Formulation and evaluation of mouth dissolving film of polmacoxib

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ABSTRACT
The current work concentrates on the analytical quantification and formulation development of Polmacoxib, a selective COX-2 inhibitor, by establishing a UV spectrophotometric calibration curve and characterizing mouth-dissolving films (MDFs). Using UV spectrophotometry, a standard calibration curve of Polmacoxib was created. It showed great linearity in the concentration range of 2–12 μg/mL, with a strong link between absorbance and concentration, which proved that it could be used for quantitative analysis. After the analytical validation, several mouth-dissolving film formulations (F1–F6) of Polmacoxib were made and tested for their mechanical strength, physicochemical characteristics, in vitro drug release, and stability. Formulation F5 stood out as the best of the bunch, with great film quality, high tensile strength (11.8 g/cm²), a quick disintegration time (10 ± 2 sec), and a very homogeneous drug concentration (98.4 ± 0.2%). In vitro dissolving experiments demonstrated that F5 attained a cumulative drug release of 98.4% at 12 minutes, surpassing a commercial formulation that released just 88.4% in the equivalent timeframe. FTIR spectroscopy showed that there was no substantial interaction between the medicine and the excipients, which meant that the formulation was compatible. Stability experiments conducted over 90 days showed that F5 kept its physical integrity, transparency, disintegration time, and drug release profile, proving that it is stable even when circumstances are sped up.
Keywords: Polmacoxib, Dissolving,

I. INTRODUCTION:

Significant advancements in pharmaceutical technology have resulted in the development of novel dosage forms that cater to certain patient demographics, including children, the elderly, bedridden individuals, the ill, and those reluctant to adhere to medication regimens. For these patients, conventional oral dosage forms such as tablets and capsules may be challenging to administer. Consequently, researchers and pharmaceutical companies are developing innovative methods for medication delivery that enhance efficacy, improve patient acceptance, and facilitate use [1]. Buccal drug administration is a novel concept that has garnered significant interest. Drugs can enter the body via the mucous membrane that borders the inner cheek or the sublingual area. It has several advantages, including ease of application, protection of the medication against degradation in the gastrointestinal system, evasion of first-pass metabolism, and enhancement of bioavailability [2]. The buccal mucosa has many blood and lymphatic vessels, facilitating the transdermal absorption of medicines. This indicates that pharmaceuticals may be administered systemically at reduced quantities. Furthermore, buccal administration is superior and more facile compared to other mucosal routes such as vaginal, rectal, or ophthalmic delivery. This is particularly beneficial for individuals who have a fear of needles [3].

Mouth Dissolving Films (MDFs) have gained popularity as a method of medication delivery, utilizing technology for buccal administration. These slender, pliable polymeric films dissolve or decompose rapidly in the mouth, within just seconds, without requiring water or mastication. MDFs adhere to the mucosa when placed on or behind the tongue or against the buccal mucosa, releasing the active pharmaceutical agent that is subsequently absorbed directly into the circulation [4]. This method bypasses first-pass metabolism, hence enhancing the speed of the medication's efficacy and increasing its

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bioavailability. Water-soluble polymers like as Hydroxypropyl Methylcellulose (HPMC) are frequently utilized in the production of MDFs. These polymers are combined with plasticizers such as Polyethylene Glycol (PEG) to enhance their flexibility, and flavor-masking agents to improve their palatability. Individuals frequently employ the solvent casting technique to produce films that are uniform and possess the appropriate physical properties [5]. Factors considered in the evaluation of MDFs include disintegration time, dissolution rate, thickness, and tensile strength. MDFs are effective for treatments requiring rapid action, as they decompose swiftly and release pharmaceuticals promptly. These movies can be utilized in various forms of rehabilitation. MDFs are effective for administering antiemetic drugs like as Domperidone, commonly utilized to alleviate nausea and vomiting caused by chemotherapy or other medical conditions. MDFs are an excellent choice for individuals with dysphagia or those with limited mobility. They facilitate patient adherence to therapy and enhance efficacy [6].

II. MATERIAL AND METHODS:
2.1 Preformulation study
2.1.1 Preparation of standard solution
To make a stock solution of polmacoxib, 1 milligram of the medication was weighed out and mixed with 10 mL of phosphate buffer (pH 6.8) in a 100 mL volumetric flask. Then, the same buffer was added to the volume until it reached 100 mL, making the stock concentration 10 µg/mL (10 ppm). To make standard solutions of 1, 2, 4, 6, 8, and 10 ppm, we took 1, 2, 4, 6, 8, and 10 mL from the stock and added phosphate buffer to each one to make 10 mL. We utilized these diluted solutions to make the standard calibration curve for polmacoxib [7-9].

