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पेटेंट प्रमाणपत्र
PATENT CERTIFICATE

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पेटेंट सं. / Patent No.	:	388898
आवेदन सं. / Application No.	:	202131022799
फाइल करने की तारीख / Date of Filing	:	21/05/2021
पेटेंटी / Patentee	:	WEST BENGAL CHEMICAL INDUSTRIES LTD

प्रमाणित किया जाता है कि पेटेंटी को उपरोक्त आवेदन में यथाप्रकटित A process for synthesis of ferric derisomaltose complex नामक आविष्कार के लिए, पेटेंट अधिनियम, १९७० के उपबंधों के अनुसार आज तारीख 21st day of May 2021 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 A process for synthesis of ferric derisomaltose complex as disclosed in the above mentioned application for the term of 20 years from the 21st day of May 2021 in accordance with the provisions of the Patents Act,1970.

एकस्य कार्यालय THE PATENT OFFICE GOVT.OF INDIA भारत सरकार

अनुदान की तारीख :
Date of Grant : 10/02/2022

पेटेंट नियंत्रक
Controller of Patent

टिप्पणी - इस पेटेंट के नवीकरण के लिए फीस, यदि इसे बनाए रखा जाना है, **21st day of May 2023** 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 21st day of May 2023 and on the same day in every year thereafter.

388898

Indian Patent

Patent Number: 388898
Date of Patent: 10 Feb, 2022

Solvent Free and Economic process for the synthesis of water soluble Ferric Derisomaltose

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Application: **202131022799**

Filed: **21 May, 2021**

ABSTRACT:

The present invention provides a process for synthesis of solvent free water soluble Ferric derisomaltose which is free of toxic impurities. The process includes use of in situ preparation of modified dextran which is free of low molecular weight carbohydrate and have molecular weight in range of 850 Dalton-1800 Dalton. The Ferric derisomaltose obtained by the process readily soluble in water and was dark brown, non-transparent aqueous solution with pH 5.0-7.0, containing ferric derisomaltose which was used for preparation of parenteral compositions.Bydissolving in water for injections and filled into glass vials. Each 1 mL of solution contains 100 mg of elemental iron as ferric derisomaltose in water for injection.

9 Claims, No Drawings

Claims

1. A process for synthesis of ferric derisomaltose complex comprises the steps of:
   i. preparation of modified dextran comprising in-situ reduction of dextran ;
   ii. oxidizing electrolytic iron with 10.0% hydrogen peroxide to make nascent ferric iron which is highly feasible for coupling with reduced dextran of step (i) to obtain a ferric iron-dextran;
   iii. heating the nascent ferric iron of step (ii) with reduced dextran of step (i) in presence of an alkali, followed by cooling;
   iv. adjusting the pH in the range of 5.50-6.50 using mineral acid; and
   v. filtering, drying the filtrate in a spray dryer to obtain the product.

   wherein step (i) comprises in-situ reduction of dextran in presence of a reducing agent.

2. The process as claimed in claim 1, wherein the dextran and reducing agent is present in ratio of 1: 0.010 to 0.25 .
3. The process as claimed in claims 1, wherein step (I) comprises a step of hydrolysis prior to in situ reduction of the dextran.
4. The process as claimed in claims 1, wherein the reducing agents are selected from sodium cyanoborohydride, lithium borohydride, sodium borohydride.
5. The process as claimed in claims 1 to 4 wherein in step (iii) the nascent ferric iron of step (ii) with reduced dextran of step (i) is heated at a temperature of about 80°C to about 85°C for a period of 1 hour to 7 hours.
6. The process as claimed in claims 1 to 5 wherein step (iii) further comprises the step of cooling the ferric derisomaltose complex solution to temperature of about 40°C and the pH is adjusted in the range of 7.0 to 8.0 by addition of mineral acid.
7. The process as claimed in claim 1 to claim 6 wherein ferric derisomaltose complex solution is filtered by passing the solution through diatomaceous earth.
8. The process as claimed in claim 1 to claim 7 wherein ferric derisomaltose complex solution is filtered through 20µm, 2.5µm, 0.45µm and 0.2µm filter paper.
9. The process as claimed in claim 1 wherein ferric derisomaltose complex has an iron content of 25-30% w/w with reduced toxicity.

