International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 8 Issue 3, May-June 2024 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

Development and Assessment of Floating Pulsatile Drug Delivery Systems for Felodipine

Mr. Kalpesh S. Patil, Prof. Kalpeshkumar S. Wagh

KVPS's Institute of Pharmaceutical Education, Boradi, Maharashtra, India

ABSTRACT

This study developed various formulations of floating pulsatile drug delivery systems (FPDDS) for Felodipine using different polymers and excipients, aiming to synchronize drug release with physiological rhythms for improved hypertension and angina treatment. Optimization involved adjusting polymer concentrations, excipients ratios, and coating thicknesses to achieve desired release behavior. In vitro studies demonstrated promising results regarding floating behavior and release kinetics, with favorable drug release profiles in simulated conditions. Comprehensive data analysis confirmed the efficacy and feasibility of the drug delivery system. Materials, including Felodipine and various excipients, were procured and their identities confirmed via UV-visible scans and FT-IR spectra. Felodipine showed maximum absorbance at 363 nm with a linear calibration curve in methanol. Solubility studies indicated variable solubility across different solvents. The formulations exhibited excellent flow properties, with formulation F4 showing optimal characteristics. Post-compression parameters for tablets (C1-C3) met USP criteria, with formulation F8 demonstrating the best performance. Compatibility studies and DSC analysis indicated good stability and compatibility of components. Overall, the FPDDS tablets showed promising results in achieving the desired drug release profile, with formulation F8 emerging as the most effective.

KEYWORDS: *Felodipine, FPDDS, DSC, FT-IR etc*

How to cite this paper: Mr. Kalpesh S. Patil | Prof. Kalpeshkumar S. Wagh "Development and Assessment of Floating Pulsatile Drug Delivery Systems for Felodipine" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-8 | Issue-3, June 2024, pp.1134-1146, URL: www.ijtsrd.com/papers/ijtsrd67104.pdf

IJTSRD67104

INTRODUCTION

Floating Pulsatile Drug Delivery Systems (FPDDS): Pulsatile drug delivery systems (PDDS) are specifically designed to cater to diseases where a constant drug release is not required, but rather a timed release is crucial. These systems aim to release a predetermined quantity of drug after a certain delay, ensuring an optimal therapeutic effect. Various technologies exist for pulse-type drug release, such as micro flora-activated delivery, time-dependent systems, and pH-dependent systems. These approaches are tailored to the drug molecule's properties and the disease's physiological requirements. The primary objective of research in this field is to innovate PDDS techniques for potential industrial and commercial applications, thus advancing treatment efficacy and patient care.[1-5]

Floating Pulsatile System: The floating pulsatile system is developed based on the following approaches:

1. Low density for buoyancy.
2. High density to stick the tablet at the bottom part of the stomach.
3. Method of bioadhesion.
4. Reduction of the pyloric sphincter by swelling polymers.

Diseases Requiring Pulsatile Drug Delivery: Understanding the physiology of diseases has led to the development of pulsatile drug delivery systems. Table No. 01 highlights various diseases and their chronological behavior.

Future Trends in Pulsatile Drug Delivery Systems: Formulating a pulsatile drug delivery system presents significant challenges as it requires precise timing and dosage for effective drug delivery. These systems play a crucial role in targeting specific sites and administering drugs at optimal times, particularly in chronic diseases like arthritis and diabetes. Multiparticulate systems offer

distinct advantages over single-type drug delivery methods by preventing dose dumping and ensuring reproducible gastric retention times. Table No. 02 showcases some of the latest advancements in pulsatile drug delivery technologies, which hold promise for enhancing treatment outcomes and patient care in various medical conditions.

Recent Advancements in Oral Pulsatile Drug Delivery Technology: Recent advancements in oral pulsatile drug delivery technology have expanded the range of drugs suitable for this method. Drugs such as Propranolol hydrochloride, Ranitidine HCl, Verapamil HCl, Ketoprofen, Acetaminophen, Theophylline, Diclofenac sodium, Isoniazid, Nifedipine, Antipyrine, Valsartan, Diltiazem hydrochloride, Salbutamol sulfate, 5-aminosalicylic acid, Aceclofenac, Isosorbide-5-mononitrate, and Indomethacin can now be administered using innovative systems. Notable examples of these advancements include technologies like SODAS, IPDAS, OSDrC Technology, Intelli Matrix Technology, and Versetrol Technology, enhancing drug delivery precision and offering improved therapeutic outcomes for patients.

Single Unit Systems: Capsular System: Single unit systems are primarily developed in capsule form. The lag time is sustained by a plug, which is displaced by swelling or erosion, resulting in the release of the drug as a pulse from the insoluble capsule body. For instance, the Pulsincap® system operates as follows: The system consists of a water-insoluble body containing the drug formulation, enclosed with a swellable hydrogel. A plug (insoluble but permeable and swellable) is positioned at the open end of the system. Upon contact with gastrointestinal fluid or dissolution medium, the plug swells, pushing itself out of the capsule after a lag time. The position and dimensions of the plug are critical for controlling the lag time. For rapid release of water-insoluble drugs, effervescent or disintegrating agents may be added.

The plug material is typically composed of the following:

A. Swellable materials coated with permeable polymer (e.g., polymethacrylates).
B. Erodible compressed polymer (e.g., HPMC, polyvinyl alcohol).
C. Congealed melted polymer (e.g., glyceryl monooleate).
D. Enzymatically controlled erodible polymer (e.g., pectin).

Introduction to Floating Pulsatile Drug Delivery System: The oral route stands out as the most favored method of administering drugs due to factors such as cost-effectiveness, ease of administration, patient compliance, and formulation flexibility. Over the past few decades, a plethora of oral drug delivery systems have been developed to serve as reservoirs from which active substances can be released over a specified period at a predetermined and controlled rate.

1. Recent scientific and patent literature demonstrates heightened interest in novel oral controlled release dosage forms designed to remain in the gastrointestinal tract (GIT) for extended and predictable durations.
2. Various approaches are currently employed to prolong gastric residence times (GRT), with floating drug delivery systems (FDDS) being prominent among them.
3. Low-density systems.
4. Raft systems incorporating alginate gels.
5. Bioadhesive or mucoadhesive systems.
6. High-density systems.
7. Superporous hydrogels.
8. Magnetic systems.

The current review briefly addresses FDDS, one of the leading methodologies in gastro retentive drug formulations.[6-10]

Drug Candidates Suitable for FDD: Drugs with a narrow absorption window in the gastrointestinal tract (GIT) (e.g., L-DOPA, para-aminobenzoic acid, furosemide, riboflavin). Drugs with local activity in the stomach (e.g., Misoprostol, antacids). Drugs susceptible to instability in the intestinal or colonic environment (e.g., Felodipine, Captopril, Ranitidine HCl, Metronidazole). Drugs that disrupt normal colonic microbes (e.g., antibiotics for Helicobacter pylori eradication, such as tetracycline, Clarithromycin, amoxicillin). Drugs with low solubility at high pH values (e.g., Diazepam, Chlordiazepoxide, Verapamil).

