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Original Article

EFFECT OF VARIOUS SUSTAINED RELEASE POLYMERS ON FLOATING TABLETS OF CARVEDILOL PHOSPHATE-A COMPARATIVE STUDY

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ABSTRACT

Objective: This study aimed to develop floating tablets of Carvedilol phosphate containing various excipients such as HPMC K100M, Carbopol, Polyox WSR, HPMC K4M, and sodium bicarbonate to generate gas. Additionally, the impact of DCP, spray dried lactose, and HPβCD on drug release was investigated.

Methods: A total of eighteen formulations were prepared using the direct compression method and evaluated for hardness, drug content, friability, floating lag time, floatation time and drug release properties.

Results: FTIR analysis confirmed that there were no chemical interactions between Carvedilol phosphate and the excipients used in the formulation of the floating tablets. Most of the Carvedilol phosphate floating tablets, except for F_9 and F_{10}, did not disintegrate in water, alkaline fluids (pH 7.4), or acidic aqueous solutions (pH 1.2). These tablets exhibited satisfactory quality attributes in terms of hardness, drug content, and friability, making them suitable for sustained release. The floating lag time of the tablets ranged from 25 seconds to 34 min, while the floating duration varied from 2 to 24 h. The drug release from the tablets was gradual and sustained over 12 h, depending on the composition of the tablets. Polyox WSR (F_9 and F_{10}) resulted in a rapid drug release, whereas an increase in the polymer concentration led to a decrease in the rate of drug release across all formulations.

Conclusion: The study reveals that the use of hydrophilic polymers enhanced the drug release, whereas hydrophobic polymers decreased the drug release. As such, formulations, F_{11}, F_{15}, and F_{16}, which gave 100% drug release within 12 h are finalized as the optimized formulations of Carvedilol phosphate floating tablet.

Keywords: Carvedilol phosphate, Floating, Polymers, Sustained release

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INTRODUCTION

The drug administration through oral route is the most reliable drug delivery system because of its comfort and easy way of consumption. A solid drug dosage is more robust stable and also exhibits additional advantages such as easy to handle and popular way of medicine consumption. Hence, better subject compliance and drug treatment can be observed with oral route of medications than with any other administration routes of dosage forms. Carvedilol is chemically named as "(±)-1-(Carbazol-4-yloxy)-3-[[2-(o-methoxyphenoxy)ethyl]amino]-2-propanol". Carvedilol is preferred in the management of hypertension, decreases rate of heart myocardial contractility rate and also reduces systolic pressure when diastolic pause increases. It is a third-generation lipophilic molecule, which is highly nonselective β_1 adrenergic receptor blocking agent selectively blocks the $\beta_1$adrenoceptor with α1-blocking activity coordinated vascular dilatory action and significant action on the function of vascular endothelial cells [1, 2]. Blocking receptors have effects like decreases in stroke and cardiac output capacity, heart muscle oxygen consumption, plasma renin activity, and inhibition of norepinephrine release [3].

Carvedilolcomes under Class II of BCS Classification which distinguish by low dissolution rate (due to its less aqueous solubility) and has a less plasma half-life of about 6 h with an elimination half-life of 2 h. Due to its poor solubility in alkaline pH environments, the bioavailability of Carvedilol Phosphate is negatively affected, limiting its absorption at the intended site [4]. Therefore, Carvedilol Phosphate is a suitable candidate for the formulation of gastroretentive floating tablets, as it can enhance its bioavailability by prolonging gastric residence time and achieving sustained release for twice-daily administration over 12 h [3]. This study aims to develop and assess floating tablets of Carvedilol Phosphate using various matrix-forming polymers such as HPMC K100 M, Carbopol, Polyox WSR, and HPMC K4M. The tablets will be evaluated for hardness, drug content, friability, disintegration time, floating time, floating lag time, as well as drug release kinetics and mechanisms.

MATERIALS AND METHODS

Chemical/reagents

Carvedilol phosphate and was a gift sample from M/s Aizant Drug Research Solutions Pvt. Ltd., Hyderabad. HPMC K100 and K4M, Carbopol, Polyox WSR, sodium bicarbonate, dicalcium phosphate (DCP), lactose were procured from commercial sources. All other materials used were of Pharmacopoeial grade**.**

Formulation of carvedilol phosphate floating tablets

The preparation of Carvedilol phosphate tablets involved utilizing HPMC K100M, Carbopol, Polyox WSR, and HPMC K4M as matrix-forming polymers, while sodium bicarbonate was employed as a gas-generating agent. Lactose and dicalcium phosphate were used as fillers. A total of twenty different formulations of Carvedilol phosphate floating tablets were developed using various combinations of matrix-forming agents and fillers through the direct compression method [5].

