Processability of extended-release tablets containing Carbopol® 971P NF polymer by roller-compaction

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OBJECTIVE

To determine the processability of formulations containing Carbopol® 971P NF polymer via roller compaction and study the influence of formulation and process variables on the properties of granules and tablets.

METHODOLOGY

Materials

Theophylline USP (Shandong Xinhua Pharmaceutical Co. Ltd., Shandong, China), Guaifenesin (Delta Synthetic Co. Ltd., Taiwan), Carbopol® 971P NF polymer (Lubrizol Advanced Materials Inc., Cleveland, OH) – CBP, Emcocel® 50M microcrystalline cellulose (JRS Pharma LP, Patterson, NY), Foremost™ NF Fast Flo® Lactose 316 (Sheffield Pharma Ingredients, Norwich, NY), Magnesium stearate (Ferro Corporation, Walton Hills, OH).

Methods

Theophylline (50% w/w) or guaifenesin (25% w/w) formulations – Table 1 - containing Carbopol® 971P NF polymer (10 or 20% w/w) were roller-compacted using an Alexanderwerk WP120X40 Roller Compactor. The compaction parameters were: roll speed (6–12 rpm), feed screw speed (20–28 rpm), roll pressure (80–100 bar), roll gap (1.5 mm). The granules were blended with lubricant and compressed into tablets (800 mg).

The properties of the granules and tablets and the drug dissolution (USP apparatus 2, 100 rpm, pH-6.8 phosphate buffer) were evaluated.

Table 1. Composition of tablet formulations (% w/w)

Formulation (% w/w)	Theophylline (10% CBP)	Theophylline (20% CBP)	Guaifenesin (10% CBP)
Theophylline	50.0	50.0	-
Guaifenesin	-	-	25.0
Carbopol® 971P NF polymer	10.0	20.0	10.0
Emcocel® 50M microcrystalline cellulose	10.0	10.0	10.0
Foremost™ NF Fast Flo® Lactose 316	29.0	19.0	54.5
Magnesium stearate (intra-granular)	0.5	0.5	-
Magnesium stearate (extra-granular)	0.5	0.5	0.5
Total	**100**	**100**	**100**

RESULTS

- The roller compaction parameters did not have a significant influence on the particle size distribution of any formulation (Fig. 1–2).
- The properties of the granule (Table 2) were only slightly affected by the processing conditions: higher compaction pressure determined a minor increase in density.
- The tablets obtained from all formulations had acceptable weight, thickness, breaking force and friability values across the process variables tested (Table 3).
- The roller-compaction parameters studied did not influence the dissolution performance of the theophylline tablets.
- Theophylline release was affected by the level of Carbopol® 971P NF polymer in the formulation: dissolution at 20% w/w polymer level was longer and showed lower intra-batch variability compared to 10% w/w polymer (Fig. 3).
- For guaifenesin tablets, the drug release showed low intra-batch variability. Processing parameters did not influence the dissolution behavior of the tablets (Fig. 4).

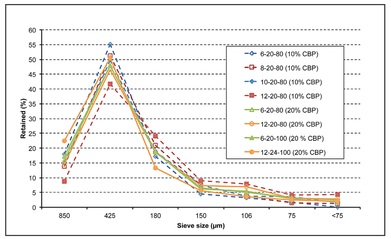

*Fig. 1. Influence of compaction parameters and polymer level on the particle size distribution of theophylline granules (*aa-bb-cc = roll speed - feed screw speed - roll pressure)*

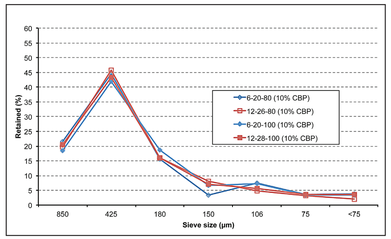

*Fig. 2. Influence of compaction parameters on the particle size distribution of guaifenesin granules (*aa-bb-cc = roll speed - feed screw speed - roll pressure)*