Advantages of FDDS:

1. Floating systems are beneficial for drugs intended for local action in the stomach, such as antacids.
2. Acidic substances like aspirin can cause irritation to the stomach wall upon contact, making FDDS suitable for their administration.
3. Floating systems are advantageous for drugs absorbed through the stomach, such as ferrous salts and antacids.

4. Administration of prolonged-release floating dosage forms (tablets or capsules) facilitates drug dissolution in gastric fluid. The dissolved drug becomes available for absorption in the small intestine after the stomach contents are emptied.
5. It is expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine.

Disadvantages of Floating Drug Delivery Systems:

1. Floating systems are not suitable for drugs with solubility or stability issues in the gastrointestinal (GI) tract.
2. These systems necessitate a high level of fluid in the stomach for efficient drug delivery and buoyancy, which may not always be present.
3. Only drugs significantly absorbed throughout the gastrointestinal tract and undergoing substantial first-pass metabolism are desirable candidates for floating drug delivery.

Felodipine: Mechanism of Action: Felodipine is a calcium channel blocker that works by inhibiting the influx of calcium ions into vascular smooth muscle and cardiac muscle cells. This action relaxes and dilates the blood vessels, reducing blood pressure and decreasing the heart's workload, which helps in managing hypertension and angina.

Side Effects:

- Common: Headache, dizziness, flushing, swelling of ankles/feet, fatigue.
- Serious (rare): Rapid/irregular heartbeat, shortness of breath, fainting, signs of liver problems.

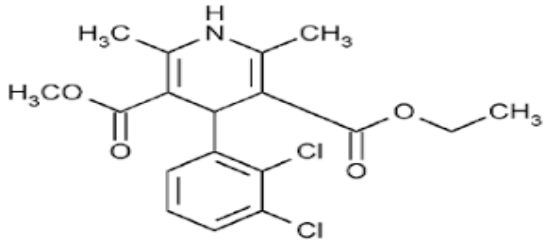
Precautions:

- Use cautiously in patients with liver disease, heart failure, or aortic stenosis.
- Avoid during pregnancy unless necessary.
- May interact with other medications.

Monitoring:

- Regular blood pressure checks.
- Periodic liver function tests may be needed.

Chemical Information:



- IUPAC Name: Mixed (methyl, ethyl) diester of 4-(2, 3-dichlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acid.
- Structure: Comprises a dihydropyridine ring with specific substituent's that confer its pharmacological properties.

Experimental:

Chemical and reagent: Felodipine was procured from Nivedita Chemicals Pvt. Ltd., Mumbai. Lactose Monohydrate and Microcrystalline cellulose were provided by DFE Pharma, Germany and JRS Pharma, Germany respectively, as gifts. HPC EXF and EC N20 were sourced from Signet Chemical, Mumbai, India, and DOW Chemical, Mumbai, India respectively. Sodium starch glycolate was obtained from DFE Pharma.

The procured samples were tested to confirm their identity and this included UV-visible wavelength scan, and recording of FT-IR spectra. The UV-Visible spectra of Felodipine were recorded using methanol as solvent was recorded using water as solvent on Shimadzu 1900 Instrument.

Preformulation studies: Preformulation may be described as a phase of the research and development process where the formulation scientist characterizes the physical, chemical and mechanical properties of new drug substances, in order to develop stable, safe and effective dosage forms. Ideally the Preformulation phase begins early in the discovery process such the appropriate physical, chemical data is available to aid the selection of new chemical entities that enter the development process during this evaluation possible interaction with various inert ingredients intended for use in final dosage form are also considered in the present study.

Materials used include Felodipine, lactose monohydrate, microcrystalline cellulose, HPC, EC N20, sodium starch glycolate, and magnesium stearate. Instruments include analytical balances, sieves, tablet compression machines, dissolution test apparatus, UV spectrophotometers, FTIR spectrophotometers, pH meters, stability chambers, friabilator, disintegration apparatus, and hardness testers.

Preformulation studies will evaluate Organoleptic properties, melting point, solubility, UV-visible spectrophotometry, bulk density; tap density, Carr's index, Hausner ratio, and angle of repose. Tablets will be prepared using direct compression, followed by compression coating. Evaluations will include weight variation, thickness, hardness, friability, drug content, disintegration, and in vitro dissolution. Stability studies will assess formulation stability under various conditions for one month.[11-15]

Results and discussion:

Procurement and Confirmation of Identity of Felodipine and other excipients:

Felodipine was sourced from Nivedita Chemicals Pvt. Ltd., Mumbai. Lactose Monohydrate and Microcrystalline Cellulose were gifted by DFE Pharma, Germany, and JRS Pharma, Germany. HPC EXF and EC N20 were obtained from Signet Chemical and DOW Chemical, Mumbai, respectively. Sodium starch glycolate came from DFE Pharma. The identity of all samples was confirmed using UV-visible wavelength scans and FT-IR spectra. UV-visible spectra for Felodipine, using methanol as the solvent, were recorded on a Shimadzu UV-1900 instrument.

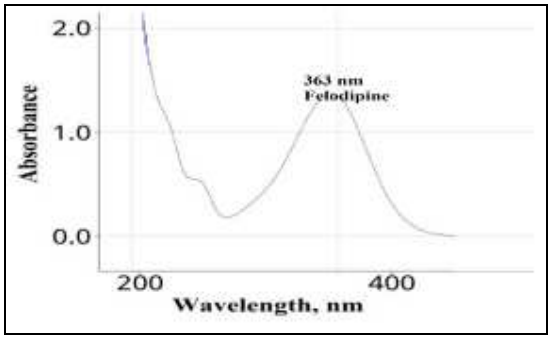


Figure no. 02: Felodipine λ-max maximum absorbance at 363 nm.

Table no.01: Calibration curve for Felodipine:

Concentration µg/ml	Absorbance
00	0.00
10	0.161
20	0.322
30	0.492
40	0.641
50	0.849
60	1.202

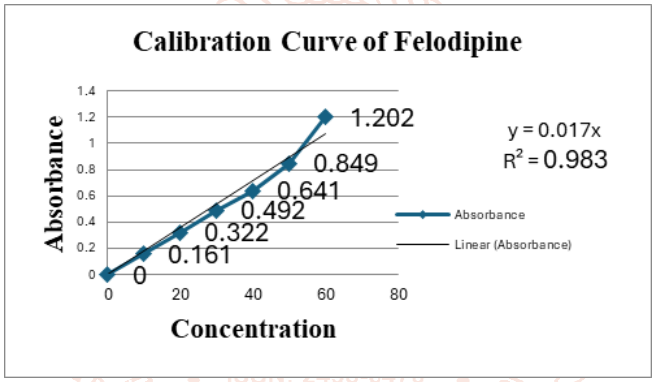


Figure no. 03: Calibration curve for Felodipine.

