

Investigation of Mini-Tab Capsule Filling Using a Zanasi Lab 16 Machine

APPLICATION DATA SUMMARY

- Coated placebo 2 mm mini-tabs were successfully filled into size 0 capsules using a Zanasi Lab 16 (IMA) capsule filling machine.
- Desired filling performance was achieved in all cases - each capsule contained 18, the target number of mini-tabs.
- Weight variation of filled capsules was not affected by the machine speed (3,000, 6,000 or 12,000 capsules/hour) and was below 1.6% in all cases. Since all capsules received 18 mini-tabs, this variation was attributed to mini-tab and capsule shell weight variation.
- Mini-tabs were successfully combined with either placebo powder or sugar spheres in one capsule. The resulting weight variation of filled capsules was found to be 0.7%.

INTRODUCTION

Mini-tabs combine the advantages of multiparticulate (MP) dosage forms with the established manufacturing techniques of tableting, and have fewer constraints compared to extrusion-spheronization. Mini-tabs produced via direct compression are an attractive alternative to pellets since the use of liquids is avoided. Like other MP systems, mini-tabs are filled into hard capsules to be taken whole or used for paediatric administration.¹

Capsule filling technologies for mini-tabs are now available from companies such as Bosch (Germany) and IMA (Italy). Mini-tabs in hard gelatine capsules are dosage forms which have become more and more popular during the past few years. Mini-tab shapes and sizes vary widely and require different technical approaches to enable their filling into capsules. Their scope of requirements ranges from volume-dosing to a precisely counted dosing of the mini-tabs.

This study investigated the possibility of filling 2 mm diameter coated placebo mini-tabs into capsules size 0, using a Zanasi Lab 16 (IMA) capsule filling machine.

MATERIALS AND METHODS

Placebo mini-tabs contained: lactose monohydrate (Friesland Foods Domo, Netherlands), powdered cellulose (Elcema F150, JRS Pharma GmbH, Germany), pregelatinized starch (Starch 1500[®], Colorcon, Inc., USA), fumed silica (Aerosil 200, Evonik Degussa, Germany) and magnesium stearate (Akcros, Netherlands). They were manufactured by direct compression (35 rpm, 1.1 kN compression force) on a modified instrumented 10-station rotary press (Piccola, Riva, Argentina) fitted with 2 mm standard concave tooling.² The mini-tabs were coated with Opadry[®], complete film coating system, clear (Colorcon, UK) to 3% weight gain.

Placebo powder containing 50% w/w starch, 48% w/w lactose (88 µm) and 2% w/w magnesium stearate and sugar spheres (18/20 mesh, 0.85-1.00 mm) was provided by IMA (Italy).

The materials were filled into hard gelatine capsules size 0 (Capsugel, Bornem, Belgium) using a Zanasi Lab 16 (IMA, Italy) capsule filling machine^{3,4} (Table 1).

Table 1. Technical Specification for Zanasi Lab 16 Machine

Max. output (capsules/hour)	16000
No. capsules processed/work cycle	2
Capsule size	5-000, DB, DBAA
Max. installed powder (kW)	8
Standard voltage	230/240 V 50/60 Hz
Suction	3.600 litres/min 2200 mm H ₂ O
Compresses air	50 dm ³ /min – 6 bar
Vacuum	40 m ³ /hour – 3 mbar
Weight (kg)	1000

Filling of powder and sugar spheres was carried out by means of dosators and pistons, moving with a double vertical and rotary movement, to penetrate the powder bed and compress it and then eject the powder slug in the capsule body.

Filling of mini-tabs into capsules was done by using a dosing wheel specifically designed according to the size of the mini-tabs and the number of them required per capsule. The dosing wheel is accurately designed to allow only one mini-tab per cavity that is held in place by vacuum. Insufficient dosing can only occur if inadequate level of vacuum is applied.

Multi-configuration capsule filling was also tested where the possibility of a combination of different material in a single capsule, ie, mini-tabs with placebo powder or pellets, was investigated. One of the reasons for combination filling is to enable the formulator to prepare products that have different release characteristics in a single capsule, ie, immediate, delayed and/or extended release, and therefore allowing the active ingredients to be released at different sites along the gastrointestinal tract.

