS 1	0.303788	0.747762	0.999981		0.909623	0.998078

		day 30							
5	B	AVS 1 day 0	1.000000	0.999910	0.956039	0.909623			0.968360
6	B	AVS 1 day 10	0.998438	0.999998	0.999756	0.998078	0.968360		
7	B	AVS 1 day 20	0.922422	0.990268	1.000000	1.000000	0.486541	0.973561	
8	B	AVS 1 day 30	0.744082	0.918987	0.999322	0.999946	0.160145	0.718493	

Table 9 (continued)

Cell number	7	8
	5.8429	6.4143
1	0.922422	0.7444082
2	0.990268	0.918987
3	1.000000	0.999322
4	1.000000	0.999946
5	0.486541	0.160145
6	0.973561	0.718493
7		0.997664
8	0.997664	

[0089] For AVS 2 further analysis for the repeated measures of variance was undertaken and shown in Table 10.

Table 10-AVS 2

Effect	Sum of Squares	Degree of liberty	Mean square	Degree of freedom F	p value
ordinate of origin	1685.498	1	1685.498	44.34161	0.000011
treatment	18.498	1	18.498	0.48664	0.496854
error	532.163	14	38.012		
time	47.379	3	15.793	6.23770	0.001335
time of treatment	2.416	3	0.805	0.31814	0.812179
error	106.338	42	2.532		

[0090] A significant difference was observed regarding the time factor. In effect augmentation was observed between D0 (day 0) and D30 (day 30).

[0091] A Tukey's HSD Post-hoc test was then utilized to calculate the data from the ANOVA statistical test set forth above in Table 10. The results are set forth in Table 11 below.

Table 11

Cell	treatment	time	1	2	3	4	5	6
------	-----------	------	---	---	---	---	---	---

number			3.6667	4.3222	5.1667	5.3667	4.3000	5.1571
1	A	AVS 2 day 0		0.986915	0.494237	0.335567	0.999936	0.985107
2	A	AVS 2 day 10	0.986915		0.947367	0.8555610	1.000000	0.999596
3	A	AVS 2 day 20	0.494237	0.947367		0.999995	0.999485	1.000000
4	A	AVS 2 day 30	0.335567	0.8555610	0.999995		0.998030	1.000000
5	B	AVS 2 day 0	0.999936	1.000000	0.999485	0.998030		0.970745
6	B	AVS 2 day 10	0.985107	0.999596	1.000000	1.000000	0.970745	
7	B	AVS 2 day 20	0.750965	0.921349	0.995766	0.998649	0.251635	0.839301
8	B	AVS 2 day 30	0.520436	0.750447	0.950741	0.972791	0.047718	0.372257

Table 11 (continued)

Cell number	7	8
	6.3714	7.0286
1	0.750965	0.520436
2	0.921349	0.750447
3	0.995766	0.950741
4	0.998649	0.972791
5	0.251635	0.047718
6	0.839301	0.372257
7		0.993737
8	0.993737	

Inappropriate Urination in the Home

[0092] With respect to the results concerning inappropriate urination in the home that were recorded by the cats' owners, no significant difference was observed between the treatment and the placebo. The Fisher's exact statistical test was used in this analysis of a bilateral situation. The results are shown below in Table 12.

Table 12

Day	p value
T0 (day 0-inclusion visit)	1.0000
T1 (day 10)	1.0000
T2(day 20)	0.3024
T3 (day 30)	0.2821

[0093] Chi-squared statistics were used to analysis the data for inappropriate urination in the household of

multi-cat owners. Tables 13 to 16 were the results for the inappropriate urination at day 0, day 10, day 20, and day 30, respectively.

Table 13

Urination at day 0	Column 1	Column 2	Gross total
Effectives line 1	6	3	9
Percentage of total	37.500%	18.750%	56.250%
Effectives line 2	4	3	7
Percentage of total	25.000%	18.750%	43.750%
Total in column	10	6	16
Percentage of total	62.500%	37.500%	
Chi ² (dl=1)	0.15	p=.6963	
V ² (dl=1)	0.14	p=.7055	
Chi ² Yates corrected	0.02	p=.8965	
Phi ²	0.00952		
P exact Fisher, unilateral		p=.5490	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	0.44	p=.5050	
Chi ² (B/C)	0.00	p=1.0000	

Table 14

Urination at day 10	Column 1	Column 2	Gross total
Effectives line 1	2	7	9
Percentage of total	12.500%	43.750%	56.250%
Effectives line 2	2	5	7
Percentage of total	12.500%	31.250%	43.750%
Total in column	4	12	16
Percentage of total	25.000%	75.000%	
Chi ² (dl=1)	.08	p=.7711	
V ² (dl=1)	.08	p=.7782	
Chi ² Yates corrected	.08	p=.7711	
Phi ²	.00529		
P exact Fisher, unilateral		p=.6077	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	.57	p=.4497	
Chi ² (B/C)	1.78	p=.1824	

