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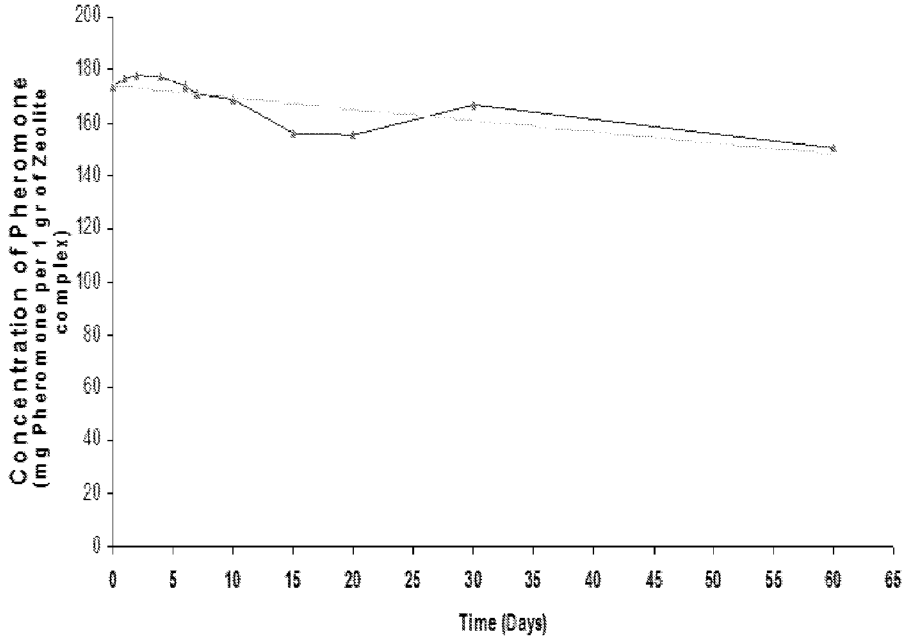

Figure 1

(57) **Abstract:** A slow-release composition comprising: first host material essentially comprising a mesoporous molecular sieve; guest material within the first host material, the guest material comprising at least one pheromone, wherein the pheromone is selected from a group consisting of: 1,7- dioxaspiro-5,5-undecane; Z-7-Tetradecenal; E-l l-hexadecenal; E-l l-Hexedecenyl-l- acetate; E,E-8,l l-dodecandien-l-ol; Z,E-9,11,13-Tetradecatrienal, and E,Z,Z-3,8,11- Tetradecatrienyl acetate, and mixtures thereof.

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PHEROMONE CLATHRATES

BACKGROUND

Pesticides are one of several broad technologies used to grow the food needed to feed the threefold growth in the world's population since 1950. Unfortunately, the use of pesticides has also caused tremendous damage to the world's environment, and much of this damage is long lasting because of the effects of persistent organic pollutants and bioaccumulation of toxic substances.

Integrated Pest Management (IPM), which has been in continuous development since the 1950s manages to greatly reduce the use of pesticides while not usually harming yields. The principles of IPM, which has been applied in different ways for different crops over the years, are avoidance of prophylactic use of pesticides, monitoring crops for pest infestation, determining thresholds that demand intervention and staged use of various tools against infestation with traditional pesticides usually acting as the last intervention if other tiers fail. Of particular interest are the push-pull variants of IPM developed during the past decade that use semiochemicals, pheromones or other chemicals that convey a signal from one organism to another so as to modify the behavior of the recipient organism, to either attract or repel pests. The use of semiochemicals to modify pest behavior increases the efficacy of IPM, and in some cases allows crops to be harvested without use of any pesticides at all.

As an approach, IPM has many advantages, mainly in its adaptability to various crops, climates and economic circumstances. But it must be stressed that it is an approach rather than a discrete technology which means that measurements of its efficacy can never be performed on a broad scale but only in case by case comparisons. As an approach its advantages, as many studies show, is that it can equal or in some cases exceed the yields of crops grown with traditional use of insecticides. This reduces the risk of insects developing resistance (as they often do) to specific insecticides, reduces direct cost of insecticides applications, reduces risks of insecticides traces in produce, and reduces potential damage to farm workers' health while protecting the general environment from the deleterious effects of the insecticides. The disadvantages include a higher level of knowledge needed by the farmer; more labor costs, and in some cases a higher percentage of blemished fruit.

Most agronomical experts agree that the advantages of IPM far outweigh the disadvantages, yet its acceptance has been in general slower than many anticipated a few decades ago. One of the major problems has been the complexity of IPM implementation and the amount of time it demands from farmers. Another major problem is that pheromones, one of the most potent tools in the IPM tool chest, are hard to apply in a manner that is easy and cost effective for farmers. Insect sex pheromones, by their nature, must be small-size molecules with relatively low molecular weight and high volatility that are released in the air during key times of the breeding cycle to attract insects to mating targets. Both the volatility and instability are problems. Resolution of these problems can greatly increase the use of pheromones in the market and increase the application of IPM principles.

Pheromones can be used in four ways in IPM applications.

Monitoring: pheromone based lures are needed to alert the farmer to the pest's presence to start the tiered IPM intervention.

Mass trapping: pheromone lures can attract insects of one sex to traps and thus reduce the number of fertile insects available for mating.

Mating disruption: Pheromones can offer false lures to insect seeking mates thus reducing the effectiveness of the mating process and the number of eggs laid in crops.

Part of push-pull IPM solutions: either on the push side by using alert pheromones or on the pull side by using sex pheromones.

A functional problem facing use of pheromones in each of these four applications is that pest control systems that involve use of pheromones must be in tune with the breeding cycles of the pests. In many if not most pests there are several breeding cycles during the years with a large degree of overlap, meaning that not all females start releasing sex pheromones during the exact same day or week. This means that IPM solutions that use pheromones must be attractive for the pest during the entire season.

Zeolites and clays are aluminosilicate minerals of alkali or alkaline earth metal which contain crystal water. Their general chemical formula is $A_mX_pO_{2p} \cdot nH_2O$, where A represents Ca, Na, K, Ba, and Sr; X represents Al and Si and m,p and n are integers. Aluminosilicates consist of three dimensional networks of AlO_4 and SiO_4 tetrahedra linked by sharing of all oxygen atoms. The aluminosilicate frameworks are remarkably open and contain channels, and interconnected voids partially filled with cations and water molecules. The intracrystalline voids make up from 20 to 50% of the total crystal volume of most zeolites.

SUMMARY

According to one aspect of the disclosure, compositions are provided that each comprise at least one host material, each hosting a guest material such as a pheromone, for example oleane.

Some embodiments comprise host materials that have desirable and improved guest material release profiles.

According to one aspect of the disclosure, compositions are provided that each comprises a mixture of host materials, each host material hosting a guest material such as a pheromone, for example oleane.

In some particular embodiments the mixture is selected to provide clathrates having complementary guest material release properties, such that guest material is first predominantly released at a high rate and then predominantly released at a substantially slower rate.

According to one aspect of the disclosure, a slow-release composition is

provided comprising: first host material essentially comprising

a mesoporous molecular sieve;

guest material within the first host material, the guest material comprising at least one pheromone, wherein the pheromone is selected from a group consisting of: 1,7-dioxaspiro-5,5-undecane; Z-7-Tetradecenal; E-11-hexadecenal; E-11-Hexedecenyl-1-acetate; E,E-8,11-dodecandien-1-ol; Z,E-9,11,13-Tetradecatrienal, and E,Z,Z-3,8,11-Tetradecatrienyl acetate, and mixtures thereof.

In some embodiments the mesoporous molecular sieve is selected from: silica; Al_2O_3, K-10 Montmorillonite and derivatives thereof, and mixtures thereof.

According to another aspect of the disclosure, a slow-release composition is provided comprising: A variable-release composition comprising:

first host material essentially comprising a mesoporous molecular sieve;

second host material selected from a second group consisting of: Na-X and derivatives thereof, Na-Y and derivatives thereof, and mixtures thereof;

guest material within the first host material and within the second host material, the guest material comprising at least one pheromone, wherein the pheromone is independently selected for each of the first host material and the second host material from a group consisting of: 1,7-dioxaspiro-5,5-undecane; Z-7-Tetradecenal; E-11-hexadecenal; E-11-Hexedecenyl-1-acetate; E,E-8,11-dodecandien-1-ol; Z,E-9,11,13-Tetradecatrienal, and E,Z,Z-3,8,11-Tetradecatrienyl acetate, and mixtures thereof.

In some embodiments the mesoporous molecular sieve is selected from a group that consists of:

silica; Al_2O_3, K-10 Montmorillonite and derivatives thereof, and mixtures thereof.

In some embodiments the composition is not incorporated into a matrix made of a polymeric material.

In some particular embodiments the first host material consists of silica.

Some embodiments further comprise spinosids.

In some embodiments the spinosids comprise spinosyn A and spinosyn D. In some embodiments spinosyn A and spinosyn D are in a w/w ratio respectively of 20/1 to 15/5. In some embodiments the ratio is between 16/4 and 18/2.

In some embodiments Na-X and derivatives thereof is selected from a group consisting of: Na-X; H-X, Zn-X, Ca-X, K-X and combinations thereof.

In some embodiments Na-Y and derivatives thereof is selected from a group consisting of: Na-Y; K-Y, Ca-Y, Zn-Y, H-Y, NH_4-Y, Al-Y, and combinations thereof.

Some embodiments further comprise at least one protective agent, the protective agent being effective in protecting the guest material against at least one of a group consisting of oxidation, photodegradation, hydrolysis, and thermal decomposition.

In some embodiments the at least one agent is situated in the first host material or adjacent thereto.

In some embodiments the agent is at least one antioxidant.

Some embodiments comprising an opaque coating on the first host material.

Some embodiments further comprise an opaque coating on the first host material and/or second host material.

According to yet another aspect a dispenser is provided comprising any of the compositions defined above.

In some embodiments the dispenser is essentially opaque.

According to another aspect of the disclosure a product or process are provided substantially as described below with reference to any one of the Examples, tables and/or to any one of the accompanying drawings.

DEFINITIONS

A mesoporous material: a material containing pores with diameters typically between 2 and 50 nm.

A clathrate: an inclusion compound in which a guest molecule is in a cage formed by a host molecule or by a lattice of host molecules.

Molecular sieve: a material with pores of essentially uniform size.

