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**Research**

# Formulation and Evaluation of Flupirtine Malate Sustained Release Bilayer Tablet

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## Abstract

The study aimed to formulate and evaluate colon-targeted Flupirtine Maleate tablets using HPMC K100M and HPMC K4M. FT-IR analysis confirmed no drug-polymer interactions, and pre-compression studies indicated good powder flow properties. Tablets were prepared by direct compression and evaluated for various physicochemical parameters. In-vitro dissolution studies showed minimal drug release in acidic and small intestinal environments, with complete release in colonic conditions. The optimized formulation (F4) followed a first-order diffusion-controlled Peppas release mechanism and remained stable over three months. The bilayer tablet approach effectively sustained drug release, enhancing patient compliance and pain management. The study concluded that the bilayer tablet approach effectively sustained the release of Flupirtine Maleate, improving patient compliance and enhancing pain management. The combination of HPMC K100M and HPMC K4M as rate-controlling polymers in the sustained release layer demonstrated promising results, making this formulation a viable option for controlled drug delivery.

**Keywords:** Flupirtine Maleate, Bilayer Tablet, Sustained Release, HPMC K100M and HPMC K4M, In-vitro Dissolution, Drug Release Kinetics.

## INTRODUCTION

Bilayer tablet technology represents an advanced approach in oral drug delivery systems, enabling the incorporation of multiple release profiles in a single dosage form. This system is especially beneficial when combining drugs with different pharmacokinetic profiles or when a single drug requires both immediate and

sustained release effects [1]. Bilayer tablets help physically separate incompatible active pharmaceutical ingredients (APIs) and can tailor drug release to match therapeutic needs.

**Applications and Therapeutic Advantages**

Bilayer tablets are widely used for drugs targeting chronic diseases such as hypertension, diabetes, inflammation, and pain, where combination therapy or controlled drug delivery improves treatment efficacy [2]. The first layer provides a loading dose via immediate release, while the second layer provides a maintenance dose through sustained release. This delivery system helps in reducing dosing frequency, improving patient compliance, and minimizing side effects associated with peak drug concentrations.[3]

**Design Challenges in Bilayer Formulations**

While bilayer tablets offer significant therapeutic advantages, their development involves technical challenges such as: [4]
Layer separation (delamination)
Cross-contamination between layers
Poor interlayer bonding
Layer weight variability
To overcome these, specialized bilayer tablet presses and optimized formulation strategies are required.

**Rationale for Choosing Flupirtine Maleate**

Flupirtine Maleate is a non-opioid, centrally acting analgesic, used for managing acute and chronic pain. However, its short biological half-life necessitates frequent administration, which may lead to reduced patient adherence [6]. By formulating Flupirtine into a bilayer tablet with sustained release features, its therapeutic effectiveness can be prolonged, dosing frequency reduced, and overall treatment compliance improved.

**Sustained Release Drug Delivery Systems (SRDDS)**

Sustained Release Drug Delivery Systems (SRDDS) are designed to release drugs at a controlled rate, maintaining consistent therapeutic levels for extended periods while minimizing side effects. These systems are gaining attention due to limited new drug approvals and resistance from irrational drug use, especially antibiotics. The primary aim of SRDDS is to enhance drug performance by prolonging action, reducing dosing frequency, minimizing side effects, and improving patient compliance. They achieve this through mechanisms such as coated tablets to control solubility, or encapsulated particles of various sizes to regulate dissolution rates, allowing drug release over 8–12 hours in the GI tract. Advantages include reduced toxicity, improved stability, and better palatability. These systems may use diffusion-controlled membranes and are often localized near the target tissue to maximize therapeutic impact. Examples include oral sustained release (e.g., Aspirin SR) and controlled release forms (e.g., Adalat CR for nifedipine), with durations ranging from hours (oral) to months (parenteral). [5]

**Sustained Release Dosage Forms**

Sustained Release (SR) systems are designed to maintain consistent drug levels in the bloodstream for extended periods. These formulations:
Improve therapeutic efficiency
Decrease fluctuation in plasma concentration
Minimize dosing frequency
Provide better patient compliance [6]
SR systems are particularly suitable for drugs with short half-lives, narrow therapeutic windows, or high dosing frequencies.

