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(54) Titre : COMPOSITION HERBICIDE
(54) Title: HERBICIDAL COMPOSITION

(57) **Abrégé/Abstract:**

A herbicidal composition, comprising preferably an aqueous solution of a salt of paraquat or diquat, or a mixture thereof, in admixture with a gelling agent that will gel at the pH of human gastric juice, (e. g. magnesium silicate), and further comprising (1) an emetic, (e.g. a triazolopyrimidine emetic) or (2) a purgative (e. g. magnesium sulphate), or (3) both an emetic and a purgative. In the event of ingestion of the composition, these additives act synergistically to reduce absorption of bipyridylum compound from the gastrointestinal tract into the bloodstream, and thereby reduce the oral toxicity of the composition.



ABSTRACTHERBICIDAL COMPOSITION

5 A herbicidal composition, comprising preferably an aqueous solution of a salt of paraquat or diquat, or a mixture thereof, in admixture with a gelling agent that will gel at the pH of human gastric juice, (e.g. magnesium silicate), and further comprising (1) an emetic, (e.g. a triazolopyrimidine emetic) or (2) a purgative (e.g. magnesium sulphate), or (3) both an emetic and a purgative.

10 In the event of ingestion of the composition, these additives act synergistically to reduce absorption of bipyridylum compound from the gastrointestinal tract into the bloodstream, and thereby reduce the oral toxicity of the composition.

HERBICIDAL COMPOSITIONS

This invention relates to herbicidal compositions containing a herbicidal bipyridylium diquaternary salt as an active ingredient.

5 Various herbicidal bipyridylium diquaternary salts are described in United Kingdom Patent Specification No. 785732, 813531 and 813532. Certain of these compounds (e.g. salts of paraquat and diquat; the chemical identity of these compounds is given later in this specification) are in widespread use in agriculture, and are manufactured for sale in the form of concentrated aqueous solutions. When required for use, these concentrated solutions are diluted with water to form a solution which is then sprayed upon unwanted plants. When used with due care, and in accordance with recommended procedures, the concentrated aqueous solutions present no hazard. However, hazards may develop if adherence to the recommended handling practices is not maintained. Thus it may happen that an operator may decant some of the concentrate into a domestic container such as a beverage bottle for subsequent use in his own garden at home. The hazard associated with such a practice is of course that a child or incautious adult coming upon the bottle may swallow some of the contents, with possible serious consequences.

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20 Various methods have been proposed to reduce the likelihood of accidental swallowing of concentrated solutions of bipyridylium diquaternary salts in the circumstances described above. These include the inclusion of an odourant in the concentrate as a warning (see UK Patents 1406881 and 1570981), the inclusion of a water-soluble blue dye, and the inclusion of a substance to convert the concentrate into a thixotropic gel (see UK Patent 1395502).

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30 Another approach to reducing the possibility of harmful effects following the ingestion of a bipyridylium salt concentrate has been to include an emetic in the concentrate, so that the concentrate will be removed by vomiting shortly after its ingestion (see UK Patent 1507407). A further approach has been to formulate the bipyridylium diquaternary salt as a multiple emulsion, as proposed in published European Patent Application No. 276911. In addition to methods of formulating bipyridylium herbicides so as to reduce the likelihood of accidental ingestion, a variety of methods has been proposed for formulating bipyridylium herbicides so as to improve their suitability for particular applications. Thus, it has been proposed to formulate an aqueous solution of paraquat as

an invert emulsion in oil (see United States Patent 4115098) in order to reduce drift and evaporation of the droplets of spray when the paraquat is applied as a herbicide.

5 According to the present invention, there is provided a herbicidal composition comprising a salt of paraquat or diquat, or a mixture thereof, in admixture with a gelling agent that will gel at the pH of human gastric juice, and further comprising (1) an emetic, or (2) a purgative, or (3) both an emetic and a purgative.

The compositions may be solid or liquid.

10 According to a preferred aspect of the present invention, there is provided a herbicidal composition comprising an aqueous solution of a salt of paraquat or diquat, or a mixture thereof, in admixture with a gelling agent that will gel at the pH of human gastric juice, and an emetic.