In the discussion unless otherwise stated, adjectives such as “substantially” and “about” modifying a condition or relationship characteristic of a feature or features of an embodiment of the invention, are understood to mean that the condition or characteristic is defined to within tolerances that are acceptable for operation of the embodiment for an application for which it is intended. Unless otherwise indicated, the word “or” in the specification and claims is considered to be the inclusive “or” rather than the exclusive or, and indicates at least one of, or any combination of items it conjoins.

“Essentially” is to be viewed in the context that a material with desired properties is made of discrete particles. Some of said particles may not have the desired properties, for example desired pore size. However, at least a majority of the particles in the material have the desired properties, e.g., a desired pore size that imparts to the discrete particle the desired properties. In bulk, such majority or predominance of the desired particles impart to the material the same properties or properties related to the desired properties of the particles.

This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the detailed description. This summary is not intended to identify key features or essential features of the claimed subject matter, nor is it intended to be used to limit the scope of the claimed subject matter.

BRIEF DESCRIPTION OF FIGURES

Figure 1 illustrates the loading and release of oleane from silica;

Figure 2 illustrates the loading and release of oleane from Al_2O_3;

Figure 3 illustrates the loading and release of oleane from K-10 Montmorillonite (Na-K10);

Figure 4 illustrates the loading and release of oleane from Al-K10;

Figure 5 illustrates the loading and release of oleane from Ca-K10;

Figure 6 illustrates the loading and release of oleane from Cu-K10;

Figure 7 illustrates the loading and release of oleane from NaX(25°C) zeolite;

Figure 8 shows loading and release from H-X oleane clathrates;

Figure 9 shows loading and release from Na-Y oleane clathrates;

Figure 10 shows loading and release from K-Y oleane clathrates.

Non-limiting examples of embodiments of the invention are described below with reference to figures attached hereto that are listed following this paragraph. Identical structures, elements or parts that appear in more than one figure are generally labelled with a same numeral in all the figures in which they appear. Dimensions of components and features shown in the figures are chosen for convenience and clarity of presentation and are not necessarily shown to scale.

DETAILED DESCRIPTION

In the detailed description below, pertaining to improved compositions comprising host materials and guest materials, the compositions also referred to below as “clathrates”. Their syntheses and methods of use are described.

Pest control systems that involve use of pheromones require a suitable host material to store and release the pheromones. One purpose of some embodiments described below is to provide clathrates comprising pheromones that can slowly release the pheromones, to provide prolonged effective treatment against pests, to minimize frequency of expensive and labor intensive treatment for example.

Another purpose of some embodiments described below is to provide compositions wherein the guest pheromones are highly loaded in their host materials, to prolong an effective treatment and/or provide high release rates, at least at initial periods of the release.

Criteria for host material selection in clathrates for pheromone dispensing are generally as follows:

1. Particle size – to provide sufficient surface area
2. Particle cavity and channel shape – to fit guest pheromones
3. Matrix structure to allow desired equilibrium and release rate
4. Host Polarity – to suit host-guest interactions

See for example EP1064843, which describes a process for preparing an emitter for controlled and durable release of a semiochemical substance (n-decyl alcohol, trimedlure, 2,3- or 2,5-dimethylpyracine) from a support selected from zeolites and aluminosilicates and aluminophosphates, wherein the process includes adapting physiochemical properties of the support to characteristics of the semiochemical substance and to specific needs of release kinetics, by modifying at least one property selected from Si/Al ratio, acidity, compensation cations, pore size, compactation and surface/weight ratio of the support.

Despite the general guidelines for host selection in EP1064843, selection of the host is largely empirical. Finding compositions that have a high loading of the pheromone/s as well as an extended release, with a high release remaining available after an extended period in the field, is difficult. Furthermore, a problem with the use of such clathrates is that often there is an immediate pest problem that needs to be swiftly dealt with, and subsequently there is a substantial danger of reinfestation within a short period after the immediate eradication. Modifying Si/Al ratio, acidity, compensation cations, pore size, compactation and surface/weight ratio of the support, for example, is generally not sufficient to solve such a problem.

Therefore, another purpose of some embodiments described below is to provide compositions that have a release rate and/or rate constant that is highest upon initial exposure of the compositions to field conditions, i.e. under conditions similar or identical to the conditions under which they are intended to be used, and at a lower rate/rate constant thereafter, such as to solve the problem of how to provide both immediate treatment of infestation and prevention of reinfestation in one treatment. Some embodiments that exhibit an inconstant rate/and or variable rate constant of release for effective immediate treatment and prolonged treatment comprise a single host material but several guest materials, each host material particle typically hosting one guest material, e.g. oleane, whereas other embodiments comprise a mixture of host materials, each hosting a guest material. The proportion of each host material may be adjusted to achieve a desired release profile.

The compositions having a higher initial release rate and/or rate constant followed by a slower release rate and/or lower rate constant may allow quick eradication of pests in orchards, followed by a lengthy prophylactic treatment of the same orchards, with a single distribution of the composition, as opposed to pest treatment with commercially available compositions that typically require multiple treatments and high dosages over the life cycle of the targeted pest, as well as excessive and/or inadequate release and frequent monitoring against reinfestation.

According to one aspect, compositions are provided comprising at least one host material, each a solid support such as a meso-porous material, and guest material, for example a sex pheromone.

In some embodiments a pheromone composition is provided comprising at least one host material and from about 0.1% to about 35%, by weight of the composition, of a pheromone.

Typically the pheromone is included within pores of the host material.

Some embodiments comprise host material selected from a group consisting of large-pore zeolites with channels having a free diameter from 12Å to 5.9Å, zeolites such as Clinoptilolite, Beta, Linde X, Linde Y, Linde L, Mordenite, and mixtures thereof.

Some embodiments comprise host material selected from a group consisting of medium-pore zeolites with channels having a free diameter from 5.9Å to 5.0Å, such as ZSM-5, Silicalite, Ferrierite types, Linde-T, Merlinoite types, Linde W, and mixtures thereof.

In some embodiments the host material comprises clays selected from the group consisting of Kaolinite, montmorillonite KSF clay, montmorillonite K10 clay, and mixtures thereof. In some embodiments the host material consists of clays selected from said group.

Some embodiments comprise host material selected from the group consisting of ion-exchanged forms of the zeolites and clays described above. In some embodiments the compositions consist of compositions selected from said group.

In some embodiments the ion-exchanged materials are zeolites and clays cation-exchanged with metal ions, such as K^+, Na^+, Li^+, Cs^+, Be^{+2}, Cr^{+3}, Ce^{+3}, Cu^{+2}, Ca^{+2}, Mg^{+2}, Fe^{+2}, Fe^{+3}, Ag^+, Ba^{+2} or Zn^{+2}, and mixtures thereof.

In some embodiments the host material is selected from the group consisting of hydrophobic (organophilic) pentasil zeolites with high Si:Al ratio.

In some embodiments the host material essentially comprises compositions selected from the group of mesoporous solids consisting of silica SiO_2, aluminum oxide Al_2O_3, and mixtures thereof. In some embodiments the host material essentially consists of mesoporous solids selected from said group.

In some embodiments the silica is provided in the form of silica gel.

The compositions may be provided as a powder, pellets, beads, or granules.

In some embodiments particle sizes of the clathrates are from about 1 micron to about 100 microns.

In some embodiments the compositions are provided as a suspension in liquid, for example in water.

Some embodiments further comprise at least one additive selected from the group consisting of protective colloids, adhesives, binding agents, chelating agents, thickening agents, thixotropic agents, penetrating agents, stabilizing agents, sequestering agents, anti-foam agents, antioxidants, natural or synthetic seasonings and/or flavors, dyes and/or colorants, vitamins, minerals, nutrients, enzymes, insecticides, deodorants, and mixtures thereof.

According to another aspect, a process is provided for preparing a composition comprising at least one pheromone as guest material and essentially at least one mesoporous solid host material.

Materials and methods

Method 1: preparation of clathrates

Solid host material was added to a solution of a pheromone in a hydrophobic solvent having a concentration of 10-15% w/w, until the concentration of the host material was 10-50% w/w in the mixture of host material, pheromone and solvent. The mixture was stirred at a controlled temperature for 2h-overnight (about 12hr), to create a suspension of the host material in the solvent and facilitate the incorporation of the guest material into the host material. The mixture was cooled to room temperature and vacuum filtered through sintered filter disc size #1-3. The precipitate solid was washed with a small quantity of cold solvent and then vacuum dried at room temperature for 2-12hr. The dried solid may then be packed in preparation for use.

In some embodiments the filtrate is recycled for further preparations of pheromone clathrates by adding some guest material to the filtrate and repeating the preparation as described above.

Suitable solvents are for example alkanes such as pentane, hexane, heptane, octane, iso-octane or haloalkanes such as dichloromethane, dichloroethane, chloroform, carbon tetrachloride, dibromomethane, ethyl acetate or mixtures thereof.

The filtration may alternatively be carried out by regular filtration, centrifuge or freeze drying for example.

Method 2: preparation of clathrates

A solid host material is calcined at a temperature of 100-400°C, as appropriate to the material, and is cooled protected from air to remain dry. The dry host material is placed in one flask, protected from air, and a pheromone is placed in another flask. The flasks are connected via a common tube and sealed from the atmosphere. The pheromone condenses on and within the host material. After 2-12hr the clathrate can be removed from the flask and packaged.

Method 3: Analyses of clathrates

Loading of the guest material in the host material is determined by extraction of the guest material from the clathrates in an organic solvent and injection of the extracts into a GC-MS. The retention time of the pheromone guest material and the mass spectrum serve to identify the pheromone and to quantify the loading of the pheromone in the host material.

The clathrates are distributed in a field and samples are collected at various times and extracted for quantitative and qualitative analysis. Release profiles of the clathrates can be derived from the analysis results of the samples.

Example 1: Loading and release of oleane from oleane clathrates

Table 1 summarizes the loadings of 36 various host materials with the guest material olive fruit fly pheromone oleane (1,7-dioxaspiro-5,5-undecane) for potentially suitable clathrates. Samples of the various host materials with oleane were simultaneously held in a field in eppendorf tubes under temperatures generally varying between 15 and 35°C, and were collected from the field at various times and analyzed according to the analysis method 3 described above. The loadings, expressed in units of mg guest per g of host material in Table 1, decrease over time as a result of the release of the pheromone. The release rate of the pheromone can be inferred from the tabulated results. The pheromone is released as a result of replacement by water entirely originating from the humidity of the air.

