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पेटेंट प्रमाणपत्र
PATENT CERTIFICATE

(Rule 74 of The Patents Rules)

पेटेंट सं. / Patent No.	:	412127
आवेदन सं. / Application No.	:	202231025214
फाइल करने की तारीख / Date of Filing	:	29/04/2022
पेटेंटी / Patentee	:	WEST BENGAL CHEMICAL INDUSTRIES LIMITED

प्रमाणित किया जाता है कि पेटेंटी को, उपरोक्त आवेदन में यथाप्रकटित PHARMACEUTICAL ACCEPTABLE IRON (III) COORDINATION COMPLEX HAVING HIGH PHOSPHATE BINDING CAPACITY AND PREPARATION THEREOF नामक आविष्कार के लिए, पेटेंट अधिनियम, 1970 के उपबंधों के अनुसार आज तारीख अप्रैल 2022 के उन्नतीसवें दिन से बीस वर्ष की अवधि के लिए पेटेंट अनुदत्त किया गया है।

It is hereby certified that a patent has been granted to the patentee for an invention entitled PHARMACEUTICAL ACCEPTABLE IRON (III) COORDINATION COMPLEX HAVING HIGH PHOSPHATE BINDING CAPACITY AND PREPARATION THEREOF as disclosed in the above mentioned application for the term of 20 years from the 29th day of April 2022 in accordance with the provisions of the Patents Act,1970.

एकस्व कार्यालय THE PATENT OFFICE GOVT.OF INDIA भारत सरकार

अनुदान की तारीख :
Date of Grant : 22/11/2022

पेटेंट नियंत्रक
Controller of Patent

टिप्पणी - इस पेटेंट के नवीकरण के लिए फीस, यदि इसे बनाए रखा जाना है, अप्रैल 2024 के उन्नतीसवें दिन को और उसके पश्चात प्रत्येक वर्ष मे उसी दिन देय होगी।

Note. - The fees for renewal of this patent, if it is to be maintained will fall / has fallen due on 29th day of April 2024 and on the same day in every year thereafter.

412127

Indian Patent

Patent Number: 412127
Date of Patent: 22 November, 2022

Pharmaceutical Acceptable Iron (Iii) Coordination Complex Having High Phosphate Binding Capacity and Preparation Thereof

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Application: **202231025214**

Filed: **29 April, 2022**

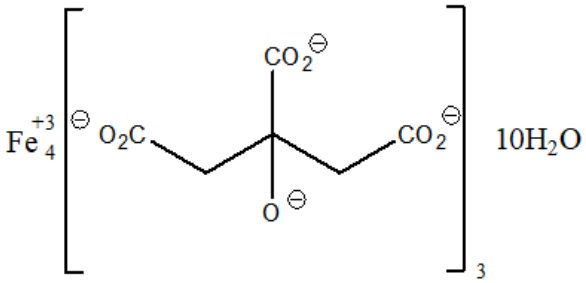
ABSTRACT:

The present invention relates to a pharmaceutical acceptable iron (III) coordination complex having high phosphate binding capacity prepared through a cost-effective and an organic solvent free route. The present invention provides a pharmaceutical composition of iron (III) coordination complex which not only releases the desired amount of elemental iron in the desired pH level which is absorbed and assimilated into iron stores but also binds the ferric iron with the higher dietary phosphate which is finally excreted through stool being insolvable. The pharmaceutical composition is industrially acceptable, consumable with less or no side-effects, more effective.

13 Claims, No Drawings

Claims

1. A pharmaceutically acceptable Iron (III) coordination complex prepared through an organic solvent free route and represented by formula I;



characterized in that,
the complex having:
   a) purity of 90-95% pure
   b) Phosphate binding capacity in the range of70.26-90 mg-P/g of elemental Iron at pH 7.5 ;
   c) moisture content in the range of 19.05 to 28 %.
   d) particle size distribution in the range of Dv (0.1)- 125µm, Dv (0.5)-726µm and Dv (0.9)- 1940µm.