15 Preferably the aqueous compositions contain 50, and more preferably, 100 grams per litre or more of paraquat or diquat, or a mixture thereof.

The aqueous compositions may contain, for example, 200 grams or more per litre of paraquat or diquat or a mixture thereof.

20 The aqueous compositions of the invention may further comprise a purgative. They may also comprise a suspending agent to assist in keeping the gelling agent evenly dispersed throughout the composition during storage and transport.

25 If a quantity of a composition according to the invention is ingested, the acidity of the gastric juice (which ranges from pH1.5 to pH3.5) will cause the composition to gel in the stomach. Increasing the viscosity of the gastric contents slows down the rate of gastric emptying. The bipyridylum herbicide will consequently be trapped in the gel, and its movement from the stomach and into the absorptive small intestine will be impeded. Ideally, the gelling agent is one which will also reduce gastric acidity and therefore reduce local irritation of the gastric mucosal lining. The emetic present in the composition is absorbed rapidly and will in a short time cause expulsion of the gel containing the bipyridylum herbicide by vomiting, thereby preventing the ingested herbicide from moving further down the gastrointestinal tract, where absorption of the bipyridylum compound would otherwise take place. In preferred
35 compositions according to the invention, a purgative is present in the composition, to assist in removing any non-absorbed bipyridylum herbicide which has passed from the stomach into the small intestine despite the action of the emetic. In the event of a bipyridylum composition according

to the invention being ingested, the combined effects of the gelling agent, emetic, and when included, the purgative, will be to substantially reduce the absorption of the bipyridylum compound from the gastrointestinal tract into the bloodstream, and thereby to reduce the oral toxicity of the concentrate.

5 Paraquat is the common name of the 1,1'-dimethyl-4,4'-bipyridylum cation, having the structure (I) (see formula sheet).

Diquat is the common name of the 1,1'-ethylene-2,2'-bipyridylum cation, having the structure (II) (see formula sheet).

10 Salts of paraquat and diquat necessarily contain anions carrying sufficient negative charges to balance the two positive charges on the bipyridylum nucleus.

15 Since the characteristic herbicidal effect of a bipyridylum quaternary cation is independent of the nature of the associated anion, the choice of the anion is a matter of convenience, depending, for example, on cost. Preferably the anion is one which gives rise to a salt of convenient water solubility. Examples of anions, which may be mono- or poly-valent, include acetate, benzenesulphonate, benzoate, bromide, butyrate, chloride, citrate, fluorosilicate, fumarate, fluoroborate, iodide, lactate, malate, 20 maleate, methylsulphate, nitrate, propionate, phosphate, salicylate, succinate, sulphate, thiocyanate, tartrate, and p-toluenesulphonate. The salt of the herbicidal bipyridylum cation may be formed from a number of similar anions or mixtures of different ones. A salt having any particular desired anion may be prepared either by direct synthesis from reactants 25 which include the desired anion, or by exchanging the anion of a previously prepared salt of the preferred anion by methods well known in the art, for example by passage of a solution of the previously prepared salt through an ion-exchange resin. For reasons of convenience and economy, paraquat is normally manufactured and sold as paraquat dichloride while diquat is 30 manufactured and sold as diquat dibromide.

35 Since the characteristic herbicidal activity of a salt of a herbicidal bipyridylum quaternary cation resides in the cation only, it is customary to quote concentrations of active ingredient and rates of application in terms of the amount of bipyridylum quaternary cation used. Application rates and concentrations quoted in this specification therefore relate to the amount of bipyridylum quaternary cation unless otherwise stated.

Preferably, aqueous compositions according to the invention contain at least 50 grams per litre of paraquat or diquat or mixtures thereof. The

compositions may contain 100 grams per litre or more of paraquat or diquat or mixtures thereof. Compositions containing 200 grams or more per litre, for example 300 grams per litre, may be prepared.

The gelling agent is preferably magnesium silicate, although other gelling agents may be used.

As commercially manufactured, (e.g. by reaction of sodium silicate with magnesium sulphate), magnesium silicate has a somewhat variable composition; thus, the ratio of silica (SiO₂) to magnesium oxide (MgO) in commercial technical grades of this material may range for example from about 3.3 to 1.5. Typical chemical analyses for two commercial technical grades of magnesium silicate (designated PDM15 and PDM 33) are given below.

