Effect of Tablet Surface Area/Volume on Drug Release From Carbomer Matrix Tablets

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OBJECTIVE

To evaluate dissolution of multiple strength guaifenesin tablets (25 – 250 mg) containing carbomer (Carbopol® 971P NF polymer) and to determine the effect of tablet surface area/volume ratio (SA/V) on drug release.

METHODOLOGY

Materials

Guaifenesin (Delta Synthetic Co Ltd, Taiwan), Carbopol® 971P NF polymer (Lubrizol Advanced Materials, Inc., Cleveland, OH), Lactose monohydrate (Sheffield Pharma Ingredients, Norwich, NY), Emcocel® 50 microcrystalline celullose (JRS Pharma LP, Patterson, NY), Cab-O-Sil® M5 fumed silica (Cabot Corp, Billerica, MA), Synpro® magnesium stearate NF (Ferro Corporation, Walton Hills, OH).

Methods

Multiple strength guaifenesin tablets (25 – 250 mg / tablet) having the composition described in Table 1 – were manufactured by high shear aqueous granulation.

The drug and the excipients were added to a high-shear granulator (Glatt TMG), and granulated with water. The dried granules were sized, blended with magnesium stearate and fumed silica and compressed on an automated Korsch PH100/DMS Rotary Press, using various standard-concave and capsule-shape size punches to accommodate different tablet weight (100 – 1000 mg), surface area and volume; the target mechanical strength was similar for all tablets (10 kP).

Table 1. Composition of guaifenesin tablets

Ingredient	% w/w
Guaifenesin	25.0
Carbopol® 971P NF polymer	10.0
Emcocel® 50 microcrystalline cellulose	9.0
Lactose monohydrate	55.0
Cab-O-Sil® M5 fumed silica	0.5
Magnesium stearate	0.5
Total	100.0

The tablets were evaluated for physical characteristics (weight, thickness, mechanical strength), and their area, volume, and ratio of surface area/volume (SA/V) were calculated.

Drug release was tested according to USP 32 – NF 27 procedure, in apparatus 2 at 50 rpm, in 1000 mL pH=6.8 phosphate buffer. The automated test system consisted of a Model Total Solution VK7010, Vankel tester coupled to a Cary 50 UV-Vis spectrophotometer.

RESULTS

The guaifenesin dose ranged from 25 to 250 mg (tablet weight 100 – 1000 mg) and the tablet surface area/volume (SA/V) from 0.602 – 1.213 mm^{-1}. All tablets had consistent mechanical strength (9.4 – 12.6 kP) and exhibited extended drug release properties.

The release profiles and properties of the tablets having extreme doses (25 – 250 mg) or SA/V (0.602 – 1.213 mm^{-1}) are represented in Fig. 1, and Table 2. All other tablets released the drug within these limits.

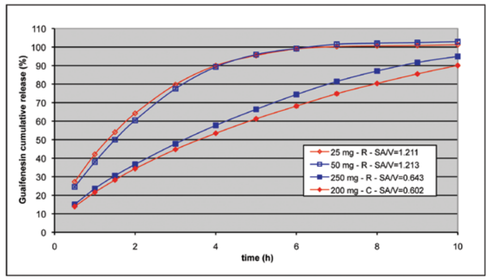

Figure 1. Guaifenesin release from tablets having extreme doses or SA/V

Table 2. Characteristics of guaifenesin tablets having extreme doses or SA/V

Tablet	Dose (mg)	Average weight (mg)	Shape	Radius	SA/V
25 mg - R - SA/V=1.211	25	100.72	Round	2.50	1.211
50 mg - R - SA/V=1.213	50	199.33	Round	4.76	1.213
200 mg - C - SA/V=0.602	200	801.00	Capsule	NA(*)	0.602
250 mg - R - SA/V=0.643	250	994.87	Round	7.94	0.643

(*) Not applicable; capsule shape (8.128 x 17.018 mm)

The results clearly suggest that the tablet surface area/volume (SA/V) is a key factor in controlling the drug release. Typically, the tablets with larger SA/V had faster release profiles, regardless of the dose or shape – Figure 2, Table 3. The dependency of the release rate as function of SA/V was not exactly linear.

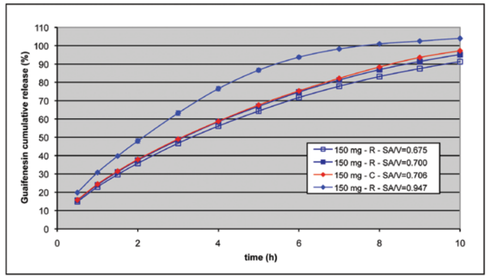

Figure 2. Release from guaifenesin 150 mg tablets having different SA/V or shape

Table 3. Characteristics of guaifenesin 150 mg tablets of different SA/V or shape

Tablet	Dose (mg)	Average weight (mg)	Shape	Radius	SA/V
150 mg - R - SA/V=0.675	150	601.18	Round	5.56	0.675
150 mg - R - SA/V=0.700	150	599.26	Round	5.95	0.700
150 mg - C - SA/V=0.706	150	604.36	Capsule	NA(*)	0.706
150 mg - R - SA/V=0.947	150	600.13	Round	7.94	0.947

(*) Not applicable; capsule shape (8.128 x 17.018 mm)

A mathematical model was developed to describe the dynamics of the drug release as function of SA/V and time.

$$\text{Guaifenesin cumulative release (\%)} = 100 \times \left[1 - e^{-t\varphi(SA/V)}\right]$$

where t – time (hours), and φ is a function of SA/V.

The model applies across the entire duration of the dissolution process, and was assessed using checkpoint formulations – Fig. 3, Table 4. The similarity between the predicted and actual dissolution profiles of those formulations was confirmed with the f2 test, resulting in f2>50.

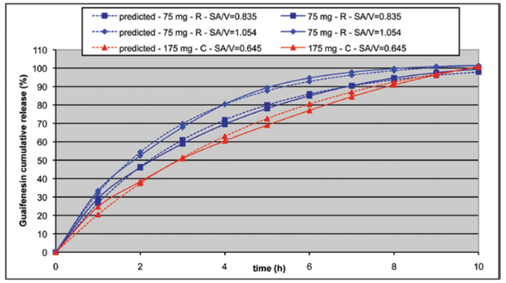

Figure 3. Predicted and actual release from guaifenesin tablets

Table 4. Characteristics of guaifenesin tablets

Tablet	Dose (mg)	Average weight (mg)	Shape	Radius	SA/V
75 mg - R - SA/V=0.835	75	300.06	Round	3.97	0.835
75 mg - R - SA/V=1.054	75	298.54	Round	5.56	1.054
175 mg - C - SA/V=0.645	175	696.64	Capsule	NA(*)	0.645

(*) Not applicable; capsule shape (8.128 x 17.018 mm)

The model can work as a tool for tablet analysis and design, for the following purposes:

- Predict the drug release process, based on SA/V
- Estimate the SA/V for a desired drug release profile.

CONCLUSIONS

Tablet surface area/volume (SA/V) was a significant factor in controlling drug release from carbomer based tablets. Tablets with larger SA/V typically had faster release profiles, regardless of the dose or shape.

Guaifenesin release from multiple strength tablets was modeled as function of tablet surface area/volume ratio (SA/V) and the model was validated using checkpoint formulations.

SA/V can be used as a tool to achieve target dissolution or to design multiple strength tablets with similar release profiles.