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(54) **Controlled Release Glass**

(57) A range of glass compositions for the controlled release of iron into solution is based on P_2O_5 as principal glass former and contains up to 20 moles% of iron oxide (calculated as Fe_2O_3) and at least one alkali metal oxide.

The drawings originally filed were informal and the print here reproduced is taken from a later filed formal copy.

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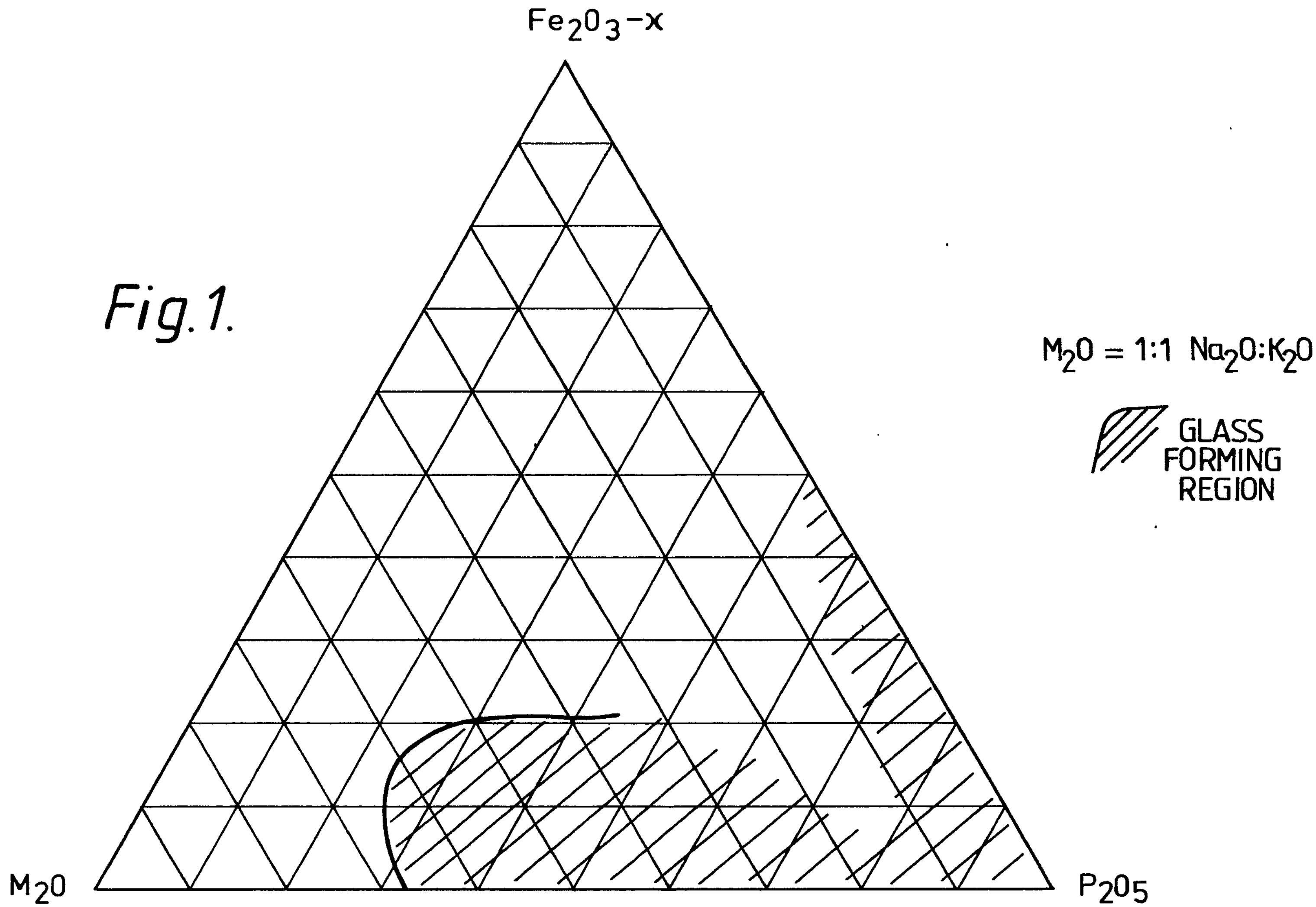

Fig.1.

