

Drug Release From Carbomer Tablets As A Function of Tablet Surface Area-To-Volume Ratio

INTRODUCTION

Carbopol[®] polymers (carbomers) are efficient gel matrix formers for extended release dosage forms. The main phenomena governing the drug release from carbomer matrix tablets are water penetration, polymer swelling, drug dissolution and diffusion and matrix erosion [1].

The aim of this study was to investigate the influence of surface area / volume ratio (SA/V) on drug release from extended release tablets containing Carbopol[®] 971P NF polymer (10% w/w). Multiple strength tablets were formulated using guaifenesin as a water soluble model drug; the dose ranged between 25 - 250 mg / tablet.

The practical implications of this study are for demonstrating the modulation of the drug release without altering tablet composition. The findings are also relevant when designing multiple strength tablets, with similar release profiles.

EXPERIMENTAL

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 cellulose (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.

Table 1. Composition (%w/w) of guaifenesin tablets

Ingredient (% w/w)	% 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 drug, polymer and fillers 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).

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.

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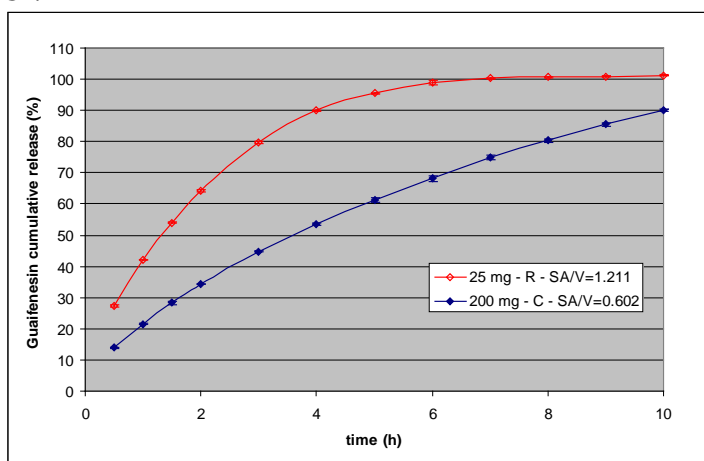
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Drug release was tested according to USP 32 – NF 27 procedure, in apparatus 2 at 50 rpm, in 1000 mL pH=6.8 phosphate buffer. The automated test system consisted of a Model Total Solution VK7010, Vankel tester coupled to a Cary 50 UV-Vis spectrophotometer.

RESULTS

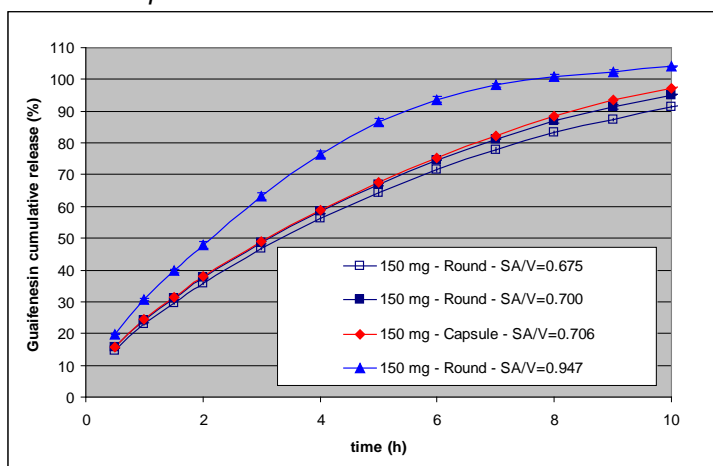
The guaifenesin dose ranged from 25 to 250 mg (tablet weight 100 - 1000 mg) and the tablet surface area / volume (SA/V) from 0.60 - 1.21 mm⁻¹. All tablets had consistent mechanical strength (9.4 - 12.6 kP) and exhibited extended drug release properties – Fig. 1.

Fig. 1. Release from guaifenesin tablets having extreme SA/V



The tablet surface area / volume (SA/V) was 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. The dependency of the release rate as function of SA/V was not exactly linear.

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



The dynamics of the drug release as function of SA/V and time was described using a non-linear mathematical model.

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

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

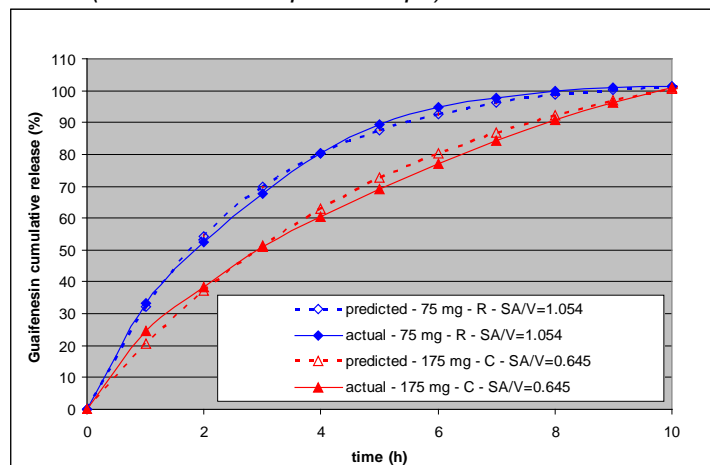
Independent experiments (Table 2) conducted to verify the theoretical predictions indicated good agreement between the predicted and actual results – Figure 3.

Table 2. Characteristics of guaifenesin tablets used for model verification

Tablet	Dose (mg)	Average weight (mg)	Shape	Radius	SA/V
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)

Fig. 3. Predicted and actual release from guaifenesin tablets (R-round or C-capsule shape)



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.

REFERENCES

- [1] Lubrizol Pharmaceutical Polymers for Controlled Release Tablets and Capsules - Bulletin 30.
<http://www.lubrizol.com/Pharmaceutical/Literature/Bulletins.html>

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