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Water Soluble Cellulose Acetate: A Versatile Polymer for Film Coating

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ABSTRACT The objective of this study was to investigate the use of water soluble cellulose acetate (WSCA) as a film coating material for tablets. Aspirin (ASA) tablets were prepared by direct compression and coated with either WSCA or HPMC (hydroxypropyl methylcellulose) dispersions. Coatings of 1–3%, depending on the intended application, were applied to the model drug (ASA) tablets employing a side-vented coating pan. Free films of WSCA, prepared by cast method, are crystal clear and, depending on the viscosity grade, are flexible, strong and durable. WSCA has the capability of forming free films without plasticizers and the films dry at room temperature. Glass transition temperature, *Tg*, was determined by differential scanning calorimetry. The *Tg* of WSCA is significantly higher relative to HPMC. Inclusion of plasticizer lowers the *Tg* of WSCA and effective plasticizers were PEG 400 and glycerin. Low viscosity WSCA was more soluble in water (25–30%) relative to medium viscosity WSCA (10–15%). WSCA solutions exhibited no increase in viscosity with an increase in temperature. Samples of coated (WSCA and HPMC) tablets and uncoated ASA cores were packaged for stability studies at room and elevated temperature storage. Physical stability of ASA tablets coated with 2:1 LV: MV (low viscosity: medium viscosity) WSCA formulations was better when compared to tablets coated with HPMC. Dissolution stability of WSCA coated ASA was similar to the physical stability results. After three months at elevated temperature (35 and 45°C), the WSCA coated tablets complied with USP dissolution requirements for ASA, while the HPMC coated tablets did not. There was no difference in moisture (weight) gain of ASA tablets coated with either WSCA or HPMC. The WSCA coated tablets were not sticky or tacky, while the HPMC coated tablets were tacky and stuck together.

KEYWORDS Water soluble cellulose acetate, Polymer, Thermal properties, Plasticizers, Coating, Coated tablet stability

INTRODUCTION

Water soluble cellulose acetate (WSCA) is a variation of commercially available cellulose acetate. Regular cellulose acetate has approximately 2.4 of the 3-hydroxyl groups per anhydroglucose unit substituted with an acetyl

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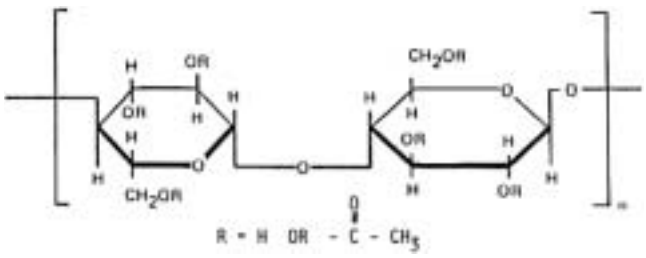

FIGURE 1 **Molecular Structure of Cellulose Acetate.**

group (Fig. 1). WSCA has a lower degree of substitution, with less than one of the hydroxyl groups converted to the acetate.

Commercial cellulose acetate is water insoluble and is produced by controlled esterification of pure raw cellulose with acetic acid and acetic anhydride. In this process acetyl groups are substituted for all or a portion of the hydroxyl units on the cellulose chain. In order to obtain soluble cellulose acetate (WSCA), the acetylation is carried to completion first to form cellulose triacetate and then followed by hydrolysis to lower the acetyl content to the desired level. In commercial cellulose acetate, hydrolysis is stopped when a 2.4 degree of substitution (DS) is reached. For WSCA, hydrolysis is continued until 0.8 DS is obtained.

The preparation of soluble cellulose acetate (WSCA) was first reported in 1938 (Fordyce, 1938). The report (patent) relates to cellulose acetate that has been hydrolyzed to an acetyl content of 13–28%. Fordyce stated that, "cellulose acetate having an acetyl content of 13–19% is water soluble and is useful for water soluble films or coatings." Water soluble cellulose acetate films and fibers, the processes for producing them and their uses, have been reported by several investigators (Malm et al., 1957; Bohrer, 1969; Mukherjee et al., 1981). In addition, a Russian patent discloses using WSCA as a tablet binder for use by the pharmaceutical industry. These early reported water soluble cellulose acetate films and fibers, however, often have limited utility because they are difficult to process or have low tensile properties or both.

Domeshek & Zazzara (1991) reported on water soluble cellulose acetate compositions having improved processability and tensile properties suitable for applications as films, coatings and fibers. The compositions comprised one or more lower molecular weight and one or more higher molecular weight WSCA components. Wheatley et al. (1993a,b,c) investigated the use of WSCA film forming compositions to coat pharmaceutical dosage forms, such as tablets. They employed blends of low viscosity (LV) and medium viscosity (MV) WSCA. These investigations were conducted at the FMC BioPolymer Research Laboratory, Princeton, NJ between 1987 and 1989.The objective of this paper is to report in more detail the use of WSCA as a film coating material for tablets.

