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Original Research Article

Formulation Development and Evaluation of Oral Dissolving Film of Lornoxicam

Alok Kumar[1], Mohit Khandelwal[2], Dilip Agrawal[3], Rakesh Goyal[4]

[1]Research Scholar, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur
[2]Associate Professor, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur
[3]Principal, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur
[4]Professor, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur

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Corresponding author: Alok Kumar
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Abstract

The study focuses on the formulation and evaluation of oral dissolving films (ODFs) of lornoxicam, aiming to improve patient compliance and achieve rapid onset of action. Lornoxicam, a non-steroidal anti-inflammatory drug (NSAID), is effective in pain management but suffers from low bioavailability and gastric irritation when administered orally in conventional forms. To address these challenges, ODFs were developed using the solvent casting method with hydroxypropyl methylcellulose (HPMC) as the film-forming polymer. The films were evaluated for various physicochemical parameters including thickness, tensile strength, disintegration time, and drug content uniformity. Additionally, in vitro dissolution studies were conducted to assess the release profile of lornoxicam from the films. The optimized formulation demonstrated desirable mechanical properties, rapid disintegration (within 60 seconds), and enhanced dissolution rate compared to conventional oral tablets. The weight of films range from 18.45-22.99 mg. The thickness of films were range from 0.046- 0.055 mm. The pH of films range from 6.55-7.95.The folding endurance of films range from 216-267.The disintegration time range from 10-42 seconds. Tensile strength of given formulation is 4.124 to 7.885gm/mm2. The drug content of films was found to be between 94.20-96.80%.These findings suggest that ODFs of lornoxicam are a promising alternative for improving patient adherence and therapeutic efficacy in pain management. Further in vivo studies are recommended to validate these results and explore the potential clinical benefits of this novel drug delivery system.

Keywords: Lornoxicam, HPMC, NSAID, Folding Endurance, Tensile Strength

Introduction

Lornoxicam, a potent non-steroidal anti-inflammatory drug (NSAID) belonging to the oxicam class, is widely used for its analgesic and anti-inflammatory properties in the management of acute and chronic pain conditions. Despite its clinical efficacy, lornoxicam faces significant challenges such as low bioavailability and gastrointestinal side effects when administered through conventional oral dosage forms. These limitations often lead to reduced patient compliance, particularly among those who experience difficulty swallowing tablets or capsules, such as pediatric, geriatric, and bedridden patients. To overcome these challenges, the development of novel drug delivery systems has gained considerable attention. Oral dissolving films (ODFs) have emerged as a promising alternative, offering numerous advantages including ease of administration without the need for water, rapid disintegration and dissolution, improved bioavailability, and better patient adherence. ODFs are thin, flexible strips that rapidly disintegrate and dissolve upon contact with saliva, releasing the drug for quick absorption through the oral mucosa. This study aims to formulate and evaluate ODFs of lornoxicam, leveraging their potential to enhance therapeutic outcomes and patient compliance. The solvent casting method was employed for the preparation of the films, using hydroxypropyl methylcellulose (HPMC) as the primary film-forming polymer. The formulated films were subjected to comprehensive physicochemical characterization, including assessments of thickness, tensile strength, disintegration time, and drug content uniformity. Furthermore, in vitro dissolution studies were conducted to evaluate the release profile of lornoxicam from the films. By addressing the limitations of conventional oral dosage forms, this research endeavors to provide a novel and effective delivery system for lornoxicam,

potentially transforming its clinical use and improving patient quality of life. The subsequent sections detail the materials and methods used, followed by the results and discussion of the findings, leading to conclusions on the efficacy and future potential of lornoxicam-loaded ODFs.