Table 15

Urination at day 20	Column 1	Column 2	Gross total
Effectives line 1	2	7	9
Percentage of total	12.500%	43.750%	56.250%
Effectives line 2	4	3	7

Urination at day 20	Column 1	Column 2	Gross total
Percentage of total	25.000%	18.750%	43.750%
Total in column	6	10	16
Percentage of total	37.500%	62.500%	
Chi ² (dl=1)	2.05	p=.1523	
V ² (dl=1)	1.92	p=.1658	
Chi ² Yates corrected	0.83	p=.3624	
Phi ²	.12804		
P exact Fisher, unilateral		p=.1818	
Bilateral		p=.3024	
Chi ² McNemar (A/D)	0.00	p=1.0000	
Chi ² (B/C)	0.36	p=.5465	

Table 16

Urination at day 30	Column 1	Column 2	Gross total
Effectives line 1	1	7	8
Percentage of total	6.667%	46.667%	53.333%
Effectives line 2	3	4	7
Percentage of total	20.000%	26.667%	46.667%
Total in column	4	11	15
Percentage of total	26.667%	73.333%	
Chi ² (dl=1)	1.76	p=.1847	
V ² (dl=1)	1.64	p=.2001	
Chi ² Yates corrected	.55	p=.4586	
Phi ²	.11729		
P exact Fisher, unilateral		p=.2308	
Bilateral		p=.2821	
Chi ² McNemar (A/D)	.80	p=.3711	
Chi ² (B/C)	.90	p=.3428	

[0094] Chi-squared statistics were used to analysis the data for aggressivness in the household of multi-cat owners. The results are shown at day 10 and day 20 in Tables 17 and 18, respectively.

Table 17

Aggressiveness at day 10	Column 1	Column 2	Gross total
Effectives line 1	6	4	10
Percentage of total	35.294%	23.529%	58.824%
Effectives line 2	5	2	7
Percentage of total	29.412%	11.765%	41.176%
Total in column	11	6	17

Aggressiveness at day 10	Column 1	Column 2	Gross total
Percentage of total	64.706%	35.294%	
Chi ² (dl=1)	0.24	p=0.6275	
V ² (dl=1)	0.22	p=0.6378	
Chi ² Yates corrected	.00	p=0.9758	
Phi ²	.01385		
P exact Fisher, unilateral		p=0.5158	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	1.13	p=0.2889	
Chi ² (B/C)	0.00	p=1.0000	

Table 18

Aggressiveness at day 20	Column 1	Column 2	Gross total
Effectives line 1	6	4	10
Percentage of total	35.294%	23.529%	58.824%
Effectives line 2	4	3	7
Percentage of total	23.529%	17.647%	41.176%
Total in column	10	7	17
Percentage of total	58.824%	41.176%	
Chi ² (dl=1)	.01	p=.9062	
V ² (dl=1)	.01	p=.9090	
Chi ² Yates corrected	0.15	p=.7018	
Phi ²	0.00082		
P exact Fisher, unilateral		p=.6461	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	0.44	p=.5050	
Chi ² (B/C)	0.13	p=.7237	

[0095] For day 30 of aggressiveness the Chi² test had a value of 1.0018 and the Fisher test had a value of Pr<=1.0000.

[0096] Besides the 17 households that were analyzed as set forth above the data was further analyzed for 15 households since household numbers 14 and 24 lacked certain data. In the case of household 14, AVS 1 and AVS 2 was missing for day 30 and in the case of household 24, the data for inappropriate urination for day 0 to day 30 was missing.

[0097] The data that was obtained was recalculated without household numbers 14 and 24 that lacked certain data and thus was partially incomplete. A comparison was made of the aggressive behavior and the confidence given by the owner to let their cats alone in the same room in the house.

[0098] The statistical analysis was based on the Mann Whitney U test for independent examples. The

results are shown in Table 19 below.

Table 19

variable	Placebo			Treatment					
	average	median	Standard deviation	Average	median	Standard deviation	U	Z	p value
AVS 1 D0	4.58	5.10	2.80	4.10	4.70	1.34	20.00	0.8679	0.385
AVS 1 D10	5.02	7.00	3.51	4.98	4.70	1.62	23.00	0.5207	0.602
AVS 1 D20	5.82	7.70	3.85	5.84	5.00	2.20	27.00	0.0578	0.953
AVS 1 D30	5.50	6.10	3.35	6.41	6.40	2.44	24.00	-0.4050	0.685
AVS 2 D0	4.10	3.95	3.68	4.30	2.60	3.10	26.00	-0.1735	0.862
AVS 2 D10	4.66	4.80	3.70	5.15	5.20	2.54	25.00	-0.2893	0.772
AVS 2 D20	5.30	6.05	4.11	6.37	7.60	2.51	27.00	-0.0578	0.953
AVS2 D30	4.93	5.15	3.75	7.02	9.00	3.13	18.00	-1.0994	0.271

[0099] Tests that were significant had a p<0.05000.

