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EVALUATION OF PENTAERYTHRITOL (ROSIN) ESTERGUM AS COATING MATERIALS

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Rosin was heated with pentaerythritol and intermediate reaction products with the different acid values were obtained. Their physical properties were studied. Aspirin granules were coated with these coating materials. Coated drug granules were evaluated for moisture absorption, flow properties, friability loss and dissolution studies in gastric medium and intestinal medium. The results have shown that these coating materials have excellent film forming properties and impart moisture protective coatings. The dissolution studies revealed that these exhibit different degree of resistance to gastric and intestinal pH's and can be used for delayed release of drug. The study of the dissolution kinetics revealed that the release characteristics obey the Hixson-Crowell cube root dissolution law and the values of cube root dissolution constants have been reported.

INTRODUCTION

Rosin and rosin derivatives have been widely used in paints, varnishes, vinyl resins and rubber products for their film forming properties. These have also been used in chewing gum bases, dental varnishes and

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as pharmaceutical aid in bandage preparations. We have reported the use of rosin and rosin esters with glycerol, sorbitol and mannitol as coating materials[1]. It has also been reported that rosin-glycerol intermediates have very good film forming properties[2] and a quantitative correlationship was found between the release characteristics and physico-chemical properties of rosin glycerol esters[3]. Juerzy et al[4] have reported the use of rosin glycerol heated product as an anhydrous binding agent in tablet formulation. Pathak et al[5,6] have reported the usefulness of rosin and rosin derivatives in tablet formulation as an anhydrous binding agents. Rosin forms an ester with pentaerythritol and Bent and Johnson[7] have patented a method for preparation of rosin-pentaerythritol estergum. Cerbert[8] has reported that pentaerythritol rosin ester has better hardness, gloss, durability and resistance to water and alkali than rosin or rosin-glycerol ester.

This communication relates the attempt to evaluate pentaerythritol rosin estergums as coating materials. It is found that pentaerythritol ester and the intermediates exhibit excellent film forming properties and impart moisture protective properties and can be used for delayed release of drugs.

MATERIALS AND METHODS

Rosin N Grade (ISI), Pentaerythritol(pure grade, Fluka, Germany), Aspirin (IP), Starch(IP).

Preparation of Pentaerythritol(Rosin) Ester gums: Rosin was heated with pentaerythritol (4:1 parts) in an aluminium vessel, at 210-220°C. At every alternate hour, a 2-5 g sample was withdrawn, its acid value was determined using IP procedure. Heating was continued till there was no further drop in the acid value. Intermediate products PR 115(acid value 115), PR 90

(A.V.90), PR 55(A.V.55), PR 35(A.V.35) and PR 15 (A.V.15) were collected pouring part of the reaction mixture in water with vigorous stirring to remove excess of pentaerythritol. These were further filtered and dried in an oven at 55°C overnight.

Study of Physical Properties: Physical properties like colour, softening point, acid value, specific gravity and equilibrium solubility[9] in different solvents was determined. The moisture absorption studies[10] were carried out using dessicators maintained at different Relative humidities. Samples were kept for 15 days to achieve equilibrium.

Coating of drug: For all the experimental purposes aspirin was used as a drug of choice. A standard coating technique was used for coating purposes[1]. Aspirin granules (20/30 mesh) were used and coated with 10% solution of coating material in acetone. In all experiments 15 no. of coats were imparted for comparative study of the materials.

Evaluation of the coated drug: The coated drug was evaluated for its moisture absorption studies[10], Flow characteristics were determined using fixed funnel cone method, angle of repose was determined. Friability loss[11] was determined by shaking the coated granules in a glass bottle for 15 min. at a constant speed and these were further sieved through mesh no.20 to determine the friability loss. Release characteristics of the drug from the coated granules were determined using a standard dissolution rate appratus USP XVIII model. All studies were carried out at 37°±1°C and at a speed 150 rpm. The release patterns were studied in two media that is gastric medium USP (without enzyme) and intestinal medium USP (without enzyme). The drug content in the sample withdrawn was determined using Ferric Nitrate

Reagent[12], the colour developed was read at 540 in the colorimeter (Bausch & Lamb).