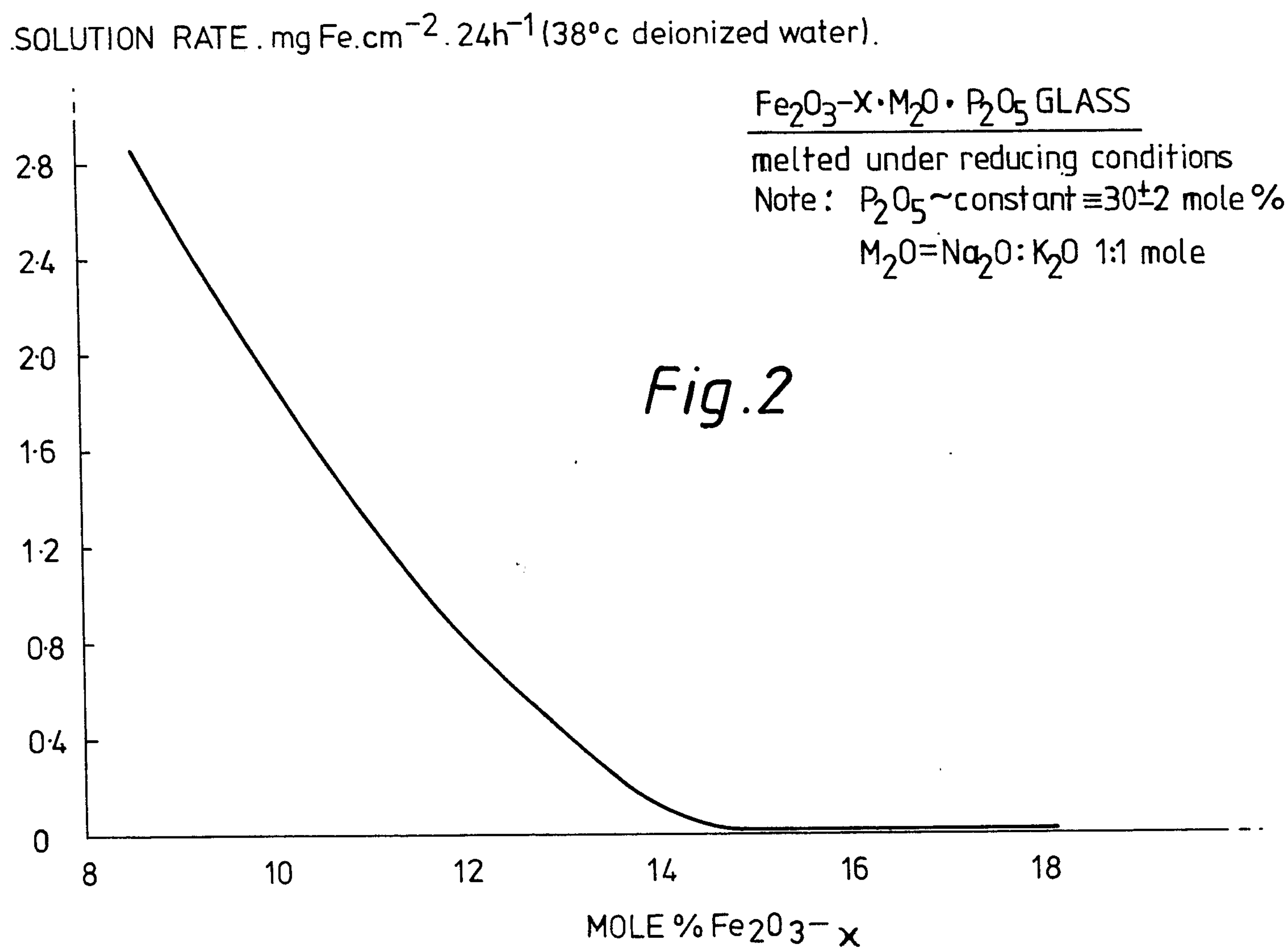
SOLUTION RATE . mg Fe.cm^{-2} . 24h^{-1} (38°c deionized water).
Fe_2O_3–X·M_2O·P_2O_5 GLASS
melted under reducing conditions
Note: P_2O_5 ~ constant ≡ 30±2 mole %
M_2O = Na_2O : K_2O 1:1 mole
2·8
2·4
2·0
1·6
1·2
0·8
0·4
0
8
10
12
14
16
18
MOLE % Fe_2O_{3-x}