[0100] There was no significant difference observed between Group A (placebo) and Group B (treated).

[0101] A student T test was then performed on Groups A and B. The results are shown in Table 20 below:

Table 20

Variable	Average A	Average B	t value	df	p	Number of actives Group A	Number of actives Group B	Standard deviation Group A	Standard Deviation Group B
AVS 1 day 0	4.587500	4.100000	0.41865	13	0.682305	8	7	2.801243	1.346601
AVS 1 day 10	5.025000	4.985714	0.02707	13	0.978813	8	7	3.512732	1.624221
AVS 1 day 20	5.825000	5.842857	-0.01077	13	0.991571	8	7	3.857368	2.209719
AVS 1 day 30	5.500000	6.414286	-.59419	13	0.562583	8	7	3.359422	2.446377
AVS 2 day 0	4.100000	4.300000	-.11263	13	0.912046	8	7	3.687043	3.105908
AVS 2 day 10	4.662500	5.157143	-.29667	13	0.771402	8	7	3.703642	2.546146
AVS 2 day 20	5.300000	6.371429	-.59728	13	0.560580	8	7	4.110266	2.513772

Variable	Average A	Average B	t value	df	p	Number of actives Group A	Number of actives Group B	Standard deviation Group A	Standard Deviation Group B
AVS 2 day 30	4.937500	7.028571	1.15094	13	0.267288	8	7	3.759155	3.137257

[0102] The ratio of F variances and the p variances are set forth in Table 21 below based on the data from the student T test for Group A and Group B in Table 20.

Table 21

variable	Ratio F variance	p variance
AVS 1 day 0	4.327370	0.093954
AVS 1 day 10	4.677347	0.078946
AVS 1 day 20	3.047250	0.195800
AVS 1 day 30	1.885742	0.457315
AVS 2 day 0	1.409221	0.691911
AVS 2 day 10	2.115883	0.379936
AVS 2 day 20	2.673549	0.251528
AVS 2 day 30	1.435755	0.675425

[0103] No significant difference was observed between Group A and Group B.

[0104] The normality statistical test was performed using the Shapiro-Wilk test. The following results are found in Table 22.

Table 22

Variable	Group A	Group B	Normality
AVS 1 day 0	0.04214	0.33781	No
AVS 1 day 10	0.01661	0.48727	No
AVS 1 day 20	0.06299	0.47791	Yes
AVS 1 day 30	0.78681	0.30573	Yes
AVS 2 day 0	0.22194	0.20306	Yes
AVS 2 day 10	0.09212	0.72960	Yes
AVS 2 day 20	0.08154	0.34576	Yes
AVS 2 day 30	0.33217	0.06120	Yes

[0105] A Mann Whitney U test was performed and the results are shown in Table 23 below.

Table 23

Variable	Total Regression A	Total Regression B	U	Z	p value	Adjusted z	p value	Number active A
AVS 1 day 0	72.00000	48.00000	20.00000	0.86796	0.385419	0.86951	0.384569	8
AVS 1 day 10	69.00000	51.00000	23.00000	0.52077	0.602525	0.52124	0.602200	8
AVS 1 day 20	65.00000	55.00000	27.00000	0.05786	0.953857	0.05792	0.953816	8
AVS 1 day 30	60.00000	60.00000	24.00000	-0.40505	0.685444	-0.40541	0.685178	8
AVS 2 day 0	62.00000	58.00000	26.00000	-0.17359	0.862187	-0.17390	0.861943	8
AVS 2 day 10	61.00000	59.00000	25.00000	-0.28932	0.772338	-0.28932	0.772338	8
AVS 2 day 20	63.00000	57.00000	27.00000	-0.05786	0.953857	-0.05792	0.953816	8
AVS 2 day 30	54.00000	66.00000	18.00000	-1.09941	0.271590	-1.09941	0.271590	8

[0106] Evaluation of only the treated group by the Mann-Whitney U test is set forth in Table 24 below.

Table 24

variable	Number of active B	2*(1-p) p exact
AVS 1 day 0	7	0.396892
AVS 1 day 10	7	0.612587
AVS 1 day 20	7	0.955089
AVS 1 day 30	7	0.694328
AVS 2 day 0	7	0.866511
AVS 2 day 10	7	0.778866
AVS 2 day 20	7	0.955089
AVS 2 day 30	7	0.280963

[0107] There was no significant difference observed between group A and B in the treatment.

[0108] An analysis using ANOVA was performed for AVS 1. The results are shown in Table 25 below.

