

### MUCOADHESIVE EFFECT OF CARBOPOL ON DRUG RELEASE RATE FROM DOUBLE PHASED SUPPOSITORIES

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#### ABSTRACT

Suppositories are the reliable alternative dosage form for patients at home or experiencing frequent attacks of hypertension and angina pectoris. Propranolol hydrochloride, a selective  $\beta$ -adrenergic antagonist used in the treatment of hypertension and angina pectoris, which undergoes extensive hepatic metabolism, has been formulated as suppositories. In order to restrict the drug absorption to only the lower rectum, mucoadhesive Propranolol hydrochloride suppositories were prepared using cocoa butter as a base, carbopol 934P and white bees wax as additives. Carbopol has a mucoadhesive property and beeswax gives the required stiffness to the suppositories. The effect of these additives on the physico-chemical behavior and drug release rates from the suppositories were studied. Beeswax at higher concentration considerably increased the melting point and hardness of the base whereas carbopol showed little effect on the melting point of the base. The drug release profile indicated that with decreased carbopol concentration (2 %w/w) the release rate was increased. These findings suggest that carbopol can be used not only as a release rate enhancer but also as a mucoadhesive material to prevent the suppositories moving to the upper rectum susceptible to first pass metabolism.

**Keywords:** Double-phased suppositories, Propranolol hydrochloride, Muco adhesive, Carbopol, White beeswax

#### INTRODUCTION

Drugs released from suppositories in the lower rectum can bypass first pass metabolism. As suppositories move slightly to the upper rectum while dissolving or melting, might prove disadvantageous for the drugs susceptible to first pass metabolism. So an attempt has been made to restrict drug absorption from suppositories to the lower rectum, which can be achieved by enhancing mucoadhesion by using some selected mucoadhesive materials. Carbopol is one such material, which is a carboxyvinyl polymer with proven mucoadhesive property<sup>1</sup>. White beeswax was added to raise the melting point of the base, which helps the suppository retain its shape and prevent it from melting and extending over a wide area. Propranolol Hcl was selected as a model drug, which undergoes extensive first pass metabolism<sup>2</sup>.

#### MATERIALS AND METHODS

Propranolol hydrochloride I.P (generously donated by Mano Pharma, Chennai), Carbopol-934P (gift sample

from Bangalore Pharmaceutical & Research Lab. Pvt. Ltd, Bangalore). All other chemicals used were of L.R/ A.R grade.

#### Preparation of Single and Double Phased Suppositories Base mixture

Suppositories were prepared by fusion method. Cocoa butter and wax were melted and mixed at about 60°C, Carbopol-934P (2%, 4%, 6% and 8%w/w) was then mixed by ultrasonication for 10 minutes. Propranolol Hcl (120mg) was then mixed with the base mixture and poured into 2gm suppository mold at room temperature (Single Phased suppositories).

Suppositories containing Propranolol hydrochloride and Carbopol-934P alone (excluding beeswax) were prepared by same method.

#### Double phased suppository

First a base mixture for the front layer was poured into the mold, cooled, removed from the mold and the top

20mm of the base was cut off and used. The front layer was put into the mold again and the terminal layer was poured next to it at 60°C and cooled at room temperature. The resultant suppositories were stored at 100C and used for the study.

### Measurement of hardness of the base

The hardness was tested using a tablet crushing strength tester. The effects of CP and wax on base hardness were examined and shown in table 1.

### The melting point of the base

The melting point was determined by macro melting range test<sup>3</sup> and the readings are as shown in the table 2.

### Softening and liquefaction temperature

This can be determined by using Setniker and Fantelli method<sup>4</sup>. The readings are shown in table 2.

### In vitro drug release profile

The release tests were carried out according to the method reported by Iwata et al<sup>5</sup>. The dissolution cell was rotated at 120rpm in 500ml of phosphate buffer pH 6.8 at 37±0.5°C. At a predetermined rate 5ml of the sample was collected and analyzed spectrophotometrically at 290nm. Each sampling was compensated by the addition of same amount of test fluid maintained at same

temperature (Graphs 1 and 2).