The UV-Visible spectra of Felodipine were recorded using methanol and water as solvents on a Shimadzu UV-1900 instrument, with a maximum absorbance at 363 nm. FT-IR spectra of pure Felodipine help identify its functional groups. Absence of peaks at 3200-3600 cm^{-1} indicates no hydroxyl groups. Peaks at 2800-3000 cm^{-1} correspond to C-H stretching, while those at 1700-1750 cm^{-1} indicate C=O stretching from ester and amide groups. Peaks at 1000-1500 cm^{-1} are due to C-C and C-N stretching. The fingerprint region below 1500 cm^{-1} provides a unique pattern for confirming Felodipine identity.

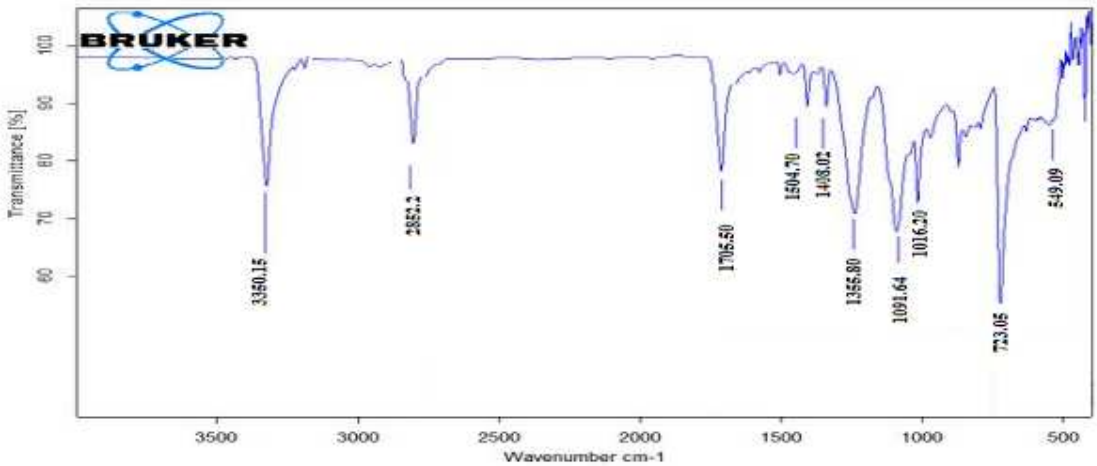


Figure no. 04: FT-IR spectra of pure Felodipine.

Organoleptic Properties: Felodipine appears white to light yellow, with a characteristic odor and bitter taste.

Melting Point: The melting point, determined using the capillary tube method, is 146°C, within the standard range of 145-147°C.

Solubility: Felodipine solubility varies with different solvents: Sparingly soluble in water, chloroform, and dichloromethane. Moderately soluble in ethanol, methanol, acetone, and Acetonitrile Highly soluble in dimethyl sulfoxide. Practically insoluble in oil. Solubility in buffered solutions depends on pH and ionic strength. Solubility can be enhanced with specific formulations of surfactants or co-solvents.

Table no. 02: Result of Angle of Repose (θ), Loose Bulk Density (gm/cm3), and Tapped Bulk Density (gm/cm3), % Compressibility, Carr's index, Hausner's ration of FPDDS for Felodipine tablets:

Formulation Code	Angle of Repose (θ)	Loose Bulk Density (gm/cm3)	Tapped Bulk Density (gm/cm3)	% Compressibility	Carr's index (%)	Hausner's ratio
F1	26.44±0.02	0.38±0.01	0.48±0.01	35.28±0.04	12.44±0.02	1.18±0.01
F2	27.36±0.02	0.38±0.02	0.48±0.02	34.42±0.03	12.36±0.02	1.38±0.02
F3	28.77±0.01	0.39±0.01	0.47±0.01	30.38±0.05	12.77±0.01	1.19±0.01
F4	27.99±0.01	0.39±0.01	0.44±0.01	31.21±0.02	12.99±0.01	1.19±0.01
F5	25.13±0.03	0.38±0.03	0.45±0.02	30.42±0.03	12.13±0.03	1.38±0.03
F6	24.55±0.04	0.38±0.03	0.53±0.02	31.93±0.02	12.55±0.04	1.28±0.03
F7	25.65±0.02	0.38±0.02	0.48±0.03	30.83±0.01	12.65±0.02	1.38±0.02
F8	**24.22±0.04**	**0.36±0.01**	**0.47±0.03**	**25.23±0.04**	**12.22±0.04**	**1.26±0.01**
F9	29.62±0.03	0.38±0.02	0.49±0.01	30.78±0.03	12.62±0.03	1.38±0.02

Each data represents Mean ±SD (n=3)

Preparation and Optimization of Floating Pulsatile Drug Delivery Systems (FPDDS) for Felodipine:
As per table no. 03 and 04 chapters no 04 Core tablet (C1- C3) was characterized for post-compression parameters like weight variation, thickness, hardness, friability, and drug content and disintegration time.

Table no. 03: Post-compression parameters of core tablet (FPDDS) for Felodipine:

Batch code	Weight Variation (mg)	Thickness	Hardness (Kg/cm^2)	Friability	In-Vitro FT (Sec.)
C1	101 ± 0.05	3.19 ± 0.26	3.5 ± 0.53	0.41 ± 0.08	28 ± 2.38
C2	101 ± 0.50	3.21 ± 0.36	3.6 ± 0.82	0.56 ± 0.06	23.0 ± 2.03
C3	102 ± 0.80	3.26 ± 0.25	3.6 ± 0.86	0.42 ± 0.08	19.0 ± 2.87

Batch codes C1, C2, and C3 underwent evaluation for weight variation, thickness, hardness, friability, and in vitro Floating Time (FT). Results showed weight deviation within 10%, meeting USP criteria. Hardness tests indicated satisfactory mechanical strength, and friability tests displayed excellent mechanical resistance (<1%). Consistent drug content was observed. Formulation C3, containing 6% Sodium Starch Glycolate, exhibited the shortest disintegration time, thus chosen as the optimized core tablet for further development.

Compatibility study of Drug and Excipients:
Compatibility Study of Drug and Excipients which used FPDDS for Felodipine tablet formulation were mixed in equal proportions and stored at Storage different environmental conditions of, 4^0,25^0 C /RH 60%, and 40^0C /RH 75% for three month. The samples were analyzed for the content of Felodipine. The samples were also observed for any change in the physical appearance. FT-IR spectrum for FPDDS for Felodipine tablet formulation F9 was recorded. At the after three month and compared with the standard Felodipine spectrum shown in figure no 18.