Table 25-AVS 1

Effect	Sum of Squares	Degree of liberty	Mean square	Degree of freedom	p value
Ordinate of origin	1668.453	1	1668.453	64.20662	0.000002
treatment	0.153	1	0.153	0.00590	0.939934
error	337.814	13	25.986		
time	25.644	3	8.548	4.24363	0.010923

Effect	Sum of Squares	Degree of liberty	Mean square	Degree of freedom	p value
time of treatment	3.862	3	1.287	0.63902	0.594467
error	78.559	39	2.014		

[0109] A significant difference is observed regarding the time factor. In effect an augmentation of the AVS 1 was observed between D0 (day 0) and D30 (day 30).

[0110] A post-hoc Tukey's HSD test was then performed. The results are shown in Table 26 below.

Table 26

Cell number	treatment	time	1 4.5875	2 5.0250	3 5.8250	4 5.5000	5 4.1000	6 4.9857
1	A	AVS 1 day 0		0.998473	0.659686	0.898654	0.999969	0.999992
2	A	AVS 1 day 10	0.998473		0.946694	0.997409	0.997910	1.000000
3	A	AVS 1 day 20	0.659686	0.946694		.999787	0.928984	0.998890
4	A	AVS 1 day 30	0.898654	0.997409	0.999787		0.975653	0.999956
5	B	AVS 2 day 0	0.999969	0.997910	0.928984	0.975653		0.936378
6	B	AVS 2 day 10	0.999992	1.000000	0.998890	0.999956	0.936378	
7	B	AVS 2 day 20	0.986767	0.999059	1.000000	0.999997	0.320791	0.946084
8	B	AVS 2 day 30	0.907131	0.976650	0.999890	0.998065	0.071427	0.570106

Table 26 (continued)

Cell number	7 5.8429	8 6.4143
1	0.986767	0.907131
2	0.999059	0.976650
3	1.000000	0.999890
4	0.999997	0.998065
5	0.320791	0.071427
6	0.946084	0.570106
7		0.994577

8

0.994577

[0111] The date for AVS 2 is shown in Table 27 below using Repeated Measures Anova statistical analysis.

Table 27-AVS 2

Effect	Sum of Squares	Degree of liberty	Mean square	Degree of freedom F	p value
ordinate of origin	1635.219	1	1635.219	40.25694	0.000026
treatment	13.886	1	13.886	0.34185	0.568773
error	528.054	13	40.620		
time	31.320	3	10.440	5.49860	0.003007
time of treatment	7.787	3	2.596	1.36710	0.267056
error	74.049	39	1.899		

[0112] A significant difference was observed regarding the time factor. In effect an augmentation was observed between D0 (day 0) and D30 (day 30).

[0113] A post-hoc Turkey HSD evaluation was performed and the results are shown in Table 28 below.

Table 28

Cell number	treatment	time	1 4.1000	2 4.6625	3 5.3000	4 4.9375	5 4.3000	6 5.1571
1	A	AVS 1 day 0		0.991167	0.661020	0.922389	1.000000	0.998416
2	A	AVS 1 day 10	0.991167		0.981687	0.999915	0.999999	0.999990
3	A	AVS 1	0.661020	0.981687		0.999468	0.998900	1.000000

		day 20						
4	A	AVS 1 day 30	0.922389	0.999915	0.999468		0.999943	1.000000
5	B	AVS 2 day 0	1.000000	0.999999	0.998900	0.999943		0.937395
6	B	AVS 2 day 10	0.998416	0.999990	1.000000	1.000000	0.937395	
7	B	AVS 2 day 20	0.890548	0.972845	0.998277	0.989814	0.121276	0.718638
8	B	AVS 2 day 30	0.708945	0.869503	0.971139	0.924876	0.013809	0.209107

Table 28 (continued)

Cell number	7 6.3714	8 7.0286
1	0.890548	0.708945
2	0.972845	0.869503
3	0.998277	0.971139
4	0.989814	0.924876
5	0.121276	0.013809
6	0.718638	0.209107
7		0.985128

8	0.985128	
---	----------	--

[0114] The results for cat urination as set forth below in Tables 29 to 32.

Table 29

Urination at day 0	Column 1	Column 2	Gross total
Effectives line 1	5	3	8
Percentage of total	33.333%	20.000%	53.333%
Effectives line 2	4	3	7
Percentage of total	26.667%	20.000%	46.667%
Total in column	9	6	15
Percentage of total	60.000%	40.000%	
Chi ² (dl=1)	0.04	p=.8327	
V ² (dl=1)	0.04	p=.8383	
Chi ² Yates corrected	0.10	p=.7513	
Phi ²	0.00298		
P exact Fisher, unilateral		p=.6224	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	0.13	p=.7237	
Chi ² (B/C)	0.00	p=1.0000	

Table 30

Urination at day 10	Column 1	Column 2	Gross total
Effectives line 1	2	6	8
Percentage of total	13.333%	40.000%	53.333%
Effectives line 2	2	5	7
Percentage of total	13.333%	33.333%	46.667%
Total in column	4	11	15
Percentage of total	26.667%	73.333%	
Chi ² (dl=1)	.02	p=.8760	
V ² (dl=1)	.02	p=.8802	
Chi ² Yates corrected	.18	p=.6678	
Phi ²	.00162		
P exact Fisher, unilateral		p=.6615	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	0.57	p=.4497	
Chi ² (B/C)	1.13	p=.2889	

