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EVALUATION OF HYDROXYPROPYL CELLULOSE AND HYDROXYPROPYL METHYL CELLULOSE AS AQUEOUS BASED FILM COATINGS

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ABSTRACT

Aqueous solutions of hydroxypropyl cellulose and hydroxypropyl methyl cellulose were evaluated as pharmaceutical film coatings from completely water based systems. The first phase of the study was to identify suitable plasticizers for the two polymers. The second was to examine possible interactions between the polymer solutions,and new color concentrates prepared for aqueous coating systems, based on viscosity measurements. The third phase of the study was to coat tablets with the various polymer aqueous solutions,in an air suspension tower,and in a side-vented coating pan, (while establishing coating conditions for each process). The final phase of the study was to evaluate the tablets coated by the various formulations.

INTRODUCTION

The use of natural and synthetic polymers as coatings in the pharmaceutical industry was originally employed (utilizing cellulose acetate phthalate and shellac) for enteric coating purposes and as a sealing coat previous to

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sugar coating. Film coating was next developed as a substitute for sugar coating for non-enteric, gastric dissolving, protective coatings. The first industrial applications of non-enteric film coating occurred late in 1953 with the patented Abbott "Filmtab" tablet coatings. A rapidly growing interest in film coating as a new coating process followed, not only as quickly soluble, protective, or enteric coatings, but also as controlled release coatings. A major research effort directed toward the improvement and understanding of the process, and the identification of new film coating materials followed during the 1960's, with the production of several hundred patents and many papers on the subject, as nearly every major drug company worked to develop its own system. Currently most major drug companies appear to be marketing film coated tablets as a replacement for some if not all of their previously sugar coated dosage forms. The reason for this change-over to solvent based film coating is obvious when the advantages of that process, as they existed in the 1960's, are considered. This advantages included; speed of operation (a few hours to complete the operation compared to days for sugar coating), great economies of process, economies of space, the process could be readily automated, anhydrous capability, the superior mechanical properties of the coatings compared to sugar coating, the minimal increase in tablet disintegration time which was normally seen for rapidly soluble films, the minimal increase in tablet size, product identification could be facilitated, there were no shape restrictions in the tablet being coated, various drug delivery capabilities were possible, the coatings were safer than sugar coatings (children did not readily mistake them for candy), a skilled artisan was not required for application, and the coating organosols were not microbial media.

The major drawbacks that were seen for the film coating process all related to the use of the organic solvents (with one exception). The disadvantages seen for solvent based film coating were; the tablet requirements (a harder, attrition resistant and solvent resistant tablet substrate was needed), solvent flammability or exposion danger, solvent toxicities, high

solvent cost compared to water used in sugar coating, environmental regulations (EPA), worker protection regulations (OSHA), concern over solvent residues in the coated tablets, and the high cost of solvent recovery systems.

In the 1970's the disadvantages of film coating, particularly those related to solvent use, began to out-weigh the advantages of the process. EPA and OSHA requirements became increasingly stringent. The cost of solvents drastically esculated. As a result pharaceutical manufacturers began to again turn to water as a coating media. Some manufacturers returned to the sugar coating process, using perhaps a modified sugar coating which included a water soluble polymer to allow the deposition of a thinner sugar coating, and one with improved mechanical properties. Other manufactures have focused their attention on water based film coatings. This paper will discuss properties of some of these newer water based film systems containing color pigments.

EXPERIMENTAL

Evaluation of the Interaction of Water Soluble Polymers (Methocel E5, Methocel Methocel E15, Klucel EF) with Five Colorcon Pigment Dispersions.

To examine the interaction of the water soluble polymers with the various pigment dispersions, viscosity measurements were taken on the samples over a period of three weeks, using a Brookfield Viscosmeter, Model RVT. The concentrations of the polymers and pigments used in this study, are listed in Table 1.

Evaluation of the Coatability of Aqueous Pigmented Coating Dispersion in a 6" Glatt-Wurster Tower

The coatability of an aqueous pigmented coating dispersions was determined by examining the ability to produce continuous, elegant film coating, on the placebo tablets, without employing unusual conditions or procedures. The physical properties of the tablets were determined by standard procedures. The hardness, friability and disintegration time of the coated tablets were evaluated and compared to the uncoated tablets. Air suspension coating, using a 6" Wurster tower, was employed in the initial coatability study. Shallow

concave and monogrammed tooling was used to prepare blank lactose based tablets as the tablet substrates. All Klucel EF, Methocel E5 and E15 solutions were prepared by adding the polymer to water at 50-53^{0} with stirring, allowing the polymer to hydrate 7-10 minutes, adding cold water to volume, and stirring to produce a uniform solution. The polymer solution was then slowly added to the pigment concentrate and stirred well. Table 2 provides a summary of the coating formulations prepared and evluated. The conditions employed for tablet air suspension coating were as follows:

500 g - coating solution prepared and applied
2.1 Kg - of tablets used for the coating process
60^{0} - temperature of incoming air maintained during coating process
11-13 units/min - proportioning pump setting
2.2 Kp/cm^{2} - Air spray setting (except formulation #1,2,3. Those three coatings were applied at settings of 2.0 Kp/cm^{2}
36-40 minutes - total coating time (except formulations #1,2,3)
3-4 minutes - drying time after tablets are coated

Table 1: Formulations Evaluated by Viscosity Measurements for Interaction Between the Water Soluble Polymers and the Pigments.

