Drug Development and Industrial Pharmacy, 28(4), 381–387 (2002)

RESEARCH PAPER

Synthesis and Evaluation of Rosin-Based Polymers as Film Coating Materials

P. M. Satturwar, P. M. Mandaogade, S. V. Fulzele,*
G. N. Darwhekar, S. B. Joshi, and A. K. Dorle

Department of Pharmaceutical Sciences, Nagpur University Campus, Amravati Road, Nagpur 440 010, India

ABSTRACT

Rosin-based polymers (R-1 and R-2) were synthesized and characterized for physicochemical properties, molecular weight (M_w), polydispersity (M_w/M_n), glass transition temperature (T_g), and thermogravimetry (TGA). Films of the polymers were cast on a mercury substrate by solvent evaporation technique. Free films were characterized for surface topography by scanning electron microscopy (SEM), water vapor transmission rate (WVTR), tensile strength, percentage elongation, and modulus of elasticity. The polymers were further evaluated as film coating materials by evaluating drug release from coated pellets with diclofenac sodium as a model drug. Drug was loaded on non-pareil seeds by a solution-layering technique and coated with varying concentrations of polymer solutions. Sustained release of the drug was observed from coated pellets. The newly synthesized rosin-based polymers promise considerable utility for pharmaceutical coating.

INTRODUCTION

Polymeric film coatings have been applied to pharmaceutical dosage forms for a variety of reasons, e.g., taste-masking, as a moisture-resistant barrier, and as a method of controlling the release characteristics of drugs (1). Film coating has been studied extensively in the pharmaceutical industry, and the use of polymers has been widely accepted (2–5). Drug release is to a large extent influenced by penetration of dissolution fluid into a polymer matrix, which in turn depends upon the properties of

*Corresponding author. E-mail: fsuniket@yahoo.com

the polymer itself (6). The main polymers used for film formation have been classified into three categories: gastrosoluble, gastroresistant (enteric), and insoluble (7). The characterization of their films is carried out using various experiments which enable the evaluation of the mechanical properties and permeability to humidity, gas, or various drugs (8).

Rosin is a solid resinous material that occurs naturally in the oleoresin of pine trees (9). Rosin and rosin derivatives are widely used in paints, varnishes, printing inks, paper, and wood products for their film-forming properties. They are also used in chewing gum bases, dental varnishes, and cosmetics. Rosin esters have been widely evaluated for their pharmaceutical applications as coating (10) and microencapsulating (11,12) materials, and as anhydrous binding agents in tablets (13). Rosin being of natural origin, rosin-based polymers are expected to be ecofriendly and biodegradable (14). The present work deals with the evaluation of newly synthesized rosin derivatives as film-coating materials.

MATERIALS AND METHODS

Materials

Rosin N grade (Swastik Acids & Chemicals, Nagpur, India), maleic anhydride (S.D. Fine Chemicals, Mumbai, India), fumaric acid (S.D. Fine Chemicals, Mumbai, India), glycerol (Qualligen Laboratories, Mumbai, India), castor oil (Apex Laboratories, Mumbai, India), chloroform (E. Merck, Mumbai, India), acetone (Loba Chemie, Mumbai, India), isopropyl alcohol (S.D. Fine Chemicals, Mumbai, India), potassium nitrate (S.D. Fine Chemicals, Mumbai, India), potassium acetate (S.D. Fine Chemicals, Mumbai, India), potassium carbonate (S.D. Fine Chemicals, Mumbai, India) were used. Diclofenac sodium was received as a gift sample from Zim Laboratories, Nagpur, India, and used as received.

Methods

Synthesis of Rosin-Based Polymers

Rosin and all other ingredients were charged in a four-neck glass reactor (2 L) fitted with a condensor, stirrer, and temperature control arrangement; 5% xylene was added as solvent. Synthesis was carried out at different temperatures, with constant stirring at 60 rpm. The composition of the derivatives and the different temperature conditions, along with the time schedule, are shown in Tables 1 and 2, respectively. Xylene was stripped off from the final product by heating under vacuum. The synthesized polymers were characterized for various physicochemical properties, like color, acid value, and softening point (Hercules drop method).