Ten filled capsules from each trial were weighted on the analytical balance to ± 0.1 mg (Sartorius, Göttingen, Germany). Then the arithmetic mean and relative standard deviation were calculated.

RESULTS AND DISCUSSION

It was found that for all trials conducted with mini-tabs the filled capsules contained 18 mini-tabs. Weight variation of filled capsules was not affected by the machine speed (Table 2) and was below 1.6%. Since exactly 18 mini-tabs were contained in every capsule in each case, any weight variation was attributed to the low weight variation associated with the mini-tabs or capsule shells (1.53% and 1.98% respectively).

Table 2. Effect of Zanasi Lab 16 Machine Speed on Weight Variation of Capsules Filled with Mini-Tabs

Machine speed (capsules/hour)	Weight variation of filled capsules (%)
3000	1.55
6000	1.31
12000	1.28

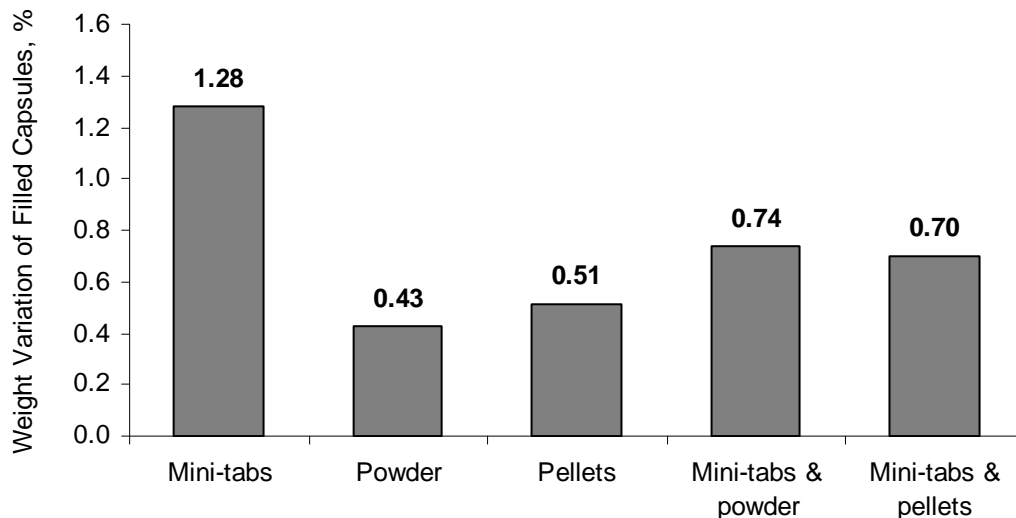
Figure 1 shows capsules filled with mini-tabs, mini-tabs with powder and mini-tabs with sugar spheres. Figure 2 shows the relative standard weight deviations for each trial conducted in this study where capsules were filled with mini-tabs, placebo powder, sugar spheres; and mini-tabs combined with either powder or sugar spheres.

Figure 1. Capsules Filled with (a) Mini-Tabs, (b) Mini-Tabs with Powder and (c) Mini-Tabs with Sugar Spheres



- a. 18 Mini-tabs only
- b. Powder and 18 mini-tabs
- c. Pellets and 18 mini-tabs

Figure 2. Weight Variation of Filled Capsules (12000 capsules/hour)



CONCLUSIONS AND RECOMMENDATIONS

- Coated placebo 2 mm mini-tabs were successfully filled into size 0 capsules using a Zanasi Lab 16 (IMA) capsule filling machine.
- Desired filling performance was achieved in all cases - each capsule contained 18, the target number of mini-tabs.
- Weight variation of filled capsules was not affected by the machine speed (3,000, 6,000 or 12,000 capsules/hour) and was below 1.6% in all cases. Since all capsules received 18 mini-tabs, this variation was attributed to a low mini-tab and capsule shell weight variation.
- Filling of mini-tabs using a dosing wheel offers high accuracy as the wheel is accurately designed to allow only one mini-tab per cavity. Hence, the accuracy is independent of capsule size, which merely acts as a container. Therefore, larger capsule size can also be used if needed.
- Mini-tabs were successfully combined with either placebo powder or sugar spheres in one capsule. The resulting weight variation of filled capsules was found to be 0.7%.

ACKNOWLEDGEMENTS

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