Process for the purification of dimethyl sulphoxide (DMSO)

The present invention relates to a process for the purification of dimethyl sulphoxide (DMSO) and to the DMSO thus purified.

The DMSO currently available on the market is a product which is already of good purity. Its commercial specifications are generally:

purity	: ≥ 99.7% by chromatography
acidity	: ≤ 0.04 mg KOH/g by potentiometry
crystallization point	: ≥ 18.2°C
visual appearance	: clear
water content	: ≤ 0.15% by weight relative to the total weight
colour (APHA)	: ≤ 10

Patent application FR 2,014,385 describes a process for the preparation of purified DMSO. This process uses a cationic ion exchanger which can be regenerated by a treatment with acids. On the other hand, the DMSO treated with this ion exchanger has a very high water content. Furthermore, the examples indicate the use of a strongly basic resin of the Amberlite IR-A 400 or Merck III type for dimethyl sulphide/DMSO/10% sulphuric acid ternary mixtures, which possibly leads to the neutralization of the acidity but also the introduction of the counterion of the basic resin into the mixture thus treated. Indeed, in this process the purification appears to be afforded essentially by fractional distillation of an aqueous DMSO solution treated beforehand with one or more ion exchangers.

Analyses of traces of metals have now been carried out on several samples (1 to 6) of commercial DMSO, from different sources. These analyses are reported in Table I.

The sodium, iron, potassium, calcium, chromium, copper, nickel and zinc concentrations were measured by

ICP (plasma-torch atomic emission spectrometry, Perkin Elmer machine, Optima 3000 model) and are expressed in ppb (1 ppb = 1 part by weight per billion = 1 μg per kg).

The list of metal elements featured in Table I is not exhaustive as regards the metal elements present in these samples.

TABLE 1

Sample	Metal cations							
	Na	Fe	K	Ca	Cr	Cu	Ni	Zn
1	40	13	60	20	2	10	8	10
2	39	60	3	13	13	< 2	18	3
3	30	40	3	20	12	< 2	15	3
4	30	40	3	14	13	< 2	15	3
5	30	< 1	20	25	< 2	< 2	< 3	< 3
6	70	90	65	55	15	2	25	60
Detection limit	2	1	3	2	2	2	3	3

For certain applications such as, for example, in electronics or in pharmacy, the DMSOs analysed above contain too many metal impurities. In general, a DMSO containing less than 10 ppb of each alkali metal and alkaline-earth metal contaminant would be necessary for most of the uses in the two abovementioned technical fields.

The aim of the present invention is to find a process for the purification of commercial DMSO which is already of good purity but which is, however, of insufficient purity for certain applications.

This aim is achieved by a process for the purification of dimethyl sulphoxide (DMSO) in order to decrease the content of cations other than H^+ therein, characterized in that it includes the following steps:

1) a DMSO in the liquid state and with a low water content is selected,

2) this DMSO is placed in contact with a solid consisting of an ion exchange resin of sulphonic type having its active groups in sulphonic acid (SO_3H) form,

3) the liquid consisting of the purified DMSO with very low contents of cations other than H^+ is then separated from the solid by any suitable known means, in particular filtration, percolation or centrifugation.

Advantageously, the DMSO selected in step 1) has a water content of less than or equal to 0.15% by weight relative to the total weight.

Ion exchange by the use of resins is a very widely used technique for aqueous media and makes it possible in particular to obtain deionised water. The exchange of anions in liquid DMSO medium with a low water content has already been performed by Alan M. Phipps, Anal. Chem. 40(12) pp. 1769-1773, 1968, for the purpose of measuring the amounts of anions bound to the resin under experimental conditions approaching thermodynamic equilibrium.

We have found in the present invention that any cation M^{n+} (n being an integer greater than or equal to 1) is retained and exchanged by $n.H^+$ protons by a

sulphonic resin in protonic form, working with DMSO which has a low water content or is virtually anhydrous.

Preferably, the sulphonic resin is based on a polystyrene-divinylbenzene copolymer. The reason for this is that these resins have a skeleton which resists chemical attack and, in particular, they are not dissolved in DMSO which has a low water content or is virtually anhydrous. These resins are generally defined by their divinylbenzene content. Indeed, the latter determines the degree of crosslinking of the resin and thus the pore size in which the cationic exchange takes place at the atomic level.

Preferably, in the copolymer the divinylbenzene represents from 50 to 60% by weight and the polystyrene from 50 to 40% by weight relative to the total weight of the copolymer, without taking into account the sulphonic groups (SO_3H). This divinylbenzene content ensures good kinetic activity of the exchange of cations M^{n+} by $n.H^+$.

The placing in contact at step 2) takes place at a temperature ranging from 18.45°C (the melting point of DMSO) to 120°C. The temperature of 120°C is the limit temperature of thermal stability of the resins.

