



(51) International Patent Classification:

C08B 13/00 (2006.01)

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(21) International Application Number:

PCT/US2018/022364

Published:

— with international search report (Art. 21(3))

(22) International Filing Date:

14 March 2018 (14.03.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/472,731

17 March 2017 (17.03.2017)

US

(71) Applicant: DOW GLOBAL TECHNOLOGIES LLC

[US/US]; 2040 Dow Center, Midland, MI 48674 (US).

(72) Inventors: PETERMANN, Oliver; August-Wolff-Strasse

13, 29699 Bomlitz (DE). ZHAO, Jin; 1801 Larkin

Center Drive / Larkin Lab, Midland, MI 48674 (US).

KELLING, Rene; August-Wolff-Strasse 13, 29699 Bom-

litz (DE). SPREHE, Matthias; August-Wolff-Strasse 13,

29699 Bomlitz (DE).

(74) Agent: JOHNSON, Christopher et al.; The Dow Chem-

ical Company, Intellectual Property, P.O. Box 1967, Mid-

land, Michigan 48641-1967 (US).

(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,

CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,

HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP,

KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME,

MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,

OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,

SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,

TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every

kind of regional protection available): ARIPO (BW, GH,

GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,

UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,

TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,

MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,

(54) Title: PROCESS FOR RECOVERING AN ESTERIFIED CELLULOSE ETHER FROM A REACTION PRODUCT MIXTURE

(57) Abstract: A process for recovering an esterified cellulose ether from a reaction product mixture obtained from a reaction of (a) a cellulose ether with (b) an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride, comprises the steps of (i) contacting the reaction product mixture with an aqueous liquid and precipitating the esterified cellulose ether from the reaction product mixture, and (ii) isolating the precipitated esterified cellulose ether from the mixture obtained in step (i). Tackiness of the esterified cellulose ether can be reduced when before or in step (i) a stearic acid salt is dispersed in the reaction product mixture, the aqueous liquid or a combination thereof at a weight ratio of at least 0.04 weights part stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether.



PROCESS FOR RECOVERING AN ESTERIFIED CELLULOSE ETHER FROM A REACTION PRODUCT MIXTURE

FIELD

- 5 The present invention relates to an improved process for recovering an ester of a cellulose ether from a reaction product mixture.

INTRODUCTION

- 10 Esters of cellulose ethers, their uses and processes for preparing them are generally known in the art.

- A common process for producing esterified cellulose ethers is described in WO 2013/148154. Typically a cellulose ether is reacted with an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride in the presence of
15 an aliphatic carboxylic acid and optionally an esterification catalyst.

- Some esterified cellulose ethers have importance uses. Hydroxypropyl methyl cellulose acetate succinate (HPMCAS), hydroxypropyl methyl cellulose acetate (HPMCA) and hydroxypropyl methyl cellulose phthalate (HPMCP) are useful in pharmaceutical dosage forms. HPMCAS is useful as an enteric polymer for pharmaceutical dosage forms.
20 Enteric polymers are those that remain intact in the acidic environment of the stomach. Dosage forms coated with such polymers protect the drug from inactivation or degradation in the acidic environment or prevent irritation of the stomach by the drug.

- In a conventional method of recovering an esterified cellulose ether, such as HPMCAS, HPMCA or HPMCP, from its reaction product mixtures after esterification, cold
25 water is poured to the reaction product mixture in order to initiate the precipitation of the product and to dilute and remove the impurities. However, applying this method, esters of cellulose ethers in the form of a fine powder or granules cannot be obtained because inter-particle coagulation occurs to a very large extent. Esterified cellulose ethers, such as HPMCAS or HPMCA, tend to exhibit a very tacky nature in the reaction product mixture in
30 the presence of an aliphatic carboxylic acid, such as acetic acid, and an alkali metal carboxylate, such as sodium acetate. The inter-particle coagulation prevents water from penetrating between the particles, so that it becomes difficult to effectively remove

impurities like acetic acid, sodium acetate, succinic acid, phthalic acid, unreacted hydroxypropyl methyl cellulose (HPMC) and others. Moreover, additional milling or crushing of the product is required to obtain a granular product.

Several methods have been suggested to address this problem.

5 U.S. Patent No. 4,226,981 and International Patent Application WO 2005/115330 disclose a process for preparing mixed esters of cellulose ethers, such as HPMCAS or HPMCA, by esterifying hydroxypropyl methyl cellulose with succinic anhydride and acetic anhydride in the presence of an alkali carboxylate, such as sodium acetate, as the esterification catalyst and acetic acid as the reaction medium. After completion of the esterification reaction, a large volume of water, specifically 10 times by volume of water, is added to the reaction product mixture so that the reaction product is precipitated. The precipitated product is then subjected to a thorough washing with water to remove impurities and dried to produce a mixed ester in the powdery or granular form.

10 European Patent Application EP 0 219 426 discloses a process for producing HPMCP or HPMCAS, followed by addition of a large amount of water to the reaction product mixture and the precipitate formed in the mixture is collected by filtration and repeatedly washed with water until the washing precipitate is no longer acidic.

US Patent Application Publication No. US 2004/0152886 addresses the need of preventing coagulation of HPMCP particles so that impurities like phthalic acid and acetic acid present between the particles can contact with water and be washed away. US 2004/0152886 suggests increasing the fluidity of the reaction product mixture by adding a fluidization solvent as a post-treatment process, and spraying it into water through a spray nozzle.

25 In International patent application WO 2013/148154, an improved process is described for precipitating an esterified cellulose ether from its reaction product mixture. According to this method a reaction product mixture comprising the esterified cellulose ether is contacted with water and the combination of water and the reaction product mixture is subjected to a shear rate of at least 800 s^{-1} . Substantial coagulation of the particles of the esterified cellulose ether during or after precipitation and during the washing of the esterified cellulose ether can be prevented. A non-tacky finely powdered ester of a cellulose ether is obtained.

