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EVALUATION OF PROPYLENE GLYCOL ROSIN ESTER AS MICROENCAPSULATING MATERIAL AND STUDY OF DISSOLUTION KINETICS

Y.V. Pathak**
College of Pharmacy, Manipal 576119 India

A.K. Dorle
Department of Pharmaceutical Sciences
Nagpur University, Nagpur 440010 India

Propylene glycol rosin ester (PgR Ester) was prepared by heating rosin with propylene glycol at 220°C. The physicochemical properties were studied. Aspirin granules were encapsulated using a standardized coating technique. The microcapsules were evaluated for moisture absorption, flow properties and friability studies. The dissolution studies were carried out in five different pH media to know the effect of pH on release characteristics. The dissolution studies revealed that PgR Ester films impart varying degrees of resistance to different pH media. The t50% values were found to be 57,47,63,93 and 88 min in pH 1.2,3.0,5.0,7.2 and 8.0 media, exhibiting potential usefulness of PgR Ester as film coating material. The release patterns obey Hixson Crowell cube root dissolution law, the values of cube root constant are given.

*Present address - Department of Pharmacy, School of Pharmacy, Hebrew University of Jerusalem. P.O. Box 12065, Jerusalem 91120 Israel

INTRODUCTION

Rosin and rosin derivatives are widely used in paints and varnishes, chewing gum bases, dental varnishes and food products. We have reported the usefulness of rosin and rosin derivatives as film coating materials for enteric coating and for delayed release of drug.[1-5] Juerzy et al[6] have reported the use of glycerol rosin heated product as anydrons binding agent. We have reported the application of different rosin esters and modified rosins as binding agents in tablet formulations.[7,8] The propylene glycol rosin ester (PgR Ester) is used in paints and varnishes [9,10] The lacquers prepared from PgR Ester are reported to be tough and flexible products.[11,12] The purpose of the present study is to prepare the PgR Ester and evaluate it as a miroencapsulating material by pan coating method. An attempt is also made to find out the effect of pH on in vitro release characteristics from the coated microcapsules and study dissolution kinetics.

MATERIALS AND METHODS

Rosin N Grade (ISI), Propylene Glycol (Lab Grad B.D.H.), Aspirin (I.P.), Starch (I.P.).

Preparation of PgR Ester

Rosin was powdered and heated with propylene glycol (4:1 proportion) in an aluminum vessel at 210-220°C. At every alternate hour, a sample of 2 to 5 g was withdrawn. Acid value of the sample was determined. Heating was continued till there was no further decrease in the acid value of withdrawn samples. The hot mass was poured in a thin stream with vigorous stirring in water, filtered and dried in an oven at 55°C overnight.

Study of physico-chemical properties

Physical properties like color, softening point, acid value, specific gravity and equilibrium solubility[13] in different solvents, were determined. The moisture absorption studies were carried out using dessicators maintained at different relative

humidities. Samples were kept for 15 days to achieve equilibrium.[3] Viscosity of PgR Ester was determined by Allana method.[14] To evaluate the hydrophilicity of coating materials used for delayed release of drug, a method described by Raghunathan et al[15] was used for determining water uptake in time.

Preparation of microcapsules

Aspirin (I.P.) was used as a model drug. A standardized pan coating method[3] was used to encapsulate the aspirin granules. The coated granules retaining on 30 mesh were used for further evaluation.

Evaluation of microcapsules

The coated drug microcapsules were studied for their flow characteristics[16] (angle of repose), moiosture absorption studies [3] and friability loss.[17] For evaluating efficacy of PgR Ester as oating material as well as studying the effect of pH conditions prevailing in gastrointestinal tract, (pH 1.2 to pH 8.0) on release characteristics from PgR Ester coated drug, the dissolution studies were carried out in five different pH media e.g. 1.2,3.0,5.0,7.2 and 8.0. For this purpose USP XVIII model was used at 150 rpm maintained at 37°±1°C. The release characteristics were studied for 3 hr in each media. The drug estimation in the withdrawn samples was done using ferric nitrate reagent (Bordelin and Pankratz method).[18]

RESULTS AND DISCUSSION

Study of the physical properties show that on esterification of rosin with propylene glycol there was a change in color from pale yellow to dark brown (Table 1). There was a sharp increase in the softening point of rosin from 65°-82°C of rosin to 87°-95°C of PgR Ester. The maximum decrease in acid value after 18 hr heating was from 145 to 27.43.