2. The coordination complex as claimed in claim 1, wherein the purity of Iron (III) coordination complex and water adduct in solution is 70-80%.
3. The coordination complex as claimed in claim 1, wherein the complex is present in the amorphous form.
4. The pharmaceutically acceptable Iron (III) coordination complex as claimed in claim 1, wherein the complex comprises of ferric tricitratedecahydrate.
5. A process for preparing the pharmaceutically acceptable iron (III) coordination complex through an organic free solvent route comprising the steps of:
   a) reacting an anhydrous ferric halide with a metal salt of acid in water with stirring at a temperature ranging between 55-85°C for a period of 24-36 hour to obtain a brown precipitate;
   b) filtering the brown precipitate obtained in step (a) in a nitrogen gas atmosphere at an optimum pressure range to obtain wet cake material;

c) drying the wet cake material obtained in step (b) at a temperature in the range of 55 to 85oC for a period of 1 to 8 hours followed by sequential increasing of temperature at 5 degree per 30 to 35 minutes to obtain the pharmaceutically acceptable Iron (III) coordination complex.

6. The process as claimed in claim 5, wherein the ferric halide used is in the range of 50 to 65%.
7. The process as claimed in claim 6, wherein the halide is a chloride.
8. The process as claimed in claim 5, wherein the metal salt is used in the range of 50 to 65%.
9. The process as claimed in claim 5, wherein the metal salt of acid is citric acid.
10. The process as claimed in claim 9, wherein the metal in metal salt is a sodium-based salt.
11. The process as claimed in claim 5, wherein the stirring in step (a) is maintained in the range of 25-40 rpm.
12. The process as claimed in claim 5, wherein the filtering is performed in step (a) in a nitrogen gas atmosphere at pressure in the range of 600-700 mmHg.
13. The process as claimed in claim 5, wherein the 5 drying is done in drying chamber at a temperature ranging between 50 to 85^{o}C for a period of 60-480 minutes.

TITLE OF THE INVENTION

PHARMACEUTICAL ACCEPTABLE IRON (III) COORDINATION COMPLEX HAVING HIGH PHOSPHATE BINDING CAPACITY AND PREPARATION THEREOF

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PREAMBLE TO THE DESCRIPTION

The following specification particularly describes the invention and the manner in which it is to be performed.

FIELD OF THE INVENTION

The present invention relates to a pharmaceutical acceptable iron (III) coordination complex and preparation thereof. Particularly, the present invention relates to 90-95% pure iron (III) coordination complex prepared without using any organic solvent. More particularly, the present invention relates to pharmaceutical composition of consumable tetra ferric tricitratedecahydrate (TFTD) having high serum phosphate binding capacity which is more effective and shows less side-effects having direct relation with the moisture content.

BACKGROUND OF THE INVENTION

Ferric iron containing compounds are useful in the treatment of a number of disorders, including, but not limited to, hyperphosphatemia, metabolic acidosis and anemia. Previous studies and inventions have listed the ferric compounds having the capacity to bind phosphate and form non-absorbable complexes with phosphate having relation with the active surface area; such co-ordination complexes of ferric citrate and ferric compounds are potentially useful for the treatment of hyperphosphatemia in renal failure patients.

Phosphate plays a very critical role in cellular processes. It is an important component of the skeleton and an integral component of the nucleic acids that make up DNA and RNA, Phosphate functions as a buffer in bone, serum, and urine. Addition or deletion of phosphate groups from the cellular enzymes and proteins is a common mechanism for the regulation of their activity. Due to the large impact of phosphate in cellular processes, the homeostasis of phosphate is a highly regulated process.

Patients with Chronic Kidney Disease typically demonstrate elevated levels of serum phosphate as kidney function is lost and the body loses its ability to excrete phosphate through the urine. This means that chronic kidney disease patient typically experiences hyperphosphatemia, which is an electrolyte disturbance in which there is an abnormally elevated level of phosphate in the blood.