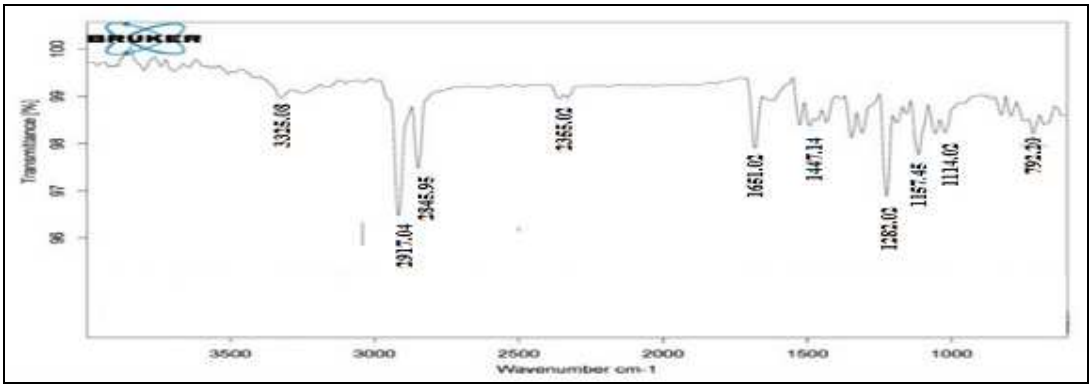


Figure no. 05: FT-IR spectra of Felodipine and excipients for Compatibility study.

Interpretation:

In drug-excipients compatibility studies, analyzing FT-IR spectra helps detect interactions. If the mixture's spectra show no significant shifts, disappearances, or new peaks compared to individual components, it suggests good compatibility. Conversely, noticeable changes indicate potential interactions, requiring further investigation.

Characterization of the FPDDS for Felodipine tablets:

The FPDDS for Felodipine tablet formulations were analyzed for free Felodipine using the UV-Spectrophotometric method at 363 nm against appropriate blank. To determine entrapped Felodipine, weighed accurately about 250 mg of dried FPDDS for Felodipine tablets and dissolved in distilled water. The appropriate dilutions were made with distilled water to get the absorbance in the range of standard curve. To determine the free Felodipine were formed was diluted appropriately with distilled water and read the absorbance on UV-Visible spectrophotometer at 363 nm

The FPDDS for Felodipine tablets formulations were characterized using UV-spectrophotometric methods to determine both free and entrapped Felodipine.

For free Felodipine, tablets dissolved in water were analyzed at 363 nm using UV-spectrophotometry. For entrapped Felodipine, dried tablet samples were dissolved diluted, and their absorbance measured at 363 nm.

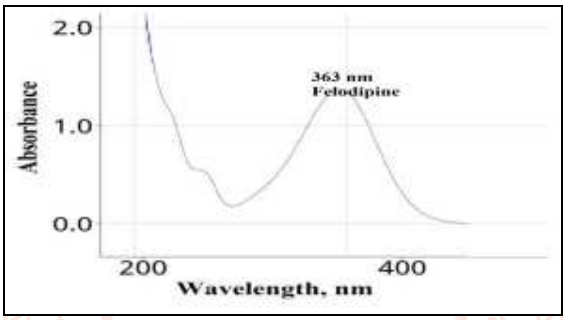


Figure no. 06: Determination for Free Felodipine from FPDDS for Felodipine tablets.

Quantification of both free and entrapped Felodipine in FPDDS tablets provides crucial insights into formulation efficacy and desired drug release. Felodipine FTIR spectrum reveals characteristic peaks: hydroxyl (OH) stretching at 3300-3500 cm-1, carbonyl (C=O) at 1700-1750 cm-1, and aromatic C=C stretching at 1600-1650 cm-1. Peaks at 1300-1400 cm-1 signify C-H bending, while 1000-1100 cm-1 represent C-O stretching vibrations. Analyzing these peaks aids in understanding Felodipine chemical structure. Any alterations in peak characteristics may suggest interactions or compatibility issues with excipients, influencing formulation integrity.

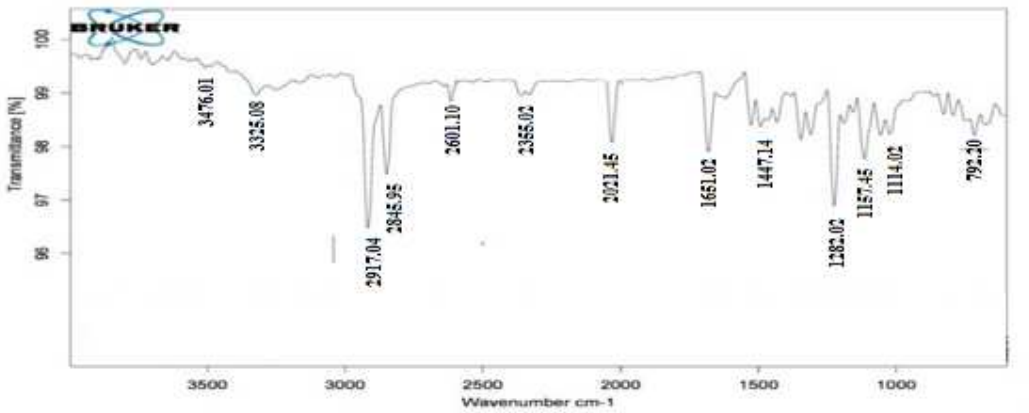


Figure no. 07: FTIR-Spectra for FPDDS for Felodipine tablets F8 formulation.

FTIR analysis of Felodipine with Sodium starch glycolate, Microcrystalline Cellulose, Lactose monohydrate, Magnesium stearate, HPC-EXF, and EC N20 reveals potential chemical interactions. Comparison of characteristic peaks in the combined spectrum with individual Felodipine and excipients spectra identifies shifts, disappearances, or new peaks, indicating interactions. Sodium starch glycolate may affect carbonyl (C=O) or hydroxyl (OH) vibrations, while Microcrystalline Cellulose and Lactose monohydrate could alter methyl (CH3) or ether group (C-O-C) vibrations. Magnesium stearate might influence alkyl chain vibrations. FTIR may also

detect hydrogen bonding shifts. This analysis aids in assessing compatibility, interactions, and formulation stability, crucial for effective drug delivery system development.

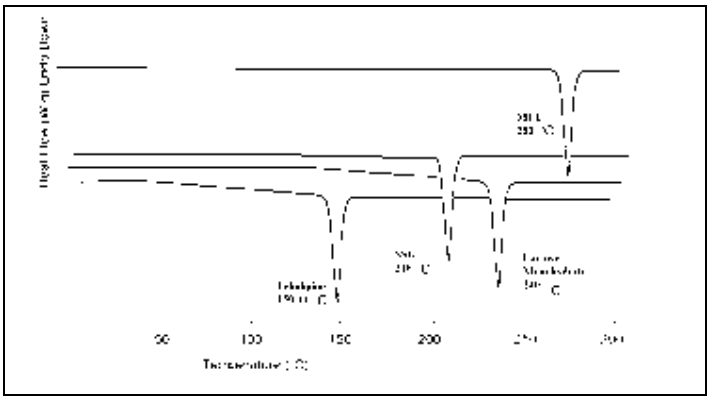


Figure no.08: DSC for physical mixture of for Felodipine tablets F8 formulation.