MATERIALS AND METHODS

Materials

The following chemicals were used as received. Experimental grades of low viscosity (LV) and medium viscosity (MV) WSCA were from Hoechst Celanese Corporation, Charlotte, NC. Polyethylene glycol (PEG 400) and hydroxypropylmethyl cellulose (HPMC E-5) were obtained from Dow Chemical Company, Midland, MI. Glycerin was from Penta Chemical Company, Fairfield, NJ; titanium dioxide (TiO_2) from Whittaker, Clark and Daniels, South Plainfield, NJ; dioctyl sodium sulfosuccinate (DOSS) from American Cyanamide Corporation, NY; Sepisperse® AP 3027 from Seppic, Paris, France and Cotolene®- PG Orange from H. Kohnstam, NY.

Preparation of Aspirin Tablets

Aspirin (ASA) was chosen as the model drug. Tablets containing 81.25% aspirin USP (40 mesh crystalline), microcrystalline cellulose Avicel® PH-101, Starch 1500, croscarmellose sodium Ac-Di-Sol®, colloidal silicon dioxide Cab-O-Sil® and stearic acid were prepared by direct compression on a B-2 tablet press (F. J. Stokes Corporation, Philadelphia). The tablet tooling was 13/32″ deep concave and average tablet weight of 400 mg. Tablet friability ($n = 20$) was typically between 0.1–0.2% and tablet disintegration (USP 20 for uncoated tablets) 15–25 sec.

Preparation of Coating Dispersions

Coating dispersions of water soluble cellulose acetate were prepared by one of two methods, i.e. blending aqueous solutions of low viscosity (LV) and

medium viscosity (MV) WSCA or by first dry blending LV and MV WSCA polymer powder and then preparing the coating dispersion. Detailed description of the preparation procedures follow:

Blending of Aqueous Polymer Solutions

1. Appropriate amounts of low viscosity (LV) and medium viscosity (MV) WSCA were mixed in deionized (DI) water in separate containers to make 15% by weight (LV) and 10% by weight (MV) solutions, respectively
2. The solutions were mixed (standard variable speed propeller-type mixers) for 60–120 min, covered and allowed to stand over night to ensure complete hydration of the polymer.
3. Appropriate amounts of each polymer solution were combined and mixed for 15 min to achieve the desired polymer ratio.
4. With continued mixing, plasticizer such as PEG 400 or glycerin was added to the LV:MV WSCA polymer solution, and mixed for 15–30 min.
5. With continued mixing, color, such as Sepisperse® AP aqueous pigment dispersion or Cotolene® PG orange, was added to the plasticized polymer solution and mixed for 15–30 min.
6. Water was added to the suspension to adjust the solids content in the final composition to 12.5% by weight and the suspension mixed thoroughly for 15–30 min. A typical coating dispersion formula is shown in Table 1

TABLE 1 **Coating Dispersion From WSCA Polymer Solutions**

Components	Suspension	Solids	(%)
WSCA, low viscosity* (15% w/w solution)	2963.0	444.5	59.3
WSCA, medium viscosity* (10% w/w solution)	2222.3	222.2	29.6
PEG 400 or glycerin	33.3	33.3	4.4
Sepisperse® AP-3027**	190.2	50.0	6.7
DI Water	591.2		
	6000.0g	750.0g	100.0

*The total solids concentration of the coating dispersion is 12.5% by weight of which approximately 89% is WSCA polymer. The ratio of LV to MV WSCA is 2:1.

**Sepisperse® AP-3027 is a commercial aqueous pigment dispersion. It contains 26.3% by weight of pigment solids and 7.5% pigment solids were used based on total polymer.

Dry Blending of Polymer Powders

1. A blend of low viscosity (LV) WSCA and medium viscosity (MV) WSCA was combined with titanium dioxide in a P-K "V" blender (Patterson Kelly, East Stroudsburg, PA) with intensifier ("I") bar. The ingredients were blended without the "I" bar for 15.5 minutes.
2. A solution of dioctyl sodium sulfosuccinate (surfactant) and PEG 400 (plasticizer) was prepared by mixing the components at low heat until a clear solution was obtained.
3. With the "I" bar on, the surfactant/plasticizer solution was added to the WSCA/TiO_2 powder mixture and blended for 1 min.
4. The resulting mixture was then ground to a fine powder by passing it through a Fitzmill ™ (The Fitzpatrick Co., Chicago) with a 1526–0014 (14 mesh) screen with hammers forward.
5. A coating dispersion containing 15% solids by weight (Table 2) was prepared by stirring the fine powder in water.

Hydroxypropylmethyl Cellulose Coating Dispersion

Dispersions of hydroxpropylmethyl cellulose (HPMC E-5) were prepared and used as controls for the coating trials. The plasticizer was PEG 400 and the dispersion was typically applied at 12.5% solids concentration by weight to the model drug tablets.

