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(54) Title: METHOD OF THE EFFECTIVE SYNTHESIS OF ACTIVE CHOLINE CHLORIDE INGREDIENT USING HETEROGENEOUS NANOCATALYSTS BASED ON COPPER AND MOLYBDENUM

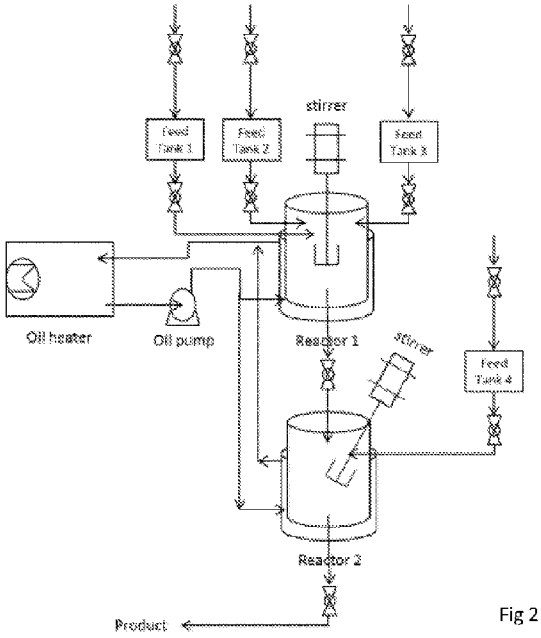

Fig 2

(57) Abstract: In this invention, the active substance of choline chloride is produced using copper and molybdenum based heterogeneous nanocatalysts which is a food supplement for livestock, poultry and aquatic animals and increases productivity. Choline chloride synthesis consists of two steps. The first step is the production of trimethylamine from ammonium chloride and paraformaldehyde, and the second step is the reaction between trimethylamine and chloroethanol, which will produce choline chloride. In the claimed invention, the production method is designed to produce high purity choline chloride from cheap raw materials in the shortest possible time. Choline chloride is an essential compound in the diet of birds and mammals and is required for the proper function of cells. Choline chloride in poultry diets is popular as vitamin B4.

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Method of the effective synthesis of active choline chloride ingredient using heterogeneous nanocatalysts based on copper and molybdenum

Technical Field

[0001] The technical background of this invention is the synthesis of choline chloride as a dietary supplement for livestock, poultry and aquatic animals and increasing productivity.

Background Art

[0002] Three nutrients in animal feed are choline, methionine, and betaine, which are interconnected and deficiency in each, affects the other. Choline has four main functions in the body, which are:

1) Manufacturing and maintaining essential cellular structure
2) An essential role in the metabolism of fat in liver
3) Manufacturing the essential acetylcholine to transferring neural messages
4) Source of Methyl group to formation of methionine from homocysteine and keratin from Guanidinoacetic acid

[0003] A survey of the sources shows that there are two different methods for the production of choline chloride on an industrial scale that their main difference is the type of raw materials.

[0004] The first method, developed by Blackett and Soliday, is the reaction of ethylene oxide gas with the trimethylamine hydrochloride salt. Firstly, trimethylamine reacts with ethylene oxide then converts to choline, and then choline chloride is obtained as the final product from the reaction of choline with hydrochloric acid. Ethylene oxide, as one of the reactants, has a high explosive potential and explodes if safety is not observed during transportation and even during the production stage and leading to harmful effects.

[0005] Considering the potential risk of using ethylene oxide gas, another method is applicable which was invented by Klein and Roland. In this method, ethylene

chloride (2-chloroethanol) reacts with aqueous solution of trimethylamine to produce choline chloride. Ethylene chloride is the product of the reaction of ethylene oxide with hydrochloric acid, which has easier transport and fewer hazards than ethylene oxide.

[0006] An invention called “Production of choline chloride” with the number US2623901A has been registered in the United States, which reveals the production of choline chloride from the reaction of chloroethanol with trimethylamine.