Table 1

Composition of Rosin-Based Polymers

Reactant	R-1	R-2
Rosin	85.0%	60.0%
Fumaric acid	2.50%	10.0%
Maleic anhydride	2.50%	—
Glycerol	10.0%	10.0%
Castor oil	—	20.0%

Table 2

Temperature Conditions and Time Intervals for Synthesis of Rosin-Based Polymers

	Temperature (°C)								
Polymer	1 hr	2 hr	3 hr	4 hr	5 hr	6 hr	7 hr	8 hr	9 hr
R-1	160	265	250	225	210	200	200	200	200
R-2	225	210	210	200	200	190	190	—	—

Polymer Characterization

Prepared polymers, R-1 and R-2, were evaluated for their molecular weight and polydispersity by size exclusion chromatography coupled to a laser light scattering detector (DAWN-DSP, Wyatt Technology). The measurements were done using a K-5-type cell at a wavelength of 633 nm. Methylene chloride was used as mobile phase with a flow rate adjusted to 1 mL/min. Molecular weight (M_w) and polydispersity index (M_w/M_n) were computed by ASTRA 4.70.07 software (Wyatt Technology).

The glass transition temperature (T_g) was determined using a differential scanning calorimeter (DSC, Schimadzu 50). Approximately 10 mg of sample was placed in the aluminum cell and scanned over a temperature range of 25–200°C at a rate of 10°C/min. The T_g was taken as the midpoint of transition and read from the thermographs. Samples were scanned in triplicate. The moisture content was determined using a thermogravimetric

analyzer (TGA, Schimadzu 50). About 10 mg of sample was scanned over a temperature range of 25–200°C at a rate of 10°C/min.

Free Film Preparation

Films of the polymers, R-1 and R-2, were prepared on a mercury substrate by solvent evaporation technique (15). A 30% w/v solution of polymers was prepared in dichloro methane and poured into a Petri dish containing mercury, allowing the solvent to evaporate for 24 hr and subsequently air-drying for an additional 48 hr. The films were stored in desiccators at ambient temperature for 24 hr before they were studied. (area of casting: 19.64 cm^2; approximate dry film thickness: 0.2 mm).

For comparison, free films of Eudragit-L 100 and hydroxy propyl methyl cellulose (HPMC, 6 cP) were prepared. Free films of Eudragit-L 100 were prepared similarly to R-1 and R-2 using a 10% w/v solution in ethanol on a mercury substrate. Free films of HPMC were prepared by casting a 5% aqueous solution within a round aluminum foil cup and drying at 40–50°C (area of casting: 12.0 cm^2; approximate dry film thickness: 0.1 mm).

Film Characterization

Films were cut into strips (12 mm width × 130 mm length) and the film thickness was measured using a micrometer screw gauge, recording the mean of five measurements. Cutting the films to proper size introduced defects at the edges of the specimens. This problem was effectively solved by cutting the films while they were quite wet with the solvent.

The mechanical properties were determined using a plastic tensile test, performed using an Instron Instrument (model 4467, Instron Corp., Canton, MA) based on the standard ASTM test method (16). The measurements were made at a gauge length of 50 mm with cross-head speed (CHS) of 25 mm/min. The test was performed at 50% relative humidity (RH) at 25°C. The thickness of the film had to fall within ±0.2 mm of the average to be acceptable for testing. The tensile strength, percentage elongation, and modulus of elasticity were computed with at least three repetitions. Similar experiments were carried out on free films of Eudragit-L 100 and HPMC (6 cP) as standard polymers using dibutyl phthalate (10% w/w of polymer) as plasticizer.

Surface topography of the films was studied under a scanning electron microscope (SEM, Stereo Scan 250-MK-III, Cambridge, UK). Samples were mounted on stubs and coated for 120 sec with a layer of gold using a sputter coater.

