kGy. (Publisher Wiley-IEEE, 1994, ISBN 0471544523, 9780471544524). US7259192 describes the depolymerization by high energy electron beam irradiation of xanthan gum at a preferred dose of 10 to 150 kGy.

SUMMARY ~~OF THE INVENTION~~

In a first aspect the present ~~invention~~disclosure provides a composition comprising

(i) a mixed metal compound containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc, calcium, lanthanum and cerium,

(ii) xanthan gum

(iii) at least one of (a) polyvinyl pyrrolidone
(b) locust bean gum
(c) methyl cellulose

wherein the composition has been irradiated with ionising radiation in an amount of at least 4kGy.

In a second aspect the present disclosure provides the use of a composition as defined above in the manufacture of a medicament for controlling serum phosphate levels.

In a third aspect the present disclosure provides the use of a composition as defined above in the manufacture of a medicament for binding phosphate.

In a fourth aspect, the present disclosure provides the use of a composition as defined above in the manufacture of a medicament for the treatment of hyperphosphataemia.

~~In a second aspect the~~The present ~~invention~~disclosure also provides a composition for use as a medicament, wherein the composition comprises

(i) a mixed metal compound containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc, calcium, lanthanum and cerium,

(ii) xanthan gum

(iii) at least one of (a) polyvinyl pyrrolidone
(b) locust bean gum
(c) methyl cellulose

wherein the composition has been irradiated with ionising radiation in an amount of at least 4kGy.

~~In a third aspect the~~The present ~~invention~~disclosure also provides a composition for binding phosphate, wherein the composition comprises

(i) a mixed metal compound containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc,

calcium, lanthanum and cerium,

(ii) xanthan gum

(iii) at least one of (a) polyvinyl pyrrolidone

(b) locust bean gum

(c) methyl cellulose

wherein the composition has been irradiated with ionising radiation in an amount of at least 4kGy.

~~In a fourth aspect the~~The present ~~invention~~disclosure also provides a composition for use in the treatment of hyperphosphataemia, wherein the composition comprises

(i) a mixed metal compound containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc, calcium, lanthanum and cerium,

(ii) xanthan gum

(iii) at least one of (a) polyvinyl pyrrolidone

(b) locust bean gum

(c) methyl cellulose

wherein the composition has been irradiated with ionising radiation in an amount of at least 4kGy.

The present ~~invention~~disclosure provides a carrier system for delivering insoluble mixed metal compounds, namely those containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc, calcium, lanthanum and cerium. The present system avoids the disadvantages of the prior art systems either with regard to the problems associated with ingestion of the carrier or the detrimental effect that the carrier may have on the insoluble compound. Critically, many prior art carriers are significantly detrimental to the phosphate binding capacity of mixed metal compounds. Phosphate binding capacity is a key property of such compounds.

Many of the prior art excipients used to modify the rheology of the carrier fluid are anionic in nature and may therefore interact with the mixed metal compound, which binds phosphate by anion exchange. Consequently, the subsequent anion binding capacity of the mixed metal compound (in this case for phosphate) is hindered.

The present ~~invention~~ disclosure provides a system in which the use of oil-based carriers is avoided. Such carriers can have the drawback of a high relative calorific value. Such high calorific values are generally considered to be undesirable and are particularly unsuitable for subjects on a calorie restricted diet and/or who may consume the composition for a prolonged period of time.

The present ~~invention~~ disclosure is further advantageous in that it allows for high loads of mixed metal compound to be delivered. This is advantageous in that the volume of product required to deliver a determined amount of mixed metal compound is kept within acceptable amounts. The use of such high loads is particularly advantageous for subjects who desire or are required to control fluid intake. Such a group is patients on dialysis who must typically restrict the volume of liquid which they consume. Any aqueous liquid dose formulation will contribute to the volume of liquid which the patient consumes, hence the volume of liquid must be kept to a minimum. As the mixed metal compound may be used for binding phosphate in a subject or for treating hyperphosphataemia, the composition is to be administered to compounds suffering from renal disease who may in turn be undergoing dialysis. Thus the need to deliver high loads is particularly applicable when delivering mixed metal compounds.