[0007] In this method, ready-to-produce trimethylamine is used, which is one of the substances with some restriction in production possibilities. Trimethylamine can also be produced in a refinery, but its use requires a close site of the production to the refinery. In the claimed method, trimethylamine is produced from cheap and available materials (including ammonium chloride and paraformaldehyde) and then used in the production of choline chloride.

Technical Problem

[0008] One of the most important problems in producing choline chloride with the commercial methods is the risk of using ethylene oxide. This material is highly flammable and can be exploded in transportation, loading and use in the production sector. Due to the cost of transportation, storage and explosion hazards, the method of producing choline chloride from ethylene oxide gas is a high-risk method.

[0009] Also, chloroethanol is a colourless liquid obtained from ethylene oxide gas and can be used as a suitable substitute for synthesis of choline chloride. -On the other hand, the lack of (mono, di and tri) methylamine production units in most petrochemical industries may reduce the synthesis of choline chloride or its production may not be economically viable.

[0010] In the producing method of trimethylamines from methanol and ammonia, the production of other methylamines such as monomethylamines and dimethylamines reduces the production efficiency and the separation of trimethylamines from other parts of the reaction is essential. On the other hand, the produced trimethylamine must enter the next stage of the reaction after

purification, which leads to a waste of time and time spent in the production process.

[0011] In this invention, a method was proposed to produce trimethylamine with higher purity using more available materials such as ammonium chloride, paraformaldehyde and caustic soda in a presence of low concentration of copper-molybdenum nanocatalyst and direct use of synthesized trimethylamine to producing choline chloride.

Solution to Problem

[0012] The synthesis of choline chloride consists of two steps. The first step is the production of trimethylamine from ammonium chloride and paraformaldehyde, and the second step is the reaction between trimethylamine and chloroethanol, which will lead to the production of choline chloride.

[0013] Trimethylamine is the simplest member of the third-type amin group. The appearance of this compound is a colourless gas. Trimethylamine also is a reason for the bad smell in spoiled fish. The most important use of trimethylamine is in the production of choline chloride, in a way that more than 80% of trimethylamine consumption in the world is spent on the production of choline chloride.

[0014] Trimethylamine is usually synthesized in two ways. The first method involves the reaction of methanol with ammonia in the presence of a suitable catalyst, in which along with the production of trimethylamine, other methylamines such as methylamine and dimethylamine are produced, which must be separated from trimethylamine using suitable methods.

[0015] In the second method, triethylamine with high purity is produced from the reaction of ammonium chloride with paraformaldehyde, which does not require a separation process. In this reaction, because other kinds of amines are not produced, the production efficiency of trimethylamine is maximized. The presence of Cu3Mo2O9 nanocatalyst in the reaction leads to an increase in the reaction rate extremely fast and enters the produced trimethylamine to the next stage of production directly, leading to the production of choline chloride in the

shortest possible time. In this invention, the reaction of ammonium chloride with paraformaldehyde was used to produce trimethylamine.

[0016] First, the Cu3Mo2O9 nanocatalyst was prepared by the reaction of nitrate salt of copper and sodium molybdate with a molar ratio (2:3) using hydrothermal method at 180 ℃ and then calcination at 500 ℃. Before starting the reaction, 50 to 100 parts of ammonium chloride and 133 to 250 parts of paraformaldehyde in a two-input balloon (one connected to a one-meter condenser and the other is closed) was added to 200 to 400 parts of 25% weight sodium hydroxide solution containing Cu3Mo2O9 nanocatalyst with a concentration of 0.1 gr/lit.

[0017] Then it was heated for 7-10 hours at a temperature of 140-180 ℃ with stirring. At this stage, the gas is released and the pressure increases with increasing temperature, so the increase in temperature must be controlled.