RESULTS AND DISCUSSION

Study of the physical properties show that on esterification of rosin there is a gradual change in colour from pale yellow to brown (Table 1). A sharp increase in the softening point is also observed, PR 15 has a much higher softening point than rosin.

Moisture absorption studies show that rosin and its pentaerythritol ester intermediates are highly hydrophobic in nature and at 100% R.H., the % moisture absorbed is less than 1% (Table 2). It clearly shows that these products can impart excellent moisture protection properties.

Study of the equilibrium solubility was carried out in four solvents. All are found to be insoluble in water and soluble in acetone and ether. Solubility in alcohol has been found to be decreasing (Table 3) and PR 15 has a very low solubility in alcohol.

Study of the coated granules :- The moisture absorption studies of the coated aspirin granules show that all the coating materials impart excellent moisture protection to the drug(Table 4). These coating materials can be used for protecting the moisture sensitive drugs.

Results of the flow properties and % friability loss are shown in Table 5. It is observed that after coating of the drug granules, there is a sharp decrease in the angle of repose (control sample angle of repose-34.3°). It is observed that coating has improved the flow properties of the drug granules. In case of friability loss it is observed that in case of rosin, it is the highest amongest all showing the brittle nature of

TABLE 1

Physical properties of the coating materials.

Coating Material	Colour	Softening point[a] °C	Acid value[a] ± S.D.	Sp.gr.[a] at 25°C
Rosin	Pale yellow	65-82	145.75±6.4958	1.110
PR 115	Yellow	87-92	115.86±2.2159	1.108
PR 90	Brownish Yellow	93-98	90.64±3.4587	1.105
PR 55	Faint brown	97-105	55.57±2.0084	1.098
PR 35	Faint brown	102-107	35.18±3.1589	1.095
PR 15	Brown	105-110	15.15±2.9219	1.080

a - Mean average of three trials.

TABLE 2

Moisture absorption studies of the coating materials.

Coating material	% Moisture Absorption[a] Relative Humidity %			
	17.5	57.0	82.5	100
Rosin	0.00	0.35	0.55	0.85
PR 115	0.00	0.15	0.25	0.65
PR 90	0.00	0.35	0.45	0.50
PR 55	0.00	0.57	0.68	0.80
PR 35	0.00	0.45	0.65	0.75
PR 15	0.00	0.10	0.50	0.75

a - Mean average of the three trials

TABLE 3

Equilibrium solubility of the coating materials in different solvents.

Coating material	Equilibrium solubility[a] mg/ml ± S.D. Solvents			
	Acetone	Alcohol	Ether	Water
Rosin	565±0.035	420±0.065	630±0.0150	Insoluble
PR 115	550±0.015	285±0.038	620±0.028	Insoluble
PR 90	535±0.018	120±0.025	615±0.035	Insoluble
PR 55	495±0.028	028±0.015	605±0.018	Insoluble
PR 35	468±0.038	020±0.005	602±0.020	Insoluble
PR 15	445±0.0308	015±0.0010	580±0.030	Insoluble

a - Mean average of the three trials.

TABLE 4

Moisture absorption studies of the coated drug granules.

Coating material	% Moisture Absorption[a] Relative Humidity %			
	17.5	57.0	82.5	100.0
Rosin	0.00	0.45	0.60	0.95
PR 115	0.00	0.00	0.35	0.68
PR 90	0.00	0.15	0.40	0.70
PR 55	0.00	0.19	0.30	0.60
PR 35	0.00	0.18	0.40	0.75
PR 15	0.00	0.15	0.55	0.80

a - Mean average of the three trials.

TABLE 5

Evaluation of the coated drug granules.