Fig.2

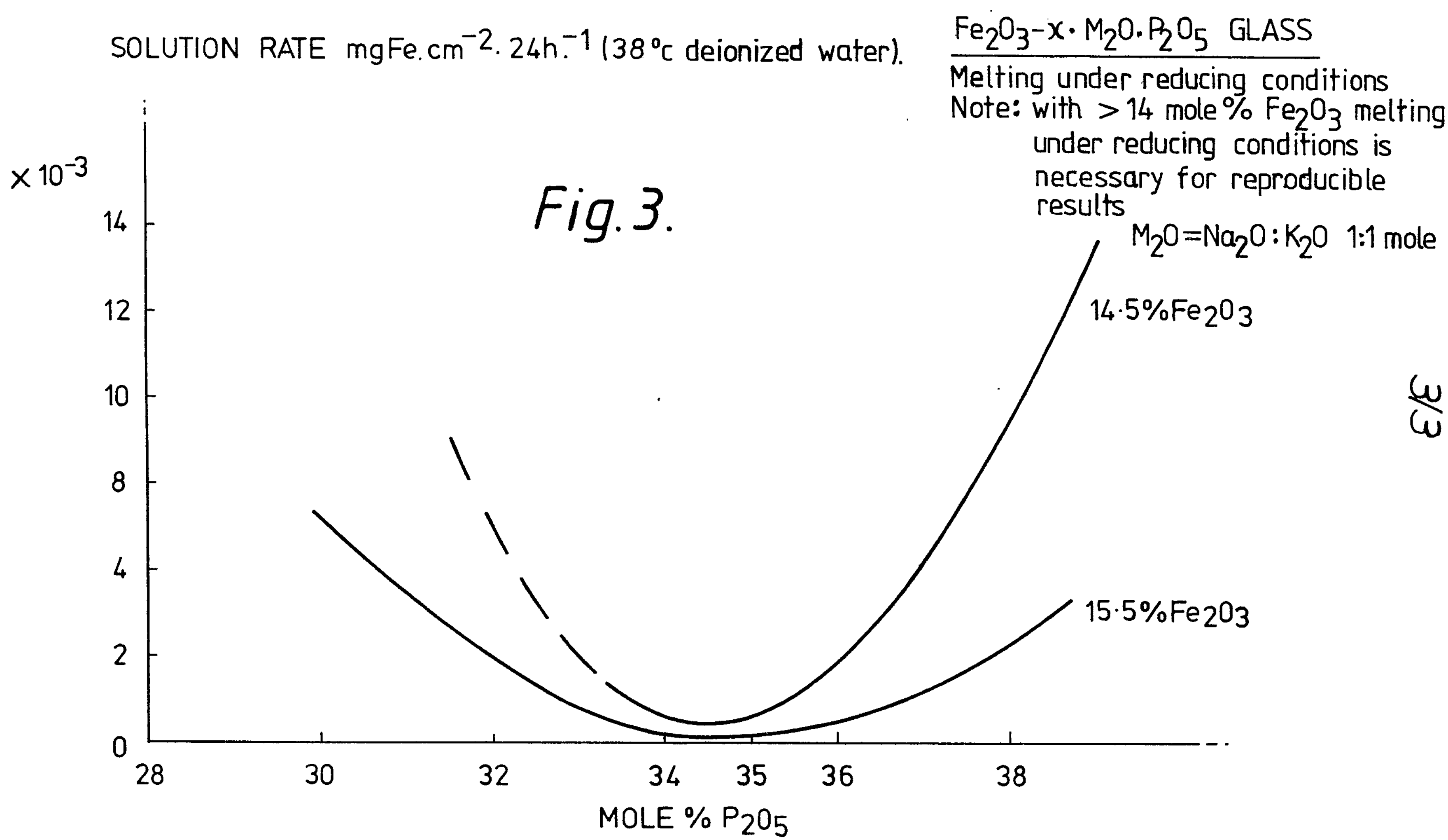
SOLUTION RATE mgFe.cm^{-2}. 24h.$^{-1}$ (38°c deionized water).
Fe_2O_3–x·M_2O·P_2O_5 GLASS
Melting under reducing conditions
Note: with > 14 mole % Fe_2O_3 melting under reducing conditions is necessary for reproducible results
M_2O=Na_2O:K_2O 1:1 mole
× 10^{-3}
14
12
10
8
4
2
0
28
30
32
34
35
36
38
MOLE % P_2O_5
14·5%Fe_2O_3
15·5%Fe_2O_3