Methods of preparation of floating tablets of carvedilol phosphate

To prepare the Carvedilol phosphate floating tablets, the predetermined quantities of Carvedilol phosphate, matrix-forming polymer, sodium bicarbonate, fillers, talc, and magnesium stearate were thoroughly mixed inside a closed polyethylene bag. The mixing process ensured the homogeneity of the powder blend. Subsequently, a multi-station tablet compression machine was

employed, along with an 8 mm round flat punch. The powder mixture was directly compressed using 9 mm flat punches, applying sufficient force to achieve a hardness ranging between 4-6 kg/cm^2. This compression step ensured the formation of tablets with the desired physical properties.

FT-IR

The *FT-IR* spectra of carvedilol and optimized solid dispersion were recorded by (Make: Bruker Optics, Model: Alpha). For this, KBR disc technique was used. The sample was combined with potassium bromide dry powder and was compacted into a transparent disc which placed in IR spectrophotometer using specialised dies at high pressure. The spectrum read in a frequency range 4000-400 cm^{-1} to evaluate polymer-drug interaction studies [6].

Characterization of tablet

The formulated Carvedilol phosphate floating tablets underwent several evaluations to assess their quality and performance. The following tests were conducted tablet Weight variation test, tablet hardness, drug content, tablet friability, *in vitro* dissolution and Buoyancy/floating test.

Weight variation

In the quality control process, twenty tablets from each batch were selected, and their individual weights were measured in grams. The average weight of the tablets was calculated by summing the weights of all the tablets and dividing by twenty. The standard deviation, which indicates the variation in tablet weights within the batch, was also determined. After obtaining the average weight and standard deviation, the results were compared against the established limitations or specifications. Compliance or non-compliance with the weight requirements was determined based on whether the average weight fell within the specified range and if the standard deviation was within acceptable limits [7].

Tablet hardness

The hardness of the tablets was determined using a hardness testing apparatus. The tablet was placed longitudinally between the two plungers of the apparatus, and the force required to break the tablet was measured. The hardness value was expressed in kilograms per square centimeter (kg/sq. cm). By measuring the tablet hardness, it was possible to assess its mechanical strength and integrity [8].

Drug content

To assess the drug content of the prepared floating Carvedilol tablets, ten tablets were selected for analysis. These tablets were powdered, and an amount equivalent to the weight of one tablet was transferred into a 100 ml volumetric flask. The powder was then dissolved in methanol and diluted with 0.1N HCL buffer solution up to the mark on the flask. The resulting solution was subjected to sonication for 10 min to ensure complete dissolution. Next, the drug concentration in the solution was determined spectrophotometrically using a UV-visible spectrophotometer (specifically, the UV 1800 Shimadzu spectrophotometer) at a wavelength of 240 nm. The solution was filtered prior to the spectrophotometric analysis. By measuring the drug concentration, the drug content in the floating Carvedilol tablets could be quantified, providing information on the amount of active pharmaceutical ingredient present in each tablet [9].

Friability test

The forces that break tablets are friction and shock. The friability test estimates a tablet's ability to resist abrasion while being handled, packaged, and transported, which is related to tablet hardness. Typically, it is assessed with a Roche friabilator. Tablets were weighted and subjected to abrasion as they fell 6 inches every time the device turned. The weight of the pills was measured after 100 spins and contrasted with the starting weight. Weight loss serves as a proxy for tablet friability, which is reported as a percentage [10]. The common consensus is that a loss of weight is not more than 1% of total weight is acceptable.

***In vitro* dissolution**

This test was executed by Type II USP as a dissolution test apparatus. The formulations thus prepared were placed into the dissolution medium holder, which holds 0.1N HCL Buffer of 900 ml at 37 °C±0.5 °C and fix at 50rpm (n=3). Aliquots of 5 ml sample collected through 0.45µm microfilter periodically at predetermined intervals of time and refill with 5 ml of new dissolution medium. The Nebivolol concentration was evaluated spectrophotometrically by UV spectrophotometer (UV 1800 shimandzu spectrophotometer) at λ max 240 nm. All drug release experiments were conducted in triplicate (n=3).

Floating time and floating lag time determination

The floating lag time and flotation time are parameters used to measure the time intervals during which the tablet enters the dissolution medium and rises to the upper third of the dissolution vessel, and the duration for which the dosage form remains afloat, respectively. These measurements were performed using a USP Type II dissolution unit, with 900 ml of 0.1 N HCl serving as the dissolution buffer. The experiments were conducted at a temperature of 37 °C. By observing and recording the floating lag time and flotation time, valuable information regarding the buoyancy and floating behaviour of the tablets in the specific dissolution conditions was obtained [11].

RESULTS AND DISCUSSION

The objective of utilizing floating tablets is to achieve an extended residence time in the stomach and upper gastrointestinal (GI) tract, leading to improved bioavailability and sustained release of the drug. In this study, the focus was on preparing floating tablets of Carvedilol phosphate.

