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RESEARCH PAPER

Evaluation of the Film-Forming Property of Hydrogenated Rosin

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ABSTRACT

The film-forming and coating properties of a new biomaterial, hydrogenated rosin (HR), is investigated in the present communication. Films produced by casting method are studied for mechanical, (tensile strength, elongation, and Young's modulus), water vapor transmission, and moisture absorption characteristics. Type of plasticizer and its concentration were observed to play an important role in modifying the film characteristics. Dibutyl sebacate (DBS), a hydrophobic plasticizer, was found to be suitable for development of flexible and smooth films. Film formulations plasticized with DBS were investigated for coating the drug layered nonpareil seeds where plasticization facilitated development of smooth and uniformly coated pellets. The increase in coat buildup, however, did not sustain the drug release significantly. The studies conclude that HR films promise utility as moisture-protective hydrophobic, film-coating materials.

Key Words: Hydrogenated rosin; Dibutyl sebacate; Mechanical properties; Coating.

INTRODUCTION

The application of polymer film coating (aqueous and nonaqueous) is well established in pharmaceutical research and industry.[1–3] The film-forming polymers have been classified into three broad categories: gastrosoluble, enteric or gastro resistant, and insoluble.[4] Films can be categorized in terms of their mechanical properties, permeability, and water vapor transmission rates.[5–7] The film-coating formulations often contain additional components, such as plasticizers, antiadherents, pigments, surfactants, and antifoaming agents.[8] These additives facilitate effective coating and improve the appearance of the final dosage form. Plasticizers are most commonly employed to improve the performance of polymeric films of pharmaceutical interest.[9] They normally function by lowering the tensile strength

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and glass transition temperature (Tg) and increasing the elongation and flexibility of films.[10] Addition of suitable plasticizer is imperative for efficient coating performance of most of the commercially available polymers.

Rosin and rosin esters have been widely used as pharmaceutically applicable coating materials.[11,12] Rosin derivatives also provide controlled-release rates of drugs in the design of matrix tablets and microcapsules.[13,14] Rosin biomaterials promise biodegradability and compatibility due to their natural origin.[15] In the present research communication a new biomaterial, hydrogenated rosin (HR), is being studied for its film-forming property and possible application to produce coated forms. The effect of a plasticizer as a film component is investigated in terms of mechanical, moisture absorption, and water vapor transmission properties. Diclofenac is used as a drug model for coating studies.

MATERIALS AND METHODS

Materials

Hydrogenated rosin was received as a gift sample from Derives Resiniques Terpeniques Inc., Gambetta, France. Dibutyl Sebacate was kindly donated by Morflex Inc., Greensboro, NC. Diclofenac sodium was obtained from Zim Laboratories, Nagpur, India and used as received. Glycerol (Qualligen Laboratories, Mumbai, India), isopropyl alcohol, potassium nitrate, potassium carbonate, and sodium chloride (S.D. Fine Chemicals, Mumbai, India) were used. All other chemicals were of analytical or pharmacopoeial grade.

Methods

Characterization of Hydrogenated Rosin

Preliminary physiochemical characteristics of hydrogenated rosin (HR) like color, acid value, softening point, and solubility were estimated using methods previously documented.[16] The average molecular weight was determined using gel permeation chromatography (GPC) with an (RI) detector. Data was based on polysterene as a reference standard. Samples were eluted through a (PL) obtain a 3μ mixed column at a flow rate of 1 mL/min with tetrahydrofuran as solvent. The glass transition temperature (Tg) was estimated by differential scanning calorimetry (DSC) (Perkin-Elmer, Norwalk, CT). Approximately 10 mg of material was placed in an aluminium pan and scanned from 25° to 250°C with the scanning rate of 10°C/min. The Tg was taken as the midpoint of the transition.

Table 1. Formulae of HR solutions for film characterization and coating studies.

	Composition (% w/w)				
Ingredients	X1	X2	X3	X4	X5
HR	30.0	30.0	30.0	30.0	30.0
GLY	—	3.0	6.0	—	—
DBS	—	—	—	3.0	6.0
Dichloromethane q.s. to	100.0	100.0	100.0	100.0	100.0

Preparation of Films

The various formulations employed for the preparation of free films are shown in Table 1. A 30% w/v solution of HR was employed for the preparation of films using varying concentration of glycerol (GLY) and dibutyl sebacate (DBS). Films were cast on a mercury substrate (area of casting: 20 cm^2), allowing the solvent to evaporate for 48 hr. Dried films were removed and carefully cut into strips with an average thickness of 0.4 mm, length 120 mm, and width 12 mm to be acceptable for tensile testing.

