Drug Release from Tablets Containing Different Carbomer Grades or Their Combination

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SUMMARY

Two grades of carbomer homopolymer (Carbopol® 971P NF and 974P NF polymers) and their combination were evaluated for controlled release properties in tablets containing model drugs of different solubility (guaifenesin and ketoprofen). Lightly crosslinked, less viscous Carbopol® 971P NF polymer was more efficient in controlling drug release than highly crosslinked, more viscous Carbopol® 974P NF polymer. The combination had a release profile intermediate to the two polymers, thus combinations can be used to modulate the drug release by varying the polymer ratio.

BACKGROUND

Carbomers (Carbopol® polymers) are high molecular weight polymers of acrylic acid, chemically crosslinked with polyalkenyl alcohols.

Due to their inherently crosslinked structure, Carbopol® polymers can form strong matrices at low concentrations, enabling them to efficiently control drug release from tablets. Drug release is mainly affected by differences in the polymer hydrogel structure, which are defined by the extent of cross linking.

OBJECTIVE

The study was designed to evaluate two grades of carbomer homopolymer (Carbopol® 971P NF and 974P NF polymers) and their combination in tablet formulations containing model drugs of different solubility (guaifenesin and ketoprofen), manufactured by wet granulation.

Carbopol® 971P NF and 974P NF polymers, differ mainly in their crosslink density:

- Carbopol® 971P NF polymer is lightly crosslinked, with long rheology and lower viscosity (viscosity range 4,000 – 11,000 mPa•s)[1, 2].
- Carbopol® 974P NF polymer is highly crosslinked and produces highly viscous gels (viscosity range 29,400 – 39,400 mPa•s)[2].

EXPERIMENTAL METHODS

Tablets containing Carbopol® 971P NF polymer (971P NF), Carbopol® 974P NF polymer (974P NF) or their combination (1:1) were manufactured by aqueous high shear granulation. Ketoprofen (low solubility) and guaifenesin (high solubility) were selected as model drugs. The polymer inclusion level was 10% w/w in the case of guaifenesin (Table 1) and 5% w/w for ketoprofen (Table 2).

Dissolution studies were conducted according to the USP 32 – NF 27 procedure, using apparatus 2, in 0.1N HCl or pH = 6.8 phosphate buffer.

Table 1. Composition of guaifenesin 200 mg tablets

Ingredient (%/tablet)	10% - 971P NF	5% - 971P NF & 5% - 974P NF	10% - 974P NF
Guaifenesin	50.00	50.00	50.00
Carbopol® 971P NF polymer	10.00	5.00	0.00
Carbopol® 974P NF polymer	0.00	5.00	10.00
Lactose monohydrate	30.00	30.00	30.00
Emcocel® 50M microcrystalline cellulose	9.00	9.00	9.00
Cab-O-Sil® M5 fumed silica	0.50	0.50	0.50
Magnesium stearate	0.50	0.50	0.50
Total	100	100	100

Table 2. Composition of ketoprofen 200 mg tablets

Ingredient (%/tablet)	5% - 971P NF	2.5% - 971P NF & 2.5% - 974P NF	5% - 974P NF
Ketoprofen	66.67	66.67	66.67
Carbopol® 971P NF polymer	5.00	2.50	0.00
Carbopol® 974P NF polymer	0.00	2.50	5.00
Lactose monohydrate	17.86	17.86	17.86
Emcocel® 50M microcrystalline cellulose	8.77	8.77	8.77
Talc	1.00	1.00	1.00
Cab-O-Sil® M5 fumed silica	0.20	0.20	0.20
Magnesium stearate	0.50	0.50	0.50
Total	100	100	100

RESULTS

All formulations had acceptable granule and tablet properties.

Carbopol® 971P NF polymer extended the release of guaifenesin for 8 -10 h in both acid and buffer media, while Carbopol® 974P NF polymer resulted in fast dissolution – Fig. 1 and 2.

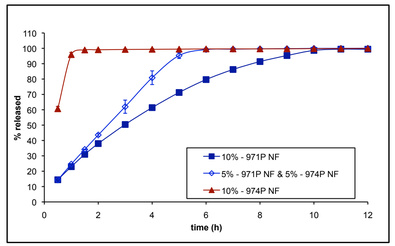

Fig. 1. Guaifenesin release in 0.1N HCl from tablets containing Carbopol® polymers

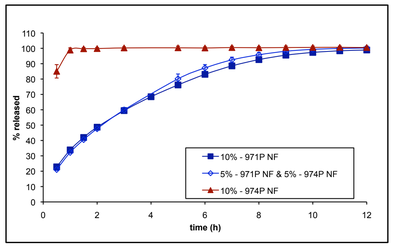

Fig. 2. Guaifenesin release in pH = 6.8 phosphate buffer from tablets containing Carbopol® polymers

The release rates followed the same order in case of ketoprofen tablets: the slowest release was observed from Carbopol® 971P NF polymer, followed by the combination and Carbopol® 974P NF polymer – Fig. 3.

The duration of release was longer in the case of ketoprofen compared to guaifenesin (due to difference in drug solubility).

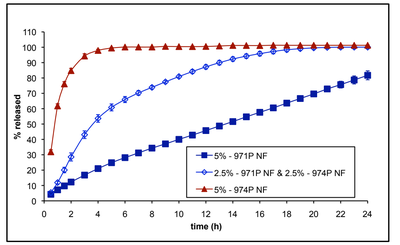

Fig. 3. Ketoprofen release in pH=6.8 phosphate buffer from tablets containing Carbopol® polymers

For both drugs, the lightly crosslinked and less viscous Carbopol® 971P NF polymer was more efficient in controlling drug release than the highly crosslinked, more viscous Carbopol® 974P NF polymer. Thus the polymer chemical nature, rather than its viscosity, controlled the release.

Upon hydration, Carbopol® 971P NF polymer, opens up easily at low concentrations, has flexible microparticles, thus resulting in a homogeneous gel structure which provides significant resistance to diffusion and erosion ("fishnet" gel structure)[3]. Highly crosslinked polymers do not open up easily, and higher concentrations are required to fill in the spaces between the swollen, rigid gel particles ("fuzzball" type of gel structure)[3].

Intermediate drug release can be achieved by combining the two polymers.

CONCLUSION

The release of guaifenesin or ketoprofen from tablets formulated with Carbopol® 971P NF polymer was slower than from tablets with Carbopol® 974P NF polymer.

The chemical nature of the polymer (crosslink degree) was more important for the drug release than its viscosity. Slower release was obtained by using the lightly crosslinked, less viscous polymer compared to the highly crosslinked, more viscous material.

Polymer combinations can be used as a formulation tool to achieve intermediate drug release.

REFERENCES

1. United States Pharmacopeia 32 – National Formulary 27, U.S. Pharmacopeia, Rockville, MD
2. Product Specifications: Carbopol® 971P NF Polymer, Carbopol® 974P NF Polymer http://www.lubrizol.com/Pharmaceutical/Literature/Specifications/Carbopol.html
3. Lubrizol Pharmaceutical Bulletin 30, http://www.lubrizol.com/Pharmaceutical/Literature/Bulletins.html

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