Formulation And Evaluation of Repaglinide Control Release Tablet

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***Abstract*—The present study aimed to formulate and evaluate controlled release tablets of Repaglinide for prolonged drug delivery in the treatment of type 2 diabetes mellitus. Controlled release tablets were prepared by the wet granulation method using hydroxypropyl methylcellulose (HPMC) and Eudragit RS100 as release-retarding polymers. Preformulation studies confirmed the acceptable physicochemical properties of Repaglinide. The prepared formulations were evaluated for pre-compression and post-compression parameters, including angle of repose, bulk density, tapped density, hardness, friability, weight variation, and drug content. All formulations showed satisfactory flow properties, mechanical strength, and uniform drug distribution. In vitro dissolution studies demonstrated sustained drug release over 12 hours. Among all formulations, F8 and F12 exhibited optimized drug release profiles with prolonged release characteristics. The study concluded that controlled release matrix tablets of Repaglinide can be successfully developed to improve therapeutic efficacy and patient compliance in diabetes management.**

***Index Terms*—Repaglinide, Controlled Release Tablets, Matrix Tablets, Sustained Drug Release, HPMC, Eudragit RS100, Wet Granulation, Diabetes Mellitus.**

I. INTRODUCTION

The oral route of drug administration remains the most preferred and widely accepted method for drug delivery because of its convenience, cost-effectiveness, ease of administration, and improved patient compliance.[1-3] However, conventional oral dosage forms often fail to maintain uniform plasma drug concentrations for prolonged periods due to rapid drug release and elimination. These fluctuations in plasma concentration may result in subtherapeutic effects or toxic manifestations, thereby reducing therapeutic efficacy. To overcome these limitations, controlled release drug delivery systems have been extensively developed to provide sustained therapeutic[4-5] action by regulating the rate and extent of drug release over an extended period of time. Controlled release formulations are specifically designed to maintain consistent plasma drug levels, minimize dosing frequency, reduce side effects, and improve overall patient adherence to therapy.[6-7]

Controlled release drug delivery systems have gained significant importance in the management of chronic diseases such as diabetes mellitus, hypertension, cardiovascular disorders,[8-9] and neurological conditions where long-term pharmacotherapy is required. These systems are capable of delivering the drug at a predetermined and controlled rate, thereby maintaining the desired therapeutic concentration in systemic circulation for an extended duration.[10] Compared with conventional immediate-release dosage forms, controlled release formulations reduce the frequency of administration and enhance patient convenience. In addition, they reduce fluctuations in plasma drug concentration, improve bioavailability, decrease dose-related adverse effects, and optimize therapeutic outcomes.[11-14]

Among various oral controlled release systems, matrix tablets are one of the most widely employed approaches due to their simplicity of formulation, ease of manufacturing, cost-effectiveness, and reproducibility. In matrix systems, the drug is uniformly dispersed within a polymeric matrix that controls drug release through mechanisms such as diffusion, swelling, and erosion. Hydrophilic polymers, hydrophobic polymers, or combinations of both are commonly used to modulate the release profile of the incorporated drug. The rate of drug release from matrix tablets depends upon several formulation variables including the type and concentration of polymer, drug solubility, tablet hardness, porosity, and dissolution medium. The

successful development of controlled release matrix tablets requires careful selection of excipients and optimization of formulation parameters to achieve the desired release kinetics and therapeutic performance.[15-18]

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The disease is associated with severe complications including cardiovascular diseases, nephropathy, neuropathy, and retinopathy, which significantly affect the quality of life of patients. Effective glycemic control is essential for reducing diabetes-related complications and improving long-term clinical outcomes.[19-22] Oral hypoglycemic agents are extensively used in the treatment of type 2 diabetes mellitus, particularly in patients who are unable to achieve adequate glycemic control through lifestyle modifications alone. Continuous and prolonged maintenance of blood glucose levels within the normal range is necessary for effective diabetes management, which highlights the importance of controlled release formulations in antidiabetic therapy.