**HPMC Polymers**

The study utilizes Hydroxypropyl Methylcellulose (HPMC) K100M and K4M as matrix-forming agents due to their proven efficacy in controlling drug release. These polymers swell upon contact with gastrointestinal fluids, forming a gel barrier that regulates diffusion and erosion-based drug release mechanisms [7].

**Advantages:**

- They are unit dosage form and offer the greatest capabilities of all oral dosage form for sustained release bilayer tablet.
- The greatest dose precision and the least content variability.
- Cost is lower compared to all other oral dosage form.
- Lighter and compact.
- Easiest and cheapest to package and strip.

- Easy to swallowing with least tendency for hang-up.
- Objectionable odour and bitter taste can be masked by coating technique.
- Suitable for large scale production.
- Greatest chemical and microbial stability over all oral dosage form.
- Product identification is easy and rapid. Requiring no additional steps when employing an embossed and/or monogrammed punch face.

**Disadvantages**

- Bilayer rotary press is expensive.
- Inaccurate individual layer weight control.
- Some drugs resist compression into dense compact, due to amorphous nature, low density nature.
- Insufficient hardness, layer separation, reduced yield.
- Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
- Bitter tasting drugs, drugs with an objectionable odour or drugs that are sensitive to oxygen may require encapsulation or coating.
- Difficult to swallow in case of children and unconscious patients.
- Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.

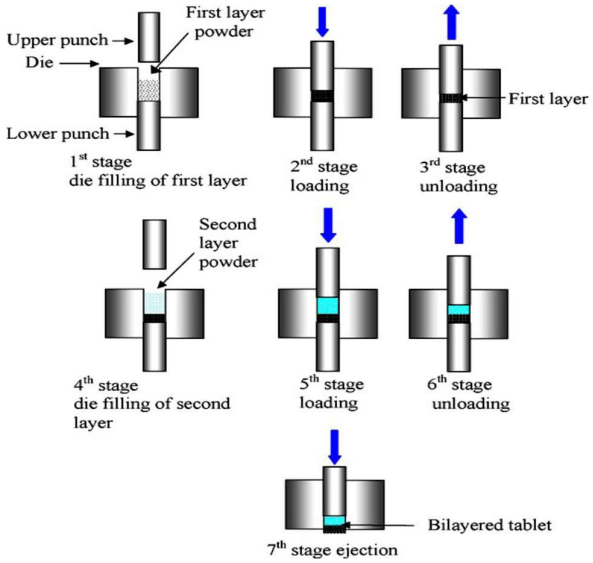


**Fig 1: Preparation of a Bilayer Tablet**

**Aim and Scope**

The aim of the present study is to formulate and evaluate bilayer tablets of Flupirtine Maleate that provide an immediate release followed by sustained release to enhance therapeutic efficacy, improve patient compliance, and reduce dosing frequency. The formulation incorporates HPMC K100M and HPMC K4M as rate-controlling polymers to develop a stable, colon-targeted delivery system using the direct compression method**.**

- Pre-formulation studies (e.g., solubility, flow properties),
- Compatibility studies using FT-IR spectroscopy,
- Tablet formulation using selected excipients and polymers,
- Evaluation of physicochemical parameters like hardness, friability, weight variation, disintegration, and in vitro drug release,
- Drug release kinetics modeling to understand the mechanism of drug release,
- Stability studies under accelerated conditions to assess shelf-life.

