CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.17819843

Available online at: http://www.iajps.com Research Article

INFLUENCE OF CASTING SOLVENT IN DESIGN AND DEVELOPMENT OF VERAPAMIL HYDROCHLORIDE MATRIX TABLETS

I. Sri Krishnanjaneyulu, B.Sannihitha, B .Sai Mouni, D .Akshita
Bapatla College of Pharmacy , Bapatla-522101

Abstract:
The present study was conducted to formulate and evaluate sustained-release matrix tablets of Verapamil hydrochloride using Rosin and Xanthan gum, and to compare the results with a marketed formulation. The effects of three granulating fluids—acetone, isopropyl alcohol, and dichloromethane—and two polymers, Rosin and Xanthan gum, on the drug-release rate were investigated with the aim of developing a controlled-release dosage form for Verapamil hydrochloride. Based on the release profiles, the polymer ratios were ranked in the following order: 1:0 > 0.75:0.25 > 0.6:0.4 > 0.5:0.5 > 0:1 (Rosin:Xanthan gum). The granulating fluids were ranked as dichloromethane > isopropyl alcohol > acetone in terms of their ability to modulate drug release. Dissolution studies indicated that the formulations followed zero-order kinetics, and the drug-release mechanism was best described by the Peppas model. The release exponent values (n > 0.5) suggested that drug release was predominantly governed by non-Fickian diffusion. Overall, the findings demonstrate that the release rate of Verapamil hydrochloride from matrix tablets can be effectively controlled by selecting appropriate granulating fluids, polymers, and polymer concentrations. The desired sustained-release profile was achieved using acetone as the granulating fluid and a Rosin:Xanthan gum ratio of 0.75:0.25.

Key Words : Rosin , Xantham gum, granulating fluids, matrix tables

Corresponding author:
I. Sri Krishnanjaneyulu,
Bapatla College of Pharmacy,
Bapatla-522101.A.P
9959579605

QR CODE

Please cite this article in press I. Sri Krishnanjaneyulu et al., ***Influence Of Casting Solvent In Design And Development Of Verapamil Hydrochloride Matrix Tablets****, Indo Am. J. P. Sci, 2025; 12(12).*

INTRODUCTION:

Verapamil hydrochloride is a calcium channel blocker widely used in the management of cardiac arrhythmias, angina pectoris, and hypertension [1]. Owing to its relatively short biological half-life (4.7 ± 1.2 hours), frequent dosing is required to maintain therapeutic plasma levels. Such repeated administration may reduce patient compliance, especially in chronic conditions like hypertension where long-term therapy is essential. To overcome these limitations, prolonged-release dosage forms are developed to extend the drug's therapeutic action, reduce dosing frequency, and enhance patient adherence[2].

In the present study, sustained-release matrix tablets of verapamil hydrochloride were formulated using both hydrophilic and hydrophobic polymers. Xanthan gum, a polysaccharide produced by the fermentation of carbohydrates by *Xanthomonas campestris*, was selected for its roles as a suspending, stabilizing, thickening, retarding, and emulsifying agent. Rosin, an oleoresin obtained after distillation of volatile oils from *Pinus* species (Family: Pinaceae), was also incorporated. Rosin and its derivatives have previously been employed as anhydrous binders and matrix-forming agents in prolonged-release formulations of water-soluble drugs. Isopropyl alcohol, acetone, and dichloromethane were used as granulating solvents during formulation[3].

MATERIALES AND METHODS:

Verapamil hydrochloride was obtained as a gift sample from Natco Pharma, Hyderabad. Rosin and Xantham gum were procured from Coveral & Co, Chennai. All other chemical reagents were of analytical grade. All materials were used as received.

Formulation of tablets:

All formulations were prepared as described in Table 1. The tablets were produced using the wet granulation method. Verapamil hydrochloride and the polymer were triturated thoroughly, passed through a #80 sieve, and mixed uniformly. The powders were then granulated with a sufficient quantity of dichloromethane, isopropyl alcohol, or acetone until a cohesive wet mass was formed. This mass was passed through a #12 sieve and the resulting granules were dried at 40 °C for 2 hours. The dried granules were re-sieved through a #16 sieve and blended with talc and magnesium stearate. Finally, the granules were compressed into tablets with an average weight of 168 mg using a single-punch tablet compression machine.