Differential Scanning Calorimetry (DSC) analyzes thermal behavior like melting points and crystallization. Felodipine shows a melting point at 150.11°C, Sodium Starch Glycolate at 218°C, Microcrystalline Cellulose at 280°C, and Lactose Monohydrate at 240°C.

Evaluation of the FPDDS for Felodipine tablets: [20-35]

A. Weight Variation Test: Twenty tablets were individually weighed using a Sartorius balance (Model CP-224 S). The average weight was calculated, and each tablet's weight was compared to the average weight.

B. Tablet Thickness: The thickness of five tablets was measured using Vernier calipers.

C. Tablet Hardness: Tablet hardness, measured as the force required breaking a tablet in diametric compression, was determined using a Monsanto hardness tester.

D. Tablet Friability: Friability was assessed using a Roche friabilator. Twenty tablets were dedusted and subjected to 100 revolutions in the drum. Percentage friability was calculated, with a maximum allowable loss of 1%.

E. Drug Content: Twenty tablets were crushed, and the equivalent of 100 mg of drug was dissolved in methanol and phosphate buffer pH 6.8. The solution was filtered and analyzed for drug content by UV spectrophotometer at 363 nm.

Table no. 04: Evaluation parameters and results of FPDDS for Felodipine tablets:

Formulation code	Parameters				
	Average weight (mg)	Thickness (mm)	Hardness	% Friability	% drug content
F1	296.0±0.81	3.67±0.2	3.4±0.1	0.76±0.01	96.82±0.53
F2	300.1±0.26	3.75±0.2	3.3±0.1	0.79±0.01	94.36±0.44
F3	295.1±0.39	3.65±0.2	3.2±0.15	0.85±0.02	95.67±1.24
F4	348.4±0.89	3.85±0.02	3.2±0.15	0.79±0.01	94.76±1.34
F5	348.6±0.93	3.86±0.02	3.6±0.1	0.66±0.02	96.50±0.65
F6	345.1±0.32	3.76±0.02	3.8±0.15	0.78±0.01	98.62±0.61
F7	390.1±0.29	3.79±0.2	3.8±0.1	0.78±0.02	99.23±0.40
F8	**399.6±0.28**	**3.85±0.2**	**3.5±0.05**	**0.61±0.01**	**99.57±0.26**
F9	399.4±0.43	3.73±0.2	3.1±0.05	0.74±0.01	99.41±0.56

Each data represents Mean ±SD (n=3)

F8 is the optimal choice among FPDDS for Felodipine tablets due to several key factors:

1. Weight: It averages 299.6 mg, aligning with the desired dosage.
2. Thickness: Tablets measure 3.85 mm, facilitating easy handling and swallowing.
3. Hardness: With a rating of 3.5, they exhibit adequate mechanical strength.
4. Friability: F8 shows minimal loss at 0.61%, indicating robustness.
5. Drug Content: Achieving 99.57%, it ensures consistent dosage.
6. Wetting Time: Dispersing in 34 seconds, it offers rapid dissolution.

Overall, F8 excels in drug content, disintegration time, and mechanical strength, making it the preferred FPDDS formulation.

***In-vitro* release profile FPDDS for Felodipine tablets:**

A. In the in-vitro disintegration test, tablets were individually placed in tubes of a disintegration test apparatus with a stainless-steel screen bottom, submerged in a 37 ± 2°C water bath. The time for complete disintegration was recorded. Compliance with Pharmacopoeial standards requires dispersible tablets to disintegrate within 3 minutes.

B. In-vitro dissolution studies for FPDDS for Felodipine tablets utilized the USP paddle method at 50 rpm in 900 ml of phosphate buffer pH 6.8 at 37 ± 0.5°C. Samples were withdrawn at intervals, replaced with fresh dissolution medium, and their absorbance measured at 363 nm using a Shimadzu 1900 Spectrophotometer.

Table no. 05: In- Vitro dissolution studies and results of FPDDS for Felodipine tablets:

Times Hrs.	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	**0**	0
1	38.32	37.45	38.02508	39.65	41.32	41.66	46.33	**25.20**	30.00
2	42.69	42.78	41.36	42.58	49.77	48.54	54.58	**35.80**	40.56
3	49.36	47.65	49.21	68.98	68.77	55.33	67.99	**45.56**	55.05
4	56.58	99.99	56.44	74.78	82.33	86.88	82.77	**55.50**	65.05
5	99.99	99.99	99.99	99.99	99.99	99.99	99.99	**65.20**	75.50
6	99.99	99.99	99.90	99.99	99.99	99.99	99.99	**75.00**	85.96
7	99.99	99.99	99.99	99.99	99.99	99.99	99.99	**85.58**	99.99
8	99.99	99.99	99.99	99.99	99.99	99.99	99.99	**99.90**	99.99

Each data represents Mean ±SD (n=3).

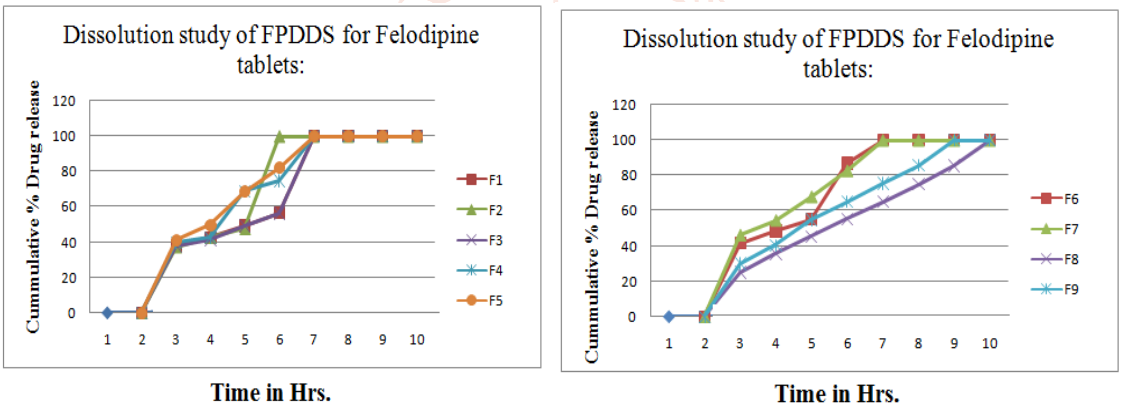


Figure no. 09: In-Vitro release Dissolution study of FPDDS for Felodipine tablet.

F8 demonstrates remarkable stability and reliability throughout the dissolution study, showcasing consistent drug release percentages over time. This underscores F8's reliability and robustness as a formulation choice.

When compared to other formulations, although some may show similar drug release percentages at specific time points, none consistently outperform F8 across all intervals. F8 emerges as the superior option, ensuring rapid and complete drug release within the designated timeframe.

Release kinetics of *In-vitro* Drug release:

The kinetics of *In-vitro* drug release was determined by applying the drug release data to various kinetic models such as zero order, first order, Higuchi, Peppas-Korsmeyer and Hixon Crowell. The result obtained were represented in table 06, and shown in figure no. 10.