	<u>PDM 33</u>	<u>PDM 15</u>
MgO	12-13%	22.6-24.6%
SiO ₂	61-65%	49.5-53.5%
Molecular ratio SiO ₂ /MgO	~ 3.3	~ 1.5
Fe	0.03%	0.03%
SO ₄	2.5%	1.5%
Loss in weight on ignition at 900°C	18-22%	20-30%

In preparing herbicidal compositions according to the present invention, it is preferred to use a grade of magnesium silicate which has a relatively high magnesium oxide content, for example magnesium silicate approximating to the composition 2MgO.3SiO₂. Magnesium silicate of this composition is often designated as magnesium silicate, and is so designated throughout this specification. Suitably purified and sterilised grades of this material are used pharmaceutically as an antacid.

Magnesium trisilicate is also known as magnesium mesotrisilicate. It is described in the Merck Index (Ninth Edition, published in 1976 by Merck and Co., Inc, Rahway, New Jersey, USA; see entry No. 5514 on pages 738-739) as an odourless, tasteless, slightly hygroscopic powder, having the chemical formula Mg₂Si₃O₈. It is usually hydrated to some extent. According to the British Pharmacopoeia, 1988, volume 1, page 348 (published by H M Stationery Office, London), magnesium trisilicate is a hydrated magnesium silicate of the approximate composition 2MgO.3SiO₂ containing water of crystallisation. The pharmaceutical grade contains not less than the equivalent of 29.0% of MgO, and not less than the equivalent of 65.0% of SiO₂, both calculated with reference to the substance after ignition at 900°C. The use of magnesium trisilicate as a gelling agent in the compositions of the present invention has the advantage that it reduces

gastric acidity, and thereby, as mentioned above, reduces local irritation of the gastric mucosal lining. Magnesium trisilicate and the silicon dioxide gel produced in the stomach both have adsorbent properties. This reduces the bioavailability of bipyridylum salts when they are in concentrated solution. The magnesium trisilicate is preferably present in a concentration of from 10 to 400 grams per litre of the composition, and more preferably in a concentration of from 10 - 100 grams per litre. Since magnesium trisilicate is insoluble in water, it may tend to settle to the bottom of the container in which the composition is stored. Liquid compositions of the invention containing magnesium trisilicate therefore preferably also comprise a suspending agent, to assist in keeping the magnesium trisilicate dispersed homogeneously throughout the composition. Examples of suitable suspending agents include bacterial polysaccharides, for example the material known as xanthan gum, and in particular the xanthan gum sold under the trade name "KELZAN". Other suitable suspending agents include alginates. The suspending agents may be present in a concentration of for example from 0.01 gram to 100 grams per litre of the composition.

A variety of known emetics may be used in the compositions of the invention. However, preferred emetics are those compounds disclosed in UK Patent No. 1507407 for use in formulations of bipyridylum herbicides, and a particularly preferred emetic is 2-amino-6-methyl-5-oxo-4-n-propyl-4,5-dihydro-5-triazolo[1,5-a]-pyrimidine, having the structural formula (A) (see formula sheet).

The amount of emetic used in the composition will vary depending upon the particular type of emetic used, but when an emetic of the class disclosed in UK Patent No. 1507407 is used, the concentration of emetic is preferably from 0.1 to 5 grams per litre of the composition.

For a composition containing 200 grams per litre of bipyridylum compound, a concentration of 1.5 to 2.0 grams per litre of emetic is preferred.

When the composition of the invention contain a purgative, this is preferably magnesium sulphate. The concentration of magnesium sulphate is preferably from 10 to 400 grams per litre of the composition, and more preferably from 10 to 100 grams per litre.

The compositions of the invention may also contain further ingredients for example one or more surface-active agents.

Surface-active agents may be cationic, non-ionic or anionic.