## MATERIALS AND METHODS

**Materials used**

**Table 1: Materials used**

| S. no | Materials used | Manufacturer |
|---|---|---|
| 1 | Flupirtine | Drugs pvt ltd, india |
| 2 | HPMC K 4M | Ferro international, japan |
| 3 | HPMC K 100M | Otto chemical, |
| 4 | Microcrystalline cellulose | FMC Bio polymer, Ireland |
| 5 | Magnesium stearate | FMC, U.S.A |
| 6 | Talc | Degussia, India |

**Equipment's Used**

**Table 2: List of Equipment used**

| S. no | Equipment | Manufacturer |
|---|---|---|
| 1 | Electronic single pan balance | Sartorius, Germany |
| 2 | Tapped density tester | Electro lab, India |
| 3 | Mechanical stirrer | Remi motors, Bombay |
| 4 | pH meter | Digisum electronics, Hyderabad |
| 5 | Dissolution test apparatus | Lab India , India |
| 6 | Stability chambers | Thermo lab, Mumbai |
| 7 | Hardness tester | Schluniger, U.S.A |
| 8 | Friabilator (USP) | Electro lab, Mumbai |
| 9 | Compression machine | Cadmach , India |

**Methodology of the current study**

**Development of analytical method for determination of wavelength of Flupirtine:**

**Determination of absorption maxima (Max):**

The ultra violet spectrophotometric method was selected for the estimation of Flupirtine. The diluted drug solution nwas scanned in between the wavelength range of about 200 – 400 nm. The λmax was obtained at 252 nm: hence it was selected and used for further quantitative analysis.

**Preparation of pH 1.2 buffer:** Dissolve 2gm of Nacl in 7 ml of concentrated hcl dilute with water and make up to 1000ml and mix.

**Preparation of pH 6.8 buffer:** 28.80gms of disodium hydrogen phosphate and 11.45 gms of potassium hydrogen phosphate were dissolved in water and volume was made upto 1000 ml.

**Preparation of pH 7.4 buffer:** Dissolve 2.38 gms of disodium hydrogen phosphate and 0.19 gm of potassium hydrogen phosphate and 0.8 gm of sodium chloride in required amount of distilled water and make up to 1000 ml.

**Preparation of calibration curve:** 100mg of Flupirtine drug was dissolved in required amount of pH 7.4 phosphate buffer and made up to 100ml , to give concentration 1000 µg/ml ( primary stock solution). From the primary stock solution, 10 ml was taken and diluted to 100 ml with same buffer to give the concentration of 100 µg/ml (secondary stock solution), aliquots of 0.5 ml to 3 ml were transferred into a series of 10 ml volumetric flasks and final volume was made up with buffer to give the concentration ranging from 5 µg/ ml to 30 µg /ml. the absorbance of these solutions was measured against a phosphate buffer pH 7.4 as a blank in UV/ Visible spectrophotometer at 252nm. Average of three determinations was taken.

**Characterization of Flupirtine compressed tablets**

**Preformulations studies**

Preformulations testing is the first step in the rational development of dosage forms of a drug substance. It can be defined as "an investigation of physical and chemical properties of a drug substance alone and when combination with Excipients". The overall objective of preformulation testing is to generate information useful to the formulations in developing stable and bio available dosage forms that can be mass produced. The preformulation testing should start at the point after biological screening, when a decision is made for further development of compound in clinical trials.

**Organoleptic properties**

These are preliminary characteristics of any substance which is useful in identification of specific material. The physical properties like color, odour of API were studied. The appearance of the active pharmaceutical ingredient was found by visual observation. The following physicochemical evaluations (precompression studies) were evaluated

**Flow behavior**

The flowability of a powder is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as reproducible filling of tablet dies, otherwise, high dose variations will occur. In order to ensure the flow properties bulk density, tapped density, angle of repose, Carr's index and Hausner's ratios were evaluated. Flow properties are the important concern in the formulations and industrial production of tablet dosage form. Angle of repose is characteristic to the flow rate of powder. In general, values of angle of repose = 40° indicate powders with poor flowability.

**Angle of repose**

The flow property was determined by measuring the angle of repose. In order to determine the flow property, the angle of repose was determined. It is the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal.

**Bulk density**

Accurately weighted power was carefully transferred into graduated measuring cylinder. The powder bed was made uniform and volume occupied by powder was noted as per graduation mark on the cylinder as ml.