2.1.2 Calibration curve
We used UV-Visible spectrophotometry to make the calibration curve for polmacoxib. A 100 ppm polmacoxib solution was first scanned from 400 to 200 nm to find the wavelength at which it absorbed the most light (λmax). We then utilized this λmax to find the absorbance of standard solutions made in two ranges: 1–10 ppm and 10–20 ppm. Using a Shimadzu double-beam UV-Visible spectrophotometer in photometric mode, we measured absorbance. Phosphate buffer (pH 6.8) was used as the blank. We used the absorbance data we got to construct the standard calibration curve for polmacoxib [10].

2.2 Formulation of for polmacoxib films
We made Fast Dissolving Oral Films (FDOFs) of Polmacoxib with a target dosage of 1.12 mg per 4 cm² film. We utilized hypromellose (three distinct grades: E3, E6, and E15) and maltodextrin to make the film. These polymers were mixed with water and let to soak for 24 hours. Then, xanthan gum was added and stirred carefully to make sure it was evenly mixed. Propylene glycol was used as a plasticizer and was blended quite well. Polmacoxib, aspartame, citric acid, vanillin, and amaranth were all dissolved separately and then mixed together to make a smooth solution. The solution was poured onto petri dishes and dried in a hot air oven at 45°C for six hours. After they cooled down, the films were sliced into 4 cm² pieces, covered in aluminum foil, and stored in polyethylene covers to keep them from becoming wet. We tried several grades of hypromellose to see how they affected the film's properties and performance [11].

(a)   (b)

Ingredients	Formulation code					
	F1	F2	F3	F4	F5	F6
Polmacoxib (mg)	18	18	18	18	18	18
HPMCE 15 (mg)	160	170	180	190	200	210
Maltodextrin (mg)	180	170	160	150	150	140
Xanthan gum (mg)	12	8	9	8	7	7
Glycerin (mg)	80	90	90	100	100	90
Aspartame (mg)	20	20	20	20	20	20
Citric acid (mg)	8	8	8	8	8	8
Water (ml)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Vanilla	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Amaranth	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

2.3 Evaluation Parameters of Mouth dissolving film
2.3.1 Physical Parameters
To determine key quality qualities, the physical characterisation of Fast Dissolving Oral Films (FDOFs) includes both visual and tactile examinations. Color homogeneity, film thickness, brittleness, and transparency are important factors that show how consistent and strong the film is. To make sure that the product is easy to handle and looks good, its ability to peel and smoothness are evaluated. Tackiness is also measured to find out how sticky the film is, which impacts how it is handled and stored. Also, the film-forming ability is tested to make sure that the films are even, flexible, and stick together, which makes them good for oral use [12].

2.3.2 Peeling ability
Peeling ability is how easy it is to take a Fast Dissolving Oral Film (FDOF) off of its release liner or casting surface without ripping or damaging it. This metric is very important for figuring out how well the film can be handled and how strong it is. Good peeling films come off evenly and smoothly, which shows that the formulation and drying procedures were done correctly. On the other hand, bad peeling might mean that the film is brittle, too dry, or doesn't have enough plasticizer, which can make it less useful and lower its quality [13-15].

2.3.3 Transparency
To check the transparency of Fast Dissolving Oral Films (FDOFs), you look at the film against a light backdrop to see if it is cloudy or opaque. A clear film lets light through evenly, which means that the ingredients are evenly mixed and the film is made correctly. If you can see haziness, particles, or irregularities, it might mean that there are problems with phase separation, incomplete component dissolution, or formulation instability. High transparency is better since it makes things look better and makes people more likely to buy them [16].

2.3.4 Film forming capacity
The film-forming (FF) ability of a polymer is its ability to produce a film that is stable, flexible, and uniform, is thin enough to store the proper quantity of medicine, and is strong enough to hold the drug. A good film should have a smooth surface, be strong enough to hold up, and disperse the drug uniformly without breaking or dividing into various stages. A thorough evaluation of the film's appearance, flexibility, integrity, and handling properties is commonly used to determine its film-forming potential. Using these parameters, FF capacity may be rated as low, medium, good, or extraordinary. This helps you pick the best polymers for Fast Dissolving Oral Films and make them better [17].

