INVESTIGATION OF PHYSICO-CHEMICAL STABILITY OF A PURE INSULIN SPRAY-DRIED POWDER FOR INHALATION SEMI-AUTOMATICALLY FILLED IN QUALI-V®-I CAPSULES

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INTRODUCTION

The Department of Food and Drug Science of the University of Parma patented a process to produce a pure insulin pulmonary powder by spray drying [1]. This powder (Ins_SD) showed remarkable high respirability (FPF: 83.6%) and, stored in glass vials, was stable at room temperature over a period of five months [2].

In this study, the chemical stability and respirability of this insulin spray-dried powder loaded in capsules and packed in blister was investigated. In particular, the powder was semi-automatically filled in HPMC Quali-V®-I capsules using a precise micro-dosing system and they were blistered and stored at different conditions. Capsules were analyzed for respirability in a commercial DPI. Degradation products were analyzed at 0, 30, 90 and 180 days after powder production and capsule filling. Finally, the in vitro respirability of Ins_SD was compared to the one of the commercial product Afrezza®.

METHODS

• A human recombinant insulin powder for inhalation (Ins_SD) was prepared by spray drying using a mini Spray Dryer Buchi® B-290 (Buchi®, CH), as previously described [1].
• Capsules Quali-V®-I size 3 (Qualicaps Europe, ES) were semi-automatically filled with 2 mg of INS_SD powder using a Omnidroste TT vacuum drum filler system (Harro Hüfner GmbH, DE) and packed in PVC/PVDC 260 mm x 250 μm, 60 μm transparent blister (Research Pharmaceutical Co., Ltd., Colomba) sealed with a standard 20 μm aluminio foil (Amcor Flexibles Soliera, SP, IT).
• The in vitro respirability of Ins_SD was assessed using the Next Generation Impactor (NGI) (Copley Scientific, UK) inserting the capsule in a R50™ medium resistance inhaler (Plastipak, IT).
• The stability study was conducted storing the capsules in blisters at room temperature (25°C-60% RH) and at refrigerate conditions (4°C) up to 6 months. Degradation products as related proteins (A21 desamido insulin and other related proteins, ORP) and high molecular weight proteins (HMWP) were analyzed.

RESULTS

Aerodynamic parameters at time zero of Ins_SD (powder loaded 2 mg corresponding to insulin 1.8 mg) and Afrezza® (powder loaded: 3.5 mg corresponding to insulin 0.7 mg) and Ins_SD stored at 25°C-60%RH

Figure 1

Figure 2

Figure 3

Table 1

CONCLUSIONS

A pure insulin pulmonary powder, produced by spray drying from an acid aqueous solution of the peptide, presented high respirability and favourable flowability properties during the semi-automatic capsule filling process. The stability data have shown that Qualicaps® Quali-V®-I capsules, together with the PVC-PVDC packaging material, can provide long-term stability and maintain good aerodynamic performance, opening the possibility of a therapy less dependent on the cold storage of drug product.

REFERENCES


CONCLUSIONS

The aerodynamic performance of both formulations Afrezza® and Ins_SD showed good emission from the device (> 90%) and high respirability, with FPF values of 68 and 92%, respectively.

The semi-automatic filling process did not affect the aerosolization performance of Ins_SD.

The percentage of all ins, SD-decomposition products (A21, CRP and HMWP) was found to be below the USP limits (dotted line) in both storage conditions for the 6 months of the investigation.

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