Table 1

		Time (days)													
No.	**Host material**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**10**	**15**	**20**	**25**	**30**	**60**
1	Na-X (25)	157.2	141.9	130.7	124.6	116.8	120.7	110.1	118.2	103.3	-	114.4	58.9	44.6	0
2	Na-X (200)	146.1	117.7	119	nd	118.2	114.1	107.2	103.8	95.8	82.2	51.9	46.8	62.6	0
3	Na-X (300)	140	122.8	116.4	115.6	111.2	106.3	104.8	102.7	83.8	61.5	-	40.6	25.3	0
4	Na-X (400)	130.3	108	105.1	105.6	99.5	101.4	100.9	96	79.3	65.5	45.5	26.6	nd	0
5	Na-X (500)	145.4	125.6	125	114	111	113.5	101.7	110.1	99.2	79	63.6	45.7	nd	0
6	Na-X (600)	157.7	114.7	120	112.4	107.9	112	90.3	107.3	89.4	75.3	61.2	24.8	nd	0
7	H-X	122	105.5	102.2	101.5	96.5	96.2	90.5	84.9	-	68.8	62.5	54.1	nd	31.6
8	Cu-X	33.8	28	24.7	18.9	16.8	12.6	8.8	8	8	5	5	5	nd	0
9	K-X	72.6	61.9	56.1	57.4	54.1	49.2	45.4	43.7	26.8	nd	0	0	0	0
10	Zn-X	175.9	139.3	135.4	121.9	105.6	115.2	97.6	96.8	94.2	nd	63.7	46	44.1	9.3
11	Ca-X	110.9	103.8	nd	86.8	98.2	109.9	100.1	75.7	65.8	nd	48.4	17.94	5.3	0
12	3A	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	4A	14.7	8.1	4.9	0	0	0	0	0	0	0	0	0	0	0
14	5A	6.5	0	0	0	0	0	0	0	0	0	0	0	0	0
15	Na-Y	173.5	131.2	nd	130.6	121.3	119.4	114.2	109.5	79.1	57.3	nd	53.5	53.3	22.8
16	K-Y	178.1	nd	125.4	129.2	121.3	117	112.6	113.9	87.6	78.1	nd	62	41.5	4.9
17	Ca-Y	195	nd	144.2	139.6	132.9	125.7	126.6	110.9	97	105.6	nd	76.1	62.9	19.8
18	SiO_2	173.7	177	178.1	170.5	177.3	nd	174.1	170.8	169.1	156.3	155.4	nd	167	150.5
19	Al_2O_3	63.8	65.5	61.7	61.6	61.7	nd	57.9	53.9	52.4	45.9	42.4	nd	52	38.4
20	Hydrophobic	16	11.3	6.7	nd	nd	nd	nd	0	nd	nd	nd	nd	0	0
21	Na-K10	92.1	nd	79.6	82.8	80.5	nd	78.3	73.5	71.9	nd	65.3	64	85.1	68.5
22	Bent (400)	31	nd	27.4	25.6	25	22.3	22.6	19.5	19	nd	12.4	12.2	10.3	7.2
23	KSF	10.1	nd	nd	nd	nd	0	nd	nd	nd	nd	0	nd	nd	nd
24	H-5A	8.8	nd	nd	nd	nd	0	nd	nd	nd	nd	0	nd	nd	nd
25	Zn-Y	220.4	147	142.6	141.7	136.5	nd	129	116.8	123.8	115.1	94.4	93	79.1	nd
26	AW (300)	19.9	17	15.8	12.3	10.9	nd	8.2	5.6	nd	nd	0	nd	3.8	0
27	AW (500)	29.5	nd	nd	20.7	18.2	nd	14.8	nd	12.7	10.6	9.1	nd	9	nd
28	H-Y	91.3	108.7	nd	79.1	nd	nd	73.5	58.6	nd	53.2	40.7	nd	22.3	0
29	NH_4-Y	176.7	154	nd	161.4	nd	nd	177.1	142	160.4	136.1	145.5	nd	129.3	82.2
30	Al-Y	61.5	74	nd	70	nd	nd	64.8	64.4	64.6	62.5	53.3	nd	48.2	26.2
31	Al-K10	77.6	68.5	70.4	71	nd	68.9	74.6	75.6	81.2	64.6	106.5	68.9	59.3	44.4
32	Ca-K10	96.5	100.6	87.6	99.5	nd	109.8	93.7	85.3	91.8	nd	70.4	82.6	66.1	58
33	Cu-K10	81.9	51.17	45.19	40.5	nd	32.9	nd	30	nd	13.8	nd	14.2	8.6	nd
34	Zn-5A	21	nd	nd	nd	nd	nd	nd	6.7	nd	nd	nd	nd	0	nd
35	Ag-5A	7.1	nd	nd	nd	nd	0	nd	nd	nd	nd	0	nd	nd	nd
36	Cu-5A	30.6	nd	nd	nd	nd	0	nd	nd	nd	nd	0	nd	nd	nd

nd= not detected

Numbers in parentheses represent the dehydration temperatures of the host materials.

In Table 1:

Na-X is a synthetic zeolite of sodium aluminate and sodium silicate, wherein the silica-to-alumina ratio is between 2 and 3;

H-X, Cu-X, K-X, Zn-X, Ca-X: Na-X are synthetic Na-X zeolites in which the sodium is respectively substituted with hydrogen, copper, potassium, zinc or calcium;

3A is a zeolite having an approximate chemical formula: $2/3K_2O \bullet 1/3Na_2O \bullet Al_2O_3 \bullet\ 2\ SiO_2 \bullet 9/2\ H_2O$ and silica-alumina ratio: $SiO_2/\ Al_2O_3 \approx 2$, wherein the zeolite can adsorb molecules whose diameters are smaller than 3 Å;

4A is a zeolite like 3A, except the zeolite can adsorb molecules whose diameters are smaller than 4 Å

5A is a zeolite like 3A, except the zeolite can adsorb molecules whose diameters are smaller than 5 Å;

Na-Y is a synthetic zeolite of sodium aluminate and sodium silicate, wherein the silica-to-alumina ratio is over 3;

K-Y, Ca-Y, Zn-Y, H-Y, NH4-Y, Al-Y are synthetic Na-Y zeolites in which the sodium is respectively substituted with potassium, calcium, zinc, hydrogen, ammonium or aluminium;

Hydrophobic is a pentasil;

Na-K10 is a sodium-substituted montmorillonite clay (a clay having two tetrahedral sheets of silica sandwiching a central octahedral sheet of alumina) having a surface area of about $250m^2/g$;

Bent (400) is a bentonite
(an absorbent aluminium phyllosilicate clay consisting mostly of montmorillonite);

KSF is an acidic montmorillonite clay having a surface area of about $10m^2/g$;

H-5A, Zn-5a, Ag-5A and Cu-5A are zeolites like 5A in which the sodium is respectively substituted with zinc, silver or copper;

AW (300) is NaZ [$(AlO_2)x(SiO_2)Y$] • $24H_2O$ molecular sieves in the form of 1.6mm sized pellets;

AW (500) is CaZ[$(AlO_2)X(SiO_2)Y$]•$13H_2O$ with 4Å sized pores;

Al-K10, Cu-K10 and Cu-K10 are montmorillonite clays like Na-K10 in which the sodium is respectively substituted with Aluminium, potassium or copper.

The desired clathrates have high-medium loading, i.e., over 5% w/w of pheromone in clathrate.

It is Apparent from Table 1 that about a third of the tested clathrates failed to adequately load.

All of the host materials listed in Table 1 theoretically had the desired pore size, sufficient to accommodate oleane. The small pore size provided a relatively large surface area per unit weight of the host material, an extremely important criterion for allowing a high loading rate for the overall packing of the host material with its pheromone. However, only 23 of them significantly loaded with the pheromone and were thus initial candidates for use in the field for pest management.

WO2012072366 describes that suitable carriers (hosts) for pheromones have typical pore widths of 3, 4, 5, 10, and 13 Angstroms, with a pore width of 5 to 15 Angstroms, especially 8 to 3 Angstroms, being preferred. However, in our experience, despite knowledge of the structures and pore dimensions of the host materials, considerable empirical effort was required to find suitable host materials. Moreover, in contrast to WO2012072366, for the guest materials tested in this disclosure we have surprisingly found that host materials with essentially larger pore sizes characterizing mesoporous host materials (2 to 50 nm, i.e., 20 to 500 Å) generally yield superior results. For example, silica, Al_2O_3; K-10 Montmorillonite (Na-K10) and its derivatives, such as Al-K10, Ca-K10, Cu-K10, at least within the use herein, are all mesoporous host materials: Compare their loading and release rates in Table 1 with the other host materials in Table 1, as further discussed below.

Some of the host materials were found to be particularly suitable for the purpose of controlled release of the pheromone, exhibiting exceptionally high loading capacities of over 15%.

In particular, mesoporous silica, for example in silica gel form, can be used to host oleane or a pheromone of similar size at a high loading and with slow release. At present I believe that the silica clathrate embodiments operate most efficiently, but other embodiments described below are also satisfactory.

Figure 1 illustrates the loading and release of oleane from silica. The points in Graph 1 represent corresponding data in Table 1 for silica clathrates.

Silica (SiO_2) has a particularly surprisingly high loading of oleane and a protracted release of the pheromone, starting with a load of over 17% and still holding a load of over 14% after 60 days. Extrapolation of the results for silica (not shown) shows that the host material remains potent after 14 months exposure to field conditions. The prolonged efficacy in very advantageous, since free oleane is highly volatile, and treatment of the affected fields/orchards is very costly and labour-intensive. Repeat treatment is minimized under the proposed regime.

Note that some silica, for example artificial silica or silica that undergoes treatment such as high temperatures, may have pore sizes that are not mesopores, i.e., less than 2 nm or more than 50 nm size. Furthermore, in general in the world, some silica samples may include a minority of mesoporous particles. Such silica is considered to be less suitable for loading and release of the pheromones considered herein.

Other mesoporous host materials that are usefully slow-release, albeit lower loading, include: Al_2O_3, see Figure 2; K-10 Montmorillonite (Na-K10), see Figure 3, and its derivatives, such as: Al-K10, see Figure 4; Ca-K10, see Figure 5; Cu-K10, see Figure 6, and combinations thereof. Figures 2-6 illustrate the respective loading and release of oleane from these host materials, and correspond to the data in Table 1.

K-10 has an average pore size of about 4 nm. US2007190092 relates to sustained release of a pheromone at a constant rate from clay/kaolin/zeolite. A sustained release pheromone formulation is described as containing a pheromone in a crystalline mineral; no particular limitations were placed on the crystalline mineral so long as this crystalline mineral is a mineral having a crystalline structure, and no particular limitations were placed on the pheromone used. Sepiolite, palygorskite, and montmorillonite were described being particularly preferable; however, sepiolite includes a very wide range of pores (M. J. Wilson, Rock Forming Minerals, Geological Society of London, 2013), whereas palygorskite is microporous (J. M. Cases et al., Clays and Clay Minerals, Vol. 39, No. 2, 191-201, 1991).