Coating material	Flow properties[a] Angle of Repose	% Friability loss[a]
Rosin	27.2°±1.45	4.12%±1.1585
PR 115	26.1 ±0.59	1.25%±0.5385
PR 90	25.24±0.95	1.35%±0.3218
PR 55	26.24±1.05	1.85%±0.7121
PR 35	27.12±0.45	2.10%±0.1518
PR 15	28.5±0.58	1.95%±0.3219

a- Mean average of the three trials.

the rosin films. But on esterification there is a decrease in the friability loss % from the coated drug granules exhibiting the harder nature of the films imparted by the esterified coating materials.

Dissolution studies in the gastric medium:- The drug release characteristics in the gastric medium from the coated aspirin granules is depicted in Fig.1 and various dissolution parameters are given in Table 6.

It is observed that rosin, PR 115, PR 90 coatings are quite resistant to acidic pH and have t_{50}% values more than 3 hr. Rosin and PR 115 release less than 20% of the drug content in 3 hr. and can be used for enteric coating purposes. PR 90 and PR 55 have intermediate resistance to the gastric pH and have higher t_{50}% values and these coating materials can be used to have a delayed release of the drug. It is further observed that decrease in the acid value of the pentaerythritol ester gums reduces the resistance to lower pH and more

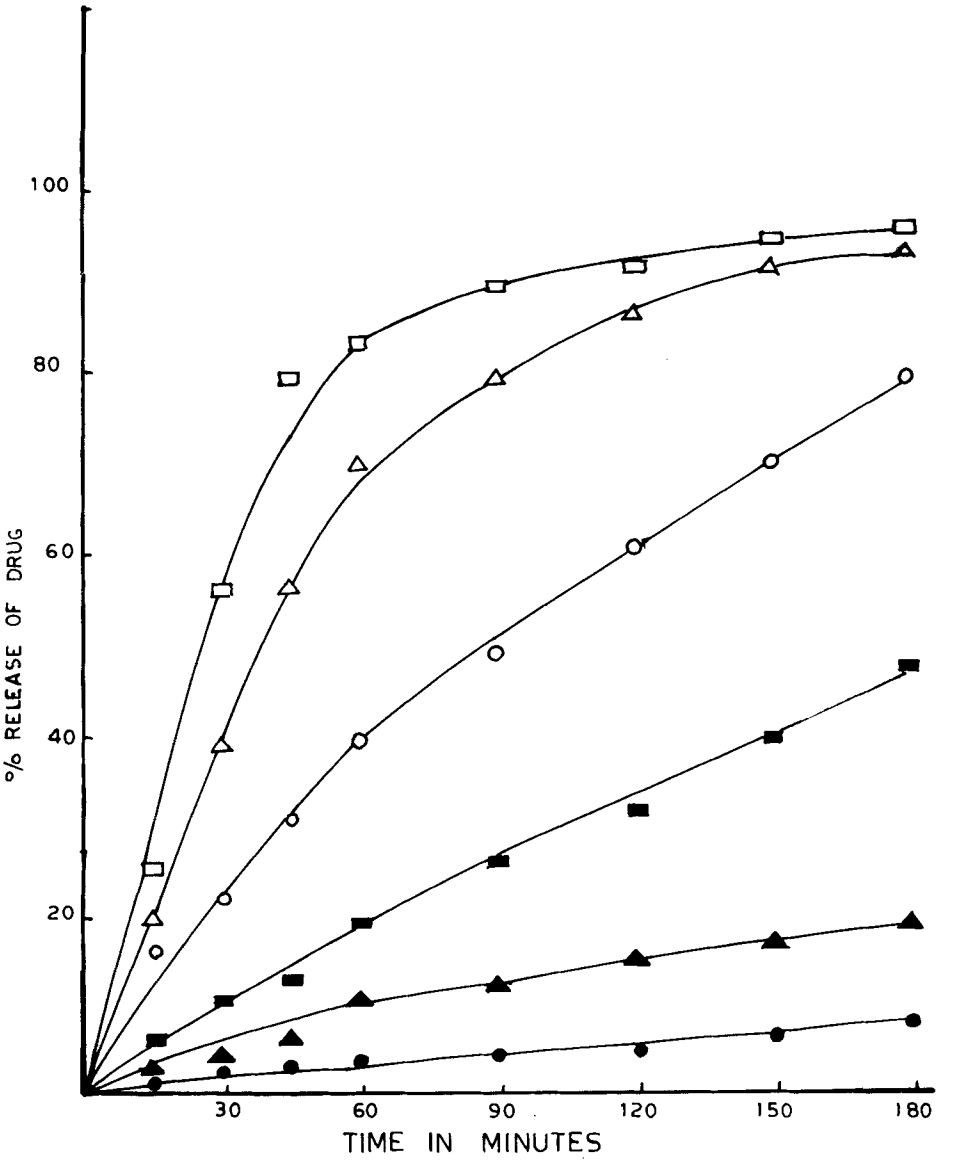

FIGURE 1