Klucel EF	6%	Methocel E5	6%
PEG 4000	0.36%	PEG 4000	0.36%
PEG 6000	0.64%	PEG 6000	0.64%
Colorcon Pigment	1.0 %	Colorcon Pigment	1.0 %
Water q.s. to	100.0 %	Water q.s. to	100.0 %

Methocel E15	5%
PEG 4000	0.36%
PEG 6000	0.64%
Colorcon Pigment	1.0 %
Water q.s. to	100.0 %

The Colorcon pigments used in this study were all water based/formulated systems of Colorcon Inc., Fort Washington, PA (See Table 2).

Table 2: Coating Formulations Applied in an Air Suspension Tower

Coating Number[a]	Polymer	% Polymer	% Plasticizer PEG 4000	% Plasticizer PEG 6000	Pigment[b]	% Pigment
1*	Methocel E5	8.5	0.53	1.28	Yellow 5	1.2
2*	Klucel EF	6.5	0.40	1.00	Yellow 5	1.2
3*	Methocel E15	6.0	0.40	1.00	Yellow 5	1.2
4	Methocel E5	8.5	0.53	1.25	Yellow 5	1.2
5	Klucel EF	6.5	0.40	1.00	Yellow 5	1.2
6	Methocel E15	6.0	0.40	1.00	Yellow 5	1.2
7	Klucel EF	5.0	0.36	0.64	Yellow 1	3.4
8	Klucel EF	5.0	0.36	0.64	-	-
9	Klucel EF	5.0	0.36	0.64	Red 1	3.4
10	Klucel EF	5.0	0.36	0.64	Brown 1	3.4
11	Klucel EF	7.0	0.40	1.00	Yellow 1	3.4
12	Klucel EF	7.0	0.40	1.00	-	-
13	Klucel EF	6.5	0.40	1.00	Yellow 1	3.4
14	Klucel EF	6.5	0.40	1.00	-	-
15	Methocel E15	5.0	0.36	0.64	Yellow 1	3.4
16	Methocel E-15	5.0	0.36	0.64	-	-
17	Methocel E-15	5.0	0.36	0.641	Red 1	3.4
18	Methocel E-15	5.0	0.36	0.64	Brown 1	3.4
19	Methocel E-5	8.5	0.53	1.28	Yellow 1	3.4
20	Methocel E-5	8.5	0.53	1.28	-	-
21	Methocel E-5	8.5	0.53	1.28	Red 1	3.4
22	Methocel E-5	8.5	0.53	1.28	Brownl	3.4

a. Coating numbers marked with an asterisk were applied to engraved lactose blank tablets

b. The water based pigment concentrates were all products of Colorcon Inc., Ft. Washington, PA, as follows:
Yellow 1 - lot 53-17-3, Yellow 2 - lot 53-17-5, Yellow 3 - lot 53-17-7, Yellow 4 - lot 53-17-8, Yellow 5 - lot 54/50/99-4, Red 1 - lot K-1-1894, Brown 1 - lot K-1-9026-L

The polymers used in this study were:

Klucel^{R} = Hydroxypropyl cellulose (HPC)

molecular weight (approximate) EF = 60,000 Viscosity (2%) 8-10 cps

From: Hercules Incorporated, 910 Market Street, Wilmington, Delaware 19899

Methocel^{R} = Hydroxypropyl methyl cellulose (HPMC)

molecular weight E5 = N.A. Viscosity (2%) 4-6 cps

E15 = N.A. " 13-18 cps

From: The Dow Chemical Company, Midland, Michigan 48640

Evaluation of a Klucel EF and Colorcon Dispersion (#53-17-3) as an Aqueous Film Coating Material in a 24" Accela-Cota Pan

A 24" Accela-Cota was selected to evaluate the coatability of a pigmented Klucel aqueous coating dispersion by a pan coating process. This Accela-Cota has been modified for aqueous film coating by adding a three-heater unit having a total heating capacity of 15,000 BTU in the air inlet of the unit. An airless spray system was used during this initial study and Avicel blank tablets were selected as the tablet substrate. The following formula was chosen for this study.

Klucel EF	325 g	6.5%
PEG 4000	20 g	0.4%
PEG 6000	50 g	1.0%
Color Pigment (#53-17-3)	485 g	3.4%
Water q.s.	5,000 g	88.7%

Coating Experiments: The pressurized tank of the Thomas Engineering Spray System was filled with coating solution and charged with air pressure to 70-80 psi. An airless spray (spray gun nozzle size 0.031 in.) was connected to the tank and the clamping pressure for exhausting the air was set at 56 psi. Ten Kg. of the blank Avicel tablets were introduced into the standard 24" Accela-Cota. Two of the specially designed heating units designed for the 24" pan (~9,000 BTU total) were used, and the temperature adjusting knob was set at 180-220^{o} F. Within approximately ten minutes of elapsed time, during which

tablets were rolling, the tablet bed temperature reached 45-50° C. At that time the coating operation was begun. The spray was directed manually to maintain a tablet temperature of 30-40°. The pan speed was kept at 18-20 rpm. On completion of coating, the heating source was turned off, and the tablets were allowed to run for an additional 7-10 minutes for drying, by allowing room air to be drawn into the apparatus during this post-coating time. The same coating experiment was repeated, without color addition in the coating solution, for comparison.

Evaulation of Klucel EF, Methocel E5 and E15 with Colorcon Pigment Dispersions as Aqueous Film Coatings and the Stability of the Coated Tablets

The three above named polymers were applied to the placebo tablets, unpigmented, and pigmented with three different Colorcon color dispersions, employing a 6" Glatt-Wurster tower and the coating procedure previously described. The tablets were evaluated for hardness and disintegration not only initially after coating, but also after 3 months of stress-aging at both 40° and 50°. Moisture uptake of the coated tablets and uncoated controls were determined by exposing the tablets to a high water-vapor pressure condition.