TABLE 2 **Coating Dispersion From WSCA Powder Blend**

	Composition	
Components	Solids*	(%)
WSCA, LV	700.0	41.6
WSCA, MV	350.0	20.8
TiO_2	525.0	31.2
DOSS	3.5	0.2
PEG 400	105.0	6.2
	1,683.5g	100.0

*A coating dispersion containing typically 15% by weight WSCA power blend was prepared and applied to tablets. In this example, approximately 62.4% of the solids composition is WSCA polymer, and the ratio of LV to MV WSCA is 2:1.

Coating Procedure

The dispersions (WSCA or HPMC) were applied to 10 kg of model drug (ASA) tablets employing a 24″ Accela-Cota™ perforated coating pan (Thomas Engineering, Inc., Hoffman Estates, IL). Coatings of 1–3% by weight were applied to the tablets depending on the intended application. Typical coating conditions are presented in Table 3.

Viscosity

Two methods were employed by the Hoechst-Celanese Company based on the solution viscosity of the WSCA sample.

1. If the solution viscosity was less than 600 cP, then capillary viscometry was employed using a modified Ostwald pipette with a precision bore, specially made by Tudor Scientific Glass, and was calibrated using Cannon oil standard at 25°C (± 0.1°C). Capillary viscosimetry was typically used for LV grades of WSCA at all solids concentration.

TABLE 3 Coating Procedures

Spray coating equipment	
Pan	24″ Accela-Cota
Baffles	4 straight and 4 mixing
Pump	Masterflex 7562-10
Pump heads	Two 7015
Spray guns	Two SS 7310–1/4 JAU
Fluid caps	1.0 mm
Air caps	134255–45° SS
Spray coating conditions	**Range**
Batch size (kg)	10
Spray rate (mL/min/gun)	15–16
Atomizing air (Bar)	1.5
Gun distance (inches)	6 at 45°
Air temperature (°C)	
Inlet	60–75
Exhaust	36–40
Bed temperature (°C)	32–35
Pan rotation (rpm)	10
Tablet bed warming (min. jogging)	10
Total coating time (min.)	65–80
Post drying	
Inlet air temperature (°C)	60
Drying time (min)	20
Tablet weight gain (wt./wt. %)	2.7–3.0

2. Brookfield viscosity was used on solutions with viscosities exceeding 500 cP, and was used at all solids concentrations for MV grades WSCA, i.e.

   Brookfield viscometer, Model RVF
   Spindle # 1 for 2–6% solutions
   Spindle # 2 for 8–15% solutions
   Speed 20 rpm.

Brookfield viscosity was used by FMC for both LV and MV grades WSCA at varying solids concentration, i.e.

Brookfield viscometer, Model RVT-7
Spindle # 3 at 20 rpm
Solution concentration – 20% w/w for LV WSCA
10% w/w for MV WSCA

Free Films

Prior to measurement of thermal properties, free films of WSCA and HPMC were prepared by the cast method. The films were prepared employing a Gardco® Microm Film Applicator (P.N. Gardner Co., Inc., Pompano Beach, FL). Polymer solutions were cast to yield films of 0.8–1 mm thickness. Thickness was measured using a Starrett micrometer, L.S. Starrett Co., Athol, MA.

Thermal Analysis

Glass transition temperature (*Tg*) measurements were made using differential scanning calorimetry (DSC) at 20°C/min heating rate under nitrogen purge. A Perkin Elmer DSC-7, Norwalk, CT was employed. The films were analyzed by DSC after over night conditioning at ambient room temperature/humidity.

Stability Protocol

Samples of coated (WSCA and HPMC) and uncoated aspirin cores were packaged for stability studies. They were prepared by placing 100 tablets in $2^1/_2$ oz high-density polyethylene (HDPE) bottles without cotton or moisture absorbent packet. The containers were closed with self sealing lined metal caps by applying 12–14 lb measured torque. They were placed on stability station at RT, 35, 45 and 40°C/80% RH (open container).

Dissolution

The stability of the coated aspirin tablets was evaluated by dissolution testing using USP dissolution apparatus 1 (basket method) at 50 rpm with 500 mL of 0.05 M acetate buffer, pH 4.5 at 37°C. Samples were withdrawn at 10, 20, and 30 min intervals and analyzed on a Beckman DU-7, UV/Vis spectrophotometer, Beckman Coulter, Inc., Fullerton, CA.

Moisture (Weight) Gain

Duplicate samples of 20 tablets from each of the WSCA and HPMC coating trials were weighed and placed in oven-dried 1 oz clear glass jars. Caps were tightly screwed into place for the "closed" samples and aluminum foil was loosely set over the "open" samples. All samples were then placed in a 40°C/80% RH chamber. On specified days, samples were removed from the chamber and equilibrated for one hour at room temperature before weighing.