Advantageously, the placing in contact of the DMSO in step 2) takes place at a temperature of from 19 to 80°C.

Preferably, this temperature ranges from 20 to 50°C for DMSO.

To have a definition of the quality of the DMSO, which has low water content or is virtually anhydrous, that is capable of being obtained purified by the process according to the invention, iron and sodium have been selected as tracer and indicator elements of the general content of cations M^{n+}, in particular alkali metal and alkaline-earth metal cations.

This DMSO is characterized in that it has a content of Fe cation tracer element of less than or equal to 1 ppb and a content of Na cation tracer element of less than or equal to 2 ppb, the respective detection limit of the method of analysis by plasma-torch atomic

emission spectrometry.

The invention will be better understood with the aid of the following experimental section describing exemplary embodiments of the present invention.

Experimental section

I - Reduction of the content of metals

I-1. Method of analysis:

Method of analysis of traces of metals in DMSO:

- ICP (plasma-torch atomic emission spectrometry): the sample is introduced into a plasma torch, the various elements present are excited and emit photons whose energy is characteristic of the element since it is defined by the electronic structure of the element considered. We routinely used a Perkin Elmer machine (Optima 3000 model).

I-2. Methodology:

Principle: the traces of metals are in M^{n+} form. By passing DMSO through a cation exchange resin, which is itself in H^+ form, the M^{n+} ions are substituted in solution by nH^+.

Since many cation exchange resins exist on the market, we chose to classify the resins according to their kinetic performance (batch reactions) and to test the most advantageous resins continuously. All the resins are:

- in sulphonic form, based on poly(styrene-divinylbenzene), the initial content, before crosslinking, of divinylbenzene and the resin supplier being variable (see Table II),

and in Table III:

- in sulphonic form, based on poly(acrylic-divinylbenzene): C 106,
- in iminodiacetic form, based on poly(styrene-divinylbenzene): S 930,
- in aminophosphonic form, based on poly(styrene-divinylbenzene): S 940,
- in acetic form, based on poly(styrene-divinylbenzene)

I-3. Selection of the resins:

Principle: out of concern to simplify the analyses, sodium and/or iron were chosen as tracers representative of all of the metal impurities contained in the DMSO.

Sodium is characteristic of atmospheric and accidental pollution (dusts, environment) and iron is characteristic of the pollution which may arise in the process (stainless steel unit).

I-4. Reduction of the content of cations (other than H^+) in DMSO.

I-4-1. Batch treatment:

DMSO doped with 1000 ppb of iron and about 1000 ppb of sodium is placed in contact with a cation exchange resin, in H^+ form (2 g of resin per 100 g of DMSO in the form of a liquid) at 25°C. Samples of this liquid are taken over time. It is thus possible to monitor the change in iron and sodium concentrations over time.

All the resins are dried by placing them in suspension in methanol and evaporation under vacuum on a rotary evaporator (90°C, 20×10^2 Pa) until a constant weight is observed.

When the commercial resins are supplied in H^+ form, they are dried as they are.

When they are in Na^+ form, they are exchanged beforehand to obtain the H^+ form in the following manner: 90 ml of resin are placed in a column. 540 ml of 5% HCl are passed through it at a constant flow rate and such that the operation lasts for 30 to 45 min. The resin is then rinsed with deionized water until the exiting water is neutral.

In certain cases (when a plateau is obtained in the case of the sodium concentration, at contents of the order of 200-300 ppb), the resins were exchanged again with 5% HCl.

Table II below collates, for each poly(styrene-divinylbenzene)-based sulphonic resin: the name of the supplier, the commercial reference of the resin, the divinylbenzene content and the iron and sodium contents

of the DMSO as a function of time. The iron and sodium assays were performed by ICP. When the results are below the detection limit inherent in the machine, they are reported as "< detection limit" (1 ppb for iron and 2 ppb for sodium).

Table III collates the results obtained with DMSO placed in contact with other resins.

TABLE II

Example No.	1		2		3		4		5		6	
Supplier	Rohm & Haas		Rohm & Haas		Purolite		Purolite		Bayer		Bayer	
References	Amberlyst® 35		Amberlyst® 36		Hypersol Macronet® MN 500		Hypersol Macronet® MN 500*		K 1221		K 2631	
% DVB	20		12		60		60		4		12	
Time	Fe	Na	Fe	Na	Fe	Na	Fe	Na	Fe	Na	Fe	Na
5 min.	230	< 2	400	200	300	540	< 1	23	800	700	380	220
10 min.	200	< 2	440	20	30	420	< 1	< 2	200	800	170	< 2
15 min.	200	< 2	440	< 2	< 1	300	< 1	< 2	300	400	170	< 2
20 min.	160	< 2	380	< 2	< 1	260	< 1	< 2	300	160	160	< 2
25 min.	160	< 2	370	< 2	< 1	260	< 1	< 2	400	170	170	< 2
30 min.	150	< 2	360	< 2	< 1	240	< 1	< 2	400	80	180	< 2
45 min.	160	< 2	360	< 2	< 1	240	< 1	< 2	120	90	170	< 2
60 min.	150	< 2	300	< 2	< 1	220	nd	nd	60	40	160	< 2
90 min.	160	< 2	260	< 2	< 1	220	nd	nd	40	20	180	< 2
120 min.	160	< 2	200	< 2	< 1	220	nd	nd	40	20	180	< 2