The present ~~invention~~ disclosure is further advantageous in that it provides for a preserved liquid composition wherein the addition of preservative components is not required. Contrary to the teaching of the prior art, we have shown that by selection of a specific combination of suspension materials and selection of a specific radiation dosage, a stable and preserved composition may be provided. Prior art teachings in the field of effluent handling (Chromate immobilisation) showed that irradiation at 1000-6000 kGy is detrimental to mixed metal compounds and enhances the formation of spinell. In particular, we have shown that preservative components are not required. Mixed metal compounds in an un-buffered aqueous system at the concentration range of interest (ca. 10% w/v) provide a relatively high pH (ca. 9.2 to 9.4). The high pH excludes the use of all known, commercially available preservatives at concentrations effective for microbial control and at levels that are safe for use in a composition in a human population. For chemical preservation, the pH of the formulation must be limited to about 8.2 or below in order to permit the use of preservatives at concentrations that are safe in the human population. The preservative may have some efficacy above pH 8.2 however there is little margin for pH increase of the formulation, for example, on storage. A significant

reduction in pH i.e. below approximately pH 8.0 cannot be made without releasing magnesium from the mixed metal compound structure. This has the effect of changing the mixed metal compound structure and may also impair properties such as phosphate binding performance of the mixed metal compound.

Hyperphosphataemia

As discussed herein ~~in one aspect~~ the present ~~invention~~ disclosure provides a composition for use in the treatment of hyperphosphataemia, wherein the composition comprises

(i) a mixed metal compound containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc, calcium, lanthanum and cerium,

(ii) xanthan gum

(iii) at least one of (a) polyvinyl pyrrolidone
(b) locust bean gum
(c) methyl cellulose

wherein the composition has been irradiated with ionising radiation in an amount of at least 4kGy.

Hyperphosphataemia is an electrolyte disturbance in which there is an abnormally elevated level of phosphate in blood. Hyperphosphataemia is frequently seen in dialysis patients, as standard dialysis regimes are unable to remove the ingested phosphate load even with a low phosphate diet, and is associated with an increased risk of death and the development of vascular calcification. The presence of hyperphosphataemia leads to hypocalcaemia, secondary hyperparathyroidism, reduced 1,25 Vit D3 and progressive metabolic bone disease. Elevated level of phosphate in blood is ultimately responsible for the increase in vascular calcification, but recent studies have also suggested that the process may additionally be influenced by 1,25 Vit D3 and an elevated calcium-phosphate product. Patients who have chronically uncontrolled hyperphosphataemia develop progressively extensive soft tissue calcifications due to the deposit of Calcium/phosphate product into skin, joints, tendons, ligaments. Eye deposits of calcium/phosphate product have also been described.

Control of serum phosphate levels using oral phosphate binders has, therefore, become a key therapeutic target in the management of dialysis patients. These binders, taken

with food, render the contained phosphate insoluble and, therefore, non-absorbable.

For ease of reference, these and further aspects of the present ~~invention~~ disclosure are now discussed under appropriate section headings. However, the teachings under each section are not necessarily limited to each particular section.

Preferred Aspects

Component (i) - Mixed Metal Compound

The mixed metal compound utilised in the present invention may be any mixed metal compound containing at least one trivalent metal selected from iron (III) and aluminium and at least one divalent metal selected from of magnesium, iron, zinc, calcium, lanthanum and cerium. In one preferred aspect, the mixed metal compound contains at least iron (III) and at least magnesium.

Preferably, the compound is of formula I

$M^{II}_{1-x}M^{III}_{x}(OH)_2A^{n-}_{y}.mH_2O$ (I)

wherein M^{II} is one or more bivalent metals and is at least Mg^{2+};

M^{III} is one or more trivalent metals and is at least Fe^{3+};

A^{n-} is one or more n-valent anions and is at least CO_3^{2-};

$(\Sigma yn)/x$ is from 0.5 to 1.5

$0 < x \leq 0.4$,

$0 < y \leq 1$ and

$0 < m \leq 10$.

$(\Sigma yn)/x$ may preferably be from 0.6 to 1.4, such as 0.7 to 1.3, such as 0.8 to 1.2, such as 0.9 to 1.1, such as approximately 1, such as 1.0.

In one preferred aspect the compound has an aluminium content of less than 10,000 ppm, more preferably less than 7,000 ppm, more preferably less than 5,000 ppm, more preferably less than 3,000 ppm, more preferably less than 1000 ppm, more preferably less than 700 ppm, more preferably less than 500 ppm, more preferably less than 300 ppm, more preferably less than 200 ppm, most preferred 100 ppm, more preferably less than 50 ppm, most preferably 30 ppm.