Fig. 3.

SPECIFICATION
Glass Compositions

This invention relates to a solid compositions which dissolve in water or other aqueous medium at a steady, predetermined rate, releasing iron ions to said medium. One of the problems involved in animal husbandry is the provision of a sufficient supply of iron to young animals. In particular the rapid rearing of piglets to a sufficient body weight for slaughtering, requires the provision of iron during the first few weeks of life over and above that which can be given by diet alone. Attempts have been made to overcome this problem by the use of iron-containing injections. Such a method does not match the rate at which iron is made available to the piglet to its requirements but it often produces local discolouring of the meat; a condition commonly known as hamstaining. Whilst such discoloured meat is still fit for human consumption, it is unattractive in appearance and cannot therefore be used in high quality meat products.

Another problem in human medicine is the problem of the supply of iron to patients suffering from some forms of anaemia. Oral preparations have various disadvantages including unpalatability, side effects, and problems of utilisation of the iron by the patients.

Yet another problem is associated with the supply in agriculture of iron to the soil in a form in which it can be used by plants.

The supply of soluble iron by known methods from conventional iron salts suffers from several further disadvantages. Thus, there are only a limited number of stoichiometric compounds from which such a material can be selected. These compounds may be so readily soluble (e.g. ferrous sulphate, ferric ammonium sulphate) that the whole 'dose' of iron is immediately released into solution, or they may be too insoluble (e.g. ferric oxide) so that insufficient iron is made available. A further problem is that in a neutral or nearly neutral pH aqueous phase, such as animal body fluids, the iron when released as iron ions Fe^{3+} (or Fe^{2+} which is rapidly oxidized to Fe^{3+}) is rapidly precipitated as insoluble ferric hydroxide or hydrocarbonate and so is rendered unavailable for processes requiring soluble iron. Finally, each given compound has a unique solution rate which cannot be adjusted to suit particular applications.

According to the invention there is provided an iron containing glass composition comprising P_2O_5 as the main glass-forming oxide and up to 20 mole % of one or more iron oxides calculated as ferric oxide (Fe_2O_3) and one or more further glass modifying oxides including at least one alkali metal oxide.

The glass compositions contain P_2O_5 as the principal glass-forming oxide together with one or more iron oxides with up to 20% (expressed as mole % Fe_2O_3) the latter acting in part as a glass modifying oxide. The solution rate of the glass is controlled to give the required value by selecting the correct ratio of the constituent oxides. In addition to iron oxide and P_2O_5 the glass contains one or more alkali metal oxides and may contain alkaline earth metal oxides, fluorides, Al_2O_3, B_2O_3, SiO_2 and others which will be obvious to those skilled in the glass making art, added in order to inhibit crystallization, modify the viscosity, or prevent phase separation. It has also been found possible to include S in the form of the SO_4'' ion in the glass by the addition of some of the metal constituents as sulphate rather than oxides and such glasses can be used to supply S as well as Fe as soil fertility improvers.

The iron can be present in the glass as both Fe II and Fe III and the relative proportion of these two states can be adjusted by controlling the atmosphere during melting. For example, if the glass is melted under oxidising conditions (an electric furnace, in air) the iron is mainly present in the ferric state, if it is melted under reducing conditions (in the presence of excess H2 or hydrocarbon in the flame furnace) a large proportion of the iron is present as Fe II. Moreover, it has been found that when the glass dissolved in an aqueous medium, the iron goes into solution in a form in which the iron ions are protected from precipitation by being present in a complexed state, as pyrophosphate or polyphosphate complexes.

