J. Indian Inst. Sci., Sept.–Oct. 1990, **70**, 451–454.

Evaluation of rosin as film-coating material for enteric coating–II—*in vivo* studies

Y. V. PATHAK*, M. SHINGAT GIRI**, AND A. K. DORLE†
* College of Pharmacy, Manipal.
** Department of Experimental Surgery, Kasturba Medical College, Manipal.
†Department of Pharmaceutical Sciences, Nagpur University, Nagpur.

Received on October 14, 1987; Revised on September 30, 1988.

Abstract

In vivo studies on rosin-coated aspirin granules carried out in dogs show that the time for peak concentration (T_p) increases from 1.8 h for plain granules to 5.10 h for rosin-coated aspirin granules. The difference in the T_p may be due to the resistance of rosin coats to the gastric contents. The results support the *in vitro* findings about the usefulness of rosin as an enteric-coating material.

Key words: Rosin, enteric coating, *in vivo* evaluation.

1. Introduction

The term bioavailability refers to the amount of drug which is made available for therapeutic action, when the drug is administered in dosage form. *In vivo* studies are the only reliable tools to know in depth about the bioavailability. Though many methods have been developed to determine the drug release characteristics from pharmaceutical dosage forms, till date no *in vitro* method has been found to be a substitute for *in vivo* studies. The extent and rate of drug absorption are affected by a number of factors depending upon the physico-chemical and biological properties of the drug and the patient factors.

The extent of drug absorbed also depends upon the variable nature of the gastrointestinal tract. The extent of bioavailability is usually determined either by the area under the blood concentration time curve or from cumulative amounts of drugs excreted in the urine.

Three main parameters describing a blood-level curve are considered to be important in evaluating the bioequivalence of the two formulations. They are: (i) the peak height concentration, (ii) the time of peak concentration, and (iii) the area under the plasma concentration time curve. To study any oral dosage form *in vivo* these three factors need to

* Present address: University of Michigan Medical Center, Department of Pediatrics and Communicable Diseases, R-5014, Kresge II, Ann Arbor, Michigan 48109-0576, USA.

be determined to evaluate the efficiency of the drug delivery system. Enteric-coated materials are resistant to acid pH in stomach and hence protect the drug in acidic pH, and release it in the gastrointestinal tract in higher alkaline range.

We have reported earlier the *in vitro* studies of rosin-coated drug granules at different pHs[1]. This communication deals with the *in vivo* evaluation of the granules, orally administered to dogs. On the basis of plasma drug concentration, various pharmacokinetic parameters were determined and reported here.

2. Materials and methods

For the present study, aspirin IP granules were coated using the standard coating technique described earlier[1]. To study the *in vivo* release characteristics, the following procedure was adopted[2]. Two healthy dogs weighing between 15 and 16 kg were used as experimental animals. A cross-over study was carried out. The dogs were fasted for 12 h before drug administration. Rosin-coated aspirin granules were suspended in 20 ml of 5% acacia solution and 20 mg/kg aspirin dose equivalent granules were administered through the stomach tube. Additional 50 ml of purified water was given through the same tube after drug administration to ensure complete washing of the tube. No food was given for one hour following the drug administration. After 1/2 and 1 h, blood samples were withdrawn from either saphenous vein (hind leg) or cephalic vein (front leg); subsequently at fixed time intervals blood samples were withdrawn till 24 h. One hour after the collection of the sample, 100 ml tinned milk was given. For better comparison, same types and amounts of food and water were maintained during the trials. Plasma was separated and analysed for total salicylate contents using the method of Levy[3]. For comparative studies, plain aspirin granules were administered adopting the same procedure and plasma concentration determined.

3. Results and discussion

Plasma drug concentration (μg/ml) was plotted against time (h). The peak height concentration is expressed in μg/ml and the time for peak concentration in hours was determined from the plasma drug concentration time curve (fig. 1). The area under plasma drug concentration time curve AUC was calculated using the trapezoidal rule[4]. The absorption constant (k) and half-life ($t_{1/2}$) were calculated using the method of residuals (Table I).