WO2016180738 pertains to sustained release of various pheromones from porous clay e.g., various zeolites. However, no discussion is dedicated to the pore size of the host material. The preferred clay is described to be clinoptilolite, which is microporous, excluding particles larger than 0.4 nm (A. Farjoo et al., Chemical Engineering Science, Volume 138, 22 December 2015, Pages 685-688).

WO2012072366, concerns pheromones in a rubber matrix into which support material is inserted. Molecular sieves such as silica gel are described as examples of support material, however the preferred pore sizes of the molecular sieves are described as 5 to 15 angstroms, with especially 8 to 3 angstroms, being preferred.

Therefore, the publications described above do not appear to indicate that mesoporous materials are particularly suitable for loading and release of the pheromones considered herein.

The release rates of the pheromones in different clathrates may greatly vary.

For example, Figure 7 illustrates the loading and release of oleane from NaX(25°C) zeolite. The points in Graph 2 represent corresponding data in Table 1 for these clathrates. Whereas like silica NaX(25°C) zeolite has a very good loading, the release rate slopes shown in Figure 1 and Figure 2 are very different. Oleane NaX(25°C) clathrates essentially finish releasing their pheromones about a month after loading.

We managed to harness this highly variable capacity in some pheromone applications to make "cocktail" embodiments characterized by an initial burst of pheromones followed by a slow and more gradual release.

The silica-pheromone clathrates and/or other slow-release clathrates may be combined with other, faster release clathrates hosting the same pheromone or others to provide variable-release compositions. The following host materials may be suitable for use for fast release and high loading of oleane or similar sized pheromones:

Na-X zeolite and its derivatives such as H-X, Zn-X and/or Ca-X and combinations thereof; K-X has slightly lower loading but has a good fast release;

Na-Y Zeolite and its derivatives, such as K-Y, Ca-Y, Zn-Y, H-Y, NH_4-Y and/or Al-Y, and combinations thereof.

As said above, Figure 7 illustrates the loading and release of oleane from

Na-X(25°C) zeolite. Figure 8 shows loading and release from H-X oleane clathrates; Figure 9 shows loading and release from Na-Y oleane clathrates; Figure 10 shows loading and release from K-Y oleane clathrates. Figures 7-10 are random examples of the loading and release of Na-X zeolite and its derivatives, Na-Y Zeolite and its derivatives and correspond to the data in Table 1.

Various Na-X zeolites and/or Na-Y zeolites may be combined to provide a tailored release profile.

Other similar pheromones tested with the same host materials are listed in Table 2.

Table 2

Insect Name	Pheromone	CAS
Dacus Oleae	1,7-dioxaspiro-5,5-undecane	180-84-7
Prays Oleae	Z-7-Tetradecenal	65128-96-3
Palpita unionalis	1) E-11-hexadecenal	57491-33-5
	2) E-11-Hexedecenyl-1-acetate	56218-72-5
Cydia Pomonella	E,E-8,11-dodecandien-1-ol	33956-49-9
Ectomyelois Ceratoniae (Carob moth)	Z,E-9,11,13-Tetradecatrienal	123314-23-8
Tuta absoluta	E,Z,Z-3,8,11-Tetradecatrienyl acetate	163041-94-9

Preliminary tests with the pheromones listed in Table 2 and the host materials listed in Table 1 indicate a surprisingly high loading and gradual release of the pheromones when the host materials are essentially mesoporous, in particular when the host material is silica, similar to the trend exhibited with oleane clathrates.

Note that for the treatment of the pest Palpita unionalis two pheromones should be incorporated in clathrates. Typically, a batch of clathrates hosting E-11-hexadecenal is prepared and another batch is prepared, hosting E-11-Hexedecenyl-1-acetate. The two clathrate batches are then mixed for use.

In addition, in some embodiments compositions comprising clathrates with various pheromones against various pests are mixed. For example, olives are often attacked by several of the insects listed in Table 2 and thus a mixture containing effective amounts of pheromones against these pests may be prepared.

One method of determining the amounts and types of pheromones and their mode of release includes monitoring a field or grove or orchard for the presence of pests. At least one adhesive plate or board may be placed therein, each spread or sprayed with at least one clathrate or mixture of the same.

The treatment against infestation may include positioning of mass traps containing the clathrates. Alternatively or in addition, mating disruption may be carried out by scattering the clathrates from a vehicle or aircraft, for example.

The treatment and compositions may further include pesticides, for example spinosad. Spinosad contains a mix of two spinosoids, spinosyn A, the major component, and spinosyn D (the minor component), in a roughly 17:3 ratio w/w respectively. The pesticides can be separately administered or together with the clathrates, for example the pesticides may cover and/or be hosted by the host materials.

In addition, several of the pheromones in Table 2 may require the hosting in the host material for the purpose of protection rather than, or in addition to, control of release. For example, from careful analysis of the clathrate samples over time we have surprisingly discovered several problems of stability of some of the pheromones such as oxidation, photo degradation, hydrolysis, and thermal decomposition. Accordingly, some composition embodiments comprise in the host material or adjacent thereto agents that at least partially counteract the degradation, such as antioxidants.

Some embodiments are provided as pheromone dispensers in which a carrier/host material loaded with pheromone is incorporated into a matrix made of a polymeric material such as, for example, rubber. However, typically the carrier/host material is not incorporated into such matrix. The dispensers may comprise a light protection material. For example, the eppendorf tubes used to store the clathrate samples in the field were each wrapped in a black layer. Alternatively, particles of the composition may be coated with light-protective material.

In the description and claims of the present application, each of the verbs, “comprise,” “include” and “have,” and conjugates thereof, are used to indicate that the object or objects of the verb are not necessarily a complete listing of components, elements or parts of the subject or subjects of the verb.

Descriptions of embodiments of the invention in the present application are provided by way of example and are not intended to limit the scope of the invention. The described embodiments comprise different features, not all of which are required in all embodiments of the invention. Some embodiments utilize only some of the features or possible combinations of the features. Variations of embodiments of the invention that are described, and embodiments of the invention comprising different combinations of features noted in the described embodiments, will occur to persons of the art. The scope of the invention is limited only by the claims.

CLAIMS

1. A slow-release composition comprising:

first host material essentially comprising

a mesoporous molecular sieve;

guest material within the first host material, the guest material comprising at least one pheromone, wherein the pheromone is selected from a group consisting of: 1,7-dioxaspiro-5,5-undecane; Z-7-Tetradecenal; E-11-hexadecenal; E-11-Hexedecenyl-1-acetate; E,E-8,11-dodecandien-1-ol; Z,E-9,11,13-Tetradecatrienal, and E,Z,Z-3,8,11-Tetradecatrienyl acetate, and mixtures thereof.

2. The slow-release composition of claim 1, wherein the mesoporous molecular sieve is selected from:

silica; Al_2O_3, K-10 Montmorillonite and derivatives thereof, and mixtures thereof.

3. A variable-release composition comprising:

first host material essentially comprising a mesoporous molecular sieve;

second host material selected from a second group consisting of: Na-X and derivatives thereof, Na-Y and derivatives thereof, and mixtures thereof;

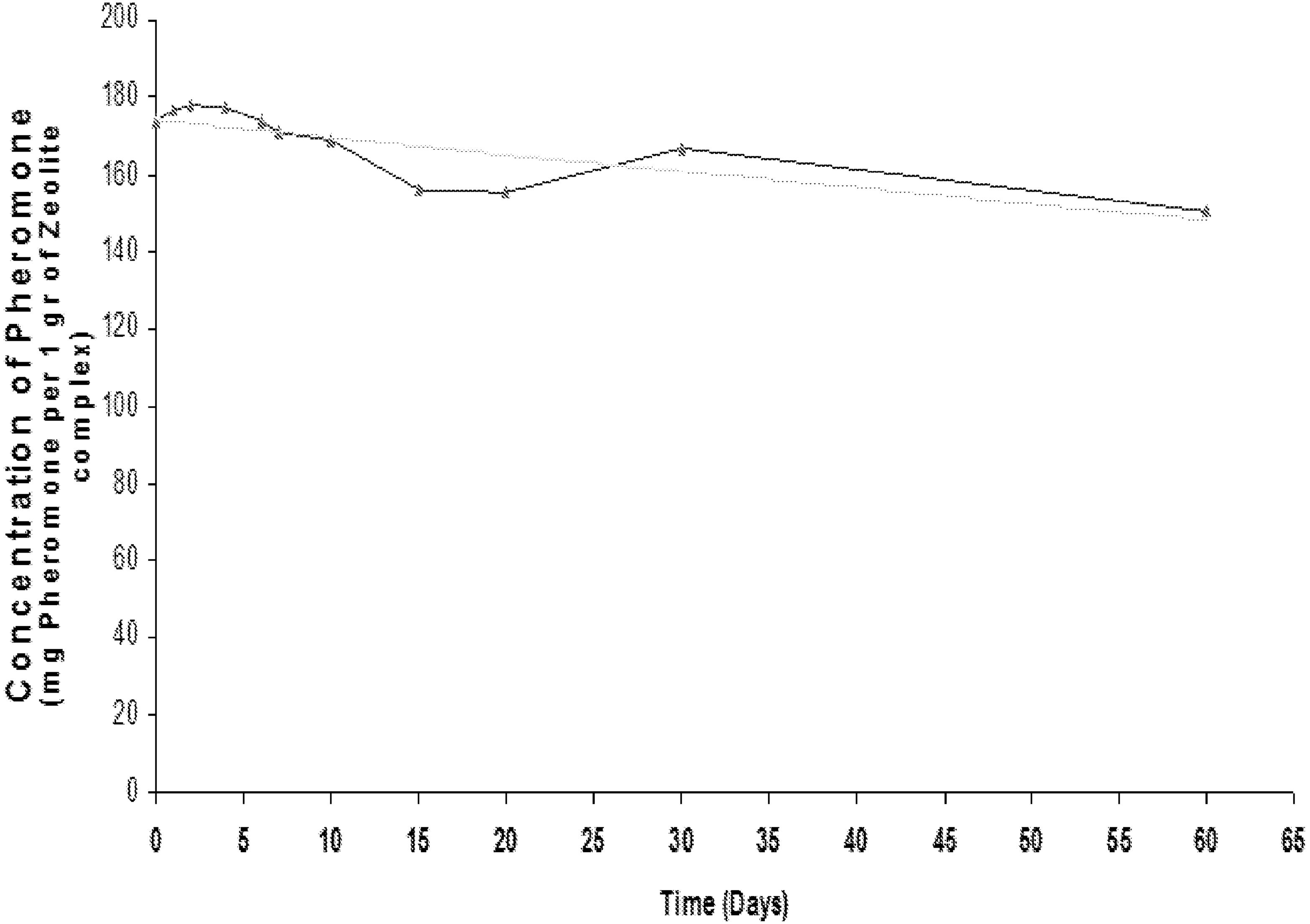
guest material within the first host material and within the second host material, the guest material comprising at least one pheromone,

wherein the pheromone is independently selected for each of the first host material and the second host material from a group consisting of: 1,7-dioxaspiro-5,5-undecane; Z-7-Tetradecenal; E-11-hexadecenal; E-11-Hexedecenyl-1-acetate; E,E-8,11-dodecandien-1-ol; Z,E-9,11,13-

Tetradecatrienal, and E,Z,Z-3,8,11-Tetradecatrienyl acetate, and mixtures thereof.

