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Content

Characterization and evaluation of natural copal gum-resin as film forming material

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Copal resin (CR) was investigated for its physicochemical properties, which are yellowish cream in colour with acid value 129.82 ± 2.38, saponification value 172.60 ± 4.03, ester value 42.78 ± 3.19, softening point 88-92°C, glass transition temperature (Tg) 85.29°C, refractive index 1.534-1.536 and moisture content (loss on drying) 0.699 ± 0.08% w/w. The free films, prepared in alcohol by solvent evaporation technique, were brittle with high tacking property. Addition of 1% w/w propylene glycol improved the mechanical properties (tensile strength, percent elongation and Young's modulus) of CR films, whereas glyceryl monostearate, sorbitan mono-oleate and sorbitan monolaurate in 15% w/w reduced the tackiness significantly. Water vapour transmission rate of CR film was $2.16 \pm 0.31 \times 10^{-5}$ g cm/cm^2 and $4.13 \pm 0.18 \times 10^{-5}$ g cm/cm^2 at relative humidity (RH) of 43% and 93%, respectively. CR films show good swelling property in phosphate buffer (pH 7.4). Present investigation proposes the film-forming natural material with its potential as a coating material for sustained release and colon-targeted drug delivery.

Key words: Copal resin, film-forming material, films, mechanical property, tackiness, swelling index

Abbreviations: Copal resin, Copal resin, WVTR, water vapour transmission rate, LOD, loss on drying, RH, relative humidity

INTRODUCTION

Polymers are widely used in healthcare products from traditional dosage forms to complex biopharmaceutical formulations in drug delivery systems. The use of film-forming material, as coating on medicine, as vehicle for drug delivery and as packaging material, has directed several studies to evaluate polymeric material for their potential as film-forming material (Knaig and Goodman, 1962). Polymer coating is widely used in the preparation of sustained and controlled release dosage forms (Phuapradit *et al.*, 1995). Pharmaceutical coating material is characterized for its mechanical properties (Rowe *et al.*, 1984; Nagarsenkar and Hegde, 1999), permeability (Sun *et al.*, 1987) and water vapour transmission (Shogren, 1997). Coating technique and the nature of dosage form do not influence the properties of free films (Sprockel *et al.*, 1990).

Natural polymers have gained the attention for their use in drug delivery systems due to their availability, compatibility and degradation under natural and physiological conditions (Bharadwaj *et al.*, 2000). Natural resins are widely used in varnishes, sealant, binding media, water proofing etc. Natural resins like rosin (pinaceae), dammar, sandarac, mastic and guaiac have been evaluated for their usefulness in pharmaceutical preparations. Copal, a resinous material, is obtained from the plants of araucariaceae and caesalpinaceae, a subfamily of leguminoaceae (Ossete-Cortina and Domenech-Carbo, 2005). It is a widely used ingredient of oil-based painting varnishes (Palomino, 1947; Mills and White, 1987; Hiscox and Hopkins, 1997) as paint media (Gettens and Stout, 1966; Cennini, 1988) and as material for coating woodwork (Hurst, 1987). It produces glossy films and protects it from the changing weather conditions (Conelly, 1985). Copal is used as pigment binder in varnishes (Billing, 1994), as emulsifier and stabilizer in paints, painting inks etc. (Langenheim, 1969). Medicinally, Copal was also used in the treatment of headache, fever, burns and stomach Ache (Whitmore, 1980). In dentistry, it is used as binding media in dental products and in treatment of microleakage in teeth (Dutton *et al.*, 1993; Anthony *et al.*, 1992). Recently, the Copal gum has been evaluated as matrix-forming material for sustaining the drug delivery (Morkhade *et al.*, 2006).

Copal resin (CR) contains agathic acid, a diterpenoid and related lobdane compounds along with cis-communic acid, trans-communic acid, polycommunic acid, sandaracopimaric acid, agathalic acid, monomethyl ester of agathalic acid, agatholic acid and acetoxy agatholic acid (Ossette-Cortina and Domenech-Carbo, 2005). CR obtained from leguminoaceae family contains copalic acid, pimaric acid, isopimaric acid, dehydro-dehydroabietic acid, dehydroabietic acid and abietic acid (Ossette-Cortina and Domenech-Carbo, 2005).