[0018] The produced Trimethylamine gas was transferred into a balloon containing 50-100 parts of chloroethanol. The solid choline chloride was produced from the reaction between trimethylamine and chloroethanol. The mentioned reaction was done within 7-10 hours and after finishing sodium hydroxide solution, the temperature of the vessel containing ammonium chloride/paraformaldehyde was increased to 100-120 degrees, and the reaction was continued for another hour.

[0019] Then, the balloon with one opening containing white choline chloride precipitation was removed from the system and the resultant precipitation was dissolved in the ethanol, and recrystallized by the evaporation of the solvent. During the reaction, the solutions were stirred by a mechanical stirrer.

[0020] [in terms of impurities, the residual level of trimethylamine in choline chloride is important in assessing "choline chloride analysis". Choline chloride is highly water-absorbent and in some vitamin supplements, based on some studies, it can possibly react with vitamins. If choline chloride is added to the mineral supplement, it has a much better result in terms of maintaining the quality of the product, but it has been proven that choline chloride absorbs the moisture of mineral items and forms an aggregated shape, although these aggregates can easily separate and have no effect on the quality of the product, but they greatly reduce the customer's satisfaction.

Advantageous Effects of Invention

[0021] In the claimed invention, the production method is designed in a way that high purity choline chloride can be obtained from cheap raw materials in the shortest possible time. Among the advantages of this invention, the following can be mentioned:

[0022] 1- Using simple equipment and no need for advanced high-tech equipment to produce the product

[0023] 2- Increasing efficiency of reaction to more than 98%

[0024] 3- Decreasing the time of production to less than 12 hours

[0025] Describing at least one executive method for using an invention

[0026] [choline chloride is an essential ingredient in the diet of birds and mammals and it is required for the suitable function of cells. Choline chloride in poultry diets is known as vitamin B4. Its effects can be the prevention and treatment of fatty liver and ketosis, as well as an increase in milk lactose.

[0027] One of the important roles of choline chloride in the liver is its participation in structure, which is an essential compound for the removal of accumulated fats in the liver around birth. In other words, because all dairy cows are in a negative energy balance during the transition period and subsequently, they are forced to use the stored fat in the body to produce energy, providing the necessary conditions for the removal of excess fat from the liver, is essential for optimal function of this organ, which is the production of glucose and prevention of metabolic diseases.

[0028] This product is used as an additive to corn powder in different proportions to produce livestock, poultry and aquatic feed. The recommended amount of choline chloride varies in different species of broilers, laying hens, mothers, turkeys, ostriches and quails.

Brief Description of Drawings

[0029] Figure 1: schematic of the production process of choline chloride

A. container related to choline chloride as the final product

B. container related to 2-chloroethyl as a precursor

C. container related to paraformaldehyde as a precursor

D. container related to trimethylamine as an intermediate product

E. container related to sodium hydroxide as a reactant in the first stage

F. container related to ammonium chloride as a precursor

G. container related to Cu-MO catalyzer as a precursor

[0030] Figure 2: the figure of the industrial process of the product

[0031] Figure 3: electron microscope image of nanocatalyst

[0032] Figure 4: X-ray diffraction pattern of nanocatalysts

[0033] Figure 5: figure of the infrared spectrum of the choline chloride product

[0034] Figure 6: images of magnetic resonance spectra of the core of the choline chloride product

Industrial Applicability

[0035] This invention in the livestock and aquaculture industry is widely used. This substance is an essential nutrient for the full growth of animals, especially poultry, pigs and pets.

Reference Signs List

[0036] Zeisell, S. H., Dietary choline; biochemistry, physiology and pharmacology. 1981, Ann. Rev. Nutr.,121-1:95.

[0037] Klein HC, Roland K, inventors; Nopco Chemical Co, assignee. Production of choline chloride. United States patent US 2,623,901. 1952 Dec 30.

[0038] Van Eygen C, inventor; UCB SA, assignee. Continuous process for the production of choline chloride. United States patent US 3,373,201. 1968 Mar 12.

[0039] Blackett EG, Soliday AJ, inventors; Wyeth Holdings LLC, assignee. Preparation of choline base and choline salts. United States patent US 2,774,759. 1956 Dec 18.