4. The composition of claim 3, the mesoporous molecular sieve selected from a group consisting of:
   silica; Al_2O_3, K-10 Montmorillonite and derivatives thereof, and mixtures thereof.
5. The composition of claim 2 or 4, wherein the composition is not incorporated into a matrix made of a polymeric material.
6. The composition of claim 2 or 4, wherein the first host material consists of silica.
7. The composition of any one of claims 1 to 4, further comprising spinosoids.
8. The composition of claim 7, wherein the spinosids comprise spinosyn A and spinosyn D.
9. The composition of claim 8, wherein spinosyn A and spinosyn D are in a 20/1 to 15/5 ratio respectively.
10. The composition of claim 9, wherein spinosyn A and spinosyn D are in a 20/2 to 16/4 ratio respectively.
11. The composition of claim 3 or 4, wherein Na-X and derivatives thereof is selected from a group consisting of: Na-X; H-X, Zn-X,Ca-X, K-X and combinations thereof.
12. The composition of claim 3 or 4, wherein Na-Y and derivatives thereof is selected from a group consisting of: Na-Y; K-Y, Ca-Y, Zn-Y, H-Y, NH_4-Y, Al-Y, and combinations thereof.
13. The composition of any one of claims 1 to 4, further comprising at least one protective agent, the protective agent being effective in protecting the guest material against at least one of a group consisting of oxidation, photodegradation, hydrolysis, and thermal decomposition.

14. The composition of claim 13, wherein the at least one agent is situated in the first host material or adjacent thereto.
15. The composition of claim 13, wherein the agent is at least one antioxidant.
16. The composition of claim 13, further comprising an opaque coating on the first host material.
17. The composition of claim 3 or 4, further comprising an opaque coating on the first host material and/or second host material.
18. A dispenser comprising the composition of any one of claims 1 to 4.
19. The dispenser of claim 18, wherein the dispenser is essentially opaque.


Concentration of Pheromone
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160
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25
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35
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Time (Days)

Figure 1

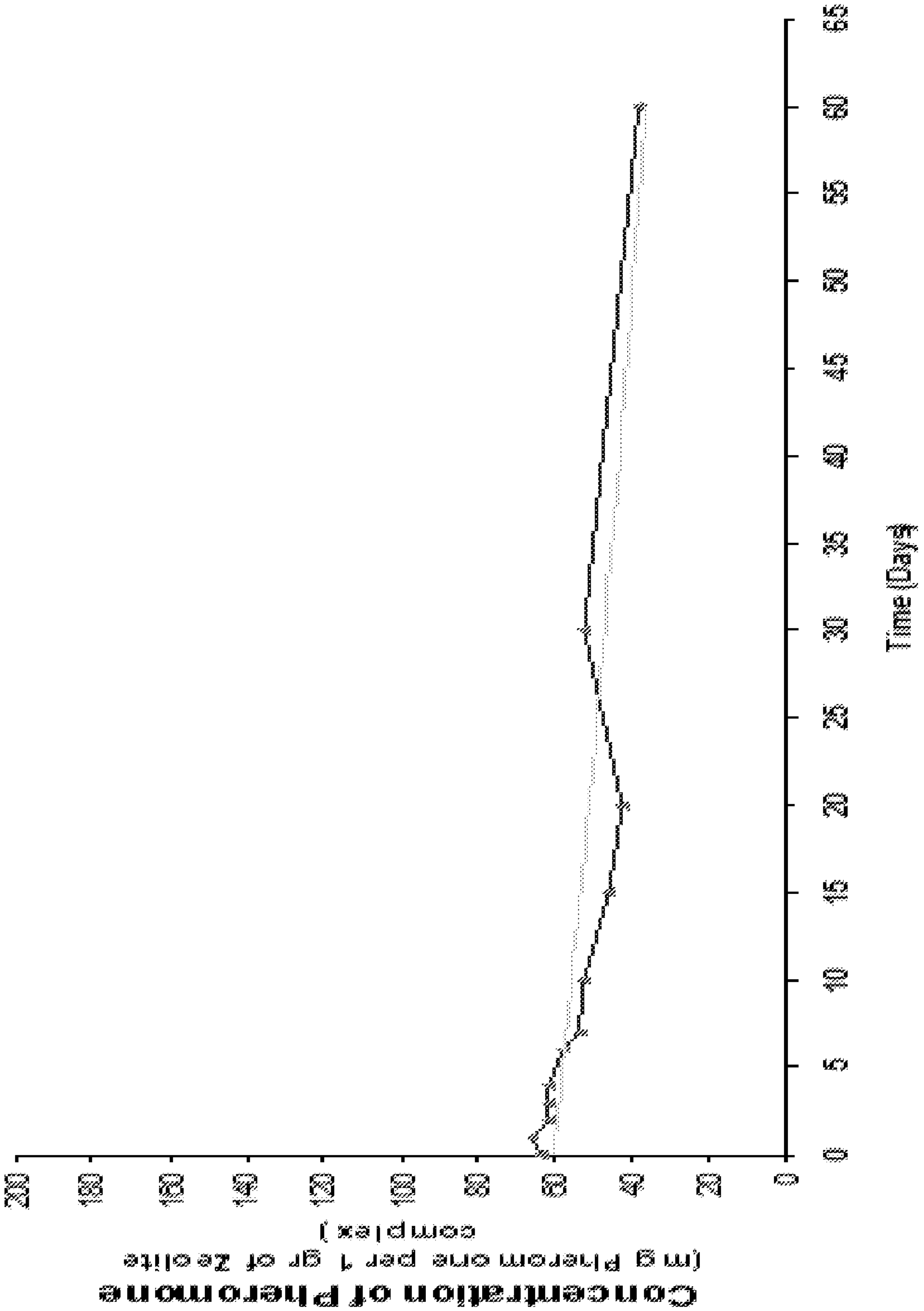
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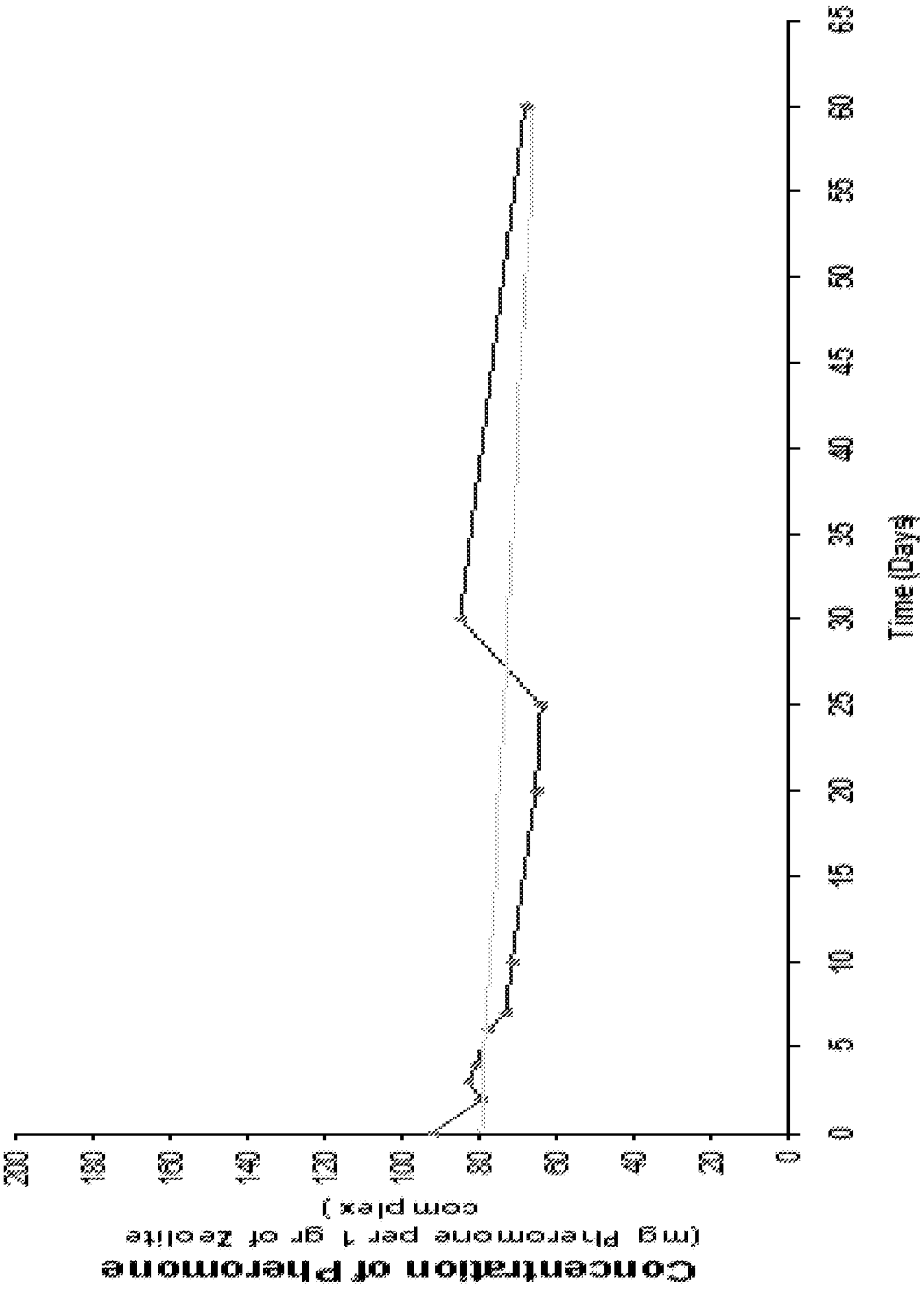
Figure 2