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CR has been used as medicine and has the ability to form glossy films. Being of natural origin, it is expected to be biodegradable and ecofriendly. Hence, it can be evaluated for polymeric properties and used in pharmaceutical coating.

MATERIALS AND METHODS

Materials

CR was purchased from Yucca Enterprises, Thane, Mumbai. Ethanol, chloroform, isopropyl alcohol, ethyl acetate and other solvents were purchased from S.D. Fine Chemicals. Potassium hydroxide, dibutyl phthalate, propylene glycol, polyethylene glycol 6000, hydroxyl propyl methyl cellulose, sodium acetate, sodium chloride and other chemicals were of analytical grade and purchased from S.D. Fine Chemicals.

Physicochemical Characterization of CR

CR resin was characterized for colour, moisture content, acid value (Indian Pharmacopoeia, 1996), saponification value (Indian Pharmacopoeia, 1996), ester value and softening point (Herculus drop softening point method). Glass transition temperature (T_g) was determined by differential scanning calorimetry (Perkin-Elmer *DSC* 7). A 5.97-mg sample was accurately weighed and scanned in the temperature range of 20-200°C at the heating rate 10°C/min. Refractive index was determined by using Abbe's refractometer. The apparatus was calibrated using distilled water; CR solution showed refractive index 1.3325 at 25°C.

Solubility Studies

One gram of CR was accurately weighed and placed in screw-capped test tubes containing 10 ml of organic solvents. The tubes were placed in a mechanical shaker for 24 h at 50 rpm and 25°C. After 24 h, 2 ml of the solution was withdrawn, poured in tarred petridish and the solvent was evaporated in an oven at 50°C. Increase in the weight of petridish relative to solvent blank was used to determine the solubility of the material in the respective solvent (Ramani *et al.*, 1996).

Free Film Preparation

Free films of CR were prepared by solvent evaporation technique on mercury substrate (Satturwar *et al.*, 2002). Thirty percent w/v solution of CR was prepared in alcohol and was casted into petridish (diameter - 20 cm) containing mercury (area of casting - 19.4 cm^2), dried at room temperature for 24 h and stored in a desiccator.

Various formulations of CR using different plasticizers were prepared. To investigate the effect of plasticizers on film characteristics, hydroxyl propyl methyl cellulose (HPMC), dibutyl phthalate (DBP), glycerine, propylene glycol and polyethylene glycol (PEG) were used. Film thickness was measured by micrometer screw gauge (15 mm; Osawa Scientific) and recorded as mean of three measurements at the length of 0.5 cm.

The prepared cast films were cut into strips (12 × 120 mm) and evaluated for stress-strain parameters using Instron instrument based on ASTM standard test principle (Lin and Lee, 1991). The measurements were made at gauge length of 50 mm, cross-head speed (CHS) of 25 mm/min at 50% RH and 25°C. Stress-strain parameters including the tensile strength, percent elongation and Young's modulus were determined for each film specimen with at least three repetitions.

Moisture Absorption by Free Films

Films were cut into 25 × 10 mm strips. The strips were transferred to tarred petridish and then into glass desiccators maintained at controlled RH of 23%, 43%, 75% and 93%. The RH in the desiccators was controlled by the use of saturated solutions of different solutes in excess. The film strips were accurately weighed, placed in RH chamber and removed at the end of day 14 and weighed. Films evaluated for increase or decrease in the weight on the 14th day, is an indication of moisture absorption. The film specimens were also observed for physical changes, if any.

