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(54) Title: PROCESS FOR THE PREPARATION OF PENTOSAN POLYSULFATE OR SALTS THEREOF

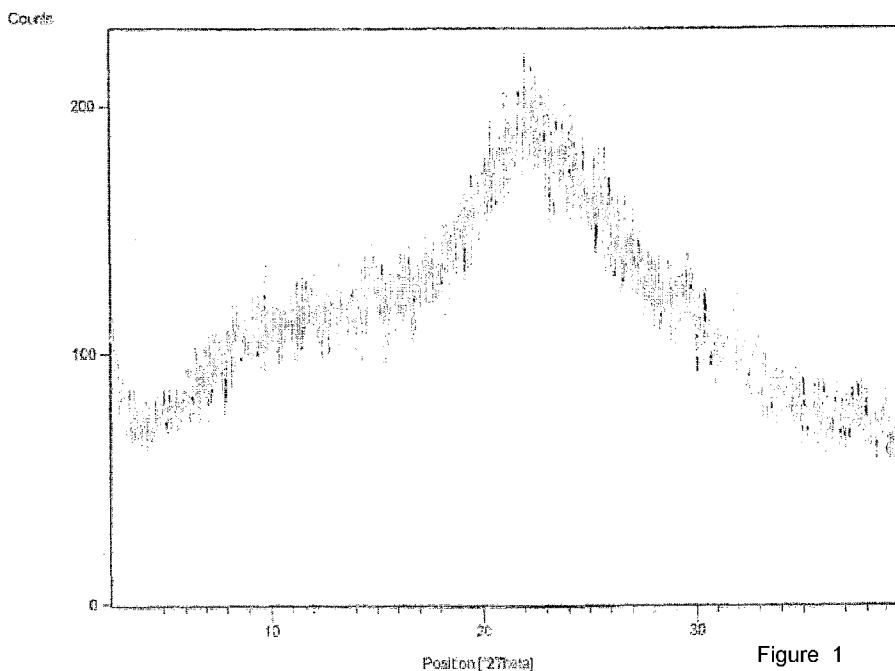


Figure 1

(57) Abstract: A process for the preparation of Pentosan polysulfate sodium comprising a step of purifying depolymerized crude Pentosan polysulfate sodium by filtration through NF membrane system.

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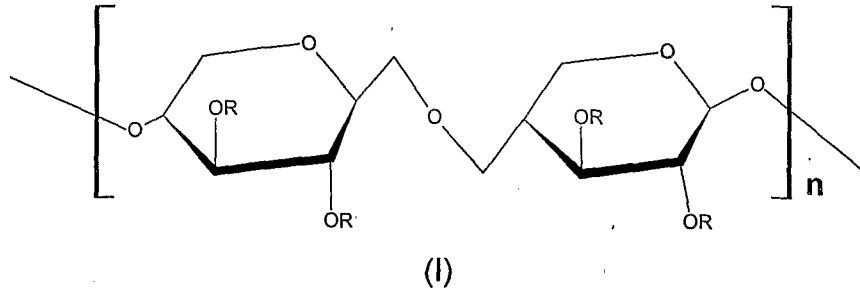
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PROCESS FOR THE PREPARATION OF PENTOSAN
POLYSULFATE OR SALTS THEREOF

Field of Invention:

The present invention relates to an improved process for the preparation of Pentosan polysulfate of formula (I)

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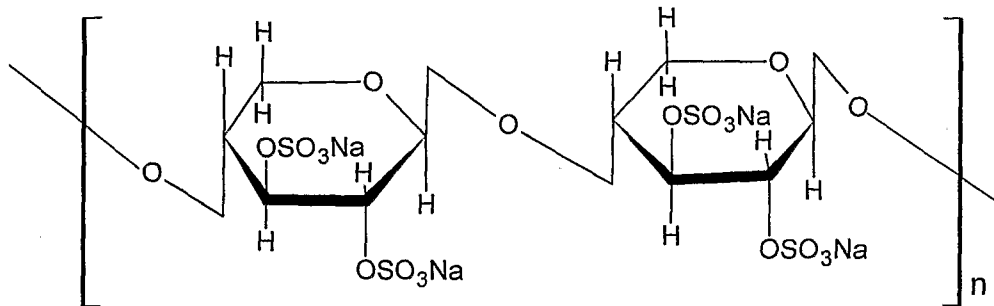


or salt thereof, wherein R represents $-SO_3Y$, and Y is at least one member selected from the group consisting of H and a pharmaceutically acceptable cation such as sodium, potassium, and magnesium. It also provides an amorphous form of Pentosan polysulfate sodium and process thereof.