Increased amounts of phosphate in the blood can be removed by administering such complexes. In this, ferric iron binds phosphate, and the ferric phosphate compounds precipitate in the gastrointestinal tract, resulting in effective removal of dietary phosphate from the body. It is also observed that the absorbed citrate from ferric citrate is converted to bicarbonate which corrects metabolic acidosis, a condition where acid get build up in the body due to kidney disease or kidney failure.

Several studies on the phosphate binding capacity of iron (III) complex have been reported following in applications and Patents:

1. CN108863771 discloses a preparation method of ferric citrate crystals. The invention mainly describes on providing the solubility of product in water and to have low content of impurities.
2. WO2020/100911 discloses a process for the synthesis of ferric citrate hydrate. The invention mainly describes on the BET specific surface area which is directly related with the dissolution rate and solubility.
3. WO2020/100912 discloses a production method of obtaining ferric citrate hydrate which mainly describes high BET specific surface area.
4. IN202021017797 discloses a method for obtaining ferric citrate having specific surface area greater than 16 sq. m/g.
5. US7767851B2 discloses ferric organic compounds, such as ferric citrate, methods of making the ferric organic compounds, and uses of the ferric organic compounds in the treatment of various disorders.

The processes disclosed in the prior art references focus on ferric organic compounds with the BET specific surface area, however the effective binding capacity has not yet been achieved. The present invention focuses on freezing the moisture content to

a definite quantity so much so that it has the highest phosphate binding capacity. The present invention opens a new era of the co- relation of moisture content with phosphate binding capacity which has not been disclosed in the references.

Unlike the previous prior arts, the pharmaceutical acceptable iron (III) coordination complex of the present invention has distinct phosphate binding capacity beneficial for patients with less dose which implies that BET surface area is not of much importance in relation to phosphate binding.

OBJECTIVE OF THE INVENTION

The primary objective of the present invention is to provide a pharmaceutical acceptable iron (III) coordination complex in the pure form prepared through an organic solvent-free route.

1. Yet another objective of the present invention is to provide an iron (III)
2. coordination complex having high serum phosphate binding capacity.
3. Yet another objective of the present invention is to maintain the moisture content in a selective range in order to provide definite phosphate binding.
4. Yet another objective of the present invention is to provide a pharmaceutical composition having less or no side effects and more effective.
5. Yet another objective of the present invention is to provide pharmaceutical composition which controls release of elemental iron in body.
6. Yet another objective of the present invention is to provide an iron (III) coordination complex having unique particle size distribution which helps in formulation of tablets.
7. Yet another objective of the present invention is to provide a cost-effective organic solvent free synthesis to derive tetra ferric tricitratedecahydrate.
8. Yet another objective of the present invention is to minimize the dose of tetra ferric tricitratedecahydrate.

Other objectives and advantages of the present invention will become apparent from the following description taken in connection with the accompanying drawings, wherein, by way of illustration and example, the aspects of the present invention are disclosed.

SUMMARY OF THE INVENTION

The present invention relates to an iron containing phosphate binder that is used to control release of elemental iron in body.The pharmaceutical acceptable iron (III) coordination complex prepared through an organic solvent free route. The process for preparing the iron (III) coordination complex comprises the reaction of ferric halide with the metal salt of low molecular weight organic acid in water at a temperature ranging between 55-85oC under stirring having speed of 25 rpm to 40 rpm for a period of ranging 24-36 hours to obtain a brown precipitate, which is then isolated through filtering under nitrogen environment to obtain a wet cake material. The wet cake material is then dried at normal condition at a temperature 55 to 85oC for first one hour and sequentially increasing the temperature in a drying chamber by 5 degree after every 30 minutes interval till the moisture content is more than 20.38 % and less than 26.38% to obtain the pharmaceutical acceptable iron (III) coordination complex having the higher serum phosphate binding capacity which is directly proportional to the moisture content until it reaches its saturation point. Preferably, the present invention provides an iron (III) coordination complex of tetra ferric tricitratedecahydrate.

