International Journal of Pharmacy and Analytical Research (IJPAR)

ISSN: 2320-2831

IJPAR |Vol.12 | Issue 3 | July - Sept -2023
www.ijpar.com

Research article ***Pharmaceutical Analysis***

Design and in-vitro characterization of rosuvastatin calcium floating tablets by employing response surface method

K. Jaganathan, D. Devanandh*, S. Chandra, N. Senthilkumar

Department of Pharmaceutics, JKKMMRF'S Annai JKK Sampoorani Ammal College of Pharmacy, Ethirmedu, Komarapalayam – 638183, Namakkal (DT), Tamil Nadu, India

Corresponding Author: K. Jaganathan
Published on: August 28, 2023

ABSTRACT

The present study aimed to design and characterize in-vitro floating tablets of Rosuvastatin Calcium using the Response Surface Method (RSM) to enhance the gastric residence time and improve bioavailability. Floating tablets were prepared using different concentrations of hydrophilic polymers and effervescent agents. The RSM was employed to optimize the formulation variables, namely the amount of hydrophilic polymer and effervescent agent, to achieve desired tablet buoyancy and drug release profile. The tablets were evaluated for physical parameters such as hardness, friability, floating lag time, total floating time, and in-vitro drug release. The drug release kinetics followed the Higuchi model, indicating diffusion-controlled release. Based on the evaluation of floating lag time and release characteristics, formula F6 was identified as the optimal formulation. F6 demonstrated a floating lag time of 171±0.81 seconds, a floatation time of 24 hours, and an impressive cumulative drug release of 99.87%. Notably, this formulation exhibited sustained release characteristics throughout the entire release period. The RSM effectively predicted the relationship between the independent variables and the responses, and the experimental values were in close agreement with the predicted values. The study successfully demonstrated the potential of designing Rosuvastatin Calcium floating tablets using RSM. The optimized formulation showed promising results in terms of buoyancy and drug release, suggesting its potential for once-daily administration and improved patient compliance.

Keywords: Rosuvastatin Calcium, Floating tablets, Response Surface Method (RSM), Hydrophilic polymers, Effervescent agents

INTRODUCTION

Novel Drug Delivery System

An oral drug delivery system that provides uniform drug delivery can only partially meet therapeutic and biopharmaceutical needs because it does not account for site-specific absorption rates within the gastrointestinal tract. As a result, designing delivery systems that release the drug at an appropriate time, at the appropriate site, as well as the desired rate is required.

To supply drugs at the proper spot means, on the one hand, delivering locally efficacious pharmaceuticals such as antibiotics, anti-inflammatory drugs, or cryostatic agents at their target site, and on the other, releasing drugs with a limited absorption window such as Digoxin, Ampicillin, Cefuroxime axetil, and so on.

To deliver drugs molecules at the appropriate moment involves avoiding constant plasma levels for medicines that acquire tolerance, such as organic nitrates, or that have biorhythmic based action profiles, such as corticosteroids or antiasthmatic agents. In this instance, the drug delivery

system must guarantee that drug-free and effective plasma levels are not altered.[1]

GASTRO retentive Drug Delivery System

The oral means for administration is the most common and convenient method of drug delivery. For dosage forms intended for oral administration, the benefits of long-term delivery technology have yet to be completely realized. This is mostly because the extent of drug absorption from the GIT is dictated by GI physiology, regardless of the device's control release qualities. Although variable absorption from different sections of the GI has been recognized for decades, drug delivery devices to target medications to other regions of the GIT have recently been developed. Examples are gastro-retentive systems, delayed release systems, and colon targeting.[2]

Hydrodynamically Balanced System (FDDS) Principle

Floating dosage form is also known as hydrodynamically balanced system (HBS). It is an oral dosage form (capsule or tablet) that is designed to prolong the residence time of the dosage form within the GI tract. It is formulation of a drug and gel forming hydrocolloids meant to remain buoyant on stomach contents. This not only prolongs GI residence time but also does so in an area of the GI tract that would maximize drug reaching its absorption site in solution and hence ready for absorption. Drug dissolution and release from the capsule retained in stomach fluids occur at the stomach, under fairly controlled condition. The retentive characteristics of the dosage form in gastric content are most significant for drugs.[3]

- Insoluble in intestinal fluid.
- That acts locally.
- That exhibits site-specific absorption.

Rosuvastatin calcium Floating tablets

Rosuvastatin calcium is a medication commonly prescribed to lower cholesterol levels in the body. It belongs to a class of drugs known as statins. Here are some of the main uses of rosuvastatin calcium:[4]

Hypercholesterolemia: Rosuvastatin is primarily used to treat high levels of low-density lipoprotein cholesterol (LDL-C), commonly known as "bad" cholesterol. It helps reduce the production of cholesterol in the liver, leading to lower LDL-C levels and improved lipid profiles.

Mixed dyslipidemia: It is also prescribed to treat mixed dyslipidemia, a condition characterized by elevated levels of both LDL-C and triglycerides. Rosuvastatin helps lower LDL-C and triglyceride levels while increasing high-density lipoprotein cholesterol (HDL-C) levels, often referred to as "good" cholesterol.

Cardiovascular risk reduction: Rosuvastatin has been shown to reduce the risk of cardiovascular events such as heart attacks, strokes, and the need for coronary revascularization procedures in individuals with or without pre-existing cardiovascular disease. It is often prescribed as a preventive measure for individuals at high risk of cardiovascular events.

Familial hypercholesterolemia: This genetic disorder causes abnormally high levels of LDL-C from birth, significantly increasing the risk of cardiovascular disease. Rosuvastatin is used as an adjunct to diet and lifestyle modifications to lower LDL-C levels in individuals with familial hypercholesterolemia.

Atherosclerosis prevention: Rosuvastatin can help slow down the progression of atherosclerosis, a condition where plaque builds up inside the arteries, leading to reduced blood flow. By lowering LDL-C levels and reducing inflammation, it helps prevent the formation of new plaques and stabilizes existing plaques.

MATERIALS AND METHODS

Drug profile

Rosuvastatin calcium

Rosuvastatin calcium is an organic calcium salt that is the hemi calcium salt of rosuvastatin. It has a role as an anti-inflammatory agent, a CETP inhibitor and a cardioprotective agent.

Preformulation studies

Formulation for floating tablets

Preparation of rosuvastatin calcium floating tablets

- TWELVE formulations (F_1, F_2, F_3, F_4, F_5, F_6, F_7, F_8, F_9, F_{10}, F_{11}, F_{12}) of varying constituents were prepared.
- TWELVE floating matrix formulations of Rosuvastatin calcium based on gas forming agent were prepared. HPMC K15M,Carbopol 940P, Guar gum were used in formulating the Matrix system. Incorporation of sodium bicarbonate into matrix resulted in the tablet floating over simulated gastric fluid for sustained release.

Direct compression

Manufacturing process

Step I: Sifting of Raw Materials

Sift Rosuvastatin calcium, HPMCK15M, sodium bicarbonate, citric acid, microcrystalline cellulose, magnesium stearate, magnesium stearate, and talc through #40 meshseparately, collect in poly bags.