To quantify the concentration of Carvedilol phosphate, an UV-visible spectrophotometer was employed, measuring absorbance at 240 nm in 0.1 N hydrochloric acid buffer. A calibration curve was constructed to verify the method's precision, linearity, and potential interference. The concentrations ranged from 0 to 10 µg/ml, adhering to Beer's rule. The method exhibited excellent reproducibility, with low relative standard deviation (RSD) values (<1.92%).

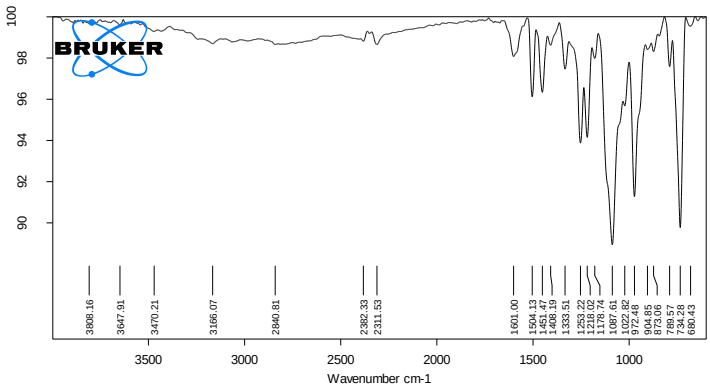

Fig. 1: FTIR spectra of carvedilol phosphate

Fig. 1-5 depict the FT-IR spectra of pure Carvedilol phosphate and physical mixtures. The IR peaks observed in the spectra of Carvedilol indicate that there are no significant interactions between Carvedilol and the excipients employed in this study. This confirms the compatibility of Carvedilol with the selected excipients, supporting their use in the formulation [10].