30

International patent application WO 2015/041973 discloses a method of improving the separability of an esterified cellulose ether from a washing liquor in which the esterified cellulose ether is suspended for purification purposes after it has been precipitated and separated from the reaction product mixture.

5 Much research effort has been spent by the skilled artisans on those esterified cellulose ethers that are useful for increasing the bioavailability of poorly water-soluble drugs, i.e., the *in vivo* absorption of such drugs by an individual upon ingestion. A common procedure is to form a solid dispersion of the drug in the esterified cellulose ether; the esterified cellulose ether is aimed at reducing the crystallinity of the drug. Known methods
10 for preparing such solid dispersion are by spray-drying or by melt-extrusion. In a melt extrusion process an esterified cellulose ether, a drug and optional additive(s) are blended and subjected to melt-extrusion, such as injection molding, melt casting or compression molding. Melt extrusion is highly desirable because unlike spray-drying no organic solvent is needed. Esterified cellulose ethers which are particularly suitable for melt extrusion have
15 a low glass transition temperature T_g due to their low viscosity and/or specific degrees of ether or ester substitution. Such esterified cellulose ethers are disclosed in International patent applications WO 2014/137778, WO 2014/137777, and 2014/137789 and in US patent applications US 2014/0357681 and US 2016/0095928. Unfortunately, such esterified cellulose ethers exhibit an even more tacky nature than other esterified cellulose ethers in
20 the reaction product mixture in the presence of an aliphatic carboxylic acid, such as acetic acid, and an alkali metal carboxylate, such as sodium acetate.

Hence, there is still the urgent need to find an improved process for recovering esterified cellulose ether from its reaction product mixture. Accordingly, an object of the present invention is to provide a process wherein substantial coagulation of the particles of
25 the esterified cellulose ether after precipitation from the reaction product mixture can be prevented. Another object of the present invention is to provide a process in which substantial coagulation and tackiness of the particles of the esterified cellulose ether during the washing of the esterified cellulose ether can be prevented to improve its handling, transportability and washability during the purification process. Yet another object of the
30 present invention is to provide a process by which a non-tacky finely powdered esterified cellulose ether can be obtained. It would be particularly desirable if one or all these objects

of the present invention were even achieved for esterified cellulose ethers which are particularly tacky after precipitation from the reaction product mixture.

SUMMARY

5 Surprisingly, a process has been found wherein i) coagulation and tackiness of the particles of the esterified cellulose ether during or after precipitation can be reduced, ii) coagulation and tackiness of the particles of the esterified cellulose ether during the washing of the esterified cellulose ether can be reduced whereby its handling, transportability and washability during the purification process is improved and iii) a non-tacky finely powdered
10 ester of a cellulose ether can be obtained.

Accordingly, one aspect of the present invention is a process for recovering an esterified cellulose ether from a reaction product mixture obtained from a reaction of (a) a cellulose ether with (b) an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or
15 tricarboxylic acid anhydride, wherein the process for recovering the esterified cellulose ether comprises the steps of (i) contacting the reaction product mixture with an aqueous liquid and precipitating the esterified cellulose ether from the reaction product mixture, and (ii) isolating the precipitated esterified cellulose ether from the mixture obtained in step (i), wherein before or in step (i) a stearic acid salt is dispersed in the reaction product mixture,
20 the aqueous liquid or a combination thereof at a weight ratio of at least 0.04 weights part stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether.

Another aspect of the present invention is a process for preparing an esterified cellulose ether wherein (a) a cellulose ether is reacted with (b) an aliphatic monocarboxylic
25 acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride in the presence of (c) an aliphatic carboxylic acid and the esterified cellulose ether is recovered from the produced reaction product mixture according to the above-mentioned process.

Yet another aspect of the present invention is a method of reducing the tackiness of an
30 esterified cellulose ether in a process for recovering the esterified cellulose ether from a reaction product mixture obtained from a reaction of (a) a cellulose ether with (b) an

aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride, which method comprises the steps of (i) contacting the reaction product mixture with an aqueous liquid and precipitating the esterified cellulose ether from the reaction mixture, and (ii) isolating the precipitated esterified cellulose ether from the mixture obtained in step (i), wherein before or in step (i) a stearic acid salt is dispersed in the reaction product mixture, the aqueous liquid or a combination thereof at a weight ratio of at least 0.04 weights part stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether.

DESCRIPTION OF EMBODIMENTS

According to the process of the present invention an esterified cellulose ether is recovered as described further below from a reaction product mixture that has been obtained from a reaction of (a) a cellulose ether with (b) an aliphatic monocarboxylic acid anhydride or with a di- or tricarboxylic acid anhydride or with a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride, optionally in the presence of (c) an aliphatic carboxylic acid and optionally (d) an alkali metal carboxylate.

The cellulose ether (a) used as a starting material for the esterification reaction preferably is an alkyl cellulose, hydroxyalkyl cellulose or hydroxyalkyl alkylcellulose. The hydroxyalkoxy groups are typically hydroxymethoxy, hydroxyethoxy and/or hydroxypropoxy groups. Hydroxyethoxy and/or hydroxypropoxy groups are preferred. Preferably a single kind of hydroxyalkoxy group, more preferably hydroxypropoxy, is present in the cellulose ether. The alkoxy groups are typically methoxy, ethoxy and/or propoxy groups. Methoxy groups are preferred. Illustrative of the above-defined cellulose ethers are methylcellulose, ethylcellulose, and propylcellulose; hydroxyethylcellulose, hydroxypropylcellulose, hydroxyethyl methylcellulose, ethyl hydroxyethylcellulose, hydroxymethyl ethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl ethylcellulose, hydroxybutyl methylcellulose, and hydroxybutyl ethylcellulose. A particularly preferred cellulose ether is one having a thermal flocculation point in water, such as, for example, methylcellulose, hydroxypropyl methylcellulose, hydroxyethyl methylcellulose, ethylhydroxy ethylcellulose, and hydroxypropyl cellulose. The cellulose

ether is preferably water-soluble, which means that it has a solubility in water of at least 1 gram, more preferably at least 2 grams, most preferably at least 5 grams in 100 grams of distilled water at 25 °C and 1 atmosphere. More preferably, the cellulose ether is a hydroxypropyl methylcellulose.