Water Vapour Transmission Rate (WVTR) Studies

To determine water vapour transmission, the permeation cell of glass body (2.25 cm internal diameter × 8.0 cm height) having cap with opening of 23.4 mm diameter (test area 4.3 cm^2) was used (Sprockel *et al.*, 1990) and its portion held in place by means of three screw clamps. The thickness of the film was determined with screw gauge and the disc of the film under investigation was clamped tightly to provide the effective surface area of 4.3 cm^2 for water vapour transmission. The RH was maintained by using saturated solutions in contact with undissolved salt (in excess). The saturated solutions of potassium acetate, potassium carbonate, sodium chloride and potassium nitrate were used to maintain the RH conditions of 23%, 43%, 75% and 93%, respectively (Patel *et al.*, 1964). The charged cells were weighed and placed in pre-equilibrated desiccators maintained at 0% RH. The cells were re-weighed after 24 h. The amount of water vapour transmitted (W) through the film was calculated by the weight loss of assembled cells. The water vapour transmission rate (WVTR) was determined using Utsumi's equation (Utsumi *et al.*, 1961) considering the thickness of the film as shown below:

$$Q = S/WL$$

where Q - water vapour transmission rate (g cm/cm^2/24 h)
W - gram of water vapour transmitted in 24 h
L - thickness of film in cm
S - surface area (cm^2)

Swelling Studies (Akhgari *et al.*, 2006; Rafiee-Tehrani *et al.*, 2007)

To investigate the swelling property, an area of 1 cm^2 (1 × 1 cm) of each film was dried in a oven at 50°C for 24 h. Dried film was accurately weighed (±0.0001 ×g) and immersed in a flask containing 250 ml of different media at 37 ± 2°C. Swollen samples were withdrawn from the medium and weighed (±0.0001 g) after removal of excess surface water by light blotting with Whatman paper. First sampling was done at 15 min and subsequent sampling was done at time intervals of 30 min up to 180 min.

To quantify the swelling process, the swelling index, Is (%), was calculated as follows (Blanchon *et al.*, 1991):

$$Is\ (\%) = \frac{W_s - W_d}{W_d} \times 100$$

where W_d = Weight of dried film

W_s = Weight of film after swelling

Swelling test was carried out using different phosphate buffer (pH 4.5, pH 6.0, pH 7.4). All the experiments were carried out in triplicate.

Effect of Different Surfactants on the Tackiness of CR Film

To investigate the effect of different surfactants on the tackiness of CR film, glyceryl monostearate (GMS), sorbitan mono-oleate (span 80), sorbitan monolaurate (span 20) and talc were used. The surfactants (except talc) were first prepared in the form of 4% w/w dispersion by homogenizing in alcohol for 15 min. The surfactant dispersions were then added into pre-plasticized (PEG 1% W/W) CR dispersion to obtain CR-surfactant dispersions of 5%, 10% and 15% (W/W) (based on polymer mass). The polymer dispersions containing 15%, 30% and 50% (w/w) talc were also prepared. The films were prepared by spraying polymer dispersion on glass plate using pneumatic nozzle. The dispersions were continuously stirred while spraying. The films were formed on the glass plate by intermittent application of warm air. The spray position was changed constantly to obtain the film with uniform thickness. The films were allowed to dry and subsequently stored over silica gel until required for the test.

The films were cut into 2.5 × 7.0 cm sections and backed with cotton cloth. The two test films were pressed together under the weight of 200 g and stored at 40°C for 60 min. The samples were cooled to 25°C at 43% RH for 60 min and T-peel test were performed using tensile tester (Instron Instrument). The films were peeled from each other through one end at cross-head at the speed of 15 mm/min. The force displacement was recorded. The average values obtained from constant force portions of the diagram were used to determine the peel forces.

RESULTS AND DISCUSSION

Various natural polymers have been investigated for their application as pharmaceutical adjuvants. CR is a biopolymer obtained from the plants and the present communication is an investigation of the physicochemical characteristics and film-forming properties of CR.

Physicochemical Characterization of CR

CR is yellowish cream in colour with softening point in the range of 88-92°C. The DSC analysis shows (Fig. 1) that the glass transition temperature (T_g) of CR is 85.29°C. The physicochemical properties of CR are given in Table 1. Higher acid value indicates the large amount of free acid groups in the CR and its suitability for enteric coating. At T_g, a solid, brittle and amorphous material undergoes its transformation to a soft and rubbery state. T_g value and softening point range are indicative of soft nature of CR.