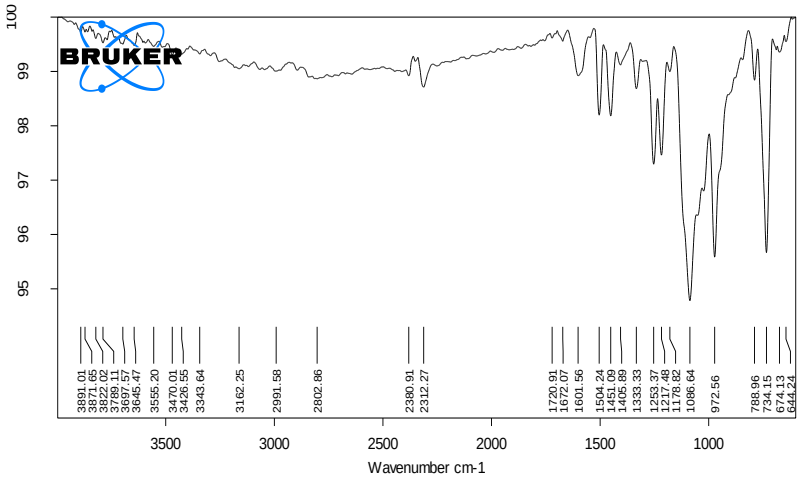

Fig. 2: FTIR spectra of carvedilol phosphate and HPCK100M

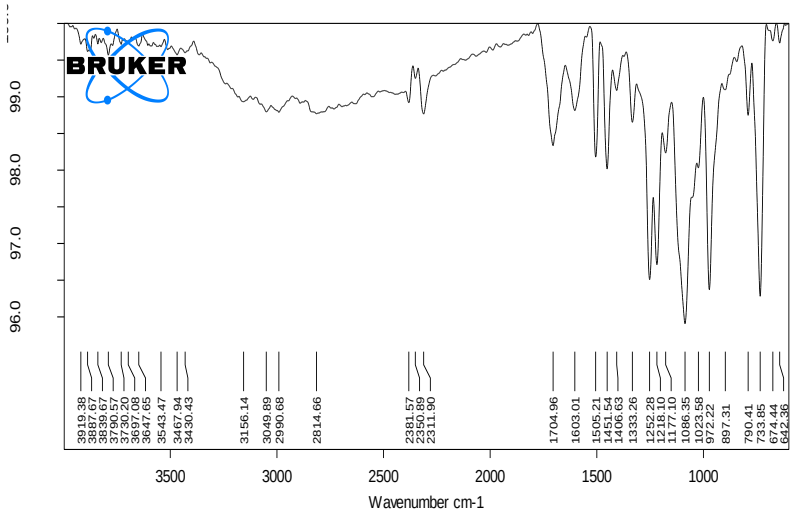

Fig. 3: FTIR spectra of carvedilol phosphate and carbopol

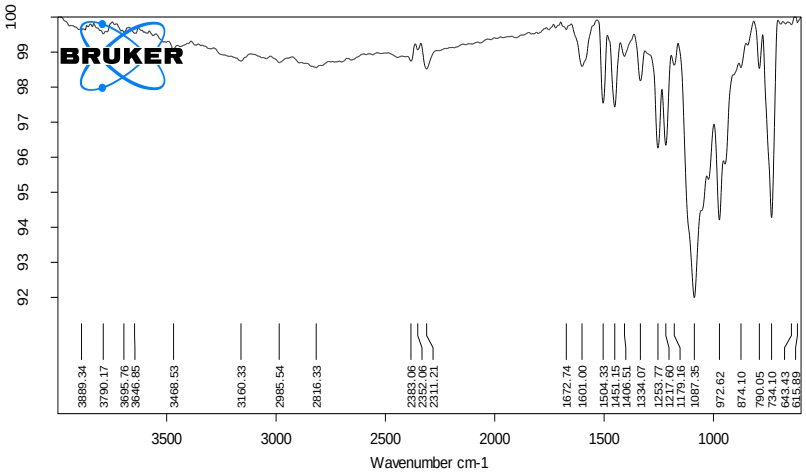

Fig. 4: FTIR spectra of carvedilol phosphate and HPMCK4M

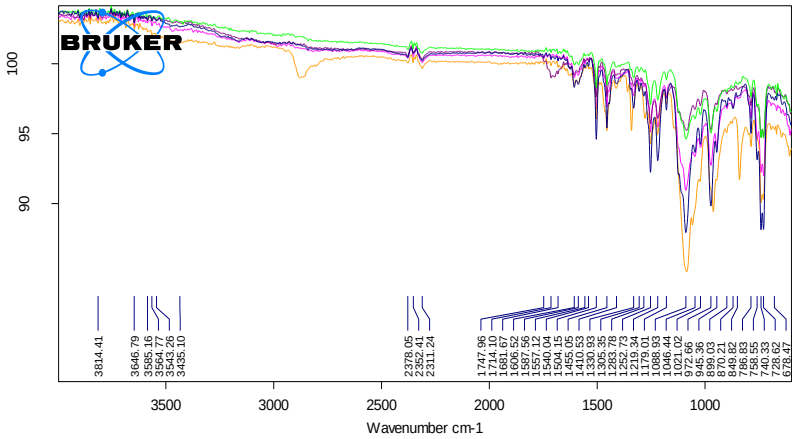

Fig. 5: Overlay of FTIR spectra of carvedilol phosphate with HPMCK100M, carbopol and HPMCK4M

Carvedilol phosphate floating tablets

Carvedilol phosphate floating tablets were developed using the concept of gas generation. Each tablet contained 20 mg of Carvedilol phosphate and was formulated using HPMC K100M, Carbopol, Polyox WSR, and HPMC K4M as matrix-forming polymers. Sodium bicarbonate was incorporated as the gas-generating agent. The impact of DCP, spray dried lactose, and HPβCD on drug release was also investigated. A total of eighteen Carvedilol phosphate floating tablets were prepared using the direct compression technique, following the specific compositions outlined in table 1-2. The formulated tablets underwent comprehensive characterization to evaluate their quality and performance. Tests conducted included hardness assessment, determination of drug content, evaluation of friability, measurement of disintegration time, determination of floating time, observation of floating lag time, and analysis of drug release characteristics. By conducting these extensive evaluations, valuable insights were obtained regarding the tablet's physical properties, drug content uniformity, mechanical strength, floating behaviour, and drug release profile [12]. These evaluations were crucial in assessing the overall performance and suitability of the Carvedilol phosphate floating tablets for their intended use (table 3).

Table 1: Composition of carvedilol phosphate floating tablets (F1-F8)

Ingredient (mg/tab)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Carvedilol phosphate	20	20	20	20	20	20	20	20
HPMC K100 M	100	50	-	-	100	50	-	-
Carbopol 934	-	-	100	50	-	-	100	50
HPβCD	-	-	-	-	30	30	30	30
Sodium bicarbonate	40	40	40	40	40	40	40	40
Dicalcium phosphate	32	82	32	82	12	52	12	52
Talc	4	4	4	4	4	4	4	4
Magnesium stearate	4	4	4	4	4	4	4	4
Total weight (mg)	200	200	200	200	200	200	200	200

Table 2: Formulae of carvedilol phosphate floating tablets (F9-F18)

