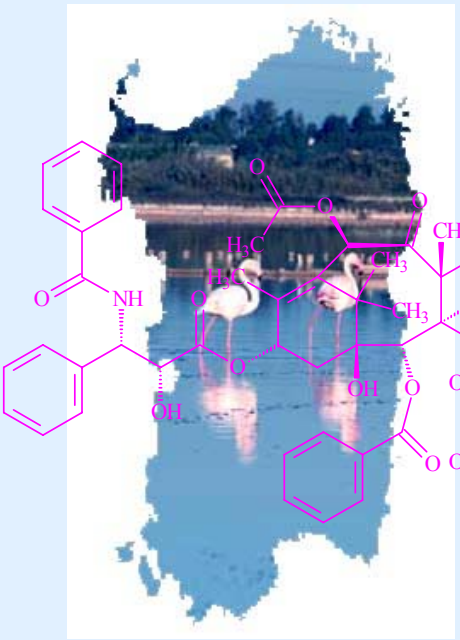
SardiniaChem 2006

GIORNATA DI STUDIO DEDICATA ALLA CHIMICA ORGANICA DELLE MOLECOLE BIOLOGICAMENTE ATTIVE

5 Giugno 2006, Complesso Universitario di Monserrato, Cagliari



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EVALUATION OF EFFECT OF THE PRIMARY PARTICLE SIZE ON COMPACTIBILITY OF SPRAY-DRIED LACTOSES

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Introduction

Spray-dried lactose is one of the most used filler-binders in direct compaction of tablets [1]. Spray-dried lactose is produced by spray-drying a suspension of α-lactose monohydrate crystals in a saturated aqueous solution of lactoses. The resulting product is composed of spherical particles, containing 80-85% crystals of α-lactose monohydrate (primary particles) and 15-20% amorphous lactose [2].

The compactibility of two commercial spray-dried lactoses, Pharmatose® DCL 11 (DCL11), prepared from α-lactose monohydrate with a median primary particle size of 34 μm and a new product, Pharmatose® DCL 14 (DCL14), prepared from 20 μm primary particles, were investigated. Both products are market from DMV International (Veghel, The Netherlands).

Methods

Flat tablets (500 mg weight; 13 mm diameter) were prepared from pure spray-dried lactose or from blends of lactose with 0.5% magnesium stearate on a programmable compaction simulator (ESH testing, Brierley Hill, UK), applying different compression forces (range 10-25 kN). The compression rates were 3 and 300 mm/s, reflecting a slow lab machine and high speed rotary press, respectively.

Tablet dimensions, weights and crushing strength were measured, after storage for at least 18 h at 20°C and 30% relative humidity (R.H.); porosity and tensile strength were calculated..

Tablet formulations were prepared by mixing DCL11 or DCL14 (90.3%) with theophylline monohydrate (5%), croscarmellose sodium (Primellose®) (4%), colloidal silica (Aerosil® 200) (0.2%) and magnesium stearate (0.5%) on the compaction simulator at 20 kN and 300 mm/s. The crushing strength, the disintegration time and the dissolution rate of theophylline monohydrate from the tablets were tested [3].

Results

The binding properties of DCL14 are significantly better than those of DCL11, because the small primary particles of DCL14 have larger surface area as well as the larger coated surface with amorphous lactose than those od DCL11.

Both lactoses have relatively low compaction speed sensitivity and rather low lubricant sensitivity. The compaction speed sensitivity is largest for DCL14, but even at high speed, the crushing strength of the tablets is significantly higher than for tablets prepared from DCL11. The compaction properties of the lubricated spray-dried lactoses are excellent and that the best performance is found for DCL14.

Comparison of theophylline monohydrate tablets with DCL11 and DCL14 as filler-binder, respectively, compressed at 20 kN, shows that the tablets containing DCL14 gave the strongest and, as a consequence, the somewhat longer disintegration time.

The dissolution rate of theophylline monohydrate for both formulations is very fast: after 8 minutes, the dissolution is complete.

Conclusions

Both spray-dried lactose investigated, Pharmatose® DCL 11 and Pharmatose® DCL 14, have rather low lubricant sensitivity and low compaction speed sensitivity in the range 3-300 mm/s.

However, the new product, Pharmatose® DCL 14 has a better compactibility than the existing product DCL11, even if compressed at high speed and even after lubrication. This effect is caused by the smaller primary particle size of α-lactose monohydrate in the spray-dried particles of DCL14.

Example of formulations show that tablets with good overall properties can be prepared using Pharmatose® DCL 14.

So, the compaction properties of spray-dried lactose could be improved by the introduction of a spray-dried lactose containing smaller primary particles

References

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