The present invention also provides a pharmaceutical composition of acceptable iron (III) coordination complex which is industrially acceptable, consumable with less or no side-effects, more effective, the composition having distinct phosphate binding capacity is useful to control phosphorus level in adults.

The present invention provides an iron-based phosphate binder having a small fraction ranging from 0.5%-0.1% of iron is absorbed and assimilated into the iron stores.

The iron (III) coordination complex have unique particle size distribution helps in the formulation of tablets.

BRIEF DESCRIPTION OF FIGURES

a) **Figure 1** illustrates Differential scanning calorimetry (DSC) of tetra ferric tricitratedecahydrate
b) **Figures 2** illustrates Thermogravimetric Analysis (TGA) of tetra ferric tricitratedecahydrate.
c) **Figures 3** illustrates X-ray diffraction of tetra ferric tricitratedecahydrate.
d) **Figure 4** illustrates retention time of citrate.

e) **Figure 5** illustrates BET Surface Area analysis of tetra ferric tricitratedecahydrate.
f) **Figure 6** illustrates the proton NMR of tetra ferric tricitrate decahydrate.

DETAILED DESCRIPTION OF THE INVENTION

The following embodiments set forth herein below are merely exemplary out of the wide variety and arrangement of instructions which can be employed in the present invention within the scope of the present claims. The present invention may be exemplified in other specific forms without departing from the spirit or essential characteristics thereof.

Accordingly, various changes and modification of the embodiments described herein can be made without departing form the scope of the invention.

Thus, accordingly those ordinarily skilled in art can recognise such alternatives, which shall not affect the novelty of the process.

Thus, unless expressly stated otherwise, they all are within the scope of the present invention.

In addition, descriptions of well-known functions and constructions are omitted for clarity and conciseness.

The terms and words used in the following description and claims are not limited to the bibliographical meanings but are merely used to enable a clear and consistent understanding of the invention. Accordingly, it should be apparent to those skilled in the art that the following description of exemplary embodiments of the present invention are provided for illustration purpose only and not for the purpose of limiting the invention.

It is to be understood that the singular forms “a”, “an” and “the” include plural referents unless the context clearly dictates otherwise.

It should be emphasized that the term “comprises/comprising” when used in this specification is taken to specify the presence of stated features, integers, steps or components but does not preclude the presence or addition of one or more other features, integers, steps, components or groups thereof.

The present invention relates to a pharmaceutical acceptable iron (III) coordination complex in the pure form prepared through an organic solvent free and cost-effective route. The iron (III) coordination complex has definite phosphate binding capacity which is directly proportional to the moisture content until it reaches its saturation point.

In an embodiment, the present invention provides a process for synthesizing a pure pharmaceutically acceptable Iron (III) coordination complex comprising the steps of:

a) reacting 50 to 65% of anhydrous ferric halide (halide=chloride, bromide or fluoride) with 55 to 65% of a metal salt of acid in water with stirring range of 25 to 40 rpm at a preferable temperature ranging between 55-85oC for period of 24-36 hour to obtain a brown precipitate;
b) obtaining the wet cake material through filtration of the brown precipitate obtained in step (a) under nitrogen atmosphere having pressure in the range of 600 -700 mmHg.
c) drying the wet cake material obtained in step (b) at a room temperature for 1 to 8 hours in the drying chamber at temperature ranging between 50-85oC for a period of 60-480 minutes followed by sequential increasing of temperature per 30 to 35 minutes to obtain the pure pharmaceutically acceptable Iron (III) coordination complex.

The process is performed through an organic solvent free route which provides the complex having highest phosphate binding capacity in the range of 60 to 90 mg-P/gm. The preferable temperature to obtain the iron (III) coordination complex is 81°C for 60-120 minutes. The amount of anhydrous ferric halide is in the range of 1.33 to 1.5 mole.