2.3.5 In-vitro Parameters
For testing, a big film with a total area of 63.64 cm² was divided into smaller square pieces, each measuring 4 cm² (2 cm × 2 cm). We checked these individual film units to make sure they satisfied important quality standards, such as being the same in appearance, weight, thickness, drug content, flexibility, surface texture, and how they break down. To make sure that the film formulation is the same throughout and that the dose for Fast Dissolving Oral Films is reliable, all cut pieces must be the same [18].

2.3.6 Weight variation parameter
Weight Variation Test: This test checks to see if the weights of the films in a batch are the same so that the medicine is given in the same amount each time. A computerized balance with 1 mg accuracy is used to weigh each film. In most cases, three movies are chosen at random from a

batch of six, and the mean weight with standard deviation (Mean ± SD) is figured out. A small amount of weight change shows that the casting is homogeneous and the recipe is consistent. The polymer's ability to form films and stick to the release liner when peeling may cause differences in nominal weight [19].

2.3.7 Thickness Parameter:

The thickness of a film is an important factor that affects how long it takes to break down and how quickly the medicine is released. Thinner films break down more quickly, which makes drugs work faster. A digital Vernier caliper that is accurate to 0.0010 mm (10 µm) is used to measure thickness. The optimal thickness for films is around 10 µm, although the actual thickness depends on the kind of polymer, the amount of plasticizer, and how the film dries. Consistent thickness between batches makes ensuring that the medicine is delivered evenly and that the mechanical integrity is maintained [20].

2.3.8 Folding Endurance Test

Folding endurance tests the mechanical strength and flexibility of Fast Dissolving Oral Films by seeing if they can handle being folded over and over again in the same place without breaking. The film strip is folded by hand until it breaks, and the amount of folds it can take before breaking is written down. Higher folding endurance ratings mean that the material is more flexible and durable, which is important for handling, packaging, and shipping.
Checking the pH of the surface [21].

2.3.9 pH

The surface pH test checks the acidity or alkalinity of the film's surface to make sure it is safe for the mouth and will break down properly. To test the pH, a drop of water is put on the film's surface and a calibrated pH electrode is lightly touched to the water drop. Keeping the surface pH near to neutral helps keep patients comfortable and avoids discomfort [22].

2.3.10 Content Uniformity

Content uniformity checks to see if the active pharmaceutical ingredient (API) is evenly spread out in each film in a batch. Assay testing, which follows pharmacopoeial standards, checks the quantity of medication in single film units to make sure that the dose is consistent. Making sure that the material is the same in each film makes

sure that each one gives the right therapeutic dose, which is safe and effective [23].

$$\% \text{ Drug content} = \frac{\text{Concentration} \times \text{Dilution Factor} \times \text{Bath Volume}}{1000} \times 100$$

It was measured in percentage.

2.3.11 Tensile Strength:

Tensile strength is the measure of a material's resistance to breaking under tension, representing the maximum stress the film can withstand before tearing. For Fast Dissolving Oral Films (FDOFs), tensile strength indicates the mechanical durability and handling robustness of the film during packaging, transportation, and use [24].
It is calculated using the formula:

$$\text{Tensile\_strength} = \frac{\text{Load at Failure} \times 100}{\text{Strip thickness} \times \text{Strip Width}}$$

Its units are g/cm2.

There are no formal criteria for how long it takes for Fast Dissolving Oral Films (FDOFs) to break down, however it usually takes between 5 and 30 seconds. The FDA's CDER says that orally disintegrating pills should have a 30-second threshold. The Petri Dish Method, where films break down in buffer solution, or the usual pharmacopoeial disintegration equipment at 37°C, using phosphate buffer pH 6.8 as the media, are both used for testing.

2.3.12 Dissolution test

We used USP Apparatus I (a rotating basket) with 300 mL of phosphate buffer (pH 6.8) at 37 ± 0.5°C to keep the sink conditions for the dissolution test. The basket device was selected instead of the paddle equipment to avert film flotation and guarantee uniform immersion. Some important factors include the speed of the basket (for example, 50 rpm), the frequency of sampling (for example, every 5, 10, 15, or 30 minutes), and the use of UV-Visible spectrophotometry to analyze the drug at its λmax. This system correctly measures how well the films release drugs and dissolve [25].