**Tapped density**

Accurately weighted power was carefully transferred into graduated measuring cylinder. The power bed was made uniform and volume occupied by powder after tapping was noted as per graduation mark on the cylinder as ml. It is expressed in gm/ ml.

**Compressibility Carr's index and Hausner's ratio:**

In the recent years, the compressibility index and the closely related Hausner's ratio have become the simple, fast and popular methods of predicting powder flow characteristics. The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials, because all of these can influence the observed compressibility index. The compressibility index and Hausner's ratio are determined by measuring both the bulk volume and tapped volume of a powder.

**In-vitro drug release studies**

Dissolution is the process by which a solid solute enters a solution in the pharmaceutical industry, it may be defined as the amount of drug substance that goes into solution per unit under standardized conditions of liquid/solid interface, temperature and solvent composition. Dissolution is considered as one of the most important quality control test performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability.[8] USP dissolution apparatus type II was employed to study the in-vitro drug release from various formulations prepared. The dissolution medium used was 900 ml of acidic buffer of Ph 1.2 for 2 hrs, phosphate buffer of pH 7.4 for 2 hrs . The tablet was kept in to the basket. the temperature was maintained at 37ºC $\pm$0.5ºC and the stirring rate was 100 rpm. samples were withdrawn at regular time intervals and the same volume was replaced with fresh dissolution medium. the samples were measured by UV-visible spectrophotometer at 252 nm at (pH 1.2, pH6.8, pH7.4) against a blank. The release studies were conducted in triplicate and the mean values were plotted versus time.

**Stability Studies**

A study was carried out to assess the stability of the Flupirtine HPMC coated tablets formulation. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies were carried out at accelerated conditions (40◦c and 75% RH) over a period 3 months. Samples were evaluated at 1,2 and 3 months for different parameters such at thickness, physical appearance, hardness, weight variation, drug content and dissolution. [9]

## RESULTS AND DISCUSSIONS

**Organoleptic Properties:**
The Flupirtine maleate used was confirmed as a white crystalline powder, matching standard specifications, indicating appropriate drug quality for formulation development. These tests were performed as per procedure given in material and method part. The results are illustrated in following table.

**Table 3: Organoleptic Properties**

| Test | Specification\ limits | Observation |
|---|---|---|
| Colour and nature | White crystalline powder | White crystalline powder |

The results of Flupirtine compiles with the specification

**Standard Calibration Curve**
A linear relationship was established between concentration and absorbance at 250 nm, suitable for further quantitative analysis.

**Table 4: Standardization Curve of Flupirtine Maleate**

| S.no | Concentration (µg/ml) | Absorbance (250nm) |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 2 | 0.0681 |
| 3 | 4 | 0.1820 |
| 4 | 6 | 0.2550 |
| 5 | 8 | 0.3276 |
| 6 | 10 | 0.4230 |
| 7 | 12 | 0.5228 |
| 8 | 14 | 0.6295 |
| 9 | 16 | 0.7291 |