RESULTS AND DISCUSSION

General

Water soluble cellulose acetate (WSCA) is an experimental variant of commercially available cellulose acetate, which is normally insoluble in water. The term water soluble cellulose acetate refers to cellulose acetate that dissolves relatively quickly in water. WSCA is soluble in water over a degree of substitution range of 0.63–0.86. In addition to degree of substitution, other ways to describe WSCA include measuring the acetyl value or acetyl content, acid content and molecular weight. Typically, molecular weight is described in terms of solution viscosity. WSCA was supplied based on "grades" depending on the solution viscosity (Domeshek & Zazzara, 1991). A capillary viscometer was used to measure solution viscosity at 6% solids solution; an LV grade WSCA has a solution viscosity of 5–50 cP and a MV grade of about 100–250 cP.

All of the WSCA supplied by Hoechst-Celanese (H-C) for the study was made on laboratory and pilot scale equipment. Since WSCA was a new experimental polymer, its properties were still being characterized by both H-C and FMC. WSCA samples were used as received from H-C except for the MV grade material, which was screened (100 mesh) prior to use. The material was supplied in the form of a white flake, or if ground, a white powder finer than 40 mesh. Ground bulk density ranged between 0.08–0.20 g/cm^3 (Hoechst-Celanese, 1987).

Physical Properties

Typical properties kindly provided by Hoechst-Celanese (1987) for the experimental polymer are reported in Table 4. Low viscosity WSCA was more soluble in water (25–30%) relative to MV WSCA (10–15%). The acetyl value for both grades was 20–26%. Viscosity versus concentration and viscosity versus. temperature profiles were provided also Figs. 2 and 3, respectively. Viscosity of the polymer solutions increased proportionally with an increase in percent solids in solution as shown in Fig. 2 and Table 5. Unlike HPMC based solutions, there is no increase in viscosity with increasing temperature. In fact, the viscosity of WSCA solutions decreased as the temperature of the solution increased (Fig. 3). The viscosity decrease was more pronounced at higher (6%) solids concentration relative to solutions containing 3% solids.

Free Films

Free films were prepared by the cast method using a film applicator. WSCA has excellent film forming properties. Typically, the films are crystal clear and depending on the viscosity "grade", they are flexible, strong and durable, i.e. films cast from LV grades WSCA tend to be somewhat brittle and cracked while films from MV WSCA are flexible and strong. WSCA solutions have the capability of forming films without the use of plasticizers and WSCA free films dry at

TABLE 4 **Properties of Water Soluble Cellulose Aacetate**

Property	Low viscostiy	Medium viscostiy
Viscostiy 6%, cps	5–50	50–300
Maximum water solubility (%) solids	25–30	10–15
Acetyl value (%)	20–26	20–26
Volatiles (%)	< 4	< 4
Sulfates (%)	< 0.01	< 0.01
pH of 1.4% solution	5–6	5–6
Ash (%)	1–2	1–2
Insolubles (%)	< 0.5	< 0.5