Generally speaking cationic and non-ionic surface-agents are preferred to anionic surface-active agents for use in the compositions of the invention, since the latter may interact undesirably with the bipyridylum quaternary salt in the compositions, but anionic surface-active agents may be used where such interactions do not occur. Examples of non-ionic surface-active agents for use in the compositions of the invention include the condensation products of ethylene oxide with alkyl phenols such as octylphenol, nonylphenol and octylcresol for example the condensation product of *p*-nonylphenol with 8 molar proportions with of ethylene oxide sold under the trade name of Synperonic NP8. Other non-ionic agents are the partial esters derived from long chain fatty acids and hexitol anhydrides, for example sorbitan monolaurate; the condensation products of the said partial esters with ethylene oxide; and the lecithins. Examples of cationic surface-active agents include quaternary salts and condensates of ethylene oxide with amines, for example the substances sold under the Trade Mark "Ethomeen", "Ethoduomeen", "Duoquad" and "Arquad". A particular example comprises the condensate of a C₁₃ to C₁₅ mixture of synthetic primary amines with 15 molar proportions of ethylene oxide sold under the trade name "Synprolam" 35x15. The proportion of surface-active agent present in the aqueous compositions of the invention is not highly critical and a suitable proportion may readily be decided upon by a person skilled in the formulation art without excessive experimentation. However by way of illustration an amount of 50 to 100 grams per litre of the composition is usually suitable; although more or less may be used depending upon the particular composition. The composition of the invention may also contain an odourant, such as a pyridine derivative, as described in UK Patent No. 1406881, or *n*-valeric acid. The compositions may also comprise a pigment or a dye to give them a distinctive colour.

In greenhouse tests, compositions according to the invention containing paraquat have been found to be equivalent in herbicidal effect to commercial aqueous formulations of paraquat, the two types of composition being applied at the same rate of application of active ingredient.

Aqueous compositions according to the invention are readily prepared by adding the various constituents of the formulation to an aqueous solution of a salt of paraquat or diquat or a mixture thereof, with suitable agitation.

Solid compositions according to the invention include compositions of the kind disclosed in UK Patent Specification No. 1,086,939, which describes a process of mixing a hydrate-forming salt (e.g. magnesium sulphate) with an aqueous solution of a bipyridylum herbicide in proportions such that the hydrate-forming salt combines with sufficient of the water present to give a solid composition. Solid compositions according to the present invention may be prepared by additionally including in the mixing process a gelling agent (e.g. magnesium trisilicate) and an emetic, in proportions in similar to those used in the aqueous composition of the present invention, relative to the paraquat or diquat.

In a variation of the invention, there are further provided herbicidal compositions comprising an aqueous solution of a salt of paraquat or diquat, or a mixture thereof, in admixture with a gelling agent that will gel at the pH of human gastric juice, and a purgative. While the compositions contain at least 50 or 100 grams per litre of paraquat or diquat or a mixture thereof, compositions containing 200 grams or more per litre may be prepared.

Preferably the gelling agent is magnesium trisilicate and the purgative is magnesium sulphate. The proportions of gelling agent and purgative present in the composition are similar to those used in the emetic-containing compositions described above.

The constituents and proportions of a composition of this kind are given below by way of example:

<u>Constituent</u>	<u>Concentration(grams/litre)</u>
Paraquat (as dichloride)	200
Magnesium trisilicate	100
Magnesium sulphate	100
Kelzan	3.0
Water	to 1 litre

Other ingredients may be included in the compositions as described above for the emetic-containing compositions. Further examples of this type of composition include the compositions described in Examples 1 to 7, but without the inclusion of the Compound A.

If a quantity of the composition containing bipyridylum herbicide, gelling agent, and purgative is inadvertently swallowed, the composition will gel in the stomach. The bipyridylum herbicide will be trapped in the

gel, and the purgative will bring about movement of the gel through the gastro-intestinal tract with increased speed, thereby reducing absorption.

5 In a further variation of the invention, there are further provided herbicidal compositions comprising an aqueous solution of a salt of paraquat or diquat or a mixture thereof, the compositions comprising 100 grams or more per litre of paraquat or diquat or a mixture thereof, and further comprising (1) an emetic and (2) a purgative. Preferably the emetic is the compound of formula (A) below, and preferably the purgative is magnesium sulphate. The proportions of these ingredients will be 10 similar to those quoted above for the compositions previously described, (i.e. 0.1 to 5 grams per litre of Compound A and 10 to 400 grams per litre of composition of magnesium sulphate).