Table 31

Urination at day 20	Column 1	Column 2	Gross total
Effectives line 1	2	6	8
Percentage of total	13.333%	40.000%	53.333%
Effectives line 2	4	3	7
Percentage of total	40.000%	20.000%	46.667%
Total in column	6	9	15
Percentage of total	40.000%	60.000%	
Chi ² (dl=1)	1.61	p=.2049	
V ² (dl=1)	1.50	p=.2207	
Chi ² Yates corrected	0.55	p=.4596	
Phi ²	.10714		
P exact Fisher, unilateral		p=.2308	
Bilateral		p=.3147	
Chi ² McNemar (A/D)	0.00	p=1.0000	
Chi ² (B/C)	.10	p=.7518	

Table 32

Urination at day 30	Column 1	Column 2	Gross total
Effectives line 1	1	7	8
Percentage of total	6.667%	46.667%	53.333%
Effectives line 2	3	4	7
Percentage of total	20.000%	26.667%	46.667%
Total in column	4	11	15
Percentage of total	26.667%	73.333%	
Chi ² (dl=1)	1.76	p=.1847	
V ² (dl=1)	1.64	p=.2001	
Chi ² Yates corrected	.55	p=.4586	
Phi ²	.11729		
P exact Fisher, unilateral		p=.2308	
Bilateral		p=.2821	
Chi ² McNemar (A/D)	.80	p=.3711	
Chi ² (B/C)	.90	p=.3428	

[0115] With respect to the results concerning inappropriate urination in the home that were recorded by the cats' owners, no significant difference was observed between the treatment and the placebo. The Fisher's exact statistical test was used in this analysis of a bilateral situation. The results are shown below in Table 33.

Table 33

Day	p value
T0 (day 0-inclusion visit)	1.0000
T1 (day 10)	1.0000
T2 (day 20)	0.3147
T3 (day 30)	0.2821

[0116] The results for aggressiveness as set forth in Tables 34 and 35 below.

Table 34

Aggressiveness at day 10	Column 1	Column 2	Gross total
Effectives line 1	5	3	8
Percentage of total	33.333%	20.000%	53.333%
Effectives line 2	5	2	7
Percentage of total	33.333%	13.333%	46.667%
Total in column	10	5	15
Percentage of total	66.667%	33.333%	
Chi ² (dl=1)	.13	p=.7144	
V-2 (dl=1)	.13	p=.7237	
Chi ² Yates corrected	.03	p=.8548	
Phi ²	.00893		
P exact Fisher, unilateral		p=.5734	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	.57	p=.4497	
Chi ² (B/C)	.13	p=.7237	

Table 35

Aggressiveness at day 20	Column 1	Column 2	Gross total
Effectives line 1	5	3	8
Percentage of total	33.333%	20.000%	53.333%
Effectives line 2	4	3	7
Percentage of total	26.667%	20.000%	46.667%
Total in column	9	6	15
Percentage of total	60.000%	40.000%	
Chi ² (dl=1)	.04	p=.8327	
V-2 (dl=1)	.04	p=.8383	
Chi ² Yates corrected	.10	p=.7513	
Phi ²	.00298		
P exact Fisher, unilateral		p=.6224	
Bilateral		p=1.0000	
Chi ² McNemar (A/D)	0.13	p=.7237	

Aggressiveness at day 20	Column 1	Column 2	Gross total
Chi ² (B/C)	0.00	p=1.0000	

Summary of the results

[0117] The cats treated with a mixture of 11.4% (wt%/wt%) of dimethyl pimelate, 7.8% (wt%/wt%) of dimethyl azelate, 35.6% (wt%/wt%) of methyl palmitate, 95.2% (wt%/wt%) methyl oleate, 11% (wt%/wt%)methyl laurate, 11% (wt%/wt%)methyl myristate, 17% (wt%/wt%)methyl linolate and 11% methyl sterate. 0.5% (wt%/wt%) of this mixture was diluted in 99.5% isopar V showed some ability to limit the aggressive behavior of cats in multi-cat households which have conflicts between the cats. Concerning the diminution of the aggressive behavior which was observed and the level of confidence of the cat owners to leave their cats together in the same room, the results were favorable for treating the cats with a mixture of 11.4% (wt%/wt%) of dimethyl pimelate, 7.8% (wt%/wt%) of dimethyl azelate, 35.6% (wt%/wt%) of methyl palmitate, 95.2% (wt%/wt%) methyl oleate, 11% (wt%/wt%)methyl laurate, 11% (wt%/wt%)methyl myristate, 17% (wt%/wt%)methyl linolate and 11% methyl sterate. 0.5% (wt%/wt%) of this mixture was diluted in 99.5% isopar V. for at least 20 days, where a decrease in aggressiveness was observed with the verum treatment compared to the placebo.