Repaglinide is an oral antidiabetic agent belonging to the meglitinide class that stimulates insulin secretion from pancreatic β-cells by blocking ATP-sensitive potassium channels. It is widely used in the management of type 2 diabetes mellitus because of its rapid onset and short duration of action. Repaglinide effectively controls postprandial blood glucose levels; however, it possesses certain pharmacokinetic limitations such as short biological half-life, rapid elimination, and the requirement for frequent administration. These characteristics may lead to fluctuations in plasma drug concentration and reduced patient compliance during long-term therapy. Therefore, the development of a controlled release formulation of Repaglinide can provide prolonged therapeutic action, maintain stable plasma drug concentrations, reduce dosing frequency, and improve patient adherence and therapeutic efficacy.[23-25]

The formulation of controlled release tablets of Repaglinide presents a promising strategy for improving the pharmacokinetic and pharmacodynamic profile of the drug. By incorporating suitable release-retarding polymers, the release of Repaglinide can be controlled in a predictable manner, thereby prolonging drug action and minimizing plasma concentration fluctuations. Hydrophilic matrix-forming polymers such as hydroxypropyl methylcellulose (HPMC), carbopol, xanthan gum, and ethyl cellulose are frequently employed in controlled release formulations due to their excellent swelling, gel-forming, and release-controlling properties. These polymers form a hydrated barrier around the tablet upon contact with gastrointestinal fluids, which regulates drug diffusion and matrix erosion, ultimately controlling the release rate of the drug.[26-30]

Several factors influence the design and performance of controlled release formulations, including drug solubility, biological half-life, absorption window, partition coefficient, stability, and dose size. Drugs with short half-lives and suitable absorption characteristics are considered ideal candidates for controlled release systems. In addition, physiological factors such as gastrointestinal pH, gastric emptying time, intestinal transit time, and food intake may also affect the in vivo performance of controlled release dosage forms. Therefore, a thorough understanding of drug properties, polymer characteristics, and gastrointestinal physiology is essential for the successful development of an effective controlled release formulation.[31-35]

The present research work focuses on the formulation and evaluation of controlled release tablets of Repaglinide using suitable polymeric systems to achieve prolonged drug release and enhanced therapeutic efficacy. The prepared formulations are evaluated for various pre-compression and post-compression parameters including angle of repose, bulk density, tapped density, hardness, friability, weight variation, drug content, swelling index, and in vitro dissolution studies. The optimization of formulation variables and release characteristics aims to develop a stable and effective controlled release dosage form capable of improving glycemic control and patient compliance in the management of type 2 diabetes mellitus.

II. MATERIALS AND METHODS

Materials:

The materials selected for the controlled-release tablets of Repaglinide include Repaglinide (API) from Microlabs Ltd, Hosur**.** Hydroxypropyl Methylcellulose (HPMC) from LOBA CHEM is used as a hydrophilic polymer to control the drug release.

Eudragit 100 from COSMO CHEM is included to modify the release rate through its film-forming properties.

Methods:[36-64]

1. Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of Repaglinide prior to formulation development. Organoleptic properties such as color, odor, and appearance were examined. The melting point of the drug was determined using Thiele's tube apparatus to confirm purity and identity. Flow properties of the powder blend were assessed by measuring the angle of repose, which indicates the frictional characteristics and flow behavior of granules. These studies provided essential information for the development of stable and effective controlled release tablets.

2. Determination of Standard Calibration Curve

The absorption maximum (λmax) of Repaglinide was determined using a UV-visible spectrophotometer by scanning the drug solution in the wavelength range of 200–400 nm. Standard calibration curves were prepared in different media including methanol, distilled water, and phosphate buffer solutions.

For calibration in 0.1 N HCl, 100 mg of Repaglinide was dissolved in 100 mL of 0.1 N HCl to obtain a primary stock solution of 1000 µg/mL. Further dilution was carried out to prepare a secondary stock solution of 100 µg/mL. Aliquots of 0.2–1.0 mL were transferred into 10 mL volumetric flasks and diluted with 0.1 N HCl to obtain concentrations of 2–10 µg/mL. The absorbance of these solutions was measured at 281 nm using a UV spectrophotometer, and the calibration curve was plotted.

3. Infrared Spectroscopy

Fourier Transform Infrared (FTIR) spectroscopy was performed to identify the characteristic functional groups and evaluate the purity of Repaglinide. The spectra were recorded using a Bruker FTIR spectrophotometer in the scanning range of 4000–400 cm^{-1}. Samples were prepared using the KBr pellet method.

