Influence of Alcohol Content in Dissolution Media on the Drug Release from Extended Release Tablets Formulated with Carbopol® Polymers

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OBJECTIVE

Evaluate the effect of alcohol content in dissolution media on drug release from extended release tablets formulated with Carbopol® polymers and investigate the risk of alcohol induced dose dumping.

METHODOLOGY

Materials

Guaifenesin (Delta Synthetic, Taiwan), Caffeine anhydrous granular 0.07/0.5 (BASF Corp., Florham Park, NJ), Metformin hydrochloride (Astroquim SA de CV, Ecatapec, Mexico), Carbopol® 971P NF polymer (Lubrizol Advanced Materials, Inc., Cleveland OH), Carbopol® 71G NF polymer (Lubrizol Advanced Materials, Inc., Cleveland OH), Emcocel® 50M microcrystalline cellulose (JRS Pharma LP, Patterson, NY), Microcrystalline cellulose PH-102 (Astroquim SA de CV, Ecatepec, Mexico), Lactose monohydrate (Kerry Bio-Science, Norwich, NY), Colloidal silicon dioxide (Astroquim SA de CV, Ecatepec, Mexico), Magnesium stearate (Ferro Corporation, Walton Hills, OH; Compañias el Fuerte SA de CV, Miguel Hidalgo, Mexico

Methods

Extended release tablets of various model drugs – guaifenesin (600 mg), caffeine (200 mg) and metformin hydrochloride (750 mg) – were formulated using Carbopol® 971P NF and/or 71G NF polymers as matrix forming excipients (10-20% w/w) – Table 1.

The drugs and excipients were granulated with deionized water. The dried granules were blended with the extragranular excipients and then compressed, using various standard-concave or capsule-shape punches to accommodate different tablet weights.

Tablets were evaluated for weight variation, mechanical strength, and friability (USP). Drug release was tested in USP apparatus I (100 rpm) or II (50 rpm) in 900 ml of 0.1N HCl solution containing ethanol (0, 20, or 40% v/v).

Table 1. Composition (%w/w) of Guaifenesin 600 mg, Caffeine 200 mg, and Metformin 750 mg Extended Release Tablets

Ingredient (%w/w)	Caffeine	Metformin	Guaifenesin A	Guaifenesin B
Guaifenesin	-	-	75.0	75.0
Caffeine	75.0	-	-	-
Metformin hydrochloride	-	75.0	-	-
Carbopol® 971P NF polymer	10.0	9.0	10.0	20.0
Carbopol® 71G NF polymer*	-	7.0	-	-
Emcocel® 50M microcrystalline cellulose	4.5	-	5.0	4.5
Microcrystalline cellulose PH-102*	-	8.0	-	-
Lactose monohydrate	10.0	-	9.5	-
Colloidal silicon dioxide*	-	0.5	-	-
Magnesium stearate*	0.5	0.5	0.5	0.5
Total	**100**	**100**	**100**	**100**
Tablet weight (mg)	266.7	1000	800	800
Dose (mg)	**200**	**750**	**600**	**600**

**Added extragranularly*

RESULTS

All formulations were characterized by acceptable tablet properties – Table 2.

Table 2. Physical Properties of Guaifenesin, Caffeine, and Metformin Tablets

Formulation	Weight (mg) (average ±SD)	Thickness (mm) (average ±SD)	Hardness (kP) (average ±SD)	Friability (%)
Caffeine	266.0±1.5	5.20±0.03	11.45±1.08	0.206
Metformin	1004.0±20.5	5.87±0.01	18.20±4.05	0.130
Guaifenesin A	800.6±5.5	7.38±0.03	16.45±0.80	0.093
Guaifenesin B	798.5±10.4	7.44±0.02	12.25±1.09	0.245

No risk of alcohol induced dose dumping was observed for the drugs/formulations tested, thus indicating the robustness of these extended release systems formulated with Carbopol® polymers.

Slower drug release was observed for caffeine and metformin hydrochloride tablets exposed to 20 or 40% v/v ethanol solution compared with exposure to 0.1N HCl – Fig.1 and 2. This can be explained by a change in drug solubility in the various media. The solubility of caffeine (1:60 water and 1:130 ethanol)[1] or metformin hydrochloride (1:2 water and 1:100 ethanol)[1] is lower in ethanol than in water.

In the case of guaifenesin, slightly slower drug release in the presence of alcohol was observed for tablets containing 10% w/w Carbopol® polymer – Fig 3. No alcohol effect was observed for the guaifenesin tablets formulated with 20% Carbopol® polymer.

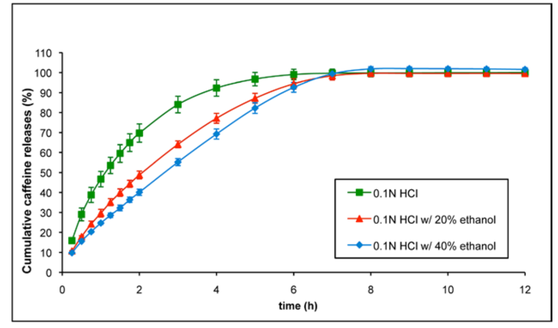

Figure 1. Influence of ethanol on the dissolution of caffeine (200 mg) tablets with 10% w/w Carbopol® 971P NF polymer in 0.1N HCl.

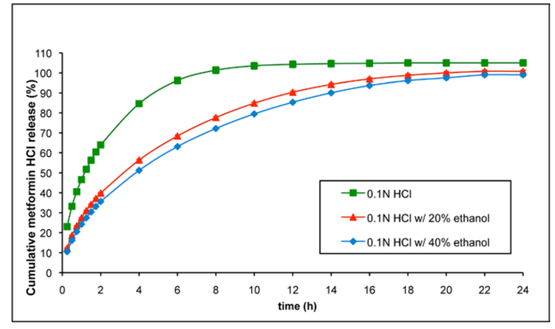

Figure 2. Influence of ethanol on the dissolution of metformin hydrochloride (750 mg) tablets with 9% w/w Carbopol® 971P NF polymer and 7% w/w Carbopol® 71G NF polymer in 0.1N HCl.

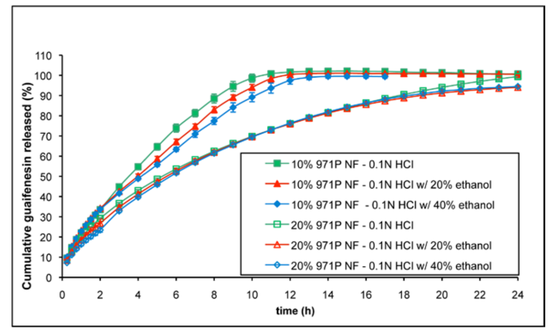

Figure 3. Influence of ethanol on the dissolution of guaifenesin (600 mg) tablets with 10% or 20% w/w Carbopol® 971P NF polymer in 0.1N HCl.

CONCLUSIONS

In vitro dissolution testing of extended release tablets of guaifenesin, caffeine and metformin hydrochloride formulated with Carbopol® polymers (10 – 20% w/w) did not indicate any alcohol-induced dose-dumping effect. Similar or slower drug release was observed when tablets were exposed to 0.1N HCl or 0.1N HCl with up to 40% v/v alcohol content.

References:

1. Moffat, A.,Osselton, N., and Widdop, B. (2004). Clarke's Analysis of Drugs and Poisons 3rd Ed., The Pharmaceutical Press, London.