Ingredient (mg/tab)	F_9	F_{10}	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}	F_{16}	F_{17}	F_{18}
Carvedilol phosphate	20	20	20	20	20	20	20	20	20	20
HPMC K100 M	-	-	-	-	-	-	-	-		
Carbopol 934	-	-	100	50	-	-	-	75		
HPMC K4M	-	-	-	-	100	50	75	-	100	50
Polyox WSR	100	50	-	-	-	-	-	-		
Sodium bicarbonate	40	40	40	40	40	40	40	40	40	40
Spray dried lactose	32	82	32	82	32	82	57	27	-	-
HPβCD	-	-	-	-	-	-	-	30	-	-
DCP	-	-	-	-	-	-	-		32	82
Talc	4	4	4	4	4	4	4	4	4	4
Magnesium stearate	4	4	4	4	4	4	4	4	4	4
Total weight (mg)	200	200	200	200	200	200	200	200	200	200

The hardness of the tablets fell within the range of 4.0-5.0 kg/cm^2, meeting the desired specifications. The tablets also exhibited excellent resistance to abrasion during the friability test, with a weight loss of less than 0.85% in each case. Furthermore, the Carvedilol phosphate drug content in all tablet formulations met the specified limit of 100±3%.

With the exception of formulations F_9 and F_{10}, all the floating tablets produced did not disintegrate in water, aqueous acidic (pH 1.2), and alkaline (pH 7.4) fluids. This indicates that the tablets had strong structural integrity and were capable of maintaining their shape under different conditions. Consequently, based on the satisfactory results obtained from the characterization tests, the manufactured floating tablets were deemed of high quality and suitable for sustained release purposes.

During the *in vitro* buoyancy evaluation, the floating lag time of multiple tablets adhered to the specified range of 25 seconds to 34 min. Additionally, the floating time varied across different floating tablets, ranging from 2 to 24 h. These results indicate that the tablets exhibited satisfactory floating behaviour and could remain buoyant for an extended period.

Table 3: Physical parameters of carvedilol phosphate floating tablets

Formulation	Hardness*1 (Kg/cm²) mean±sd	Friability*2 (% wt. loss) mean±sd	Drug *3 content (%) mean±sd	Floating lag time*4 (seconds) mean±sd	Floating time*5 (h)
F_1	4±0.05	0.82±0.015	99.6±1.98	30±0.5	>24
F_2	5±0.03	0.75±0.010	98.2±1.25	15±0.5	>24
F_3	5.5±0.06	0.65±0.012	100.3±1.50	22±0.4	>24
F_4	4±0.06	0.87±0.015	99.5±1.65	13±0.2	>24
F_5	5±0.03	0.77±0.013	97.3±1.50	90±1.5	>24
F_6	6±0.05	0.55±0.001	99.8±2.00	60±1.5	>24
F_7	5.5±0.06	0.60±0.012	98.7±1.90	28±0.4	>24
F_8	6±0.06	0.45±0.010	99.6±1.45	18±0.2	>24
F_9	6±0.05	0.34±0.006	101.2±1.50	10±0.2	Up to 4 h
F_{10}	5±0.05	0.6±0.012	100.8±1.85	14±0.2	Up to 3 h
F_{11}	5±0.05	0.74±0.010	99.5±1.56	5±0.1	Up to 10 h
F_{12}	4±0.04	0.47±0.010	98.5±1.50	5±0.1	>24
F_{13}	5±0.04	0.65±0.011	99.3±1.75	48±0.3	>24
F_{14}	6±0.04	0.52±0.010	99.5±1.50	22±0.3	>24
F_{15}	6±0.04	0.45±0.009	98.7±1.60	14±0.2	>24
F_{16}	6±0.04	0.38±0.006	98.4±175	25±0.2	>24
F_{17}	5±0.04	0.56±0.010	99.6±1.35	30±0.15	>24
F_{18}	5.5±0.05	0.29±0.005	101.5±2.00	14±0.15	>24

*1= n=10 tablets, *2= weight equal to 6.5 g., *3 = n= 10 tablets, *4= n= 10 tablets, *5= n= 10 tablets

In order to examine the release profile of carvedilol phosphate from the floating tablets, the tablets were subjected to *in vitro* dissolution testing using 0.1N HCl buffer. The drug release pattern was visually represented in fig. 6-7, while the specific drug release characteristics were summarized in table 4. The release of the drug from the tablets followed a gradual and sustained pattern over duration of 12 h. The release kinetics was influenced by the composition of the tablets, highlighting the importance of the tablet formulation in controlling the drug release behaviour [13, 14].