Stability Evaluation of the Film Coated Tablets

The hardness and distintegration time stability of the film coated tablets, with and without pigments, was carried-out on samples stored at 40 and 50° in closed screw-cap brown glass containers, over a period of three months. The color and hardness* of the tablets were periodically examined. The disintegration time of the tablets was measured after three months storage, by the USP XIX method.

The effect of high humidity on the film coated tablets was determined by exposing the tablets at 30° (± 0.5°) and 81.1% relative humidity. For this purpose, two one-ounce square amber glass bottles filled with 50 tablets were used. One of these was tightly closed and the other one was left open.

*Haberlein Hardness Tester

The bottle which was tightly closed was used as a control. The environmental chamber consisted of an air tight dessicator in which the tmperature was maintained at 30 $\pm$ 0.5^{0}. To obtain an 81.1% relative humidity, a saturated solution of ammonium sulfate was used.

The film coated tablet samples were placed inside the dessicator in their containers above the saturated salt solution. The dessicator was then placed inside the environmental chamber for temperature control. The amount of moisture uptake by the tablet at any given time was obtained from the increase in average weight of the tablets.

RESULTS

Evaluation of the Interaction of Water Soluble Polymers (Methocel E5, Methocel E15, Klucel EF) with Five Colorcon Pigment Dispersions

The results showed that the viscosity of each solution did not change over the period studied (Figure 1a-1e). It was concluded that none of the five pigments interacted appreciably with any of the polymers.

Evaluation of the Coatability of Aqueous Pigmented Coating Dispersions in a 6" Glatt-Wurster Tower

The coating results for the pigment dispersions in solutions of the three polymers or for the polymer solutions alone, applied in the Wurster tower, were excellent. The film coated tablets had a smooth, shiny, and elegant surface. The weight variation, thickness, hardness and disintegration time of identically pigmented coated tablets of the three polymers, versus uncoated control tablets, are presented in Table 3. None of the coated tablets demonstrated appreciable friability. The Klucel coated tablets (formulations 2 and 5) were somewhat softer than the Methocel formulations, probably reflecting the more flexible Klucel film. There was some trend to indicate that the Methocel E15 polymer increased tablet disintegration times while the other two polymers produced no such increase or a minimal increase.

Evaluation of Klucel EF and Colorcon Dispersion (Yellow 1) as an Aqueous Film Coating Material in a 24" Accela-Cota Pan

The amount of coating solution required for 10 Kg of blank tablets was

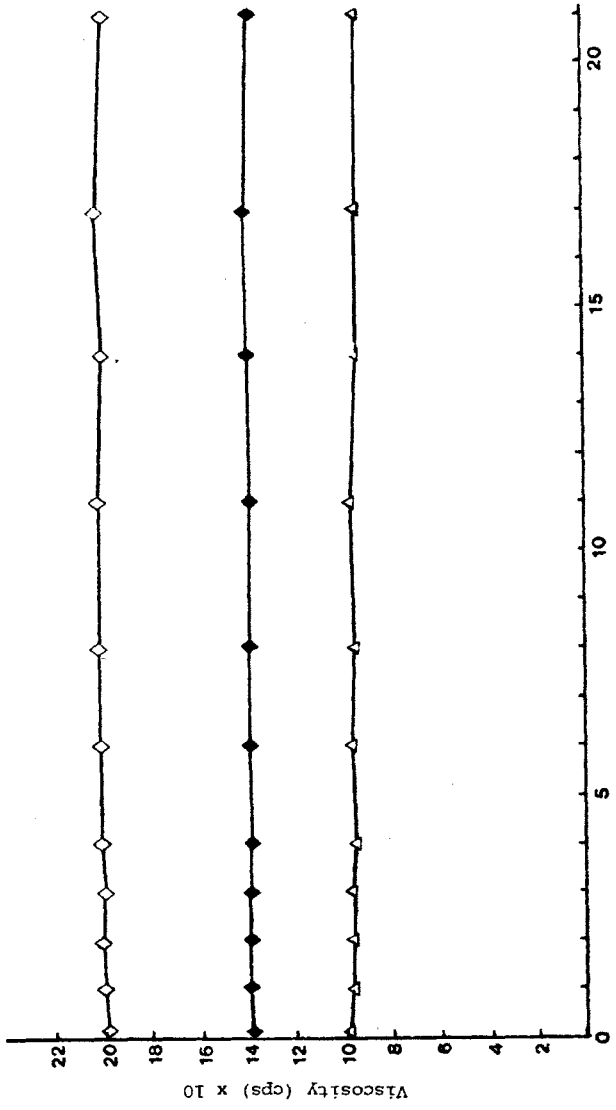

Fig. 1a. Interaction of pigment formulation (#53-17-3) with water soluble polymers.
(◇ Methocel E15, ◆ Klucel EF, △ Methocel E5).