Solubility

Relative solubility study of CR, in different solvents and under different pH conditions, indicates that CR is insoluble in water and soluble in most of the organic solvents showing highest solubility in alcohol as shown

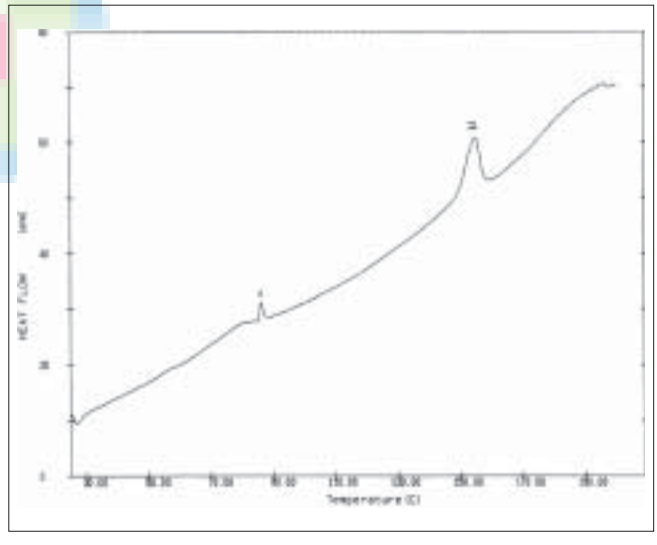

Figure 1: DSC analysis of copal resin

Table 1: Physicochemical characteristics of copal resin

Parameter	Copal resin
Colour	Yellowish cream
Moisture content (%)	0.699 ± 0.08
Acid value	129.82 ± 2.38
Saponification value	172.60 ± 4.03
Ester value	42.78 ± 3.19
Softening point (°C)	88-92
Glass transition temperature, T_g (°C)	85.29
Refractive index	1.534-1.536

± - Values are the means of three determinations

in Table 2. The pH-dependant solubility was observed, showing alkalinity favouring the solubility of CR in buffered solution.

Characterization of CR Films

The investigation shows the excellent film-forming property of CR. Resin has highest solubility in alcohol; hence alcohol was selected as a solvent for the preparation of CR films. However, the plasticizer-free films are brittle, and therefore polyethylene glycol 6000, dibutyl phthalate (DBP), propylene glycol (PEG), hydroxypropyl methyl cellulose (HPMC) and glycerine were used as plasticizers in different concentrations to improve the mechanical properties. The films prepared with HPMC, polyethylene glycol 6000 were semi-transparent; DBP-added films were difficult to dry; glycerine-added films were brittle. The films prepared using PEG (1% w/w and 2% w/w based on polymer mass) were smooth and excellent with improved mechanical properties (Table 3). Scanning electron micrographs of the plasticizer-free films and films with plasticizer are shown in Fig. 2.

Table 2: Relative solubility of copal resin

Solubility in different solvents		Solubility in different buffer solutions	
Solvent	**Solubility (g/ml)**	**pH**	**Solubility (g/ml)**
Chloroform	0.26 ± 0.013	1.6	0.023 ± 0.007
Acetone	0.26 ± 0.022	4.5	0.041 ± 0.010
Ethyl acetate	0.52 ± 0.017	6.8	0.064 ± 0.013
Isopropyl alcohol	0.36 ± 0.023	8.0	0.080 ± 0.015
Ethanol	0.83 ± 0.018	10.0	0.096 ± 0.019
Water	0.012 ± 0.007		

- Values are mean of three determinations

Moisture Absorption Studies

Results of moisture absorption studies at different RH conditions are shown in Table 4. The moisture absorption does not increase significantly with increase in RH, which indicates the hydrophobic nature of CR films.

Water Vapour Transmission Rate (WVTR) of Free Films

Water vapour transmission rate (WVTR) varies with the thickness of film. WVTR was determined by using Utsumi's equation, and inversely proportional to the thickness of the film and are shown in Table 5.

The low WVTR, viz. $4.13 \pm 0.18 \times 10^{-5}$ g cm/cm^2 at 93% RH, indicates strong moisture protecting ability of CR films (Utsumi *et al.*, 1961).

