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Formulation and Assessment of an Instant Degrading Film of the Poorly Soluble Medicament Cilnidipine

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ABSTRACT

Cilnidipine, also known as dihydropyridine, is a calcium antagonist that has that chemical formula. It does this by blocking L-type calcium channels, which prevents calcium from entering the capillaries. This results in a reduction in blood pressure. When taken orally in tablet form, the medicine has a lower bioavailability than when it is injected. This is because it is less water-soluble. A substance was produced as a result of the combination of PEG 400 and propylene glycol that was neither hard nor sticky in nature. Inclusion complexes that are produced with cyclodextrin contribute to an improvement in the drug's solubility and release. We studied the influence that PEG 400 and propylene glycol would have on the formula by using a factorial arrangement. A 32-full factorial design was utilised in order to attain the maximum level of optimization for the rapidly disintegrating film. In in vitro drug release investigations using PEG 400 and propylene glycol, independent parameters such as pH, thickness, weight uniformity, percent drug content, folding endurance, and disintegration time were examined and analysed.

Keywords- Cilnidipine, Calcium antagonist, Blood pressure, Disintegration, Capillaries.

I. INTRODUCTION

Modern-day hypertension is the most common health problem of our day. Hypertension is a problem that affects the vast majority of people. Increased risk of heart disease and stroke can be attributed to elevated blood pressure. Risk factors for high blood pressure include obesity and excessive alcohol consumption, as well as smoking and a family history of hypertension. Beta-blockers are the most commonly prescribed medication for the treatment of hypertension. In a few seconds, saliva breaks down the film, allowing it to be swallowed easily. Drug bioavailability is increased, costs are reduced, and patient compliance is increased by using oral rapid dissolving films. As an alternative to capsules and tablets, instant dissolving film is an oral instant dissolving film supplied through the buccal channel to achieve reduced dissolve time in order to reach systemic circulation with a speedy beginning of action. It has been described that the Besides its poor dissolution rate, the bitterness of quercetin also poses a challenge for further development. Using carnauba wax, shellac as the shell-forming excipient, this work aimed to microencapsulate quercetin by hot-melt extrusion for taste-masking. Hot-melt extrusion is a technique that offers many advantages over others, such as simplicity,

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continuous operation, high throughput, and the ability to operate in the absence of any organic solvent. The purpose of this work is to utilize hot-melt extrusion to microencapsulate quercetin powders for taste-masking. Cilnidipine is a calcium antagonist of the dihydropyridine class. At the L-type calcium channels in your blood vessels, cilnidipine acts as an antagonist, blocking calcium from entering your body and decreasing your blood pressure. Cilnidipine also operates on the sympathetic nerve's N-type calcium channel to limit the release of norepinephrine and reduce the rise in blood pressure associated with stress.

II. MATERIAL & METHODS

The drug received from J.B chemicals and pharmaceuticals Pvt. Ltd. Was analyased for its purity at laboratory scale. Different polymer from chemdyes corporation and solvents were received from Sigma Aldrich.

Evaluation Parameters of drugs-

Organoleptic properties: The sample drug's physical properties were compared to those of the reference drug via hand inspection of both samples. You can find the final results in the table.1

Table No .1: Organoleptic properties

Sr.no	Properties	Standard	Sample
1.	State	solid	solid
2.	Color	yellow	yellow
3.	Odor	Odorless	Odorless
4.	solubility	Soluble in ethanol, methanol and insoluble in water	Soluble in ethanol, methanol and insoluble in water

Melting Point: It was established that the melting point of cilnidipine was 111°c using the capillary technique. 108 to 113°C is the stated temperature.

Discussion: The melting point of cilnidipine was found to be 111°c, which is consistent with the reported value of 108-113°c, indicating that the medicine was received.

Spectroscopic Estimation of cilnidipine: The λ-max (Wavelength) was determined by UV spectrometer. The results for wavelength are mentioned below.

Table No .2: wavelength of drug in different solvents

Solvents	λ-max (Reported)	λ-max (observed)
Methanol	240	240
Phosphate buffer pH 6.8	246	246
1% Sodium Lauryl Sulphate (SLS)	242	242

Discussion: The submitted sample is most likely cilnidipine, as the observed values are highly consistent with the indicated values.