The metal salt of acid is selected from, but not limited to, acetic acid and citric acid. The amount of metal salt of acid is in the range of 3 to 4 moles. The metal in metal salt of acid is selected from, but not limited to, Sodium, Lithium and Potassium.

Drying of the wet cake may be performed in drying apparatus selected from, but not limited to, air tray dryer (ATD), Vacuum Tray Dryer (VTD) and Spray dryer. The wet cake material is initially dried under normal conditions at an optimized temperature and then temperature is gradually raised to achieve a predetermined moisture content. The optimized temperature ranges between 25 to 85^{o}C.

For instance, in the first hour of the reaction the drying is performed at normal condition at an optimized temperature and sequentially increasing the temperature by 5^{o}C at a time intervals of 30 to 35 minutes till the moisture content of the wet cake

material reaches in between 20.38% to 26.38 % which affords pure pharmaceutically acceptable iron (III) coordination complex having highest phosphate binding capacity. Total time period takes for drying is ranging between 1.5 to 8 hours to obtain the pure form of iron (III) coordination complex.

The whole process for preparing the pure pharmaceutically acceptable Iron (III) coordination is crucial in terms of temperature, revolution per minute (RPM) and drying pattern. The temperature and time of the reaction is regulated in a way to obtain the pure form of iron (III) coordination complex for the purpose of achieving the pharmaceutical composition.

Initially the RPM of the reaction should be 10 to 20 to initiate the reaction of anhydrous ferric halide and metal salt of acid.

The second critical part of reaction is heating and the optimizing the temperature of drying the wet cake material. The temperature during drying should be maintained in the range of 50oC-85oC, preferably 81oC. Heating the wet cake material at more than 85°C leads to the formation of the polymer which is the most critical aspect in drying pattern.

In the present invention, the phosphate binding capacity of the iron (III) coordination complex depends on its moisture content, whereby both are directly proportional to each other until the binding capacity reaches its

saturation point and does not very further with increase in moisture content. The phosphorus binding capacity does not depend on the Active Surface Area (BET) as seen in the previous arts, however in the present invention with increase in moisture content of the molecule, the molecule exhibits higher phosphate binding capacity which means more the moisture content more is the phosphate binding capacity until it reaches to a saturation point.

Table 1 illustrates the data of different batches prepared on the different conditions.

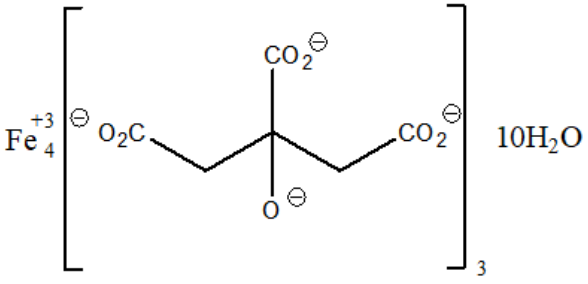
Table 1

Sr. No	Batch no	Drying temperature at 81° C (in hours)	Ferric content (in %)	Moisture content (in %)	Phosphate binding capacity (at pH 7.5) [mg-p/gm]
1	TFTD/009/08/ 21	8	16.53	19.05	70.26
2	TFTD/007/08/ 21	7	17.35	20.38	73.93
3	TFTD/009/08/ 21	6	16.53	21.60	76.00
4	TFTD/012/09/ 21	3	17.66	26.38	89.94
5	TFTD/013/09/ 21	1.5	17.75	28	89.94

From the table 1, it is seen that the obtained wet cake material dried in air tray drier at 81 °C till the moisture content reaches 26.38% as see in batch no 4 which gives the highest phosphate binding capacity of the iron (III) coordination complex. After that the phosphate binding is saturated and does not have any significant change.