Water Vapor Transmission Rate Studies

Films were prepared as described earlier. A film of appropriate dimensions was mounted on a permeation cell containing saturated salt solution with excess quantity of potassium carbonate or potassium nitrate to provide RH conditions of 43% and 93%, respectively (17,18). The charged cells were weighed and placed in pre-equilibriated desiccators maintained at 0% RH. The cells were reweighed at 24 hr intervals for 72 hr. The amount of water transmitted through the film was given by the weight loss of the assembled cell. The rate of water vapor transmission was calculated using Utsumi's equation (19), taking the film thickness into consideration as shown:

$$Q = \frac{WL}{S}$$

where:

W = water transmitted (g/24 hr);
L = film thickness (cm);
S = surface area (cm^2);
Q = water vapor transmission (g cm/cm^2/24 hr).

Polymer Coating

Drug coating was carried out by a solution-layering technique in a conventional coating pan (20). A weighed quantity of non-pareil seeds (NPS) of approximately 14/16 mesh was charged into a pan and diclofenac sodium solution (20% w/v in 95% alcohol) containing 2% w/v polyvinyl pyrrolidone (PVP) as binder was sprayed over the cascading NPS. Hot air was blown onto the cascading pellets to evaporate the solvent. Drug-loaded pellets (10% drug loading) were dried in an oven at 50°C for 24 hr. A polymer solution containing aluminum stearate (2% w/v of the polymer) was sprayed onto the cascading pellets to build up different levels of coating, i.e., 2, 4, 6, 8, and 10% on a dry weight basis. The operating conditions employed for coating are shown in Table 3.

Evaluation of Drug Release

The in vitro release of diclofenac sodium from film-coated pellets was conducted using USP XXIII

Table 3

Operating Conditions for Coating

Item	Conditions
Machine	Conventional coating pan (Retina Ind. Co.)
Coating solution (R-1 and R-2)	10% w/v in dichloromethane:isopropyl alcohol (1 : 1)
Speed	40 rpm
Coating amount	2, 4, 6, 8, and 10% on dry weight basis
Charge	50 g
Spray gun	Art master
Gun position	15 cm from the pellet bed surface
Spray rate	1 mL/min
Pressure	40 psi
Supply air temperature	70–75°C
Pellet bed temperature	40–45°C

dissolution apparatus 2 (Veego Scientific, Mumbai, India). A weighed quantity of coated pellets equivalent to 100 mg of drug was subjected to dissolution analysis conducted in 900 mL of simulated gastric fluid (without enzymes, pH 1.2) for the first 2 hr followed by 900 mL of stimulated intestinal fluid (without enzymes, pH 6.8), both at 37±0.5°C, up to 12 hr. The apparatus was operated at 100 rpm. Aliquots of the medium were withdrawn at specified time intervals for drug analysis and replaced by an equivalent quantity of fresh medium. The withdrawn samples were appropriately diluted and analyzed spectrophotometrically for diclofenac sodium at 276 nm.

RESULTS AND DISCUSSION

In the present article, two new rosin-based polymers (R-1 and R-2) are synthesized and evaluated for their film-coating properties. The synthesized polymers are glossy, brownish-yellow, and soft in nature. The physicochemical characteristics of R-1 and R-2 are shown in Table 4. The polymers do not show a sharp melting point indicative of their amorphous nature. The acid values of R-1 and R-2 are significantly reduced compared to rosin (acid value 155 mg of KOH), probably due to esterification of rosin acids (abietic and pimaric). Rosin acids on heating form levopimaric acid which reacts with maleic anhydride to form a crystalline Diels–Alder adduct. The adduct is esterified with glycerol and these esters are used extensively as protective coatings. Fumaric acid reacts more slowly with rosin than maleic anhydride but yields products of higher acid value (21).

Table 4

Evaluation of Physicochemical Characteristics of Rosin-Based Polymers

Polymer	Color	Softening Point (°C)	Acid Value (mg of KOH)
R-1	Brownish-yellow	94–96	40–45
R-2	Brownish-yellow	70–72	80–85

The weight average molecular weight (M_w) of R-1 and R-2 was found to be 1608 and 3761, respectively. The polydispersity index (M_w/M_n) of the synthesized polymers indicates a narrow range of molecular weight distribution. The lower values of T_g (59°C and 85°C) for the two polymers substantiate their soft nature. The T_g measurements show a higher value for R-2 than for R-1. Thermogravimetric analysis shows a 2.8% and 3.4% loss of initial weight for R-1 and R-2, respectively, indicative of their hydrophobic nature. The polymer characterization is presented in Table 5.