Claims

[Claim 1] Method of the effective synthesis of active choline chloride ingredient using heterogeneous nanocatalysts comprising:

a. Production of trimethylamine from ammonium chloride and paraformaldehyde

b. The reaction between trimethylamine and chloroethanol

[Claim 2] According to claim 1, Cu3Mo2O9 nanocatalyst was prepared by a reaction of nitrate salts of copper and sodium molybdate with a molar ratio of (2:3) using a hydrothermal method at 180 ℃ and then calcination at 500 ℃.

[Claim 3] According to claim 1, 2, the used trimethylamine gas was obtained from the reaction between 50 to 100 parts of ammonium chloride and 133 to 250 parts of paraformaldehyde in 200 to 400 parts of 25% weight sodium hydroxide solution containing Cu3Mo2O9 nanocatalyst with a concentration of 0.1 gr/lit at a temperature between around 140 to180 - 180 ℃, which was prepared before initiating the reaction and after finishing the sodium hydroxide solution, the temperature of the vessel containing ammonium chloride/paraformaldehyde was increased to 100 to 120 ℃, and the reaction was continued for another hour.

[Claim 4] According to claims 1, 2 and 3, the produced Trimethylamine gas was transferred into a balloon containing 50 to100 parts of chloroethanol and after 7 to10 hours the reaction between trimethylamine and chloroethanol was completed and solid choline chloride was produced.

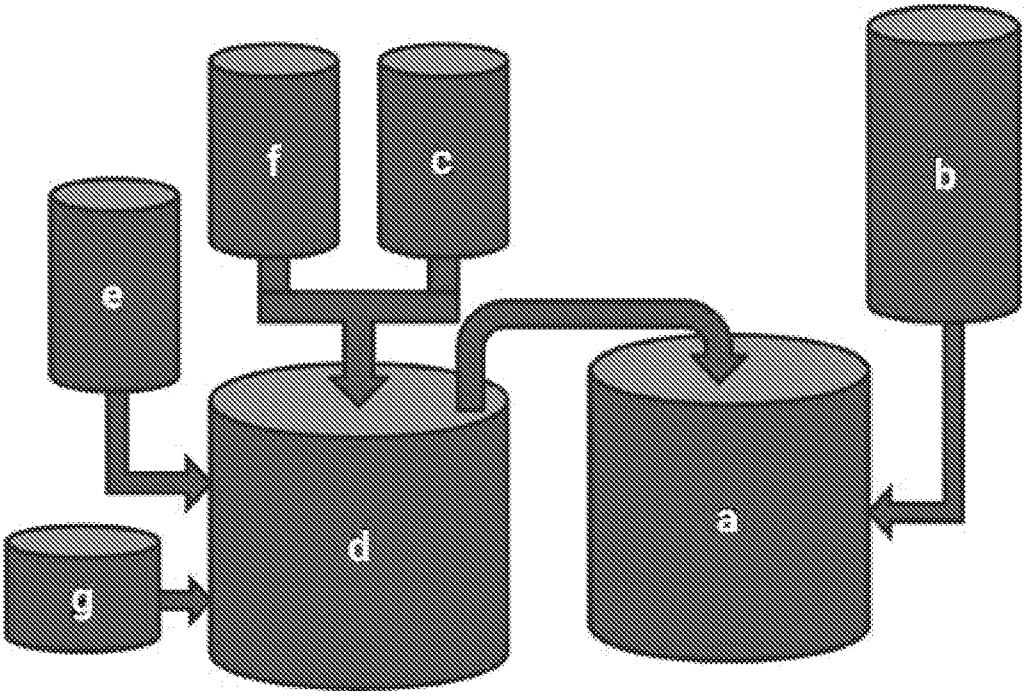
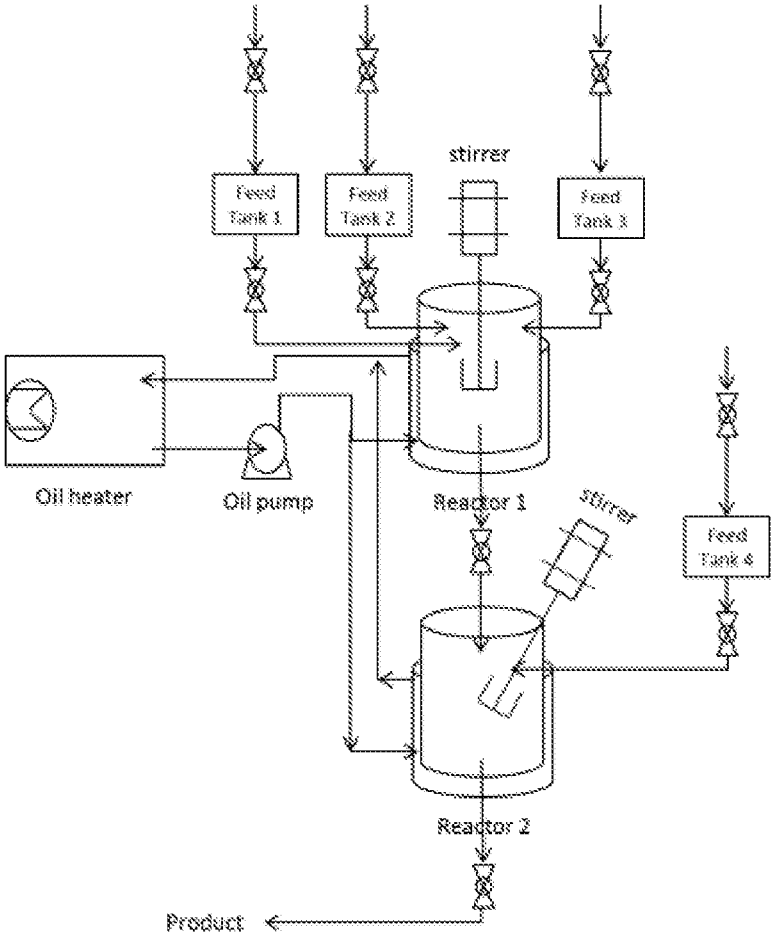