Table 4: Release parameters of carvedilol phosphate floating tablets

Formulation	Rate of release		Release exponent (n) mean±sd*
	K_0 (mg/h) mean±sd*	K_1(h^{-1}) mean±sd*	
F_1	0.76±0.01	0.0510±0.001	0.800±0.01
F_2	0.80±0.01	0.0539±0.001	0.765±0.01
F_3	0.91±0.01	0.0713±0.001	0.589±0.01
F_4	2.40±0.04	0.4075±0.008	0.688±0.01
F_5	0.89±0.01	0.0671±0.001	0.694±0.01
F_6	1.12±0.02	0.0901±0.001	0.926±0.01
F_7	1.35±0.02	0.1263±0.002	0.992±0.01
F_8	4.82±0.06	0.3152±0.006	0.657±0.01
F_9	9.87±0.15	1.868±0.036	0.169±0.003
F_{10}	8.56±0.15	1.601±0.02	0.696±0.01
F_{11}	1.57±0.03	0.240±0.006	0.656±0.01
F_{12}	2.89±0.03	0.580±0.01	0.733±0.015
F_{13}	1.03±0.01	0.083±0.002	0.733±0.01
F_{14}	2.65±0.05	0.486±0.01	0.896±0.01
F_{15}	1.50±0.02	0.143±0.002	0.709±0.01
F_{16}	1.66±0.01	0.332±0.006	0.701±0.01
F_{17}	0.95±0.01	0.067±0.001	0.945±0.01
F_{18}	2.23±0.02	0.168±0.003	0.964±0.01

*n=3 (All drug release experiments were conducted in triplicate (n=3))

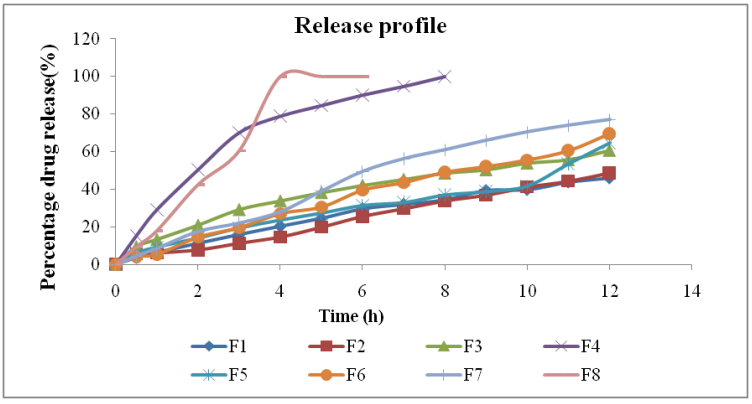

Fig. 6: Dissolution profiles of carvedilol phosphate floating tablets (F1-F8)

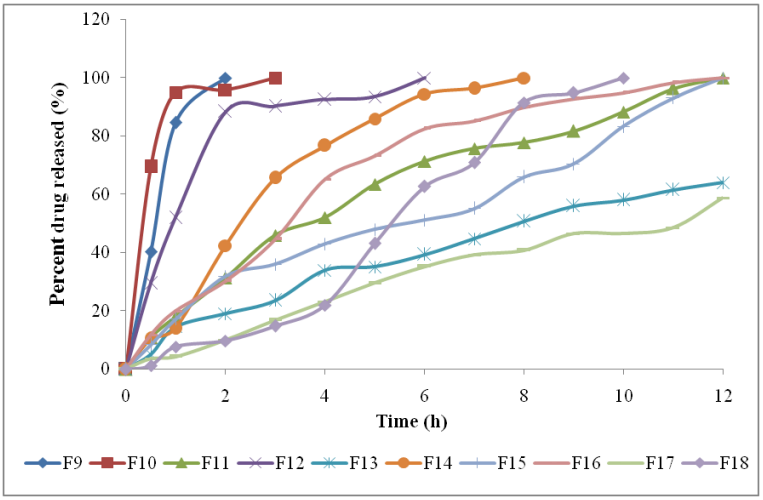

Fig. 7: Dissolution profiles of carvedilol phosphate floating tablets (F9-F18)

A notable finding from the study was that a decrease in the polymer concentration resulted in an increase in the release of the drug across the mentioned formulations. The incorporation of the hydrophilic excipients HPβCD and lactose led to an enhancement in the rate of drug release. A rapid release of the drug was observed with these formulations, which were formulated with Polyox WSR. Hence Polyox WSR was not suitable in formulation of Carvedilol floating tablets. A decrease in drug rate release was observed with dicalcium phosphate and HPMC K 100 M. Formulations F_{11}, F_{15}, and F_{16} gave 100% drug release within 12 h.

To analyse the release date, various kinetic models, including zero order, first order, Higuchi, and Korsemeyer-Peppas models were utilized [15-19]. The coefficients of determination (R2 values), which indicate the goodness of fit, were determined for each model and presented in table 5. First-order kinetics was followed by all formulations except in case of F_2, F_7, F_{11}, F_{15}, and F_{18}. A zero-order release was observed with formulations F_2, F_7, F_{11}, F_{15}, and F_{18}.