Evaluation of the formulation:

Flow properties of the prepared granules were evaluated .Other properties of the granules evaluated were bulk density, true density apparent density, and porosity using standard reported methods[4].weight variation test was conducted as per specifications of IP[5].Hardness and friability of the tablets formulated were evaluated using a Monsanto hardness tester and a Roche friabilater, respectively.

Drug content[6]:

Twenty tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 90 mg of Verapamil hydrochloride was transferred in to a 100 ml volumetric flask and extracted with distilled water by keeping in sonicator (bath) for 2 hours. Then it was filtered, suitable dilutions made and absorbance was measured by using Elico UV-Visible spectrophotometer (SL 159) at 278 nm.

In vitro drug release study[7]:

Release of Verapamil hydrochloride was determined using a six panel, USPXXIII dissolution apparatus-2 at 100 rpm. The dissolution was studied using 900 ml of water. The medium was allowed to equilibrate to temperature of 37 $\pm$ 0.5 ^{O}C. The apparatus was operated for 12 hours. At definite time intervals 5 ml of the receptor fluid was with drawn, filtered, suitable dilutions were done with distill water and analyzed spectrophotometrically at 278 nm using Elico UV-Visible spectrophotometer. The rate and the mechanism of release of Verapamil hydrochloride from the prepared matrix tablets were analyzed by fitting the dissolution data into[8], zero-order equation, $Q=Q_0 - k_0t$(1),where Q is the amount of drug released at time t, and k_0 is the release rate. First order equation, $\ln Q=\ln Q_0 - k_1t$ (2), where k_1 is the release rate constant and Higuchi's equation, $Q= k_2t^{1/2}$ (3) where Q is the amount of the drug released at time t and k_2 is the diffusion rate constant. The dissolution data was further analyzed to define the mechanism of release by applying the dissolution data following the empirical equation , $M_t/M_\alpha=Kt^n$ (4), where Mt/M_α is the fraction of drug released at time t. K is a constant and n characterizes the mechanism of drug release from the formulations during dissolution process.

RESULTS AND DISCUSSION:

The present investigation aimed to fabricate and evaluate sustained-release matrix tablets of Verapamil hydrochloride and compare their performance with a marketed product. The study examined the influence of three granulating fluids—**acetone**, **isopropyl alcohol**, and **dichloromethane**—and two polymers—**Rosin** and **Xanthan gum**—on the drug-release profile, with the objective of developing a robust slow-release formulation of Verapamil hydrochloride. All formulations were prepared to contain **80 mg** of Verapamil hydrochloride, matching the marketed

product.

Five initial formulations (F1–F5) were prepared using **dichloromethane** as the granulating fluid. The granules were evaluated for micromeritic properties such as angle of repose, bulk density, and Carr's index. Bulk density values ranged from **0.464 to 0.477 g/cm^3**, indicating good packing characteristics. The angle of repose for all formulations ranged from **25°34' to 27°91'**, suggesting good flowability, while Carr's index values between **9.6–13.58%** indicated free-flowing material.

All tablet formulations were further evaluated for weight variation, hardness, friability, and drug content. The tablets complied with **I.P. weight-variation standards**, and hardness values were within **4–5 kg**. All formulations met **USP friability requirements**, exhibiting less than **1% friability**, and the drug content ranged between **98–102%**, satisfying compendial specifications.

The dissolution profile (Fig. 1) demonstrated that drug release was significantly influenced by the polymer composition. Based on the release rate, polymer ratios were ranked as follows:

1:0 (F1) > 0.75:0.25 (F5) > 0.6:0.4 (F4) > 0.5:0.5 (F3) > 0:1 (F2)

Formulation F1 showed the slowest release, while **Formulation F5 (0.75:0.25 Rosin:Xanthan gum)** exhibited a release profile closest to that of the marketed product. Therefore, the **0.75:0.25 polymer ratio** was identified as the most suitable for developing a 12-hour sustained-release formulation.

To assess the influence of granulating fluids, additional formulations (F6 and F7) containing the optimal polymer ratio (0.75:0.25) were prepared using **isopropyl alcohol** and **acetone**, respectively. The dissolution results (Fig. 2) showed that the rate of drug release was affected by the choice of granulating fluid, with the following order:

dichloromethane > isopropyl alcohol > acetone

Formulation F7, prepared using **acetone**, was compared with the marketed formulation (Fig. 3) and exhibited a slightly slower release profile. Based on these findings, **acetone** was identified as the most suitable granulating fluid for achieving the desired sustained-release characteristics.