The constituents and proportions of a composition of this kind are given below by way of example:

15	<u>Constituent</u>	<u>Concentration(grams/litre)</u>
	Paraquat (as dichloride)	200
	Magnesium sulphate	100
	Compound A	2.5
	Water	to 1 litre

20 If a quantity of such a composition is inadvertently swallowed, the combined action of the emetic and purgative will reduce absorption of the bipyridylum herbicide.

The following Examples illustrate the invention.

EXAMPLE 1

25 This Example illustrates an aqueous composition according to the invention.

	<u>Constituent</u>	<u>Concentration(grams/litre)</u>
	Paraquat (as dichloride)	100
	Magnesium trisilicate	10
30	Magnesium sulphate	100
	Kelzan	1.0
	Emetic (Compound A)	1.2
	Water	to 1 litre

EXAMPLE 2

35 This Example illustrates an aqueous composition according to the invention.

<u>Constituent</u>	<u>Concentration(grams/litre)</u>
Paraquat (as dichloride)	200
Magnesium trisilicate	100
Magnesium sulphate	100
5 Kelzan	3.0
Emetic (Compound A)	2.5
Water	to 1 litre

EXAMPLE 3

10 This Example illustrates an aqueous composition according to the invention.

<u>Constituent</u>	<u>Concentration (grams/litre)</u>
Paraquat (as dichloride)	200.00
Synperonic	35.00
Nansa 1169PS	117.00
15 Kelzan	3.00
Magnesium sulphate heptahydrate	100.00
Magnesium trisilicate	10.00
Compound A (see page 7)	1.65
Pyridine base	10.00
20 Sulfacide Blue	5.00
Silcolapse 5020	0.25
Acetic acid 80% solution	to pH 7.0+ ⁻ 0.5
Water	to 1 litre

25 The above composition was prepared by simple admixture of the constituents or aqueous solutions thereof.

The compositions of the constituents indicated by the various trade names are as follows:-

Synperonic NP8

30 A surface-active agent comprising a condensate of p-nonylphenol with eight molar proportions of ethylene oxide.

Nansa 1169 PS

A surface-active agent comprising an aqueous solution of sodium dodecylbenzenesulphonate in a concentration of 30%.

Kelzan

35 Xanthan gum, comprising a bacterial polysaccharide, present as a suspending agent.

Pyridine base

An odourant comprising a mixture of alkyl pyridines, typically comprising methyl ethyl pyridines (40-60%), propylpyridine (20-30%), ethylpyridine (2.5%) picolines (less than 5%) and other alkyl pyridines, most of the mixture distilling in the range 180-220°C.

Sulfacide Blue

A water-soluble blue dye.

Silcolapse 5020

A silicone-based antifoaming agent

EXAMPLE 4

This Example illustrates an aqueous composition according to the invention.

<u>Constituent</u>	<u>Concentration (grams/litre)</u>
Paraquat (as dichloride)	200.00
Synperonic NP8	35.00
Nansa 1169PS	117.00
Kelzan	3.00
MgSO ₄ 1.5 H ₂ O	100.00
Magnesium trisilicate	100.00
Compound A	1.65
Sulfacide Blue 5J liquid	5.00
Silcolapse 5020	0.25
Acetic acid 80% solution	to pH 7.0 ⁺ - 0.5
Water	to 1 litre

EXAMPLE 5

This Example illustrates an aqueous composition according to the invention.

<u>Constituent</u>	<u>Concentration (grams/litre)</u>
Paraquat (as dichloride)	200.00
Synperonic NP8	35.00
Nansa 1169PS	117.00
Kelzan	3.00
MgSO ₄ 1.5 H ₂ O	100.00
Magnesium trisilicate	100.00
Compound A	1.65
Pyridine base	10.00
Sulfacide Blue 5J liquid	5.00
Silcolapse 5020	0.25

Acetic acid 80% solution to pH 7.0 ^{+ -} 0.5
 Water to 1 litre

EXAMPLE 6

This Example illustrates an aqueous composition according to the invention.