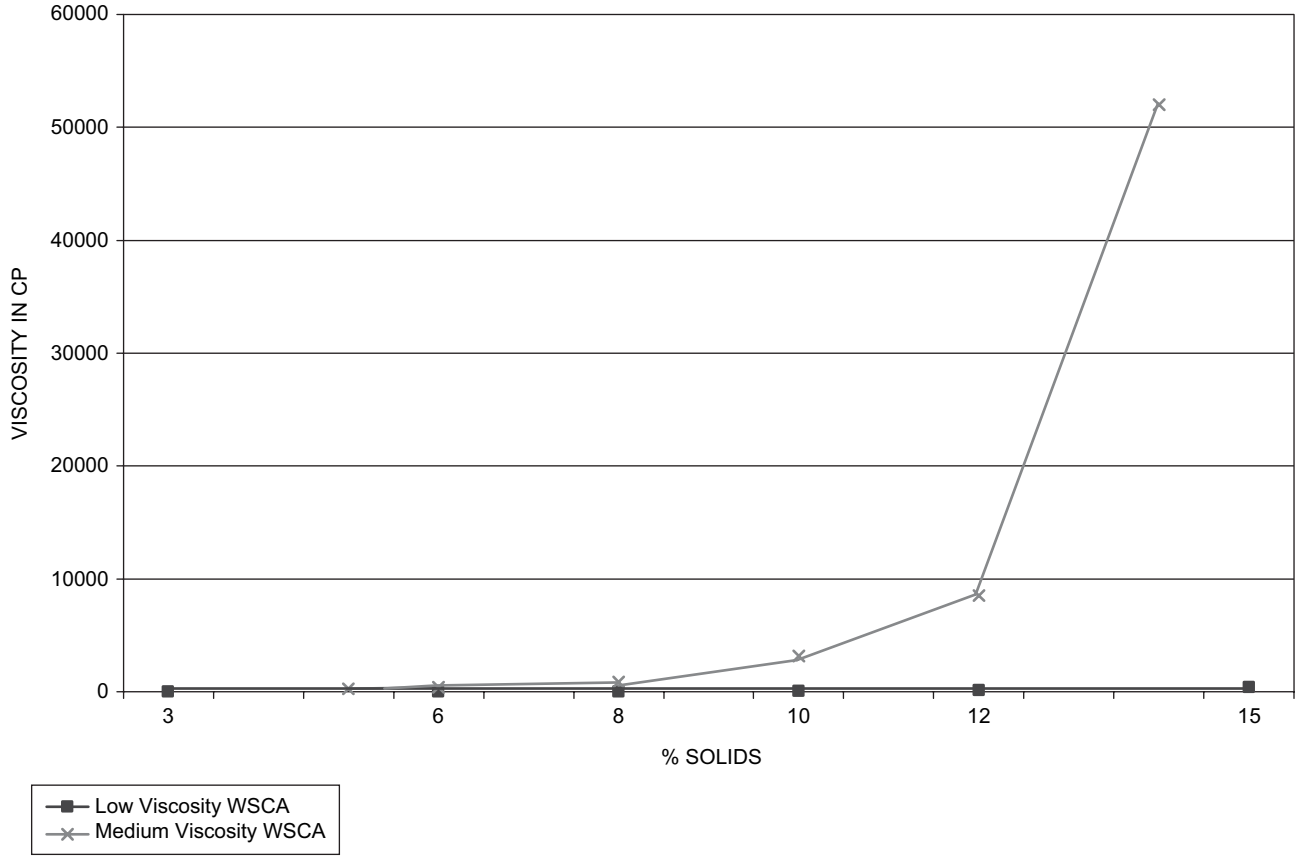

FIGURE 2 **WSCA Solution Viscosity Versus Concentration (% Solids).**

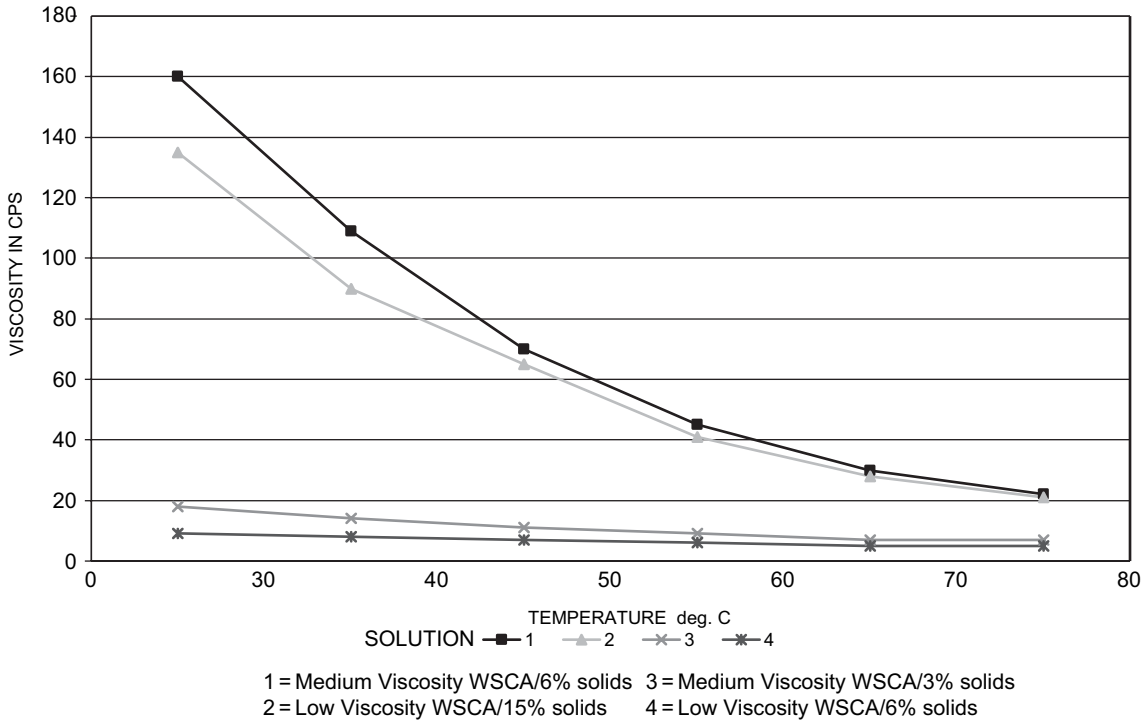

FIGURE 3 **Changes in WSCA Solution Viscosity Versus Changes (Increase) in Temperature.**

TABLE 5 Viscosity Profile Data* of Water Soluble Cellulose Acetate

Solids (%)	Low viscosity (cps)	Medium viscosity (cps)
2	–	25
3	5	–
5	–	240
6	13	393
8	32	847
10	74	3200
12	150	8500
14	–	52000
15	415	–

*Courtesy of Hoechst-Celanese.

room temperature. HPMC solutions do not dry at room temperature but require oven drying to form a film.