Swelling Studies

Figure 3 reveals the results of swelling property of CR films. Swelling of CR-free films in phosphate buffer pH 7.4 was

Table 3: Mechanical properties of free films

Film	Copal resin
Thickness (mm)	0.26 ± 0.04
Tensile strength (MN m^{-2})	0.386 ± 0.41
Elongation (%)	38.95 ± 7.12
Young's modulus	0.807 ± 0.03

CR 30% w/w with PEG 1% w/w based on polymer mass. # - Values are means of three determinations

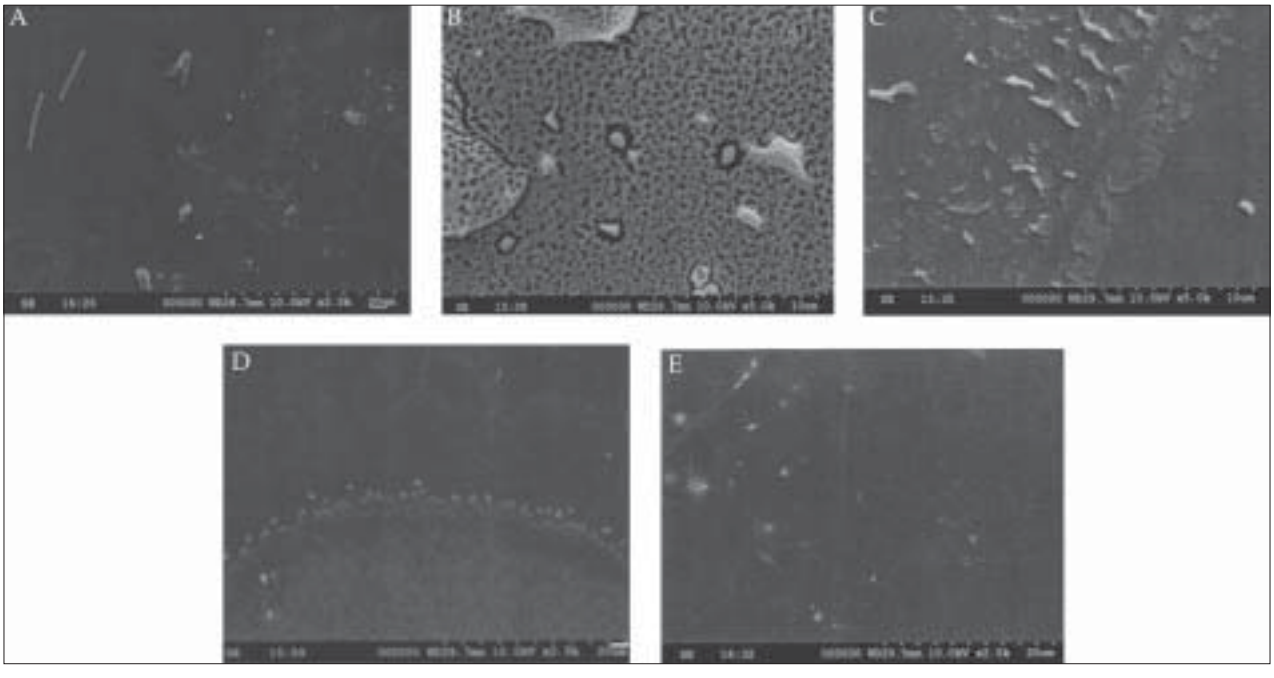

Figure 2: Scanning electron micrographs of CR films, (A) CR film without plasticizer, (B) CR film with 2% W/W HPMC, (C) CR film with 2% W/W glycerine, (D) CR film with 2% W/W dibutyl phthalate, (E) CR film with 2% W/W propylene glycol 6000

Table 4: Moisture absorption studies of copal resin films at different relative humidity conditions

Product	Percent moisture absorbed at % RH			
	23	43	75	93
CR film	0.89 ± 0.10	1.09 ± 0.14	1.67 ± 0.18	2.08 ± 0.22

- Values are means of three determinations

Table 5: WVTR of copal resin free films

Film	Thickness (cm)	Area (cm^2)	WVTR (g cm/cm^2)/24 h 10-5 at RH	
			43%	93%
CR	0.38 ± 0.04	4.30 ± 0.15	2.16 ± 0.23	4.13 ± 0.18