Table 2. Granule physical properties

Batch*	Flodex (mm)	Flow rate (g/sec)	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Carr's Index (%)
Theophylline (10% CBP)						
6-20-80	12	6.50	0.605	0.770	1.273	21.42
8-20-80	12	6.58	0.619	0.785	1.269	21.22
10-20-80	14	6.31	0.613	0.785	1.280	21.87
12-20-80	20	No flow	0.584	0.769	1.318	24.11
Theophylline (20% CBP)						
6-20-80	12	6.10	0.597	0.755	1.264	20.89
12-20-80	14	4.80	0.567	0.722	1.273	21.44
6-20-100	12	7.38	0.622	0.776	1.248	19.90
12-24-100	9	7.06	0.597	0.758	1.271	21.31
Guaifenesin (10% CBP)						
6-20-80	14	6.54	0.639	0.804	1.259	20.55
12-26-80	14	7.70	0.656	0.822	1.253	20.22
6-20-100	16	5.83	0.653	0.829	1.269	21.20
12-28-100	14	7.33	0.661	0.831	1.257	20.47

**aa-bb-cc = roll speed - feed screw speed - roll pressure*

Table 3. Tablet physical properties

Batch*	Weight (mg)	SD	Thickness (mm)	SD	Breaking force (kP)	SD	Friability 100 rot.	Friability 300 rot.
Theophylline (10% CBP)								
6-20-80	800.08	3.00	6.60	0.02	16.24	0.38	0.076	0.131
8-20-80	802.53	3.68	6.60	0.02	15.96	0.90	0.040	0.145
10-20-80	799.75	3.07	6.60	0.01	15.75	0.51	0.055	0.134
12-20-80	800.87	4.14	6.61	0.02	17.02	0.64	0.049	0.109
Theophylline (20% CBP)								
6-20-80	801.95	5.89	6.84	0.02	14.29	0.84	0.075	0.167
12-20-80	800.58	4.89	6.87	0.03	16.40	0.63	0.034	0.094
6-20-100	802.31	5.34	6.80	0.03	12.63	0.66	0.078	0.181
12-24-100	802.23	4.65	6.86	0.02	14.87	0.72	0.017	0.060
Guaifenesin (10% CBP)								
6-20-80	804.45	3.77	6.80	0.02	12.72	0.53	0.161	0.380
12-26-80	799.75	4.26	6.76	0.02	12.03	0.83	0.183	0.405
6-20-100	799.18	5.02	6.71	0.02	12.11	1.01	0.185	0.437
12-28-100	800.82	4.20	6.70	0.02	12.84	0.95	0.164	0.410

**aa-bb-cc = roll speed - f*

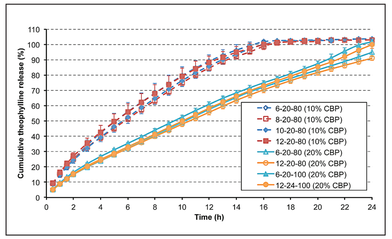

*Fig. 3. Influence of compaction parameters and polymer level on theophylline release (*aa-bb-cc = roll speed - feed screw speed - roll pressure)*

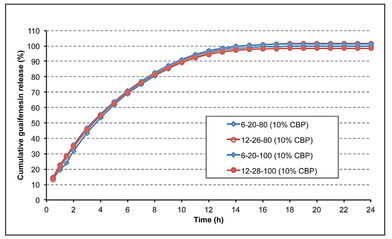

*Fig. 4. Influence of compaction parameters on guaifenesin release (*aa-bb-cc = roll speed - feed screw speed - roll pressure)*

CONCLUSIONS

Theophylline (50% w/w) or guaifenesin (25% w/w) formulations containing Carbopol® 971P NF polymer (10 or 20% w/w) could be successfully processed by roller-compaction for preparing extended-release matrix tablets.