Film Characterization

Plasticizer free films of the polymers are glossy, elastic, and translucent. The mechanical properties of free films are useful to assess the basic film-forming properties of new materials, thereby predicting their usefulness for pharmaceutical coating and drug delivery. The polymer concentration,

solvent system, and presence/absence of plasticizer are important variables. A clear polymer solution was obtained with organic solvents like dichloromethane, acetone, and chloroform. A 30% w/v solution in dichloromethane was used for the preparation of free films. Increasing the polymer concentration above 40–45% resulted in migration and subsequent deposition of polymeric material to the periphery of the circular ring used for film casting over mercury substrate in the Petri dish. The resulting films visually showed an irregular distribution of polymer, assessed by varying thickness at different points. Films produced from the plasticizer free solutions containing a polymer concentration below 15% were smooth and transparent but very brittle. This brittleness or lack of plasticity prevents the cutting of free films into proper dimensions required for mechanical testing. Therefore, in order to assess the basic film-forming properties of R-1 and R-2, free unplasticized films, 30% w/v in dichloromethane, were used for mechanical testing.

The results obtained in plastic tensile tests of free films are shown in Table 6. It is seen from the results that the tensile strength and modulus of elasticity of R-1 and R-2 are lower compared to Eudragit L-100 and HPMC. The percentage elongation of the prepared films is very high compared to the standard polymers, suggesting that the prepared polymers form films which are soft, elastic, and tough, desirable characteristics in film coating.

Scanning electron photomicrographs of the free films of R-1 and R-2 are shown in Fig. 1.

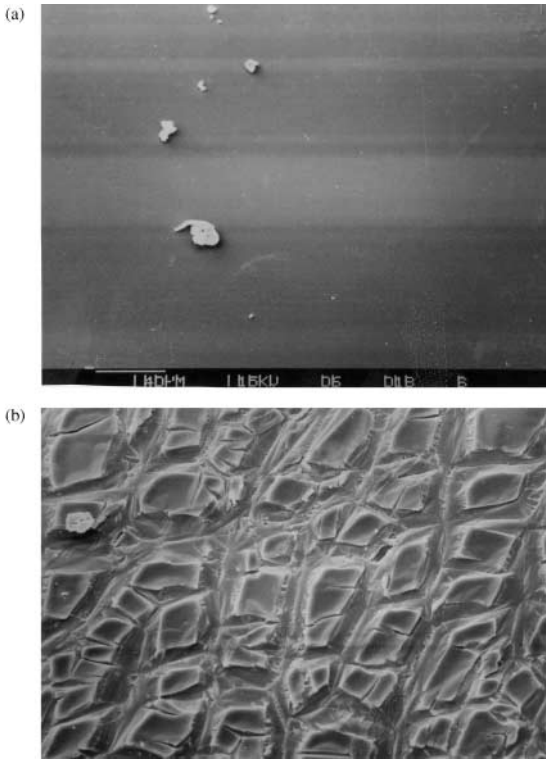

Figure 1. Scanning electron photomicrographs of free film: (a) R-1 and (b) R-2.

Table 5

Polymer Characterization

Polymer	Molecular Weight (M_w)	Polydispersity (M_w/M_n)[a]	T_g (°C)	TGA (% wt. loss)
R-1	1608	1.091(0.059)	59	2.8
R-2	3761	2.103(0.187)	85	3.4

[a]Each value represents a mean of three determinations. Numbers in parentheses indicate standard deviation.