5 The cellulose ether used as a starting material for the esterification reaction generally has a viscosity of from 1.20 to 400 mPa·s or from 1.20 to 100 mPa·s, preferably from 1.5 to 50 mPa·s, more preferably from 1.5 to 30 mPa·s, most preferably from 1.5 to 20 mPa·s and in particular from 1.5 to 10 mPa·s, measured as a 2 weight-% aqueous solution at 20 °C according to ASTM D2363 – 79 (Reapproved 2006). The process of the present
10 invention is particularly useful when the cellulose ether that is used as a starting material for the esterification reaction has a viscosity of from 1.5 to 8.0 mPa·s, measured as indicated above. In one preferred embodiment of the invention the cellulose ether that is used as a starting material for the esterification reaction has a viscosity of from 4.0 to 8.0 mPa·s; in another preferred embodiment the cellulose ether has a viscosity of from 1.5 to 2.5 mPa·s,
15 measured as indicated above. Esterified cellulose ethers produced from the latter cellulose ethers are particularly tacky. For these esterified cellulose ethers there is a special need to reduce tackiness.

 The MS(hydroxyalkoxyl) is the average number of moles of hydroxyalkoxyl groups per anhydroglucose unit. The term “hydroxyalkoxyl groups” refers to the hydroxyalkoxyl
20 groups as the constituting units of hydroxyalkoxyl substituents, which either comprise a single hydroxyalkoxyl group or a side chain, wherein two or more hydroxyalkoxy units are covalently bound to each other by ether bonding. Within this definition it is not important whether the terminal hydroxyl group of a hydroxyalkoxyl substituent is further alkylated, e.g. methylated, or not; both alkylated and non-alkylated hydroxyalkoxyl substituents are
25 included for the determination of MS(hydroxyalkoxyl). The average number of hydroxyl groups substituted by alkoxy groups, such as methoxy groups, per anhydroglucose unit, is designated as the degree of substitution of alkoxy groups (DS). In the above-given definition of DS, the term “hydroxyl groups substituted by alkoxy groups” does not only include alkylated hydroxyl groups directly bound to the carbon atoms of the cellulose
30 backbone, but also alkylated hydroxyl groups of hydroxyalkoxy substituents bound to the cellulose backbone.

In a preferred embodiment of the invention the cellulose ether is a hydroxypropyl methylcellulose which has a DS_{methoxyl} of from 1.0 to 2.7, preferably from 1.0 to 2.5, more preferably from 1.0 to 2.3, most preferably of 1.1 to 2.2, and particularly from 1.6 to 2.2, and an $MS_{\text{hydroxypropoxyl}}$ of from 0.05 to 1.30, preferably from 0.10 to 1.20, and more preferably from 0.15 to 1.10. In one preferred embodiment the hydroxypropyl methylcellulose has a $MS_{\text{hydroxypropoxyl}}$ of from 0.15 to 0.50, more preferably from 0.20 to 0.40. In another preferred embodiment hydroxypropyl methylcellulose has an $MS_{\text{hydroxypropoxyl}}$ of from 0.40 to 1.30, more preferably from 0.60 to 1.00. The DS_{methoxyl} and $MS_{\text{hydroxypropoxyl}}$ are determined according to United States Pharmacopeia and National Formulary, Hypromellose (hydroxypropyl methyl cellulose).

The process of the present invention is particularly useful when the cellulose ether that is used as a starting material for the esterification reaction is a hydroxypropyl methylcellulose which has a DS_{methoxyl} of from 1.0 to 2.7, preferably from 1.0 to 2.5, more preferably from 1.0 to 2.3, most preferably of 1.1 to 2.2, and particularly from 1.6 to 2.2, and an $MS_{\text{hydroxypropoxyl}}$ of from 0.40 to 1.30, preferably from 0.40 to 1.20, more preferably from 0.50 to 1.10, most preferably from 0.60 to 1.10, and particularly from 0.60 to 1.00. In this embodiment of the invention the sum of the DS_{methoxyl} and $MS_{\text{hydroxypropoxyl}}$ preferably is at least 1.8, more preferably at least 1.9, most preferable at least 2.5, and preferably up to 3.3, more preferably up to 3.2, most preferably up to 3.1. Esterified cellulose ethers produced from such cellulose ethers are particularly tacky and there is a special need to reduce their tackiness. The DS_{methoxyl} and $MS_{\text{hydroxypropoxyl}}$ are determined as indicated above.

The cellulose ether (a) is reacted with (b) an aliphatic monocarboxylic acid anhydride or with a di- or tricarboxylic acid anhydride or with a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride. Preferred aliphatic monocarboxylic acid anhydrides are selected from the group consisting of acetic anhydride, butyric anhydride and propionic anhydride. Preferred dicarboxylic acid anhydrides are selected from the group consisting of succinic anhydride, maleic anhydride and phthalic anhydride. A preferred tricarboxylic acid anhydride is trimellitic anhydride. A preferred aliphatic monocarboxylic acid anhydride can be used alone; or a preferred di- or tricarboxylic acid anhydride can be used alone; or a preferred aliphatic monocarboxylic acid anhydride can be used in combination with a preferred di- or tricarboxylic acid anhydride.

The production of the following esterified cellulose ethers from the above-mentioned cellulose ethers, aliphatic monocarboxylic acid anhydrides and di- or tricarboxylic acid anhydrides is particularly preferred:

- i) HPMC-XY and HPMC-X, wherein HPMC is hydroxypropyl methyl cellulose, X is A (acetate), or X is B (butyrate) or X is Pr (propionate) and Y is S (succinate), Y is P (phthalate), Y is M (maleate) or Y is T (trimellitate), such as hydroxypropyl methyl cellulose acetate phthalate (HPMCAP), hydroxypropyl methyl cellulose acetate trimellitate (HPMCAT), hydroxypropyl methyl cellulose acetate maleate (HPMCAM) or hydroxypropyl methylcellulose acetate succinate (HPMCAS); or
- ii) hydroxypropyl methyl cellulose phthalate (HPMCP); hydroxypropyl cellulose acetate succinate (HPCAS), hydroxybutyl methyl cellulose propionate succinate (HBMCPPrS), hydroxyethyl hydroxypropyl cellulose propionate succinate (HEHPCPrS); and methyl cellulose acetate succinate (MCAS).