Concentration of Pheromone
(mg Pheromone per 1 gr of Zeolite complex)
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Time (Days)
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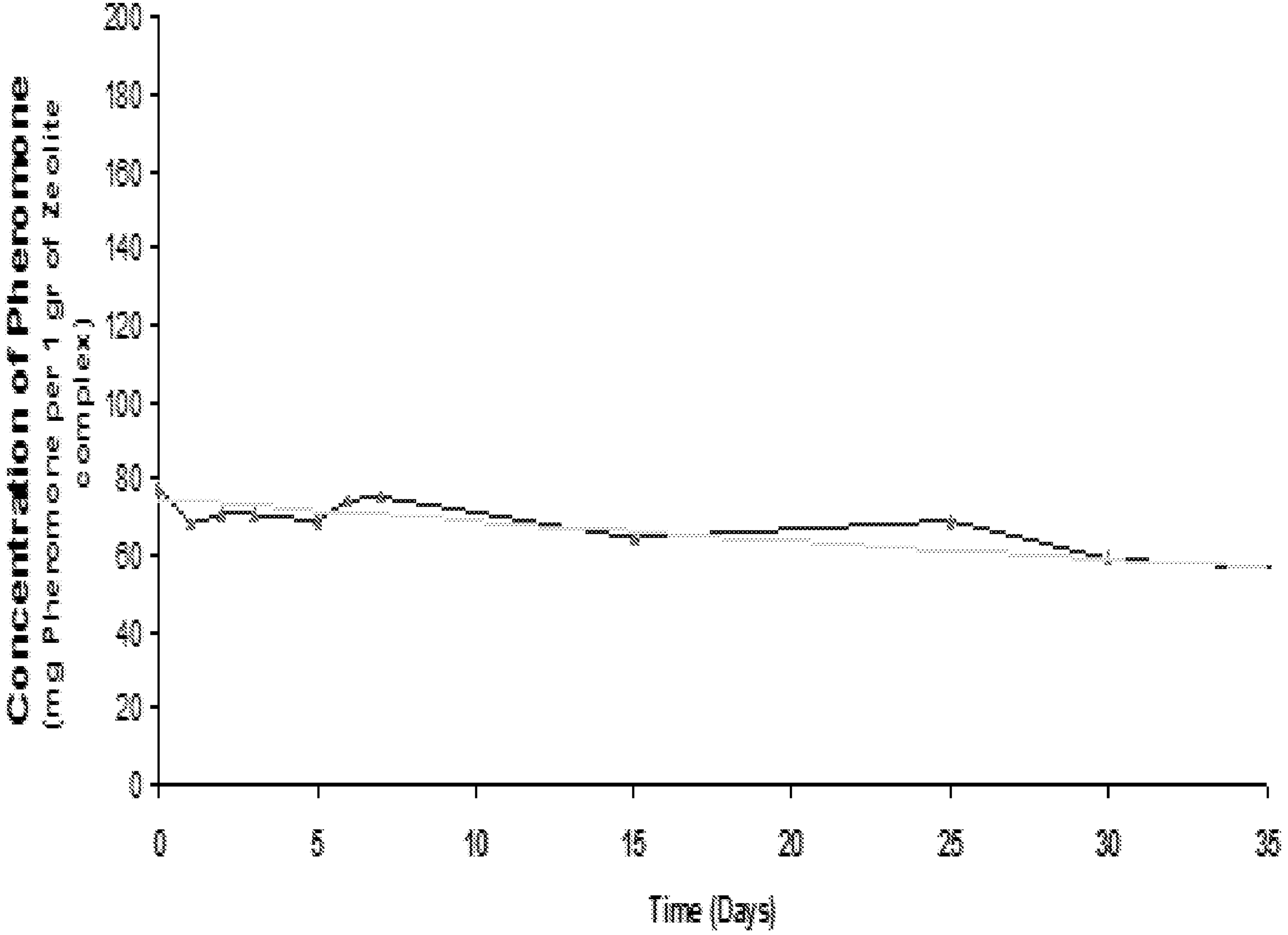
Figure 3


Concentration of Pheromone
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Time (Days)

Figure 4

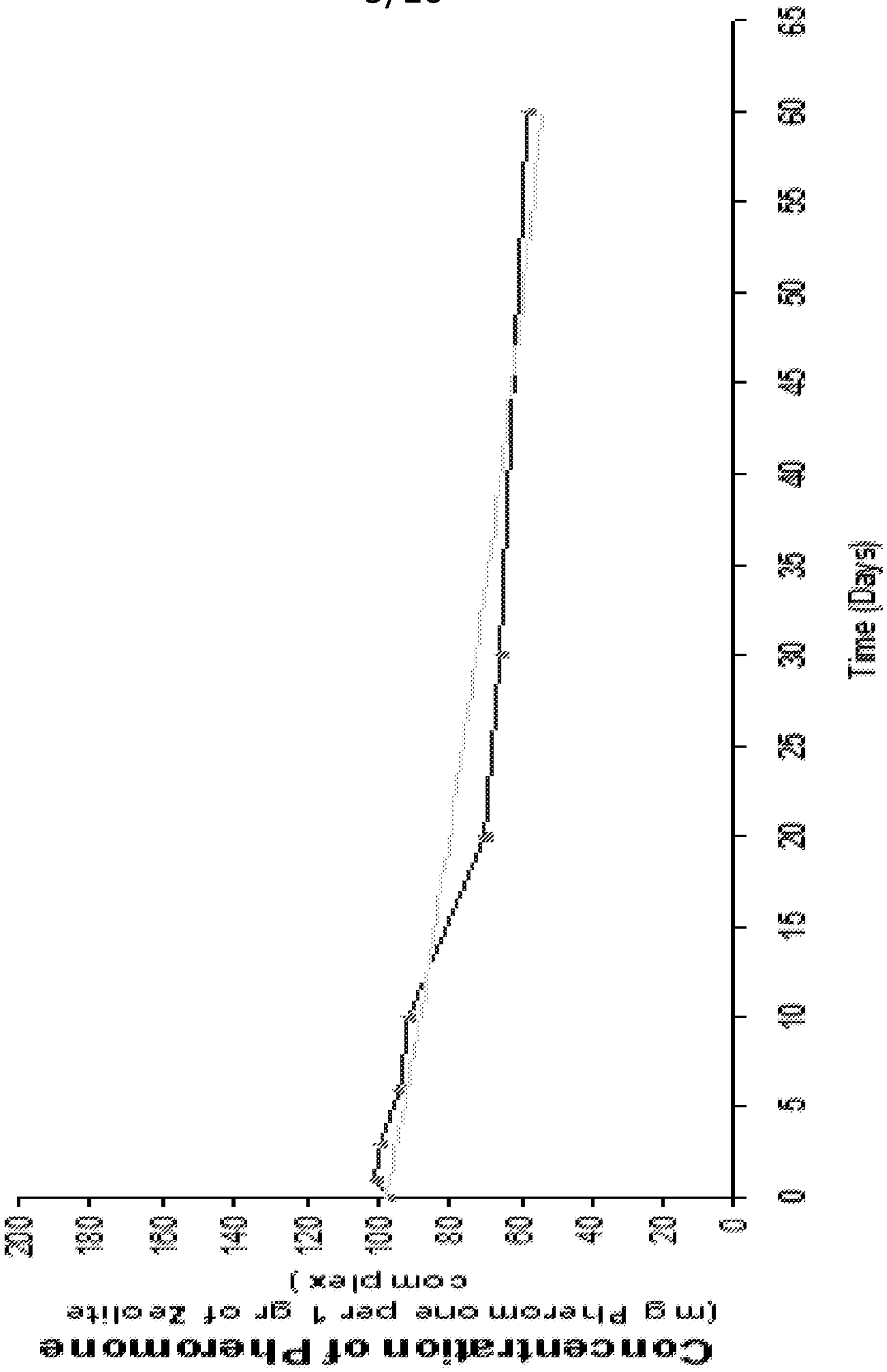
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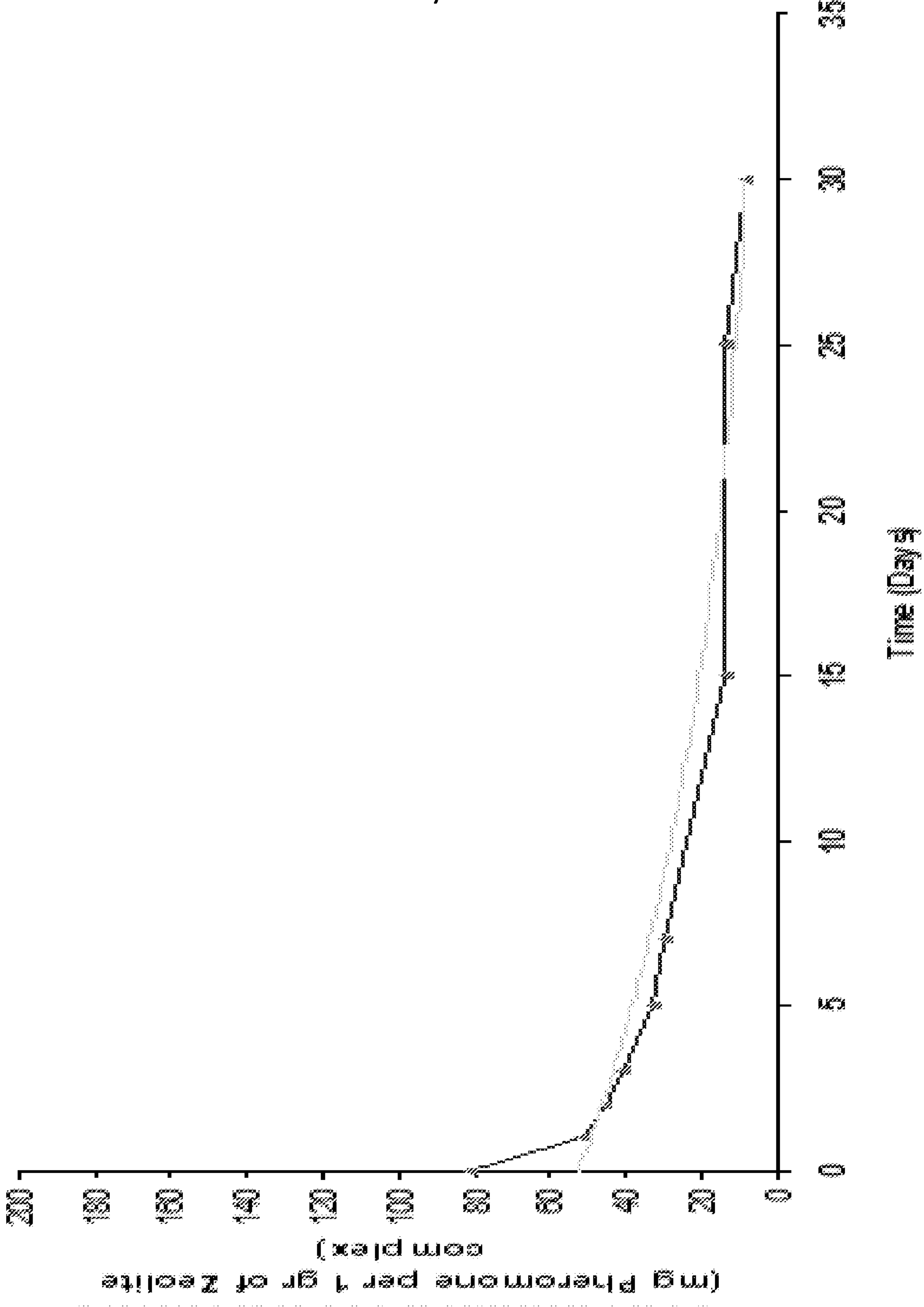
Figure 5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Time (Days)
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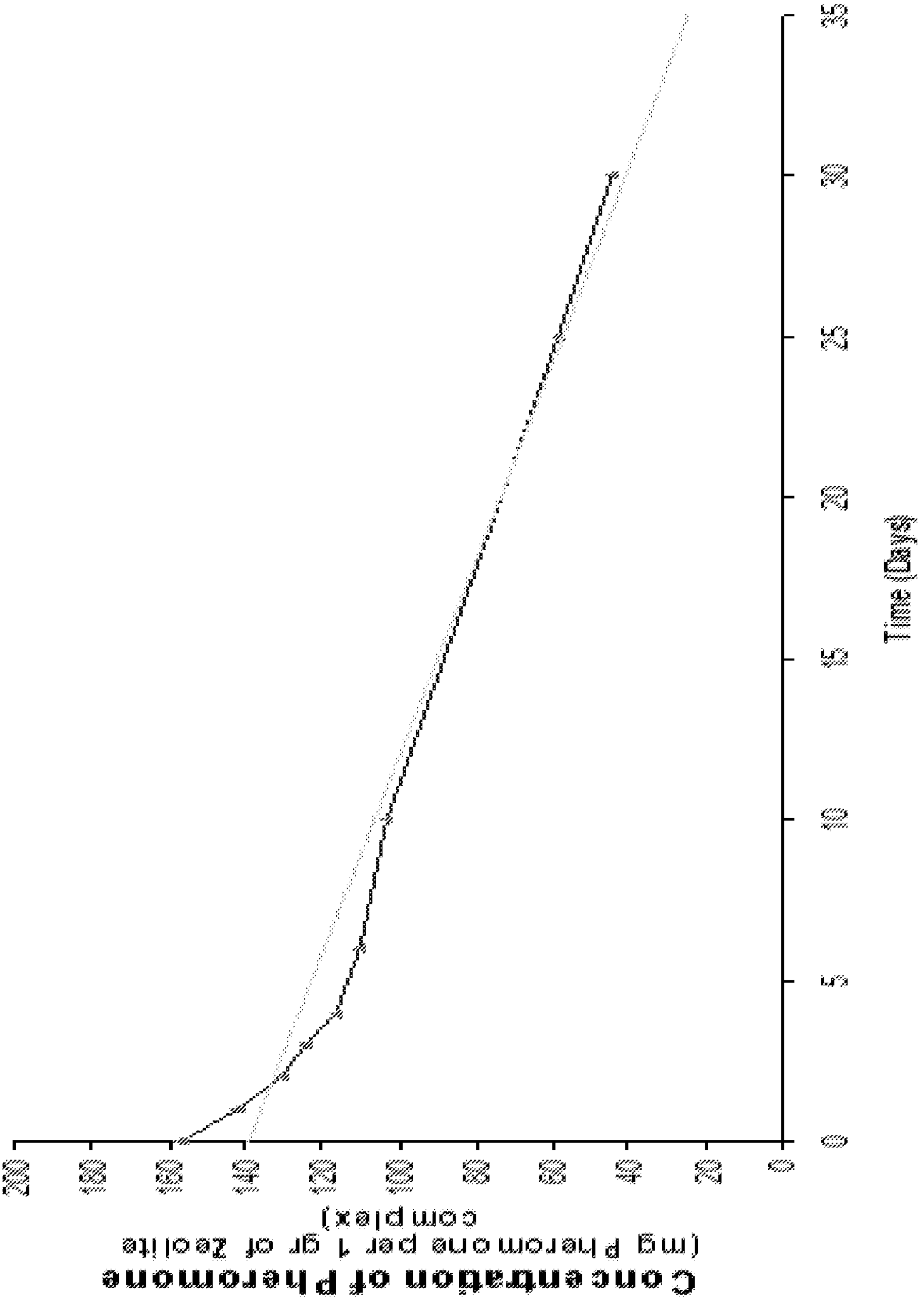
Figure 6