Step II: Pre blending

Sift Rosuvastatin calcium, HPMCK15M, sodium bicarbonate, citric acid, microcrystalline cellulose, magnesium stearate, magnesium stearate blender and mix for 10 minutes.

Step III: Compression

Fix the tablet machine and compress the powder blend using 10x10mm oblong punches as per the SOP.

Response surface methodology (RSM)

It is a powerful statistical technique utilized in the optimization of formulation designs. It involves the construction and analysis of mathematical models to study the relationship between multiple variables and the response of interest. In the context of formulation optimization, RSM aids in identifying the optimum levels of various factors to achieve desired formulation characteristics. By systematically varying the levels of input variables and analyzing the resulting responses, RSM helps determine the ideal combination of factors that yield the desired outcome. Through experimental design and statistical analysis, RSM facilitates the identification of critical formulation parameters and their optimal levels, ultimately improving the efficiency and effectiveness of the formulation development process.[5]

Design Expert software is a comprehensive and powerful tool widely used in the field of experimental design and optimization. Developed by Stat-Ease, Design Expert provides researchers, scientists, and engineers with a user-friendly interface to design, analyze, and interpret experiments. The software offers a wide range of features and functionalities, including factorial designs, response surface designs, mixture designs, and optimization tools. It allows users to efficiently explore and optimize multiple variables, identify key factors affecting the response, and generate predictive models to understand the relationship between variables and outcomes. Design Expert offers various statistical analyses, graphical tools, and visualizations to interpret experimental results and make data-driven decisions. It simplifies the complex process of experimental design, making it accessible to users of all levels of expertise. Whether for formulation development, process optimization, or quality improvement, Design Expert is a valuable tool that helps researchers achieve optimal results and streamline their experimentation process. In this research I used design expert version 13 Stat-Ease,USA.

The Box-Behnken Design (BBD) is a response surface methodology (RSM) technique widely used in experimental design and optimization. It is a three-level fractional factorial design that allows for the efficient exploration of multiple factors and their interactions. The BBD is particularly useful when the number of factors is moderate and the goal is to understand and optimize the response surface within the experimental region. By strategically selecting a subset of factor combinations and levels, the BBD reduces the number of experimental runs required while still providing sufficient information to estimate the model parameters accurately. This design approach enables researchers to efficiently analyze the impact of multiple factors, identify optimal operating conditions, and generate predictive models to guide further experimentation or process optimization. The BBD's balanced and orthogonal design structure helps ensure robust and reliable results, making it a valuable tool for experimental design and optimization in a wide range of scientific and engineering disciplines. In this research I used this design to develop the formulation.[6]

Table 1: Formulation of Rosuvastatin calcium floating tablets Using Response surface methodology

Independent variables	**Levels**		
	-1	**0**	**+1**
A_1 : HPMC K15M (mg)	20	50	80
B_2 : Carbopol 940 (mg)	10	35	60
C_3 : Guar gum (mg)	20	40	60
Dependent variables			
Y_{FLT} = Floating Lag Time (min)			
Y_{SI} = Swelling Index (%)			
$Y_{\%\ Drug\ release}$ =cumulative drug release (%)			

Table 2:Formulations of Rosuvastatin calcium floating tablets.

Name of the ingredient	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Rosuvastatin calcium	40	40	40	40	40	40	40	40	40	40	40	40
HPMC K15M	80	50	80	50	20	50	20	80	80	20	20	50
Carbopol 940	10	10	35	10	35	60	35	60	35	60	10	60
Guar gum	40	20	60	60	20	60	60	40	20	40	40	20
Sodium bicarbonate	50	50	50	50	50	50	50	50	50	50	50	50
Citric acid	20	20	20	20	20	20	20	20	20	20	20	20
Microcrystalline cellulose	55	105	10	65	110	15	70	5	50	70	115	55
Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5

Total weight	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**

RESULTS AND DISCUSSION

Table 3: Physical Characteristics ofPolymersand Excipients

Parameters	HPMC K15M	Carbopol 940p	Guar gum	Sodium bi carbonate	Citric acid
Bulk density(g/cc)	0.500	0.435	0.522	0.589	0.564
Tapped density(g/cc)	0.691	0.618	0.728	0.854	0.786
Compressibility Index (%)	27.86	27.57	22.34	26.25	28.27
Angle of repose(º')	37º46'	41 º53'	30º57'	32º52'	35º38'
Hausners ratio	1.322	0.689	1.199	1.156	0.982

Characterization of rosuvastatin calcium powder blend

The physical characteristics of the granules (F1 to F12) such as bulk density, tapped density, angle of repose, and compressibility index were determined. The results are given in the table.

Table 4: Physical characteristics of powder blend ($F_1 – F_{12}$)

Batch No	BulkDensity (g/cc)	Tapped Density (g/cc)	Angle ofrepose Tan θ=h/r	Compressibility index (%)
F_1	0.486±0.12	0.605±0.35	32º18'±0.83	24.4±0.33
F_2	0.483±0.36	0.614±0.49	29°27'±0.24	27.1±0.17
F_3	0.488±0.19	0.627±0.32	30°16±'0.36	28.48±0.12
F_4	0.519±0.37	0.579±0.18	33°41'±0.18	19.56±0.24
F_5	0.535±0.43	0.590±0.24	27°89'±0.21	18.2±0.35
F_6	0.507±0.71	0.529±0.66	31°96'±0.39	17.9±0.46
F_7	0.502±0.64	0.589±0.54	25º31º'±0.47	17.3±0.68
F_8	0.509±0.09	0.573±0.25	27°30'±0.58	19.96±0.53
F_9	0.503±0.16	0.549±0.37	29°48'±0.27	20.34±0.16
F_{10}	0.482±0.52	0.552±0.24	28°79'±0.52	28.1±0.27
F_{11}	0.501±0.14	0.548±0.78	27°96'±0.48	27.38±0.47
F_{12}	0.498±0.22	0.511±0.26	25º41º'±0.51	25.43±0.27

n=3, mean ± Standard Deviation

Evaluation of Rosuvastatin calcium floating tablets

The physical properties of the tablets ($F_1 – F_{12}$)obtained by compressing the blend using Cadmach eight punches tablet machine. The physical properties of Rosuvastatin calcium ($F_1 – F_{12}$) such as tablet size, hardness, friability, and weight variation were determined and results of the formulations ($F_1 – F_{12}$) found to be within the limits specified in Pharmacopoeia.

