

Description

The invention relates to a method of preparing solid forms of administration of lactulose from lactulose syrup.

Netherlands Patent Specifications No. 129368, 147784 and 150161 relate to methods of preparing solid forms of administration of lactulose. They relate to lactulose in powder form obtained by spray-drying lactulose syrup. The drawback of this method is that spray-drying of lactulose requires a vehicle. As a result of this the content of lactulose in the final product will always be lower than in the syrup. Moreover, the use of a vehicle has a price-raising effect.

Furthermore, German Patent Specification No. 2717707 relates to a method of preparing a solid form of administration of lactulose by heating a water-containing solution of lactulose which also comprises auxiliary substances for the caramelisation, while evaporating water so that upon cooling solid lactulose is obtained in a caramelised form. A drawback of this product is that, as a result of the caramelisation, it experiences a strong colouring, which is undesired for a pharmaceutical product. Also in the French Patent Application, published under no. 2139789, an auxiliary agent is added prior to the drying procedure, viz. konnyaku powder.

Finally it is possible to prepare lactulose in a crystalline form. However, the crystallisation of lactulose is rather laborious and the crystalline final product comprises a certain quantity of the solvent used (customarily methanol). Crystallisation increases the cost of production considerably. Another, equally laborious and time-consuming method of preparing crystal-containing lactulose is described in the Japanese Patent Application, published under no. 61-104800. This method includes the addition of seed crystals to the concentrate and the kneading thereof, followed by aging at elevated temperature of the dough obtained. It is the object of the present invention to provide a method of preparing a solid form of administration of lactulose from lactulose syrup, which method is simple and does not exhibit the drawbacks of the known methods mentioned hereinbefore.

According to the present invention this object can be achieved, (a) by evaporating the lactulose syrup, without mixing it with a konnyaku solution and in the absence of a caramelization auxiliary agent, to a water content of at most 10%, (b) by thereupon cooling the evaporated lactulose syrup to approximately 20 °C without kneading and aging, and (c) by finally grinding and sieving, or breaking the solid lactulose, obtained after cooling.

The evaporation of the lactulose syrup is generally carried out by rapidly heating it for a short period of time. This is preferably done under reduced pressure so that evaporation can be carried out at lower temperatures, for example, in a rotating film evaporator. The pressure at which evaporation is carried out depends on the apparatus used. The syrup is preferably evaporated to a water content of from 2 to 6%.

The evaporated hot, thick syrup, the final temperature of which when leaving the evaporator is chosen above the solidification point of lactulose (about 100 °C), is then cooled to approximately 20 °C. During this step the syrup solidifies.

By cooling in such a manner, that is, as rapidly as possible or in a conditioned, moisture free space so that hardly any or no water can be attracted from the air, it is achieved that the evaporated solid syrup does not stick so that further mechanical processing is possible. It has been found that the quality of the final product both after rapid cooling in air, and after slow cooling in a conditioned space is comparable.

It has further been found that the formulation properties of the final product, for example, dissolving rate and hygroscopicity, depend on the particle size chosen.

The starting syrup is preferably evaporated to a water content of from 2 to 6% at an as low as possible temperature and pressure so as to prevent decomposition.

The invention will now be described in greater detail with reference to the ensuing specific example.

EXAMPLE

Evaporation was carried out in a rotating film evaporator of the brand Canzler having a heated surface area of 1 m². The parameters to be adjusted are:

- 1) ϕ_v , i.e. the quantity supplied to the evaporator (feed stream)
- 2) P_v , i.e. the pressure in the evaporator
- 3) P_s , i.e. the pressure of the steam to heat the evaporator, and/or the steam temperature.

These parameters should be chosen to be so that the final temperature (T_a) of the evaporated syrup emanating from the evaporator is higher than the solidification point of about 100 °C.

$\phi_v(m^3/h)$	$P_v(10^5 Pa)$	$P_s(10^5 Pa)$	$T_a(^{\circ}C)$	% H ₂ O
0.0980	0.57	1.73	124	5 - 5.7
0.054	0.60	2.80	138	2.9 - 4

The cooling of the evaporated syrup was carried out

- a) on a cooling roller (drum flaker) so that flakes are obtained
- b) with a rotadropformer + cooling belt so that pastils are obtained
- c) by slowly cooling in a closed pot.

Solid lactulose which does substantially not stick and can readily be subjected to further processing, for example, grinding or breaking, sieving and packaging, is obtained both after accelerated cooling in air and after slow cooling in a closed pot.

Claims

1. A method of preparing a solid form of administration of lactulose from lactulose syrup, characterized in that lactulose syrup, without mixing it with a konnyaku solution and in the absence of a caramelization auxiliary agent, is evaporated to a water content of at most 10%, after which the evaporated lactulose syrup, without kneading and aging, is cooled to approximately 20 ° C, and the solid lactulose obtained is finally ground and sieved, or broken.
2. A method as claimed in Claim 1, characterized in that evaporation is carried out rapidly and for a short period of time at a reduced pressure.
3. A method as claimed in Claim 1, characterized in that the evaporated syrup is cooled in air as rapidly as possible or in a conditioned (moisture-free) space.
4. A method as claimed in Claim 1, characterized in that the syrup is evaporated, in a rotating film evaporator to a water content of from 2 to 6%.