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<u>Constituent</u>	<u>Concentration (grams/litre)</u>
Paraquat (as dichloride)	50.00
Diquat (as dibromide)	50.00
Synperonic NP8	35.00
10 Nansa 1169PS	117.00
Kelzan	3.00
MgSO ₄ 1.5 H ₂ O	100.00
Magnesium trisilicate	100.00
Compound A	1.65
15 Pyridine bases	10.00
Sulfacide Blue 5J liquid	5.00
Silcolapse 5020	0.25
Acetic acid 80% solution	to pH 7.0 ^{+ -} 0.5
Water	to 1 litre

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EXAMPLE 7

This Example illustrates an aqueous composition according to the invention.

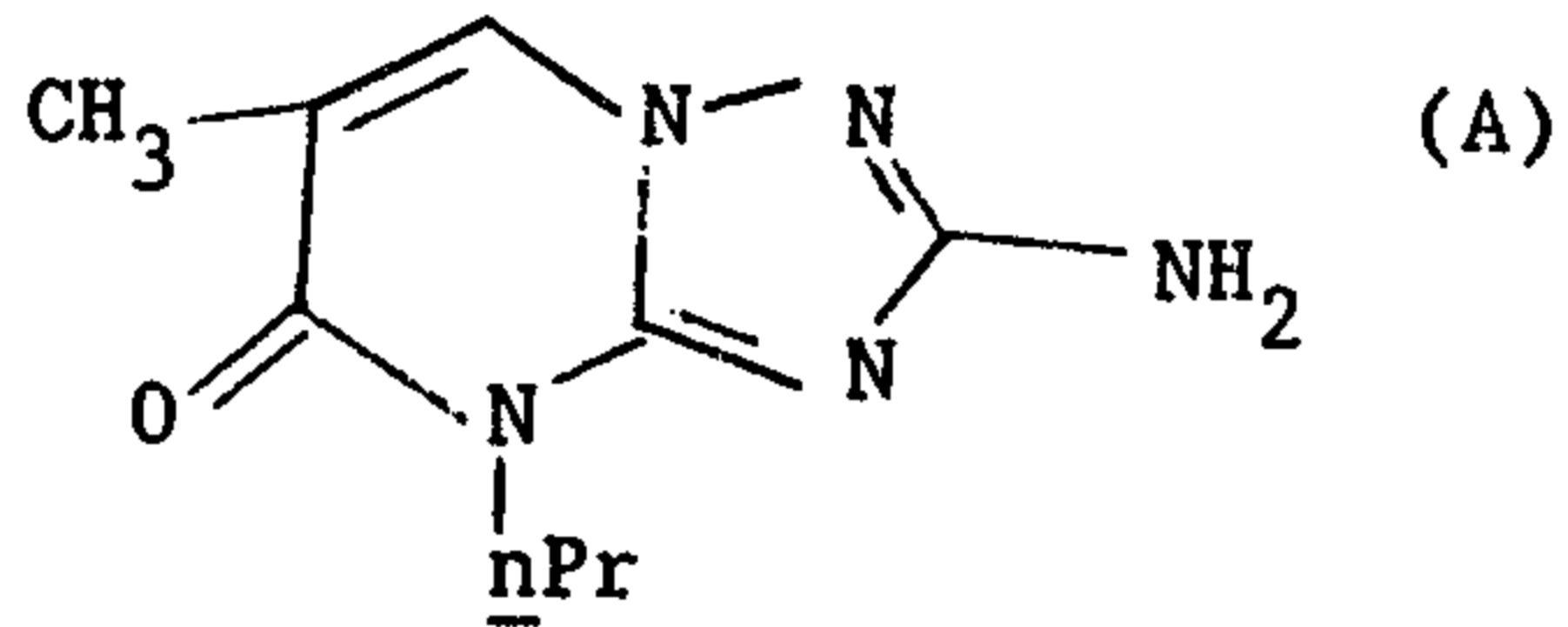
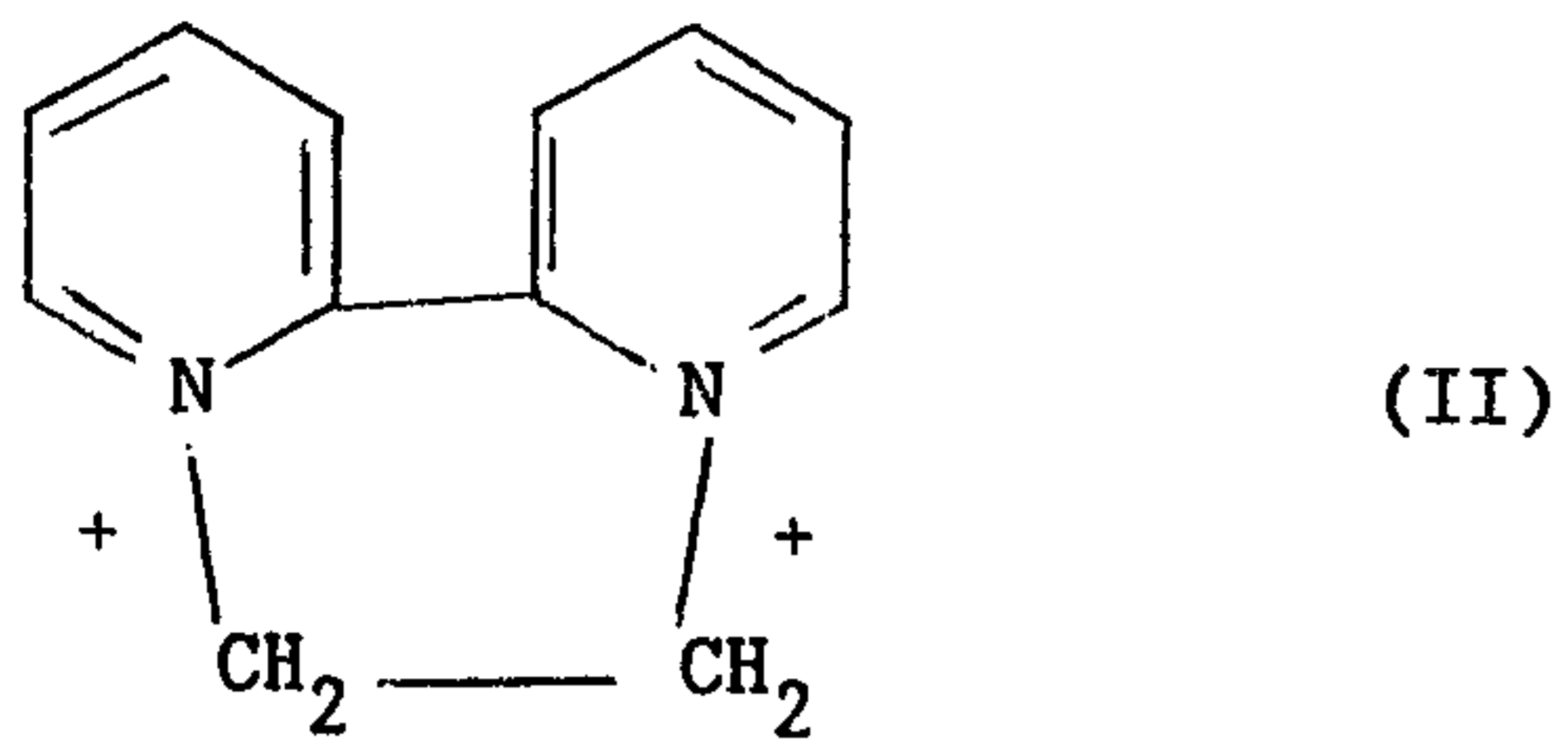
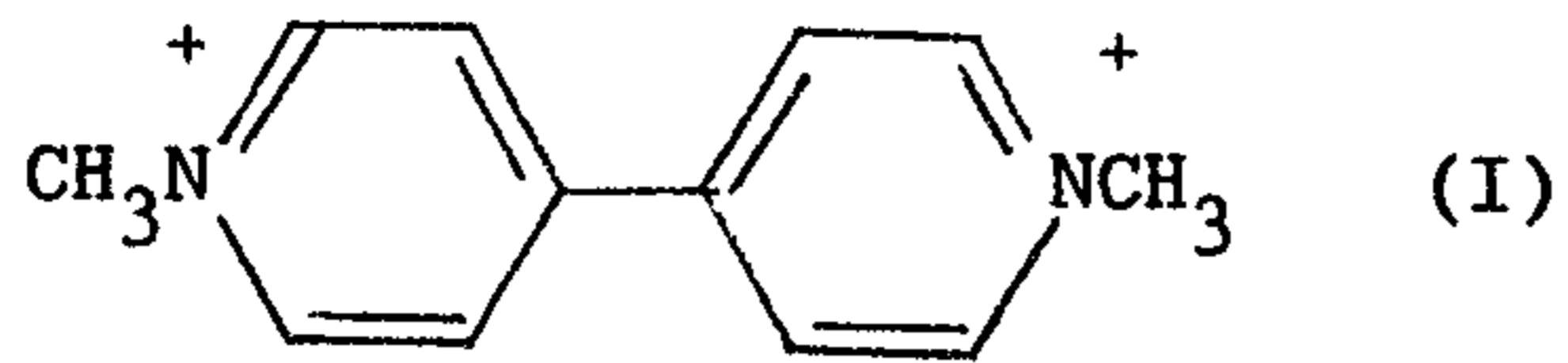
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<u>Constituent</u>	<u>Concentration (grams/litre)</u>
Paraquat (as dichloride)	200.00
25 Synperonic NP8	35.00
Nansa 1169PS	117.00
Kelzan	3.00
MgSO ₄ 1.5 H ₂ O	100.00
Magnesium trisilicate	50.00
30 Compound A	1.65
Pyridine base	10.00
Sulfacide Blue 5J liquid	5.00
Silcolapse 5020	0.25
Acetic acid 80% solution	to pH 7.0 ^{+ -} 0.5
35 Water	to 1 litre