10

Background of the invention:

15 Pentosan polysulfate sodium is chemically known as β -D-Xylan, (1-4), 2, 3-bis (hydrogen sulphate) sodium salt having molecular weight range of 4000 to 6000 Dalton. The structural formula of Pentosan polysulfate sodium represents as below:



Pentosan Polysulfate sodium

20

The current pharmaceutical product containing Pentosan polysulfate sodium salt is being sold by Ortho McNeil under the tradename Elmiron[®] in the form of capsules which is used for the treatment of bladder infection, interstitial cystitis and tumors.

- 5 Pentosan polysulfate sodium [37319-17-8] is a semi-synthetically produced heparin-like macromolecular carbohydrate derivative which chemically and structurally resembles glycosaminoglycans. It is a white odorless powder, slightly hygroscopic and soluble in water to 50% at pH 6.
- 10 Pentosan polysulfate sodium is a mixture of linear polymers of β -1 \rightarrow 4-linked xylose, usually sulfated at the 2- and 3-positions and occasionally substituted at the 2-position with 4-O-methyl- α -D-glucuronic acid 2, 3-O-sulfate.

15 Pentosan polysulfate is a semi-synthetic compound whose polysaccharide backbone, xylan is extracted from the bark of the beech tree or other plant sources and then treated with sulfating agents such as chlorosulfonic acid or sulfonyl chloride and acid. After sulfation, Pentosan polysulfate is usually treated with sodium hydroxide to yield the sodium salt.

- 20 Pentosan polysulfate is disclosed in US patent no. 2689848. The process wherein Xylan is treated with chlorosulfonic acid in the presence of pyridine to obtain sulfuric acid ester salt of xylan followed by oxidative depolymerisation in acidic or neutral aqueous medium to obtain depolymerised product which is dialyzed and followed the fractionation process to obtain desired product. However, this process does not
- 25 provide end product with desired molecular weight.

30 US patent 2689848 disclosed the process for the production of salts of sulfuric acid ester of Xylan, the steps which comprise oxidizing the aqueous solution of the a salt of a sulfuric acid ester of highly polymeric xylan in an aqueous solution of H₂O₂ and H₂SO₄ to depolymerize such highly polymeric xylan ester partially, dialyzing the depolymerized product and fractionating an aqueous solution of the dialyzate with an

organic water miscible solvent to obtain a fraction having a Z_{\square} value between 0.0030 and 0.015 and sulfur content of 13.5 to 17%.

Moreover, the process as disclosed above for the preparation of Pentosan polysulfate is tedious, costly and provides low yield of final product. Moreover, the use of cellophane tubes for dialysis makes process inapplicable at industrial scale up.

Therefore, it is necessary to develop a process for preparation of Pentosan polysulfate sodium which provides good yield as well as operationally simple and easily applicable at an industrial scale.

Surprisingly, the present inventors have found that carrying out the purification of crude Pentosan polysulfate of formula (I) or its salt by dissolving it in water, followed by filtration through NF membrane system and crystallization of resulting mixture from alcohol provides high yield with good purity of Pentosan polysulfate of formula (I) or its salt of molecular weight of 3000 to 10000 Dalton.

Objects of the invention:

It is therefore an object of the present invention is to provide an improved process for the preparation of Pentosan polysulfate of formula (I) or salt thereof.

Another object of the present invention is to provide the process for the preparation of Pentosan polysulfate of formula (I) or its salt which is operationally simple, easy to handle and applicable at an industrial scale.

A furthermore object of the present invention is to provide an amorphous form of Pentosan polysulfate of formula (I) or its salt thereof.

Another object of the present invention is to provide an amorphous form of Pentosan polysulfate sodium.

Yet another object of the present invention is to provide an improved process for preparation of Pentosan polysulfate of formula (I) or salt thereof, comprising steps of:

- 5 i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of alkali in the presence of alcoholic solvent to obtain salt of sulfuric acid ester of xylan
- ii) oxidizing the salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate of formula (I) or its salt
- 10 iii) purifying depolymerized crude Pentosan polysulfate of formula (I) or its salt by dissolving it in water, followed by filtration through NF membrane system
- iv) crystallizing the product obtained in the step (iii) from alcohol to obtain pure Pentosan polysulfate of formula (I) or its salt

15 A further object of the present invention is to provide an improved process for purification of Pentosan polysulfate of formula (I) or salt thereof, comprising steps of:

- i) dissolving crude Pentosan polysulfate of formula (I) or its salt in water
- ii) filtering the reaction mixture obtain in the step (i) with NF membrane system
- 20 iii) crystallizing the resulting product obtained in the step (ii) from alcohol to obtain pure Pentosan polysulfate of formula (I) or its salt