Patentansprüche

1. Verfahren zur Herstellung einer festen Verabreichungsform von Lactulose aus Lactulose-Sirup, dadurch gekennzeichnet, daß Lactulose-Sirup, ohne Mischen desselben mit einer Konnyaku-Lösung und in Abwesenheit eines Karamelisierungshilfsmittels, auf einen Wassergehalt von höchstens 10 % eingedampft wird, wonach der eingedampfte Lactulose-Sirup, ohne Kneten und Alterung, auf ungefähr 20 ° C abgekühlt wird, und schließlich die erhaltene feste Lactulose gemahlen und gesiebt oder zerkleinert wird.
2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß das Eindampfen rasch und während eines kurzen Zeitraums unter vermindertem Druck durchgeführt wird.
3. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß der eingedampfte Sirup so rasch wie möglich an der Luft oder in einem klimatisierten (feuchtigkeitsfreien) Raum abgekühlt wird.
4. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß der Sirup in einem Rotationsverdampfer auf einen Wassergehalt von 2 bis 6 % eingedampft wird.

Revendications

1. Procédé de préparation d'une forme solide d'administration de lactulose à partir de sirop de lactulose, caractérisé en ce qu'on fait évaporer le sirop de lactulose, sans le mélanger avec une solution de konnyaku et en l'absence d'un agent auxiliaire de caramélisation, jusqu'à une teneur en eau d'au plus 10%, après quoi on refroidit à environ 20 ° C le sirop de lactulose évaporé, sans pétrissage ni vieillissement, et enfin on broie et on tamise, ou on concasse, le lactulose solide obtenu.
2. Procédé selon la revendication 1, caractérisé en ce qu'on conduit l'évaporation rapidement et pendant une courte durée à pression réduite.

$\phi_v(\text{m}^3/\text{h})$	$P_v(10^5 \text{ Pa})$	$P_s(10^5 \text{ Pa})$	$T_a(^{\circ}\text{C})$	% H ₂ O
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Solid lactulose which does substantially not stick and can readily be subjected to further processing, for example, grinding or breaking, sieving and packaging, is obtained both after accelerated cooling in air and after slow cooling in a closed pot.

Claims

1. A method of preparing a solid form of administration of lactulose from lactulose syrup, characterized in that lactulose syrup, without mixing it with a konnyaku solution and in the absence of a caramelization auxiliary agent, is evaporated to a water content of at most 10%, after which the evaporated lactulose syrup, without kneading and aging, is cooled to approximately 20 °C, and the solid lactulose obtained is finally ground and sieved, or broken.
2. A method as claimed in Claim 1, characterized in that evaporation is carried out rapidly and for a short period of time at a reduced pressure.
3. A method as claimed in Claim 1, characterized in that the evaporated syrup is cooled in air as rapidly as possible or in a conditioned (moisture-free) space.
4. A method as claimed in Claim 1, characterized in that the syrup is evaporated in a rotating film evaporator to a water content of from 2 to 6%.

Patentansprüche

1. Verfahren zur Herstellung einer festen Verabreichungsform von Lactulose aus Lactulose-Sirup, dadurch gekennzeichnet, daß Lactulose-Sirup, ohne Mischen desselben mit einer Konnyaku-Lösung und in Abwesenheit eines Karamelisierungshilfsmittels, auf einen Wassergehalt von höchstens 10 % eingedampft wird, wonach der eingedampfte Lactulose-Sirup, ohne Kneten und Alterung, auf ungefähr 20 °C abgekühlt wird, und schließlich die erhaltene feste Lactulose gemahlen und gesiebt oder zerkleinert wird.
2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß das Eindampfen rasch und während eines kurzen Zeitraums unter vermindertem Druck durchgeführt wird.
3. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß der eingedampfte Sirup so rasch wie möglich an der Luft oder in einem klimatisierten (feuchtigkeitsfreien) Raum abgekühlt wird.
4. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß der Sirup in einem Rotationsverdampfer auf einen Wassergehalt von 2 bis 6 % eingedampft wird.

Revendications

1. Procédé de préparation d'une forme solide d'administration de lactulose à partir de sirop de lactulose, caractérisé en ce qu'on fait évaporer le sirop de lactulose, sans le mélanger avec une solution de konnyaku et en l'absence d'un agent auxiliaire de caramélisation, jusqu'à une teneur en eau d'au plus 10%, après quoi on refroidit à environ 20 °C le sirop de lactulose évaporé, sans pétrissage ni vieillissement, et enfin on broie et on tamise, ou on concasse, le lactulose solide obtenu.
2. Procédé selon la revendication 1, caractérisé en ce qu'on conduit l'évaporation rapidement et pendant une courte durée à pression réduite.



3. Procédé selon la revendication 1, caractérisé en ce qu'on refroidit le sirop évaporé aussi rapidement que possible à l'air ou dans un espace conditionné (dépourvu d'humidité).
4. Procédé selon la revendication 1, caractérisé en ce qu'on fait évaporer le sirop dans un évaporateur à film rotatif jusqu'à une teneur en eau de 2 à 6%.

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