It is observed that the peak height concentration achieved in control and rosin-coated drug was substantially different. In the case of rosin-coated drug, the maximum drug plasma concentration acquired was 4.25 μg/ml, but the time taken to reach the peak concentration was almost three times that of the control plain drug granules. Similarly, the AUC values were significantly different than those obtained in the case of plain drug granules.

It clearly shows that there was significant delay in the drug release from the rosin-coated granules because of the coating imparted. The higher values of AUC and lower values of absorption constant in the case of coated granules show that the drug was released steadily

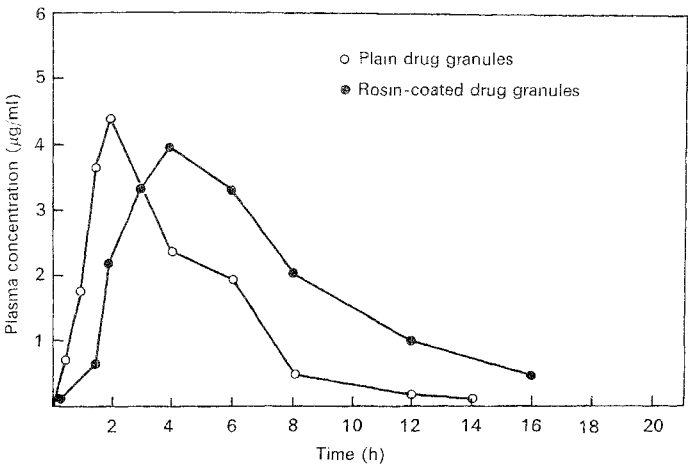

FIG. 1. *In vivo* studies. Plasma concentration time curve in dogs.

Table 1
***In vivo* evaluation–pharmacokinetic parameters**

Parameters	Control	Coated drug granules
Peak height conc. (μg/ml)	5.10	4.25
Time of peak conc. (*h*)	1.80	5.00
AUC (μg/h/l)	17.93	30.96
Absorption constant (h^{-1}) ($t_p = t/k$)	0.58	0.21
Method of residuals		
a) $t_{1/2}$ (*h*)	0.56	3.0
b) absorption constant (h^{-1})	1.21	0.23

and it remained in the plasma for comparatively longer period than the control samples. The higher values of absorption constant and lower values of $t_{1/2}$ in the case of control granules, calculated by the method of residuals, show quicker absorption and elimination of the drug. It is seen from fig. 1 that the absorption phase in the case of plain drug granules is much shorter than that of rosin-coated granules.

We have already reported the acid-resistant properties of rosin films. The *in vitro* studies reported[1] earlier have shown that less than 10% drug is released in 3 h in gastric medium and subsequently as the pH increases, there is a gradual increase in the drug release. The *in vitro* studies have shown rosin film to be useful for enteric coating. The *in vivo* studies show

that there is a substantial delay in drug release, and the time for peak concentration is around 5 h.

The normal stomach retention time varies from 1 to 3 h. The *in vivo* study shows that the films are resistant to acidic pH in the stomach but subsequently release the drug as the pH increases. *In vivo* studies confirm our *in vitro* findings and support our hypothesis regarding the usefulness of rosin as an enteric-coating material. It warrants a detailed study.

References

1. PATHAK, Y. V. AND DORLE, A. K. — *J. Indian Inst Sci.*, 1986, **66**, 549–553.
2. PATHAK, Y. V., SHINGAT GIRI, M. AND DORLE, A. K. — *J. Microencapsulation*, 1987, **4**, 107–110.
3. LEVY, G. — *J. Pharma. Sci.*, 1961, **50**, 388–392.
4. ROWLAND, T. AND TOZER, T. N. — *Clinical pharmacokinetics*, 1980, pp. 288–295, Lea and Fabiger, Philadelphia.