4. Preparation of Controlled Release Tablets

Controlled release tablets of Repaglinide were prepared by the wet granulation method using hydroxypropyl methylcellulose (HPMC), microcrystalline cellulose, and Eudragit RS100 as release-retarding polymers. All ingredients except lubricants were blended thoroughly, followed by the addition of Repaglinide for uniform mixing. Granulation was carried out using polyvinyl pyrrolidone (PVP) solution prepared in isopropyl alcohol as a binder. The wet mass was passed through sieve no. 10 and dried at 40°C for 30 minutes. The dried granules were sieved through mesh no. 22–44 and mixed with magnesium stearate and talc as lubricants. Finally, the granules were compressed using a rotary tablet compression machine to obtain tablets of suitable hardness.

Table 1: Formulation for preparation control release tablet Repaglinide

Ingredients (mg)	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12
Repaglinide	1	1	1	1	1	1	1	1	1	1	1	1
Eudragit Rs100	-	-	-	-	30	40	15	60	15	20	25	30
hydroxy propyl methyl cellulose	30	40	50	60	-	-	-	-	15	20	25	30
Micro crystallinecellulose	66	56	46	36	66	56	46	36	66	56	46	36
Magnesium Stearate	1	1	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Total	100	100	100	100	100	100	100	100	100	100	100	100

III. EVALUATION OF CONTROLLED RELEASE TABLETS

A. Weight Variation Test

The uniformity of tablet weight was evaluated to ensure consistency in the formulation process. Twenty tablets from each batch were selected randomly and weighed individually using a calibrated digital balance. The average tablet weight was calculated, and individual weights were compared with the average value according to pharmacopeial specifications.

B. Hardness Test

The mechanical strength of the tablets was determined

by measuring tablet hardness using a Pfizer hardness tester. Five tablets from each formulation batch were tested, and the force required to break each tablet under diametric compression was recorded. The hardness test was performed to ensure that the tablets possessed adequate strength to withstand handling and transportation.

C. Friability Test

Friability testing was carried out using an Electrolab friabilator to assess the resistance of tablets to abrasion and mechanical stress. Pre-weighed tablets were placed in the friabilator and rotated at 25 rpm for 100 revolutions. After completion of the test, the tablets were dedusted and reweighed. The percentage weight loss was calculated to determine the friability of the formulations.

D. Drug Content Uniformity

Drug content uniformity was evaluated to ensure uniform distribution of Repaglinide within the tablets. Ten tablets were accurately weighed and finely powdered. A quantity of powder equivalent to 10 mg of Repaglinide was transferred into a volumetric flask containing pH 7.4 phosphate buffer. The solution was filtered, suitably diluted, and analyzed using a UV-visible spectrophotometer at the selected wavelength. The percentage drug content was calculated for each formulation.

E. In Vitro Drug Release Study

The in vitro dissolution study was performed using a USP dissolution apparatus at a temperature of 37 ± 0.5°C and a rotation speed of 100 rpm. Initially, the tablets were placed in 900 mL of acidic dissolution medium (pH 1.2) for the first 2 hours, followed by phosphate buffer pH 7.4 for the remaining study period to simulate gastrointestinal conditions. At predetermined intervals, aliquots of dissolution medium were withdrawn and replaced with an equal volume of fresh medium to maintain sink conditions. The collected samples were analyzed using a UV-visible spectrophotometer at the appropriate wavelength to determine the amount of drug released from the tablets over time.

IV. RESULT AND DISCUSSION:

1. Physicochemical Properties of Repaglinide

A. Organoleptic Characteristics

The organoleptic properties of Repaglinide were evaluated to confirm its identity and purity. The drug was observed as a white crystalline powder with an odourless nature, which complied with the standard specifications. These characteristics indicated the acceptable quality of the drug sample used for formulation development.

Table 2: organoleptic properties of Repaglinide

Parameter	Specification	Observation
Color	White to off-white powder	White powder
Odour	Odourless	Odourless

B. Melting Point Determination

The melting point of Repaglinide was determined and found to be 131°C, which was in close agreement with the reported standard value of 130–131°C. The observed melting point confirmed the purity and authenticity of the drug sample.

C. Standard Calibration Curve of Repaglinide

The calibration curve of Repaglinide was developed using UV-visible spectrophotometry. Different concentrations of the drug solution (2–20 µg/mL) were prepared and scanned within the wavelength range of 200–400 nm. The maximum absorbance (λmax) was observed at 281 nm. A linear relationship between concentration and absorbance was obtained, indicating compliance with Beer-Lambert's law and confirming the suitability of the analytical method for drug estimation.