Material and Methods

Method of Preparation for Oral Dissolving Film

Calculation of Oral dissolving film

Diameter of Petri dish

(Dose of Lornoxicam as per record 8mg)

Radius of the petri dish = 6 cm Diameter = Radius/2 = 6/2 =3 cm.πr^2=3.14 x3x3 =28.26 cm^2

Now, Dose is % mg and cut the pieces in 2 cm x 2 cm = 4 $cm^2$4cm^2contain 5 mg of drug. So, 28.26 cm^2 contains = 28.26/4 = 7.06 and 7.06 x 5 = 35.32 mg drugSo2 ml contain 35.32 mg drug

Then, 10 ml contain drug =176.60 mg drug

Method of preparation of Drug free film

For the film preparation, the solvent casting method was utilised. Weighed the polymer precisely and submerged it in 10 millilitres of water. Aspartame and the specified amount of citric acid were added to this mixture, and it was agitated for 45 minutes. Stir the solution continuously while adding the polymer solution after it has been well combined. PEG 400 plasticizer was finally added, stirring constantly. After 45 minutes of vigorously stirring the final dispersion, the solution was sonicated for 15 minutes to eliminate any remaining air bubbles. The dispersion was then placed aside for an hour to allow the foams to subside. Glycerol was used to lubricate the petri dish in the interim to reduce the possibility of film damage during removal. After transferring two millilitres of the final dispersion into the measuring cylinder, the solution was poured into a 28.26 cm2 clean, dry petri plate. After that, the films were dried for one to two hours at 40°C in a vacuum tray dryer. After that, the films were taken out and chopped to a size of (2x2) cm2. After that, these films were kept in appropriate packaging at room temperature.

Table 1: Formulation of Oral Dissolving Films Drug Free

Ingredients	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9	PF10
Sodium Alginate(gm)	0.9	1.2	--	--	--	--	--	--	--	--
Eudragit (gm)	--	--	0.9	1.2	--	--	--	--	--	--
Pullulan (gm)	--	--	--	--	0.9	1.2	--	--	--	--
Sod. Starch Glycolate(gm)	--	--	--	--	--	--	0.9	1.2	--	--
HPMC (gm)	--	--	--	--	--	--	--	--	0.9	1.2
PEG-400(ml)	1	1	1	1	1	1	1	1	1	1
Citric Acid(mg)	200	200	200	200	200	200	200	200	200	200
Aspartame(mg)	10	10	10	10	10	10	10	10	10	10
Colouring Agent	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*
Flavouring Agent	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*	q.s*
Water(ml)	10	10	10	10	10	10	10	10	10	10

Table 2: Trials Taken To Study the Effect of Various Concentration of PEG 400 on Parameters of Oral Dissolving Film

Ingredients	TF1	TF2	TF3	TF4	TF5	TF6	TF7	TF8	TF9	TF10
Pullulan(gm)	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
PEG-400(ml)	--	0.2	0.4	0.8	1	1.2	1.4	1.6	1.8	2
CitricAcid(mg)	200	200	200	200	200	200	200	200	200	200
Aspartame(mg)	10	10	10	10	10	10	10	10	10	10
Colouring Agent	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
Flavouring Agent	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
Water(ml)	10	10	10	10	10	10	10	10	10	10

Method of preparation of Lornoxicam Oral Dissolving Film

Weighed the polymer precisely and submerged it in 10 millilitres of water. Ten millilitres of water were used to dissolve the necessary amount of Lornoxicam. Stirred this solution for 45 minutes after adding the specified amount of aspartame and citric acid. Stir the solution continuously while adding the polymer solution after it has been well combined. PEG 400 plasticizer was finally added, stirring constantly. After 45 minutes of stirring the final dispersion, the solution was sonicated for 15 minutes to eliminate any remaining air bubbles.

After that, the dispersion was placed aside for an hour to allow the foams to subside. Glycerol was used to lubricate the petri dish in the interim to reduce the possibility of film damage during removal. After transferring two millilitres of the

final dispersion into the measuring cylinder, the solution was poured into a 28.26 cm2 clean, dry petri plate. After that, the films were dried for one to two hours at 40°C in a vacuum tray dryer. After that, the films were taken out and sliced into 2 x 2 cm2 pieces with 5 mg of Lornoxicam within. After that, these films were kept in appropriate packaging at room temperature.