Table 6

Mechanical Properties of Free Films[a]

Mechanical Property	Polymer			
	R-1	R-2	Eudragit®	HPMC
Thickness (mm)	0.20 (0.11)	0.19 (0.23)	0.20 (0.11)	0.11 (0.12)
Tensile strength (MN/m^2)	1.08 (0.63)	0.58 (0.23)	10.01 (0.31)	44.08 (0.30)
Elongation (%)	140.76 (116.04)	178.34 (79.21)	3.22 (1.73)	3.44 (0.33)
Modulus of elasticity (MN/m^2)	1.96 (0.20)	0.49 (0.41)	359.83 (13.41)	1293.34 (11.48)

[a]Each value represents a mean of three determinations. Numbers in parentheses indicate standard deviation.

Table 7

Water Vapor Transmission Rate Study of Free Films[a]

Polymer	RH (%)	Thickness (cm)	Area (cm^2)	WVTR ($g\,cm/cm^2$) 24 hr	48 hr	72 hr
R-1	43	0.0195	4.31	2.59×10^{-5}	2.59×10^{-5}	3.77×10^{-5}
	93			4.93×10^{-5}	1.32×10^{-4}	1.86×10^{-4}
R-2	43	0.0197	4.44	6.26×10^{-5}	8.32×10^{-5}	1.11×10^{-4}
	93			1.15×10^{-4}	2.35×10^{-4}	3.89×10^{-4}

[a]Each value represents a mean of three determinations.

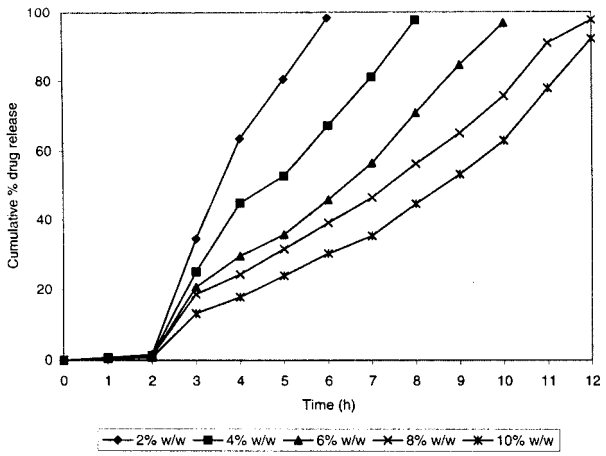

Figure 2. Drug release profile of R-1-coated pellets.

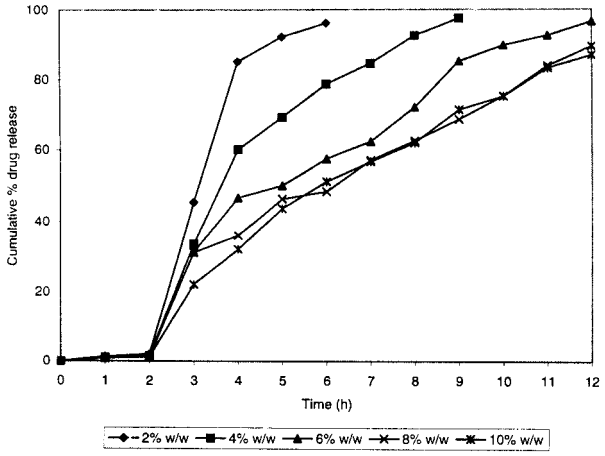

Figure 3. Drug release profile of R-2-coated pellets.

A relatively smooth surface is observed with R-1, while the surface is irregular and rough with R-2.

The results obtained in WVTR studies are depicted in Table 7. Such studies determine the effectiveness of the polymer film as a moisture barrier. The water vapor transmission at different relative humidities shows that at higher humidity WVTR is very low compared to the value for shellac ($8.813\times10^{-4}\,g\,cm/cm^2/24\,hr$), which has been suggested as a control for maximum permissible water vapor transmission (18). Such low values of WVTR for the free films of the prepared polymers are indicative of their moisture-protective ability.

Drug Release Profile

Preliminary studies show that the drug release from coated pellets was sustained up to 12 hr using the prepared polymers. The drug release profiles are shown in Figs. 2 and 3 for R-1 and R-2, respectively. The extent of film coating build-up affects the release behavior of drug from pellets. Drug release is sustained up to 12 hr with 8% w/w of film coating build-up with R-1 and 6% w/w of film coating build-up with R-2. Thus the amount of polymer used affects the release behavior. Little or no drug is released for the first 2 hr (pH 1.2) with both polymers.