Table 5: Coefficient of determination (R^2) Values in the evaluation of carvedilol phosphate drug release as per different kinetic models

Formulation	Zero-order	First order	Higuchi	Korsemeyer-Peppas
F_1	0.981	0.995	0.974	0.998
F_2	0.993	0.986	0.919	0.933
F_3	0.939	0.986	0.919	0.995
F_4	0.895	0.993	0.979	0.968
F_5	0.895	0.965	0.914	0.983
F_6	0.961	0.981	0.953	0.978
F_7	0.999	0.990	0.953	0.994
F_8	0.981	0.984	0.849	0.995
F_9	0.968	0.936	0.988	0.882
F_{10}	0.657	0.807	0.999	0.769
F_{11}	0.945	0.913	0.955	0.990
F_{12}	0.733	0.881	0.913	0.882
F_{13}	0.970	0.993	0.981	0.956
F_{14}	0.917	0.974	0.955	0.953
F_{15}	0.979	0.926	0.950	0.979
F_{16}	0.959	0.965	0.969	0.976
F_{17}	0.976	0.982	0.953	0.981
F_{18}	0.963	0.864	0.842	0.964

All the formulated tablets were shown diffusion-controlled drug release as it obtained by Higuchi plots.

When the drug release pattern analysed through Korsemeyer-Peppas gives 0.692-0.800, 0.657, 0.65-0.733, 0.709 and 0.701 as release exponent (n) for formulations F_1-F_5, F_9, F_{11}-F_{13}, F_{15} and F_{16} respectively proving the release mechanism as 'non-Fickian diffusion'. For Formulations F_6-F_8, F_{14}, F_{17} and F_{18}, the obtained release exponent 'n' are 0.916-0.992, 0.896, 0.945 and 0.965, respectively, showing drug release mechanism as Super case II transport.

Formulations F_9, F_{10}, which show fast release, exhibited drug release mechanism asfickian diffusion [17].

As such, formulations F_{11}, F_{15} (HPMCK4M 32.5% and lactose) and F_{16} (Carbopol 32.5% and HPβCD a) gave 100% drug release within 12 hand 0.696, 0.709 and 0.701 as release exponent 'n' respectively. F_{11}, F_{15} and F_{16} formulations indicating 'non-Fickian release. A zero-order release was observed with formulations F_{11} and F_{15} and a first-order release was observed in case of formulation F_{16} [20-22].

As such, formulations F_{11} (Carbopol 50% and spray-dried lactose), F_{15} (HPMCK4M 32.5% and lactose) and F_{16} (Carbopol 32.5% and HPβCD), which gave 100% drug release within 12 h are finalized as the optimized floating formulations of Carvedilol phosphate recommended for bid administration.

CONCLUSION

The present work is to formulate floating tablets of Carvedilol phosphate. The FTIR spectra analysis revealed no evidence of chemical interactions between Carvedilol phosphate and the

excipients used in the formulation of the floating tablets. With the exception of formulations F_9 and F_{10}, the Carvedilol phosphate floating tablets exhibited good quality characteristics, including hardness, drug content, and friability. The floating lag time of multiple tablets fell within the specified range of 25 seconds to 34 min, while the floating duration varied from 2 to 24 h across different tablet formulations. The drug release from the manufactured tablets followed a gradual and sustained pattern over a 12-hour period, with the release kinetics dependent on the composition of the tablets. Based on these observations, formulations F_{11} (Carbopol 50% and spray-dried lactose), F_{15} (HPMCK4M 32.5% and lactose), and F_{16} (Carbopol 32.5% and HPβCD) were identified as optimized formulations for Carvedilol phosphate floating tablets and are recommended for twice-daily administration.

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Nil

AUTHORS CONTRIBUTIONS

All authors were responsible for every part of this work and contributed to data analysis, drafting, and revision of the manuscript.

CONFLICT OF INTERESTS

The authors confirm that there are no conflicts of interest regarding the publication of this article.