Other than visual observations of the free films, FMC did not investigate the mechanical properties. Hoechst-Celanese did provide preliminary mechanical data as shown in Table 6. In general, WSCA films without plasticizer exhibit higher tensile strength and Young's modulus, but lower percent elongation relative to HPMC.

Thermal Properties

WSCA films were analyzed for glass transition temperature, *Tg* by thermal analysis. Owing to the rigid nature and high glass transition temperature of most of the polymers currently being utilized pharmaceutically, plasticizers are used to lower the *Tg* and thereby soften the polymer. The glass transition temperature was determined for films cast from solutions of WSCA LV, WSCA LV:MV (1:1) and WSCA MV. Thermal analysis is a very useful tool in the selection of the optimal type and use level of plasticizer and was used to determine the *Tg* of WSCA films containing the plasticizers PEG 400 and glycerin (Table 7).

The results show that the glass transition temperature for WSCA is significantly higher than HPMC and that blending (1:1) of WSCA LV and MV grades does not alter the *Tg*. The inclusion of plasticizer does lower the *Tg* of WSCA. Additional comments regarding plasticizer choice and concentration are discussed under tablet coating.

Table Coatings

Coating Dispersions

Polymer solutions were mixed using a standard variable speed propeller-type mixer, covered and allowed to stand for at least 12 hr (overnight) to deaerate and ensure complete hydration of the polymers. Both WSCA and HPMC solutions trapped air while dispersing the polymer and there was no apparent difference in the amount of entrapped air between the two polymer solutions. With gentle mixing the next morning, the entrapped air and foam was dispersed or dissipated. Typical viscosity of 2:1 LV:MV WSCA coating dispersions (at 12.5% solids concentration) containing either 5% PEG 400 or glycerin ranged between 700–740 cP.

Plasticizers

Plasticizers may be defined as non-volatile, high boiling organic solvents used to impart flexibility to otherwise hard or brittle polymeric materials (Pharmaceutical Coatings Bulletin, 1995). Polymeric films use plasticizers to impart flexibility, improve flow and reduce brittleness. The plasticizers evaluated were polyethylene glycol (PEG) 400, 600, 1000, 1450, and

TABLE 6 Comparison of WSCA Films to Other Water Soluble Films*

Polymer	Film thickness (mil)	Tensile strength (psi)	Young's modulus (psi)	Elongation (%)
WSCA- 100% LV	1.48	4789	435200	2.08
WSCA- 80/20 LV/MV	2.12	7903	481100	3.26
WSCA- 50/50 LV/MV	1.65	8142	511900	3.25
WSCA- 100% MV	1.50	8433	475200	5.63
HPMC (culminal 25)	1.54	5258	269700	9.56
HPC (klucel EF)	1.50	891	49200	21.22

*All films without plasticizer.

TABLE 7 Glass Transition Temperature (*Tg*) of WSCA Films With and Without Plasticizer

Sample	*Tg* (°C)
HPMC E-5	154
WSCA LV	249
WSCA LV:MV (1:1)	248
WSCA MV	253
WSCA LV:MV (2:1) with 5% PEG 400 and 7.5% color	215
WSCA LV:MV (2:1) with 5% glycerin and 7.5% color	218

3350, propylene glycol (PG), glycerin, triacetin (TRA), dibutyl sebacate (DBS), triethyl citrate (TEC) and diethyl phthalate (DEP). They were evaluated at use levels of 5–15% with respect to polymer solids in solution.

LV and MV WSCA did not respond well to high molecular weight PEG (above 1000) at 10% use levels, as the films were opaque. HPMC films also became brittle and opaque when using higher molecular weight PEG. It was also observed that DBS, TEC, TRA, and DEP, when mixed with any of the WSCA polymer solutions, resulted in opaque, white films. DBS and DEP separated from the solution after 24 hr storage. PG, glycerin and PEG 600 when mixed with LV WSCA resulted in films that were clear but cracked and brittle.

It was concluded that PEG 400 at 2–5% use levels (based on polymer solids) was best suited as a plasticizer for WSCA. PEG 400 aided in film formation, adhesion, uniformity and overall strength of the polymer film. Glycerin was the second plasticizer choice. Limited study suggested that the solubility of WSCA is enhanced when plasticizer is added to the water prior to polymer (WSCA) hydration.