TABLE 1

Physical Properties of PgR Esters

No.	Properties	Values* PgR Ester (Rosin)[a]
1	Color	Dark Brown (Pale yellow)
2	Softening range	87°-95°C (65°-82°C)
3	Acid value	27.43 (145.75)
4	Specific gravity	1.1140 (1.1100)
5	Viscosity in sec.	49.0 (42.0)
6	Water uptake in 24 hr	2.5 ml (1.8 ml)
7	Equilibrium solubility in mg/ml	
	a. Acetone	465.0 (565.0)
	b. Alcohol	5.0 (420.0)
	c. Ether	680.0 (630.0)
	d. Water	Insoluble (Insoluble)

* mean average of three values

[a]from ref. 3 and 5.

There was a significant increase in the viscosity of PgR Ester than rosin showing better cohesive forces which may lead to better film properties. The alarming increase in water uptake in 24 hr may lead to stability problems if PgR Ester is used as coating material. This was further well clarified in the moisture absorption studies (Table 2) where it is observed that at 100% Relative Humidity the % moisture absorption was around 3% in plain PgR Ester while 3.5% in coated drug microcapsules. In the case of rosin, it was less than 1% in both cases. This is a disadvantage for PgR Ester to be used as coating material. Special care and extensive studies must be carried out to overcome this disadvantage. Suitable packaging modification to maintain lower relative humidity in the container may serve the purpose.

TABLE 2

Evaluation of Microcapsules

No.	Parameter	Value*
1	Angle of repose	29.85°
2	Friability loss	0.98%
3	Moisture absorption studies	
	Relative humidity %	
	a. 17.5	0.70 (0.50)[a]
	b. 57.0	0.98 (0.84)[a]
	c. 82.5	1.75 (1.68)[a]
	d. 100.0	3.45 (2.89)[a]

* Mean average of three trials [a]values for plain PgR Ester

The flow properties were improved after PgR Ester coating which was evident from the low value of angle of repose (29.85°) as compared to that of plain aspirin granules (angle of repose 34.3°). The % friability loss was less than 1% which is much less than the rosin coated granules (4.12%). It shows that the rosin gets hardened on esterification with propylene glycol and the films formed by PgR Ester are much stronger than the rosin films. In this context PgR Ester is a better coating material than rosin.

The drug release patterns are depicted in Fig 1 in different pH media. As reported by us, rosin and rosin derivatives are found useful for delaying the drug release. These have exhibited varying degrees of resistance to gastrointestinal pHs. Hence, it was thought worthwhile to conduct the dissolution studies in five different pHs. Considering the stomach retention time of 1 to 4