Dissolution studies : release characteristics in gastric medium.

Rosin — PR 115
PR 90 — PR 55
PR 35 — PR 15

TABLE 6

Dissolution parameters in gastric medium USP (without enzyme).

Coating material	% Release of drug[a] in 3 hr.	t_{50}% in min.	Cube root rate constant in gl/3 $min.^{-1}$
Rosin	10	>180	0.0022
PR 115	20	>180	0.0045
PR 90	47.28	>180	0.0110
PR 55	78.82	90.0	0.0250
PR 35	92.80	39.0	0.0433
PR 15	94.45	28.0	0.0577

a - Average mean of the three trials.

than 90% of the drug is released in 2 hr. in case of PR 35 and PR 15, with t_{50}% less than 40 min. in both the cases. Studying the dissolution kinetics it is observed that the release pattern from the coated drug obeys the Hixson-Crowell cube root dissolution law[11]. The values of the cube root constant for each release pattern are given in Table 6. It is observed that there is a gradual increase in the value of cube root constant with the decrease in the acid value of the coating materials showing the lower resistance of the films to gastric pH exhibiting quicker release. The three assumptions 1) dissolution occures normal to the surface of the solute particles, 2) agitation is uniform over all exposed surfaces and there no stagnation and 3) the particle of solute retains its geometric shape on which the Hixson-Crowell cube root dissolution law is based hold true for