Coating Process

The coating trials were uneventful. Usual processing conditions typical of coating with HPMC were observed. Coating trials were successfully done in both a 16″ conventional stainless steel pan and a 24″ Accela-Cota. High productivity spray application equipment (pumps and spray guns) was used as is typically used for aqueous film coating. Processing temperatures were typical and post-drying time/temperatures were the usual 10–20 min. WSCA coating solutions/suspensions were applied at higher solids concentration (12.5–15% w/w) with low solution viscosity (700–740 cP). Spray gun blocking or beading was minimal and there was no difference between WSCA and HPMC. Initial appearance of the coated tablets was smooth, glossy and elegant and there was no significant difference in appearance of coated tablets, with logo, between WSCA and HPMC.

Stability

Physical Stability

Aspirin (ASA) tablets were coated with 1–1.5% WSCA and HPMC, respectively. The WSCA coating formulations were prepared by blending 1:1 and 2:1 WSCA solutions. The plasticizer was 4% PEG 400 and pigment 8% Cotolene® PG orange. Friability, disintegration and coated tablet appearance were monitored and the results presented in Table 8. After one month storage at 40°C/ 80% RH the HPMC (control) coated tablets were soft and capped with evidence of crystal formation, and the color was fading. The formulation containing 2:1 WSCA LV:MV was hard with no evidence of capping, while the 1:1 formulation tablets were soft and capped. Both formulations (1:1 and 2:1) exhibited crystal formation and fading. There was no difference in the stability between the WSCA and HPMC coated ASA tablets stored for 3 months at RT and 35°C. At 45°C, the HPMC coated ASA tablets were sticky, with severe crystal formation and strong acetic acid odor. The WSCA coated tablets were satisfactory at three months/45°C with exception of a slight acetic acid odor.

Dissolution Stability

Aspirin (ASA) tablets were coated with 3% WSCA or HPMC. The 2:1 WSCA coating formulations were prepared by dry blending the polymer powders or by blending the polymers solutions in the proper ratio. The plasticizer was PEG 400 and the pigment Sepisperse® Juane. Results of the dissolution stability study are presented in Table 9. As expected the uncoated ASA core tablets and 2:1 WSCA coated tablets met the initial USP tolerances of "not less than 80% of the labeled amount of $C_9H_8O_4$ is dissolved in 30 min". After three month storage at RT, all of the samples met USP dissolution requirements. After three months at 35°C and 45°C, however, neither the

TABLE 8 Physical Stability of Aspirin Tablets Coated with 1–1.5% WSCA and HPMC

			1 Month		3 Months		
		Initial	45°C	40°C/ 80% RH	RT	35°C	45°C
ASA cores (uncoated)	Friability (%)	0.19	0.12		0.20	0.15	0.16
	Disintegration (sec)	19	15		18–22	19–24	19–25
	Appearance	White smooth	Crystals formed	Soft and capped crystals	Crystals AA odor*	Crystals AA odor	Crystals AA odor
HPMC E-5 (control) 1.5% coating	Friability (%)	0.0	0.0		0.0	0.0	0.0
	Disint. (sec)	22–28	37		14–24	15–25	18–28
	Appearance	Orange smooth	Orange faded	Soft and capped crystals fading	No crystals no sticking no AA odor	No crystals no sticking no AA odor	Severe crystals sticking AA odor
WSCA 1:1 LV : MC 1% coating	Friability (%)	0.0	0.0		0.0	0.0	0.0
	Disint. (sec)	31–50	24–26		30–45	31–46	31–43
	Appearance	Orange smooth	Orange smooth	Soft and capped crystals fading	No Crystals No Sticking No AA odor	No Crystals No Sticking No AA odor	No Crystals No Sticking Slight AA odor
WSCA 2 : 1 LV : MV 1% coating	Friability (%)	0.0	0.0		0.0	0.0	0.0
	Disint. (sec)	25–28	16–20		20–33	22–31	23–32
	Appearance	Orange smooth	Orange smooth	Hard and no capping crystals fading	No crystals no sticking no AA odor	No crystals no sticking no AA odor	No crystals no sticking slight AA odor

**Odor of Acetic Acid.*

TABLE 9 Dissolution Stability of Aspirin Tablets Coated with 3% WSCA and HPMC. Mean % aspirin in solution ± sd (n = 3)

		Initial	3 Months		
	Time (min)		RT	35°C	45°C
ASA cores (uncoated)	10	55 ± 5.5	60 ± 1.5	39 ± 5.7	37 ± 4.4
	20	91 ± 10.4	87 ± 3.2	65 ± 13.5	60 ± 6.7
	30	101 ± 2.1	96 ± 2.5	78 ± 14.3	76 ± 9.5
HPMC E-5 (control) 3.0% coating	10	=	55 ± 8.1	30 ± 3.2	32 ± 8.7
	20	=	96 ± 3.0	53 ± 6.7	71 ± 18.9
	30	=	101 ± 1.0	64 ± 7.4	88 ± 4.7
WSCA 2:1 LV:MV 3.0% coating WSCA solution.	10	53 ± 0.6	50 ± 8.5	51 ± 9.5	44 ± 2.1
	20	95 ± 3.1	93 ± 5.5	90 ± 6.4	86 ± 6.7
	30	104 ± 1.5	98 ± 4.0	98 ± 0.6	94 ± 1.5
WSCA 2:1 LV:MV 3.0% coating WSCA dryblend	10	=	51 ± 6.6	48 ± 2.0	39 ± 4.0
	20	=	92 ± 9.0	85 ± 7.9	77 ± 5.5
	30	=	100 ± 0.6	97 ± 1.5	92 ± 4.0