Table no. 06: Different Release kinetics of In-vitro Drug release:

Sr. no	Kinetics Models				
	Zero order	First order	Higuchi model	Korsmeyer Peppas	Hixon Crowell
	R2	R2	R2	R2	R2
F1	0.9829	0.8176	0.9504	0.9486	0.9819
F2	0.9662	0.9778	0.9764	0.9861	0.9243
F3	0.9977	0.8906	0.9721	0.9846	0.9746
F4	0.9826	0.9449	0.9534	0.9729	0.9716
F5	0.9292	0.9178	0.9844	0.9762	0.9842
F6	0.9173	0.8892	0.9817	0.9718	0.9383
F7	0.9721	0.9778	0.9791	0.9971	0.9701

F8	0.9991	0.9231	0.9941	0.9998	0.9987
F9	0.9979	0.9331	0.9741	0.9998	0.9789

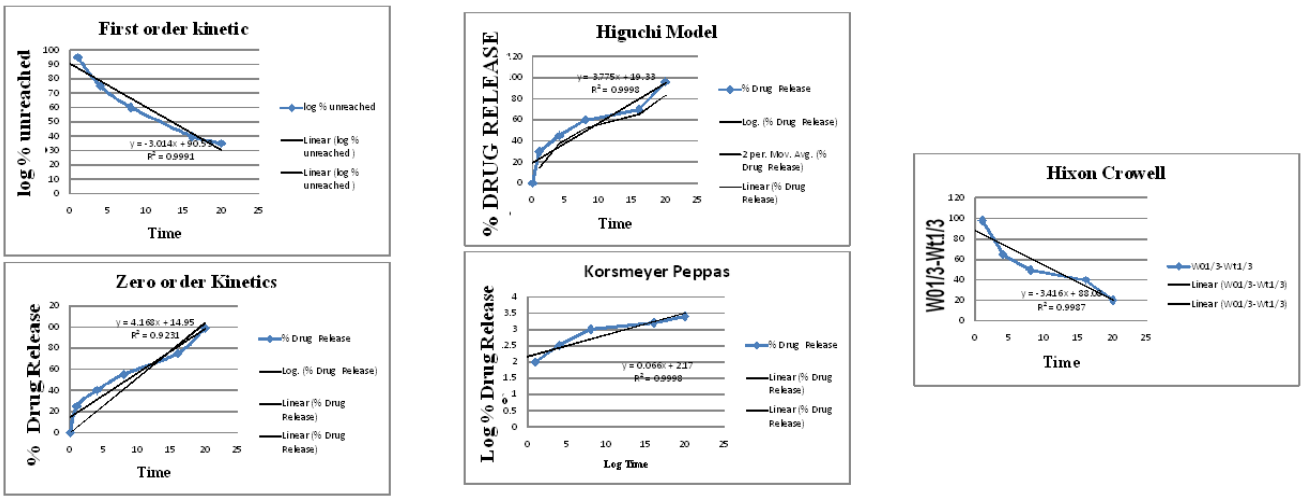


Figure no. 10: Graph of different Release kinetics of *In-vitro* Drug release

Stability studies of FPDDS for Felodipine tablets: [61-74]

The product was evaluated for following parameters: Weight variation, Hardness, Friability, Drug content, Dissolution analysis. **Storage condition at 40°C ± 2°C/75 %RH ± 5%:**

Table no. 07: Stability Study of Optimized Batch of F8 FPDDS for Felodipine tablets:

Time	Parameters				
	Hardness (Kg/cm2)	Uniformity of weight	Friability (%)	Floating time(sec)	Drug content (%)
0 Days	3.5±0.57	400.2±0.31	0.64±0.02	20 ±1.02	99.57 ± 0.09
30 Days	3.4±0.15	400.3±0.29	0.68±0.01	22 ±1.59	98.83 ± 0.11
60 Days	3.3±0.10	400.6±0.36	0.69±0.01	21 ±0.83	98.49 ± 0.12
90 Days	3.3±0.15	400.8±0.34	0.71±0.01	25 ±0.93	97.71 ± 0.15

Each data represents Mean ±SD (n=3).

Table no. 08: % drug release during Stability Study of Optimized Batch of F8 FPDDS for Felodipine tablets by dissolution testing:

Time (Sec)	0 days	30 days	60 days	90 days
0	0	0	0	0
1	26.20	29.10	24.90	24.91
4	49.80	44.20	45.10	50.10
8	67.56	66.56	69.46	65.16
16	89.50	88.56	89.59	88.50
20	99.20	99.40	99.10	99.10

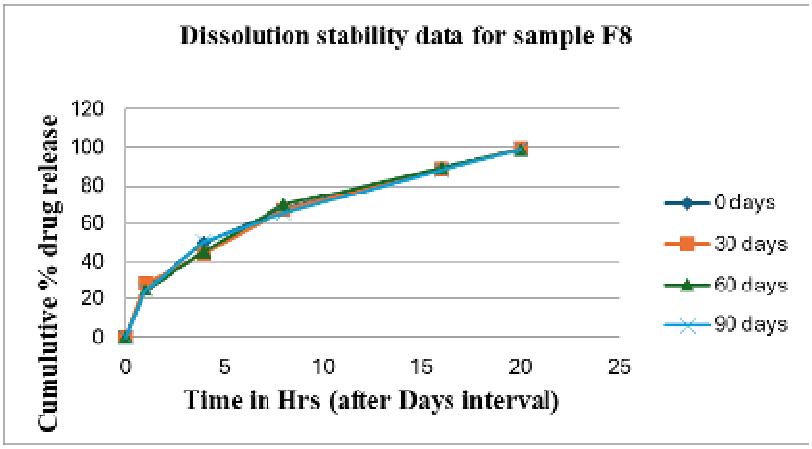


Figure no. 11: % drug release during Stability Study of Optimized Batch of F8 FPDDS for Felodipine tablets by dissolution testing.

The stability studies for optimized formulation F8 was carried out based accelerated stability conditions and study of various parameters carried out at 0, 30, 60, 90 days of intervals and the results found satisfactorily and that reveals that the optimized formulation was stable under accelerated condition.[36-48]

Discussion:

Formulation Development: Various FPDDS formulations for Felodipine were developed using different polymers and excipients to synchronize drug release with physiological rhythms for improved hypertension and angina treatment.

Optimization: Polymer concentrations, excipients ratios, and coating thicknesses were adjusted to achieve desired pulsatile release behavior.

In Vitro Studies: Promising results in floating behavior, release kinetics, and dissolution tests under simulated physiological conditions.

Data Analysis: Comprehensive analysis confirmed the efficacy and feasibility of the developed system for better patient outcomes and medication adherence.

Procurement and Testing: Felodipine and excipients were procured and confirmed via UV-visible scans and FT-IR spectra.

UV-Visible Spectra: Maximum absorbance of Felodipine at 363 nm, with a linear calibration curve in methanol.

FT-IR Spectrum: Characteristic peaks for C-H, C=O, C-C, and C-N stretching, confirming compound identity.