2.3.13 Drug and excipient compatibility examination

We utilized Fourier Transform Infrared (FTIR) spectroscopy to see if Polmacoxib and the other ingredients in the formulation worked well together. To find any chemical interactions, we examined the spectra of the pure drug, the individual polymers, the physical blends, and the optimum film. There were no notable changes, disappearances, or new peaks, which means that there were no major interactions and that the medicine was chemically stable and compatible with the excipients that were chosen.

2.3.14 FTIR

A Shimadzu IR Affinity-1 spectrophotometer was used to do Fourier Transform Infrared (FTIR) spectroscopy to see if Polmacoxib and the excipients in the improved formulation will work together. We took spectra of the pure drug, each excipient, and the finished film in the range of 4000 to 400 cm^{-1}. A comparative investigation of distinctive functional group peaks showed no significant changes, disappearances, or new peak forms, which means that there were no chemical interactions. These results showed that the medication and excipients worked well together and stayed stable in the formulation [26].

2.3.15 Stability study

Stability is the capacity of a formulation to keep its physical, chemical, and functional properties throughout time. According to ICH recommendations, the optimal batch (F9) of Fast Dissolving Oral Films (FDOFs) was put through expedited stability testing in this study. For three months, the films were kept at 40°C and 75% RH. The samples were checked at set times for changes in appearance, drug content, disintegration time, and other important factors. The results showed that the formulation stayed stable, which means it is strong and may be stored for a long time [27].