Test Procedures for Films

The mechanical properties of the films were computed using an Instron instrument (Model 4467, Instron Corp., Canton, MA) at 23°C and 50% RH. The stress-strain parameters viz. tensile strength, percent elongation, and Young's modulus were determined for each film specimen, employing a gauge length of 50 mm and crosshead speed (CHS) of 5 mm/min. All measurements were carried out in triplicate.

Films were subjected to a water vapor transmission (WVT) rate and moisture absorption study using procedures described previously.[17] Saturated salt solutions of potassium acetate, potassium carbonate, sodium chloride, and potassium nitrate were used to obtain controlled relative humidities (RH) of 23%, 43%, 75%, and 93% respectively, for

the studies. Utsumi et al.'s equation[18] was employed for the determination of WVT rate, taking into consideration the film thickness. For moisture absorption the weight gain of the films was recorded at a predetermined time interval (at the end of 14 days) and calculated as the percentage of moisture sorption. The measurements were made in triplicate.

Preparation of Coated Diclofenac Pellets

Drug layered nonpareil seeds (NPS) were prepared by spraying diclofenac sodium solution (20% w/v in 95% ethanol) containing povidone (2% w/v) as a binder over 14/16-mesh NPS in a conventional coating pan (Retina Ind., Mumbai, India) using a spray gun. Drug-loaded pellets (10% on plain NPS) were dried and coated with X1, X4, and X5 formulations of film-coating solutions until different levels of coat consumption (% weight increase) were achieved. The coating experiments were performed under conditions of inlet air temperature 60–65°C, pellet bed temperature 40–45°C, spray rate 1.5 mL/min, spray gun position 10 cm from bed surface, and automizing pressure 35 psi. The coated pellets were transferred and air dried.

Representative intact pellets and cross-sectioned pellets (X5 coated) were observed under a scanning electron microscope (Stereoscan 250-MK-III, Cambridge, England). Samples were mounted on stubs and gold coated for 120 s using a sputter coater under argon atmosphere before examination.

Dissolution Studies

Drug release analysis from coated pellets was followed in 900 mL of 0.1 N HCl (pH 1.2) for the first 2 h followed by 900 mL of phosphate buffer solution (pH 6.8) up to 10 h. The USP 23 dissolution apparatus 2 (Veego Scientific, Mumbai, India) was used for the testing and was operated at $37^\circ \pm 1^\circ$C at a speed of 100 rpm. Aliquots withdrawn at specific time intervals were analyzed for drug content spectrophotometrically at 276 nm and replaced with fresh media of the same volume. Triplicate measurements were noted.

RESULTS AND DISCUSSION

Physiochemical Characteristics

The application of polymer film coat is a common practice in sustained and controlled-release dosage forms. In vitro characterization of polymer/biomaterial and the film membrane is essential for optimization for use in drug delivery. In this study hydrogenated rosin (HR), a yellow-colored, natural product-based biomaterial, is investigated for film-forming and coating property. Hydrogented rosin has a Mw of 400 with polydispersity index close to 1. The Tg is 47°C, acid value 171.0, while the softening point range is 54–56°C. Solubility data of HR in various solvents and pH solutions are depicted in Table 2. Hydrogenated rosin soluble in organic solvents such as dichloro methane and chloroform but poorly soluble (insoluble) in water, which is indicative of its hydrophobic nature. Solubility in different buffer solutions is highly pH-dependent, with solubility increasing with increase in the pH of the solution.

Film Characterization

Films prepared from HR containing different proportions of plasticizers were studied to evaluate

Table 2. Relative solubility of hydrogenated rosin.

Solubility in different solvents (37°C)		Solubility in different pH solutions (37°C)	
Solvent	Solubility (g/mL)	pH	Solubility (g/mL) $\times 10^{-4}$
Chloroform	0.55 ± 0.026	1.6	14.4 ± 0.67
Dichloromethane	0.52 ± 0.017	4.6	36.6 ± 1.24
Acetone	0.42 ± 0.042	6.8	6.03 ± 1.92
Isopropyl alcohol	0.23 ± 0.018	8.0	144.0 ± 2.82
Ethanol	0.14 ± 0.011	10.4	217.5 ± 3.16
Water	$22.3 \pm 1.01 \times 10^{-4}$		

Each value is mean ± S.D. of four determinations.