Example 2- Testing of a Different Semiochemical

[0118] The semiochemical that was tested in this example was a mixture of 4.5% (w%/w%) methyl laurate, 4.5% (w%/w%) methyl myristate, 13.4% (w%/w%) methyl palmitate, 6.5% (w%/w%) methyl linoeate, 46.5% (w%/w%) methyl oleate, 4.5% (w%/w%) methyl stearate, 11.0% (w%/w%) dimethyl pimelate and 9.0% (w%/w%) dimethyl azelate. 0.5% (wt%/wt%) of this mixture was diluted in 99.5% isopar V.

[0119] The same testing was performed on 16 cases of aggressive cat housemates from seven different veterinary clinics as in Example 1. This aggressive behavior was studied with households having 2 or 3 cats that were aggressive among themselves, but not aggressive towards their owner. Furthermore, their aggression did not entail wounding the other cats and the cats were not on any other treatments.

[0120] This was a multicenter blinded placebo-controlled study wherein 8 placebos were tested and 8 treatments were tested. At the inclusion visit day 0 (T0) the cat owners were given a diffuser along with instructions for this study that was proposed for 1 month. The evaluation was performed every ten days; day 10, day 20, day 30 (T0,T1,T2,T3) and evaluation was by telephone. A post-treatment evaluation at T4 30 days later after the treatment was stopped was also done by telephone.

[0121] The AVS1 and AVS2 was evaluated in the same manner as in Example 1 using the same form filled out by the owner of the cats.

[0122] The results showed that there was a significant improvement between day 0 (T0) and day 30 (T3) in the AVS scores for the treated cats. The AVS 1 (aggression)score for the treated cats under ANOVA statistics was degree of freedom(df)=3;F=4.24; p=0.01. For AVS 2 (affiliation) the score for the treated cats under ANOVA statistics was: df=3; F=5.49; p=0.003. There was no significant difference between the two groups of treatments at day 0 (T0) using the Mann Whitney test; AVS 2 z=0.172 p=0.862.

[0123] At day 30 (T3) there was a higher score in the treated group than in the placebo group for the two AVS's (mean AVS 1(aggression) treated=6.4; placebo=5.5; mean AVS 2 (affiliation) treated= 7.02; placebo=4.93. As a follow up 30 days after the treatment was discontinued, the owners confirmed that the situation was stable in both the treated group and the placebo group.

Conclusion

[0124] These results show that treatment improved social facilitation in multi-cat households with stable results.

Example 3-Testing of a Third Semiochemical

[0125] The same testing was performed on cases of aggressive cat housemates as in Example 1. This aggressive behavior was studied with households having 2 or 3 cats that were aggressive among themselves, but not aggressive towards their owner. Furthermore, their aggression did not entail wounding the other cats and the cats were not on any other treatments.

[0126] The semiochemical that is tested in this example was a mixture of 15.5% (w%/w%) methyl laurate, 15.5% (w%/w%)methyl myristate, 35.4% (w%/w%)methyl palmitate, 23.5% (w%/w%) methyl linoleate, 74.6% (w%/w%) methyl oleate, 15.5% (w%/w%) methyl stearate, 11.0% (w%/w%) dimethyl pimelate and 9.0% (w%/w%) dimethyl azelate. 0.5% (wt%/wt%) of this mixture was diluted in 99.5% isopar V.

[0127] The treatment improved social facilitation and eased aggressiveness in multi-cat households.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- [US5709863A \[0008\]](#)
- [WO9623414A1 \[0008\]](#)
- [US6054481A \[0009\] \[0010\]](#)
- [US6077867A \[0009\]](#)
- [US6169113B \[0009\]](#)
- [US6384252B \[0009\]](#)
- [US7723386B \[0009\]](#)
- [WO9937297A1 \[0010\]](#)
- [WO2014001836A1 \[0011\]](#)

Non-patent literature cited in the description

- **VAN DEN BOS**Post-conflict stress-response in confined group-living cats (*Felis sylvestris catus*)*Applied Animal Behaviour Science*, 1998, vol. 59, 323-330 [0002]
- **JONGMAN, EC**Adaptation of domestic cats to confinement*Journal of Veterinary Behavior*, 2007, vol. 2, 1920196- [0005]
- **KESSLER MRTURNER DC**Effects of density and cage size on stress in domestic cats (*Felis sylvestris catus*) housed singly, in pairs and in groups in boarding catteries*Animal Welfare*, 1999, vol. 6, 243-254 [0005]
- Remington's Pharmaceutical Sciences 20050000 [0046]
- Remington's Pharmaceutical Sciences 20120000 [0057]