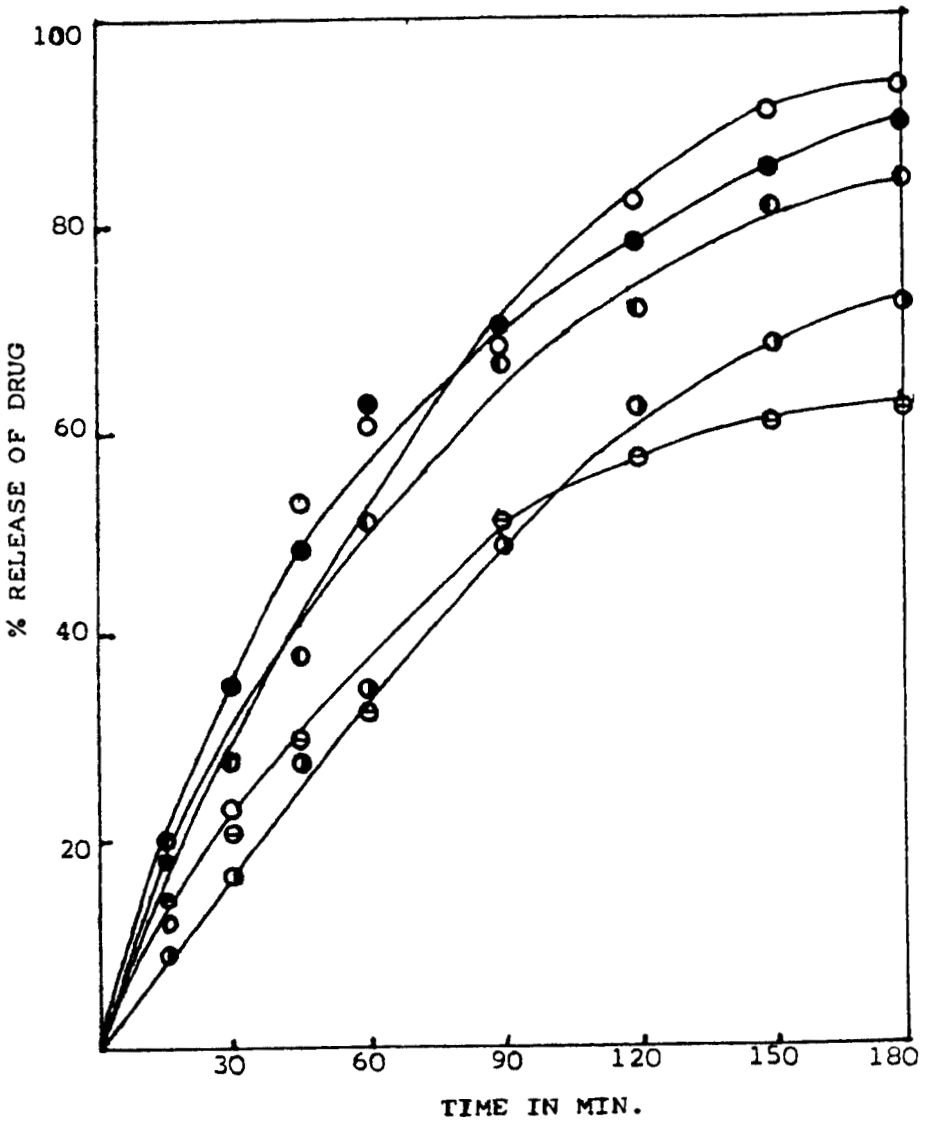

FIG. 1 EFFECT OF pH ON THE RELEASE CHARACTERISTICS OF PGR ESTER COATED ASPIRIN GRANULES.

- pH 1.2
- pH 3.0
- pH 5.0
- pH 7.2
- pH 8.0

TABLE 3

Dissolution Parameters in Various pH Media

Parameters pH	5 release of drug* in 3 hr	t50% in min	Cube root rate constant in $g^{1/3}\ min^{-1}$
1.2	93.0	57.0	0.0170
3.0	90.0	47.0	0.0187
5.0	84.0	61.0	0.0142
7.2	72.0	93.0	0.0098
8.0	64.0	88.0	0.0109

* average mean of three trials

hr, the studies were conducted in each pH for 3 hr to know the release patterns at various pH levels for 1 to 3 hr. Various dissolution parameters are given in Table 3.

The dissolution studies in different pH media have shown promising results, reflecting the usefulness of PgR Ester for delayed release of the drug. It is observed that there is a substantial delay in drug release in acid pH with t50% 57.0 min and 47.0 min in pH 1.2 and 3.0. But, subsequently, as the pH increases, it is observed that PgR films are more and more resistant to releasing the drug in a significantly delayed fashion with t50% more than 90 min at pH 7.2 and onwards. If we consider that the drug remains in the stomach for 1 to 2 hr, then the drug release can be delayed up to 3 to 6 hr with PgR Ester coating as the films are more and more resistant to alkaline pH the drug release is further delayed.

Studying the dissolution kinetics, it is observed that the release patterns from the microcapsules obey the Hixson Crowell Cube Root dissolution law. The values of cube root constant are

given in Table 3. The three assumptions 1) dissolution accurs normally to the surface of the solute particles, 2) agitation is uniform over all exposed surfaces and there is no stagnation and 3) the particle of solute retains its geometric shape, on which the cube root law is based holds true for the dissolution characteristics from PgR Ester coated microcapsules.

From the studies it can be concluded that PgR Ester has excellent film forming properties and can be used as film coating material for delayed release of the drug.

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