Fig 1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Oil pump
Reactor 1
stirrer
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Reactor 2
Product

Fig 2

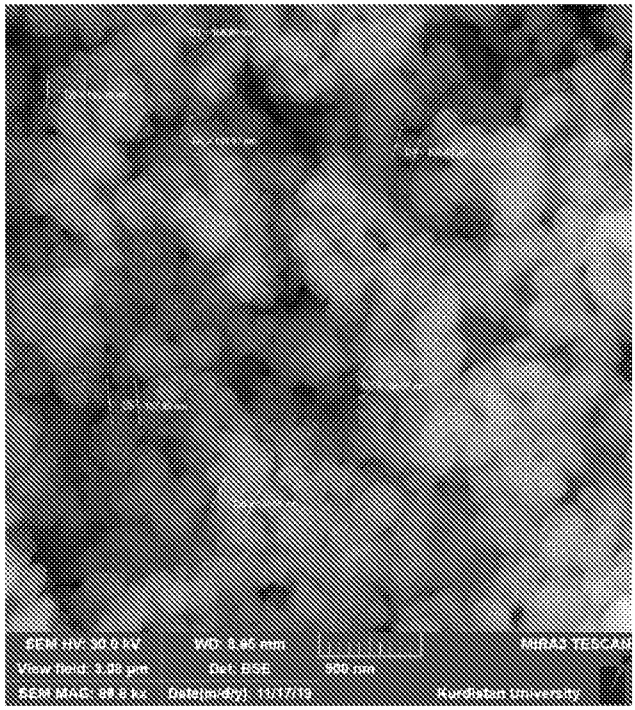
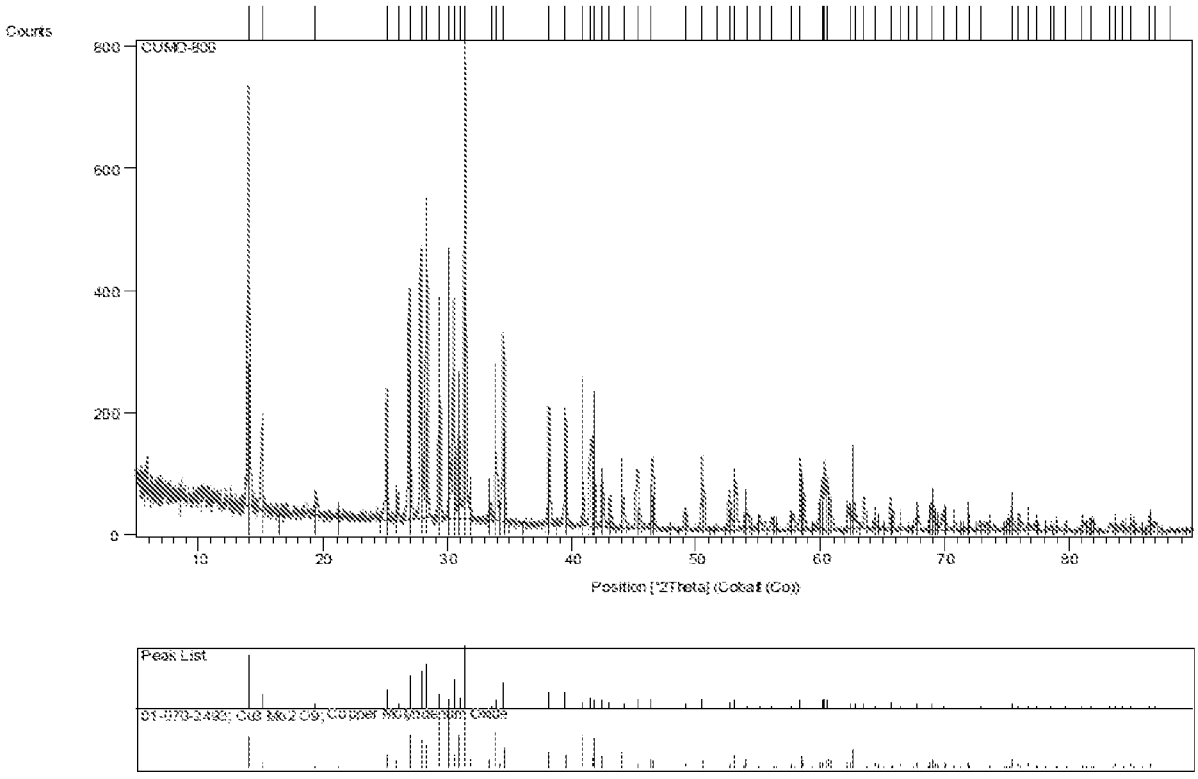


