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Stability of Pharmaceutical Carbopol®* Polymer Gels Containing Hydrogen Peroxide

Introduction

Hydrogen peroxide is a disinfectant and is used as a bleaching agent in several tooth-whitening oral care formulations.

The stability of gels based on Carbopol® polymers has been evaluated for household and personal care applications. However, several types of pharmaceutical grade polymers, such as those manufactured in ethyl acetate solvent and the Carbomer Interpolymer Carbopol® Ultrez 10 NF have not been previously evaluated.

Accordingly, Lubrizol Advanced Materials, Inc. scientists generated an experimental screening design study to determine the stability of pharmaceutical Carbopol® polymer gels with various grades of hydrogen peroxide.

The parameters studied were viscosity, pH, peroxide content, and Brookfield Yield Value, which estimates the ability of a formulation to support a stable suspension. The study was conducted at room temperature and at 45°C, with measurements taken initially and at 1, 3, 6, 9, and 12 weeks. The study was later extended to 15 weeks for some of the best formulations.

The test formulation utilized in the study is shown in Table 1.

Table 1
Stability Test Formulation

Ingredient	Weight %
Carbopol® Polymer	0.7%
Hydrogen Peroxide	4% or 7%
NaOH	q.s. to pH = 5.5
Deionized Water	q.s. 100%

Background

Carbopol® polymers are well known for their ability to thicken, stabilize and provide suspending properties in a wide variety of pharmaceutical products.

Carbopol® polymers are used in a variety of anhydrous and aqueous tooth whitening products based on both carbamide peroxide and hydrogen peroxide. Carbopol® polymer gels are stable to these peroxides, but are known to be sensitive to oxygen, which is the byproduct of degradation of the peroxides.[1-3] Accordingly, the choice of stabilizer package for the peroxide is critical to prevent viscosity loss in the gels during storage.

There are several types of stabilizers used by peroxide manufacturers, all of which are designated as trade secrets. Consequently, a phenomenological approach is necessary and it is unclear as to why the various peroxides performed differently. Several suppliers were queried as to which of their hydrogen peroxide grades would be acceptable in oral care formulations and the following grades were chosen for the study:

Table 2
Peroxides in Study

Peroxide Grade	Source
Peroxal® CG*	Atofina
Peroxal® CLG	Atofina
CG	Degussa
European CG	Degussa
Peralkali®	Degussa
Super D® CG	FMC
*CG = “Cosmetic Grade”	

Table 3
Carbopol® Polymers

• 5984 EP
• 956
• 971P NF
• 974P NF
• 980 NF
• Ultrez 10 NF

The 47 formulations of the designed experiment were prepared according to the recipe in Table 1. Special precautions had to be taken to ensure no contaminants which could catalyze peroxide decomposition were introduced into the formulations. Polyethylene beakers and Teflon® agitators were used in the preparation; the formulations were divided and stored either at room temperature or at 45°C in polypropylene jars with polyethylene slip sheets for the stability studies, and Teflon-coated spindles were used to measure the Brookfield viscosity and yield values.

Results

Viscosity Stability

The main influences on viscosity stability were found to be peroxide grade and polymer crosslink density.

Of the six peroxides studied, Peralkali® hydrogen peroxide (Degussa) was found to have the least effect on Carbomer gel viscosity. The viscosity retention of the gel containing Carbopol® 980 NF polymer in combination with the various peroxides measured to 12 or 15 weeks is presented in Figure 1. It can be noted that two of the peroxides degraded the viscosity of the carbomer gel in only two weeks. Thus the choice of peroxide source and grade is critical if even slowly decaying viscosities are desirable.

Furthermore, the formulation utilizing the lightly crosslinked Carbopol® 971P NF polymer lost all of its viscosity in Peralkali® peroxide by six weeks and was the first to lose viscosity in combination with each of the peroxides. In contrast, all of the formulations with more highly crosslinked polymers demonstrated increased viscosity retention, as shown in Figure 2. The level of peroxide in the formulations appeared to have minimal effect up to 9 weeks at 45°C, but significant relative viscosity loss occurred in the gel using Carbopol® 980 NF polymer in combination with 7% Peralkali® between weeks 9 and 12.

After 12 weeks at 45°C, several of the formulations showed viscosity retention between 56% and 62%. Notably, both of the Carbopol® Ultrez 10 NF polymer formulations (4% and 7% peroxide) had retained 59% of their viscosity. Carbopol® Ultrez 10 NF polymer may be considered as a better candidate for use in hydrogen peroxide formulations relative to the other polymers due to its ease of processing.

The viscosity retention after 15 weeks at room temperature is displayed in Table 4, below.