Yet another object of the present invention is to provide an improved process for preparation of Pentosan polysulfate sodium, comprising steps of:

- 25 i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of sodium hydroxide in the presence of alcoholic solvent to obtain sodium salt of sulfuric acid ester of xylan
- ii) oxidizing the sodium salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate sodium
- 30

- iii) purifying depolymerized crude Pentosan polysulfate sodium, by dissolving it in water, followed by filtration through NF membrane system
- iv) lyophilizing the product obtained in the step (iii) to obtain pure Pentosan polysulfate sodium

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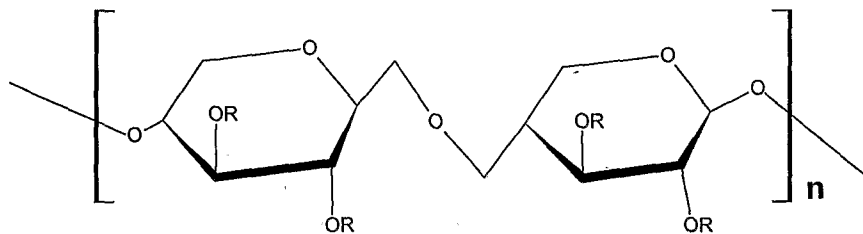
A further object of the present invention is to provide an improved process for purification of Pentosan polysulfate sodium, comprising steps of:

- i) dissolving crude Pentosan polysulfate sodium in water
- ii) filtering the reaction mixture obtain in the step (i) with NF membrane system
- iii) lyophilizing the resulting product obtained in the step (ii) to obtain pure Pentosan polysulfate sodium

10

Summary of the invention:

- 15 According to one aspect, present invention provides an improved process for the preparation of Pentosan polysulfate of formula (I),



(I)

- 20 or salt thereof, wherein R represents $-\text{SO}_3\text{Y}$, and Y is at least one member selected from the group consisting of H and a pharmaceutically acceptable cation such as sodium, potassium, and magnesium said process

comprising steps of:

- i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of alkali in the presence of alcoholic solvent to obtain salt of sulfuric acid ester of xylan;
- 5 ii) oxidizing the salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate of formula (I) or its salt;
- iii) purifying depolymerized crude Pentosan polysulfate of formula (I) or its salt by dissolving it in water, followed by filtration through NF membrane system;
- 10 iv) crystallizing the product obtained in the step (iii) from alcohol to obtain pure Pentosan polysulfate of formula (I) or its salt.

Further aspect of the present invention is to provide an improved process for purification of Pentosan polysulfate of formula (I) or salt thereof, comprising steps of:

- 15 i) dissolving crude Pentosan polysulfate of formula (I) or its salt in water;
- ii) filtering the reaction mixture obtain in the step (i) with NF membrane system;
- iii) crystallizing the resulting product obtained in the step (ii) from alcohol to obtain pure Pentosan polysulfate of formula (I) or its salt.

20

Further aspect of the present invention is to provide an improved process for preparation of Pentosan polysulfate sodium, comprising steps of:

- i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of sodium hydroxide in the presence of alcoholic solvent to obtain sodium salt of sulfuric acid ester of xylan;
- 25 ii) oxidizing the sodium salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate sodium;

- iii) purifying depolymerized crude Pentosan polysulfate sodium by dissolving it in water, followed by filtration through NF membrane system;
- iv) lyophilizing the product obtained in the step (iii) to obtain pure Pentosan polysulfate sodium.

A further object of the present invention is to provide an improved process for purification of Pentosan polysulfate sodium, comprising steps of:

- i) dissolving crude Pentosan polysulfate sodium in water
- ii) filtering the reaction mixture obtain in the step (i) with NF membrane system
- iii) lyophilizing the resulting product obtained in the step (ii) to obtain pure Pentosan polysulfate sodium

15 **Brief description of the drawings:**

Figure-1 represents the powder X-ray diffraction (XRD) pattern of an amorphous form of Pentosan polysulfate sodium.

20 **Detailed description of the Invention**

The process of the present invention for preparation of Pentosan polysulfate of formula (I) or salt thereof, is operationally simple, easy to handle and applicable at an industrial scale.