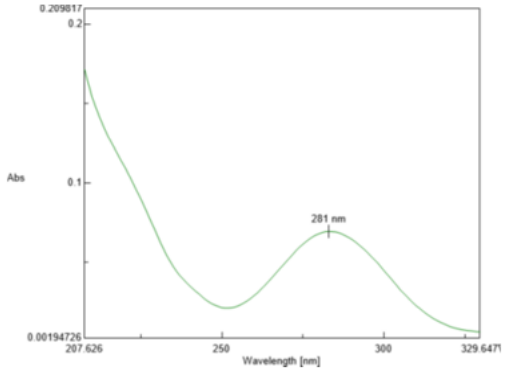

Figure 1: Calibration curve of Repaglinide

Solubility: Table showing the Solubility of Repaglinide (API) in various solvents.

Table 3: Solubility of Repeglinide

Solvents	Solubility
Water	Practically insoluble
Phosphate Buffer pH 6.8	soluble
methanol	soluble
ethanol	soluble

2. Evaluation of Controlled Release Tablets

A. Pre-Compression Parameters

The pre-compression properties of the powder blends were evaluated to determine their suitability for tablet compression. The angle of repose values ranged from 21.85° to 30.94°, indicating good flow characteristics of the granules. Bulk density and tapped density values demonstrated satisfactory packing ability of the powder blends. Carr's index and Hausner ratio values further confirmed acceptable flowability and compressibility, which are essential for uniform die filling and tablet formation. Overall, the results suggested that all formulations possessed adequate flow and compression properties suitable for the preparation of controlled release tablets.

Table 4: Pre-Compression Parameters of Repaglinide Controlled Release Tablets

Formulation Code	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner Ratio
C1	30.61	0.190	0.206	7.71	1.09
C2	25.63	0.195	0.219	6.71	1.08
C3	21.85	0.177	0.192	13.52	1.15
C4	23.74	0.145	0.154	13.46	1.14
C5	24.77	0.135	0.174	14.25	1.24
C6	25.75	0.142	0.150	9.25	1.12
C7	26.52	0.164	0.192	16.75	1.19
C8	25.74	0.199	0.230	14.92	1.10
C9	22.56	0.134	0.234	13.25	1.20
C10	25.46	0.165	0.151	12.25	1.18
C11	23.74	0.145	0.219	11.52	1.16
C12	30.94	0.170	0.220	10.33	1.15

The pre-compression evaluation indicated satisfactory flow and compressibility characteristics of all formulations. The angle of repose ranged from 21.85° to 30.94°, indicating good flow behavior of the granules. Bulk density and tapped density values demonstrated acceptable packing ability, while Carr's index and Hausner ratio confirmed suitable compressibility and flow properties for tablet compression.

B. Post-Compression Parameters

The prepared Repaglinide tablets were evaluated for various post-compression parameters to ensure quality and uniformity. The tablet weights were found within the range of 100–104 mg, indicating acceptable weight uniformity among formulations. Friability values ranged from 0.665% to 0.990%, which were below the pharmacopeial limit of 1%, demonstrating good mechanical resistance and low susceptibility to abrasion.

The hardness of the tablets ranged from 4.6 to 6.7 kg/cm², indicating sufficient mechanical strength to withstand handling and transportation. These results confirmed that the tablets possessed adequate physical integrity while maintaining controlled drug release properties.

Table 5: Post-Compression Parameters of Repaglinide Controlled Release Tablets

Formulation Code	Weight Variation (mg)	Friability (%)	Hardness (kg/cm²)	Drug Content (%)
C1	100	0.891	5.6	97.32
C2	101	0.866	5.6	95.14
C3	103	0.921	5.6	96.00
C4	101	0.891	5.6	93.26
C5	100	0.901	6.7	98.55
C6	104	0.745	6.7	96.45
C7	100	0.665	6.7	96.15
C8	101	0.990	6.7	94.22
C9	100	0.930	4.6	95.55

C10	101	0.980	4.6	98.22
C11	100	0.865	4.6	97.66
C12	100	0.891	4.6	96.42

The post-compression evaluation confirmed that all tablet formulations complied with acceptable quality standards. Weight variation was found within pharmacopeial limits, indicating uniformity in tablet weight. Friability values were below 1%, demonstrating good mechanical resistance and low susceptibility to abrasion. Hardness values indicated adequate tablet strength, while drug content analysis confirmed uniform distribution of Repaglinide within the formulations. These findings suggest that the prepared tablets possessed satisfactory physical integrity and formulation consistency.