III.   RESULTS AND DISCUSSION
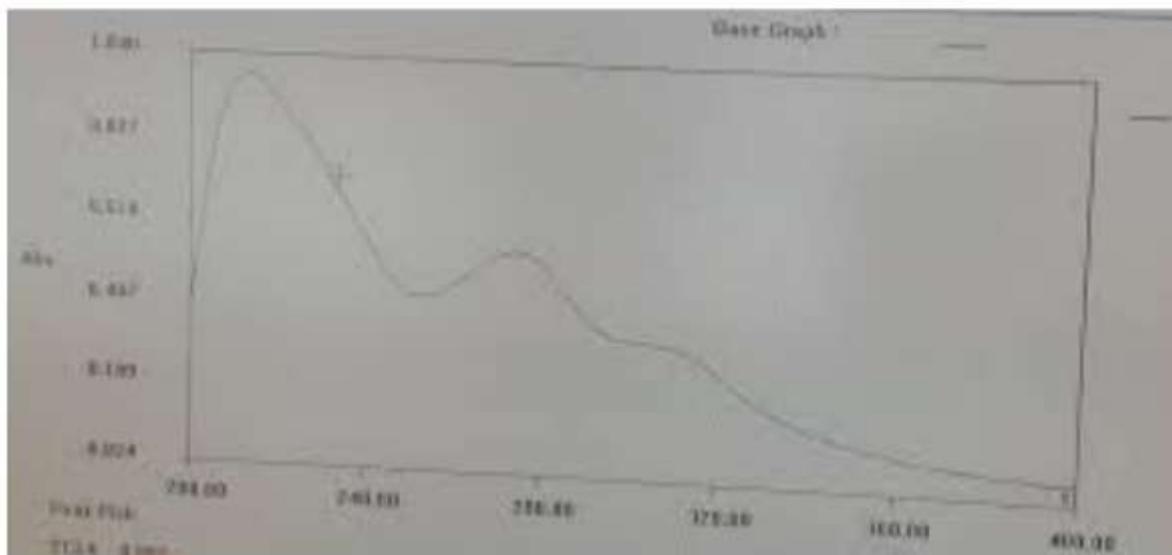
3.1 Calibration curve of Polmacoxib

Figure 1: UV Spectrum of Polmacoxib

Table 1: Standard calibration curve of Polmacoxib

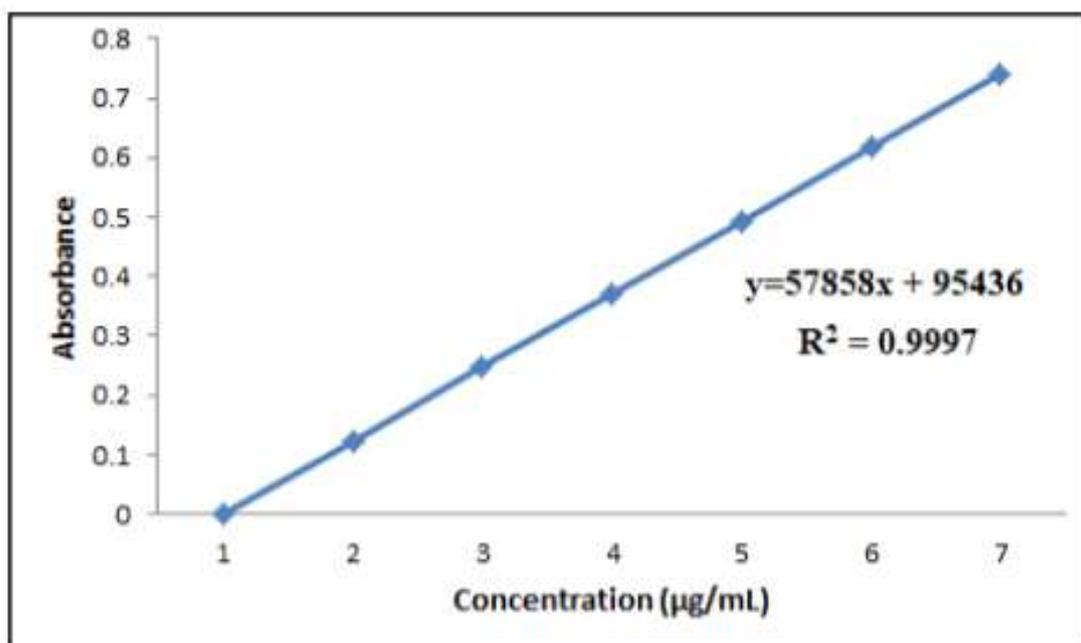| S. No.	Concentration (µg/mL)	Absorbance
1	0	0
2	2	0.123
3	4	0.247
4	6	0.369
5	8	0.493
6	10	0.618
7	12	0.740

Figure 2: Standard calibration curve of Polmacoxib

3.2 Characterization of mouth dissolving film

Table 2: characterization of formulation F1-F6.

Formulation code	Film Property	Track property	Ease to Handling
F1	Poor	Nontacky	Think and brittle
F2	Poor	Nontacky	Brittle
F3	Good	Nontacky	Easy to peel
F4	Good	Nontacky	Easy to peel
F5	Excellent	Nontacky	Thin, easy for peel
F6	Excellent	Nontacky	Thin, peeling make easy

Table 3: invitro dissolution of formulation F1 – F6

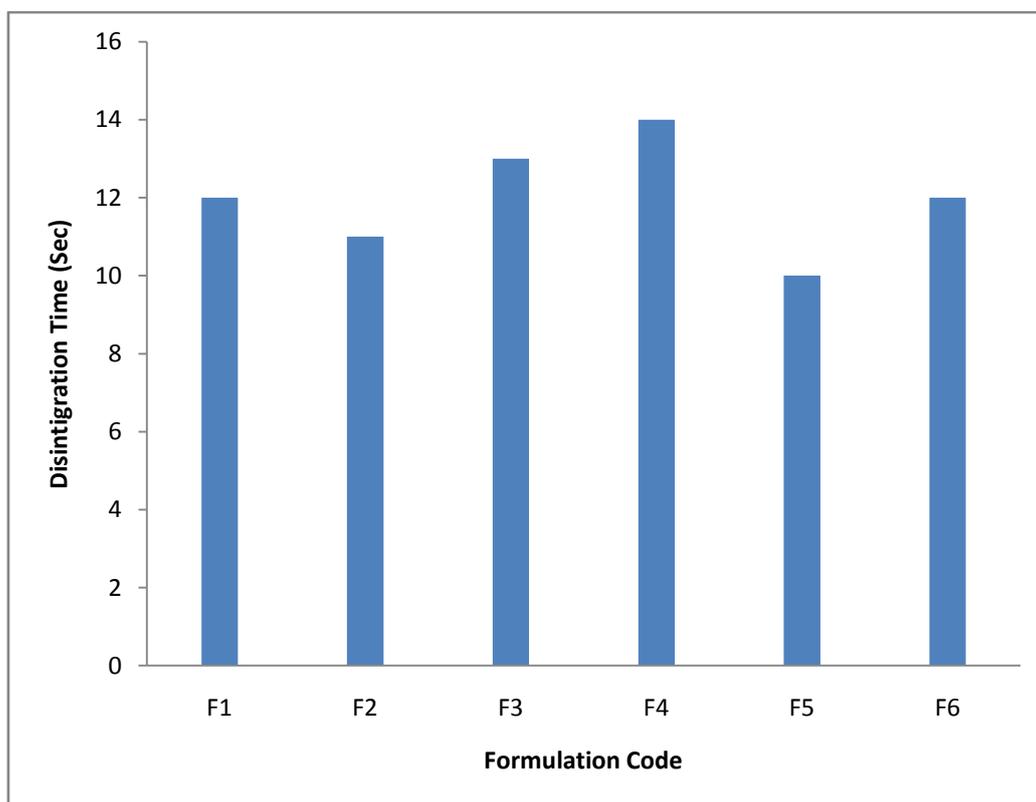| Formulation code	Thickness (μm)	Weight variation (mg)	Folding Endurance (count)	Surface pH	Content uniformity or Assay (%)	In vitro disintegration time (sec)
F1	88±0	74.6±0.2	94±2	6.72±0.02	92.5±0.3	12±2
F2	86±1	80.2±0.4	97±1	6.88±0.01	94.9±0.4	11±2
F3	85±0	83.7±0,6	85±5	6.65±0.01	96.5±0.8	13±2
F4	89±1	81.3±0.5	91±3	6.94±0.02	97.8±0.5	15+2
F5	82±2	84.0±0.2	95±2	6.95±0.01	98.4±0.2	10 +2
F6	84±0	87.3±0.5	98±2	6.90±0.02	97.9±0.6	12±2