Title of the invention

SOLVENT-FREE AND ECONOMIC PROCESS FOR THE SYNTHESIS OF WATER SOLUBLE FERRIC DERISOMALTOSE

Applicant(s)

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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 process for synthesis of water soluble Ferric Derisomaltose, which is stable and has reduced toxicity and is useful in the treatment of iron deficiency anaemia. In particular, the present invention relates to a solvent free and eco-friendly improved process for synthesis of water soluble Ferric Derisomaltose.

BACKGROUND OF THE INVENTION

Patients with iron deficiency anaemia (IDA)are prescribed iron supplementation in order to treat and manage anaemia and to replenish the body stores. Significant proportions of patients are found to benefit by supplementing iron intravenously (IV).

Treatment and management of IDA typically involve dietary changes by incorporating food groups rich in iron. Dietary supplementation with oral iron is a first line of treatment which apart from being safe is cost effective and convenient. However, where supplementation with oral iron fails to provide the desired result, parenteral therapy is employed as a second line of treatment. Intravenous iron preparations areusually available as ferric gluconate, iron sucrose, iron dextran, and ferric carboxymaltose preparations in the market,which are delivered to patients in a single administration for treatment of anaemia.

Ferric Derisomaltose (also known as Iron isomaltoside) is an iron replacement product for intravenous infusion. Ferric derisomaltose is an iron carbohydrate complex with a matrix structure composed of interchanging layers of ferric hydroxide and the carbohydrate derisomaltose. Derisomaltose consists of linear, hydrogenated isomaltooligosaccharides with an average molecular weight of 1000 Da and a narrow molecular weight distribution that is almost devoid of mono- and disaccharides. Ferric derisomaltose has an average molecular weight of 155,000 Da and has the following empirical formula: {FeO(1-3X) (OH)(1+3X) (C6H5O73-)X}, (H20)T, (C6H10O6)R(-C6H10O5-)Z(C6H13O5)R, (NaCl)Y X= 0.0311; T = 0.25; R = 0.14; Z = 0.49; Y = 0.14

It is a helical inclusion complex in which individual D glucose units are linked to form a Dextran moiety. These Dextran units, in turn, self-repeat themselves in a polymeric chain forming Ferric derisomaltose. It is a non-branched, non-anaphylactic carbohydrate [W. Richter, Hapten inhibition of passive antidextran dextran anaphylaxis in guinea pigs. Role of molecular size in anaphylactogenicity and perceptibility of dextran fractions, International Archives of Allergy and Immunology 41(1971) 826–844; K.-G. Ljungström, Invited commentary: retreatment with dextran 1 makes dextran 40 therapy safer, Journal of Vascular Surgery 43 (2006) 1070–1072], and is structurally different from branched polysaccharides used in iron dextran.

Ferric derisomaltose contains a polynuclear Fe(III)oxyhydroxide core which is stabilized by a hydrogenated (reduced) Dextran 1000 and a low amount of hydroxyl acid, which promotes the stability and solubility of compound. Synthesis of such iron-carbohydrate complexes are known and described in the art. Said synthesis processes involve use of solvents like methanol or ethanol, which makes the processes cumbersome Handling of such solvents increases the capital costs as it requires equipment and protective clothing.

However, the major challenges during the synthesis include maintaining the physico-chemical stability of trivalent iron ions/salts with low molecular weights of the saccharides/polysaccharides. The carbohydrate shell is unique for each preparation since the carbohydrate shell determines the metabolic pathway of the complexes, affectingtheir pharmacokinetics and pharmacodynamics, as well as their interaction with the innate immunesystem and, thus, side effects [Koskenkorva-Frank, T.S; et.al The complex interplay of ironmetabolism, reactive oxygen and reactive nitrogen species: Insights into the potential of different iron therapies to induce oxidative and nitrosative stress. Free Radica. Biol. Med. 2013, 65, 1174–1194]. Depending on the carbohydrate shell the preparations can be classified as (a) non-dextran based and (b) dextran/dextran based complexes. Further, low and higher molecular weight dextran complexes are not much stable as compared to modified molecular weight

dextran complex (as oligosaccharide). Higher molecular weight dextran is associated with solubility problems in formulation as well as Injection grade formulations while lower molecular weight dextran is associated with toxicity issues.

Therefore, there remains a need for an improved process for manufacture of ferric derisomaltose with good stability and reduced toxicity and which does not require solvents like methanol and ethanol.

OBJECTS OF THE INVENTION

Accordingly, it is an object of the present invention to provide a solvent free process for the synthesis of Ferric derisomaltose which provides a stable and less toxic ferric derisomaltose.