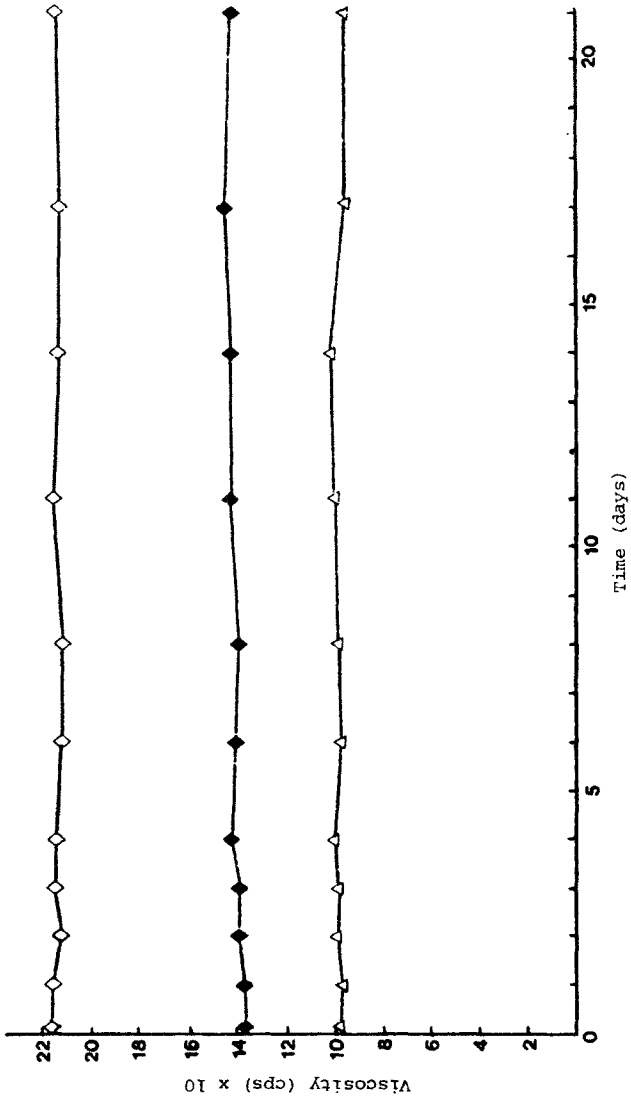

Fig. 1b. Interaction of pigment formulation (#53-17-5) with water soluble polymers.
(◇ Methocel E15, ◆ Klucel EF, △ Methocel E5).

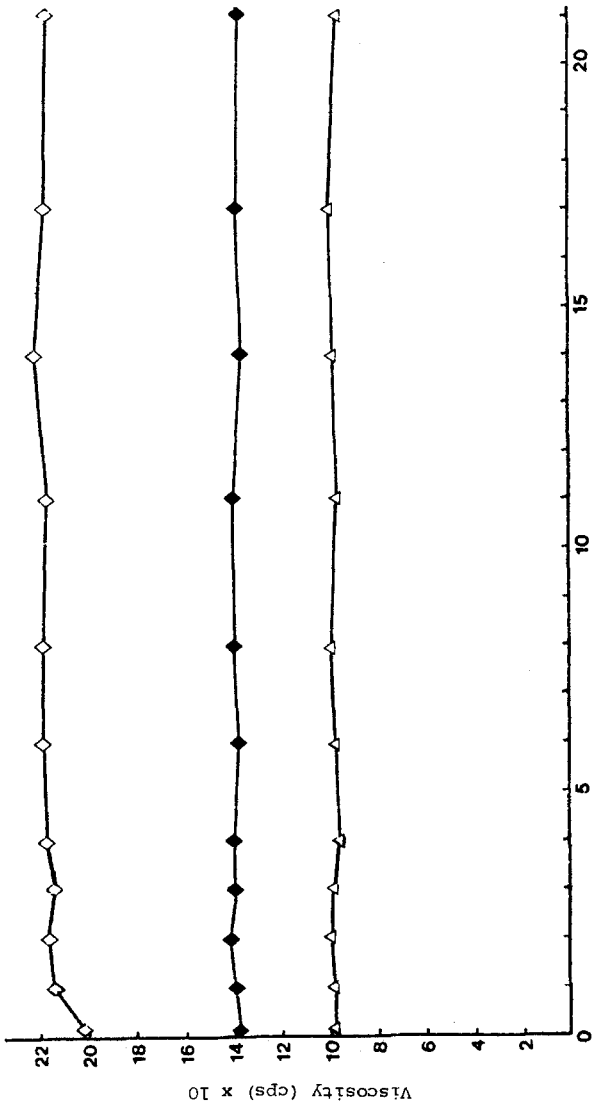

Fig. 1c. Interaction of pigment formulation (#53-17-7) with water soluble polymers.
(◇ Methocel E15, ● Klucel EF, △ Methocel E5).