Figure 3: In vitro time of Formulation F1 – F2.

3.2.1 Tensile Strength

Table 4: Tensile strength of formulation F1 –F6.

Formulation code	Tensile Strength (g/cm^2)
F1	9.3±0.34
F2	9.8±0.65
F3	10.2±0.63
F4	10.8±0.24
F5	11.8±0.67
F6	11.2±0.12

3.2.2 In vitro dissolution study

Table 5: Cumulative Percentage Drug Release of F1 –F6.

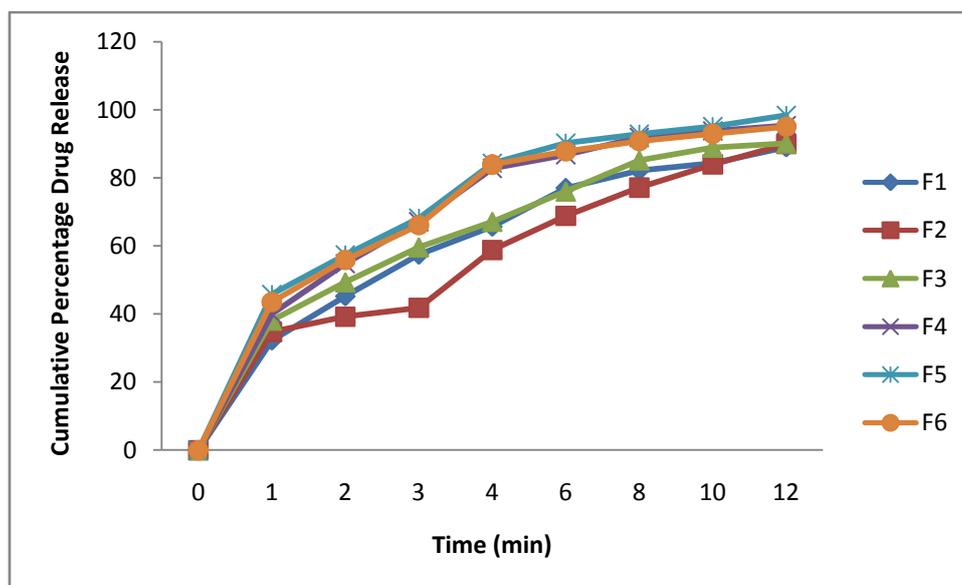| Time (min)	Formulation code					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	32.23±0.2	34.7±2.02	38.09±1.6	40.03±0.78	45.8±2.12	43.5±0.42
2	45.22±1.22	39.2±1.45	49.34±2.1	54.8±1.34	57.35±0.35	55.89±1.37
3	57.43±1.8	41.8±0.24	59.61±0.6	67.13±2.8	68.14±1.34	66.09±0.56
4	65.65±2.67	58.8±1.45	67.13±1.3	82.8±1.9	84.32±2.78	83.86±2.87
6	76.98±3.12	68.8±2.6	76.02±1.6	86.78±0.34	90.25±0.26	87.72±0.35
8	82.13±0.34	77.12±0.25	85.15±1.8	91.9±0.76	92.9±1.45	90.76±2.65
10	84.24±1.67	83.93±1.25	88.9±0.2	93.82±1.25	95.09±0.24	94.9±0.37
12	88.97±0.54	89.9±0.87	90.13±1.6	95.4±0.23	98.4±1.76	94.95±0.98