PATENTKRAV

1. Semiokemisk sammensætning omfattende mellem 1% og 8% (vægt%/vægt%) methyllaurat, mellem 1% til 8% (vægt%/vægt%) methylmyristat mellem 10% til 18% (vægt%/vægt%) methylpalmitat, mellem 3% til 10% (vægt%/vægt%) methyllinoleat, mellem 40% og 55% (vægt%/vægt%) methyloleat, mellem 1% til 8% (vægt%/vægt%) methyl stearat, mellem 5% og 15% (vægt%/vægt%) dimethylpimelat, mellem 4% til 15% (vægt%/vægt%) dimethylazelat eller salte deraf, der opretholder deres semiokemiske egenskaber, eller blandinger deraf.
10
2. Semiokemisk sammensætning ifølge krav 1, hvor sammensætningen omfatter mellem 2% og 6% (vægt%/vægt%) methyllaurat, mellem 2% til 6% (vægt%/vægt%) methylmyristat mellem 11% til 15% (vægt%/vægt%) methylpalmitat, mellem 4% og 8% (vægt%/vægt%) methyllinoleat, mellem 42% og 50% (vægt%/vægt%) methyloleat, mellem 2% til 6% (vægt%/vægt%) methylstearat, mellem 7% og 13% (vægt%/vægt%) dimethylpimelat, mellem 6% til 11% (vægt%/vægt%) dimethylazelat eller salte deraf, der opretholder deres semiokemiske egenskaber eller blandinger deraf.
15
3. Semiokemisk sammensætning ifølge et hvilket som helst af kravene 1 til 2, hvor sammensætningen omfatter 4,5% (vægt%/vægt%) methyllaurat, 4,5% (vægt%/vægt%) methylmyristat, 13,4% (vægt%/vægt%) methylpalmitat, 6,5% (vægt%/vægt%) methyllinoleat, 46,5% (vægt%/vægt%) methyloleat, 4,5% (vægt%/vægt%) methylstearat, 11% (vægt%/vægt%) dimethylpimelat, 9% (vægt%/vægt%) dimethylazelat.
20
4. Semiokemiske sammensætninger ifølge et hvilket som helst af kravene 1 til 3, yderligere omfattende et farmaceutisk acceptabelt bærer eller en veterinært acceptabel bærer eller en forstærkningssammensætning.
25
5. Semiokemisk sammensætning ifølge et hvilket som helst af kravene 1 til 4, yderligere omfattende et ikke-toksisk fyldstof udvalgt blandt gruppen af fedtsyrer, alkoholer, aminer, squalene, glycerol og blandinger deraf.
30

6. Semiokemisk sammensætning ifølge krav 4, hvor nævnte forstærkningssammensætning er aminer og fedtsyrer fra indoliske derivater, estere af disse aminer og fedtsyrer, ketoner, acetone, alkoholer eller steroler.

5 7. Opløsning omfattende den semiokemiske sammensætning ifølge et hvilket som helst af kravene 1 til 6 og et opløsningsmiddel.

8. Opløsning ifølge krav 7, hvor nævnte opløsning er i form af en spray, en aerosol, administreres i en diffusor, mikroindkapsles eller er en matrix med langsom frigivelse.

10 9. Fremgangsmåde til reduktion af sociale konflikter i husholdninger med flere katte eller i katterier eller kenneler eller til inducering af social facilitering hos katte, nævnte fremgangsmåde omfatter frigivelse af den semiokemiske sammensætning ifølge et hvilket som helst af kravene 1 til 6 eller opløsningen ifølge krav 7 eller 8 et miljø der omgiver katte.

15 10. Fremgangsmåde ifølge krav 9, hvor husholdningerne med flere katte har mindst to katte.

20 11. Fremgangsmåde ifølge krav 9 eller krav 10, hvor nævnte semiokemiske sammensætning eller nævnte opløsning frigives langsomt, og denne frigivelse finder sted mellem 3 til 5 uger.

25 12. Fremgangsmåde ifølge et hvilket som helst af kravene 9 til 11, hvor miljøet er et indendørs miljø eller et lukket miljø.

DRAWINGS

FIGURE 1

ANALOGICAL VISUAL SCALES TO BE FILLED OUT BY THE DIFFERENT OWNERS

Date _____ Scheduled time _____

Name and surname of the person:

1. A number of studies that show aggression between cats that live together in the same house and this is noticed by their owners. Please give us your perception by placing a vertical line on the two analogical visual scales below.