Calibration of Methanol: Figure 5.1(a) displays the Cilnidipine in methanol calibration curve used to quantify dissolution solutions, and Table 5.3 details the relevant absorbance readings. Cilnidipine spectra in methanol are shown in Fig. 1(b). For the calibration curve, the slope was found to be 0.0795 and the intercept was found to be 0.0396 using regression analysis, yielding a correlation coefficient of 0.9908

Table 3: Data for Calibration curve of cilnidipine in methanol at 240 nm

Sr. no.	Concentration (µg/mL)	Absorbance A=1	Absorbance A=2	Absorbance A=3	Absorbance, n=3
1	2	0.221	0.228	0.223	0.224± 0.003
2	4	0.379	0.389	0.381	0.383± 0.005
3	6	0.526	0.548	0.543	0.539± 0.011
4	8	0.673	0.696	0.677	0.682± 0.012
5	10	0.221	0.208	0.219	0.802± 0.009

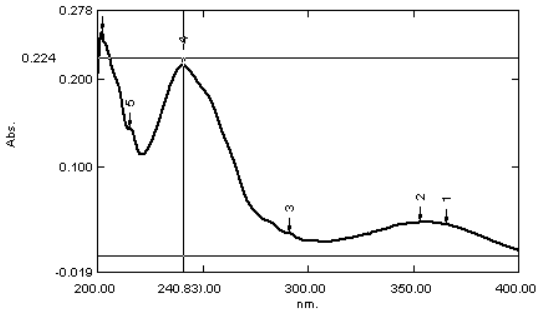

Fig. 1 (a) 2ppm spectra of Cilnidipine in Methanol at 240 nm

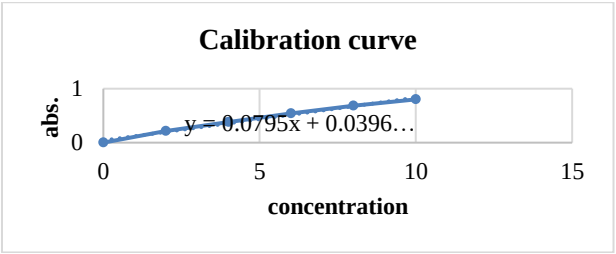

Fig. 1 (b) Calibration curve of Cilnidipine in Methanol at 240 nm

Calibration of phosphate buffer pH 6.8: The dissolution rate of Cilnidipine in phosphate buffer, pH 6.8, was measured using a calibration curve, as shown in

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Figure .2(a) and Table .4. Spectra of cilnidipine in a 6.8-pH phosphate buffer are depicted in Fig. .2. (b). With a slope of 0.0426 and an intercept of 0.0276, the calibration curve got a correlation coefficient of 0.9926 in the regression analysis.

Table 4: Data for Calibration curve of cilnidipine in phosphate buffer pH 6.8 at 246 nm

Sr. no.	Concentration (µg/mL)	AbsorbanceA=1	AbsorbanceA=2	AbsorbanceA=3	Absorbance, n=3
1	0	0	0	0	0
2	2	0.129	0.133	0.128	0.13±0.002
3	4	0.219	0.214	0.215	0.216±0.002
4	6	0.283	0.29	0.285	0.286±0.003
5	8	0.373	0.376	0.367	0.372±0.004
6	10	0.449	0.439	0.447	0.445±0.005
7	12	0.519	0.546	0.534	0.533±0.01