Hydroxypropyl methylcellulose acetate succinate (HPMCAS) is the most preferred esterified cellulose ether. The HPMCAS preferably has a DS_{methoxyl} of from 1.0 to 2.7, more preferably from 1.0 to 2.5, even more preferably from 1.0 to 2.3, most preferably from 1.1 to 2.2, and particularly from 1.6 to 2.2, and an $MS_{\text{hydroxypropoxyl}}$ of from 0.05 to 1.30, preferably from 0.10 to 1.20, and more preferably from 0.15 to 1.10. In one preferred embodiment the hydroxypropyl methylcellulose has a $MS_{\text{hydroxypropoxyl}}$ of from 0.15 to 0.50, more preferably from 0.20 to 0.40. In another preferred embodiment hydroxypropyl methylcellulose has an $MS_{\text{hydroxypropoxyl}}$ of from 0.40 to 1.30, more preferably from 0.60 to 1.00.

The process of the present invention is particularly useful when the produced HPMCAS has a DS_{methoxyl} of from 1.0 to 2.7, more preferably from 1.0 to 2.5, even more preferably from 1.0 to 2.3, most preferably from 1.1 to 2.2 and particularly from 1.6 to 2.2, and an $MS_{\text{hydroxypropoxyl}}$ of from 0.40 to 1.30, preferably from 0.40 to 1.20, more preferably from 0.50 to 1.10, most preferably from 0.60 to 1.10, and particularly from 0.60 to 1.00. In this embodiment of the invention the sum of the DS_{methoxyl} and $MS_{\text{hydroxypropoxyl}}$ preferably is at least 1.8, more preferably at least 1.9, most preferable at least 2.5 and preferably up to 3.3, more preferably up to 3.2, most preferably up to 3.1.

The produced esterified cellulose ether, particularly the HPMCAS, generally has a viscosity of from 1.20 to 400 mPa·s or 1.20 to 100 mPa·s, preferably from 1.5 to 50 mPa·s, more preferably from 1.5 to 30 mPa·s, even more preferably from 1.5 to 20 mPa·s, most preferably from 1.5 to 10 mPa·s, and in particular from 1.5 to 8.0 mPa·s, measured as a 2.0 wt. % solution of the esterified cellulose ether in 0.43 wt. % aqueous NaOH at 20 °C. In one preferred embodiment the produced esterified cellulose ether has a viscosity of from 4.0 to 8.0 mPa·s; in another preferred embodiment the produced esterified cellulose ether has a viscosity of from 1.5 to 2.5 mPa·s, measured as indicated above. The 2.0 % by weight solution of the esterified cellulose ether is prepared as described in "Hypromellose Acetate Succinate, United States Pharmacopeia and National Formulary, NF 29, pp. 1548-1550", followed by an Ubbelohde viscosity measurement according to DIN 51562-1:1999-01 (January 1999).

The esterification of the cellulose ether can be conducted in a known manner, for example as described in U.S. Patent Nos. 3,435,027 and 4,226,981, in the International Patent Applications WO 2005/115330 and WO2013/148154, or in European Patent Application EP 0 219 426. The esterification of the cellulose ether is preferably conducted in (c) an aliphatic carboxylic acid as a reaction medium, such as acetic acid, propionic acid, or butyric acid. The reaction medium can comprise minor amounts of other solvents or diluents which are liquid at room temperature and do not react with the cellulose ether, such as halogenated C₁-C₃ derivatives, such as dichloro methane, or dichloro methyl ether, but the amount of the aliphatic carboxylic acid is preferably more than 50 percent, more preferably at least 75 percent, and even more preferably at least 90 percent, based on the total weight of the reaction medium. Most preferably the reaction medium consists of an aliphatic carboxylic acid. The esterification reaction is generally conducted in the presence of 100 to 2,000 parts by weight of an aliphatic carboxylic acid as the reaction medium per 100 parts by weight of the cellulose ether. The molar ratio [aliphatic carboxylic acid / anhydroglucose units of cellulose ether] generally is from [4.9 / 1.0] to [20.0 / 1.0], preferably from [5.5 / 1.0] to [17.0 / 1.0], more preferably from [5.7 / 1.0] to [15.0 / 1.0].

The esterification reaction is preferably conducted in the presence of (d) an esterification catalyst, more preferably in the presence of an alkali metal carboxylate, such as sodium acetate or potassium acetate. The amount of the alkali metal carboxylate is

preferably 20 to 200 parts by weight of the alkali metal carboxylate per 100 parts by weight of the cellulose ether. If an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride are used for esterifying the cellulose ether, the two anhydrides may be introduced into the reaction vessel at the same time or separately one after the other.

5 The amount of each anhydride to be introduced into the reaction vessel is determined depending on the desired degree of esterification to be obtained in the final product, usually being 1 to 10 times the stoichiometric amounts of the desired molar degree of substitution of the anhydroglucose units by esterification. If an anhydride of an aliphatic monocarboxylic acid is used, the molar ratio between the anhydride of an aliphatic monocarboxylic acid and
10 the anhydroglucose units of the cellulose ether generally is 0.6 or more, and preferably 0.8 or more. The molar ratio between the anhydride of an aliphatic monocarboxylic acid and the anhydroglucose units of the cellulose ether generally is 8 or less, preferably 6 or less, and more preferably 4 or less. If an anhydride of a dicarboxylic acid is used, the molar ratio between the anhydride of a dicarboxylic acid and the anhydroglucose units of cellulose
15 ether generally is 0.1 or more, and preferably 0.13 or more. The molar ratio between the anhydride of a dicarboxylic acid and the anhydroglucose units of cellulose ether generally is 1.5 or less, and preferably 1 or less. The molar number of anhydroglucose units of the cellulose ether utilized in the process of the present invention can be determined from the weight of the cellulose ether used as a starting material, by calculating the average
20 molecular weight of the substituted anhydroglucose units from the DS(alkoxyl) and MS(hydroxyalkoxyl).