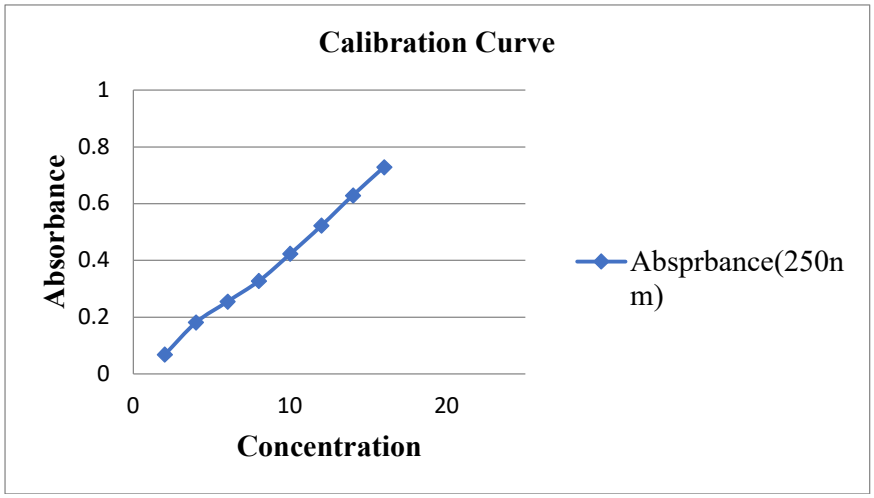


**Fig 2: Calibration curve of Flupirtine maleate in pH 6.8 buffer**

**FT-IR Spectroscopy Compatibility**
A compatibility study focuses on a binary mixture of drug substance and some selected Excipients a fixed ratio with or without added moisture. The mixture stored at elevated temperatures as 40◦c 75%RH, 55◦c 60%RH in capped vials. The results of interaction between the active drug and Excipients are determined as those IR spectra of mixture of Flupirtine maleate and HPMCK100M+HPMCK4M.

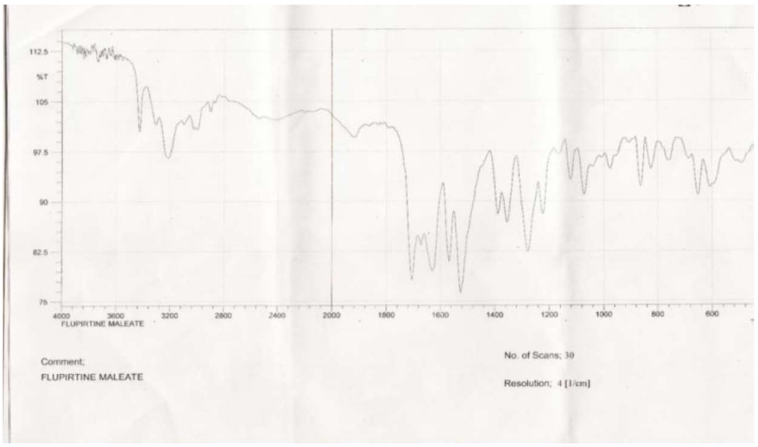


**Fig 3: FT- IR spectra of Drug Flupirtine Maleate**

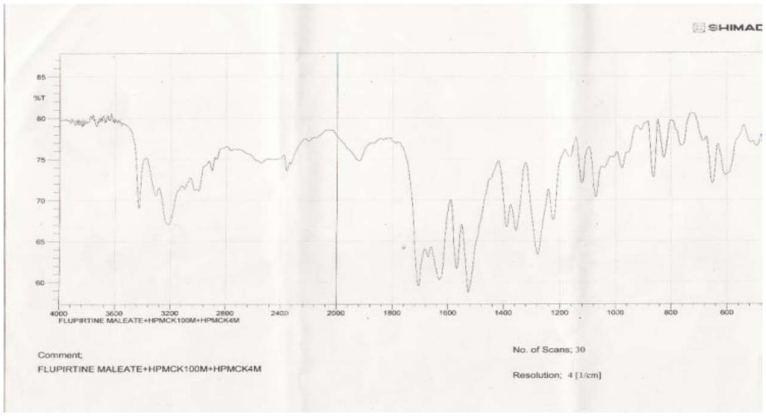


**Fig 4: FT-IR spectra of mixture of Flupirtine Maleate and HPMCK100M +HPMCK4M**

**Pre-compression Parameters**

The powder blends exhibited good flow properties, with angle of repose values below 30° and compressibility index values between 17.05%–20.33%. These results suggest suitability for direct compression method.