Table 3: Formulation of Oral Dissolving Films of Lornoxicam

Ingredients (Batch No. F5)	Quantity
Lornoxicam(mg)	140
Pullulan(gm)	0.9
PEG 400 (ml)	1
Citric Acid(mg)	200
Aspartame(mg)	10
Colouring Agent	q.s*
Flavouring Agent	q.s*
Water(ml)	10

Result

Chemical Compatibility

Compatibility study of pure drug Lornoxicam with other excipients were carried out prior to the formulation of films. IR spectra of pure drug and DSC of physical mixture of drug-excipients were obtained, which are depicted below. All the characteristics peaks of Lornoxicam were present inspectra at respective wave lengths.

Thus, it shows compatibility between drug and excipients. There was no significant change in the chemical integrity of the drug.

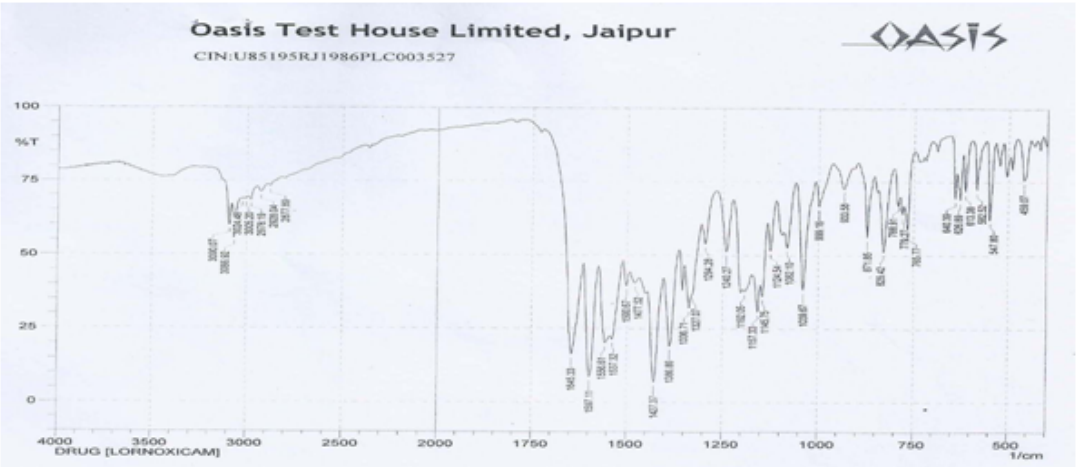

Figure 1: FTIR Spectrum of Lornoxicam

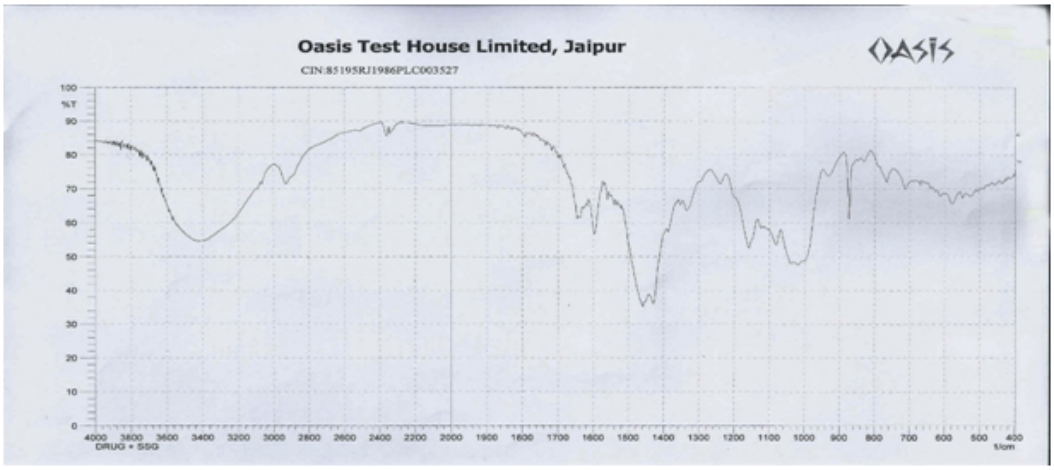