Table 5: Physical Characteristics of Rosuvastatin calcium Floating Tablets ($F_1 – F_9$)

Batch No	Thickness (mm)	Friability (%)	Hardness (kg/cm^2)	Weight Variation (mg±SD)	Percentage Content
F_1	4.6±0.14	0.47±0.17	5.2±0.34	302±1.02	94.74±0.17
F_2	4.8±0.32	0.59±0.42	5.0±0.73	305±1.45	99.25±0.20
F_3	4.6±0.44	0.43±0.12	5.6±1.92	302.5±1.23	98.77±0.27
F_4	4.8±0.25	0.45±0.2	5.1±0.34	298±1.12	97.38±0.14
F_5	4.5±0.15	0.42±0.13	5.8±0.28	304±1.11	95.48±0.27
F_6	5.1±0.62	0.51±0.30	5.9±0.37	299±1.40	95.87±0.27
F_7	46±0.14	0.64±0.70	5.7±0.89	304±0.92	98.88±0.22

F_8	4.7±0.32	0.40±0.12	5.4±0.42	294±0.98	98.52±0.11
F_9	4.6±0.42	0.49±0.50	5.8±0.56	307±1.21	97.57±0.2
F_{10}	4.8±0.35	0.39±0.21	5.1±0.22	304±1.22	99.75±0.29
F_{11}	4.5±0.29	0.35±0.23	5.8±0.12	299±0.87	99.25±0.37
F_{12}	5.0±0.56	0.40±0.31	5.2±0.41	302±0.91	96.88±0.71