**Table 5: physio chemical evaluation of Flupirtine powder**

| Pre Formu lation | Angle of repose ± SD | Bulk density ± SD | Tapped density ± SD | Carr's index ± SD | Hausner's ratio ± SD |
|---|---|---|---|---|---|
| F1 | 25.16 ± 0.05 | 0.632 ± 0.04 | 0.743 ± 0.05 | 17.53 ± 0.53 | 1.16 ± 0.04 |
| F2 | 24.11 ± 0.06 | 0.671 ± 0.12 | 0.848 ± 0.54 | 17.06 ± 0.43 | 1.243 ± 0.03 |
| F3 | 21.03 ± 0.03 | 0.671 ± 0.03 | 0.826 ± 0.09 | 18.55 ± 0.93 | 1.221 ± 0.03 |
| F4 | 24.14 ± 0.09 | 0.678 ± 0.05 | 0.784 ± 0.11 | 18.28 ± 0.06 | 1.172 ± 0.02 |

The Flupirtine tablets were prepared by direct compression method. Before compression the powder was evaluated for angle of repose, bulk density, tapped density, Hausner's ratio and compressibility index. The bulk densities of the powder were found to be in the range of 0.589 ± 0.020 to 0.716 ± 0.04 gm/ml, while the tapped densities were ranges between 0.726 ± 0.06 to 0.869 ± 0.07 gm/ml. the flow characteristics of the powder were assessed by determining their angle of repose and Carr's index . the low values of compressibility 17.05 ± 0.32 to 20.33 ± 0.88 signify good flowability. The angle of repose of all formulation were less than $30^{O}$ (21.03 ± 0.03 to26.83 ± 0.06), also indicated good flowability of the powder. This shows that the powder has smooth flow properties ensuring homogenous filling of the die cavity during the punching of tablets.

**Post-compression Evaluation**

The Flupirtine tablets were prepared by direct compression method. The results of physicochemical evaluation of prepared tablets are shown in Table 5.5. the tablets were evaluated for hardness, diameter, thickness average weight of the tablet and drug content. The tablet was evaluated for their hardness, content uniformity, diameter, thickness, friability, disintegration and in vitro drug release. The hardness test is one of the control parameters during the manufacturing of tablets. Generally, the tablets prepared with low compression force dissolves faster than that with high compression force. The recommended hardness value for tablet is 4 to 8 kg/cm. the average hardness of the tablets was found to be in range of 6.7 ± 0.19 to 7.4 ± 0.24 kg/cm2.

**Table 6: evaluation of sustained release Bilayer tablet of Flupirtine maleate**

| Formu lation | Hardness (kg/cm2) | Wt. variation(mg) | Thickness (mm) | % Friability | Invitro disintegration time (sec) |
|---|---|---|---|---|---|
| **F1** | 7.2 ± 0.31 | 720.6 ± 3.11 | 7.34 ± 0.16 | 0.72 ± 0.24 | 98.16% |
| **F2** | 7.16± 0.37 | 720.8 ± 2.31 | 7.38 ± 0.25 | 0.72 ± 0.41 | 99.65% |
| **F3** | 7.3 ± 0.21 | 718.6 ± 2.12 | 7.22 ± 0.14 | 0.72 ± 0.29 | 99.36% |
| **F4** | 7.4 ± 0.24 | 720.7± 4.076 | 7.51 ± 0.240 | 0.74± .063 | 96.62% |

The average weight variation of the tablets was found within the limits of 718.6 ± 2.12 to 720.8 ± 2.31. friability value of tablets should be in range of 0.5 to 1% limits, which is the usual friability range of tablets range of 0.72 ± 0.24 to 0.74 ± 0.63. The content uniformity of drug Flupirtine present in the tablet's formulation ranged from the thickness of the tablet was found to be 7.22 ± 0.14 to 7.51 ± 0.240. It was found that the physicochemical parameters of the prepared tablets comply with standards.

**In Vitro Drug Release Studies**

For immediate release layer Dissolution rate was studied by using USP type-I apparatus at 75 rpm using 900ml of 0.1 N HCl solutions as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°C, aliquot of 5 ml of dissolution medium was withdrawn at every 15 min interval the absorbance of solution was measured by UV spectrophotometric method at 250 nm and concentration of the drug was determined from standard calibration curve. The volume of the dissolution medium was adjusted to 900ml at every sampling time by replacing 5 ml with same dissolution medium. The in vitro release of drug from sustained layer was carried out for 24 hours using basket type tablet dissolution apparatus USP type-I containing 900 ml of dissolution medium maintained at 37±0.5◦C and speed of agitation at 75 rpm. Using 900 ml of pH 6.8 phosphate buffers as a dissolution medium.