Figure 2: FTIR Spectrum of Lornoxicam + Sodium starch glycolate

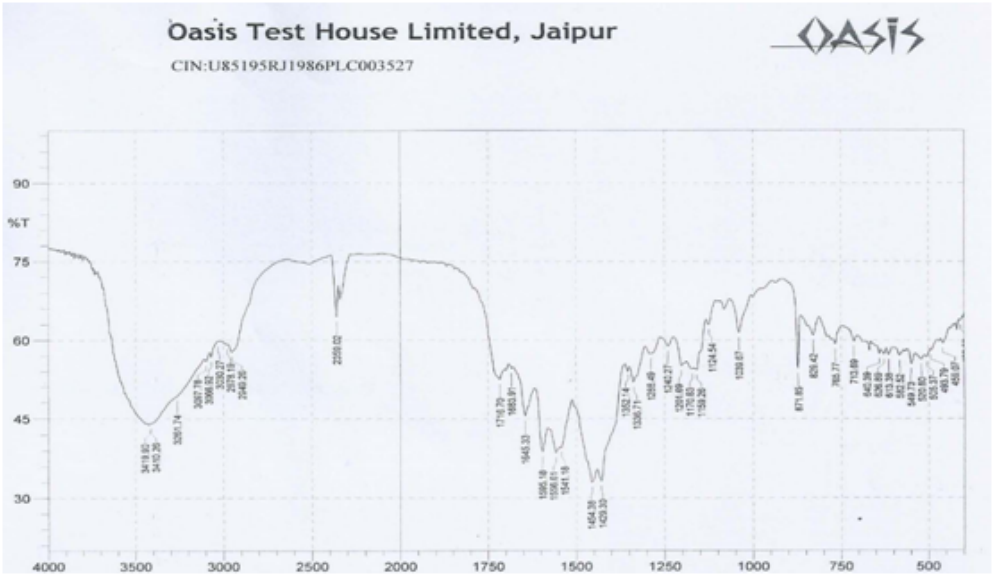

Figure 3: FTIR Spectrum of Lornoxicam + Eudragit

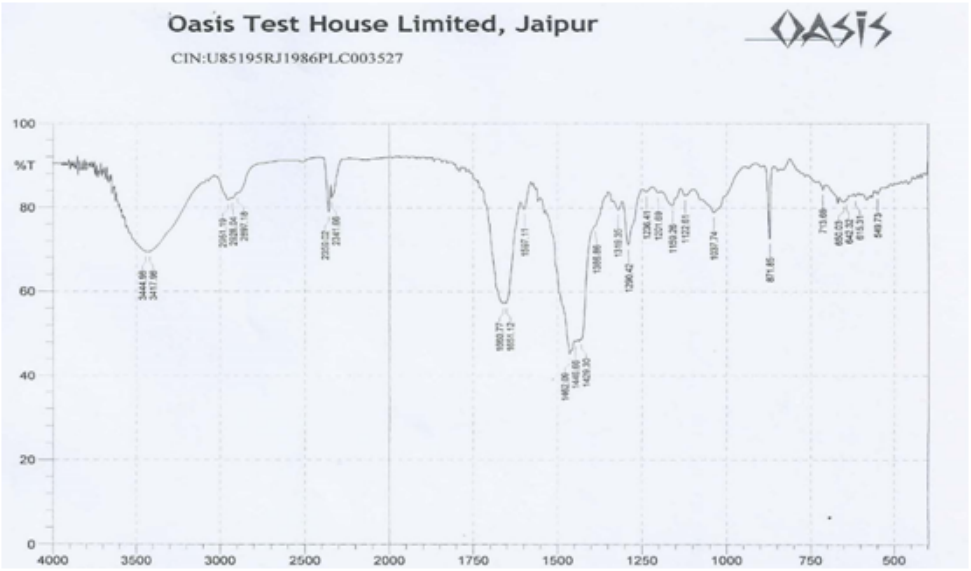

Figure 4: FTIR Spectrum of Lornoxicam + HPMC

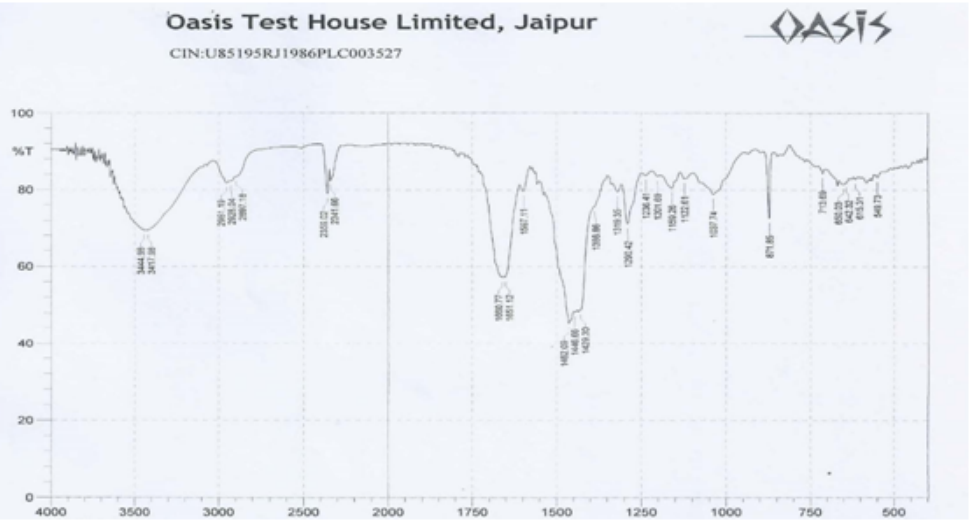

Figure 5: FTIR Spectrum of Lornoxicam + Pullalan

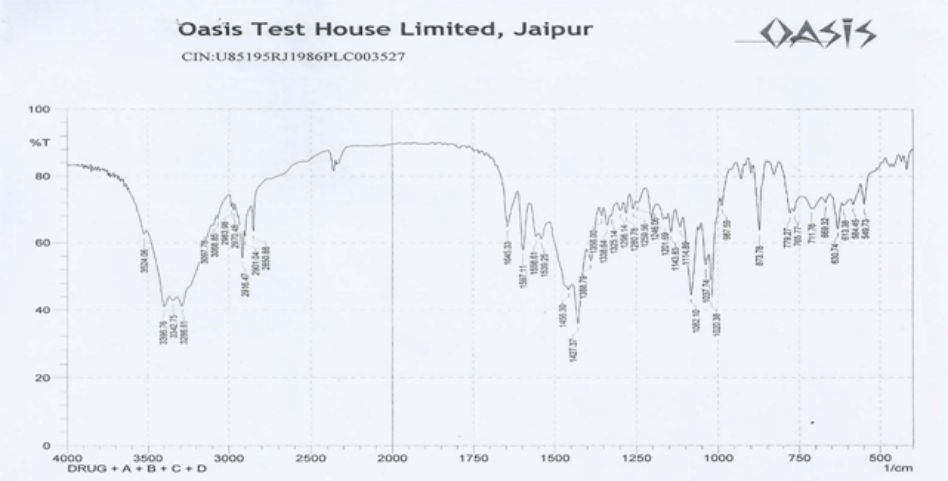

Figure 6: FTIR Spectrum of Lornoxicam + All polymers excipients

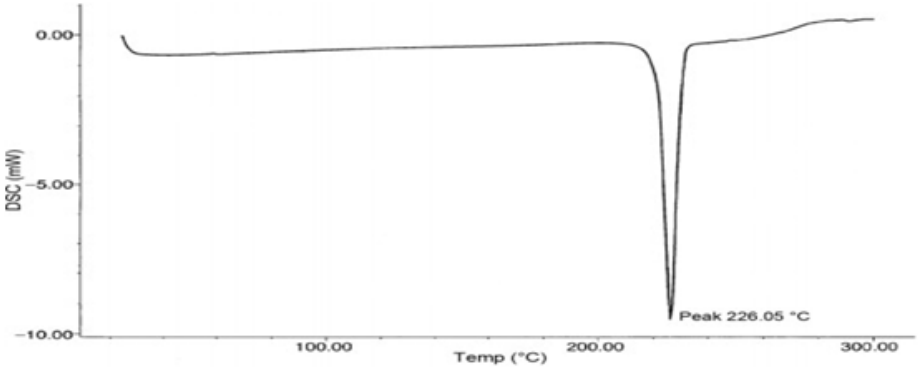

Figure 7: DSC of Lornoxicam

The calibration curve of Lornoxicam was prepared in Phosphate Buffer pH 7.4 at 258 nm and the absorbance values of different concentrations of Lornoxicam solutions in Phosphate Buffer p.

Table 4: Calibration Curve Data of Lornoxicam

Concentration	Absorbance (258 nm)
0.0	0
2.0	0.168
4.0	0.284
6.0	0.413
8.0	0.539
10.0	0.687
12.0	0.912

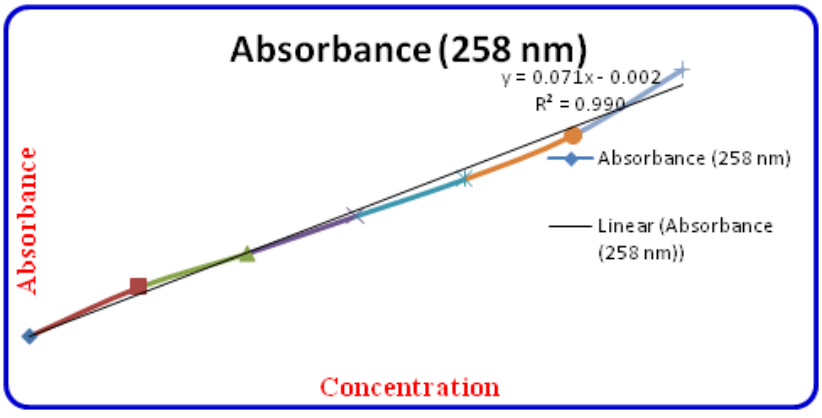