## RESULTS AND DISCUSSION

Suppositories of Propranolol hydrochloride, both single and double phased were prepared by fusion method by adapting selected mucoadhesive like carbopol 934P and white bees wax, a thickening agent. The influence of carbopol, especially on the physical properties and release profile of drug from both the forms of suppositories were studied. It was found that carbopol has least influence on the hardness and melting point of the suppositories. But the white bees wax used in different amounts has increased the melting point of the suppositories to retain their shape for a longer time. The effect of carbopol on drug release rate at different percentages indicated that it promotes the increased drug release from the suppositories in the concentration of 2%w/w than at higher concentrations. The drug release from single phase suppository was not sustained for a longer time compared to double phased suppositories. This may be due to the water-soluble property of carbopol i.e., addition of a small amount of carbopol improved the water absorbability of the base and facilitated the release of Propranolol hydrochloride. But a large amount of carbopol forms a highly viscous gel layer and suppresses the drug release.

Single-Phased Suppositories

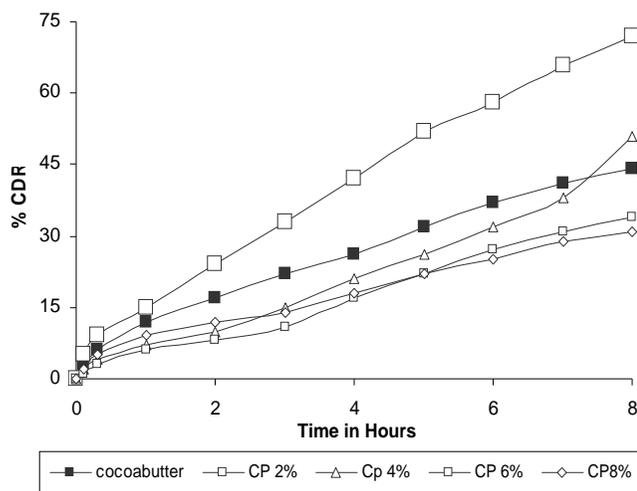


Figure 1

Double-Phased Suppositories

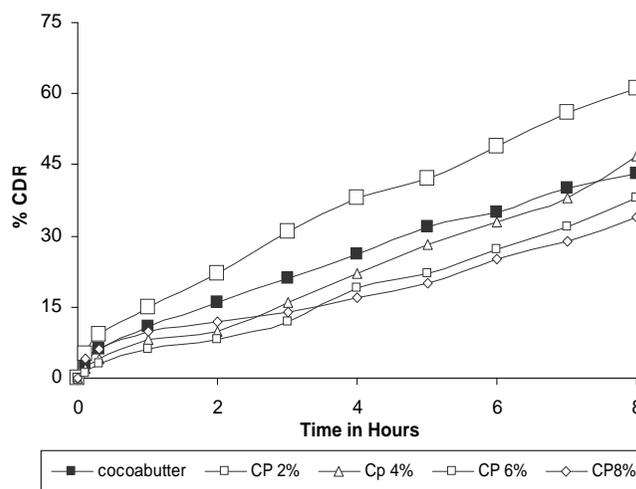


Figure 2

Figure 1 and 2: Release profiles of Propranolol hydrochloride from single and double phased suppositories

**Table 1: Effect of additives on suppository base hardness**

Carbopol % w/w	White bees wax % w/w	Hardness
0	0	1.3 ± 0.12
2	5	1.6 ± 0.34
4	10	1.9 ± 0.26
6	20	2.6 ± 0.14
8	30	2.0 ± 0.08

**Table 2: Reading of various physical parameters of double phased suppositories**

Suppositories with varied temperature* amount of CP and Wax	Melting point*	Softening temperature*	Liquefaction
CP 2% w/w and Drug	340C	320C	340C
CP 2% w/w and Wax 5 %	480C	390C	430C
CP 4% w/w and Wax 10 %	540C	390C	480C
CP 6% w/w and Wax 20 %	580C	380C	540C
CP 8% w/w and Wax 30 %	600C	400C	580C

CP-Carbopol \* average of three readings

## CONCLUSION

The results suggest that double phased suppositories with varied carbopol concentration can produce rectal stagnation and moderate drug release facilitating drug absorption in the lower rectum. This approach is highly beneficial for enhancing the bioavailability of drugs undergoing extensive first pass metabolism

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