Thus, it is concluded that the phosphate binding capacity of iron (III) coordination complex is at its highest peak in between the moisture content 20.38%-26.38% whereby the phosphate binding increases with increase in moisture content. After the moisture content reaches above 26.38 %, the phosphate binding does not have any significant change.

In a preferable embodiment, the present invention provides a pharmaceutical acceptable iron (III) coordination complex of tetra ferric tricitratedecahydrate (Formula 1) having the binding capacity in the range 60.00 to 90.00 mg-p/gm and moisture content in the range of 19.05% to 28%.



Formula 1

In an exemplary embodiment, the present invention provides the physio- chemical properties of Tetra Ferric Tricitratedecahydrate (TFTD) obtained through an organic-free solvent route are elaborated in the Table 2:

Table 2

Physio-Chemical Properties

S.No.	Test parameter	TFTD
1	Appearance	Brown to beige powder
2	Purity of pharmaceutical compound	NLT 90 to 95% w/w (ODB)
3	Assay content of pharmaceutical compound non-related substances in solution state	0.4-0.5%
4	Assay content of pharmaceutical compound in solution state	NMT 20 to 30 %
5	Assay content of ferric iron	16.5-20.0% (as is basis)
6	Limit of ferrous iron	NMT 0.5%
7	Water Content	NMT 27% (by KF)
8	Identification	Positive for iron and citrates
9	BET Active Surface Area	NMT $1m^2/g$
10	IR Spectrum	Complies
11	LC/MS	m/z Ferric Citrate- 279.8 (-ve mode) [M+2H_20-1]
12	XRD	Amorphous
13	Phosphate Binding Capacity	84-90 mg-P/g of Elemental Iron at pH 7.5
14	Particle size distribution	D_v (0.1)- 125µm D_v (0.5)- 726µm D_v (0.9)- 1940µm*

NOTE:
NMT stands for Not More Than
NLT stands for Not Less Than
ODB stands for On Dry Basis
µm* stands for micron
D_v (0.1)- 10% of the particles is 125µm
D_v (0.5)- 50% of the particles is 726µm
D_v (0.9)- 90% of the particles are in the range of 1940µm

The physio chemical properties such as purity and other characteristic properties which supports the other parameters like polymorphism, citrate content and moisture content illustrated in Table 2 establish the purity and justify the phosphate binding capacity of tetraferrictricitrate decahydrate.

The purity of tetraferrictricitrate decahydrate can be ascertained by negative mode LCMS at mass ion at m/z 279.8 which represents (M+2H20-1). While XRD corresponds to amorphous form (Figure 3) and HPLC shows the citrate content in the range of 50-60% by HPLC area normalization. Figure 2 provide the

thermogravimetric (TGA) analysis having three transition temperature of the tetraferrictricitrate decahydrate. In figure 5, BET Surface area represents the active surface area of the molecule. In figure 1, DSC indicates the melting point and proton NMR of tetra ferric tricitrate decahydrate is indicated in figure 6. The efficacy of tetraferrictricitrate decahydrate depends on the rate of interaction or binding of the molecule with the receptor.

In another embodiment, the present invention provides a pharmaceutical composition comprising:

a) 90-95% pure pharmaceutically acceptable Iron (III) coordination complex as first active ingredient in the range of 16.5-20 wt%;
b) at least one excipient in the range of 25 to 30 wt% .

Purity of pharmaceutically acceptable Ferric tricitratedecahyrate is 70-80% as basis when it is with water in solution state.

The excipient is selected predominantly from, but not limited to, Polyvinylpyrrolidone (PVP) K-30, Ethyl Cellulose, Microcrystalline Cellulose Powder (MCCP).

The particle size distribution (PSD) of a component influence important properties of the final product, such as the content uniformity of tablets and the dissolution rate of the drug to the patient. Particle size distribution of tetraferrictricitrate decahydrate is Dv (0.1)- 10% of the particles are 125µm Dv (0.5)- 50% of the particles are 726µm Dv (0.9)- 90% of the particles are 1940µm which is favorable in the formation of tablets. The composition is formulated as tablets, capsules, granules, troche and pills.