REFERENCES:

1. Aachal Kolhe, Akshda Chauhan, Aishwarya Dongre. To Study the effect of Cross linking of Sodium Alginate on the Rate of Drug Release. Research Journal of Pharmaceutical Dosage Forms and Technology.2022; 14(2):127-2.

2. Sanjay D, Bhaskar M, Sankha C, Das MK, Samrendu S, Ganguly S, Kakali D, Mridula M. Polymers derived from xanthomonas compesteries and retardant materials for the formulation of sustained release floating matrix tablet of atenolol. Int J BioL Macromol 2014; 651:345-56..

3.Thapa P., Lee A.R., Choi D.H., Jeong S.H. Effects of moisture content and compression pressure of various deforming granules on the physical properties of tablets. Powder Technol. 2017;310:92–102. .

4.Kuwata A, Ishikawa A, Ono T, Yonemochi E. Granulation Methods and the Mechanisms for Improving Hardness of Loxoprofen Sodium Hydrate-Containing Tablets. Pharmaceutics. 2025;17(4):445-455.

5. Hirai N., Takatani-Nakase T., Takahashi K. Preparation and Evaluation of Ibuprofen Solid Dispersion Tablets with Improved Dissolution and Less Sticking Using Porous Calcium Silicate. J. Pharm. Pharmacol. 2018;6:1–8..

6.Arndt O.-R., Baggio R., Adam A.K., Harting J., Franceschinis E., Kleinebudde P. Impact of Different Dry and Wet Granulation Techniques on Granule and Tablet Properties: A Comparative Study. J. Pharm. Sci. 2018;107:3143–3152. .

7.Maharjan R., Lee J.C., Kim N.A., Jeong S.H. Preparation of seeded granules to improve mechanical properties and various drug loading for pharmaceutical application. Powder Technol. 2021;392:650–660.

8. Waghmare RS. Dry Granulation by Slugging Method for Sustained Release of Model Drug. International Journal of Pharmacy and Pharmacutical Research. 2020;17(3):29-77.

Table 1: FORMULATION OF VERAPAMIL HYDROCHLORIDE MATRIX TABLETS

S. No.	Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)
		1:0	0:1	0.5:0.5	0.6:0.4	0.75:0.25	0.75:0.25	0.75:0.25
1.	Verapamil hydrochloride	80	80	80	80	80	80	80
2.	Rosin	80	---	40	48	60	60	60
3.	Xantham Gum	---	80	40	32	20	20	20
4.	Magnesium Stearate	4	4	4	4	4	4	4
5.	Talc	4	4	4	4	4	4	4
6.	Dichloromethane	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	---	---
7.	Isopropyl alcohol	---	---	--	--	--	Q. S.	--
8.	Acetone	--	--	--	--	--	--	Q. S.
Total		168	168	168	168	168	168	168

TABLE 2 CORRELATION COEFFICIENT (R) VALUES OF VERAPAMIL HYDROCHLORIDE TABLETS

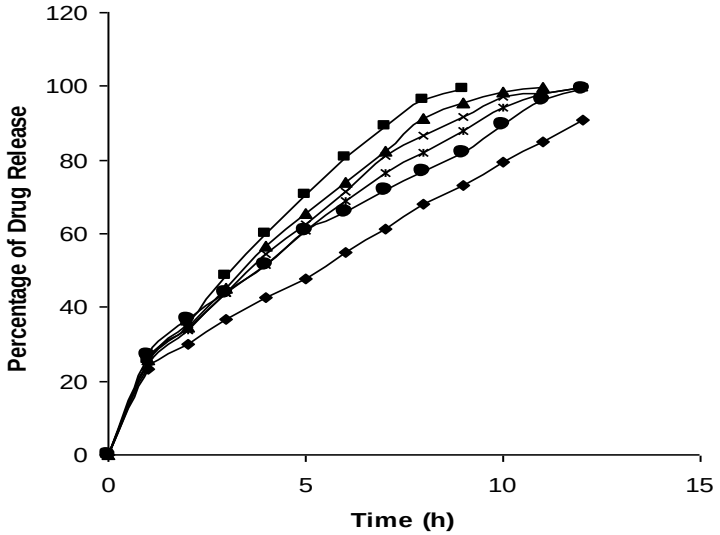
FORMULATION	CORRELATION COEFFICIENT (R) VALUES			
	ZERO-ORDER MODEL	FIRST ORDER MODEL	MATRIX	PEPPAS
F1	0.9689	0.9492	0.9867	0.9904
F2	0.9578	0.8869	0.9867	0.9971
F3	0.9331	0.8892	0.9902	0.9956
F4	0.9197	0.9124	0.9916	0.9958
F5	0.9315	0.8809	0.9929	0.9981
F6	0.9436	0.8729	0.9907	0.9987
F7	0.9524	0.9109	0.9875	0.9986
MARKETED	0.9153	0.8697	0.9961	0.9972