 The mixture is generally heated at 60 °C to 110 °C, preferably at 70 to 100 °C, for a period of time sufficient to complete the reaction, that is, typically from 2 to 25 hours, more typically from 2 to 8 hours. The cellulose ether as the starting material is not always soluble
25 in the aliphatic carboxylic acid, but can only be dispersed in or swollen by the aliphatic carboxylic acid, especially when the degree of substitution in the cellulose ether is relatively small. The esterification reaction can take place even with such a dispersed or swollen cellulose ether and, as the esterification reaction proceeds, the cellulose ether under reaction generally dissolves in the reaction medium, to finally give a homogeneous solution.

30 The resulting reaction product mixture comprises the esterified cellulose ether, typically an aliphatic carboxylic acid used as a reaction medium, typically a reaction

catalyst, such as an alkali metal carboxylate, typically residual amounts of one or more esterification agents and by-products, such as an aliphatic monocarboxylic acid and/or a di- or tricarboxylic acid. The resulting reaction product mixture generally comprises from 3 to 60, typically from 7 to 35 weight percent of the esterified cellulose ether; from 10 to 95, typically from 20 to 70 weight percent of an aliphatic carboxylic acid, from 1 to 50; typically from 5 to 30 weight percent of a reaction catalyst, such as an alkali metal carboxylate, and from 0.1 to 50, typically from 2 to 40 weight percent of minor components, such as non-reacted anhydrides of an aliphatic monocarboxylic acid and/or of a di- or tricarboxylic acid.

10 In step (i) of the process of the present invention the above-described reaction product mixture is contacted with an aqueous liquid and the esterified cellulose ether is precipitated from the reaction product mixture.

In a preferred embodiment of step (i) of the process of the present invention, the reaction product mixture is first diluted with a first amount of aqueous liquid without precipitating the esterified cellulose ether from the reaction product mixture and the diluted reaction product mixture is then contacted with a second amount of aqueous liquid to precipitate the esterified cellulose ether from the diluted reaction product mixture. The first amount of aqueous liquid is optional, i.e., it can be zero. Preferably the first amount of aqueous liquid is from 0.2 to 10 weight parts, more preferably from 0.5 to 5 weight parts, and most preferably from 1 to 3.5 weight parts of aqueous liquid per weight part of cellulose ether used for esterification. The first amount of aqueous liquid is used to quench the reaction product mixture. When the reaction product mixture is quenched, remaining amounts of anhydrides in the reaction product mixture are hydrolyzed and the esterification reaction is stopped. However, such quenching should be conducted without precipitating the esterified cellulose ether from the reaction product mixture. Preferably the second amount of aqueous liquid, that is used to precipitate the esterified cellulose ether from the diluted reaction product mixture, is from 5 to 400 weight parts, more preferably from 8 to 300 weight parts, most preferably from 10 to 100 weight parts, and particularly from 12 to 50 weight parts of aqueous liquid per weight part of cellulose ether used for esterification.

30 In another embodiment of step (i) of the process of the present invention, the reaction product mixture is directly contacted i.e., without intermediate dilution step, with an

aqueous liquid to precipitate the esterified cellulose ether from the reaction product mixture. Preferably, the amount of aqueous liquid that is used to precipitate the esterified cellulose ether from the reaction product mixture is from 5 to 400 weight parts, more preferably from 8 to 300 weight parts, most preferably from 10 to 100 weight parts, and particularly from 12 to 50 weight parts of aqueous liquid per weight part of cellulose ether used for esterification.

The aqueous liquid used in step (i) may comprise a minor amount of an organic liquid diluent; however, the aqueous liquid should comprise at least 55, preferably at least 65, more preferably at least 75, most preferably at least 90, and particularly at least 95 weight percent of water, based on the total weight of the liquid components of the aqueous liquid. Preferably the aqueous liquid is water.

The reaction product mixture comprising the esterified cellulose ether generally has a temperature of from 60 °C to 110 °C. It can be contacted with the aqueous liquid without previous cooling of the reaction product mixture. The temperature of the aqueous liquid preferably is from 1 to 98 °C, more preferably from 10 to 90 °C. When an optional dilution, i.e., quenching step is carried out, the first amount of liquid used for quenching and the second amount of liquid used for precipitation each independently preferably have a temperature of from 1 to 98 °C, more preferably from 10 to 90 °C.

Step (i) can be conducted under low shear, but it is preferably conducted as described in the International patent application WO 2013/148154, wherein the combination of aqueous liquid and the reaction product mixture is subjected to a shear rate of at least 800 s⁻¹, preferably at least 1500 s⁻¹, more preferably at least 3000 s⁻¹, and most preferably at least 8000 s⁻¹. The shear rate is generally up to 300,000 s⁻¹, typically up to 200,000 s⁻¹, more typically up to 100,000 s⁻¹ and most typically up to 50,000 s⁻¹.

It is an essential feature of the present invention that before or in step (i) a stearic acid salt is dispersed in the reaction product mixture, the aqueous liquid or a combination thereof at a weight ratio of at least 0.04 weight part stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether. The amount of the stearic acid salt is preferably at least 0.06 weight parts, more preferably at least 0.08 weight parts, even more preferably at least 0.10 weight parts, and most preferably at least 0.12 weight parts of stearic acid salt per weight part of cellulose ether utilized for producing the esterified

cellulose ether. The amount of the stearic acid salt is generally up to 2 weight parts, preferably up to 1.0 weight part, more preferably up to 0.5 weight parts, and most preferably up to 0.2 weight parts of stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether.