n=3, mean ± Standard Deviation

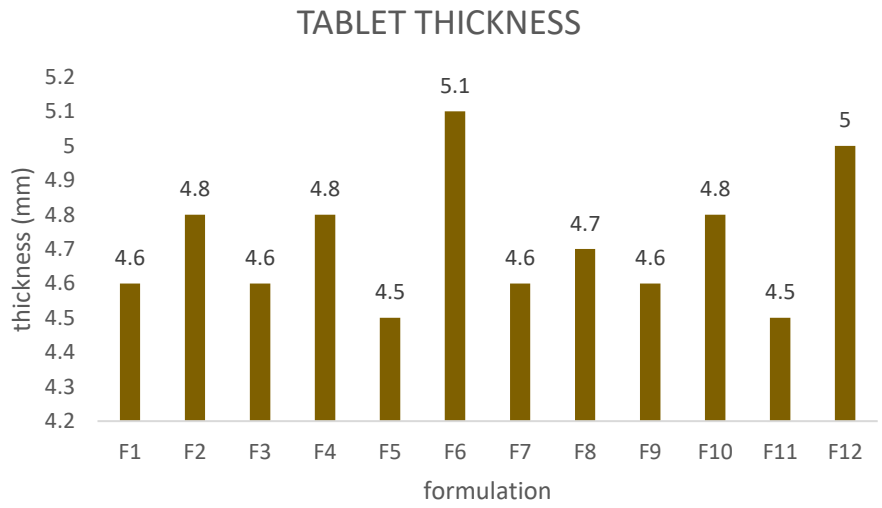


Fig 1: Thickness of Rosuvastatin calcium floating tablets

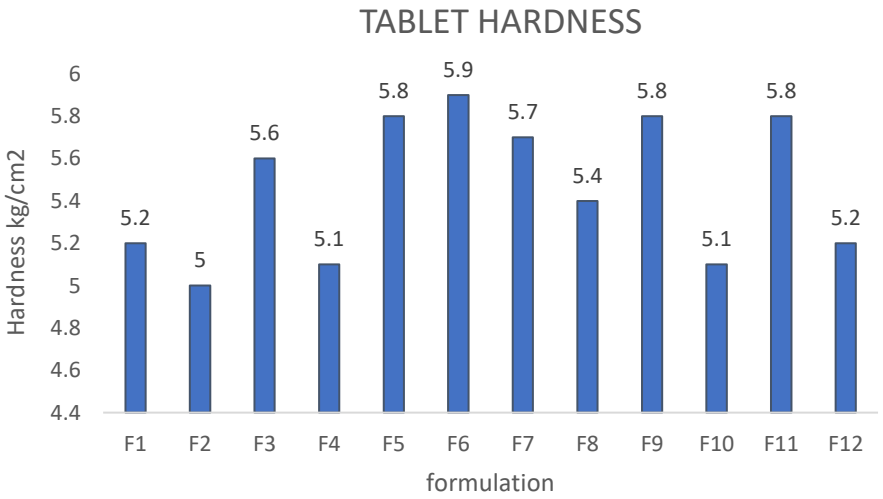


Fig 2: Hardness of Rosuvastatin calcium floating tablets

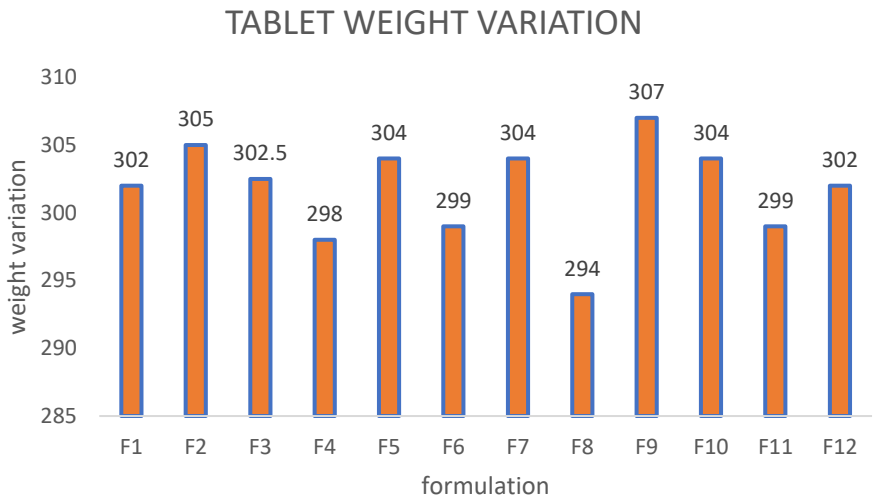


Fig 3: Weight variation of Rosuvastatin calcium floating tablets

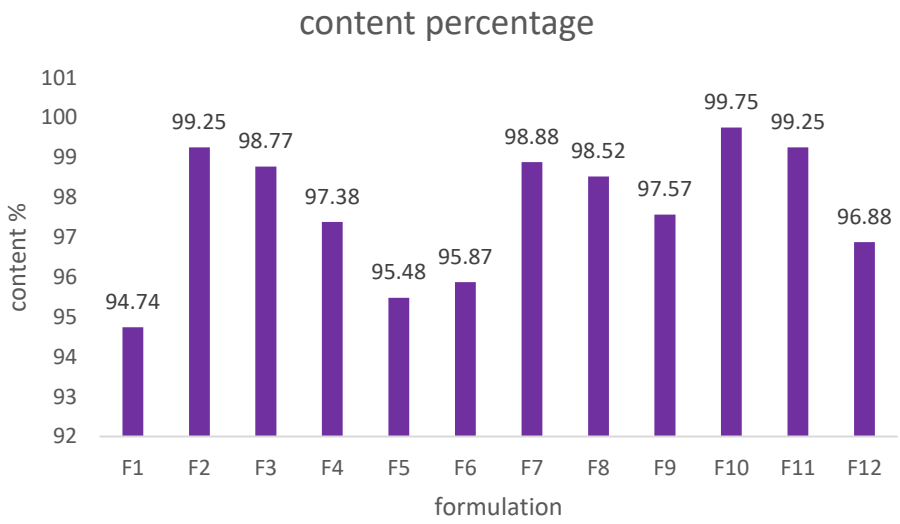


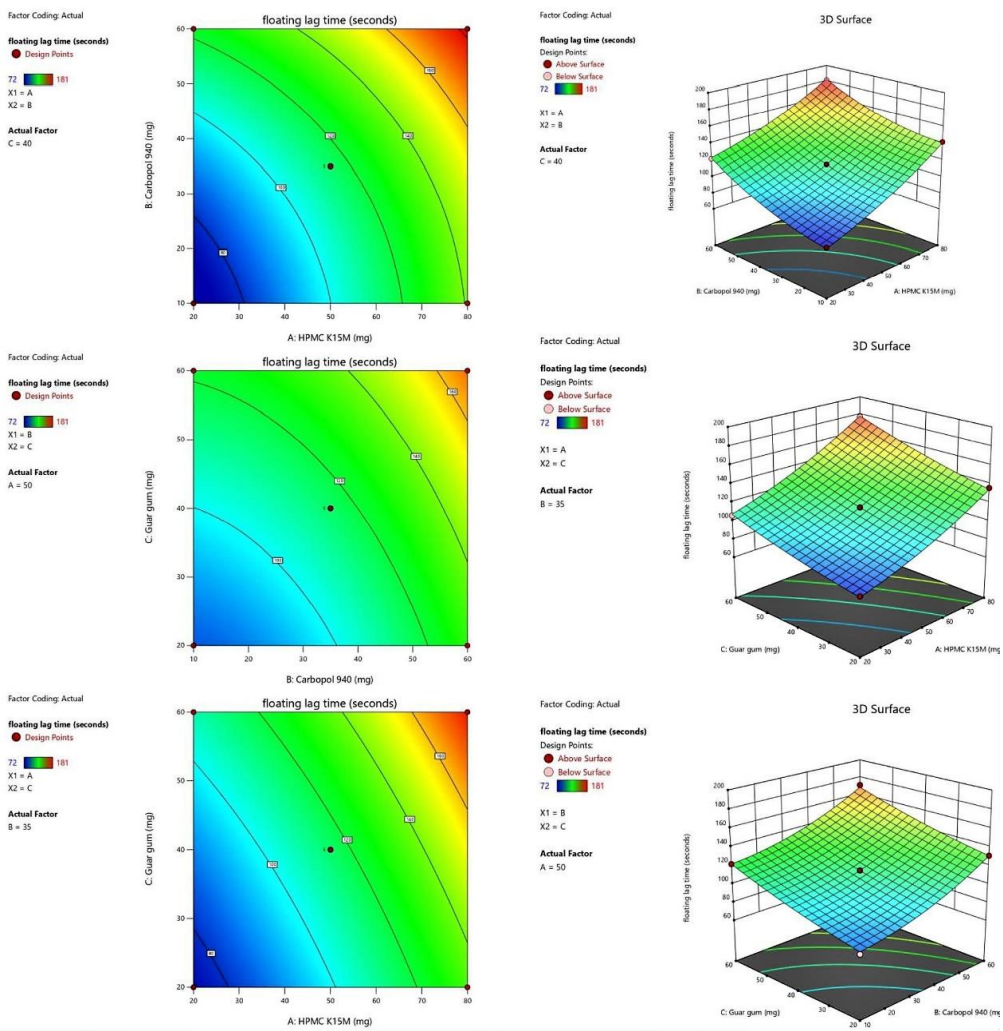
Fig 4: Percentage of contents of Rosuvastatin calcium floating tablets

Table 6: Observed response

		Factor 1	Factor 2	Factor 3	Response 1	Response 2	Response 3
Std	**Run**	**A:HPMC K15M**	**B:Carbopol 940**	**C:Guar gum**	**floating lag time**	**swelling index**	**DRUG RELEASE T90%**
		mg	mg	mg	seconds	%	%
2	1	80	10	40	142	46	7.1
9	2	50	10	20	81	44	6.4
8	3	80	35	60	177	69	8.2
11	4	50	10	60	122	43	6.9
5	5	20	35	20	76	63	7.9
12	6	50	60	60	171	99.8	10.8
7	7	20	35	60	106	75	7.8
4	8	80	60	40	181	99.5	10.6
6	9	80	35	20	136	82	8.9

3	10	20	60	40	122	96	9.6
1	11	20	10	40	72	49	7.4
10	12	50	60	20	131	99	10.2

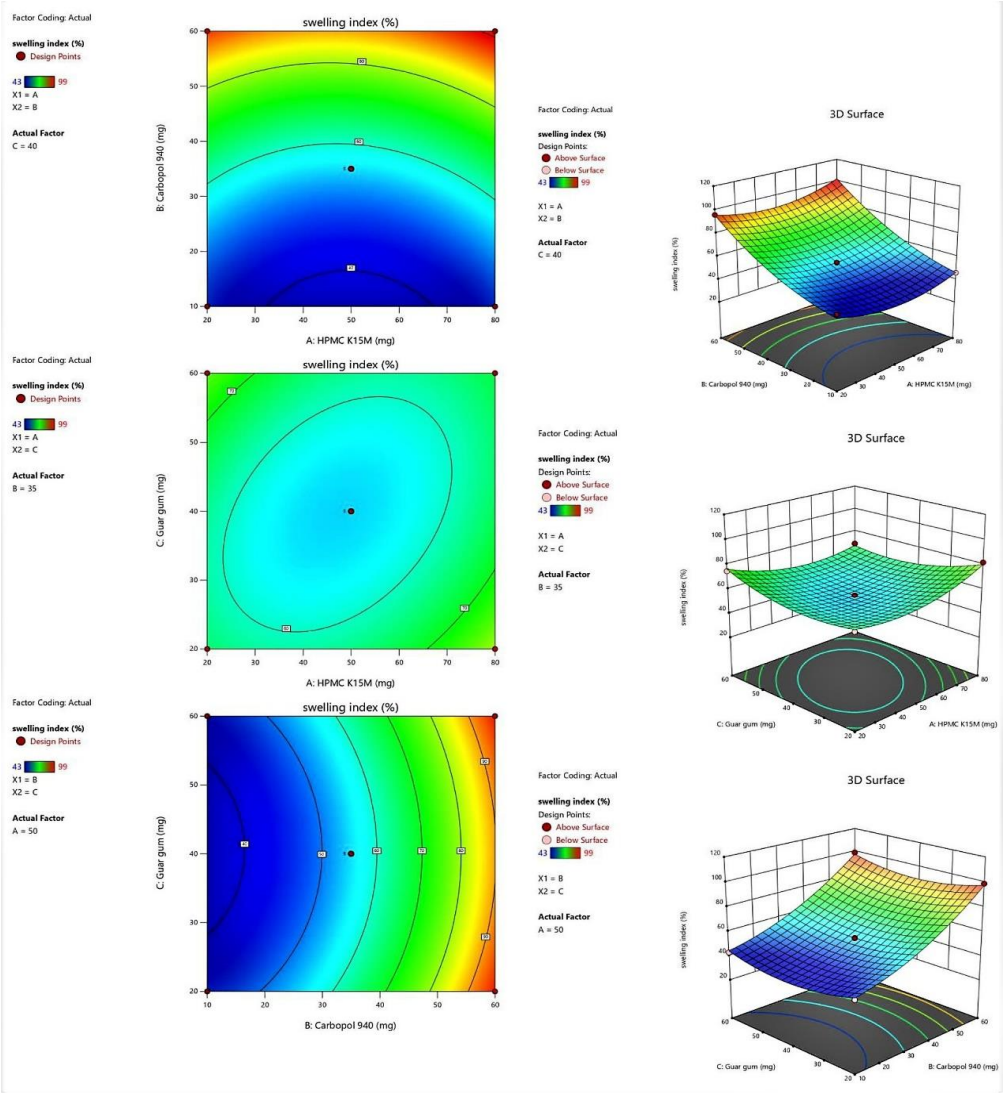
Countour plot and 3d-response plot of floating lag time