Figure 8: Calibration Curve of Lornoxicam

Table 5: Solubility Profile of Lornoxicam

S. No.	Solvents	Solubility
1.	Distilled water	++
2.	0.1N Hydrochloric acid	++++
3.	Ethanol	+++
4.	Ethyl ether	+++
5.	Dichloro methane	++
6.	Chloroform	++
7.	DMSO	+++

Practically insoluble + Slightly soluble ++ Soluble ++++

Evaluation of Lornoxicam Oral Dissolving Films

a) Appearance

Formulations containing drug with lower concentration of pullulan were transparent, higher concentration of pullulan were translucent and films containing eudragit and sodium alginate were opaque in appearance.

HPMC films were also transparent but the films containing pullulan had good texture and feel.

b) Weight of film

Films of area 4 cm^2 were weighed using electronic balance and the average weight was calculated. The weight of films range from18.45-22.99 mg.

c) Thickness of film

The thickness of three randomly selected films was determined using a standard Vernier caliper. The thickness of films were range from 0.046-0.055 mm.

d) Surface pH of film

The surface pH of the film was determined in order to investigate the possibility of any side effect in vivo. As an acidic oral alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to then eutral as possible. The pH of films range from 6.55-7.95.

e) Folding endurance

Folding endurance was determined by repeatedly folding the film at same possible position until it breaks. The folding endurance of films range from 216-267.

f) Disintegration Time

2 ml of distilled water was placed in petridish and one film was added onthe surface of the water and the time measured until the film was dissolved completely. The disintegration time range from 10-42 seconds.