It is another object of the present invention to provide a process for the synthesis of Ferric derisomaltose which is industrially feasible and economic.

It is yet another object of the present invention to provide a ferric derisomaltose which is stable and non-toxic.

SUMMARY OF THE INVENTION

Accordingly, the present invention provides a simple and solvent free and an economic process for synthesis of ferric derisomaltose complex with high iron content, good stability and reduced toxicity.

In an aspect, the present invention provides a solvent free process for synthesis of ferric derisomaltose complex comprises the steps of:

i. preparation of modified dextran comprising in-situ reduction of dextran;
ii. oxidizing electrolytic iron with 10.0% hydrogen peroxide to make nascent ferric iron which is highly feasible for coupling with reduced dextran of step (i) to obtain a ferric iron-dextran;
iii. heating the nascent ferric iron of step (ii) with reduced dextran of step (i) in presence of an alkali, followed by cooling;
iv. adjusting the pH in the range of 5.50-6.50 using mineral acid; and
v. filtering, drying the filtrate in a spray dryer to obtain the product.

In a second aspect, the present invention provides a ferric derisomaltose complex so obtainable that has improved stability, yield and reduced toxicity.

DETAILED DESCRIPTION OF THE INVENTION

The following description with reference to the accompanying drawings is provided to assist in a comprehensive understanding of various embodiments of the present disclosure as defined by the claims and their equivalents. It includes various specific details to assist in that understanding but these are to be regarded as merely exemplary. Accordingly, those of skilled in the art will recognize that various changes and modifications of the various embodiments described herein can be made without departing from the scope and spirit of the present disclosure. In addition, descriptions of well-known functions and constructions may be omitted for clarity and conciseness. Further it is to be understood that the singular forms "a," "an," and "the" include plural referents unless the context clearly indicates otherwise.

Described herein is an improved process for synthesis of ferric derisomaltose complex, which does not use any solvent. In other words, the synthesis process described herein is solvent free.

The present invention provides a process for synthesis of ferric derisomaltose complex comprises the steps of:

i. preparation of modified dextran comprising in-situ reduction of dextran;
ii. oxidizing electrolytic iron with 10.0% hydrogen peroxide to make nascent ferric iron which is highly feasible for coupling with reduced dextran of step (i) to obtain a ferric iron-dextran;
iii. heating the nascent ferric iron of step (ii) with reduced dextran of step (i) in presence of an alkali, followed by cooling;
iv. adjusting the pH in the range of 5.50-6.50 using mineral acid; and
v. filtering, drying the filtrate in a spray dryer to obtain the product.

In particular, the process for synthesis of said ferric derisomaltose complex comprises the step of selecting a suitable Dextran. As already discussed, low molecular weight and high molecular weight Dextran complexes are not suitable; the inventors of the present invention have provided selection of suitable dextran as a key step to control the toxicity and stability of the compound. In a preferred embodiment, Dextran-5 is selected as starting material for the process of synthesis of ferric derisomaltose, Said Dextran -5 is converted to dextran – 1 by controlled hydrolysis which can be performed according to standard methods. Thereafter, the dextran undergoes in situ reduction yield Dextran -1 having molecular weight of between 850 and 1100 Dalton, preferably between 800 and 1100 Dalton and

most preferably it has a molecular weight of 1000 Dalton.

Surprisingly, the present inventors found that the 'in situ' synthesis of dextran-1 under controlled condition of a residual reducing agent in the reacting solution, results in production of modified dextran which is substantially free from low molecular weight carbohydrate. Dextran-1 so produced is substantially free of any low molecular weight carbohydrate that is it comprises less than equal to 2%.

'In-situ' synthesized dextran avoids the need for costly purification steps to obtain reduced/hydrogenated dextran of molecular weight in the range of 850 to 1100 Da. The step of reduction also reduces the concentration of unreduced dextran in the solution resulting in a low concentration of unreduced dextran which further diminishes the chances of reduction of ferric ions to undesired ferrous ions, thereby reducing impurity formation. Thus, the present process avoids the use commercial variety of Dextran -1 that is used by existing processes and subsequently obviates use of a costly separation process typically carried out by membrane filtration or solvent isolation to remove lower molecular weight dextran from the modified dextran compound.