Concentration of Pheromone
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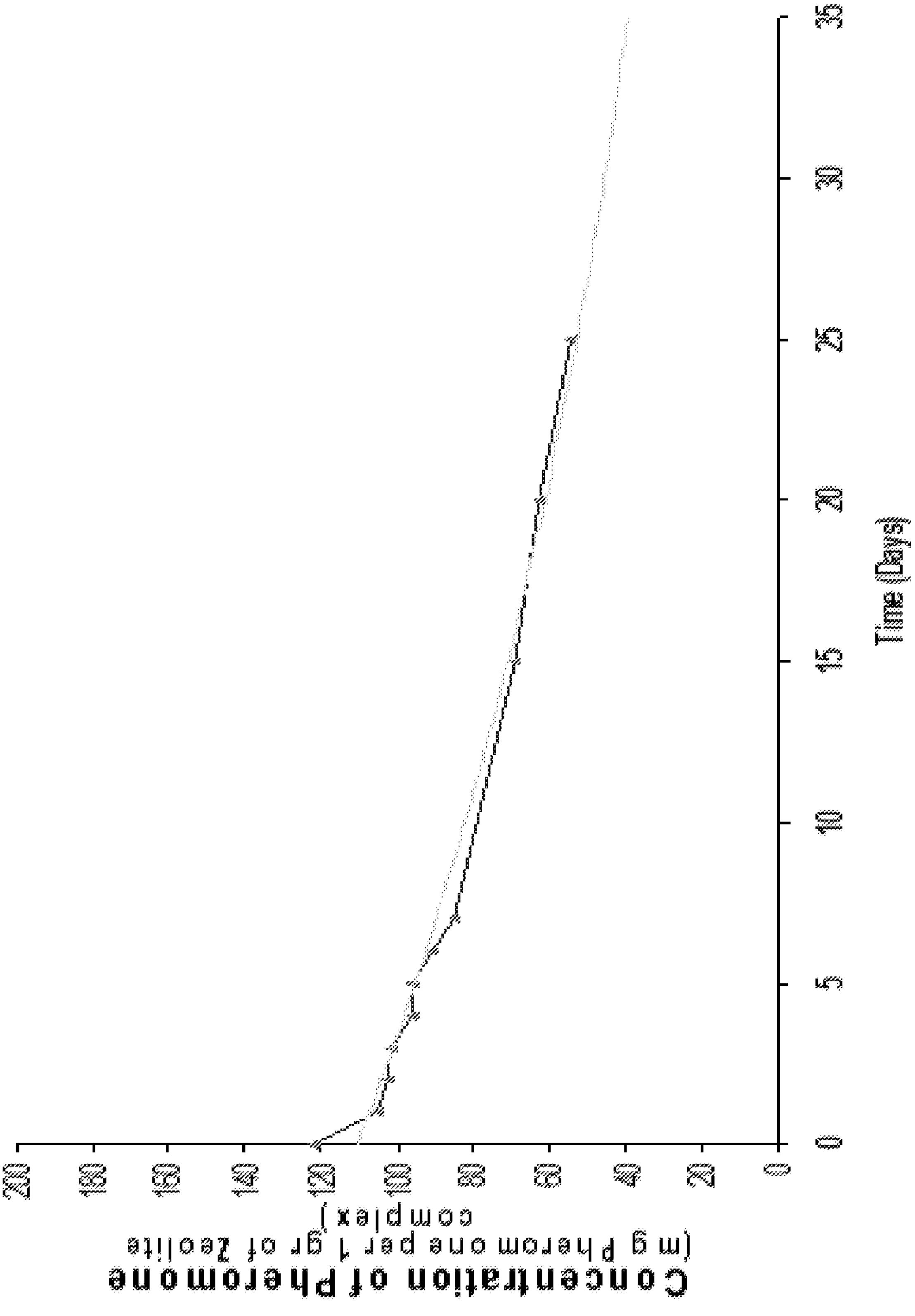
Time (Days)