This is particularly important when the Fe has to remain available in solution long enough for it to be delivered to the site at which it is to be utilized, for example to diffuse or be transported from the site of implantation in animals or from the particle source to the plant roots in agricultural applications.

An example of the range of glass compositions is provided by the phase diagram of Fig. 1 in which the region of glass-formation in the (0.5 K_2O:0.5Na_2O)—Fe_2O_3—P_2O_5 system is hatched.

In one application, iron may be supplied in the form of a glass bullet which is sub-cutaneously implanted in an animal.

The following Example illustrates the invention:

A glass was prepared by melting a batch of the composition.

Fe_2O_3	1.44g
$NH_4H_2PO_4$	4.00g
Na_2CO_3	1.35g
K_2CO_3	1.76g

in a fireclay crucible in a O_2/H_2 furnace with the flame having a large excess of H_2 at a temperature of 1000°C for 10 min. The molten glass was poured into 3 mm diameter 1cm long, cylindrical holes in a pyrophylite mould and the resultant 'bullets' pressed out of the mould when cold. The resultant glass had an Fe II/Fe III~0.97. This composition dissolved in deionized water at 30°C at the rate of 25mg (Fe) $.cm^{-2}$ $.day^{-1}$.

A second example is an iron glass suitable for incorporation in a non-aqueous medium for use as an injection as a suspension of fine particles in a medium, for example peanut oil.

The batch weight was: Fe_2O_3(87.1%Fe_2O_3) 13.2g:$NH_4H_2PO_4$ 43.43g: Na_2CO_3 13.27g : K_2CO_3 17.1g : loss on melting 31.91g.

It was melted in a Morgan fireclay crucible in an oxy-hydrogen furnace with excess H_2 at 1000°C for 15 min, cast onto steel plate, and ground to a powder.

By analysis, the composition of the glass was

Fe_2O_3	8.52 mole %
(2FeO)	6.08 mole %
P_2O_5	34.8 mole %
Na_2O	25.5 mole %
K_2O	25.1 mole %

The solution rate was 0.15 mg Fe/day/g glass, equivalent to 10 mg Fe.day:g glass for 10μm diameter glass particle.

It will be clear that the surface area per g of glass will be proportionally higher as the particle size (diameter of the powder is reduced and it is therefore necessary to formulate a glass with a solution rate R (mg.cm^{-2}.d^{-1}) much smaller than when the first method of dosing with an implanted monolithic rod is used. For example, the surface area per g of a powder of grain size 500—700μm is approximately 10 times the surface area of 1g of a 4mm diameter rod.

These glasses may also be formulated for oral administration. In this case there can be an advantage in covering the iron containing glass with a skin of another soluble glass not containing iron. This skin is designed so that it remains substantially intact until the dose has passed through the stomach so that effectively little or no iron is released until post-stomach parts of the alimentary canal is reached. Alternatively the skin may contain iron but be formulated so that the release of iron is slow compared with the release occurring when the core is exposed.

In the case of ruminants oral administration may be in the form of a bolus for retention in the reliculum. Generally it is necessary to load the glass with denser material in order to increase the mean density of the bolus to a value at which it is less likely to become dislodged from the reticulum.

For oral administration the glass does not need to be in the form of individual pellets, but may be in the form of powder, for instance having a particle size of about 10 microns, either made up as a tablet or dispersed in a pharmaceutically inert non-aqueous medium. This form is particularly suited for administration to young piglets for which a suitable dose would typically be about 1 gram per day of the formulation of example 2.

In powder form the glasses are also suitable for application to soil to remedy iron deficiency.

A further use for the glasses is as a material over which drinking water is caused to flow whereby iron in the form of a stable solution is released at a controlled rate for drinking water for livestock and fowl.