Floating lag time=115 + 32.5 * A + 23.5 * B + 19 * C + -2.75 * AB + 2.75 * AC + -0.25 * BC + 5.875 * A^2 + 8.375 * B^2 + 2.875 * C^2

Std. Dev.	1.91	**R^2**	0.9984
Mean	123.06	**Adjusted R^2**	0.9964
C.V. %	1.55	**Predicted R^2**	0.9751
		Adeq Precision	76.5106

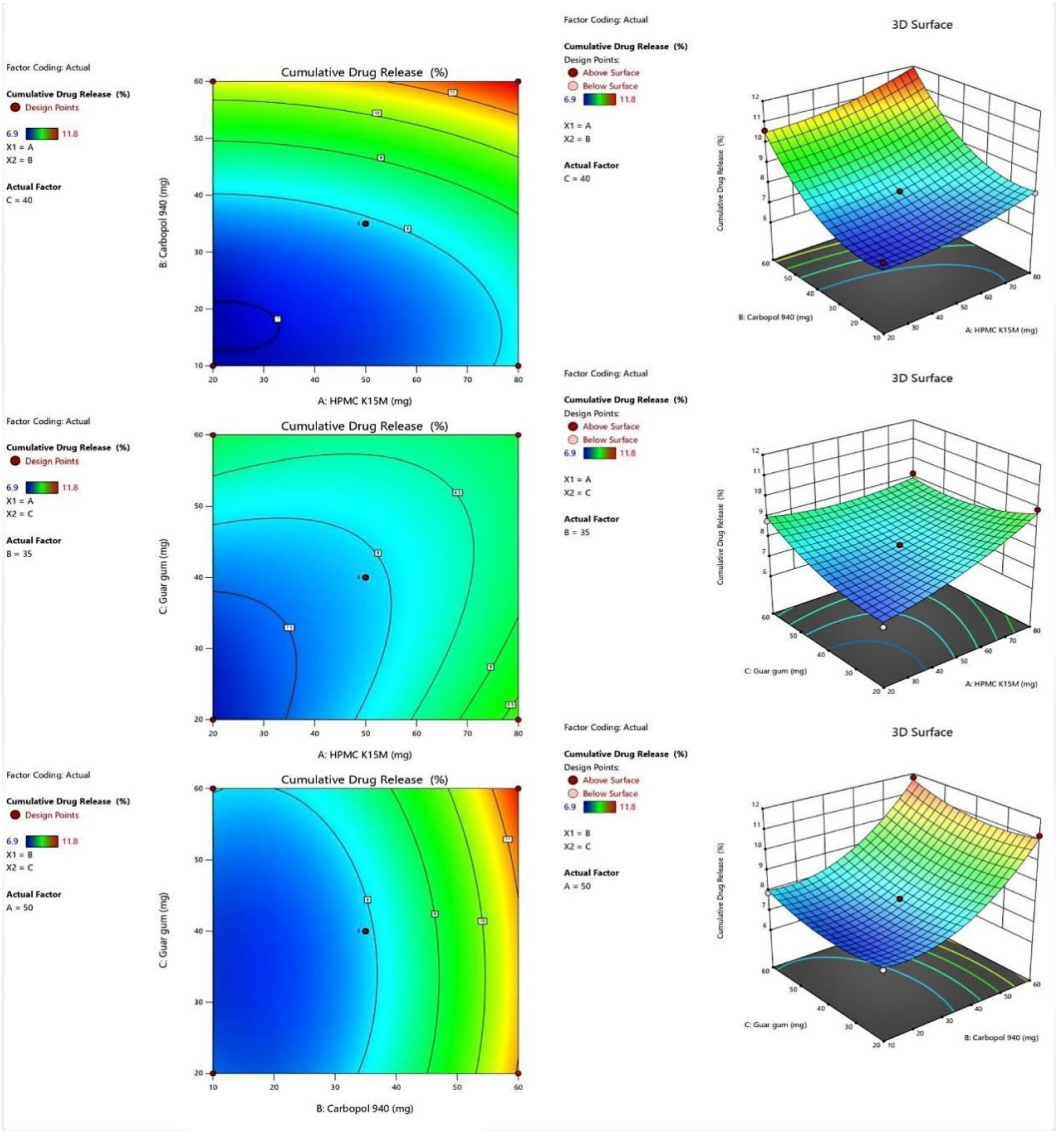
Countour plot and 3d-response plot of swelling index



SWELLING INDEX=55 + 1.625 * A + 26.375 * B + -0.25 * C + 1.5 * AB + -6.25 * AC + 0.25 * BC + 9.25 * A^2 + 8.25 * B^2 + 8 * C^2

Std. Dev.	2.28	**R^2**	0.9947
Mean	67.00	**Adjusted R^2**	0.9878
C.V. %	3.40	**Predicted R^2**	0.9149
		Adeq Precision	33.0165

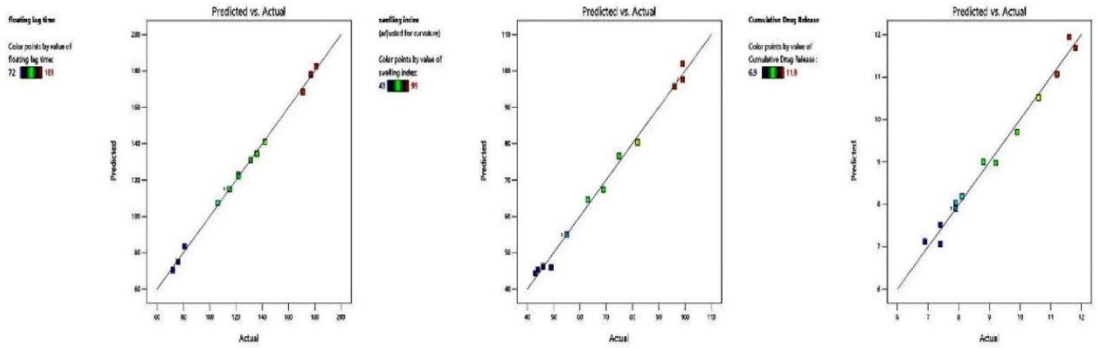
Contour plot and 3d-response plot of cum. Drug release%



CUMULATIVE DRUG RELEASE %= 7.9 + 0.6375 * A + 1.8 * B + 0.2875 * C + 0.075 * AB + -0.65 * AC + 0.025 * BC + 0.325 * A^2 + 1.2 * B^2 + 0.475 * C^2

Std. Dev.	0.2639	**R^2**	0.9878
Mean	8.84	**Adjusted R^2**	0.9722
C.V. %	2.98	**Predicted R^2**	0.8053
		Adeq Precision	24.0858

Predicted vs actual responses of rosuvastatin calcium from response surface methodology Floating lag time, swelling index, cumulative drug release %



Dissolution Studies7

Observation

From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling, drug diffusion and matrix erosion. It was observed that all the tablets ascended to the upper one third of the dissolution vessels within a short time and remained floated until the completion of release studies. The drug release study is carried out up to 24hrs.