25 The present invention provides an improved process for preparation of Pentosan polysulfate of formula (I) or salt thereof, comprising steps of:

- i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of alkali in the presence of alcoholic solvent to obtain salt of sulfuric acid ester of xylan

- ii) oxidizing the salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate of formula (I) or its salt
 - iii) purifying depolymerized crude Pentosan polysulfate of formula (I) or its salt by dissolving it in water, followed by filtration through NF membrane system
 - iv) crystallizing the product obtained in the step (iii) from alcohol to obtain pure Pentosan polysulfate of formula (I) or its salt
- 10 The suitable alkali in step (i) is selected from alkali metal salt of carbonate, bicarbonate, hydroxide or mixtures thereof. The most preferable is sodium hydroxide. The suitable alcoholic solvent in step (i) is selected from methanol, ethanol, propanol, isopropanol, butanol or mixtures thereof. The most preferable is methanol. The suitable alcohol in step (iv) is selected from methanol, ethanol,
- 15 propanol, isopropanol, butanol or mixtures thereof. The most preferable is methanol. Crystallization provides an amorphous form of Pentosan polysulfate of formula (I) or its salt.

The present invention also provides an improved process for preparation of Pentosan polysulfate sodium, comprising steps of:

- i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of sodium hydroxide in the presence of alcoholic solvent to obtain sodium salt of sulfuric acid ester of xylan
- ii) oxidizing the sodium salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate sodium
- iii) purifying depolymerized crude Pentosan polysulfate sodium by dissolving it in water, followed by filtration through NF membrane system

- iv) lyophilizing the product obtained in the step (iii) to obtain pure Pentosan polysulfate sodium

The suitable alcoholic solvent in step (i) is selected from methanol, ethanol, 5 propanol, isopropanol, butanol or mixtures thereof. The most preferable is methanol. Lyophilization provides an amorphous form of Pentosan polysulfate of formula (I) or its salt.

10 According to present invention, pyridine is added in chlorosulfonic acid slowly at below 40-50°C. The resulting salt was heated to 60-65°C before addition of xylan and raised the temperature to 75-80°C. After completion of reaction, reaction mixture is cooled to 25-30°C and added methanol to isolate the pyridinium salt. The isolated pyridinium salt is dissolved in water and decolorized with chlorine dioxide, then it is quenched with alkaline methanol. It is then adjusted pH 6.5-7.0 with glacial acetic 15 acid, filtered and dried the material at 50-55°C under reduced pressure to get the sodium salt of sulfuric acid ester of xylan.

Sodium salt of sulfuric acid ester of xylan is dissolved in water and heated to 90-100°C, then added preheated mixture of 5N H₂SO₄ and 30% hydrogen peroxide. 20 The reaction mixture is maintained at 90-100°C. After completion of reaction, the reaction mixture is cooled to 25-30°C and adjusted pH 7.5-7.3 with 5N sodium hydroxide solution. Then this reaction mixture is precipitated with methanol, filtered and dried to get the depolymerized product i.e. crude Pentosan polysulfate sodium.

25 The depolymerized product is dissolved in water and subjected to NF Membrane system of cut off molecular weight of 3000 Dalton and monitored the rejection of lower molecular weight material with gel permeation chromatography. After the completion of reaction, the concentrate was subjected to water recovery at 40-50°C. Finally residue was crystallized with methanol to get the pure amorphous form of

Pentosan polysulfate sodium having Z_{\square} value 0.006 and Molecular weight of 6543 Dalton. X-ray powder diffraction pattern is matching with Figure-1.

5 Moreover, after the completion of filtration, the concentrate is transferred in a single neck round bottom flask and fitted to Lyophilizer (BT4KZL-105) and starts the operation of lyophilization. It takes about 24 hr to complete the lyophilization and provides an amorphous form of Pentosan polysulfate having Z_{\square} value -0.007 and Mol weight of 5406 Dalton. X-ray powder diffraction pattern is matching with Figure-1.

10 In the present invention, the purification step as discussed hereinabove is carried out by using "PERMA" Pilot Membrane System manufactured by PERMIONIC Membranes Pvt. Ltd., 3/29, 4/19, B.I.D.C., Gorwa Estate, Vadodara-390016, Gujarat, India.

15 In accordance with the aspects of this invention, purification of crude Pentosan polysulfate of formula (I) or its salt is carried out in following manner:

The crude Pentosan polysulfate of formula (I) or its salt is dissolved in water. Feeding the resultant solution and allow it to pass through micron filter membrane system and concentrate flow meter, thereby filtering out the Pentosan polysulfate of
20 formula (I) or its salt with desired molecular weight in the range of 3000 to 10000 Dalton.

For the purpose of this specification, the meaning of the term "NF membrane system" is nano-filtration accompanied by membrane which is capable to pass the
25 undesired product having molecular weight of at least 3000 Dalton.

Advantages of the present invention over prior art:

- i) The present invention provides process which is economical, operationally and industrially applicable.

- ii) The present invention provides cheaper as well as less time consuming process for the preparation of Pentosan polysulfate sodium.
- iii) The process is simple and easy to handle and does not require special handling care or critical conditions.
- 5 iv) The process provides the desired Pentosan polysulfate sodium with molecular weight of 3000 to 10000 Dalton specifically.