their application to produce coated forms. The 30% w/v solution in dichloromethane was used for film casting onto mercury substrate. Neat HR films were brittle and broke easily upon handling. The type of plasticizer was found to influence the film-forming property of HR. Two categories of plasticizers were tested viz. dibutyl sebacate (DBS): hydrophobic and glycerine (GLY): hydrophilic, differentiated mainly by their aqueous solubility. Glycerol, a hydrophilic plasticizer, was found to be ineffective since it failed to produce clear and flexible films. It is well known that to be effective, the liquid plasticizer must blend uniformly and homogenously with the polymer and remain blended when cooled to room temperature.[19] Film-forming solutions plasticized with GLY resulted in brittle, nonuniform, and opaque films. This may be attributed to the incompatibility between GLY and HR, possibly due to their respective hydrophilic and hydrophobic natures. Films plasticized with DBS (10% and 20% w/w) were sufficiently flexible to be bent in their dried state. The mechanical properties of HR film are shown in Table 3. Due to the brittle and nonuniform nature of films it was difficult to compute the mechanical properties of films produced with film formulations X1, X2, and X3. The tensile strength values of films produced from formulations X4 and X5 indicate risk of film cracking, but no such defects in the coated pellets or films were observed, which may be attributed to the high percentage values of elongation.[20] Addition of DBS increased the elongation, producing more flexible films. The increase in elongation, and subsequent decrease in Young's modulus due to plasticizer addition may favorably contribute to adhesion between film and coating surface.[21]

Extremely low rates of WVT were demonstrated by HR films plasticized with DBS (X4 and X5). The values are in the range of 10^{-5} g cm/cm^2/24 h. This is further supportive of the hydrophobic nature of HR. There was a significant influence of the relative humidity condition on the WVTR as evident from the results shown in Table 4.

The moisture absorption isotherm of X4 and X5 HR films showed an increase in moisture absorption with increase in relative humidity (Fig. 1). The X4 films absorbed more moisture than X5 films.

Table 3. Mechanical properties of films.

Formulae of film solutions	Thickness (mm)	Tensile strength (MPa) (mean ± S.D.)	Elongation (%) (mean ± S.D.)	Young's modulus (MPa) (mean ± S.D.)
X1[a]	—	—	—	—
X2[a]	—	—	—	—
X3[a]	—	—	—	—
X4	0.37 ± 0.04	0.247 ± 0.032	10.92 ± 0.17	2.69 ± 0.08
X5	0.39 ± 0.01	0.293 ± 0.016	18.27 ± 0.93	2.00 ± 0.09

Values are mean ± S.D. of three determinations.
[a]No data generated.

Table 4. WVTR study of films.

Formulae of film solutions	Thickness (mm)	Area (cm^2)	WVTR (g cm/cm^2/24 h) × 10^{-5} at RH	
			43 (%)	93 (%)
X1[a]	—	—	—	
X2[a]	—	—	—	—
X3[a]	—	—	—	—
X4	0.038	4.34	2.32 (0.32)	4.74 (0.13)
X5	0.040	4.32	1.67 (0.56)	4.17 (0.27)

Values are mean of three determinations. Figures in parentheses indicate S.D.
[a]No data generated.

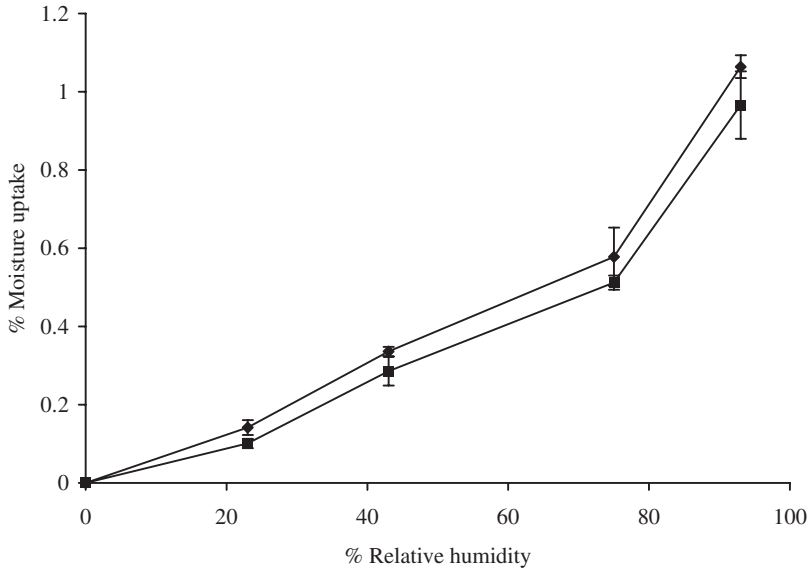


Figure 1. Moisture absorption curves of HR films at different % RH; (◆) X4, (■) X5 at the end of 14 days. Data represents mean ± S.D. of four determinations. No data generated with X1, X2, and X3 films.