The percentage drug release from batch F_1 to F_{12}vary from 42.69 to 99.87%. Large concentration of high viscosity polymer induces the formation of strong viscous gel layer that slowed down the rate of water diffusion into the tablet matrix, which may result in the retardation of drug release. Being water-soluble polymers, they dissolve and form pores filled liquid in which drug can thereafter diffuse in dissolution medium. All the formulations were designed as dosage form for 24 hrs. To check the 100 % dissolution release profile, optimized formulations were subjected to dissolution studies for 24 hrs.

The dissolution studies of the formulation (F_1 to F_{12}) were carried out in USP dissolution apparatus (paddle) in 900 ml of Simulated Gastric Juice of 0.1N HCl of pH 1.2 as dissolution medium. The formulation F_6 showed a constant release in a sustained manner with 99.87% as like zero order kinetics and hence $F_6$was chosen as the best formulation.

Table 7:*In Vitro* release profile of Rosuvastatin calcium floating Tablets (F_1 - F_3)in 0.1N HCl of pH 1.2

S.No	Time(hrs)	F_1	F_2	F_3
	0	**0**	**0**	**0**
1	**1**	0	0	0
2	**2**	12.87	18.58	18.1
3	**3**	28.35	36.28	28.5
4	**4**	42.38	58.68	39.73
5	**5**	57.98	68.87	52.93
6	**6**	69.87	78.75	69.8
7	**7**	89.68	89.58	79.79
8	**8**	99.79	99.89	88.83
9	**9**			99.8
10	**10**			
11	**11**			
12	**12**			

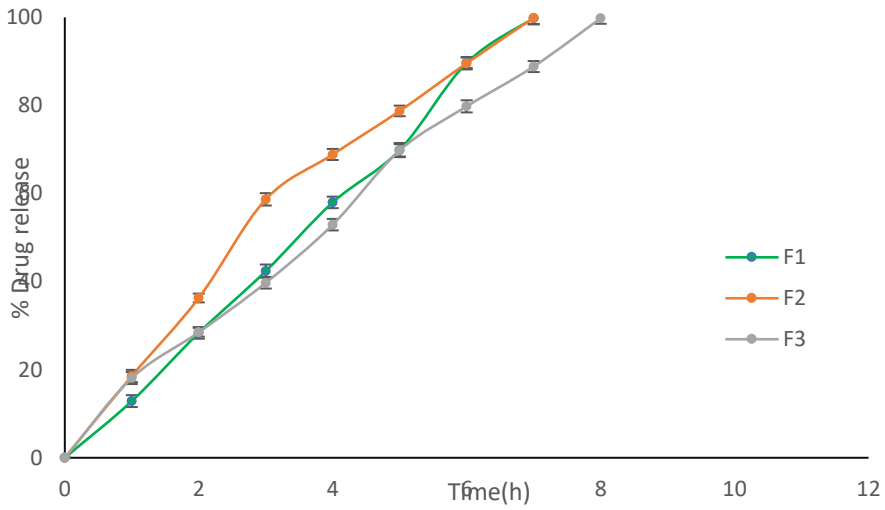


Fig 5: In *vitro* release profile of Rosuvastatin calcium Floating Tablets (F_1-F_3)in in simulated gastric fluid of pH 1.2 0.1N HCl.

Table 8:*In Vitro* release profile of Rosuvastatin calcium floating Tablets (F_4 – F_5) in0.1N HCl of Ph 1.2

S.no	Time(hrs)	F_4	F_5	F_6
0	**0**	**0**	**0**	**0**
1	**1**	11.2	13.24	8.767
2	**2**	26.54	25.35	16.8
3	**3**	42.68	37.24	25.77
4	**4**	56.58	48.52	34.77
5	**5**	67.35	64.98	42.8
6	**6**	78.94	79.78	54.63
7	**7**	89.38	90.36	67.93
8	**8**	99.47	99.65	74.8
9	**9**			80.6
10	**10**			88.63
11	**11**			93.77
12	**12**			99.87

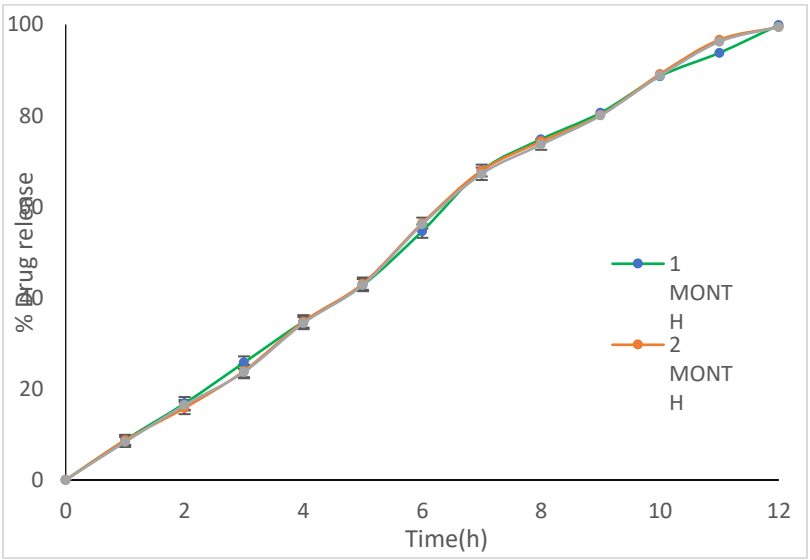


Fig 6: *In Vitro* release profile of Rosuvastatin calcium floating Tablets (F_4 F_6) in 0.1N HCl of pH 1.2

Table 9: *In Vitro* release profile of Rosuvastatin calcium floating Tablets (F_7- F_9) in simulated gastric fluid of pH 1.2 0.1N HCL

S.No	Time (hrs)	F_7	F_8	F_9
	0	**0**	**0**	**0**
1	**1**	13.87	8.767	12.1
2	**2**	27.87	16.8	24.5
3	**3**	40.77	25.77	34.73
4	**4**	58.67	34.77	44.93
5	**5**	70.67	42.8	56.8
6	**6**	82.8	52.63	67.79
7	**7**	89.77	66.93	83.83
8	**8**	99.6	72.8	92.8
9	**9**		79.6	99.8
10	**10**		89.63	
11	**11**		99.88	
12	**12**			