Figure 7


Concentration of Pheromone
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Time (Days)
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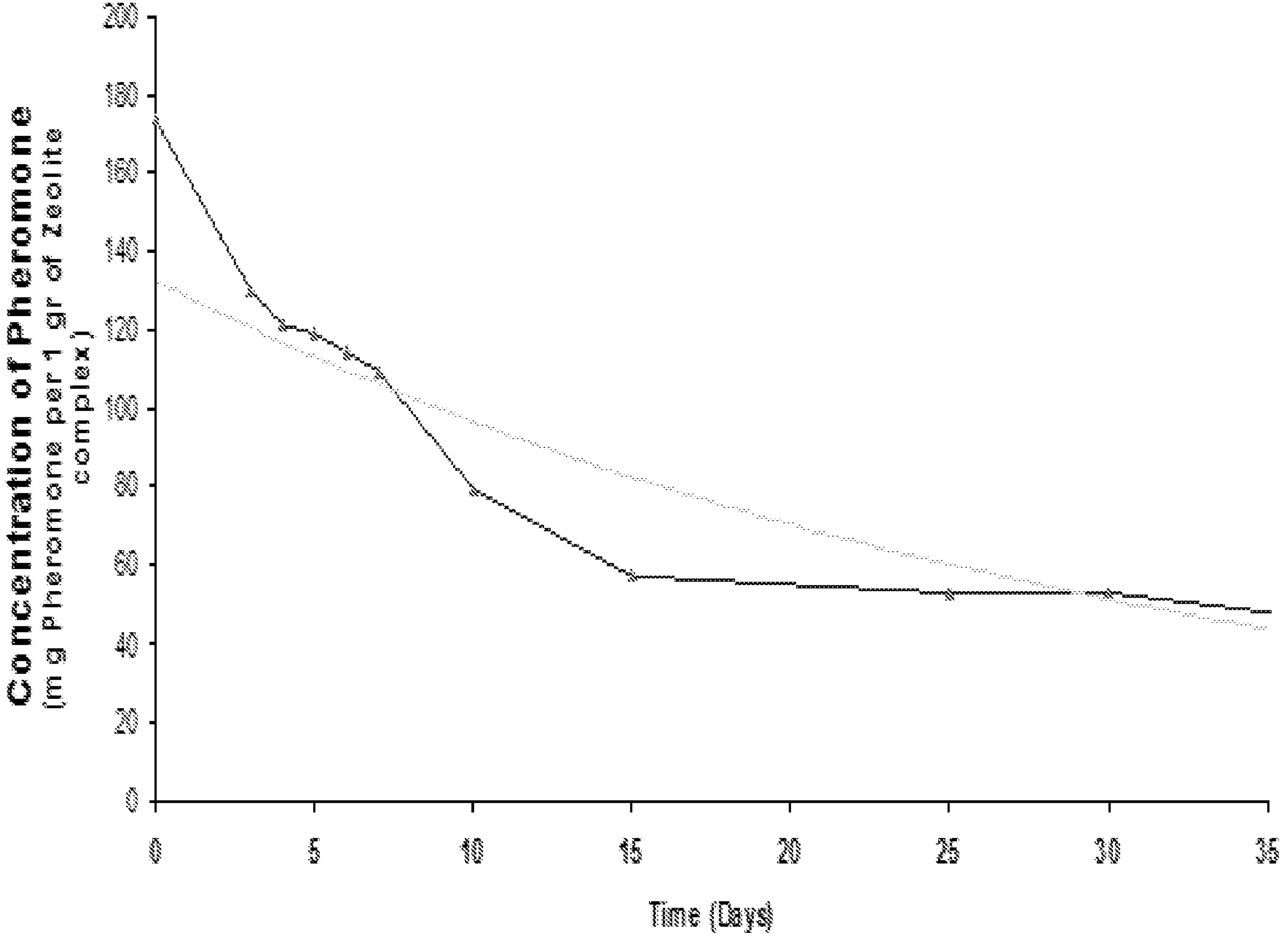
Figure 8


Concentration of Pheromone
(mg Pheromone per 1 gr of Zeolite complex)
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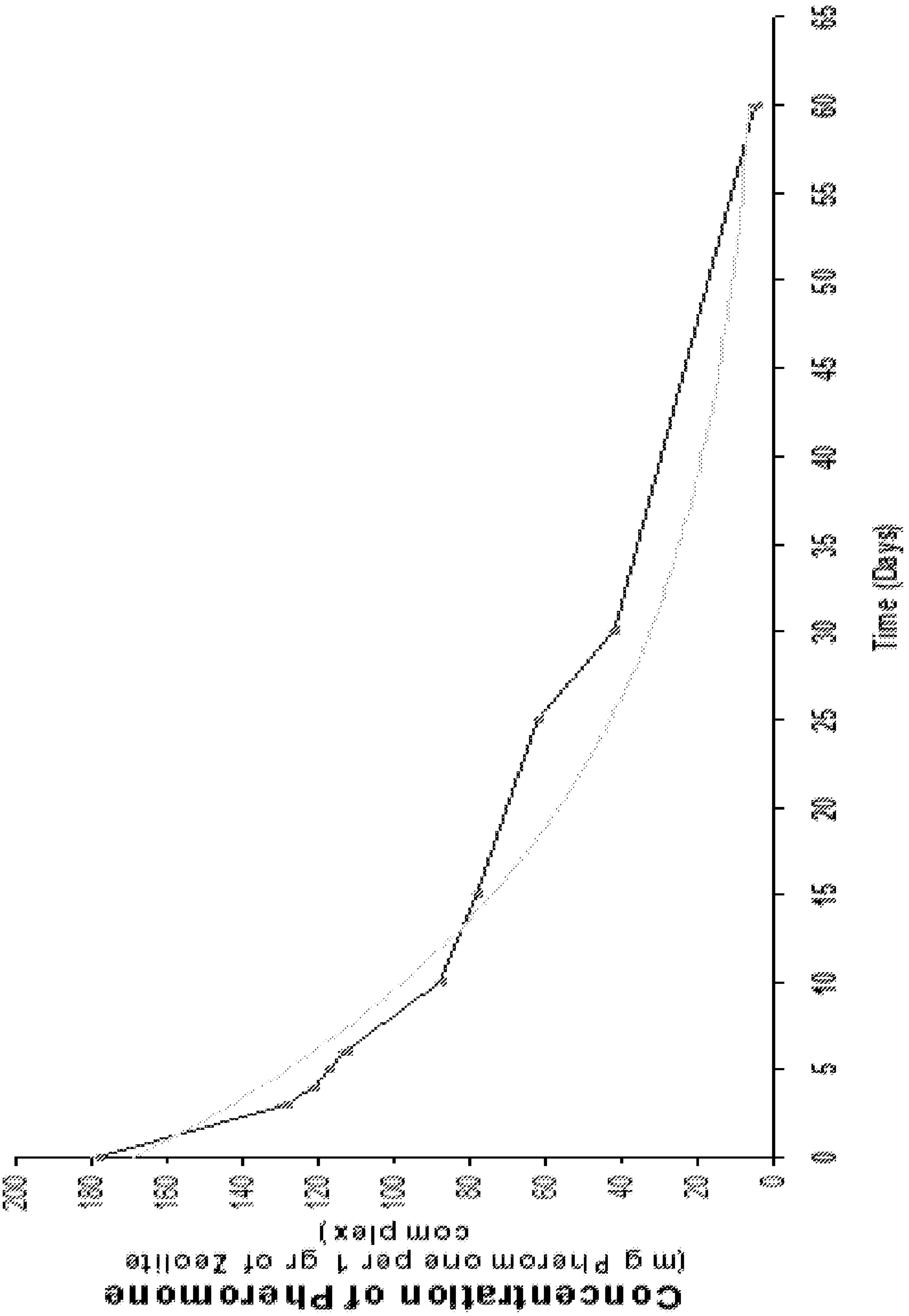
Time (Days)

Figure 9


Concentration of Pheromone
(mg Pheromone per 1 gr of Zeolite complex)
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Time (Days)
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Figure 10

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL2018/050947

A. CLASSIFICATION OF SUBJECT MATTER

IPC (2018.01) A01N 25/18, A01N 25/08, C01B 39/02, C07C 47/21, C07C 69/738, C07C 33/035

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC (2018.01) A01N 25/18, A01N 25/08, C01B 39/02, C07C 47/21, C07C 69/738, C07C 33/035

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Databases consulted: CAPLUS, BIOSIS, INSPEC, PatBase, COMPENDEX

Search terms used: pheromone, slow release, variable release, mesoporous molecular sieve, silica, alum, spinosoid, spinosad, spinosyn

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1064843 A1 CONSEJO SUPERIOR DE [ES]; UNIV VALENCIA POLITECNICA [ES] 03 Jan 2001 (2001/01/03) abstract, [009], [0010], [0017], [0019], [0033] cited in the application	1,2,5,6
Y	abstract, [0009], [0010], [0019], [0033]	3,4,7-19
Y	DE 102004048579 A1 CONTITECH ELASTOMER BESCH GMBH [DE] 13 Apr 2006 (2006/04/13) [0001], [0006]- [0008], [0014], [0015], [0017], [0020]	3,4,6,11,12,18,19
Y	WO 2012087630 A1 DU PONT [US]; XU MING [US] 28 Jun 2018 (2018/06/28) p. 60 lines 1-4, p. 64 example B, p. 80 Table A, p. 82 Table B1, p. 88 lines 18, 19, 31, p. 101 lines 30-31	7-10,13-15
Y	WO 2008057547 A2 ISCA TECHNOLOGIES [US] MAFRA-NETO AGENOR [US] 15 May 2008 (2008/05/15) abstract, p. 4 lines 19-20, p. 8 lines 23-26, p. 13 lines 5-7, p.18 lines 14-17, p. 19 lines 22-24, p. 23 lines 7-10	7-10,13-19

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 18 Nov 2018	Date of mailing of the international search report 19 Nov 2018
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616	Authorized officer YUDBOROVSKI Evgenia Telephone No. 972-2-5651654

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IL2018/050947

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
EP 1064843 A1	03 Jan 2001	EP 1064843 A1	03 Jan 2001
		EP 1064843 B1	11 Feb 2004
		AT 259144 T	15 Feb 2004
		BR 9908620 A	31 Oct 2000
		CA 2322816 A1	10 Sep 1999
		DE 69914727 D1	18 Mar 2004
		DE 69914727 T2	07 Oct 2004
		ES 2156481 A1	16 Jun 2001
		ES 2156481 B1	01 Feb 2002
		ES 2216489 T3	16 Oct 2004
		JP 2002505347 A	19 Feb 2002
		PT 1064843 E	31 May 2004
		US 6432476 B1	13 Aug 2002
		WO 9944420 A1	10 Sep 1999
DE 102004048579 A1	13 Apr 2006	DE 102004048579 A1	13 Apr 2006
		EP 1799035 A1	27 Jun 2007
		WO 2006037546 A1	13 Apr 2006
WO 2012087630 A1	28 Jun 2018	WO 2012087630 A1	28 Jun 2012
WO 2008057547 A2	15 May 2008	WO 2008057547 A2	15 May 2008
		WO 2008057547 A3	27 Nov 2008
		AU 2007317844 A1	15 May 2008
		BR PI0713456 A2	07 Feb 2012
		CA 2669036 A1	15 May 2008
		CA 2669036 C	18 Feb 2014
		CO 6210738 A2	20 Oct 2010
		EP 2088857 A2	19 Aug 2009
		EP 2088857 A4	08 Sep 2010
		MX 2009004887 A	24 Sep 2009

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.	PCT/IL2018/050947

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		US 2008254083 A1	16 Oct 2008
		US 7887828 B2	15 Feb 2011