Organoleptic Properties and Melting Point: Felodipine is white to light yellow, with a characteristic odor, bitter taste, and a melting point of 146°C.

Solubility Studies: Felodipine is sparingly soluble in water, chloroform, and dichloromethane; moderately soluble in ethanol, methanol, acetone, and Acetonitrile; and highly soluble in Dimethyl sulfoxide.

Flow Properties: Formulations had well to excellent flow, with F4 showing the best characteristics (Carr's index 12.99%, Hausner's ratio 1.13).

Post-Compression Parameters: Tablets (C1-C3) met USP criteria for weight variation, mechanical strength, and friability.

Compatibility Study**:** FT-IR spectra showed good compatibility between Felodipine and excipients after storage.

FPDDS Analysis: Free and entrapped Felodipine quantified using UV-spectrophotometry at 363 nm, ensuring desired drug release profile.

DSC Analysis: Revealed characteristic endothermic peaks for Felodipine and excipients, indicating thermal stability and compatibility.

Evaluation of Tablets: F8 formulation showed the best overall performance: Average weight: 399.6 mg, Thickness: 3.85 mm, Hardness: 3.5 Kg/cm², Friability: 0.61%, Drug content: 99.57%, floating time: 18 seconds.

Conclusion:

The development and optimization of various FPDDS formulations for Felodipine, utilizing different polymers and excipients, successfully synchronized drug release with physiological rhythms, enhancing treatment for hypertension and angina. Adjustments in polymer concentrations, excipient ratios, and coating thicknesses achieved the desired pulsatile release behavior. In vitro studies demonstrated promising floating behavior, release kinetics, and dissolution profiles under simulated physiological conditions. Comprehensive data analysis confirmed the efficacy and feasibility of the developed system, indicating potential improvements in patient outcomes and medication adherence.

Felodipine and excipients were procured and verified through UV-visible scans and FT-IR spectra, with Felodipine showing maximum absorbance at 363 nm and characteristic FT-IR peaks confirming compound identity. Organoleptic properties and a melting point of 146°C were consistent with known standards. Solubility studies indicated varied solubility across different solvents.

Formulations exhibited well to excellent flow properties, with F4 showing the best flow characteristics (Carr's index 12.99%, Hausner's ratio 1.13). Post-compression parameters confirmed that tablets (C1-C3) met USP criteria for weight variation, mechanical strength, and friability. Compatibility studies showed no significant interactions between Felodipine and excipients after storage.

FPDDS analysis quantified free and entrapped Felodipine using UV-spectrophotometry at 363 nm, ensuring the desired drug release profile. DSC analysis revealed characteristic endothermic peaks for Felodipine and excipients, indicating thermal stability and compatibility.

Among the formulations, F8 demonstrated the best overall performance with an average weight of 399.6 mg, thickness of 3.85 mm, hardness of 3.5 Kg/cm², friability of 0.61%, drug content of 99.57%, and a

floating time of 18 seconds, making it the optimal formulation for effective and reliable drug delivery.

Conflict of interest:
Authors do not have any conflict of interest

Acknowledgement:
I would like to express my heartfelt gratitude to KVPS's Institute of Pharmaceutical Education, Boradi, including all teaching and non-teaching staff, and to Principal Dr. Vikas V. Patil for their unwavering support throughout this research. A special thanks to my research guide, Prof. Kalpeshkumar S. Wagh, for his invaluable guidance and encouragement. Without their collective assistance, this work would not have been possible.

References:

[1] Gennaro AR. The Science and Practice of Pharmacy. 1st ed. USA: Lippincott Williams & Wilkins, 2000:903-905.

[2] Bussemer T, Otto I, Bodmeier R. Pulsatile drug delivery systems Crit Rev. Ther Drug Carrier Syst.2001;18(5):433-458.

[3] Patel JD, Aneja K, Majumdar SH. Pulsatile drug delivery system: An "User-Friendly" dosage form. J Pharma ResHealth Care. 2010; 2(2):204-215.

[4] Martin RJ, Banks-Schlegal S. Chronobiology of asthma. Am J Resp Crit Care Med. 1998; 158:1002-1007.

[5] Kikuchi A, Okano T. Pulsatile drug release control using hydrogels. Advanced Drug Delivery Review.2002; 54:53–77.

[6] Ogihara T, etal.The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH2009). Hypertens Res 2009; 32: 70–77.

[7] Qureshi J, Amir M, Ahuja A, Baboota S, Ali J. Chronomodulated drug delivery system of salbutamol sulphate forthe treatment of nocturnal asthma. Indian J. Pharm. Sci. 2008; 70(3):351-356.

[8] Yehia SA, Elshafeey AH, Sayed I, Shehata AH. Optimization of Budesonide compression-coated tablets forcolonic delivery. AAPS PharmSciTech. 2009; 10(1):147- 157.

[9] Bailpattar P, Karwa P, Patel K, Mondal MD, Sahidullah, PM. Formulation and evaluation of time controlled drugdelivery system of Montelukast sodium. Int. J. Pharm. Innovations. 2012;2(3):1-12.

[10] Veerareddy PR, Manthri R. Formulation and evaluation of compression coated Piroxicam tablets for colonspecific drug delivery. Acta Pharma. 2010; 52:281-294.

[11] Bhatt Y, Deshmukh A, Joshi M, Nalle S, Paladi R. Evaluation and characterization of dispersibleEtoricoxibtablets. Int. J. Pharm. Sci. 2009;1(2):310-314

[12] Amin AF, Patel MM, Patel SL, Bhadani MN, Shah TJ. A synchronous colon-specific drug delivery system fororally administered Mesalamine. Acta Pharm. 2009; 51: 251- 260.

[13] Patel MR, Patel KR, Patel NM, Mehta TJ, Patel AD. Development and optimization of colon targetedcompression coated tablet of Methotrexate. J Chem. Pharm. Res. 2011; 3(2):786-791.

[14] Bussmer T, Peppas NA, Bodmeier R. Evaluation of the swelling, hydration and rupturing properties of theswelling layer of a rupturable pulsatile drug delivery system. Eur J Pharm Biopharm. 2003; 56(2):261-270.

[15] Moon A, Kondawar M, Shah R. Formulation and evaluation of press coated Indomethacin tablets for pulsatiledrug delivery system. J. Pharm. Res 2011; 4(3):564-566.

[16] Gandhi SD, Pandya PR, Jani GK, Upadhyay NN, Nagaich U. Formulation development and evaluation of colontargeted tablets of Secnidazole for the treatment of amoebiasis. Int. J. Pharm. Sci. Rev. Res. 2010; 5(3):64-71.

[17] Bauskar M, Nandedkar S, Wagh R. Formulation, design and optimization of pulsatile release tablet ofDoxofylline with swelling and erodiable layers for treatment of nocturnal asthma. Int. J. Pharmacy andPharmaceutical.Sci.2012; 3(5):218-223.