**Table 7: cumulative percent drug release data for bilayer tablet for sustained release**

| S. No. | Time (hr) | Cumulative percent drug release | | | | |
|---|---|---|---|---|---|---|
| | | **F1** | **F2** | **F3** | **F4** | **Marketed product** |
| 1 | 0 | 0 | 0 | 0 | 0 | **0** |
| 2 | 1 | 29.25 | 28.19 | 30.75 | 26.45 | **25.80** |
| 3 | 2 | 33.42 | 35.95 | 38.54 | 33.36 | **32.40** |
| 4 | 3 | 38.24 | 45.24 | 47.62 | 41.16 | **38.25** |
| 5 | 4 | 46.14 | 54.09 | 52.81 | 44.86 | **42.54** |
| 6 | 5 | 52.78 | 60.27 | 58.38 | 48.71 | **48.70** |
| 7 | 6 | 60.50 | 66.87 | 63.17 | 52.25 | **51.25** |
| 8 | 7 | 69.25 | 68.23 | 67.40 | 56.86 | **55.80** |
| 9 | 8 | 78.86 | 74.49 | 71.37 | 61.63 | **58.62** |
| 10 | 9 | 85.10 | 76.98 | 78.23 | 64.95 | **62.50** |
| 11 | 10 | 92.174 | 82.26 | 81.51 | 70.15 | **68.30** |
| 12 | 11 | 95.38 | 87.85 | 87.49 | 75.36 | **72.86** |
| 13 | 12 | 98.16 | 92.95 | 95.35 | 80.92 | **74.12** |
| 14 | 14 | - | 99.65 | 96.30 | 83.6 | **81.78** |
| 15 | 16 | - | - | 99.36 | 89.30 | **90.82** |
| 16 | 18 | - | - | - | 96.62 | **96.59** |

**Drug Release Kinetics [10]**

All formulations followed zero-order kinetics**,** with strong correlation to Higuchi's model**,** indicating diffusion-controlled release. The Korsmeyer–Peppas model revealed non-Fickian (anomalous) transport (n = 0.478–0.689), suggesting a combination of drug diffusion and matrix erosion. The rate and mechanism of release of Flupirtine Maleate from the prepared bilayer tablets were analysed by fitting the dissolution data into the zero order, First order, Higuchi, Korsmeyer-Peppas and hexon crowel equations. All the Formulations (F1-F4) followed Zero order release Mechanism. Higuchi plots for all the formulations were linear indicating the drug release by diffusion controlled. The erosion model was applied to *in vitro* release data, the linearity was observed with r2value and also Hixon-Crowell cube root model showed high r2 value of 0.959 to 0.972 suggested that the geometrical shape of tablet diminished proportionality due to erosion of hydrophilic gel layer. To explore the release pattern, results of the in vitro dissolution data were fitted to the Korsmeyer-Peppas equation, which characterizes the transport mechanism. The value of release exponent (n) for all formulations were in between 0.478 to 0.689 indicates the non fickian transport or anomalous diffusion it refer to combination of both diffusion and erosion rate release.

**Table 8: Mathematical modeling and drug release kinetics of optimized formulation F4 and marketed product**

| Formulation | Drug release kinetics (R2) | | | | Release exponential(n) |
|---|---|---|---|---|---|
| | Zero- order | First –order | Huguchi | Korsmeyer | |
| F4 | 0.926 | 0.911 | 0.993 | 0.972 | 0.987 |
| Marketed product | 0.934 | 0.912 | 0.993 | 0.974 | 0.990 |