5 Preferred stearic acid salts are ammonium, alkali metal or alkaline earth metal salts of stearic acid, such as ammonium stearate, trimethylammonium stearate, sodium stearate, potassium stearate, calcium stearate or magnesium stearate. Sodium stearate is the most preferred stearic acid salt.

10 The stearic acid salt can added in one or more portions or continuously to disperse it in the reaction product mixture, the aqueous liquid or a combination thereof. Preferably, the stearic acid salt is dispersed in the aqueous liquid before contacting the reaction product mixture with the aqueous liquid. It is important that the stearic acid salt is dispersed rather than dissolved in the reaction product mixture, the aqueous liquid or a combination thereof.

15 When the stearic acid salt is directly added as a solid to the reaction product mixture, the reaction product mixture should have a temperature that the stearic acid salt is dispersed but not dissolved therein. In this case the reaction product mixture preferably has a temperature of from 50 to 65 °C, more preferably from 50 to 60 °C. However, preferably the stearic acid salt is not added as a solid to the reaction product mixture.

20 In a preferred embodiment of the invention, the stearic acid salt is dispersed in the aqueous liquid which is used for diluting the reaction product mixture, and/or in the aqueous liquid which is used for precipitating the esterified cellulose ether from the reaction product mixture. More preferably, the stearic acid salt is dispersed in the aqueous liquid which is used for precipitating the esterified cellulose ether from the reaction product mixture.

25 Alternatively, the stearic acid salt can be added as a separate aqueous dispersion to the reaction product mixture before or preferably during contacting the reaction product mixture with an aqueous liquid which is used for precipitating the esterified cellulose ether from the reaction product mixture. The aqueous liquid should have a temperature that the stearic acid salt is dispersed but not dissolved therein. The aqueous dispersion of the stearic acid salt, preferably has a temperature of from 1 to 65 °C, more preferably from 5 to 55 °C, and 30 most preferably from 10 to 40 °C, regardless whether this aqueous dispersion of the stearic acid salt is a separate aqueous dispersion, an aqueous dispersion used for diluting the

reaction product mixture without precipitation or an aqueous dispersion used for precipitating the esterified cellulose ether from the reaction product mixture.

In step (ii) of the process of the present invention the precipitated esterified cellulose ether is isolated from the remainder of the mixture obtained in step (i). Step (ii) of isolating
5 the precipitated esterified cellulose ether from the mixture obtained in step (i) can be conducted in a known manner in a separation device, such as by centrifugation or filtration or upon settling by decantation or a combination thereof. Preferred separation devices are filtration devices or decanters, such as vacuum filters, pressure filters, screen and filter centrifuges or decanter centrifuges.

10 The isolated esterified cellulose ether is preferably purified by steps (iii) suspending the isolated esterified cellulose ether in an aqueous liquid to provide a suspension, and (iv) recovering the esterified cellulose ether from the suspension of step (iii).

In step (iii) the isolated esterified cellulose ether is preferably contacted with 2 to 400 weight parts, more preferably 3 to 300 weight parts, and most preferably 4 to 150 weight
15 parts of aqueous liquid per weight part of esterified cellulose ether. The aqueous liquid may additionally comprise a minor amount of an organic liquid diluent, as described further above. The esterified cellulose ether is preferably suspended in the aqueous liquid under agitation, such as high-shear or low-shear blending.

Step (iv) can be conducted in a known manner in a separation device, such as by
20 centrifugation or filtration or upon settling by decantation. Preferred separation devices are filtration devices or decanters, such as vacuum filters, pressure filters, screen and filter centrifuges or decanter centrifuges or a combination thereof. In step (iv) a purified esterified cellulose ether is obtained.

The sequence of steps (iii) and (iv) as described above can be repeated once or several
25 times, preferably once to 5 times. E.g., a sequence of step (iii), step (iv), step (iii) and step (iv) can be conducted.

In at least one suspension step (iii) preferably the esterified cellulose ether is contacted with an aqueous liquid that has a temperature of from 25 °C to 95 °C, preferably from 30 °C to 85 °C. In this suspension step (iii), stearic acid salt is dissolved in the aqueous
30 liquid and separated from the esterified cellulose ether. When the sequence of steps (iii) and (iv) as described above is conducted several times, preferably in the last suspension step

- (iii) the aqueous liquid has the above-mentioned temperature of from 35 °C to 95 °C, preferably from 40 °C to 85 °C. When the sequence of steps (iii) and (iv) is conducted several times, the aqueous liquid utilized in the other suspension steps (iii) generally has temperature of from 3 °C to 95 °C, preferably from 10 °C to 90 °C, and more preferably from 20 °C to 70 °C, and most preferably from 30 °C to 50 °C.

Some embodiments of the invention will now be described in detail in the following Examples.

EXAMPLES

- Unless otherwise mentioned, all parts and percentages are by weight. In the Examples the following test procedures are used.

Content of ether and ester groups in Hydroxypropyl Methyl Cellulose Acetate Succinate (HPMCAS)

- The content of ether groups in the esterified cellulose ether is determined in the same manner as described for “Hypromellose”, United States Pharmacopeia and National Formulary, USP 35, pp 3467-3469.

- The ester substitution with acetyl groups ($-\text{CO}-\text{CH}_3$) and the ester substitution with succinoyl groups ($-\text{CO}-\text{CH}_2-\text{CH}_2-\text{COOH}$) are determined according to Hypromellose Acetate Succinate, United States Pharmacopeia and National Formulary, NF 29, pp. 1548-1550. Reported values for ester substitution are corrected for volatiles (determined as described in section “loss on drying” in the above HPMCAS monograph).

Properties of hydroxypropyl methylcellulose (HPMC)

- The content of methoxyl groups and of hydroxypropoxyl groups in HPMC are determined as described for “Hypromellose”, United States Pharmacopeia and National Formulary, USP 35, pp 3467-3469.

- The viscosity of HPMC is determined as a 2% by weight solution in water at 20°C by Ubbelohde viscosity measurement as described in the United States Pharmacopeia (USP 35, “Hypromellose”, pages 423 – 424 and 3467 - 3469 and in ASTM D-445 and ISO 3105 referenced therein).