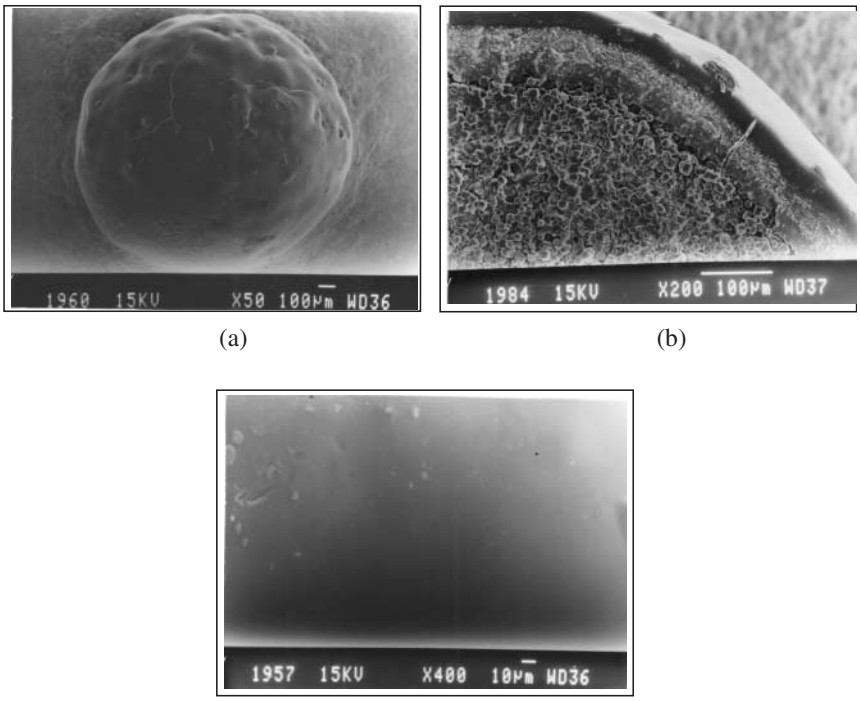
Slight visual changes were observed in the films stored at 93% RH, with the films exhibiting a sticky and soft appearance at the end of the study. The results of the moisture uptake and WVTR study indicate a possible moisture-resistant ability of HR films, suggesting their role as moisture-resistant barriers on spherical units. The WVTR is very low as compared with values for Shellac (8.813×10^{-4} g cm/cm^2/24 h), which has been suggested as a control for maximum permissible water vapor transmission.[22]

Coating and Dissolution Studies

Dibutyl sebacate was found to be an effective plasticizer in the concentration range of 10% and 20% w/w (based on polymer weight). Drug-layered NPS were coated with X1, X4, and X5 coating solutions to achieve different coat build-ups. Coating with formulation X1, however, posed a number of problems such as agglomeration, cracking, sticking, and long processing times. The brittle film structure and internal stresses when applied to the solid surface seem to render coating difficult with X1. However, a plasticizer (DBS) addition resulted in effective coating, free of cracks and other defects. The representative scanning electron micrographs of pellets coated with X5 are shown in Fig. 2. As illustrated, the coated pellet shows a continuous and uniform spherical appearance. At higher magnification the cross-sectioned, coated pellet shows distinct layers of coat, drug, and NPS. The physical nature of each of the three layers is clearly visible. The drug layer is grained and compacted between coat and NPS. The surface of the coated pellet is smooth and homogenous with uniform surface. The drug-release profile from pellets coated with X4 and X5 is shown in Fig. 3 and Fig. 4, respectively. Coat build-ups even up to 10% w/w did not produce sufficient sustaining of drug release.

CONCLUSION

In this study, HR, a rosin-based biomaterial, was investigated for its film-forming property. Preliminary physiochemical characterization revealed that HR is a low molecular weight biomaterial that is freely soluble in organic solvents. Dibutyl sebacate, a hydrophobic plasticizer, was found to be effective in improving the mechanical properties, making the films more flexible as evidenced by increase in elongation. Hydrogenated rosin films plasticized with DBS demonstrated low WVT rates with increase in relative humidity. In summary, it may be concluded that DBS is an effective plasticizer in HR film formulations. The HR films plasticized with



(a) (b)

(c)

Figure 2. Representative scanning electron micrographs of pellets coated with formulation X5, (a) coated pellet; (b) cross-section of coated pellet; (c) surface of coated pellet.