g) Tensile Strength

Tensile strength of given formulation is 4.124 to 7.885gm/mm^2

Table 6: Physical Characterization of Fast Dissolving Oral Films

Parameters	Formulation Code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Weight variation	18.97 ±0.12	21.86 ±0.13	21.04 ±0.33	20.90 ±0.17	18.50 ±0.01	18.45 ±0.12	21.75 ±0.11	19.72 ±0.22	21.08 ±0.25	21.03 ±0.15
Thickness	0.048 ±0.01	0.049 ±0.12	0.052 ±0.01	0.055 ±0.09	0.045 ±0.01	0.051 ±0.02	0.049 ±0.05	0.052 ±0.02	0.054 ±0.08	0.046 ±0.04
SurfacepH	7.67	7.95	7.43	6.87	6.55	6.89	7.58	6.98	7.07	6.75
Folding endurance	218	216	235	240	260	222	236	248	267	265
Disintegration time	28 ±0.18	24 ±0.05	19 ±0.06	24 ±0.15	10 ±0.12	35 ±0.08	42 ±0.15	35 ±0.05	29 ±0.09	31 ±0.16
Tensile Strength	0.675 ±0.12	7.746 ±0.04	7.885 ±0.09	4.124 ±0.11	4.243 ±0.18	4.345 ±0.04	5.521 ±0.01	5.582 ±0.02	5.624 ±0.11	6.876 ±0.06
Percent Elongation (%)	2.51	2.45	3.48	2.41	4.55	338	2.34	3.28	3.32	2.38
Drug content	94.45 ±0.15	94.58 ±0.19	95.30 ±0.11	95.50 ±0.17	96.80 ±0.15	96.15 ±0.08	95.40 ±0.03	94.20 ±0.08	94.80 ±0.14	94.90 ±0.09

Drug Content

A sample of size 2x2 cm^2 which were placed in the beaker containing 100ml of distilled water. Dilute 10 ml of this solution to 10 ml with distilled water. Than Absorbance of standard preparation and test preparation was taken using UV double beam spectrophotometer. The drug content of films was found to be between 94.20-96.80%.

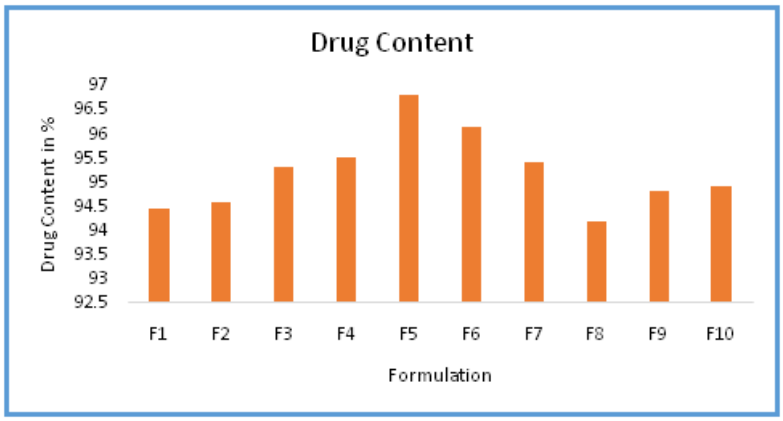

Figure 9: Drug Content

Conclusion

In vitro release studies showed that the formulation F5 match with the required dissolution profile, the drug release retarded in F1, F2 and F3 formulations due to different concentration of polymer and plasticizer, which did not match with the required dissolution profile. The invitro release of formulation F5 was found to be most promising as it was in accordance required dissolution profile.

In the present study we found the results between the following range that shows good formulation among all. The pH of films range from 6.55-7.95. The folding endurance of films range from 216-267. The disintegration time range from 10-42 seconds. Tensile strength of given formulation is 4.124 to 7.885gm/mm2. The drug content of films was found to be between 94.20-96.80%. Further stability study was conducted on films of F5 formulation and stored for one month in air tight plastic pack. Films were then evaluated for assay, content uniformity, pH, weight, tensile strength, Percent elongation and invitro release profile. No significant changes were observed in any of studied parameters during the study period.. The films were found to be uniform, flexible and 96.80% of drug was released by the formulation F5 within ten minutes which was desirable for the fast absorption, thus it could be concluded that the developed formulation was stable.

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