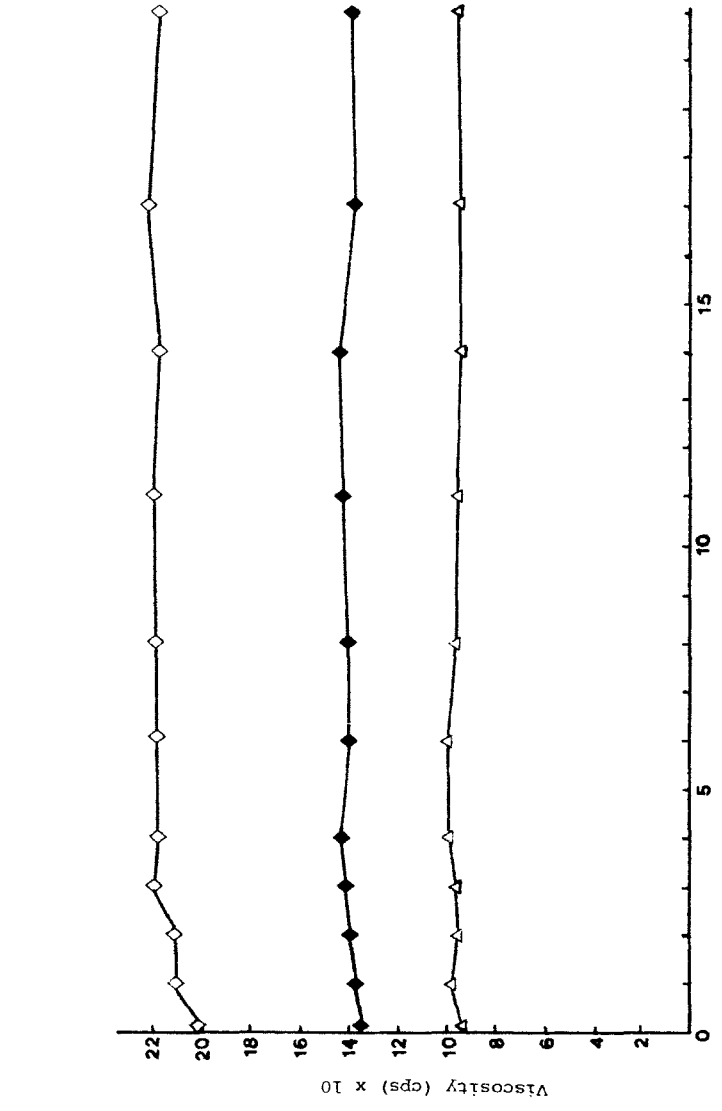

Fig. 1d. Interaction of pigment formulation (#53-17-8) with water soluble polymers.
(◇ Methocel E15, ◆ Klucel EF, △ Methocel E5).

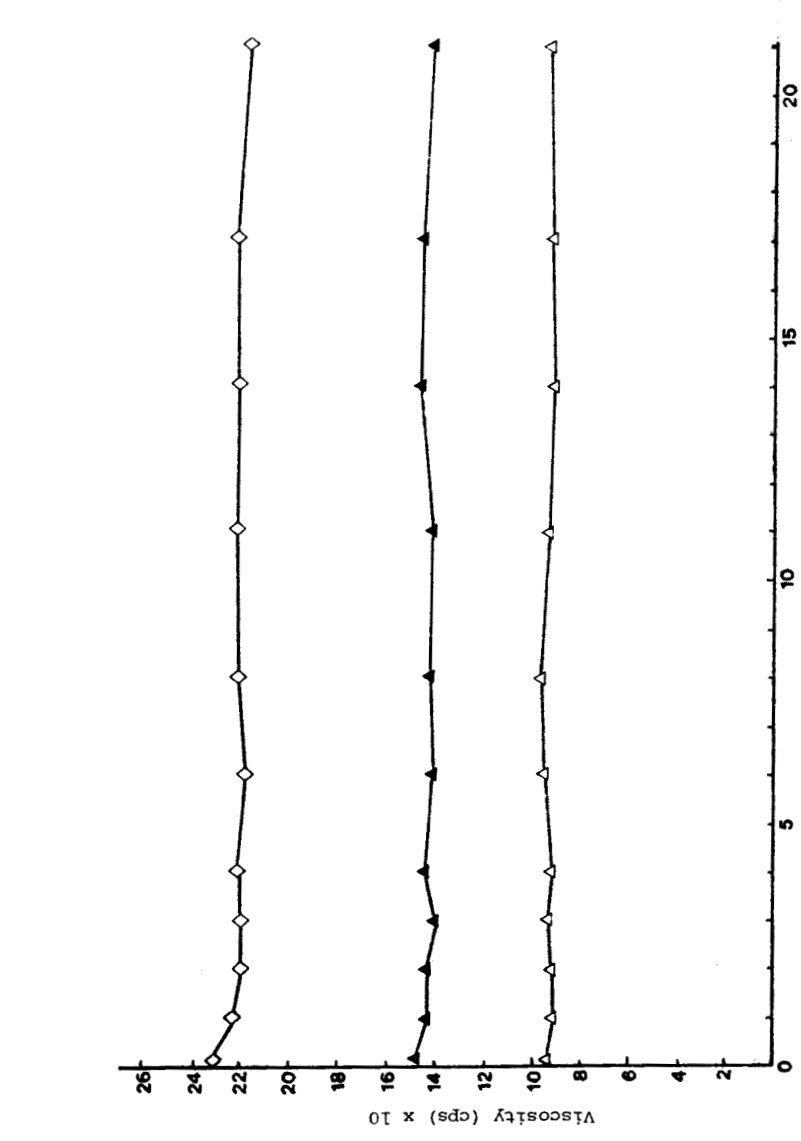

Fig. 1e. Interaction of pigment formulation (#54/50/99-4) with water soluble polymers.
(◇ Methocel E15, ◆ Klucel EF, △ Methocel E5).

Table 3. Evaluation of Coated Tablets vs Uncoated Tablets

Tablet or Coating Number[a]	Hardness (sc) n = 10	Thickness (in.) n = 10	Weight (mg) n = 20	Disintegration Time (minutes)
Uncoated (engraved blank)	15.70 ± 5.28	.204 ± .003	481.60 ± 12.19	18.9 ± 1.38
1	22.59 ± 2.06	.216 ± .020	497.26 ± 15.5	21.0 ± 3.41
2	19.11 ± 2.47	.207 ± .003	493.70 ± 11.99	23.8 ± 6.24
3	24.23 ± 1.17	.207 ± .003	494.17 ± 15.92	25.9 ± 3.32
Uncoated (shallow concave blank)	13.24 ± 1.46	.181 ± .002	344.19 ± 6.94	27.6 ± 4.23
4	19.96 ± 1.60	.186 ± .002	354.90 ± 7.65	25.0 ± 7.36
5	14.23 ± 1.61	.186 ± .003	351.57 ± 9.06	27.0 ± 3.13
6	18.06 ± 1.60	.187 ± .002	350.24 ± 11.16	29.7 ± 3.82