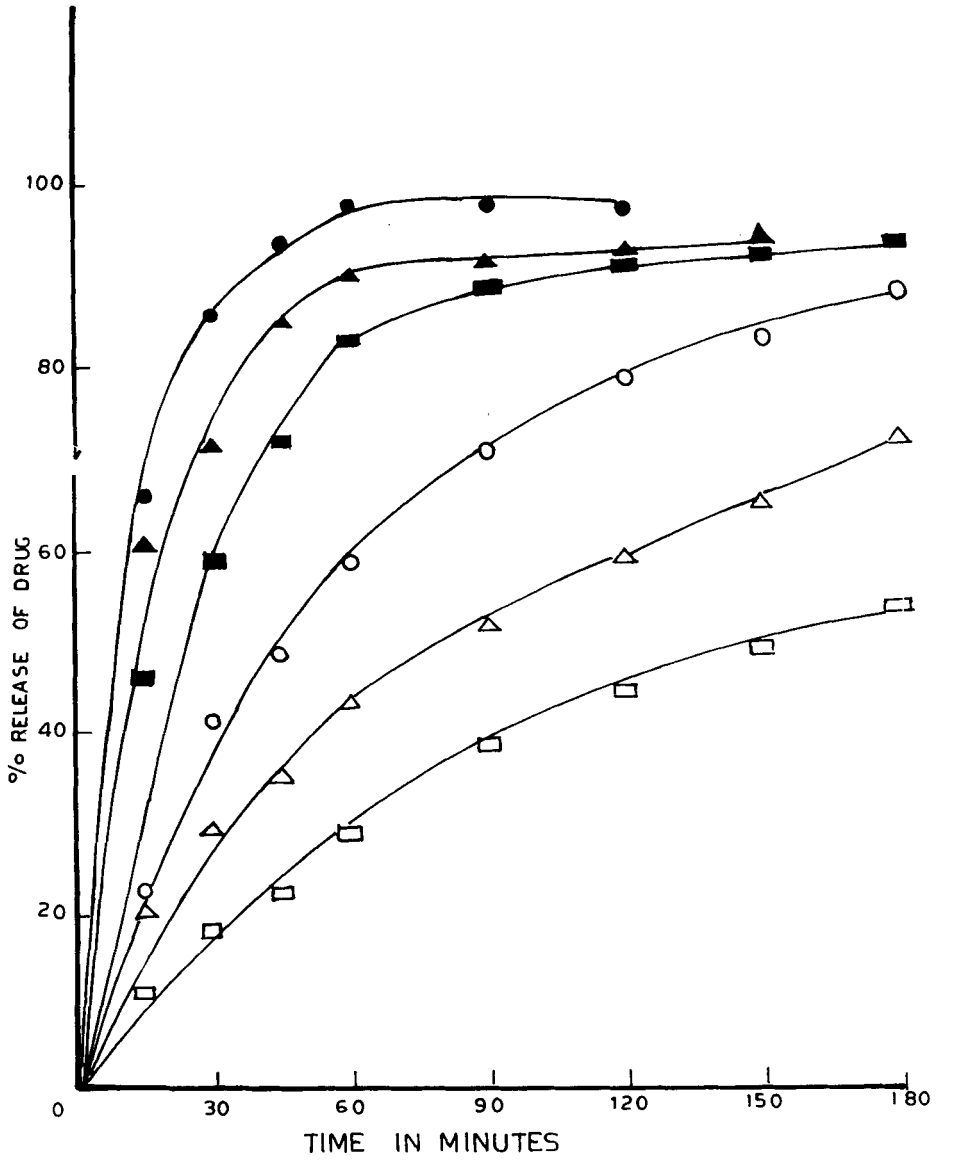

FIGURE 2
Dissolution studies - release characteristics in intestinal medium

Rosin
PR 90
PR 35
PR 115
PR 55
PR 15

TABLE 7

Dissolution parameters in intestinal medium USP (without enzyme).

Coating material	Release of drug[a] in 3 hr.	t_{50} in min.	Cube root rate constant in g 1/3 $min.^{-1}$
Rosin	97.10	9.0	0.1568
PR 115	94.10	16.0	0.0814
PR 90	93.75	24.0	0.0670
PR 55	88.90	45.0	0.0395
PR 35	72.35	80.0	0.0275
PR 15	53.52	150.0	0.0165

a - Average of the three trials.

the dissolution phenomena of the pentaerythritol estergum film coatings also.

Dissolution studies in Intestinal Medium:- It is observed that there is a reversal of release characteristics in the intestinal medium (Fig.2). There is a quick release of drug from Rosin, PR 115 and PR 90 coated drug granules with t_{50}% less than 15 min. It is observed that in case of rosin coated drug within 30 min. 90% of the drug is released. There is a gradual increase in the resistance of pentaerythritol estergums to the alkaline pH with reduction in the acid value (Table 7). The PR 55 and PR 35 exhibit an intermediate resistance to the intestinal pH with t_{50}% values 45 min. and 80 min. respectively.

In case of PR 15 it is observed that only 53% of the drug is released in 3 hr. with t_{50}% about 2½ hr. These pentaerythritol estergums exhibit interesting

characteristics of delayed release of drugs in the alkaline pH. These can be used for sustained release of the drug in the higher pH's provided these are double coated with acid resistant materials, like cellulose acetate pthalate or rosin or higher acid value pentaerythritol estergums. Study of the dissolution kinetics show a sharp decrease in Hixson-Crowell cube root dissolution constant with decrease in the acid value of the coating materials.

CONCLUSIONS

It can be concluded that pentaerythritol rosin estergums show excellent film forming properties and can impart moisture protective coating to the drugs. These can be used for enteric coating of the acid sensitive drugs. Different acid value intermediates can be used for sustained release of drug throughout the GIT with varying resistance to different pH's.

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