CONCLUSION

In the present study, the film-forming properties of two new rosin-based polymers, R-1 and R-2, have been investigated to assess their potential for use in film coating. Both R-1 and R-2 could be used at a concentration of 30% w/v in dichloromethane to form free films. Addition of a suitable

plasticizer may be attempted to improve their mechanical properties. Coating experiments did not result in any serious agglomeration of pellets. Coated pellets sustained the release of drug up to 12 hr. The polymers prevented a significant amount of drug release under gastric conditions. The synthesized polymers therefore promise considerable utility in film coating and in the design of gastroresistant delivery dosage forms.

ACKNOWLEDGMENTS

The authors are thankful to Dr. V. D. Labhasetwar, Nebraska Medical Centre, Omaha, NE for his guidance. One of the authors (P. M. M.) would like to thank C.S.I.R., New Delhi for financial support and V.R.C.E., Nagpur for the Instron facility.

REFERENCES

1. Felton, L.A.; McGinity, J.M. Int. J. Pharm. **1997**, *154*, 167.
2. Phuapradit, W.; Shah, N.H.; Raikar, A.; Williams, L.; Infeld, M.H. Drug Dev. Ind. Pharm. **1995**, *21* (8), 955.
3. Lim, L.Y.; Wan, L.S.C. Drug Dev. Ind. Pharm. **1994**, *20* (6), 1007.
4. Lu, S.M.; Chen, S.R. J. Contr. Rel. **1993**, *23*, 105.
5. Kokubo, H.; Obara, S.; Nishiyama, Y. Chem. Pharm. Bull. **1998**, *46* (11), 1803.
6. Rosilio, V.; Treupel, L.R.; de Laurdes, M.; Baszkin, A. J. Contr. Rel. **1988**, *7*, 171.
7. Benita, S.; Dor, Ph.; Aronhime, M.; Marom, G. Int. J. Pharm. **1986**, *33*, 71.
8. Lopez, C.R.; Bodmeier, R. Drug Dev. Ind. Pharm. **1996**, *22* (12), 1201.
9. Pathak, Y.V.; Dorle, A.K. Drug Des. Del. **1990**, *6*, 223.
10. Pathak, Y.V.; Nikore, R.L.; Dorle, A.K. Int. J. Pharm. **1985**, *24*, 351.
11. Sheorey, D.S.; Dorle, A.K. J. Microencaps. **1991**, *8*, 243.
12. Pathak, Y.V.; Dorle, A.K. Indian J. Pharm. Sci. **1986**, *48*, 15.
13. Ramani, C.C.; Puranik, P.K.; Dorle, A.K., Int. J. Pharm. **1996**, *137*, 11.
14. Sahu, N.H.; Mandaogade, P.M.; Deshmukh, A.M.; Meghre, V.S.; Dorle, A.K. J. Bioact. Comp. Polym. **1999**, *14*, 344.
15. Rama Rao, P.; Diwan, P.V. Drug Dev. Ind. Pharm, **1998**, *24* (4), 327.
16. Munden, B.J.; Dekay, H.G.; Banker, G.S. J. Pharm. Sci. **1964**, *53*, 395.
17. Woodruff, C.W.; Peck, G.E.; Banker, G.S. J. Pharm. Sci. **1972**, *61*, 1956.
18. Patel, M.; Patel, J.M.; Lemberger, A.P. J. Pharm. Sci. **1964**, *53*, 286.
19. Utsumi, I.; Ida, T.; Takahashi, T.; Sugimoto, N. J. Pharm. Sci. **1961**, *50*, 592.
20. Swarbrick, J.; Boylan, J.C. In *Encyclopedia of Pharmaceutical Technology*; Marcel Dekker: New York, 1997; Vol. 1, 337.
21. Mundhe, B.N.; Morey, S.P.; Gogte, B.B. Paint. India, **1993**, *44*, 77.