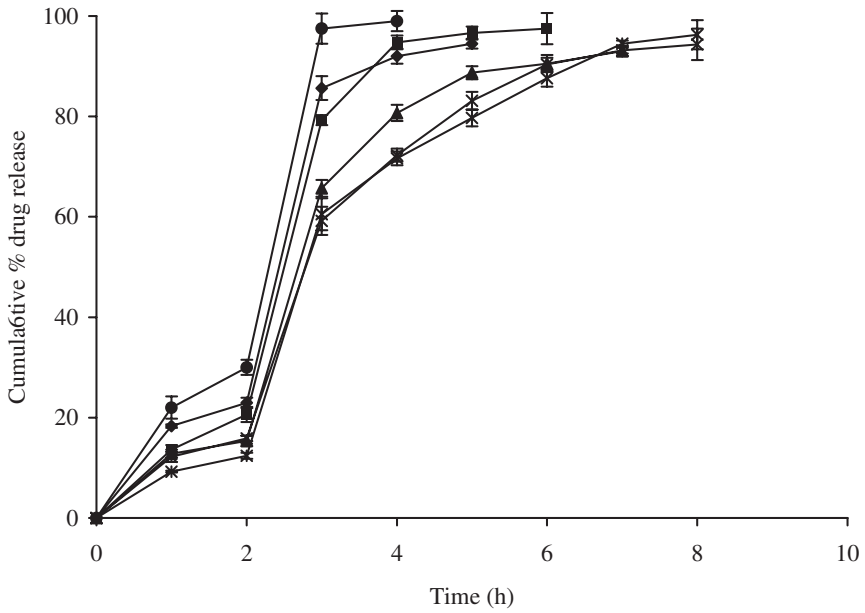


Figure 3. In vitro drug release from (●) uncoated pellets; X4 coated pellets (♦) 4% w/w; (■) 6% w/w; (▲) 8% w/w; (×) 10% w/w; (∗) 12% w/w.

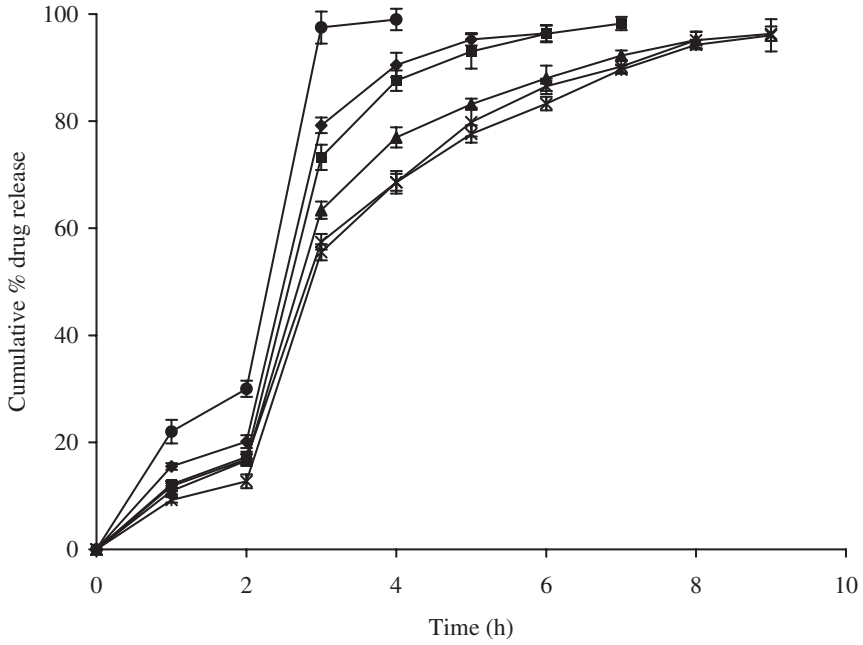


Figure 4. In vitro drug release from (●) uncoated pellets; X5 coated pellets, (◆) 4% w/w; (■) 6% w/w; (▲) 8% w/w; (×); 10% w/w; (∗) 12% w/w.

DBS, however, promise utility as moisture-protective film-coating materials.

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