[a]See Table 2 for identification

Table 4. Evaluation of Pan Coated Tablets vs. Uncoated Tablets

	Friability (n = 10)		Hardness (sc) n = 10	Thickness (in.) n = 10	Weight (mg) n = 20	Disintegration (min.)
	before (g)	after (g)				
Uncoated Tablet	-----	-----	18.63 ± 1.33	.193 ± .002	448.5 ± 2.8	12 ± 2
Coated with Pigment	4.63	4.63	20.05 ± 1.61	.201 ± .002	465.0 ± 3.5	30 ± 5
Coated without Pigment	4.64	4.64	17.66 ± 2.2	.197 ± .002	462.0 ± 5.0	26 ± 4

Table 4a. Hardness of film coated tablets stored at 40°C (Unit: sc)

Coating Number[a]	Polymer %	Pigment #	Time (day) 0	2	5
Uncoated	---	---	14.48 ± 2.92	13.24 ± 1.37	13.52 ± 1.65
7	Klucel EF 5%	Yellow 1	14.53 ± 1.54	13.81 ± 1.97	14.60 ± 1.69
8	"	---	13.23 ± 1.82	12.41 ± 1.62	12.74 ± 1.50
9	"	Red 1	15.74 ± 1.73	15.58 ± 2.16	15.53 ± 2.07
10	"	Brown 1	15.83 ± 2.40	14.29 ± 2.53	15.49 ± 2.05
11	Klucel EF 7%	Yellow 1	18.30 ± 1.91	17.75 ± 1.87	18.19 ± 1.99
12	"	---	15.35 ± 2.37	14.31 ± 1.70	15.49 ± 2.11
13	Klucel EF 6.5%	Yellow 1	17.64 ± 2.09	16.85 ± 2.28	18.17 ± 1.74
14	"	---	14.01 ± 1.87	13.48 ± 1.46	13.92 ± 1.88
15	Methocel E15 5%	Yellow 1	20.28 ± 2.13	19.01 ± 3.66	19.78 ± 1.93
16	"	---	19.94 ± 1.85	19.80 ± 1.76	20.41 ± 2.31
17	"	Red 1	21.65 ± 1.44	21.35 ± 2.40	21.17 ± 2.32
18	"	Brown 1	21.93 ± 1.73	21.86 ± 1.98	20.96 ± 2.53
19	Methocel E5 8.5%	Yellow 1	21.64 ± 2.72	21.77 ± 1.66	21.46 ± 2.10
20	"	---	20.83 ± 1.51	20.89 ± 1.91	20.39 ± 2.10
21	"	Red 1	21.45 ± 2.40	21.57 ± 1.92	20.87 ± 2.24
22	"	Brown 1	22.10 ± 2.23	21.16 ± 2.35	21.94 ± 1.98

a. See Table 2 for coating compositions.

12	23	40	52	90
13.76 ± 1.65	13.31 ± 1.72	13.54 ± 1.83	13.63 ± 2.10	14.22 ± 1.29
13.94 ± 1.79	14.82 ± 1.72	13.19 ± 1.72	13.01 ± 2.00	12.95 ± 2.12
12.80 ± 1.47	12.95 ± 1.60	13.95 ± 1.53	11.99 ± 2.10	12.15 ± 1.59
14.99 ± 2.18	15.15 ± 1.66	13.49 ± 2.19	14.00 ± 1.95	14.08 ± 3.09
15.09 ± 1.65	14.75 ± 2.58	15.41 ± 2.81	14.93 ± 1.96	15.09 ± 2.31
19.14 ± 2.14	18.85 ± 1.60	17.25 ± 2.36	18.01 ± 1.25	17.52 ± 3.27
15.28 ± 2.21	14.76 ± 2.03	13.75 ± 1.55	13.63 ± 1.62	13.34 ± 1.09
18.11 ± 2.10	18.81 ± 2.88	17.66 ± 1.62	16.95 ± 2.50	16.71 ± 2.30
13.54 ± 1.66	13.69 ± 1.31	13.10 ± 1.40	13.32 ± 1.29	13.49 ± 1.35
20.38 ± 1.86	19.73 ± 1.48	19.44 ± 1.81	19.59 ± 1.63	19.42 ± 1.99
19.94 ± 2.05	21.40 ± 1.77	20.58 ± 2.16	20.12 ± 3.10	20.43 ± 2.54
21.87 ± 2.49	21.94 ± 2.19	20.00 ± 1.80	20.95 ± 2.54	20.03 ± 1.88
21.54 ± 2.30	20.96 ± 2.00	20.69 ± 1.77	21.63 ± 2.08	22.10 ± 1.98
21.64 ± 1.80	20.65 ± 1.23	19.23 ± 1.79	19.75 ± 1.89	20.30 ± 1.29
20.48 ± 1.35	20.95 ± 2.47	18.92 ± 3.75	19.05 ± 2.19	19.69 ± 1.98
22.43 ± 2.10	22.09 ± 1.74	19.81 ± 2.48	21.02 ± 2.31	20.65 ± 2.00
20.85 ± 1.32	21.89 ± 2.57	19.52 ± 2.01	20.52 ± 1.63	21.25 ± 1.93

Table 4b. Hardness of film coated tablets stored at 50°C. (Unit = sc)