TABLE II (continued)

Example No.	7		8		9		10		11	
Supplier	Mitsubishi		Mitsubishi		Rohm & Haas		Rohm & Haas		Rohm & Haas	
References	Relite®EXC04		Relite®EXC29		XN 1010		XN 1010*		Amberlyst® 35	
% DVB	60		?		50		50		20	
Time	Fe	Na	Fe	Na	Fe	Na	Fe	Na	Fe	Na
5 min.	80	17	80	200	360	360	10	30	130	100
10 min.	20	< 2	20	140	160	320	5	27	80	20
15 min.	20	< 2	20	50	100	320	< 1	13	80	25
20 min.	20	< 2	20	50	60	360	< 1	10	66	10
25 min.	8	< 2	2	40	60	440	< 1	< 2	65	< 2
30 min.	< 1	< 2	8	40	20	400	< 1	< 2	60	< 2
45 min.	< 1	< 2	10	40	nd	nd	nd	nd	nd	nd
60 min.	< 1	< 2	10	30	nd	nd	nd	nd	nd	nd
90 min.	< 1	< 2	nd	nd	nd	nd	nd	nd	nd	nd
120 min.	< 1	< 2	2	20	nd	nd	nd	nd	nd	nd

* resin exchanged again in the laboratory :

nd : not determined

TABLE III

Example No.	12		13		14		15		16	
Supplier	Purolite		Purolite		Purolite		Purolite		Purolite	
References	MN 600		C 160		S930		S940		C106	
Ionic form			Sulphonic		Iminodiacetic		Aminophosphonic		Carboxylic	
Structure	Styrene-divinyl-benzene		Styrene-divinyl-benzene		Styrene-divinyl-benzene		Styrene-divinyl-benzene		Acrylic-divinyl-benzene	
Time	Fe	Na	Fe	Na	Fe	Na	Fe	Na	Fe	Na
0 min.	1460	1330	1500	1400	1270	1360	1390	1330	1430	1350
30 min.	800	1470	57	320	760	1260	64	1120	1430	1360
60 min.	760	1460	37	380	600	1270	< 1	960	1430	1380
90 min.	765	1500	37	400	460	1320	< 1	880	1160	1380
120 min.	760	1500	37	400	430	1340	< 1	800	1090	1360

The preferred resins are those which, in the selection test I-3 above, lead in 30 min. to iron and sodium concentrations below or equal to the detection limits, i.e. 1 ppb for iron and 2 ppb for sodium.

Any resin not featured in Table II but which satisfies the criteria of test I-3 would also be preferred in the present invention.

On examining Table II, it may be seen that the resins Purolite MN 500*, Relite® EXC04 and Rohm & Haas XN 1010* are the most active, and are consequently preferred. Their divinylbenzene percentage is from 50 to 60%.

I-4-2. Continuous treatment:

From the batch results, several continuous tests were carried out.

Test conditions: according to the rules commonly followed by those skilled in the art as regards the column diameter/grain size ratio, the column height/diameter ratio and the linear speed so as not to be diffusion-limited. The resin is suspended in 90 ml of DMSO in a beaker with gentle stirring (to remove the air bubbles) and this suspension is then introduced into a vertical polyethylene column whose lower part is fitted with a polyethylene sinter of porosity 70 μm. The beaker is rinsed with 10 ml of DMSO. Under the sinter, the column is fitted with a PTFE tap. This tap is closed during the filling operation. Once the resin has been loaded onto and packed in the column, the tap is opened and the column is fed continuously with DMSO by means of a pump fitted with a PTFE head. Samples are taken at regular intervals, either manually or using an automatic sampler. All the tubes and joints are made of PTFE. The flasks are made of high-density polyethylene.

I-4-2-1. Example 17

Relite® EXC04 resin

Volume of dry resin: 35 cm^2

Grain size: 0.3 - 0.8 mm

Column diameter: 1.5 cm

Bed height: 21 cm
Flow rate of DMSO: 0.35 l/h
Assay of iron and sodium in the samples by ICP.