Example 1I. Production of a Reaction Product Mixture comprising HPMCAS

514.07 g of glacial acetic acid, 204.73 g (dry content 97.69 g) of a hydroxypropyl
5 methylcellulose (HPMC), and 43.54 g of sodium acetate (water free) were introduced into a
glass reactor with an inner diameter of 147 mm and intensively mixed by use of a MIG™
stirrer (two blade axial flow impeller, company EKATO, Schopfheim, Germany) with an
outer diameter of 120 mm running at 300 rpm. The HPMC had a viscosity of about
5 mPa•s, measured as a 2 % aqueous solution at 20 °C, a degree of methoxyl substitution,
10 DS(methoxyl), of 2.0, and a hydroxypropoxyl substitution, MS(hydroxypropoxyl), of 0.86.

The glass reactor was put in a heated bath and the mixture was heated to 85° C. 33.84
g of succinic anhydride and 147.69 g of acetic anhydride were added. Mixing was continued
for 30 minutes, then 130.61 g of sodium acetate (water free) were added. Intense mixing
was continued for 3 hours to effect esterification while the bath temperature was kept at 85°
15 C.

II: Recovering HPMCAS according to the Process of the Present Invention

The hot reaction mixture as obtained in Procedure I above was quenched by addition
of 318.46 g of water. The water had room temperature. The reaction mixture was diluted by
20 quenching and became less viscous.

HPMCAS was precipitated from the diluted reaction mixture by adding a suspension
of 30 g of sodium stearate in 2 L of water having room temperature.

During the addition of water for quenching and the aqueous sodium stearate
suspension for precipitation, the content of the glass reactor was stirred using the above
25 described MIG™ stirrer running at 300 rpm.

HPMCAS was isolated from the resulting suspension via filtration. A filter cake was
obtained that was only very slightly tacky.

The filter cake was re-suspended 6 times in 3 L of water having room temperature
using an Ultra-Turrax stirrer S50-G45 (rotor diameter 36 mm, inner stator diameter 38 mm)
30 running at 5000 rpm. HPMCAS was again isolated from the resulting suspension via
filtration. The resulting filter cake after the last washing step was not tacky.

One portion of the filter cake was dried at 55 °C. Another portion of the filter cake was washed 5 times with 1.5 L of water having a temperature of 40 °C to remove residual amounts of stearate before drying at 55 °C.

5 Examples 2 and 3

Example 1 was repeated, except that in Example 2 a suspension of 22 g of sodium stearate in 2 L of water was used and in Example 3 a suspension of 15 g of sodium stearate in 2 L of water was used for precipitation. In each example HPMCAS was isolated from the resulting suspension via filtration. The tackiness of the filter cake after precipitation was
10 higher in Example 3 than in Example 2, which in turn was higher than in Example 1. However, even in Example 3 the filter cake after precipitation and after the last washing step with water having room temperature was less tacky than the filter cake in the corresponding steps in Comparative Examples A and B below.

15 Comparative Example A:

I. Production of a Reaction Product Mixture comprising HPMCAS

A reaction product mixture comprising HPMCAS was produced as in Example 1.

II. Recovering HPMCAS Without Sodium Stearate Addition

20 The hot reaction product mixture as obtained in Procedure I was quenched by addition of 318.46 g of water. The water had room temperature. The reaction product mixture was diluted by quenching and became less viscous.

HPMCAS was precipitated from the diluted reaction product mixture by adding 2 L of water having room temperature.

25 During the addition of water for quenching and precipitation, the content of the glass reactor was stirred using the above described MIG™ stirrer running at 300 rpm.

HPMCAS was isolated from the resulting suspension via filtration. An extremely tacky filter cake was obtained that had the appearance of chewing gum.

The filter cake was re-suspended in 3 L of water having room temperature using an
30 Ultra-Turrax stirrer S50-G45 (rotor diameter 36 mm, inner stator diameter 38 mm) running at 5000 rpm. HPMCAS was again isolated from the resulting suspension via filtration. The

resulting filter cake was clearly tacky.

The filter cake was again re-suspended in 3 L of water having room temperature. Again the Ultra-Turrax stirrer S50-G45 running at 5000 rpm was used for re-suspension. HPMCAS was isolated from the resulting suspension via filtration. The resulting filter cake
5 was still slightly tacky.

The filter cake was thoroughly washed 5 times by re-suspension at 200 rpm in 3 L of water having room temperature and separation by filtration. The resulting filter cake was still slightly tacky. After the final filtration HPMCAS was dried at 40°C.

10 Comparative Example B

Example 1 was repeated, except that a suspension of 5 g of sodium stearate in 2 L of water was used for precipitation. HPMCAS was isolated from the resulting suspension via filtration. The obtained filter cake was very tacky. The filter cake after the last washing step with water having room temperature was only slightly less tacky than in Comparative
15 Example A.

Comparative Example C

Example 1 was repeated, except that HPMCAS was precipitated from the diluted reaction mixture by first adding 30 g of sodium stearate to the diluted reaction mixture
20 having a temperature of 85 °C wherein the sodium stearate dissolved and then adding 2 L of water having room temperature. HPMCAS was isolated from the resulting suspension via filtration. The obtained filter cake was very tacky as in Comparative Example A.

Comparative Example D

25 Example 1 was repeated, except that a suspension of 30 g of sodium oleate in 2 L of water having a temperature of 2 °C was used for precipitation. (Water having a temperature of 2 °C was used to avoid dissolution of sodium oleate and to enable a direct comparison with Example 1 wherein sodium stearate was not dissolved but dispersed in water.) HPMCAS was isolated from the resulting suspension via filtration. The obtained filter cake
30 was very tacky as in Comparative Example A.