Fig 3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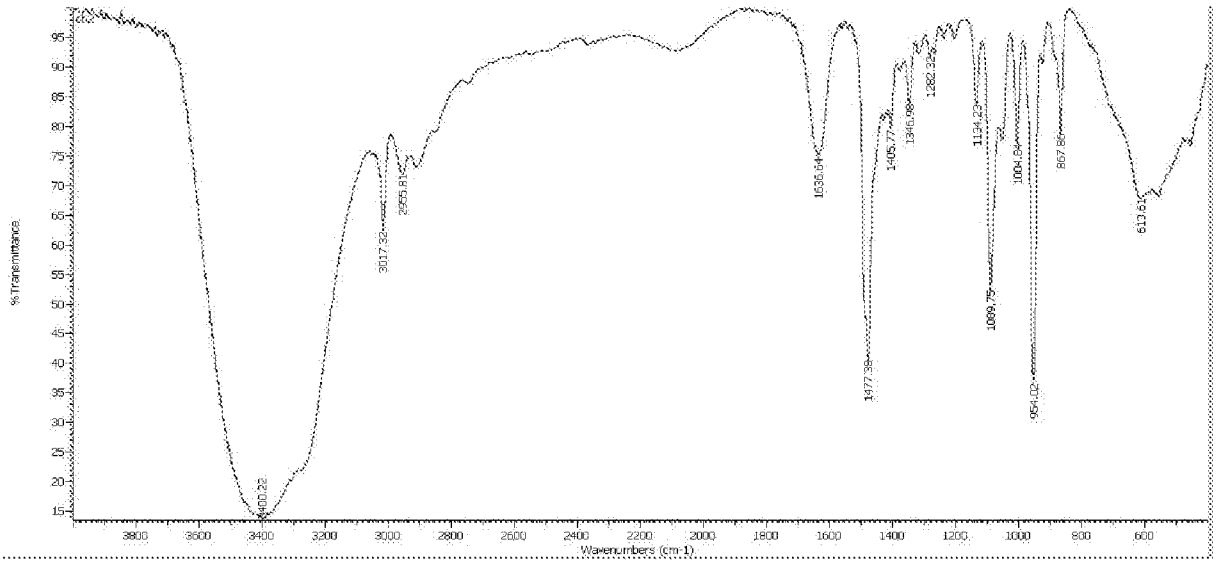
Peak List

Fig 4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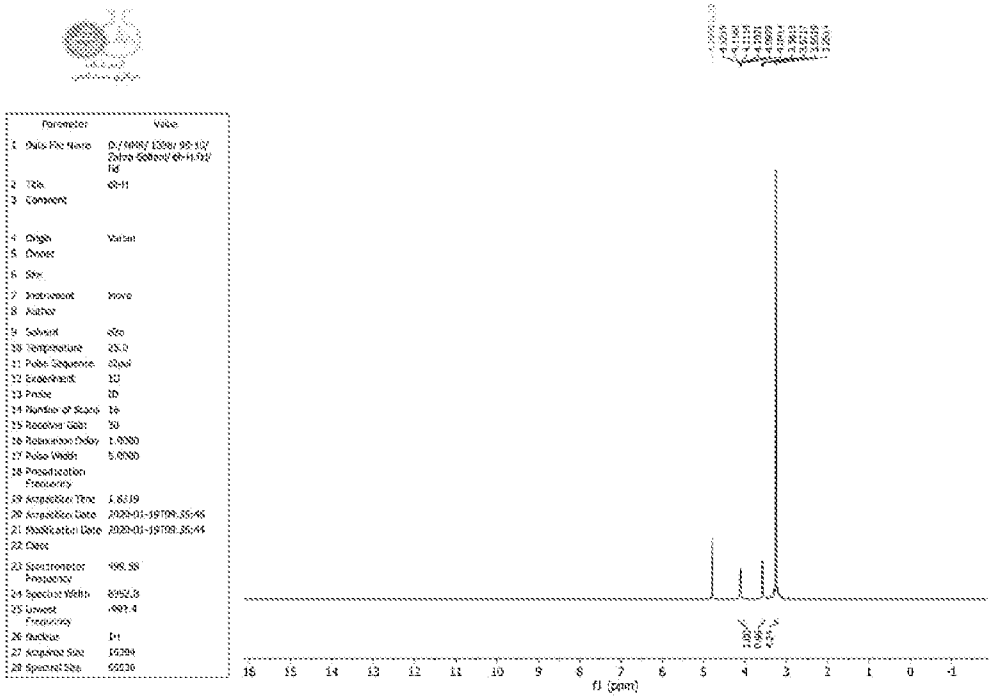
867.86
613.61