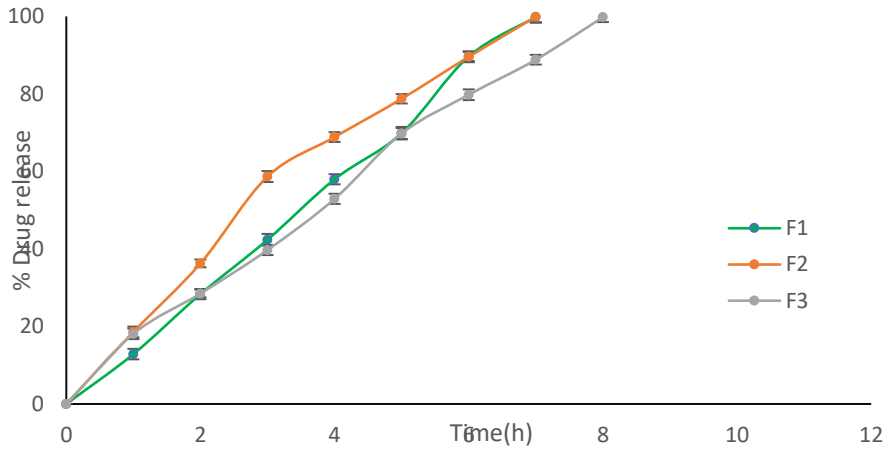


Fig 7: *In Vitro* release profile of Rosuvastatin floating Tablets (F_7- F_9) in 0.1NHCl of pH1.2

Table 10:*In Vitro* release profile of Rosuvastatin calcium floating Tablets (F_7- F_9) in simulated gastric fluid of pH 1.2 0.1N HCL

S.No	Time (hrs)	F_{10}	F_{11}	F_{12}
	0	**0**	**0**	**0**
1	**1**	0	0	0
2	**2**	12.21	14.24	19.23
3	**3**	21.1	26.35	29.2
4	**4**	32.54	38.24	40.67
5	**5**	46.22	49.54	52.45
6	**6**	57.65	62.98	66.67
7	**7**	68.24	78.78	75.51
8	**8**	79.58	89.36	86.38
9	**9**	88.67	99.65	98.96
10	**10**	92.68		
11	**11**	99.87		
12	**12**			

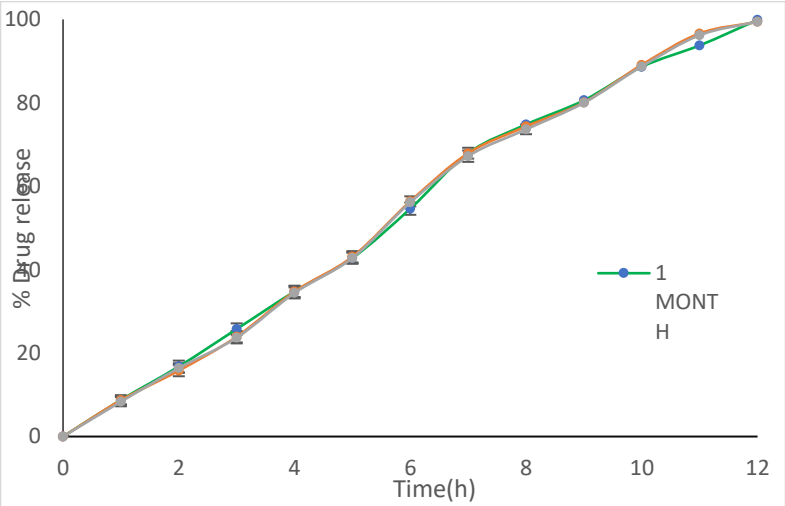


Fig 8: *In Vitro* release profile of rosuvastatin floating Tablets (F_{10}- F_{12}) in 0.1NHCl of pH1.2

Accelerated stability studies

In any rationale design and evaluation of dosage forms for drugs, the stability of the active component must be major criteria in determining their acceptance or rejection.

During the stability studies the product is exposed to normal conditions of temperature and humidity. However, the studies will take a longer time and hence it would be convenient to carry out the accelerated stability studies where the product is stored under extreme conditions of temperature. In the present study, stability studies were carried out on formulation F_9. The tablets were stored at 40 ± 2^0 C/75 ± 5 % RH for a duration of one month.

Theselected formulation was evaluated for stability studies. The formulation was stored at 40°C at 75%RH for 3 months and analysed for their physical parameters, drug content and friability after 3rd month the data were showed in table no 21.

Table 11: Accelerated stability studies

	Drug content(%)	**Hardness (kg/cm^2)**	**Friability(%)**
After one month	99.63±0.17	5.8±0.45	0.45
After 3 months	99.59±0.15	5.7±0.42	0.46

Table 12: *In Vitro* Dissolution Studies

Time(hrs)	**Initial**	**1^{s}month**	**3rdmonth**
0	**0**	0	0
2	8.767	8.72	8.35
2	16.8	15.82	16.42
3	25.77	23.93	23.71
4	34.77	34.75	34.43
5	42.8	43.1	42.81
6	54.63	56.38	56.13
7	67.93	67.91	67.21
8	74.8	74.33	73.63
9	80.6	80.11	80.01
10	88.63	89.11	88.73
11	93.77	96.63	96.21
12	99.87	99.42	99.46

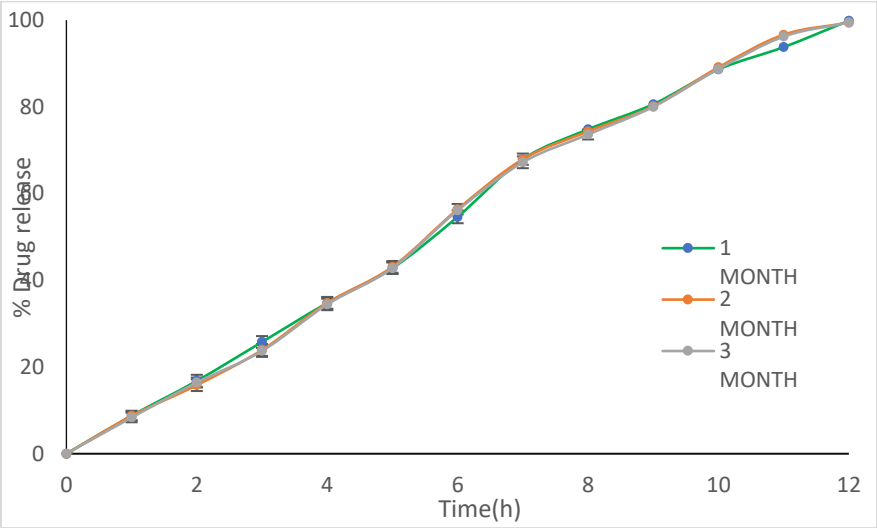


Fig 9: Accelerated Stability Studies

Rosuvastatin calcium floating tablets are a pharmaceutical formulation designed to release the medication slowly and provide extended drug delivery in the gastrointestinal tract. These tablets contain rosuvastatin, a potent statin medication used to lower cholesterol levels and reduce the risk of cardiovascular events. The floating property allows the tablets to remain buoyant in the stomach, ensuring prolonged contact with the gastric fluid and improving drug absorption. Various formulation techniques and excipients can be employed to achieve the desired floating behavior and drug release profile. Rosuvastatincalcium floating tablets offer a promising approach for controlled release, enhancing patient compliance by reducing dosing frequency and maintaining therapeutic drug levels.[8]