The step of reduction of the dextran into modified dextran is carried out in presence of a mild reducing agent under controlled conditions. Mild reducing agents can be selected from sodium cyanoborohydride, lithium borohydride, sodium borohydride, preferably the mild reducing agent is sodium borohydride . Further the ratio of the amount of the mild reducing agent and that of dextran is preferably is in the range of 0.010 to 0.25: 1. In a preferred embodiment, the ratio of sodium borohydride to dextran-1 is maintained at 0.019:1. Typically the reduction of dextran-5 is carried out for a period of about 120 minutes.

In an embodiment, the step of reduction is performed at a controlled condition. The dextran is subjected to reduction in presence of a residual reducing agent at a temperature of 25°C to 35°C.

In a preferred embodiment, Dextran-1 undergoes reduction under controlled condition in presence of a sodium borohydride at room temperature followed by quenching to reduce the affinity of oxidizing agent that may hinder the nascent ferric ion in further complexation reaction. The process continues until the unreduced dextran-1 concentration in the solution was in the range of 0.05 to 0.1%. Samples are tested by standard methods such as NELSON method for monitoring the carbohydrate content.

In an embodiment of the present invention, the reduced hydrolysed dextran is passed through celite bed to improve the stability of modified dextran.

In the step of oxidizing electrolytic iron as recited under step (ii) with an oxidizing agent to make nascent ferric ion, the electrolytic iron is oxidized by 10% of hydrogen peroxide.

In the step of heating the nascent ferric iron of step (ii) with reduced dextran of step (i) in presence of an alkali, followed by cooling, wherein the alkali is hydroxide alkali and is free from chloride. In said step water is added to the nascent ferric ions of step (ii) with continuous stirring. Reduced dextran of step (i) is added followed by alkali solution for about 25 to 35 minutes.

The electrolytic iron is oxidized in the presence of 10 % hydrogen peroxide in aqueous medium at specific pHof range 4.0-4.5, and is monitored until the free iron and ferrous content is less than about 0.5% level in reaction mass at specific pH 4.0-4.5. Said step produces the nascent ferric ion in solution. Consequently, it reduces the impurities and obviates the need for further steps of purification thereby decrease the cost of manufacturing the ferric derisomaltose.

The process also comprises steps of (iv) adjusting the pH in the range of 5.50-6.50 using mineral acid; and(v) filtering, drying the filtrate in a spray dryer to obtain the ferric derisomaltose complex.

The ferric derisomaltose complex so obtained is heated at a temperature of about 80°C to about 85°C for a period of 1 hour to 7 hours. Preferably, heating is carried out for a period of 2 to 3 hours. The reaction mass is cooled to temperature of about 40°C and the pH is adjusted in the range of 7.0 to 8.0 by addition of mineral acid.

In an embodiment the solution is filtered through 20µm, 2.5µm, 0.45µm and 0.2µm filter paper. In a preferred embodiment, the solution is filtered over diatomaceous earth (Celite bed) to remove any undissolved residue from reaction mass followed by filtration through 1.2 micron membrane. The solution is then transferred to the spray dryer for drying the reaction mass.

In a preferred embodiment, the ferric derisomaltose complex so produced is further reduced to reduce the content of the dimer saccharide of ferric derisomaltose to less than 1.8% which results in an iron complex having more stable and increased the half life of the initial products like iron Isomaltoside. This reduction in dimer content also resulted in improved stability as well

as toxicity based on accelerated stability testing. The dimer content of Ferric Derisomaltose is less than 1.8%. Table 1 provides the stability data of the Ferric Derisomaltose produced by the method of the present invention.

The ferric derisomaltose obtained can be spray dried according to standard procedure. Preferably the inlet temperature of the dryer is maintained at about 140°C and the outlet temperature is at about 115°C-140°C to obtain a brown red powder with iron content in the complex in the range of 25-30%w/w and molecular weight of the complex in the range of 100kDa to 160kDa.

Ferric derisomaltose complex, in the spray dried form can be obtained is dark brown, non-transparent powder ~~aqueous solution~~ with pH 5.0-7.0, readily soluble in water and was used for preparation of parenteral compositions. Ferric derisomaltose has an average molecular weight of 155,000 Da and has the following empirical formula: {FeO(1-3X) (OH)(1+3X) (C6H5O7 3-)X}, (H20)T, (C6H10O6)R(-C6H10O5-)Z(C6H13O5)R, (NaCl)Y X= 0.0311; T = 0.25; R = 0.14; Z = 0.49; Y = 0.14

The ferric derisomaltose so obtained in the present invention consists of linear, hydrogenated isomalto-oligosaccharides with an average molecular weight of 1000 Da and a narrow molecular weight distribution that is almost devoid of mono- and disaccharides.