C. In Vitro Dissolution Study

The in vitro dissolution study was carried out to evaluate the drug release behavior of the prepared controlled release tablets. The formulations exhibited sustained drug release patterns over an extended period. Among all formulations, F8 and F12 demonstrated better controlled release characteristics with prolonged drug release up to 12 hours. Formulation F8 showed 84.91% drug release, whereas formulation F12 exhibited 99.92% cumulative drug release at the end of the dissolution study.

Table 6: Dissolution Study of Repaglinide Control Release Tablets

Time (hr.)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	38.50	25.85	34.53	31.78	24.67	36.26	36.21	21.43	31.73	36.95	36.89	34.44
1.5	62.90	40.69	53.71	50.19	38.46	57.20	57.18	34.06	49.96	50.21	54.05	47.51
2	83.27	73.92	95.40	91.95	70.66	92.98	90.32	97.40	89.50	86.35	92.26	95.47

The results indicated that the selected polymers effectively controlled the release of Repaglinide from the matrix tablets and maintained prolonged drug release behavior suitable for sustained-release therapy.

Table 7: Kinetic Values of Repaglinide control release Tablets

Formulation code	Regression coefficient values of				Slope value (n)	
	Zero order	First order	Peppas	Higuchi	Peppas	Higuchi
F1	0.889	0.984	0.659	0.963	0.996	33.90
F2	0.863	0.986	0.656	0.960	0.995	30.82
F3	0.911	0.980	0.740	0.955	1.077	31.70
F4	0.888	0.983	0.618	0.977	0.923	28.11
F5	0.946	0.887	0.720	0.972	1.064	34.60
F6	0.888	0.986	0.665	0.969	0.997	31.43
F7	0.946	0.979	0.735	0.957	1.065	31.70
F8	0.892	0.987	0.641	0.979	0.942	27.95
F9	0.925	0.990	0.638	0.960	0.974	33.57
F10	0.901	0.993	0.691	0.965	1.035	31.73
F11	0.884	0.966	0.737	0.956	1.079	31.77
F12	0.887	0.986	0.630	0.978	0.931	27.76

The percentage drug release of all the formulations in acidic medium (pH 1.2) for 2 h, and in alkaline medium (pH 7.4) for remaining 10 h. The release was found to be 84.91 to 99.92 %. Formulation F8 and F12 showed prolonged release over a period of 12 h and % drug release found to be 84.91 %.

V. CONCLUSION

The present investigation successfully developed and evaluated controlled release matrix tablets of Repaglinide for prolonged drug delivery in the management of type 2 diabetes mellitus. Preformulation studies confirmed the acceptable physicochemical properties of the drug, including organoleptic characteristics, melting point, and compatibility profile. The developed analytical

method showed good linearity and reliability for quantitative estimation of Repaglinide. The prepared formulations exhibited satisfactory pre-compression and post-compression characteristics, indicating good flow properties, compressibility, mechanical strength, and content uniformity. In vitro dissolution studies demonstrated effective sustained drug release from the matrix tablets over an extended period. Among the formulations, F8 and F12 showed optimized release profiles with prolonged drug release up to 12 hours. Overall, the study confirmed that controlled release matrix tablets of Repaglinide can successfully formulated using suitable polymers to achieve sustained therapeutic action. The developed formulation may improve patient compliance, reduce dosing frequency, and enhance therapeutic effectiveness in the treatment of diabetes mellitus.

VI. CONFLICTS OF INTERESTS

The authors declares that there is no conflict of interest.

REFERENCES

[1] Javadzadeh Y, Hamedeyazdan S, Adibkia K, Kiafar F, Zarrintan MH, Barzegar-Jalali M. Evaluation of drug release kinetics and physico-chemical characteristics of metronidazole floating beads based on calcium silicate and gas-forming agents. Pharmaceutical Development and Technology. 2010 Aug 1; 15(4):329-38.

[2] Murata Y, Sasaki N, Miyamoto E, Kawashima S. Use of floating alginate gel beads for stomach-specific drug delivery. European journal of pharmaceutics and biopharmaceutics.2000 Sep 1; 50(2):221-6.

[3] Gholap SB, Banarjee SK, Gaikwad DD, Jadhav SL, Thorat RM. Hollow microsphere: A review. International Journal of Pharmaceutical Sciences Review and Research. 2010 Mar;1(1):74-9.