The process of the present invention is described by the following examples, which are illustrative only and should not be construed so as to limit the scope of the
10 invention in any manner.

Example-1

To a three neck 3lt round bottom flask the pyridine (800ml) and chlorosulfonic acid
15 (200ml) was added slowly at below 40-50⁰ C. The resulting salt was heated to 60-65⁰C then added xylan (100g) and raised the temperature to 75-80⁰ C. After completion of reaction, reaction mixture was cooled to 25-30⁰C and methanol was added (2500ml) to isolate the pyridine salt of xylan. The isolated pyridine salt of xylan was dissolved in water 500ml and decolorized with chlorine dioxide (200ml),
20 then it was added a mixture of methanol (2000ml) and 33% Sodium hydroxide (200ml). It was then adjusted to pH to neutral with acetic acid, filtered and dried the material at 50-55⁰ C under reduced pressure to get 240 gm sodium salt of sulfuric acid ester of xylan.

25 To a three neck 3lt round bottom flask charged sodium salt of sulfuric acid ester of xylan (500g) in water (1500ml) and heated to 90-100⁰C, then added the preheated mixture of 5N sulfuric acid (25ml) and 30% hydrogen peroxide (250ml). Monitored the reaction with HPLC, after completion of reaction till average molecular weight came about 4000-8000 Dalton, cooled the reaction mixture and solution was
30 adjusted pH to neutral with dilute sodium hydroxide solution. Then the reaction

mixture was precipitated with methanol (12lt), filtered and dried at 50-55⁰C to get crude Pentosan polysulfate sodium having yield of 450 gm and Z \square value -0.006.

5 The 450 gm of the crude Pentosan polysulfate sodium was dissolved in water (20lt) and subjected to the NF membrane of cut off molecular weight of 3000 Dalton, filtration. The NF Membrane system was monitored the rejection of lower molecular weight material with HPLC. After the completion of filtration, the concentrate was subjected to water recovery at 40-50⁰C under reduced pressure up to 340ml. Finally residue was crystallized with methanol (2.7lt) to get the pure Pentosan polysulfate sodium. Filtered the material and dried it at 45-50⁰C under vacuum. The yield of
10 pure Pentosan polysulfate sodium was 170gm having Z \square value 0.006 and Molecular weight of 6543 Dalton.

X-ray powder diffraction pattern is matching with Figure-1.

15 **Example-2**

To a three neck 3lt round bottom flask the pyridine (800ml) and chlorosulfonic acid (200ml) was added slowly at below 40-50⁰ C. The resulting salt was heated to 60-65⁰C then added xylan (100g) and raised the temperature to 75-80⁰ C. After completion of reaction, the reaction mass was cooled 25-30⁰C and added methanol
20 (2500ml) to isolate the pyridine salt of xylan. The isolated pyridine salt of xylan was dissolved in water 500ml and decolorized with chlorine dioxide (200ml), then it was added a mixture of methanol (2000ml) and 33% Sodium hydroxide (200ml). It was then adjusted to pH to neutral with acetic acid, filtered and dried the material at 50-55⁰ C under reduced pressure to get 240 gm of sodium salt of sulfuric acid ester of
25 xylan.

To a three neck 1lt round bottom flask, charged sodium salt of sulfuric acid ester of xylan (200g) in water (600ml). The reaction was heated to 90-100⁰C, then added preheated mixture of 5N sulfuric acid (10ml) and 30% hydrogen peroxide (100ml).

Monitored the reaction with HPLC after completion of reaction, till average molecule weight came about 4000-8000 Dalton cooled the reaction mixture and the solution was adjusted pH to neutral with diluted sodium hydroxide solution. Then the reaction mixture was subjected to NF membrane system.

5

The above reaction mixture was diluted with water (20lt) and subjected to the NF membrane of cut off molecular weight of 3000 Dalton, filtration. The NF Membrane system was monitored the rejection of lower molecular weight material with HPLC. After the completion of filtration, the concentrate was transferred in a single neck

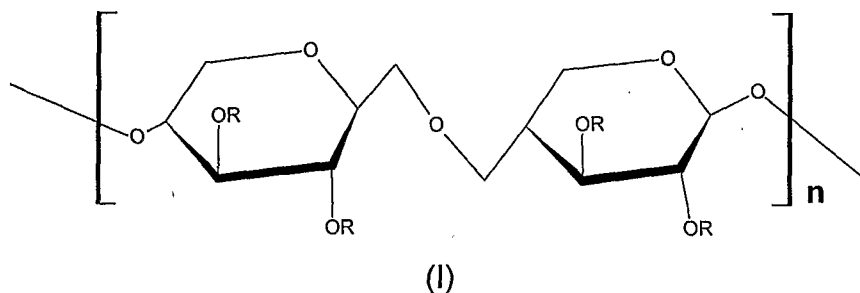
10 round bottom flask and fitted to Lyophilizer (BT4KZL-105) and started the operation of lyophilization. It took about 24 hr to complete the lyophilization. The yield of amorphous form of Pentosan polysulfate was 60gm and Mol wt.-5406 and $Z\eta$ value -0.007.