Ferric derisomaltose so obtained by the process of the present invention is stable and has an iron content of 25-30%w/w with reduced toxicity.

In a further embodiment the present invention also provides a parenteral composition comprising 100 mg of elemental iron as ferric derisomaltose in 1mL in water for injection. Further, the aqueous solution of ferric derisomaltose can be suitably used for preparation of injections by adjusting the concentration of iron and by adding suitable amount of sodium chloride in order to make the solution isotonic using standard technique.

Among other advantages of the present invention, the inventors found that said process offers high dosing flexibility with optimized administration convenience to treat patients with iron deficiency. Further the ferric derisomaltose obtainable by the present process is stable and has good yield. It can be used to prepare parenteral administration to the patients suffering from iron deficiency anaemia.

Further embodiments will be explained by some illustrative examples.

Example 1: Preparation of reduced dextran

100g Dextran-1 was passed through a Celite bed to improve the quality of it. Dextran-1 was mixed with sodium borohydride at room temperature followed by quenching by using dil. HCl (10%) to reduces the affinity of reducing agent which may hindered the nascent Ferric ion in further complexation reaction. The concentration of sodium borohydride was maintained between 0.3 to 0.7mg/ml; preferably at 0.5mg/ml and the temperature below 35°C. The reduction was carried using a ventilated reactor to exhaust the inflammable hydrogen gas produced during the reduction reaction. The process was continued until the unreduced Dextran-1 concentration in the solution was in the range of 0.05 to 0.1%. The ratio of sodium borohydride to dextran-1 was maintained at 0.019:1.

Example 2: Preparation of nascent ferric ions

~~Electrolytic~~ iron was oxidized by 10% of hydrogen peroxide in aqueous medium by electrolysis method at specific pH and was monitored by titration method until the free iron and ferrous content is less than about 0.5% level in reaction mass at specific pH 4.50- pH 5.5.

Example 3: Formation of Ferric Derisomaltose complex:

The nascent ferric ions (Freshly prepare) as obtained in Example 2 was added to water with continuous stirring. Reduced dextran of example 1 was later added followed by alkali solution and for about 25 to 35 minutes. Ferric Derisomaltose complex so obtained was heated and the temperature was maintained at 80°C-85°C for 1-7 hours preferably 2-3 hrs. The reaction mass was cooled to temperature of about 40°C and the pH was adjusted in the range of 7.0-8.0 by addition of mineral acid.

The ferric derisomaltose complex so produced was further reduced to reduce the content of the dimer saccharide of ferric derisomaltose to less than 1.8% which results in an iron complex having more stable and increased the half life of the initial products like iron Isomaltoside. This reduction in dimer content also resulted in improved stability as well as toaxicity based on accelerated stability testing. The dimer content of Ferric Derisomaltose is less than 1.8%. Table 1 provides the stability data of the Ferric Derisomaltose produced by the method of the present invention.

The solution was filtered over Celite bed to remove any undissolved residue from reaction mass followed by filtration through 1.2 micron and the solution was transferred to the spray dryer for drying the reaction mass. The inlet temperature of the dryer was

maintained at about 140°C and the outlet temperature at about 115°C to obtain brown red powder with iron content in the complex in the range of 25-30%w/w and molecular weight of the complex in the range of 100kDa to 160kDa. The ferric derisomaltose complex so obtained was readily soluble in water and was dark brown, non-transparent aqueous solution with pH 5.0-7.0, containing ferric derisomaltose which was used for preparation of parenteral compositions.

Stability studies were carried out to observe the shelf life of the ferric derisomaltose complex at a storage temperature of 30 ± 2°C and humidity of 40% ± 5%.

Table 1: Stability Data of the Ferric Derisomaltose

Period completed [In Month]	Description	Loss on Drying	pH (5% solution)	Carbohydrate (on dried Basis)	Iron Content (on dried Basis)	Filtration Test (100 mg/ ml solution)	Endotoxin
	Brown or dark brown	NMT 6.0%	5.50-8.5	NLT 30.0% w/w	NLT 20%w/w	a. Should pass	0.5 Eu/mg of Iron
	free flowing powder	w/w				0.45 µ b. Should pass 0.20 µ	
Initial (0 Month)	Complies	3.22%	6.7	33.32%	26.22%	Complies	Complies
1 Month	Complies	3.59%	6.8	33.16%	26.55%	Complies	Complies
3 Month	Complies	3.66%	6.7	33.67%	26.82%	Complies	Complies
6 Month	Complies	3.92%	6.7	33.56%	26.02%	Complies	Complies
9 month	Complies	4.12%	6.7	33.86%	26.52%	Complies	Complies
12 month	Complies	4.22%	6.7	33.92%	26.31%	Complies	Complies

As observed, the ferric derisomaltose complex was found to have long term stability.