TABLE 3: DISSOLUTION PARAMETERS OF VERAPAMIL **HYDROCHLORIDE TABLETS**

TABLETS	DISSOLUTION PARAMETERS			
	DIFFUSION EXPONENT (n)	ZERO ORDER K (mg/h)	T_{50} (h)	T_{90} (h)
F1	0.5668	7.86	5.09	9.16
F2	0.6498	7.61	5.25	9.46
F3	0.6112	6.82	5.86	10.55
F4	0.5968	7.09	5.64	10.15
F5	0.5973	7.77	5.14	9.26
F6	0.6159	7.48	5.34	9.62
F7	0.6380	6.66	6.0	10.81
Marketed	0.5361	7.03	5.68	10.24

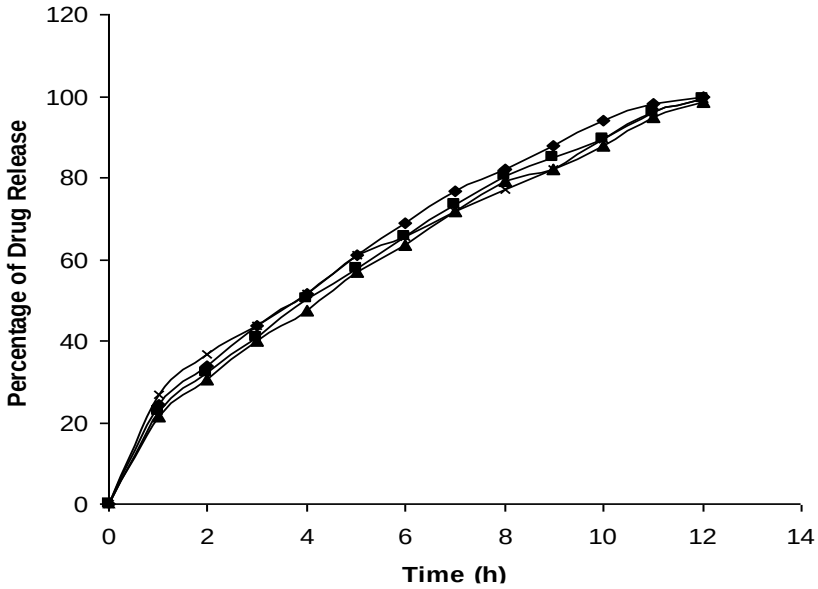
Fig 1.

Fig 1. Dissolution profiles of Verapamil hydrochloride tablets prepared with Rosin and Xanthum gum in different ratios.



(♦) F_1 - Tablets prepared with Rosin and Xanthum gum in 1:0
(■) F_2 - Tablets prepared with Rosin and Xanthum gum in 0:1
(▲) F_3 - Tablets prepared with Rosin and Xanthum gum in 0.5:0.5
(×) F_4 - Tablets prepared with Rosin and Xanthum gum in 0.6:0.4
(✳) F_5 - Tablets prepared with Rosin and Xanthum gum in 0.75:0.25
(●) M - Marketed tablets

Fig 2. Dissolution profiles of Verapamil hydrochloride tablets prepared with different granulating fluids.



(•) - Tablets prepared with Dichloromethane
(■) - Tablets prepared with Isopropyl alcohol
(▲) - Tablets prepared with Acetone
(×) - Marketed tablets