X-ray powder diffraction pattern is matching with Figure-1.

15

CLAIMS

1. A process for preparation of Pentosan polysulfate of formula (I)



or salts thereof, wherein R represents $-\text{SO}_3\text{Y}$, and Y is at least one member selected from the group consisting of H and a pharmaceutically acceptable cation such as sodium, potassium, and magnesium, comprising steps of:

10

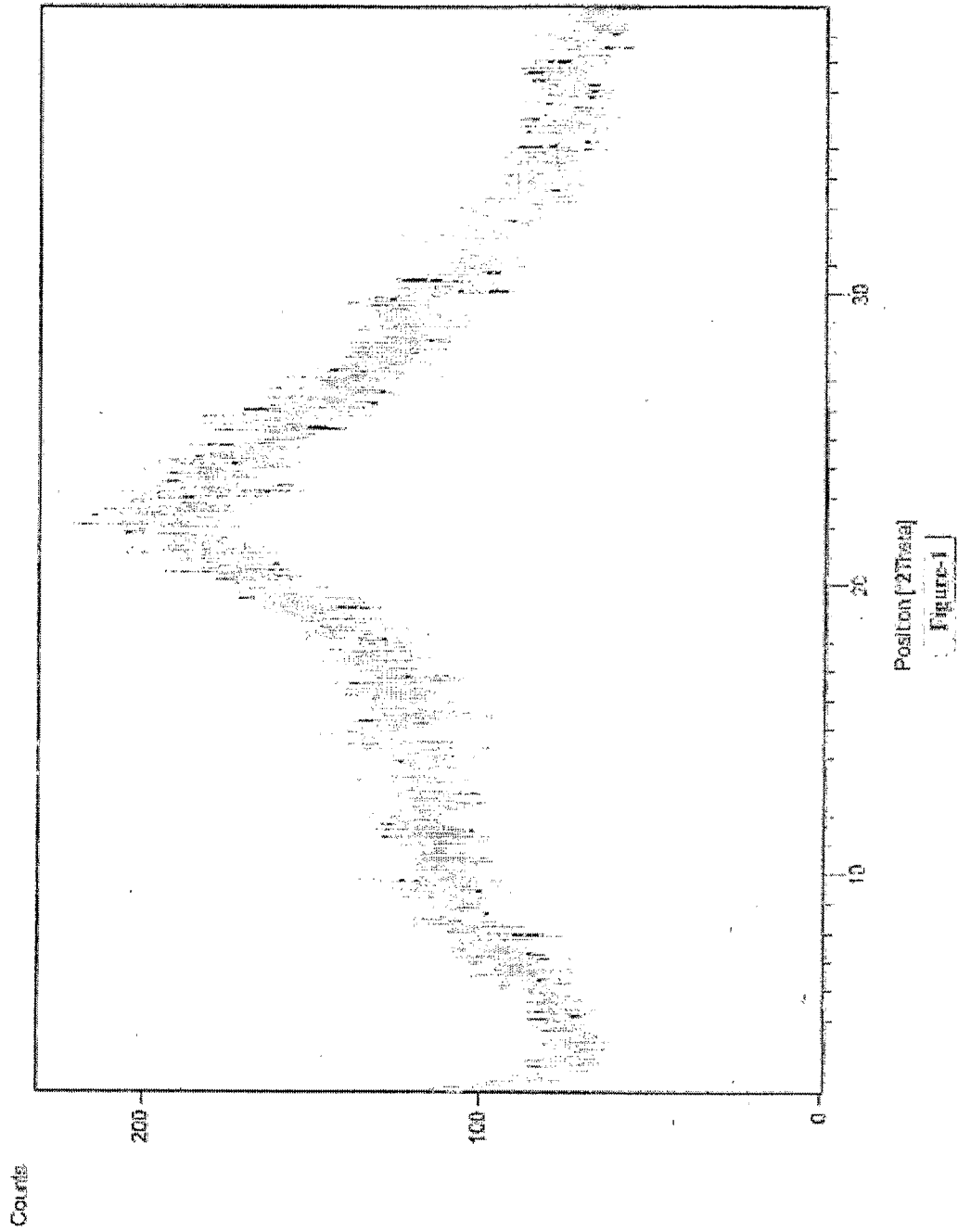
- 15
- i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of alkali in the presence of alcoholic solvent to obtain salt of sulfuric acid ester of xylan
 - ii) oxidizing the salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate of formula (I) or its salt
 - iii) purifying depolymerized crude Pentosan polysulfate of formula (I) or its salt by filtration through NF membrane system
 - iv) crystallizing the product obtained in the step (iii) from alcohol to obtain
- 20

2. A process as claimed in claim 1, wherein said alkali in step (i) is selected from alkali metal salt of carbonate, bicarbonate, hydroxide or mixtures thereof.