Table 4
Viscosity Retention in Peralkali® after 15 weeks at Room Temperature

Carbopol® Polymer	% Peroxide	% Ret.
980 NF	(4)	96
5984 EP	(7)	93
956	(4)	92
974P NF	(7)	90
Ultrez 10 NF	(7)	83
971P NF	(7)	82
980 NF	(7)	52
Ultrez 10 NF	(4)	32

Viscosity retention at room temperature was much better overall than at 45°C, but the two poorest results are inconsistent when compared to high-temperature results for those polymers.

Figure 1
Viscosity Retention of Carbopol® 980 NF Polymer in Various Peroxides at 45°C

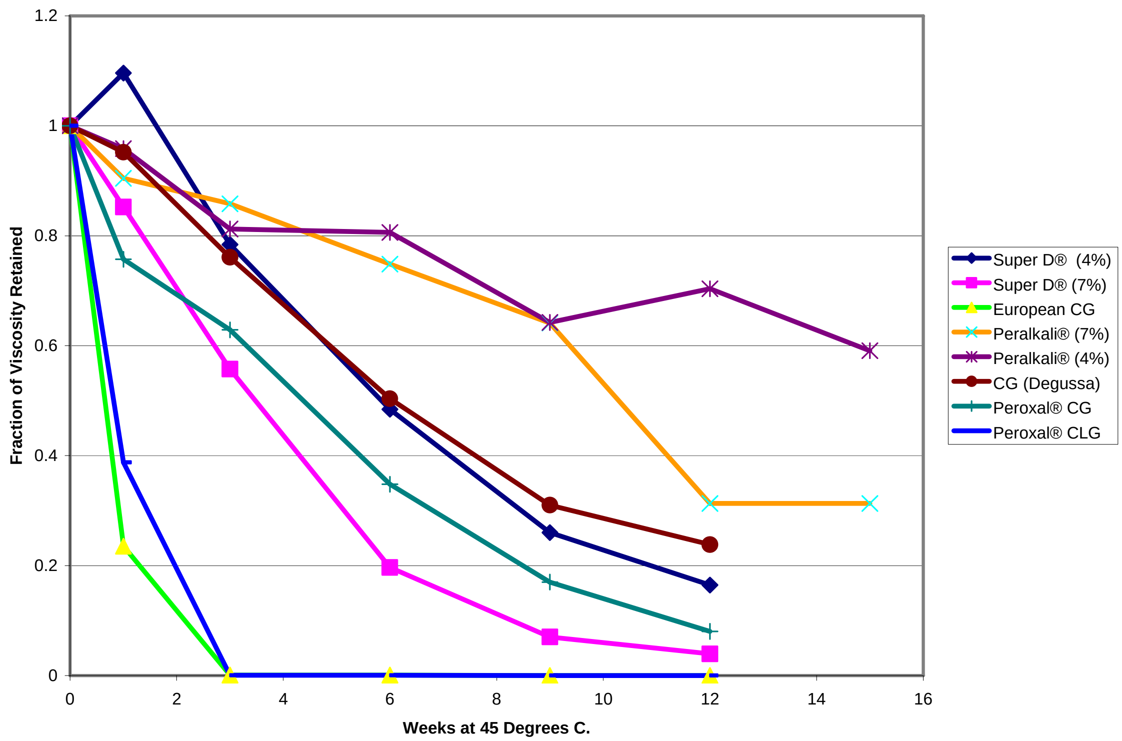
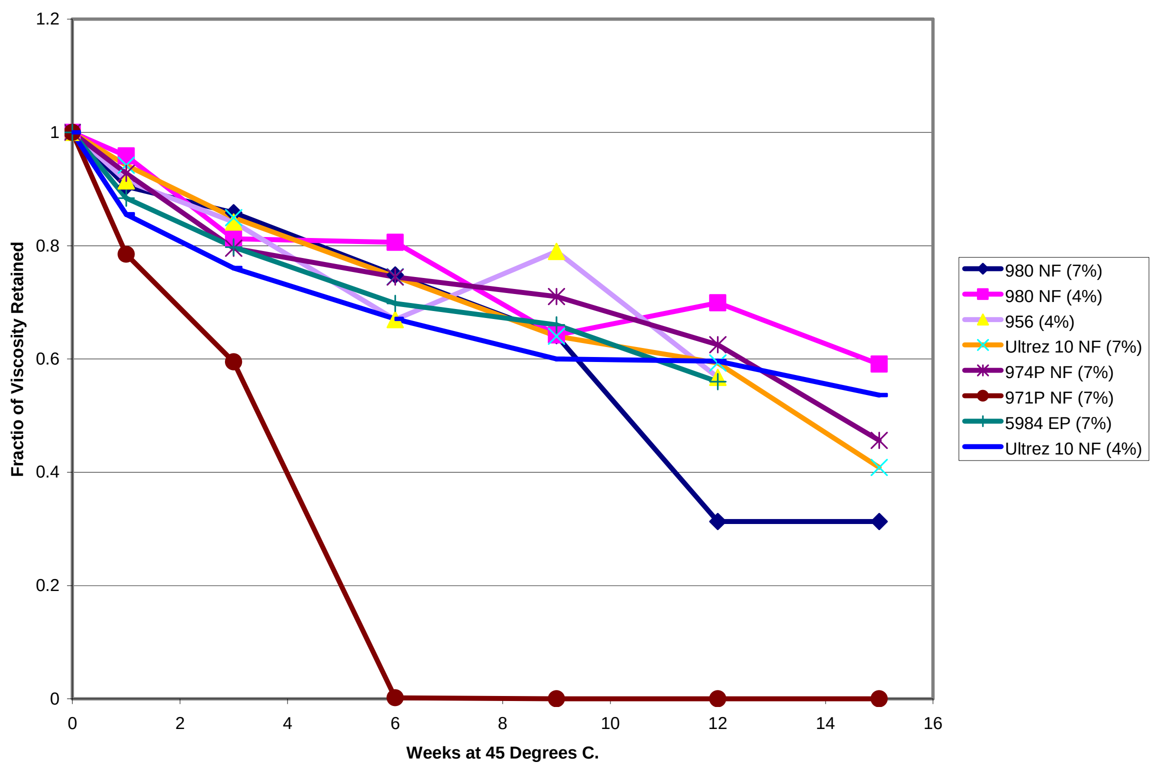