[4] Soppimath KS, Aminabhavi TM, Agnihotri SA, Mallikarjuna NN, Kulkarni PV. Effect of coexcipients on drug release and floating property of nifedipine hollow microspheres: A novel gastro retentive drug delivery system. Journal of applied polymer science. 2006 Apr5; 100(1):486-94.

[5] Babu VB, Khar RK. In vitro and in vivo studies of sustained-release floating dosage forms containing salbutamol sulfate. Die Pharmazie. 1990 Apr 1; 45(4):268-70.

[6] Wagner JG. Interpretation of percent dissolved-time plots derived from in vitro testing of conventional tablets and capsules. Journal of pharmaceutical sciences. 1969 Oct 1; 58(10):1253-7.

[7] Barzegar-Jalali M. Kinetic analysis of drug release from nanoparticles. Journal of Pharmacy & Pharmaceutical Sciences. 2008 May 7; 11(1):167-77.

[8] Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm. 2010 May 1; 67(3):217-23.

[9] Arifin DY, Lee LY, Wang CH. Mathematical modeling and simulation of drug release from microspheres: Implications to drug delivery systems. Advanced drug delivery reviews. 2006 Nov 30; 58(12-13):1274-325.

[10] Adibkia K, Hamedeyazdan S, Javadzadeh Y. Drug release kinetics and physicochemical characteristics of floating drug delivery systems. Expert opinion on drug delivery. 2011 Jul 1; 8(7):891-903.

[11] Timmermans J, Moes AJ. Measuring the resultant-weight of an immersed test material: II. Examples of kinetic determinations applied to monolithic dosage forms. Acta pharmaceutica technologica. 1990; 36(3):176-80.

[12] Khan AD. MeenakshiBajpai: Floating Drug Delivery System: An Overview. International Journal of PharmTech Research, CODEN (USA): IJPRIF ISSN. 2010:0974-4304.

[13] Gopalakrishnan S, Chenthilnathan A. Floating drug delivery systems: A Review. Journal of Pharmaceutical science and technology. 2011; 3(2):548-54.

[14] Fell JT, Whitehead L, Collett JH. Prolonged gastric retention: using floating dosage forms. Pharmaceutical technology. 2000 Mar; 24(3):82-90.

[15] Moursy NM, Afifi NN, Ghorab DM, El-Saharty Y. Formulation and evaluation of sustained release floating capsules of Nicardipine hydrochloride. Die Pharmazie-An International Journal of Pharmaceutical Sciences. 2003 Jan 1; 58(1):38-43.