Coating[a] number	Polymer %	Pigment #	Time (day) 0	2	5
Uncoated	---	---	14.48 ± 2.92	13.07 ± 2.64	13.74 ± 1.92
7	Klucel EF 5%	Yellow 1	14.53 ± 1.54	14.54 ± 1.42	14.01 ± 1.56
8	"	---	13.23 ± 1.82	12.72 ± 1.65	12.60 ± 1.64
9	"	Red 1	15.74 ± 1.73	15.28 ± 2.29	15.45 ± 1.71
10	"	Brown 1	15.83 ± 2.40	15.18 ± 2.41	15.09 ± 1.88
11	Klucel EF 7%	Yellow 1	18.30 ± 1.91	18.28 ± 2.39	17.93 ± 2.18
12	"	---	15.35 ± 2.37	15.31 ± 1.43	14.89 ± 1.63
13	Klucel EF 6.5%	Yellow 1	17.64 ± 2.09	18.17 ± 1.81	18.47 ± 1.87
14	"	---	14.01 ± 1.87	13.55 ± 1.40	13.87 ± 1.63
15	Methocel E15 5%	Yellow 1	20.28 ± 2.13	19.42 ± 2.53	19.51 ± 1.54
16	"	---	19.94 ± 1.85	20.45 ± 1.89	20.58 ± 2.35
17	"	Red 1	21.65 ± 1.44	20.05 ± 2.36	19.86 ± 4.24
18	"	Brown 1	21.93 ± 1.73	20.97 ± 2.23	21.21 ± 2.63
19	Methocel E5 8.5%	Yellow 1	21.64 ± 2.72	21.29 ± 2.63	20.55 ± 1.67
20	"	---	20.83 ± 1.51	18.86 ± 4.30	19.23 ± 3.03
21	"	Red 1	21.45 ± 2.40	21.25 ± 1.64	20.45 ± 2.68
22	"	Brown 1	22.10 ± 2.23	21.34 ± 2.01	21.36 ± 1.80

a. See Table 2 for coating compositions.

Table 4b (cont'd.)

12	23	40	62	90
13.37 ± 1.93	13.75 ± 2.22	13.67 ± 1.69	13.81 ± 2.10	13.95 ± 2.55
14.27 ± 2.07	14.76 ± 1.40	14.05 ± 1.91	15.06 ± 3.09	15.24 ± 1.50
12.55 ± 1.53	13.04 ± 1.79	12.61 ± 1.64	13.43 ± 1.94	12.29 ± 1.27
14.85 ± 2.44	15.13 ± 2.38	15.08 ± 2.79	14.96 ± 2.11	14.90 ± 2.52
14.84 ± 2.22	15.05 ± 2.03	15.52 ± 1.62	14.69 ± 2.59	15.26 ± 1.88
17.99 ± 1.81	18.87 ± 2.22	17.86 ± 2.83	19.01 ± 1.31	18.46 ± 2.10
14.39 ± 1.31	14.92 ± 1.30	14.96 ± 2.47	14.42 ± 2.70	15.38 ± 1.73
17.56 ± 2.70	18.49 ± 2.72	17.70 ± 1.71	16.89 ± 2.30	16.92 ± 3.08
13.69 ± 2.01	13.29 ± 1.63	13.15 ± 1.41	12.89 ± 2.11	13.00 ± 1.39
18.96 ± 2.33	20.03 ± 2.14	18.91 ± 2.33	20.31 ± 2.57	20.52 ± 1.64
20.71 ± 3.02	19.65 ± 2.20	19.44 ± 2.57	20.67 ± 3.42	20.16 ± 2.03
20.19 ± 1.68	21.76 ± 2.53	20.56 ± 1.69	21.14 ± 1.42	20.93 ± 2.93
21.37 ± 2.19	21.26 ± 2.32	21.86 ± 1.81	20.86 ± 2.63	20.44 ± 2.41
20.95 ± 1.93	20.79 ± 1.30	19.17 ± 1.89	20.06 ± 1.72	19.33 ± 2.81
20.34 ± 1.90	19.29 ± 1.35	19.78 ± 1.54	21.30 ± 2.72	20.60 ± 1.41
21.73 ± 2.45	21.35 ± 2.57	21.47 ± 2.18	21.87 ± 1.24	21.97 ± 1.65
21.99 ± 3.31	20.87 ± 2.95	20.68 ± 2.00	21.47 ± 2.45	22.01 ± 1.97

Table 5 : Disintegration time of film coated tablets.

Coating Number[a]	Polymer %	Pigment #	Disintegration Time (minutes) Original	After 3 months Storage at 40°	After 3 months Storage at 50°
Uncoated	---	---	14.86 ± 1.62	9.75 ± 0.87	9.07 ± 0.54
7	Klucel EF 5%	Yellow 1	16.83 ± 1.98	17.80 ± 1.92	16.57 ± 5.90
8	"	---	12.10 ± 0.95	10.06 ± 0.65	4.41 ± 2.10
9	"	Red 1	20.17 ± 1.25	19.66 ± 1.31	24.30 ± 1.95
10	"	Brown 1	19.50 ± 2.21	24.01 ± 2.11	26.10 ± 2.20
11	Klucel EF 7%	Yellow 1	19.04 ± 0.97	37.03 ± 5.14	35.17 ± 4.95
12	"	---	11.75 ± 0.83	12.08 ± 0.74	12.11 ± 1.49
13	Klucel EF 6.5%	Yellow 1	20.21 ± 1.02	38.30 ± 5.73	35.16 ± 4.31
14	"	---	11.50 ± 0.63	11.20 ± 0.74	10.45 ± 0.54
15	Methocel E15 5%	Yellow 1	20.56 ± 0.79	20.74 ± 3.47	26.50 ± 2.05
16	"	---	12.10 ± 0.75	10.56 ± 0.97	9.94 ± 0.93
17	"	Red 1	19.06 ± 2.08	24.45 ± 5.12	26.28 ± 2.70
18	"	Brown 1	18.69 ± 2.80	20.16 ± 2.94	24.75 ± 4.10
19	Methocel E5 8.5%	Yellow 1	17.61 ± 2.36	7.78 ± 2.65	6.70 ± 5.50
20	"	---	12.1 ± 0.80	11.27 ± 1.66	10.75 ± 0.87
21	"	Red 1	17.90 ± 1.69	26.29 ± 1.37	21.31 ± 0.91
22	"	Brown 1	18.67 ± 1.74	23.02 ± 2.91	28.50 ± 5.09

a. See Table 2 for coating compositions.