- Values are means of three determinations

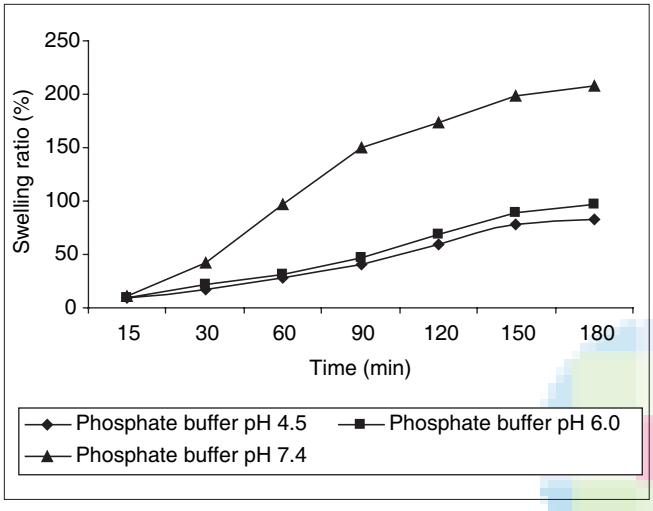

Figure 3: Swelling ratio (%) versus time (min) for CR film immersed in different media

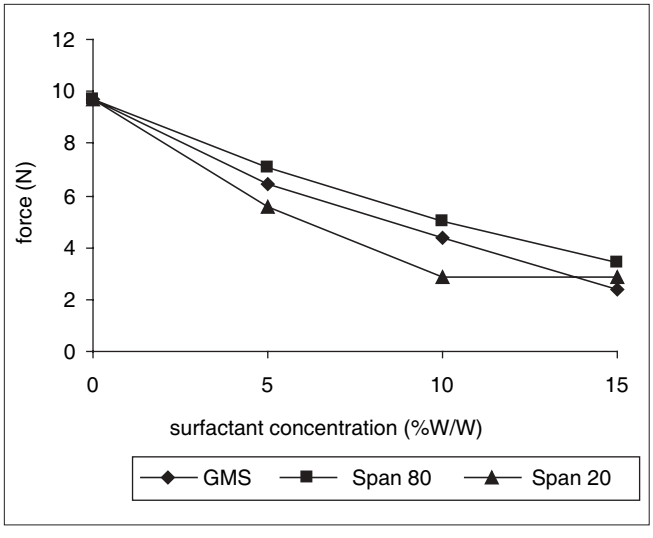

Figure 4: Effect of surfactants on free CR films

significant as compared to phosphate buffer pH 4.5 and phosphate buffer pH 6.0. Swelling in phosphate buffer pH 7.4 shows the possibility of CR as coating agent for colon-targeted drug delivery.

Table 6: Effect of talc on tackiness of free CR films

Additive	Force (N, Mean ± SD)
No additive	9.7 ± 0.3
Talc (% w/w)	
15	10.4 ± 0.4
30	8.3 ± 0.7
50	5.6 ± 0.6

- Values are the means of three determinations

Effect of Surfactants on Tackiness of CR Films

Film tackiness is represented by the force required to peel the pressed films and helps to compare the anti-tacking property of different surfactants (Wesselling *et al.*, 1999). As the casting method could sediment the additives, spraying technique was used to study the effect of talc and surfactants on the tackiness of CR films Fig. 3.

The effect of talc on the tackiness of CR film is shown in Table 6. Talc could not reduce the tackiness of CR films significantly when used in 15%, 30% and 50% (w/w), whereas GMS, span 80 and span 20 significantly reduce the tackiness of CR films when used in 15% (w/w) (Fig. 4).

CONCLUSION

In the present study, CR was evaluated for its physicochemical properties, mechanical properties, moisture absorption, water vapour transmission and swelling property. WVTR and swelling studies direct towards the potential of CR as a good film-forming material and can be evaluated for hydrophobic matrix material for sustained, pH-dependant and colon-targeted drug delivery. Anti-tacking effect of GMS, span 80 and span 20 on CR film can improve the performance of material when used as coating agent.

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