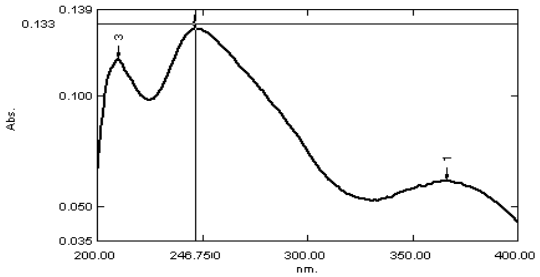

Fig. .2. (a) 2ppm spectra of Cilnidipine in phosphate buffer pH 6.8 at 246 nm

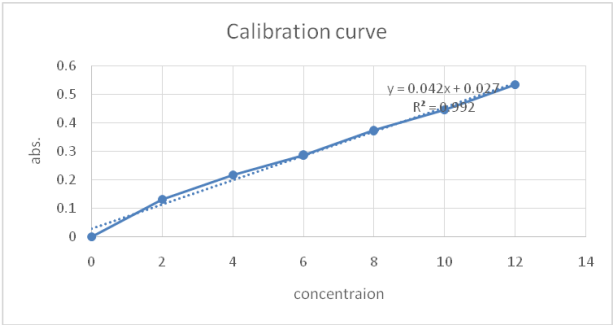

Fig. .2. (b) Calibration curve of Cilnidipine in phosphate buffer pH 6.8 at 246 nm

Calibration of 1% Sodium Lauryl Sulphate (SLS): Dissolution solutions were calibrated using a cilnidipine in 1% SLS calibration curve (figure 3(a) and absorbance data (table.5). Spectrum of Cilnidipine in 1% SLS is shown in Fig. 3(b).

Table.5: Data for Calibration curve of cilnidipine in 1% SLS at 242nm

Sr. no.	Concentration (µg/mL)	Absorbance A=1	Absorbance A=2	Absorbance A=3	Absorbance, n=3
1	2	0.274	0.263	0.285	0.274±0.010
2	4	0.366	0.385	0.392	0.381±0.013
3	6	0.489	0.512	0.496	0.499±0.011
4	8	0.624	0.668	0.673	0.655±0.026
5	10	0.815	0.836	0.812	0.821±0.013
6	12	0.979	0.987	0.986	0.984±0.004

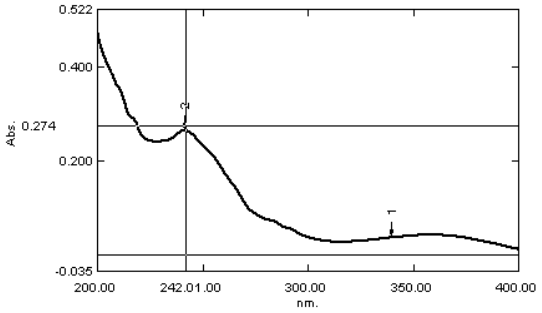

Fig. 3. (a) 2ppm spectra of Cilnidipine in1% SLS at 242 nm

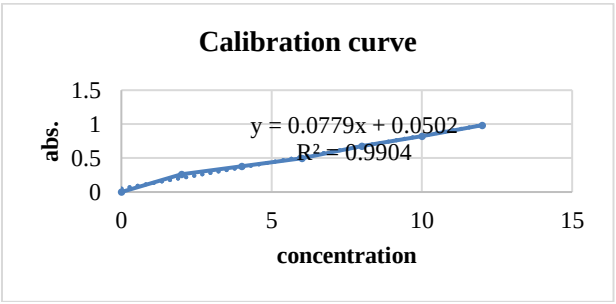

Fig. 3. (b) Calibration curve of Cilnidipine in 1% SLSat 242 nm

III. IDENTIFICATION OF CILNIDIPINE BY FTIR

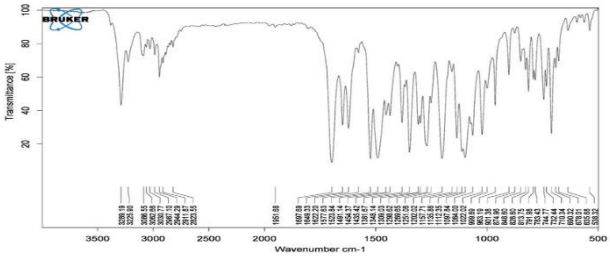

Fig..4. Reference FTIR spectrum of cilnidipine

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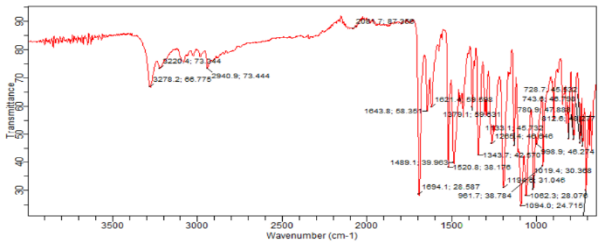