3. A process as claimed in claim 1, wherein said alcoholic solvent in step (i) is selected from methanol, ethanol, propanol, isopropanol, butanol or mixtures thereof.
- 5 4. A process as claimed in claim 1, wherein said purification in step (iii) is carried out by dissolving crude Pentosan polysulfate of formula (I) or its salt in water and followed by filtration through NF membrane system.
- 10 5. A process as claimed in claim 1, wherein said alcohol in step (iv) is selected from methanol, ethanol, propanol, isopropanol, butanol or mixtures thereof.
6. A process for preparation of an amorphous form of Pentosan polysulfate Sodium, comprising steps of:
 - 15 i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of sodium hydroxide in the presence of methanol to obtain sodium salt of sulfuric acid ester of xylan
 - ii) oxidizing the sodium salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate sodium
 - 20 iii) purifying depolymerized crude Pentosan polysulfate sodium by filtration through NF membrane system
 - iv) crystallizing the product obtained in the step (iii) from methanol to obtain an amorphous form of Pentosan polysulfate sodium
- 25 7. A process as claimed in claim 6, wherein said purification in step (iii) is carried out by dissolving crude Pentosan polysulfate sodium in water and followed by filtration through NF membrane system.
- 30 8. An amorphous form of Pentosan polysulfate sodium with molecular weight of range 3000 to 10000 Dalton as shown in figure-1.

9. A process for the purification of Pentosan polysulfate of formula (I) or salts thereof, comprising steps of:
- i) dissolving crude Pentosan polysulfate of formula (I) or its salt in water
 - 5 ii) filtering the reaction mixture obtain in the step (i) with NF membrane system
 - iii) crystallizing the resulting product obtained in the step (ii) from alcohol to obtain pure Pentosan polysulfate of formula (I) or its salt
- 10 10. A process as claimed in claim 9, wherein said alcohol in step (iii) is selected from methanol, ethanol, propanol, isopropanol, butanol or mixtures thereof.
11. A process for the purification of Pentosan polysulfate sodium, comprising steps of:
- 15 i) dissolving crude Pentosan polysulfate sodium in water
 - ii) filtering the reaction mixture obtain in the step (i) with NF membrane system
 - iii) crystallizing the resulting product obtained in the step (ii) from alcohol to obtain pure Pentosan polysulfate sodium
- 20 12. A process as claimed in claim 11, wherein said alcohol in step (iii) is selected from methanol, ethanol, propanol, isopropanol, butanol or mixtures thereof.
13. A process for the preparation of Pentosan polysulfate sodium comprising a
25 step of purifying depolymerized crude Pentosan polysulfate sodium by filtration through NF membrane system.
14. A process as claimed in claim 13, wherein said purification is carried out by
30 dissolving crude Pentosan polysulfate sodium in water and followed by filtration through NF membrane system.

15. A process for preparation of amorphous form of Pentosan polysulfate sodium, comprising steps of:
- 5
- i) treating xylan with chlorosulfonic acid in the presence of pyridine followed by addition of sodium hydroxide in the presence of alcoholic solvent to obtain sodium salt of sulfuric acid ester of xylan
 - ii) oxidizing the sodium salt of sulfuric acid ester of xylan with the mixture of H_2SO_4 and 30% H_2O_2 to obtain depolymerized crude Pentosan polysulfate sodium
 - 10 iii) purifying depolymerized crude Pentosan polysulfate sodium by filtration through NF membrane system
 - iv) lyophilizing the product obtained in the step (iii) to obtain amorphous form of Pentosan polysulfate sodium
16. A process as claimed in claim 15, wherein said alcoholic solvent in step (i) is selected from methanol, ethanol, propanol, isopropanol, butanol or mixtures thereof.
17. A process as claimed in claim 15, wherein said purification in step (iii) is carried out by dissolving crude Pentosan polysulfate sodium in water and followed by filtration through NF membrane system.
- 20
18. A process for the purification of Pentosan polysulfate sodium, comprising steps of:
- 25 i) dissolving crude Pentosan polysulfate sodium in water
 - ii) filtering the reaction mixture obtain in the step (i) with NF membrane system
 - iii) lyophilizing the resulting product obtained in the step (ii) to obtain pure Pentosan polysulfate sodium
- 30



INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2007/000198

A. CLASSIFICATION OF SUBJECT MATTER INV. C08B37/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) C08B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CH 290 145 A (VON KAULLA KURT NIKOLAI DR MED [CH]; A WANDER GMBH DR [DE]) 15 April 1953 (1953-04-15)	8
Y	*Patentanspruch, Unteranspruch* examples	1-7,9-18
X	US 2 689 848 A (ELFRIEDE HUSEMANN ET AL) 21 September 1954 (1954-09-21) cited in the application	8
Y	examples 1-8	1-7,9-18
X	EP 0 184 480 A (SANOFI SA [FR]; SCLAVO SPA [IT]) 11 June 1986 (1986-06-11)	8
Y	examples 1-9	1-7,9-18
X	WO 88/00211 A (PHARMACIA AB [SE]) 14 January 1988 (1988-01-14)	8
Y	example 1	1-7,9-18
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<input checked="" type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input checked="" type="checkbox"/>
		See patent family annex.
* Special categories of cited documents :		
A document defining the general state of the art which is not considered to be of particular relevance		*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
E earlier document but published on or after the international filing date		*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
O document referring to an oral disclosure, use, exhibition or other means		*&* document member of the same patent family
P document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 24 January 2008		Date of mailing of the international search report 01/02/2008
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Gerber, Myriam

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2007/000198

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>YUAN Q ET AL: "PILOT-PLANT PRODUCTION OF XYLO-OLIGOSACCHARIDES FROM CORNCOB BY STEAMING, ANZYMATIC HYDROLYSIS AND NANOFILTRATION" JOURNAL OF CHEMICAL TECHNOLOGY AND BIOTECHNOLOGY, WILEY & SONS, CHICHESTER, GB, vol. 79, no. 10, October 2004 (2004-10), pages 1073-1079, XP001235875 ISSN: 0268-2575 abstract</p> <p style="text-align: center;">-----</p>	1-7,9-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IN2007/000198

Patent document cited in search report	Publication date	Patent family member(s)	Publication date																																												
CH 290145	A	15-04-1953	NONE																																												
US 2689848	A	21-09-1954	NONE																																												
EP 0184480	A	11-06-1986	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 25%;">AU</td> <td style="width: 25%;">4984585</td> <td style="width: 25%;">A</td> <td style="width: 25%;">15-05-1986</td> </tr> <tr> <td>CA</td> <td>1247091</td> <td>A1</td> <td>20-12-1988</td> </tr> <tr> <td>DK</td> <td>510585</td> <td>A</td> <td>08-05-1986</td> </tr> <tr> <td>ES</td> <td>8605286</td> <td>A1</td> <td>16-08-1986</td> </tr> <tr> <td>FR</td> <td>2572731</td> <td>A1</td> <td>09-05-1986</td> </tr> <tr> <td>GR</td> <td>852681</td> <td>A1</td> <td>10-03-1986</td> </tr> <tr> <td>JP</td> <td>61197601</td> <td>A</td> <td>01-09-1986</td> </tr> <tr> <td>NZ</td> <td>214094</td> <td>A</td> <td>08-01-1988</td> </tr> <tr> <td>PT</td> <td>81440</td> <td>A</td> <td>01-12-1985</td> </tr> <tr> <td>US</td> <td>4713373</td> <td>A</td> <td>15-12-1987</td> </tr> <tr> <td>ZA</td> <td>8508532</td> <td>A</td> <td>30-07-1986</td> </tr> </table>	AU	4984585	A	15-05-1986	CA	1247091	A1	20-12-1988	DK	510585	A	08-05-1986	ES	8605286	A1	16-08-1986	FR	2572731	A1	09-05-1986	GR	852681	A1	10-03-1986	JP	61197601	A	01-09-1986	NZ	214094	A	08-01-1988	PT	81440	A	01-12-1985	US	4713373	A	15-12-1987	ZA	8508532	A	30-07-1986
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WO 8800211	A	14-01-1988	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 25%;">SE</td> <td style="width: 25%;">453394</td> <td style="width: 25%;">B</td> <td style="width: 25%;">01-02-1988</td> </tr> <tr> <td>SE</td> <td>8603008</td> <td>A</td> <td>08-01-1988</td> </tr> <tr> <td>US</td> <td>4814437</td> <td>A</td> <td>21-03-1989</td> </tr> </table>	SE	453394	B	01-02-1988	SE	8603008	A	08-01-1988	US	4814437	A	21-03-1989																																
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