The physical mixtures were assessed for bulk density, tapped density, Carr's index, and Hausner ratio to evaluate their powder characteristics. Further characterization of the drug and polymer mixture was conducted using FTIR analysis. The results indicated no interaction between the drug and polymer, as the key peaks of the drug remained unchanged in the IR spectra of the drug-polymer physical mixture.[9]

In the current study, the focus was on the development of floating tablets of Rosuvastatin calcium using the Effervescent floating technique. To achieve the desired floating behavior, different polymers including HPMC K4M, carbopol 940, and Guar gum were utilized, along with the incorporation of NaHCO3 into the tablet formulation. This combination of polymers and the effervescent agent facilitated the floating of the tablets in simulated gastric fluid.[10]

The formulations were prepared using various ratios of HPMC K4M and carbopol 940, both individually and in combination. The purpose of this approach was to optimize the floating properties and drug release characteristics of the tablets. The prepared formulations underwent evaluation through physical tests to assess their appearance, hardness, and weight uniformity. Additionally, buoyancy lag time, which indicates the time taken for the tablet to start floating, and dissolution testing were performed to evaluate the release of the active ingredient.[11,12]

By conducting these evaluations, the researchers aimed to determine the most suitable combination of polymers and formulation ratio that would result in tablets with desirable floating behavior, optimal physical properties, and consistent drug release. Such floating tablets have the potential to improve drug absorption and provide prolonged drug release in the stomach, enhancing therapeutic outcomes and patient compliance.

Overall, this study sought to explore the feasibility of developing floating tablets of Rosuvastatin calcium using the Effervescent floating technique and assess their performance through various evaluation parameters, ultimately aiming to enhance the drug delivery system for improved patient treatment.

Based on the evaluation of floating lag time and release characteristics, formula F6 was identified as the optimal formulation. F6 demonstrated a floating lag time of 171±0.81 seconds, a floatation time of 24 hours, and an impressive cumulative drug release of 99.87%. Notably, this formulation exhibited sustained release characteristics throughout the entire release period. To further assess its performance, formulation F6 was compared to a commercially available marketed formulation.

The in-vitro release data of Rosuvastatin calcium from the floating tablets were analyzed using various kinetic models. The fitting of the data to these models aimed to elucidate the release kinetics of the drug. Specifically, for formulation F6, the obtained 'n' value of 1.542 indicates that the drug release mechanism involves high polymer relaxation and swelling/erosion.

CONCLUSION

Rosuvastatin floating tablets present a viable strategy for controlled drug release and improved therapeutic outcomes. The floating characteristic allows the tablets to reside in the stomach for an extended period, increasing drug absorption and optimizing the bioavailability of rosuvastatin. By maintaining consistent drug levels over an extended duration, these tablets offer potential benefits such as reduced dosing frequency, enhanced patient adherence, and improved

efficacy in managing hyperlipidemia and reducing cardiovascular risk. However, the development of effective rosuvastatin floating tablets requires careful formulation design, considering factors such as polymer selection, tablet geometry, and release modifiers to achieve the desired floating behavior and drug release profile. Further research and development in this area hold promise for advancing the field of Prolonged-release formulations and improving patient outcomes in the treatment of dyslipidemia. Basedon these findings, it can be concluded that the developed formulation holds promise and should be considered for further *in vivo* studies.

REFERENCES

1. Homayun B, Lin X, Choi HJ. Challenges and recentprogress in oraldrugdeliverysystems for biopharmaceuticals.Pharmaceutics.2019Mar19;11(3):129. doi: 10.3390/pharmaceutics11030129, PMID 30893852, PMCID PMC6471246.
2. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oraldrugdelivery.Front Pharmacol.2021Feb19;12:618411. doi: 10.3389/fphar.2021.618411, PMID 33679401, PMCID PMC7933596.
3. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: a review. AAPS PharmSciTech.2005Oct19;6(3):E372-90. doi: 10.1208/pt060347, PMID 16353995, PMCID PMC2750381.
4. NBI. Medline plus. Rosuvastatin.Available from: https://medlineplus.gov/druginfo/meds/a603033.html#:~:text=Rosuvastatin%20is%20in%20a%20class,other%20parts%20of%20the%20body.[Posted;07/20/2021].
5. Response surfacemethod. Mechatronics and manufacturingengineering;2012.Available from: https://www.sciencedirect.com/topics/engineering/response-surface-method.
6. The openeducator. Box-Behnkenresponsesurfacemethodology[citedJul 172023]. Available from: https://www.theopeneducator.com/doe/Response-Surface-Methodology/Box-Behnken-Response-Surface-Methodology.
7. Maggi L, Segale L, Torre ML, Ochoa ME, Conte U. Dissolution behaviour of hydrophilic matrix tablets containing two different polyethylene oxides (PEOs) for the controlled release of a water-soluble drug. Dimensionality study.Biomaterials.2002Feb;23(4):1113-9. doi: 10.1016/s0142-9612(01)00223-x, PMID 11791914.
8. Luvai A, Mbagaya W, Hall AS, Barth JH. Rosuvastatin: a review of the pharmacology and clinical effectiveness in cardiovascular disease. Clin Med Insights Cardiol.2012;6:17-33. doi: 10.4137/CMC.S4324. PMID 22442638, PMCID PMC3303484.
9. Wadher KJ, Kakde RB, Umekar MJ. Formulation and evaluation of a sustained-release tablets of metformin hydrochloride using hydrophilic synthetic and hydrophobic natural polymers. Indian J Pharm Sci.2011Mar;73(2):208-15. doi: 10.4103/0250-474x.91579, PMID 22303065, PMCID PMC3267306.
10. NaveedA, SyedZ.shaikaliabbas, Mohdirfan. Formulation and evaluation of rosuvastatin calciumoralfloatingtablets. ResJ Pharm Technol. Nov2012;5(11):1389-92. Available from: https://www.researchgate.net/publication/281638137_Formulation_and_Evaluation_of_Rosuvastatin_Calcium_Oral_Floating_Tablets.
11. Arshad MS, Kiran M, Mudassir J, Farhan M, Hussain A, Abbas N. Formulation, Optimization, in vitro and in-vivo evaluation of levofloxacinhemihydrate Floating Tablets. BrazJ PharmSci. 2022Mar14;58:e18630. doi: 10.1590/s2175-97902022e18630.
12. Li S, Lin S, Daggy BP, Mirchandani HL, Chien YW. Effect of HPMC and Carbopol on the release and floating properties of Gastric Floating Drug Delivery System using factorial design.Int J Pharm.2003Mar6;253(1-2):13-22. doi: 10.1016/s0378-5173(02)00642-7, PMID 12593933.