CHEMICAL FORMULAE
(in description)



Claims:

1. An aqueous liquid herbicidal composition comprising a salt selected from the group consisting of a salt of paraquat, a salt of diquat, and a mixture thereof, in a concentration of at least 50 grams per litre, in admixture with from 10 to 400 grams per litre of a gelling agent that will gel at the pH of human gastric juice, the composition further comprising an additive selected from the group consisting of an emetic, a purgative and a mixture thereof.
2. An aqueous liquid herbicidal composition comprising:
 - (i) a herbicidal component comprising a salt selected from the group consisting of a salt of paraquat, a salt of diquat, and a mixture thereof;
 - (ii) a gelling agent that will gel at the pH of human gastric juice; and
 - (iii) an additive selected from the group consisting of an emetic, a purgative and a mixture thereof;wherein the ratio of the herbicidal component to the gelling agent is from 1:1 to 20:1.
3. An aqueous liquid herbicidal composition as claimed in claim 1 or claim 2 comprising an aqueous solution of a salt selected from the group consisting of a salt of paraquat, a salt of diquat, and a mixture thereof in admixture with a gelling agent that will gel at the pH of human gastric juice and an emetic.
4. A composition as claimed in any one of claims 1 to 3 comprising at least 100 grams per litre of paraquat or diquat or a mixture thereof.
5. A composition as claimed in any one of claims 1 to 4 comprising at least 200 grams per litre of paraquat or diquat or a mixture thereof.
6. A composition as claimed in any one of claims 2 to 5 which further comprises a purgative.
7. A composition as claimed in any one of claims 1 to 6 wherein the gelling agent comprises magnesium silicate.
8. A composition as claimed in any one of claims 1 to 7 wherein the gelling agent comprises magnesium trisilicate.
9. A composition as claimed in any one of claims 1 to 8 wherein the emetic comprises 2-amino-6-methyl-5-oxo-4-n-propyl-4,5-dihydro-5-triazolo-[1,5-a]-pyrimidine.

10. A composition as claimed in any one of claims 1 to 9 wherein the purgative comprises magnesium sulphate.
11. A composition as claimed in any one of claims 1 to 10 which further comprises a suspending agent.