REFERENCES

1. https://en.org/wiki/carvedilol.wikipedia. [Last accessed on 13 Oct 2023]
2. https://go.drugbank.com/drugs/DB01136. [Last accessed on 13 Oct 2023]
3. Mohapatra PK, Satyavani CH, Sahoo SA. The Design and development of carvedilol gastroretentive floating drug delivery systems using hydrophilic polymers and *in vitro* characterization. Int J Pharm Pharm Sci. 2020 Jul 1;12(7):66-73. doi: 10.22159/ijpps.2020v12i7.38024.
4. Qin C, Wu M, Xu S, Wang X, Shi W, Dong Y. Design and optimization of gastro-floating sustained-release tablet of pregabalin: *in vitro* and *in vivo* evaluation. Int J Pharm. 2018 Jul 10;545(1-2):37-44. doi: 10.1016/j.ijpharm.2018.04.011, PMID 29649518.
5. Tran PHL, Tran TTD. Dosage form designs for the controlled drug release of solid dispersions. Int J Pharm. 2020 May 15;581:119274. doi: 10.1016/j.ijpharm.2020.119274, PMID 32234566.
6. Djuris J, Milovanovic S, Medarevic D, Dobricic V, Dapcevic A, Ibric S. Selection of the suitable polymer for supercritical fluid assisted preparation of carvedilol solid dispersions. Int J Pharm. 2019 Jan 10;554:190-200. doi: 10.1016/j.ijpharm.2018.11.015, PMID 30414899.
7. Desai S, Bolton S. A floating controlled-release drug delivery system: *in vitro-in vivo* evaluation. Pharm Res. 1993 Sep;10(9):1321-5. doi: 10.1023/a:1018921830385, PMID 8234170.
8. Hilton AK, Deasy PB. *In vitro* and *in vivo* evaluation of an oral sustained-release floating dosage form of amoxycillin trihydrate. International Journal of Pharmaceutics. 1992 Oct 10;86(1):79-88. doi: 10.1016/0378-5173(92)90033-X.
9. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: a review. AAPS PharmSciTech. 2005 Sep;6(3):E372-90. doi: 10.1208/pt060347, PMID 16353995.
10. Namdev A, Jain D. Floating drug delivery systems: an emerging trend for the treatment of peptic ulcer. Curr Drug Deliv. 2019 Dec 1;16(10):874-86. doi: 10.2174/1567201816666191018163519, PMID 31894738.
11. Kotreka UK, Adeyeye MC. Gastroretentive floating drug-delivery systems: a critical review. Crit Rev Ther Drug Carrier Syst. 2011;28(1):47-99. doi: 10.1615/critrevtherdrugcarriersyst.v28.i1.20, PMID 21395515.
12. Hofmann AF, Pressman JH, Code CF, Witztum KF. Controlled entry of orally administered drugs: physiological considerations. Drug Dev Ind Pharm. 1983 Jan 1;9(7):1077-109. doi: 10.3109/03639048309046314.
13. Nagarwal RC, Ridhurkar DN, Pandit JK. *In vitro* release kinetics and bioavailability of gastroretentive cinnarizine hydrochloride tablet. AAPS PharmSciTech. 2010 Mar;11(1):294-303. doi: 10.1208/s12249-010-9380-5, PMID 20182827.
14. Sauzet C, Claeys Bruno M, Nicolas M, Kister J, Piccerelle P, Prinderre P. An innovative floating gastro retentive dosage system: formulation and *in vitro* evaluation. Int J Pharm. 2009 Aug 13;378(1-2):23-9. doi: 10.1016/j.ijpharm.2009.05.027, PMID 19465095.
15. Taghizadeh Davoudi E, Ibrahim Noordin M, Kadivar A, Kamalidehghan B, Farjam AS, Akbari Javar H. Preparation and characterization of a gastric floating dosage form of capecitabine. BioMed Res Int. 2013;2013:495319. doi: 10.1155/2013/495319, PMID 24288681.
16. Chavanpatil M, Jain P, Chaudhari S, Shear R, Vavia P. Development of sustained release gastroretentive drug delivery system for ofloxacin: *in vitro* and *in vivo* evaluation. Int J Pharm. 2005 Nov 4;304(1-2):178-84. doi: 10.1016/j.ijpharm.2005.08.009, PMID 16198522.
17. Srikanth Meka V, Wee Liang VA, Dharmalingham SR, Sheshala R, Gorajana A. Preparation and *in vitro* characterization of non-effervescent floating drug delivery system of poorly soluble drug, carvedilol phosphate. Acta Pharm. 2014;64(4):485-94. doi: 10.2478/acph-2014-0038, PMID 25531788.
18. Rajora A, Nagpal K. A critical review on floating tablets as a tool for achieving better gastric retention. Crit Rev Ther Drug Carrier Syst. 2022;39(1):65-103. doi: 10.1615/CritRevTherDrugCarrierSyst.2021038568, PMID 34936318.
19. Uppala P, Shaik S, Valluru S, Nalluri B. Development of enteric coated sustained release matrix tablets of sertraline hydrochloride. J App Pharm Sci 2015;5(4):58-64. doi: 10.7324/JAPS.2015.50410.
20. Jeganathan B, Prakya V. Preparation and evaluation of floating extended release matrix tablet using a combination of polymethacrylates and polyethylene oxide polymers. Int J Pharm Pharm Sci. 2014 Jul 19;6(8):584-92.
21. Chaitanya K, Velmurugan SE. Formulation and evaluation of levodopa effervescent floating tablets. Int J Pharm Pharm Sci. 2015;7:189-93.
22. Niharika MG, Krishnamoorthy K, Akkala M. Overview on floating drug delivery system. Int J App Pharm. 2018 Oct 4;10(6):65-71. doi: 10.22159/ijap.2018v10i6.28274.