uncoated ASA cores nor the HPMC coated tablets met the requirements. The WSCA coated ASA tablets complied with the USP dissolution requirements at all three-month stability stations. The ASA tablets coated with 2: 1 WSCA from solution exhibited slightly faster release at 10 and 20 min relative to the tablets coated with WSCA from the powder blend, but the differences were not statistically significant.

TABLE 10 **Moisture Gain (% Weight Increase)**

	Percent Weight Increase*			
	After 3 Days		After 7 Days	
	Open	Closed	Open	Closed
HPMC E-5 (control) with 5% PEG 400	0.876	0.233	1.100	0.406
WSCA LV : MV 1 : 1 with 5% PEG 400	0.976	0.243	1.160	0.422
WSCA LV : MV 2 : 1 with 5% PEG 400	1.028	0.240	1.174	0.422
WSCA LV : MV 2 : 1 with 5% glycerin	0.926	0.226	1.098	0.378
WSCA LV w 5% PEG 400	0.916	0.236	1.012	0.386
WSCA LV w 5% glycerin	0.903	0.228	1.033	0.396

*Data averaged.

Moisture (Weight) Gain

The objective of the investigation was to determine the percent increase in weight due to moisture uptake by aspirin (ASA) tablets coated with either WSCA or HPMC E-5 (control) stored in a 40°C/80% RH chamber. Results of the moisture gain (percent weight increase) are presented in Table 10. There was no significant difference in weight gain between the ASA tablets coated with either WSCA or HPMC. While there was no difference in weight gain, the WSCA film coated tablets were not sticky or tacky, whereas the HPMC coated tablets were tacky and stuck together.

CONCLUSION

The use of WSCA as an aqueous polymeric film coating for tablets was investigated. WSCA has excellent film forming properties. Typically, the films are crystal clear and, depending on the viscosity grade used, they are flexible, strong and durable. Both grades have the capability of forming free films without plasticizer and WSCA free films dry at room temperature. The glass transition temperature, *Tg*, for WSCA is considerably higher relative to HPMC. Inclusion of plasticizers such as PEG 400 or glycerin lowers the *Tg* of WSCA. Preparation of WSCA polymer solutions was typical for the methods commonly used to prepare aqueous film coatings. Typical aqueous film coating conditions and equipment were used. Aspirin tablets coated with 2:1 WSCA formulations exhibited better physical and dissolution stability after extended storage especially at elevated temperature. There was no significant difference in moisture (weight) gain between ASA tablets coated with either WSCA or HPMC, but WSCA film coated tablets were not tacky or sticky. The HPMC coated tablets were tacky and stuck together.

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REFERENCES

Bohrer, T. C. (1969). *U.S. Patent* 3,482,011.

Domeshek, K. A., & Zazzara, K. L. (1991). *U.S. Patent* 4, 983, 730.

Fordyce, C. E. (1938). *U.S. Patent* 2,129,052.

Hoechst–Celanese, *Product Characterization* literature, 1986 and 1987.

"Influence of Plasticizers on the Dissolution and Physical Properties of Ethyl-cellulose Films and Coated Beads," (1995). Pharmaceutical Coatings Bulletin, Morflex Inc., 102–103.

Malm, C. J., Barkey, K. T., Salo, M., & May, D. C. (1957). Far-hydrolyzed cellulose acetates preparation, properties and uses. *Ind. Eng. Chem.*, *49*, 79–83.

Mukherjee, A. K., Agarwal, R. K., Chaturvedi, H. K., & Gupta, B. D. (1981) Water soluble cellulose acetate and its application. *Indian J. Textile Res.*, *6*, 120–123.

Pharmaceutical Coatings Bulletin (1995). *Influence of Plasticizers on the Dissolution and Physical Properties of Ethyl-cellulose Films and Coated Beads*, *102–3*, Morflex Inc.

Russian Patent No. 1740744, Water-Soluble Cellulose Acetate, Its properties and Use, 20.

Wheatley, T. A., Bridges, C. I., & Steuernagel, C. R. (1993a). *U.S. Patent* 5,206,030.

Wheatley, T. A., Bridges, C. I., & Steuernagel, C.R. (1993b). *U.S. Patent* 5,248,516.

Wheatley, T. A., Bridges, C. I., & Steuernagel, C. R. (1993c) *U.S. Patent* 5,258,436.