Starting with a DMSO containing 10 ppb of sodium and 50 ppb of iron, 35 litres of DMSO containing less than 2 ppb of sodium and 1 ppb of iron (detection limits of each element by this technique) were obtained. The experiment was not continued to the saturation point of the resin.

I-4-2-2. Example 18
Relite® EXC29 resin
Volume of dry resin: 35 cm^3
Grain size: 0.3 - 0.8 mm
Column diameter: 1.5 cm
Bed height: 26 cm
Initial DMSO containing 40 ppb of sodium and 40 ppb of iron.
Flow rate of DMSO: 0.40 l/h
Assay of iron and sodium in the samples by ICP. See Table IV.

Table IV

Volume of DMSO treated in litres	Na (ppb)	Fe (ppb)
0, (starting DMSO)	40	40
1.46	≤ 2	≤ 1
4.06	25	≤ 1

I-4-2-3. Example 19
Hypersol Macronet® MN 500 resin
Volume of dry resin: 35 cm^3
Grain size: 0.3 - 1.2 mm
Column diameter: 1.5 cm
Bed height: 21 cm
Initial DMSO containing 25 ppb of sodium and 78 ppb of

iron
Flow rate of DMSO: about 2 l/h
Assay of iron and sodium in the samples by ICP.

The results are given in Table V below:

Time in h	Volume treated in litres	Na in ppb	Fe in ppb
0	0	25	78
104	208	≤ 2	≤ 1
120	240	20	≤ 1

I-4-2-4. Example 20
Relite® EXC04 resin
Volume of dry resin: 32 cm^3
Grain size: 0.3 - 0.8 mm
Column diameter: 1.5 cm
Bed height: 19 cm
Initial DMSO containing 20 ppb of sodium and 40 ppb of iron
Flow rate of DMSO: about 2 l/h
Assay of iron and sodium in the samples by ICP.

The results are given in Table VI below:

Time in h	Volume treated in litres	Na in ppb	Fe in ppb
0	0	20	40
53	106	≤ 2	≤ 1
77	154	≤ 2	≤ 1

I-4-2-5. Examples 21 and 22.

Hypersol Macronet® MN 500 resin
Volume of dry resin: 31 cm^3
Grain size: 0.3 - 0.8 mm
Internal diameter of the column: 2 cm
Bed height: 10 cm
Initial DMSO: 10 ppb of sodium and 20 ppb of iron
DMSO flow rate: 3.14 l h^{-1} (results - Table VII)
DMSO flow rate: 8.3 l h^{-1} (results - Table VIII)

Table VII

Equivalent volume 1 of DMSO/1 of resin*	Na ppb	Fe ppb
0	< 2	< 1
1700	< 2	< 1
2400	< 2	< 1
4100	< 2	< 1
7200	< 2	25
8948	< 2	26

* volume of DMSO treated per volume of resin, in litres.

Table VIII

Equivalent volume 1 of DMSO/1 of resin*	Na ppb	Fe ppb
0	< 2	< 1
4887	< 2	< 1
6761	< 2	4
11313	< 2	5
13319	5	5
17806	18	24
19613	25	25

* volume of DMSO treated per volume of resin, in litres.

During these tests of Examples 21 and 22, it was verified that the calcium, zinc, magnesium and silicon contents were respectively less than 2, 2, 1 and 2 ppb.

* C L M S *

CLAIMS

1. Process for the purification of dimethyl sulphoxide (DMSO) in order to decrease the content of cations other than H^+ therein, characterized in that it includes the following steps:

1) a DMSO in the liquid state and with a low water content is selected,

2) this DMSO is placed in contact with a solid consisting of an ion exchange resin of sulphonic type having its active groups in sulphonic acid (SO_3H) form,

3) the liquid consisting of the purified DMSO with very low contents of cations other than H^+ is then separated from the solid by any suitable known means, in particular filtration, percolation or centrifugation.

2. Process according to Claim 1, characterized in that the DMSO selected at step 1) has a water content of less than or equal to 0.15% by weight relative to the total weight.

3. Process according to either of Claims 1 and 2, characterized in that the resin is based on a polystyrene-divinylbenzene copolymer.

4. Process according to Claim 3, characterized in that the divinylbenzene represents from 50 to 60% by weight of the copolymer, without taking into account the sulphonic groups $-SO_3H$.

5. Process according to one of Claims 1 to 4, characterized in that the placing in contact of the DMSO at step 2) takes place at a temperature of from 19 to 80°C.

6. Process according to Claim 5, characterized in that the temperature is from 20 to 50°C.

7. DMSO capable of being obtained according to one of Claims 1 to 8, characterized in that it has a content of Fe cation tracer elements of less than or equal to 1 ppb and a content of Na cation tracer elements of less than or equal to 2 ppb, the respective detection limit of the method of analysis by plasma-torch atomic emission spectrometry.

This Sheet Has Been Replaced

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