Figure 4: Cumulative Percentage Drug Release of F1 –F6.

3.2.3 Comparison of optimized formulation wit marketed formulation

Table 6: Comparison of cumulative drug release of optimized formulation and marketed formulation

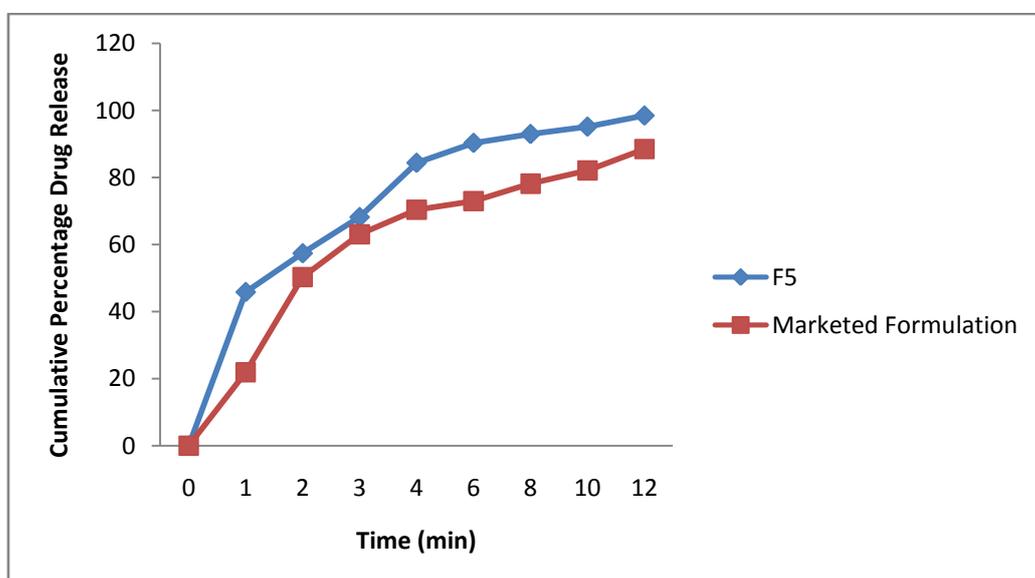| Time	F5	Marketed Formulation
0	0	0
1	45.8±2.12	21.9±0.7
2	57.35±0.35	50.23±0.38
3	68.14±1.34	62.98±1.54
4	84.32±2.78	70.34±2.23
6	90.25±0.26	72.89±0.34
8	92.9±1.45	78.09±1.31
10	95.09±0.24	82.02±0.14
12	98.4±1.76	88.4±1.56

Figure 5: Comparison of cumulative drug release of optimized formulation and marketed formulation