Fig 5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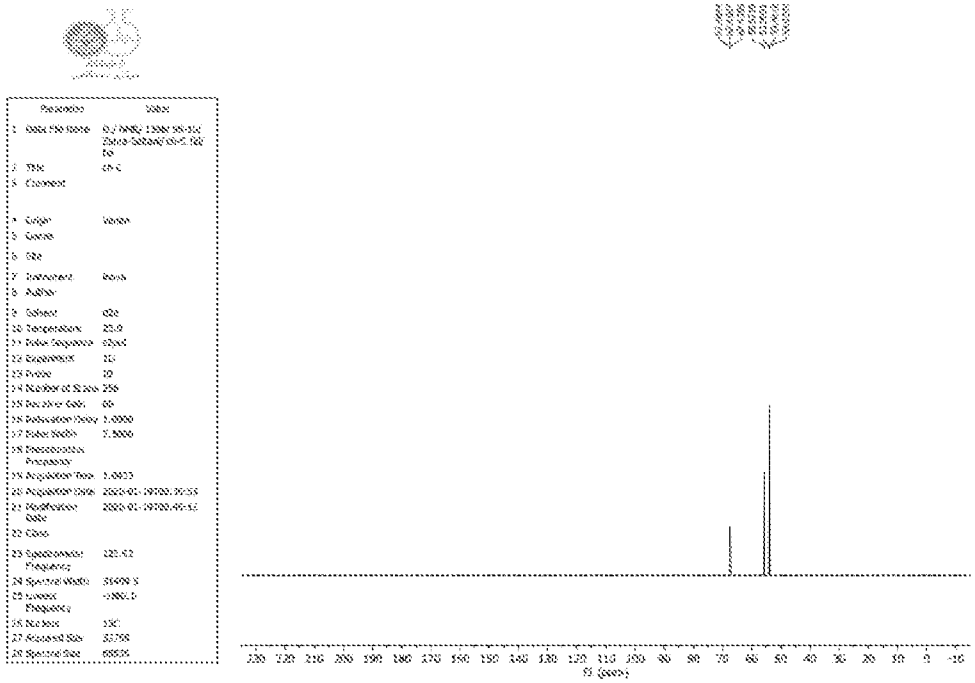
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16 Relaxation Delay 1.0000
17 Pulse Width 7.5000
18 Preacquisition Frequency
19 Acquisition Time 1.0923
20 Acquisition Date 2020-01-19T09:39:55
21 Modification Date 2020-01-19T09:40:52
22 Class
23 Spectrometer Frequency 125.72
24 Spectral Width 31499.5
25 Lowest Frequency -1860.5
26 Nucleus 13C
27 Acquired Size 32768
28 Spectral Size 65536
f1 (ppm)

Fig 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2022/051273

A. CLASSIFICATION OF SUBJECT MATTER
C07C213/04,C07C215/40 Version=2022.01

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)

C07C

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 practicable, search terms used)

PatSeer, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CN 1053057 A (HUBEI PROVINCIAL INST OF CHEMI [CN]) 17 JULY 1991 (FAMILY NONE) Abstract; embodiments 1-5; claims 1-5	1-4
A	EP 0074072 A1 (BASF AG [DE]) 16 MARCH 1983 Abstract; claim 1; example 1	1-4
A	WO 1998018753 A1 (COA L P DU [US]) 07 MAY 1998 Abstract; examples 1-2	1-4
A	ROMAN A. et al., "A Kinetic Model of the Choline Chloride Synthesis", ORGANIC PROCESS RESEARCH & DEVELOPMENT 1999, Vol. 3, pages 357362, https://doi.org/10.1021/op980080f page 357	1-4

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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"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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16-06-2022	16-06-2022
Name and mailing address of the ISA/ Indian Patent Office Plot No.32, Sector 14,Dwarka,New Delhi-110075 Facsimile No.	Authorized officer Sankara Rao Yamala Telephone No. +91-1125300200

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2022/051273

Citation	Pub.Date	Family	Pub.Date
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WO 1998018753 A1	07-05-1998	AU 5156098 A	22-05-1998
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		US 5684191 A	04-11-1997