[16] Vasave VS. A review on: floating drug delivery system. World Journal of Pharmaceutical Research. 2023; 12(2):641-69.
[17] Chaudhary S, Dua JS, Prasad DN. Recent Development in Floating Drug Delivery System: An Overview. Journal of Drug Delivery and Therapeutics. 2022 Jan 15; 12(1):185-93.
[18] Dhone PG, Sahu YP, Sabitri B, Khandelwal PN. Formulation and Evaluation of Floating Tablet of Levofloxacin. International Journal of Health Sciences. JUN 2022 (I):13468-77.
[19] Fang D, Pan H, Cui M, Qiao S, Li X, Wang T, Meng Q, Xu L, Pan W. Fabrication of three-dimensional-printed ofloxacin gastric floating sustained-release tablets with differentstructures. Journal of Drug Delivery Science and Technology. 2022 Jan 1; 67:102992.
[20] Naseem F, Shah SU, Rashid SA, Farid A, Almehmadi M, Alghamdi S. Metronidazole based floating bioadhesive drug delivery system for potential eradication of H. pylori: preparation and in vitro characterization. Polymers. 2022 Jan 27; 14(3):519.
[21] Rajora A, Nagpal K. A critical review on floating tablets as a tool for achieving better gastric retention. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2022; 39(1).
[22] Charoenying T, Patrojanasophon P, Ngawhirunpat T, Rojanarata T, Akkaramongkolporn P, Opanasopit P. Design and optimization of 3D-printed gastroretentive floating devices by central composite design. AAPS PharmSciTech. 2021 Jul; 22:1-8.
[23] Sakamoto A, Izutsu KI, Yoshida H, Abe Y, and Inoue D, Sugano K. Simple bicarbonate buffer system for dissolution testing: Floating lid method and its application to colonic drug delivery system. Journal of Drug Delivery Science and Technology. 2021 Jun 1; 63:102447.
[24] Aundhia C, Shah N, Patel S, Sen AK, Patel P. Formulation and Evaluation of Floating Tablet of Norfloxacin. International Journal of Pharmaceutical Research. 2020 Jan 2; 12(1).
[25] Harish C. Formulation and Evaluation of Bilayer Tablets: Glimepiride in Floating Drug Delivery and Metformin in Sustained Release (Doctoral dissertation, PSG College of Pharmacy, Coimbatore).
[26] Ji J, He X, Yang XL, Du WJ, Cui CL, Wang L, Wang X, Zhang CF, Guo CR. The in vitro/vivo evaluation of prepared gastric floating tablets of Berberine hydrochloride. AAPS Pharm SciTech. 2017 Aug; 18:2149-56.
[27] Sharma P, Verma Am, Chaudhary R, Joshi V. Formulate And Evaluate Floating Tablet Of Ofloxacin Using HPMC. Asian Journal of Pharmaceutical Science & Technology. 2016 OCT Vol 6, Issue 2 115-119.
[28] Ahsan M, Abbas N, Hussain A, Saeed H, Shah PA, Mohammad S, Arshad MS. Formulation optimization and in-vitro evaluation of oral floating captopril matrix tablets using factorial design. Tropical Journal of Pharmaceutical Research. 2015; 14(10):1737- 48.
[29] Gul S, Sajid S. Formulation of improved norfloxacin HCl tablets: quality control assessment and comparison study of acidic and basic form of norfloxacin in tabletformulation. J Develop Drugs. 2015; 5(145):2.
[30] Kesarla RS, Vora PA, Sridhar BK, Patel G, Omri A. Formulation and evaluation of floatingtablet of H2-receptor antagonist. Drug development and industrial pharmacy. 2015 Sep 2;41(9):1499-511.
[31] Rathore J, Parmar HK. Formulation and evaluation of floating tablet norfloxacin. International Journal of Pharma Sciences and Research. 2015; 6(1):23-7.
[32] Verma P, Khinchi MP, Soni SL. Formulation and Evaluation of Ranitidine Floating Tablets. Asian Journal of Pharmaceutical Research and Development. 2015 Jul 1:15-20.
[33] Kavitha K, Rajesh G, Ramesh S, Shivaleela S, Lavanya P. Formulation and Evaluation of Ranitidine Floating Tablets. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2013 Jul 1; 3(3).
[34] Mahde BW, Ghareeb MM, Abdulrasool AA. Formulation and evaluation of gastroretentive floating tablet of bromocriptine mesilate. International Journal of Pharmacy and Pharmaceutical Sciences. 2013; 5(1):361-5.
[35] Malisetty SC, Allena RT, Sandina S, Gangadharappa HV. Formulation and evaluation of modified-release effervescent floating tablets of ofloxacin. Int J Health Allied Sci. 2013 Apr 1; 2(2):99-107.
[36] Nanjwade BK, Adichwal SA, Sutar KP. Development and evaluation of glipizide floating