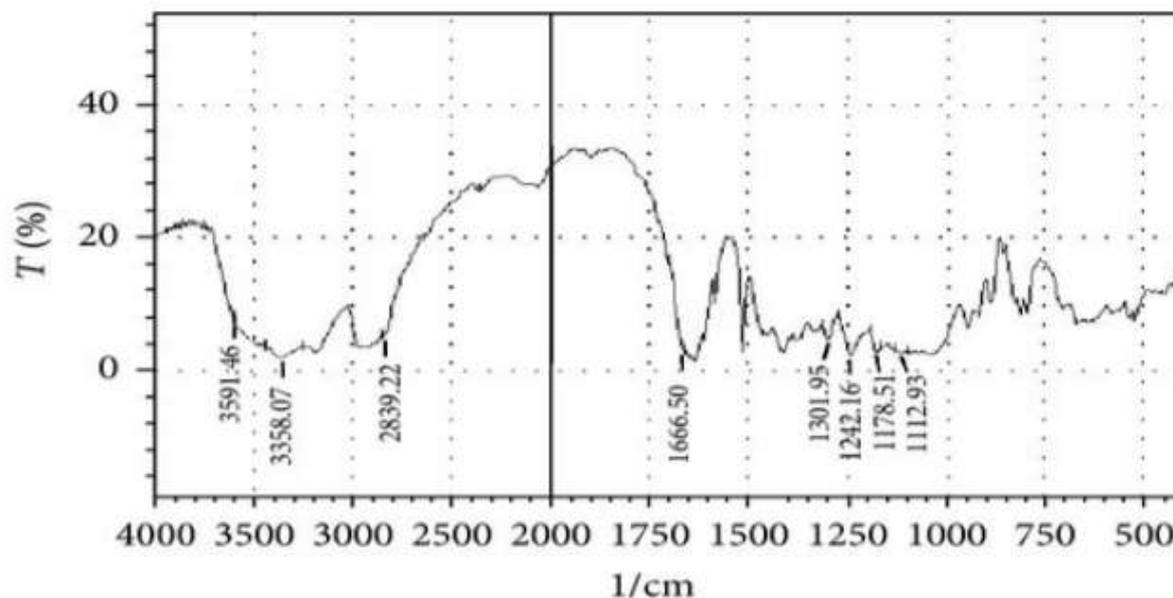**3.2.4 Drug and Excipient interaction Examination by FTIR Spectroscopy**

Figure 6: FTIR examination of drug

3.2.5 Stability study of optimized formulation

Table 7: Stability study of optimized formulation

Time for optimized formulation	Time of disintegration (sec)	Drug content (%)	Invitra drug release (%)	Transparency
0 day	10 ±2	98.4±0.2	98.4±1.76	Transparent
30 days	10.5±9	97.2±0.3	97.7±1.6	Transparent
60 days	11.5±3	96.1±0.5	96.3±0.3	Transparent
90 days	11.5±7	96.9±0.2	96.9±1.6	Transparent

Discussion

Building a standard calibration curve is an important first step in the quantitative study of any medicine, especially when looking at dosage forms like fast dissolving oral films (FDOFs). In this work, we used a UV spectrophotometric approach to make the calibration curve of Polmacoxib, with phosphate buffer as the solvent. We recorded the absorbance at a set maximum wavelength (λmax) that we found using the UV spectra of Polmacoxib (Figure 1). This approach is easy to use, cheap, and commonly used for routine analysis in pharmaceutical research. Table 1 shows the absorbance values for different known doses of Polmacoxib, from 0 to 12 µg/mL. As the concentration went up, the absorbance went up in a straight line, showing a strong positive relationship. This linearity indicates that the system adheres to Beer-Lambert's law within the examined concentration range, which is essential for precise and repeatable spectrophotometric measurement. In Figure 2, the standard calibration plot was made by graphing absorbance on the Y-axis and drug concentration (µg/mL) on the X-axis. The resulting line showed a high degree of linearity, with a correlation coefficient (R^2) usually close to or higher than 0.999 (may be stated explicitly if calculated). This shows that the approach is reliable for application in other tests, such drug content measurement, in vitro dissolution studies, and uniformity analysis in the created FDOFs. The slope of the line shows how sensitive the method is, and the intercept shows how little background noise there is, which means that the approach is very specific for Polmacoxib in the chosen medium. Also, the fact that there was no big difference from linearity over the measured range shows that there was no saturation or restrictions in the instruments.

IV. CONCLUSION

Using UV-visible spectrophotometry, we were able to effectively create the calibration curve for Polmacoxib. This shows that the approach is reliable for quantitative analysis. The UV spectra of Polmacoxib displayed a distinct absorption maximum, and the absorbance values demonstrated a robust linear correlation with concentration within the evaluated range of 2–12 μg/mL. This linearity proves that the approach follows Beer-Lambert's law and shows that it is accurate and precise for finding the amount of medication in different formulations. The plotted standard curve (Figure 2) demonstrated exceptional correlation, signifying that the analytical method is both robust and appropriate for subsequent pharmaceutical evaluations, including content uniformity, in vitro dissolution studies, and assay determinations of Polmacoxib-containing formulations. The lack of variations or abnormalities in the absorbance values further substantiates the method's consistency and specificity. The established UV calibration curve is a strong analytical basis for accurately measuring Polmacoxib in the mouth-dissolving films that have been made. This is very important for quality control and making sure that each batch is the same during formulation development.

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