Figure 2
Viscosity Retention of Various Carbopol® Polymers in Peralkali® at 45°C



pH Stability

The 47 formulations of the study began with an average pH of 5.52 (Std. Dev. 0.038) while after 12 weeks the average pH was 5.43 (Std. Dev. 0.096). Thus, there was little pH drift over the course of the study.

Peroxide Stability

Hydrogen peroxide content was determined by thiosulfate titration.[4] The initial concentration was estimated by averaging the initial and one-week results and the test standard deviation was 0.18. The 12-week concentration was estimated by averaging the 12-week results with the 9-week 45°C results and the standard deviation had improved to 0.096. Only six of the 47 formulations showed a statistically significant drop (>0.27) in peroxide concentration. Only one of these contained Peralkali®, but interestingly this formulation had the highest retained viscosity after twelve weeks.

Brookfield Yield Value

Yield value, rather than viscosity, is the major factor governing the stability of suspensions. Brookfield Yield value is an estimate of the resistance to initial flow, by extrapolation of the torques at 0.5 and 1 RPM, back to 0 RPM. It is semi-quantitative, but for each material to be suspended, there seems to be a threshold yield value below which the suspensions settle, but above which suspensions are maintained.

Results are displayed in Tables 5 and 6. Table 5 shows the 12-week results for the formulation with Carbopol® 980 NF polymer in combination with various peroxides. The various peroxides performed the same with regard to Brookfield Yield Value retention as to viscosity retention.

Table 5
12-Week Yield Value Retention of Carbopol® 980 NF Polymer Gels in Various Peroxides at 45°C

Peroxide Grade	% Peroxide	% Ret.
Peralkali®	(4)	82
Peralkali®	(7)	78
Degussa CG*	(4)	55
FMC	(4)	44
Peroxal® CG	(7)	20
FMC	(7)	6
Degussa Europe CG	(7)	0
Peroxal® CLG	(7)	0

*CG = Cosmetic Grade

In contrast, a difference in performance was observed among the polymers (Table 6). For example, formulations with Carbopol® 971P NF polymer, a low level crosslinked polymer, lost its yield value, and the formulations with highly-crosslinked polymers performed much better. The formulations using the ethyl acetate polymers Carbopol® 974P NF and Carbopol® 956 polymers retained 97 - 98% of their yield value.

Table 6
12-Week Yield Value Retention in Peralkali® at 45°C

Carbopol® Polymer	% Peroxide	% Ret.
956	(4)	98
974P NF	(7)	97
980 NF	(4)	82
980 NF	(7)	78
Ultrez 10 NF	(7)	69
Ultrez 10 NF	(4)	68
5984 EP	(7)	66
971P NF	(7)	0

Conclusions

In hydrogen peroxide formulations, peroxide source and grade are critical factors to consider with regard to polymer stability. Peralkali® hydrogen peroxide from Degussa performed the best of those used in this study and should be used as a control in evaluating carbomer performance in other hydrogen peroxide formulations.

Study results indicate that Carbopol® 980 NF polymer would be the polymer of choice if viscosity retention is critical to formulation performance. Carbopol® Ultrez 10 NF polymer might be a good alternative if easy processing is critical. Additionally, if yield value retention is a critical formulation parameter then Carbopol® 956 and Carbopol® 974P NF polymers would be the most suitable choices.

Polymer crosslink density is also important as highly crosslinked Carbopol® polymers best retained their viscosity and yield values.

Finally, higher peroxide levels may shorten shelf life.

References

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