It has been found that the solution rate of the glasses which are subject of this invention are dependent primarily upon two factors: the total molar percentage of alkali metal oxides, and secondly, the mole % of iron expressed as Fe_2O_3, the solution rate decreasing very rapidly as the percentage of iron increases. Fig. 2 and 3 illustrate this behaviour. It will be clear that the solution rate R decreases as the amount of iron is increased, for any ratio of P_2O_5/M_2O, reaching very low values as Fe_2O_3 15.5 mole% if the P_2O_5 is greater than 34 mole %. The effect of the M_2O content is more complex. For all Fe_2O_3 contents, a decrease in M_2O decreases the value of R until M_2O=51 mole % and a further decrease in M_2O leads to an increase in R if Fe_2O_3 is less than 15 mole %. It will now be obvious to those skilled in the art how to formulate a glass composition according to the teaching of this patent to have a solution rate appropriate for a particular application.

Claims

1. An iron containing glass composition comprising P_2O_5 as the main glass-forming oxide and up to 20 mole % of one or more iron oxides calculated as ferric oxide (Fe_2O_3) and one or more further glass modifying oxides including an alkali metal oxide.

2. A glass composition as claimed in claim 1 in which there is at least 24 mole % P_2O_5.

3. A glass composition as claimed in claim 1 formulated according to the teaching of this patent to give a predetermined rate of release of Fe to an aqueous solution.

4. A charge of glass as claimed in any preceding claim coated with a skin of a soluble glass that will not release iron as fast as the core.

5. A charge of glass as claimed in claim 4 formulated as a therapeutic oral dose for human or animal administration wherein the thickness and composition of the skin is such that the dose passes through the stomach with the skin substantially intact and iron is not released in significant quantities until the dose reaches the post-stomach regions of the alimentary canal.

6. A glass as claimed in any preceding claim which glass is in the form of a fine powder dispersed in a nonaqueous medium for injection.

7. A glass as claimed in any claim of claims 1 to 5 wherein the glass is in the form of a loaded bolus for retention in the reticulum of a ruminant.

8. A glass composition as claimed in any claim or claims 1 to 5 for the continuous provision of a dosed quantity of iron as a stable solution for supply in drinking water for livestock or fowl.

9. A glass composition as claimed in any claim of claims 1 to 5 in the form of powder for application to soil to ameliorate iron deficiency.

10. A glass composition as claimed in claim 6 wherein the glass has a composition substantially as described in the foregoing Example 2.

New Claims or Amendments to Claims filed on 9/6/1981
Superseded Claims 1—10
New of Amended Claims:—

1. A water soluble glass composition adapted to release ferrous and/or ferric iron into aqueous solution, the composition comprising glass forming proportions of phosphorus pentoxide as the principle glass forming oxide, one or more iron oxides, and one or more further glass modifying oxides including an alkali metal oxide, and wherein the composition of the glass is such that, when contacted with water, dissolution of the glass is effected releasing ferrous and/or ferric ions into solution at a predetermined rate.

2. A glass as claimed in claim 1, wherein the proportion of phosphorus pentoxide is at least 24 mole %.

3. A glass as claimed in claim 1 or 2, and which includes one or more alkaline earth metal oxides or fluorides.

4. A glass as claimed in claim 1, 2 or 3, and which further includes sulphur.

5. A glass as claimed in any one of claims 1 to 4, wherein said alkali metal oxide comprises a substantially equimolar mix of radium and potassium oxides.

6. A water soluble glass composition substantially as described herein with reference to the accompanying drawings.

7. A glass composition as claimed in any one of claims 1 to 6, and in the form of a monolithic body for ingestion by or implantation into an animal.

8. A glass body as claimed in claim 7, and coated with an outer skin of a further soluble glass having a relatively low or zero iron content.

9. A glass body as claimed in claim 8 and formulated as a therapeutic oral dose for animal or human administration, wherein the thickness and composition of said outer skin is such that the body, when administered, is passed through the stomach with the skin substantially intact thereby confining release of iron from the glass body to the port stomach regions of the alimentary tract.

10. A glass body as claimed in any one of claims 7 to 9, and in the form of a bolus for lodgement in the reticulum of a reminant animal.

11. A glass composition as claimed in any one of claims 1 to 6, and in the form of a powder.

12. A powdered glass as claimed in claim 11 disposed in a non-aqueous medium for injection into a human or animal.

13. A fertiliser incorporating a glass powder as claimed in claim 11.

14. A method of treating an animal for iron deficiency substantially as hereinbefore described.

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