[18] Bhowmik D., Chiranjib B., Krishnakanth, Pankaj, Chandira R.M. (2009). Fast dissolving tablet: An overview. *Journal of Chemical and Pharmaceutical Research*, 1(1): 163-177.

[19] Yourong Fu, Schicheng Yang, Seong hoonJeong, Susumu Kimura, Kinam Park. Orally Fast disintegrating tablets: Development technologies, Taste Masking and Clinical studies. *Crit Rev Ther drug carrier systems* 2004; 21(6): 433-475.

[20] Behnke k, Sogaard J, Martin S, Bauml J, Ravindran AV, Agren H, et al. Mirtazapine orally disintegrating tablet versus sertraline: A

prospective onset of action study. *J. Clin. Psychopharmacol*. 2003; 23:358-64.

[21] Jaccard TT, and Leyder J. "Une Nouvelle formegalenique: Le Lyoc", *Ann. Pharm. Fr.* 1985; 43(2):123- 131.

[22] Dollo G, Chevanne F, Le Corre P, Chemtob C, Le Verge R. Bioavailability of phloroglucinol in man. *J Pharm Belg* 1999; 54:75-82.

[23] Gafitanu E, Dumistracel I, Antochi S. Formulations and bioavailability of propyphenazone in lyophilized tablets. *Rev Med Chir Soc Med Nat Iasi* 1991; 95:127-8.

[24] Bhandari S., Mittapalli R.K., Ganu R., Rao Y.M. (2008). Orodispersible tablets: *An overview. Asian J. Pharm*., 2(1):2-11.

[25] Swamy P.V., Gada S.N., Shirsand S.B., Kinagi M.B. and Shilpa H. (2010). Design and evaluation of costeffective orodispersible tablets of diethylcarbamazine citrate by effervescent method. *International Journal of Pharma Sciences and Research*, 1(6): 258-264.

[26] Srinivas M., Parambil A., Krishnan M., Achutha N.U. (2008). Enhancement of dissolution rate and bioavailability of aceclofenac. *International Journal of Pharmaceutics,* 350: 279–290.

[27] Indian Pharmacopoeia (2007). *Ministry of Health and Welfare; Controller of Publication*; 63.

[28] Wagh M.P., Yewale C.P., Zate S.U., Kothawade P.I. and Mahale G.H. (2010). Formulation and evaluation of fast dispersible tablets of aceclofenac using different superdisintegrants. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2: 154-157.

[29] Malakar S., Rao S.B., Kumar A.P. and Kulkarni S.V. (2010). Formulation and evaluation of fast dispersible aceclofenac tablets: effect of functionality of super disintegrates. *Journal of Global Pharma Technology*; 2(5): 90-96.

[30] Banker G.S. and Anderson N. R. (1987). In: Lachman L., Lieberman H.A. and Kanig J.L. *The Theory and Practice of Industrial Pharmacy*. 3rd ed., Mumbai, Varghese Publishing House, 293-399.

[31] Ravikumar, Patil S.R., Patil M.B., Paschapur M.S. and Mahalaxmi R. (2010). Design and characterization of aceclofenac mouth dissolving tablets by effervescent formulation approach,.*Der Pharmacia Lettre*, 2(1) :220-236.

[32] Chakraborthy S., Khandai M., Singh S.P. and Patra N. (2008). Comparative study on effect of natural and synthetic superdisintegrant in the formulation of fast dissolving tablets. *International Journal of Green Pharmacy*, 22-25.

[33] 11. Patel H.A., Patel J.K., Patel K.N. and Patel R.R. (2010). Studies on formulation and *in-vitro* evaluation of fast dissolving tablets of domperidone. *Int. J. Ph. Sci.,* 2(1): 470-476.

[34] 12. Shah D.P., Jain V.C., Sonani N.G., Dalvadi H.P. and Patel N.J. (2010). Influence of various excipients on quality control parameter of aceclofenac tablets containing SSG. *International Journal OF Pharmaceutical Sciences,* (1):113-121.

[35] Clarke A, Brewer F, Johnson ES, Mallard N, Hartig F, Taylor S, et al. A new formulation of selegiline: Improved bioavailability and selectivity for MAO-B inhibition. J Neural Transm. 2003; 110:124-5.

[36] Ohwavworhu F., Adelakun T., Phosphoric acid mediated depolymerization and decrystallization of α-Cellulose obtained from Corn Cob: Preparation of Low Crystallinity Cellulose and some Physicochemical Properties, Tropical J.Pharm. Res 2004,4(2), 509-516.

[37] Reddy K, Mutalik S., Reddy S., Once daily sustained release matrix Tablets of Nicorandi: Formulation and In Vitro Evaluation. AAPS Pharm Sci Tech 2003 ,4(4), E61- E66.

[38] Chaudhari PD, Chaudhari SP, Kohle SR, Dave KV, More DM. formulation and evaluation of fast dissolving tablets of famotidine. Indian Drug 2005; 42: 641-9.

[39] Bankar GS, Anderson NR. Tablets. In: Lachman L, Lieberman HA, Kanig JL, editor. The theory and practice of industrial pharmacy. 3rded. Mumbai: Varghese Publishing House; 1987.p.293-9.

[40] JinichiFukami, EtsuoYonemochi, Yasuo Yoshihashi, Katsuhide Terada. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose", International journal of pharmaceutics 2006; 310:101-109.

[41] Bi XY, Sunada H, Yonezawa Y and Danjo. "Evaluation of rapidly Disintegrating tablets

prepared by a direct compression method", Drug Dev. Ind.Pharm, 1999; 25:571-581.

[42] Adamo Fini , Valentina Bergamante , Gian Carlo Ceschel , Celestino Ronchi , Carlos Alberto Fonseca de Moraes. Fast dispersible/slow releasing ibuprofen tablets. Eur J Pharm sci .2008;69:335–341.

[43] Allen LV. Rapid-dissolve technology: An interview with Lloyd. Allen. IJPC. 2003;7(6), 449–450.

[44] Amin.D, Gupta SS, Prabhu NB, Wadhwani AR. fast disintegrating dosage forms of ofloxacin and metronidazole benzoate: Indian drugs. 2005; 42:614-617.

[45] Beatrice Perissutti, FulvioRubessa, MariarosaMoneghini, Dario Voinovich. Formulation design of carbamazepine fast-release tablets prepared by melt granulation technique. Int J Pharma .2003; 256: 53–63.

[46] Bhaskaran S. Narmada G.V. Indian Pharmacist. 2002; 1, 9-12. 6. Chang RK, Guo X, Burnside A, Couch RA. Fastdissolving tablets. Pharm Technol. 2000; 6:52–58.

[47] Chaudhari PD, Chaudhari SP, Kolhe SR, Dave KV, More DM. Formulation and evaluation of fast dissolving tablets of famotidine; Indian drugs. 2005; 42:641-649.

[48] Chaudhari PD, Kolhe SR, Chaudhari SP, More DM. Use of cation exchange resins to optimize the taste masking of bitter drug Rizatriptan benzoate. Indian drugs. 2006; 43:795-799.