Comparative Example E

Example 1 was repeated, except that a solution of 30 g of sodium oleate in 2 L of water having room temperature was used for precipitation. HPMCAS was isolated from the resulting suspension via filtration. The obtained filter cake was very tacky as in

5 Comparative Example A.

Comparative Example F

Example 1 was repeated, except that HPMCAS was precipitated from the diluted reaction mixture by adding a solution of 30 g of sodium stearate in 2 L of water having a
10 temperature of 90 °C. (Water having a temperature of 90 °C was used to enable dissolution of the sodium stearate in water). The obtained filter cake was very tacky as in Comparative Example A.

Comparative Example G

15 Example 1 was repeated, except that a suspension of 10 g of sodium lauryl sulfate (SLS) in 2 L of water having room temperature was used for precipitation. HPMCAS was isolated from the resulting suspension via filtration. The obtained filter cake was very tacky as in Comparative Example A.

Claims

1. A process for recovering an esterified cellulose ether from a reaction product mixture obtained from a reaction of (a) a cellulose ether with (b) an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride, wherein the process comprises the steps of

(i) contacting the reaction product mixture with an aqueous liquid and precipitating the esterified cellulose ether from the reaction product mixture, and

(ii) isolating the precipitated esterified cellulose ether from the mixture obtained in step (i),

wherein before or in step (i) a stearic acid salt is dispersed in the reaction product mixture, the aqueous liquid or a combination thereof at a weight ratio of at least 0.04 weights part stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether.

2. The process of claim 1 wherein the stearic acid salt is dispersed in the aqueous liquid before contacting the reaction product mixture with the aqueous liquid.

3. The process of claim 1 or 2 wherein the reaction product mixture has been obtained from a reaction of (a) a cellulose ether with (b) an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride in the presence of a combination of (c) an aliphatic carboxylic acid and (d) an alkali metal carboxylate.

4. The process of any one of claims 1 to 3 wherein the stearic acid salt is an ammonium, alkali metal or alkaline earth metal salt of stearic acid.

5. The process of any one of claims 1 to 4 wherein before or in step (i) from 0.06 to 2 weight parts of stearic acid salt are dispersed per weight part of cellulose ether utilized for producing the esterified cellulose ether.

6. The process of claim 5 wherein before or in step (i) from 0.10 to 0.5 weight parts of stearic acid salt are dispersed per weight part of cellulose ether utilized for producing the esterified cellulose ether.
7. The process of any one of claims 1 to 6 wherein the esterified cellulose ether is an esterified alkyl cellulose, a hydroxyalkylcellulose or a hydroxyalkyl alkylcellulose.
8. The process of any one of claims 1 to 7 wherein the cellulose ether has a viscosity of from 1.5 to 50 mPa·s, measured as a 2 weight-% aqueous solution at 20 °C.
9. The process of any one of claims 1 to 8 wherein the aliphatic monocarboxylic acid anhydride is selected from the group consisting of acetic anhydride, butyric anhydride and propionic anhydride.
10. The process of any one of claims 1 to 9 wherein the di- or tricarboxylic acid anhydride is selected from the group consisting of succinic anhydride, maleic anhydride and phthalic anhydride.
11. The process of any one of claims 1 to 10 wherein hydroxypropyl methylcellulose is esterified with succinic anhydride and acetic anhydride to produce hydroxypropyl methyl cellulose acetate succinate.
12. The process of claim 11 wherein the hydroxypropyl methylcellulose acetate succinate has a DS_{methoxyl} of from 1.0 to 2.7 and an $MS_{\text{hydroxypropoxyl}}$ of from 0.40 to 1.30.
13. A process for preparing an esterified cellulose ether wherein (a) a cellulose ether is reacted with (b) an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride in the presence of (c) an aliphatic carboxylic acid and the esterified cellulose ether is recovered from the produced reaction product mixture according to the process of any one of claims 1 to 12.

15. A method of reducing the tackiness of an esterified cellulose ether in a process for recovering the esterified cellulose ether from a reaction product mixture obtained from a reaction of (a) a cellulose ether with (b) an aliphatic monocarboxylic acid anhydride or a di- or tricarboxylic acid anhydride or a combination of an aliphatic monocarboxylic acid anhydride and a di- or tricarboxylic acid anhydride, which method comprises the steps of

(i) contacting the reaction product mixture with an aqueous liquid and precipitating the esterified cellulose ether from the reaction mixture, and

(ii) isolating the precipitated esterified cellulose ether from the mixture obtained in step (i),

wherein before or in step (i) a stearic acid salt is dispersed in the reaction product mixture, the aqueous liquid or a combination thereof at a weight ratio of at least 0.04 weights part stearic acid salt per weight part of cellulose ether utilized for producing the esterified cellulose ether.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/022364

A. CLASSIFICATION OF SUBJECT MATTER
INV. C08B13/00
ADD.

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 practicable, search terms used)

EPO-Internal, BIOSIS, COMPENDEX, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2015/041973 A1 (DOW GLOBAL TECHNOLOGIES LLC [US]) 26 March 2015 (2015-03-26) cited in the application claims; examples -----	1-13,15
A	WO 2015/156922 A1 (DOW GLOBAL TECHNOLOGIES LLC [US]) 15 October 2015 (2015-10-15) claims; examples -----	1-13,15



Further documents are listed in the continuation of Box C.



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

"E" earlier application or patent but published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

"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

"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

17 May 2018

Date of mailing of the international search report

30/05/2018

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Vaccaro, Eleonora

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/022364

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2015041973 A1	26-03-2015	CN 105829352 A	03-08-2016
		EP 3049446 A1	03-08-2016
		JP 6073526 B2	01-02-2017
		JP 2016532725 A	20-10-2016
		KR 20160044586 A	25-04-2016
		US 2016222133 A1	04-08-2016
		WO 2015041973 A1	26-03-2015

WO 2015156922 A1	15-10-2015	CN 106163564 A	23-11-2016
		EP 3129060 A1	15-02-2017
		JP 6254719 B2	27-12-2017
		JP 2017517592 A	29-06-2017
		KR 20160142329 A	12-12-2016
		US 2017173159 A1	22-06-2017
		WO 2015156922 A1	15-10-2015