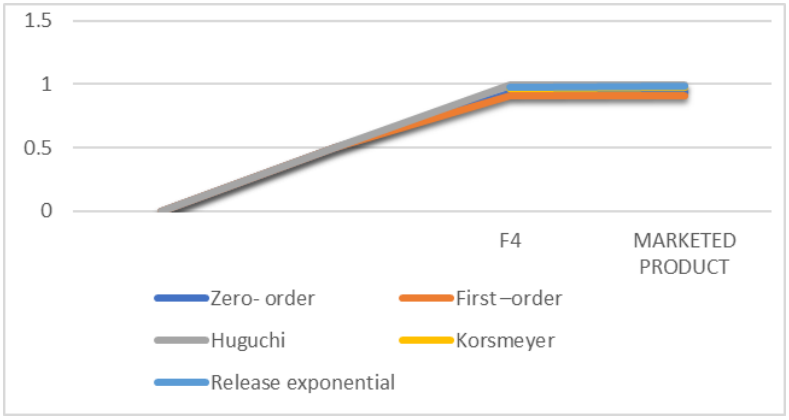


**Fig 5: Mathematical modeling and drug release kinetics of optimized formulation F4 and marketed product**

**Stability Studies**

Tablets stored under accelerated conditions (40°C/75% RH) for 3 months showed no significant changes in physical properties or drug content, confirming formulation stability.

**Table 9: Results of Flupirtine Maleate Stability Studies**

| **Parameters tested** | **Storage conditions** | | | |
|---|---|---|---|---|
| | **Initial** | **40◦c ± 2◦c / 75% ± 5% RH** | | |
| | | **1 st month** | **2nd month** | **3rd month** |
| Description | White crystalline powder | Non change | No change | No change |
| Weight(mg) variation | 520 | 520 | 520 | 519 |
| Thickness (mm) | 7.51 | 7.51 | 7.51 | 7.49 |
| Hardness (kp) | 7.4 | 7.4 | 7.4 | 7.1 |
| Friability (%) | 0.74 | 0.74 | 0.74 | 0.73 |

## SUMMARY

The aim and present study was to formulate and evaluate colon targeted tablets of Flupirtine by using HPMC K100M, HPMC K4M. FT-IT study was carried out to check any possible interactions between the drug and the Polymer HPMC K100M, HPMC K4M. the study confirmed that no interaction between the selected drug and the polymer. Flupirtine tablets were prepared by direct compression method using HPMC K100M, HPMC K4M as a polymer, magnesium stearate is used as a glidant, sodium starch glycolate is used as super disintegrating agent.

Before compression, the powder evaluated for angle of repose, bulk density, tapped density and compressibility index. The precompression studies of the powder were assessed by determining their angle of repose and Carr's index. The values of compressibility index and angle of repose signify good flowability of the powder for all the batches. After compression the compressed tablets were evaluated for its hardness, weight variation, content uniformity, diameter, thickness and friability, disintegration. The In- vitro dissolution studies were carried out for compressed and coated tablets using USP dissolution apparatus.

The cumulative percentage of drug release from the tablets varies and depends on % weight buildup of the polymer on tablet. The selected formulations F8 were subjected to release kinetics, stability studies. The drug release from the selected formulations (F4) was first order diffusion controlled and release mechanism was Peppas release. The stability study indicated that the prepared formulations was stable and retained their pharmaceutical properties at 40◦c/75% RH over a period of 3 month.

The HPMC K100M, HPMC K4M coated tablet formulations having release less amount of drug hostile acidic environment of stomach (pH 1.2) and in pH 6.8 phosphate buffer (small intestine) due to protective polymer coating but release total amount of the drug in the colonic environment (pH 7.4).

## CONCLUSION

The present study was carried out to develop Sustained Release Bilayer Tablets of Flupirtine Maleate Immediate release layer and sustained release layer by direct compression method. Concluded that, the bilayer tablet technology can be successfully applied for Flupirtine Maleate using of polymers such as HPMC K100M, and HPMC K4M, can be used as rate controlling polymers by appropriate selection of the level of polymers in the Sustained release layer of Bilayer tablet. It can be concluded that the optimized batch F4 by adopting biphasic drug release pattern in a single dosage could improve patient compliance and give better pain management.

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