The composition is useful for treating the diseases like especially to treat hyperphosphatemia, metabolic acidosis and anemia but not limited to the same.

Since the entire process for preparing the iron (III) complex is organic solvent free not only it is cost-effective but also renders the phosphate binding of the pharmaceutical composition to be better. Thus, the pharmaceutical composition of pure iron (III) complex is industrially acceptable, consumable with less or no side-effects, more effective.

The pharmaceutical composition of iron (III) coordination complex of the present invention has higher phosphate binding capacity, hence less dose is required for patients.

In general, the ferric iron component binds with dietary phosphate in the Gastro Intestinal (GI) tract and precipitates as ferric phosphate. Ferric iron component is insoluble, and is excreted in the stool. Additionally, it has been shown to increase serum iron parameters through systemic absorption, which is managed by body's GI mechanism. As it is an iron-based phosphate binder, a small fraction (0.5% to 1%) of the iron is absorbed and assimilated into iron stores.

The pharmaceutical composition not only releases the desired amount of elemental iron in the desired pH level which is absorbed and assimilated into iron stores but also binds ferric iron with the higher dietary phosphate which is finally excreted through stool being insolvable. The amount of elemental iron released is in the range of 16.5 to 20% at pH 1.9 to 3.

The pharmaceutical composition helps in controlling phosphorous level in adults.

EXAMPLES

The following examples are given by way of illustration of the working of the invention in actual practice and should not be constructed to limit the scope of the present invention in any way.

Example 1

<u>Preparation of pure Tetra Ferric Tricitratedecahydrate</u>:

The reaction is carried out with 1.33 mole of anhydrous ferric chloride with 3 moles of metal citrate in water at most preferable temperature of 81°C under stirring for a desired amount of time to derive the pure tetra ferric tricitratedecahydrate.

<u>Drying Method</u>:

The wet cake material collected can be dried in air try drier at desired temperature until the phosphate binding capacity is that desired, keeping in mind to find a co-relation between the moisture content and phosphate binding capacity.

The sequence of drying the wet cake should be as follows:

a) Drying at room temperature (RT) for 1 h.
b) Sequential increase of temperature by 5oC per 30 min and total 8 h with monitoring of moisture content.

Example 2

Batch No: TFTD/009/08/21

The drying was carried for 8 hours at 81°C temperature in ATD which resulted in the moisture contain to be 19.05% , the Ferric (III) content available to bind the phosphate was 16.53 %, however, the phosphate binding capacity of the same was 70.26 mg-p/gm of Fe at pH level 7.5

Example 3

Batch no: TFTD/007/08/21

The drying was carried for 7 hours at 81°C temperature in ATD which resulted in the moisture contain to be 20.38%, the Ferric (III) content available to bind the phosphate was 17.35 %, however, the phosphate binding capacity of the same was 73.93 mg-p/gm of Fe at pH level 7.5

Example 4

Batch No: TFTD/009/08/21

The drying was carried for 6 hours at 81°C temperature in ATD which resulted in the moisture content to be 21.60%, the Ferric (III) content available to bind the phosphate was 16.53%, however, the phosphate binding capacity of the same was 76 mg-p/gm of Fe at pH level 7.5.

Example 5

Batch No: TFTD/012/09/21

The drying was carried for 3 hours at 81°C temperature in ATD which resulted in the moisture content to be 26.38%, the Ferric (III) content available to bind the phosphate was 17.66%, however, the phosphate binding capacity of the same was 89.94 mg-p/gm of Fe at pH 7.5.