approximately 3.6 Kg. The coated tablets, including the tablet edges, appeared smooth and uniform. Properties of the coated and uncoated tablets are summarized in Table 4. When the tablets of Table 4 are compared to the Klucel coated tablets of Table 3, there is an indication that pan coating tended to increase disintegration times in comparison to the uncoated blanks, while air suspension coating did not.

Evaluation of Klucel EF, Methocel EF and E15 with Colorcon Pigment Dispersions as Aqueous Film Coatings and the Stability of the Coated Tablets

The hardness of the coated tablets and uncoated controls on storage at 40^{o} over 90 days or at 50^{o} over 90 days are shown in Table 4a and 4b respectively. Although the Klucel coated tablets were initially somewhat softer than the Methocel coated tablets, there was no consistent change in hardness observed with any coating at either temperature over the 90 day period. Likewise, no change in color intensity was seen at either temperature over the 90 day period with any of the coatings in Table 4.

The disintegration times of the coated tablets and uncoated controls, initially and after three months storage at 40^{o} and 50^{o}, are shown in Table 5. In general there was little change in disintegration time for any sample at 40^{o}. At 50^{o} the disintegration time of 5 out of 6 Methocel pigmented coated tablets had increased. The unpigmented coated tablets did not undergo an increase in disintegration time on high temperature exposure.

The amount of moisture uptake by the tablets is shown in Table 6. It is clear that the films containing pigments have a tendency to lower the moisture uptake, as compared to the coated tablets containing no pigment. The pigment formulations clearly have some benefit in reducing moisture uptake in these aqueous based film coated tablets.

SUMMARY

Hydroxpropyl cellulose and hydroxypropyl methyl cellulose have been evaluated as plasticized film coatings applied from a totally aqueous system. Elegant coatings of both polymers were obtained, employing either

Table 6: Percentage of moisture uptake of polymer film coated tablets

Coating Number[a]	Polymer %	Pigment #	Time (day) 1 Control	1 Sample	2 Control	2 Sample
7	Klucel EF 5%	Yellow 1	0.0061	0.7967	0.0096	1.2898
8	"	---	0.0069	0.9126	0.0101	1.4596
9	"	Red 1	0.0069	0.6303	0.0074	1.0408
11	Klucel EF 7%	Yellow 1	0.0046	0.7343	0.0064	1.1857
12	"	---	0.0052	0.9692	0.0073	1.5558
13	Klucel EF 6.5%	Yellow 1	0.0018	0.7616	0.0035	1.2245
14	"	---	0.0052	0.9403	0.0079	1.4736
15	Methocel E15 5%	Yellow 1	0.0028	0,6970	0.0039	1.1370
16	"	---	0.0041	0.9771	0.0052	1.5876
17	"	Red 1	0.0015	0.6563	0.0040	1.0878
19	Methocel E5 8.5%	Yellow 1	0.0059	0.6410	0.0079	1.0682
20	"	---	0.0071	0.9941	0.0059	1.5865
21	"	Red 1	0.0011	0.6420	0.0037	1.0787

a. See Table 2 for coating compositions.

Table 6 (Cont'd)

3		4		5		7	
Control	Sample	Control	Sample	Control	Sample	Control	Sample
0.0107	1.6493	0.0107	1.9465	0.0109	2.1813	0.0112	2.5145
0.0110	1.8645	0.0114	2.1762	0.0114	2.3947	0.0129	2.7148
0.0079	1.3684	0.0079	0.6545	0.0081	1.8992	0.0079	2.2183
0.0068	1.5564	0.0068	1.8552	0.0071	2.0820	0.0092	2.4044
0.0085	2.0087	0.0085	2.3634	0.0101	2.6200	0.0102	2.9602
0.0080	1.5950	0.0074	1.9063	0.0081	2.1583	0.0093	2.5032
0.0079	1.8705	0.0087	2.1936	0.0100	2.4430	0.0111	2.7946
0.0039	1.4731	0.0051	1.7501	0.0054	1.9679	0.0052	2.3075
0.0059	2.0139	0.0071	2.3512	0.0069	2.6000	0.0080	2.9261
0.0055	1.4157	0.0055	1.6878	0.0040	1.9041	0.0059	2.2149
0.0079	1.3971	0.0092	o16741	0.0090	1.8991	0.0105	2.2280
0.0072	2.0099	0.0089	2.3507	0.0089	2.5984	0.0102	2.9431
0.0021	1.4327	0.0042	1.7215	0.0040	1.9452	0.0079	2.2863

clear of pigmented polymer aqueous solutions, and utilizing either pan or (Accela Coata)or air suspension coating methods. Coating conditions and properties of the coated tablets are described. Unpigmented coatings generally had shorter disintegration times than pigmented coated tablets, and were much less prone to undergo disintegration time increases at 40^{0} or 50^{0} storage for three months, compared to the pigmented coatings. Hydroxylpropyl cellulose (Klucel EF) coating compositions are described which are at least equal to hydroxypropyl methyl cellulose coatings when applied from totally aqueous systems.