AVS 1

Aggressiveness

The cats never stop fighting when they are together | _____ longer (threats, scratching, biting) cats do not fight any (threats, scratching, biting)

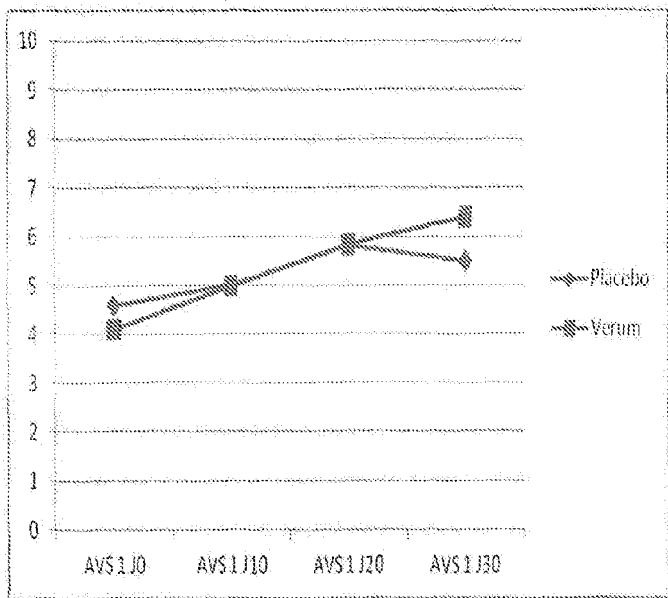
AVS 2

Affiliation

I am not confident to let my cats together in the same room | _____ I am totally confident to let my cats together in the same room

2. In the home were there episodes of inappropriate urination (outside the litter box):

Yes No

FIGURE 2**AVS 1**
Aggressiveness

0=Cats never stop fighting when they are together (threat, scratching, bite)

10= Cats do not fight ever (threat, scratching, bite)

FIGURE 3

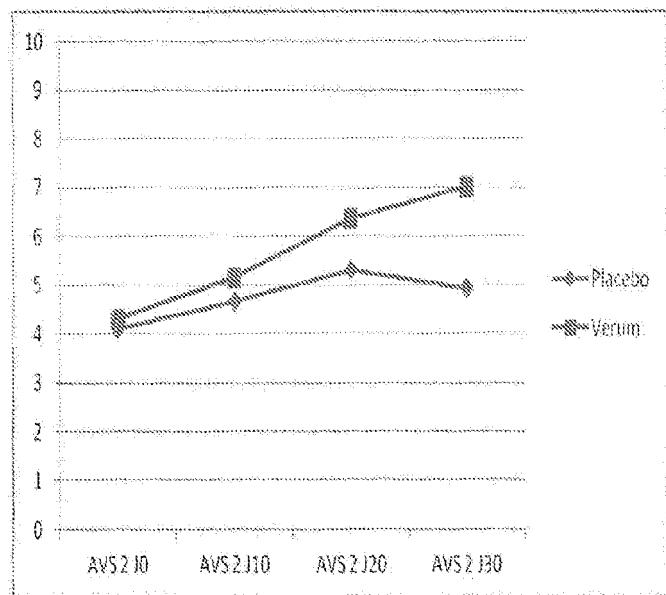
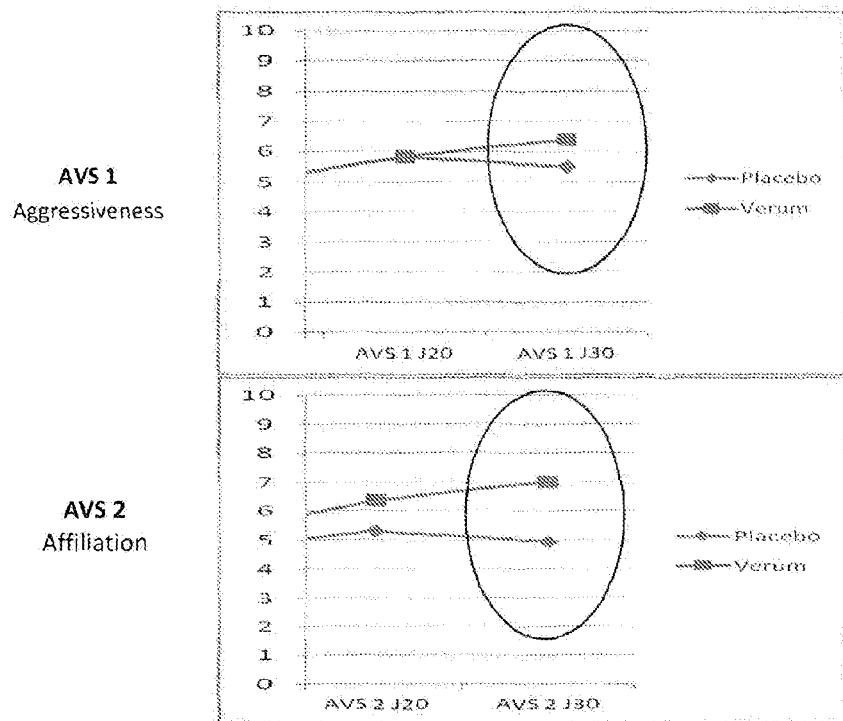
AVS 2
AFFILIATION

FIGURE 4



For AVS 1: 0=Cats never stop fighting when they are together (threat, scratching, bite)

10= Cats do not fight ever (threat, scratching, bite)

For AVS 2: 0=Not confident to let cats together in the same room

10=Totally confident to let cats together in the same room