Example 6

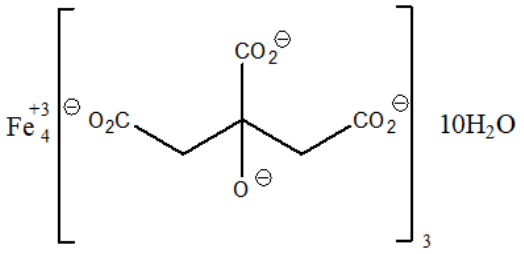
Batch No: TFTD/013/09/21

The drying was carried for 1.5 hours at 81°C temperature in ATD which resulted in the moisture content to be 28%, the Ferric (III) content available to bind the phosphate was 17.75%, however, the phosphate binding capacity of the same was 89.94 mg-/gm of Fe at pH 7.5.

While this invention has been described in connection with what is presently considered to be the most practical and preferred embodiment, it is to be understood that the invention is not limited to the disclosed embodiments, but, on the contrary, is intended to cover various modifications and equivalent arrangements included within the scope of the appended claims.

We Claims

1. A pharmaceutically acceptable Iron (III) coordination complex prepared through an organic solvent free route and represented by formula I;



characterized in that,
the complex having:

a) purity of 90-95% pure
b) Phosphate binding capacity in the range of70.26-90 mg-P/g of elemental Iron at pH 7.5 ;
c) moisture content in the range of 19.05 to 28 %.
d) particle size distribution in the range of Dv (0.1)- 125µm, Dv (0.5)-726µm and Dv (0.9)-1940µm.

2. The coordination complex as claimed in claim 1, wherein the purity of Iron (III) coordination complex and water adduct in solution is 70-80%.
3. The coordination complex as claimed in claim 1, wherein the complex is present in the amorphous form.
4. The pharmaceutically acceptable Iron (III) coordination complex as claimed in claim 1, wherein the complex comprises of ferric tricitratedecahydrate.

5. A process for preparing the pharmaceutically acceptable iron (III) coordination complex through an organic free solvent route comprising the steps of:
   a) reacting an anhydrous ferric halide with a metal salt of acid in water with stirring at a temperature ranging between 55-85°C for a period of 24-36 hour to obtain a brown precipitate;
   b) filtering the brown precipitate obtained in step (a) in a nitrogen gas atmosphere at an optimum pressure range to obtain wet cake material;
   c) drying the wet cake material obtained in step (b) at a temperature in the range of 55 to 85oC for a period of 1 to 8 hours followed by sequential increasing of temperature at 5 degree per 30 to 35 minutes to obtain the pharmaceutically acceptable Iron (III) coordination complex.
6. The process as claimed in claim 5, wherein the ferric halide used is in the range of 50 to 65%.
7. The process as claimed in claim 6, wherein the halide is a chloride.
8. The process as claimed in claim 5, wherein the metal salt is used in the range of 50 to 65%.
9. The process as claimed in claim 5, wherein the metal salt of acid is citric acid.
10. The process as claimed in claim 9, wherein the metal in metal salt is a sodium-based salt.
11. The process as claimed in claim 5, wherein the stirring in step (a) is maintained in the range of 25-40 rpm.
12. The process as claimed in claim 5, wherein the filtering is performed in step (a) in a nitrogen gas atmosphere at pressure in the range of 600-700 mmHg.
13. The process as claimed in claim 5, wherein the 5 drying is done in drying chamber at a temperature ranging between 50 to 85^{o}C for a period of 60-480 minutes.

PHARMACEUTICAL ACCEPTABLE IRON (III) COORDINATION COMPLEX HAVING HIGH PHOSPHATE BINDING CAPACITY AND PREPARATION THEREOF

ABSTRACT:

The present invention relates to a pharmaceutical acceptable iron (III) coordination complex having high phosphate binding capacity prepared through a cost-effective and an organic solvent free route. The present invention provides a pharmaceutical composition of iron (III) coordination complex which not only releases the desired amount of elemental iron in the desired pH level which is absorbed and assimilated into iron stores but also binds the ferric iron with the higher dietary phosphate which is finally excreted through stool being insolvable. The pharmaceutical composition is industrially acceptable, consumable with less or no side-effects, more effective.