Further, table 2 provides the toxicity data for the Ferric derisomaltose produced by the present invention.

Description	Iron Content (on dried Basis)	Abnormal Toxicity Test								
		10 Times			20 Times			50 Times		
Brown free flowing powder	26.22%	Concentration	Weight of sample injected	Procedure	Concentration	Weight of sample injected	Procedure	Concentration	Weight of sample injected	Procedure
		0.333 mg Fe/ 0.5 ml per mouse IV	254.00 mg	254.00 mg of sample dissolved in 100 ml of sterile water for injection by heating in a water bath	0.666 mg Fe/ 0.5 ml per mouse IV	508.00 mg	508.00 mg of sample dissolved in 100 ml of sterile water for injection by heating in a water bath	1.665 mg Fe/ 0.5 ml per mouse IV	1270.02 mg	1270.02 mg of sample dissolved in 100 ml of sterile water for injection by heating in a water bath
Results		No Mortality Observed			No Mortality Observed			No Mortality Observed		

As observed, the ferric derisomaltose obtained is safe and not toxic.

By dissolving in water for injections and filled into glass vials. Each 1 mL of solution contains 100 mg of elemental iron as ferric derisomaltose in water for injection.

Claims

1. A process for synthesis of ferric derisomaltose complex comprises the steps of:
   i. preparation of modified dextran comprising in-situ reduction of dextran ;
   ii. oxidizing electrolytic iron with 10.0% hydrogen peroxide to make nascent ferric iron which is highly feasible for coupling with reduced dextran of step (i) to obtain a ferric iron-dextran;
   iii. heating the nascent ferric iron of step (ii) with reduced dextran of step (i) in presence of an alkali, followed by cooling;
   iv. adjusting the pH in the range of 5.50-6.50 using mineral acid; and
   v. filtering, drying the filtrate in a spray dryer to obtain the product.

   wherein step (i) comprises in-situ reduction of dextran in presence of a reducing agent.
2. The process as claimed in claim 1, wherein the dextran and reducing agent is present in ratio of 1: 0.010 to 0.25 .
3. The process as claimed in claims 1, wherein step (I) comprises a step of hydrolysis prior to in situ reduction of the dextran.
4. The process as claimed in claims 1, wherein the reducing agents are selected from sodium cyanoborohydride, lithium borohydride, sodium borohydride.
5. The process as claimed in claims 1 to 4 wherein in step (iii) the nascent ferric iron of step (ii) with reduced dextran of step (i) is heated at a temperature of about 80°C to about 85°C for a period of 1 hour to 7 hours.
6. The process as claimed in claims 1 to 5 wherein step (iii) further comprises the step of cooling the ferric derisomaltose complex solution to temperature of about 40°C and the pH is adjusted in the range of 7.0 to 8.0 by addition of mineral acid.
7. The process as claimed in claim 1 to claim 6 wherein ferric derisomaltose complex solution is filtered by passing the solution through diatomaceous earth.
8. The process as claimed in claim 1 to claim 7 wherein ferric derisomaltose complex solution is filtered through 20µm, 2.5µm, 0.45µm and 0.2µm filter paper.
9. The process as claimed in claim 1 wherein ferric derisomaltose complex has an iron content of 25-30% w/w with reduced toxicity

Solvent Free and Economic process for the synthesis of water soluble Ferric Derisomaltose

ABSTRACT

The present invention provides a process for synthesis of solvent free water soluble Ferric derisomaltose which is free of toxic impurities. The process includes use of in situ preparation of modified dextran which is free of low molecular weight carbohydrate and have molecular weight in range of 850 Dalton-1800 Dalton. The Ferric derisomaltose obtained by the process readily soluble in water and was dark brown, non-transparent aqueous solution with pH 5.0-7.0, containing ferric derisomaltose which was used for preparation of parenteral compositions. By dissolving in water for injections and filled into glass vials. Each 1 mL of solution contains 100 mg of elemental iron as ferric derisomaltose in water for injection.