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Solid State Form of Sugammadex Sodium and Process for Preparation Thereof

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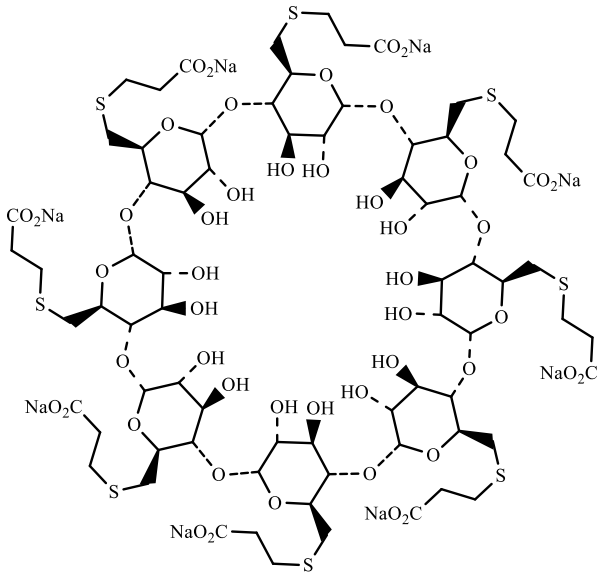
Introduction:

Sugammadex sodium is a modified cyclodextrin having the following structural formula:



Formula-1a

The chemical name of Sugammadex sodium is 6^{A},6^{B},6^{C},6^{D},6^{E},6^{F},6^{G},6^{H}-octakis-S-(2-carboxyethyl)-6^{A},6^{B},6^{C},6^{D},6^{E},6^{F},6^{G},6^{H}-octathio-γ-cyclodextrin sodium salt (1:8).

Sugammadex sodium is approved by USFDA on Dec 15, 2015 and is being sold under the brand name Bridion. It is indicated for the reversal of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide in adults undergoing surgery. It is administered intravenously by injection in the form of a sterile solution. The approved dosage strengths in USA are EQ 200MG BASE/2ML (EQ 100MG BASE/ML) and EQ 500MG BASE/5ML (EQ 100MG BASE/ML).

Provided herein is a solid state form of Sugammadex sodium and process for its preparation.

Solid state form of Sugammadex sodium:

The authors of the present publication provide solid state form of Sugammadex sodium designated herein as crystalline Form-M and process for preparation thereof.

The crystalline Form-M of Sugammadex sodium is characterized by its PXRD (Powder X-Ray Diffraction) pattern having peaks at 5.9, 7.6, 8.4, 12.0, 13.3, 14.1, 15.3, 16.9, 17.9, 18.9, 19.4, 20.3, 21.5, 22.4 and 24.0 ± 0.2º of 2θ.

The measurements of the PXRD peak locations (2θ values) and/or intensity will vary within a margin of error. The margin of error for 2θ values is ± 0.2º.

The crystalline Form-M of Sugammadex sodium described herein is useful for the preparation of various pharmaceutical compositions formulated in a manner suitable for the route of administration to be used.

Experimental procedure:

Preparation of crystalline Form-M of Sugammadex sodium:

Crystalline Form-M of Sugammadex sodium was prepared as follows:

13 gm of Sugammadex sodium was added to a mixture of 26 ml of methanol and 26 ml of water at 25-30ºC under nitrogen atmosphere. The obtained mixture was stirred for 15 min at 25-30ºC. Filtered the mixture through hyflow bed and washed the hyflow bed with 13 ml of water. Heated the filtrate to 55-60ºC and 260 ml of methanol was slowly added to it. Slowly cooled the mixture to 40-45ºC and the resulting precipitate was filtered and washed with methanol. The solid obtained was dried to afford 12.48 gm of Sugammadex sodium as a crystalline solid.

PXRD analysis of the sample obtained was carried out by using the below provided method of analysis.

Method of Analysis and Equipment:

The PXRD analysis was carried out by using BRUKER/D8 ADVANCE diffractometer using CuKα radiation of wavelength 1.5406A° and at a continuous scan speed of 0.03°/min.

Results and Discussion:

The results of PXRD analysis revealed that Sugammadex sodium prepared according to the above described process is crystalline in nature. The resulting PXRD pattern is presented in the following figure-1.

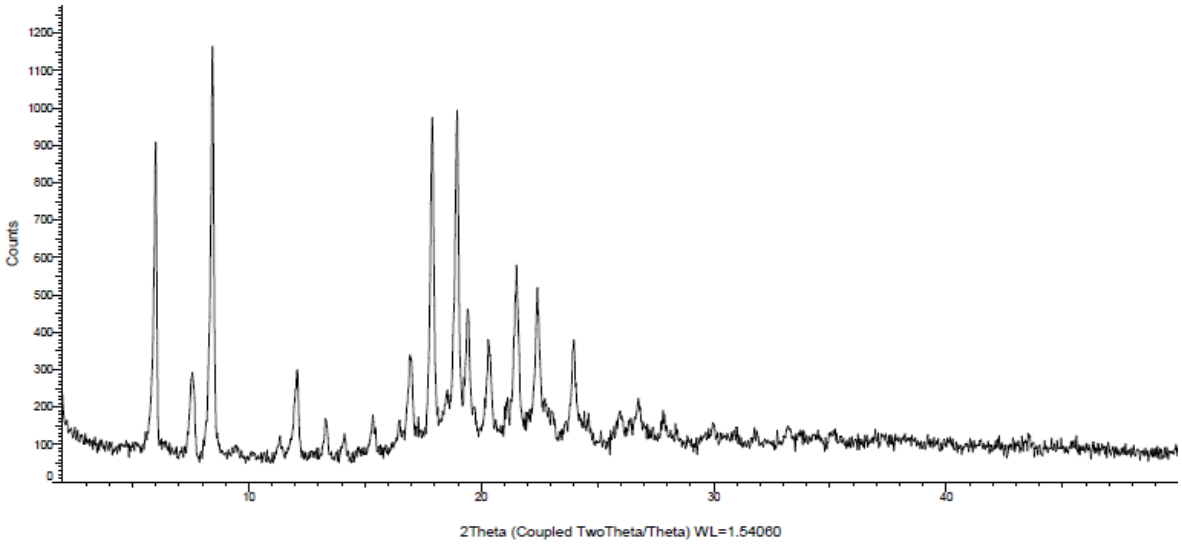


Figure-1: *Powder X-Ray diffraction (PXRD) pattern of Sugammadex sodium form-M*

PXRD peak listing for crystalline Form-M of Sugammadex sodium is provided in Table-1:

Table-1: PXRD peak listing for Sugammadex sodium crystalline Form-M

S.No	2θ value
1	5.9
2	7.6
3	8.4
4	9.4
5	11.3
6	12.0
7	13.3

8	14.1
9	15.3
10	16.5
11	16.9
12	17.9
13	18.5
14	18.9
15	19.4
16	20.3
17	21.1
18	21.5
19	22.4
20	24.0
21	26.0
22	26.7
23	27.8