tablet. In vitro. 2012 Jan 1; 10:15.
[37] Prajapati PH, Nakum VV, Patel CN. Formulation and evaluation of floating matrix tablet of stavudine. International Journal of pharmaceutical investigation. 2012 Apr; 2(2):83.
[38] Rangapriya M, Manigandan V, Natarajan R, Mohankumar K. Formulation and evaluation of floating tablets of Pioglitazone hydrochloride. International Journal of Pharmaceutical and Chemical Sciences. 2012; 1(3):1048-53.
[39] Saigeethika S, Singhvi G. Formulation and evaluation of floating tablets of ofloxacin. International Journal of Pharmaceutical Sciences and Research. 2012 Nov 1; 3(11):4291.
[40] Chander Shekar B, Shireesh Kiran R, Nagendra Babu B. Preparation and evaluation of gastro retentive floating tablets of ketoconazole. Int J Pharm. Research & Development. 2010; 2(9):174-84.
[41] Karkhile VG, Karmarkar RR, Sontakke MA, Badgujar SD, Nemade LS. Formulation and evaluation of floating tablets of furosemide. Int J Pharm Res Dev. 2010; 1:1-9.
[42] Ram HA, Lachake P, Kaushik U, Shreedhara CS. Formulation and evaluation of floating tablets of liquorice extract. Pharmacognosy research. 2010 Sep; 2(5):304.
[43] Bomma R, Naidu RA, Yamsani MR, Veerabrahma K. Development and evaluation of gastroretentive norfloxacin floating tablets. Acta pharmaceutica. 2009 Jun 1; 59(2):211- 21.
[44] Khan F, Razzak SM, Khan ZR, Azad MA, Chowdhury JA, and Reza S. Theophylline loaded gastroretentive floating tablets based on hydrophilic polymers: preparation and in vitro evaluation. Pakistan journal of pharmaceutical sciences. 2009 Apr 1; 22(2).
[45] Kumar R, Patil MB, Patil SR, Paschapur MS. Formulation and evaluation of effervescent floating tablet of famotidine. Int J Pharm Tech Res. 2009 Jul; 1(3):754-63.
[46] Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: A review. Int J Pharm Tech Res. 2009 Jul 1; 1(3):623-33.
[47] Gangadharappa H, Pramod K, Shiva KH. Gastric floating drug delivery systems: a review. Indian Journal of Pharmaceutical Education and Research. 2007 Oct 1; 41(4):295-305.
[48] Jaimini M, Rana AC, Tanwar YS. Formulation and evaluation of famotidine floating tablets. Current drug delivery. 2007 Jan 1; 4(1):51-5.
[49] Patel NM, Patel VF, Yeole PG. Studies on Formulation and Evaluation of Ranitidine Floating Tablets. Indian Journal of Pharmaceutical Sciences. 2005 Dec 1; 67(6):703-709.
[50] Srivastava AK, Wadhwa S, Ridhurkar D, Mishra B. Oral sustained delivery of atenolol from floating matrix tablets—formulation and in vitro evaluation. Drug development and industrial pharmacy. 2005 Jan 1; 31(4-5):367-74.
[51] Jiménez-Castellanos MR, Zia H, Rhodes CT. Design and testing in vitro of a bioadhesive and floating drug delivery system for oral application. International Journal of Pharmaceutics. 1994 Apr 25; 105(1):65-70.
[52] Gangadharappa H, Pramod K, Shiva KH. Gastric floating drug delivery systems: a review. Indian Journal of Pharmaceutical Education and Research. 2007 Oct 1; 41(4):295-305.
[53] Deshmukh K, Ahamed MB, Deshmukh RR, Pasha SK, Bhagat PR, Chidambaram K. Biopolymer composites with high dielectric performance: interface engineering. InBiopolymer composites in electronics 2017 Jan 1 (pp. 27-128). Elsevier.
[54] Francis FJ. Wiley encyclopedia of food science and technology. John Wiley and Sons Inc. 1999.
[55] Lewis RJ. Food additives handbook. Springer Science & Business Media; 1989.
[56] Snyder CH. The extraordinary chemistry of ordinary things. (No Title). 1995 Feb 7.
[57] Ann Bazar J, Rahimi M, Fathinia S, Jafari M, Chipakwe V, Chehreh Chelgani S. Talc flotation—an overview. Minerals. 2021 Jun 22
[58] Britannica T. Editors of encyclopaedia. Argon. Encyclopedia Britannica. 2020 Jul.;11(7):662.
[59] Wentzensen N, O'Brien KM. Talc, body powder, and ovarian cancer: a summary of the epidemiologic evidence. Gynecologic Oncology. 2021 Oct 1; 163(1):199-208.
[60] Yang X, Andersen J, Dinovi M, Veerabhadra M. Magnesium stearate of certain food additives and contaminants. 2015:37.
[61] Okoye PC. The Magnesium Stearate Handbook. iUniverse; 2016 Nov 18.
[62] Mutalik S, Manoj K, Reddy MS, Kushtagi P, Usha AN, Anju P, Ranjith AK, Udupa N.

Chitosan and enteric polymer based once daily sustained release tablets of aceclofenac: invitro and in vivo studies. AAPS PharmSciTech. 2008 Jun; 9:651-9.

[63] Dutta S, Sengupta M. Modified release dosage form and drug delivery. J Pharm Res. 2009 Nov;2(11):1728-9.

[64] Perioli L, Ambrogi V, Giovagnoli S, Ricci M, Blasi P, Rossi C. Mucoadhesivebilayeredtablets for buccal sustained release of flurbiprofen. AAPS pharmscitech. 2007 Sep; 8: E20-7.