Fig. .5. Sample FTIR spectrum of cilnidipine

Table 6. IR scan of cilnidipine:

Functional group	Reference value (cm-1) of cilnidipine	Observed values (cm-1) of cilnidipine
-NO_2 stretching	1523.84	1520.8
-N-H stretch	3289.19	3278.2
-C-H stretch	2944.29	2940.9
>C=O stretching of ester	1697.69	1694.1
C-O stretching of ester	1097.84	1094.0

Discussion:

These results are consistent with reference standards, suggesting that the sample provided here is really cilnidipine. As a result of this study's efforts to positively identify the drug, it is safe to assume that the cilnidipine in the sample is of the highest possible quality.

Infrared spectroscopy studies of drug-excipient compatibility (FTIR):

The following FTIR spectrum displays chlorocilnidipine and a mixture of chlorocilnidipine, pullulan, PEG 4000, and -cyclodextrin. Here is a rundown of several possible spectrum interpretations.

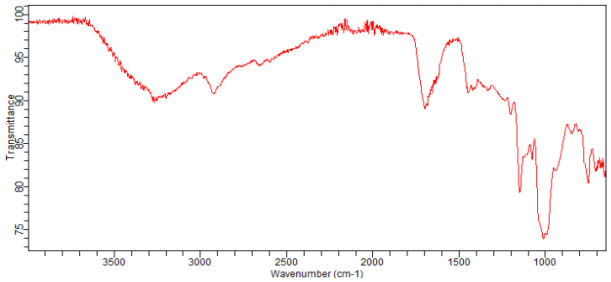

Fig. 6. FTIR spectra of pullulan

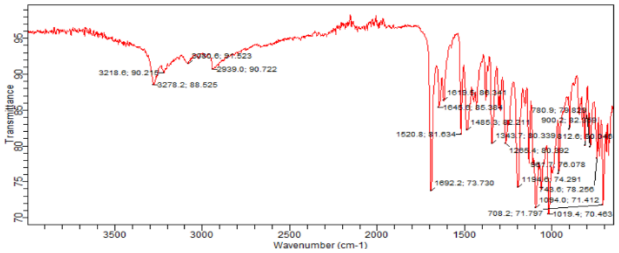

Fig. 7. FTIR spectra of cilnidipine + pullulan

Discussion:

The FT-IR spectrum shows that pullulan did not affect the effectiveness of the drug.

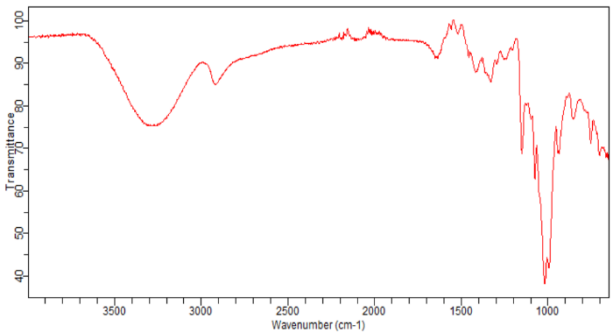

Fig..8. FTIR spectra of β-CD

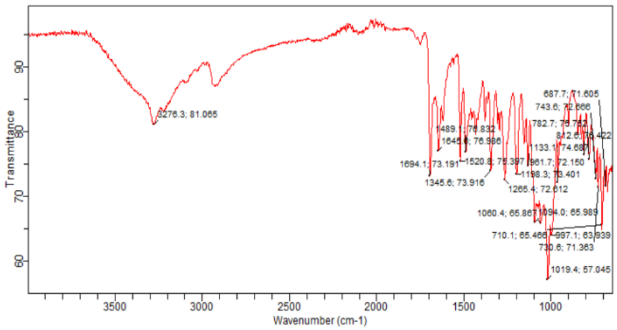

Fig..9. FTIR spectra of β-CD + cilnidipine

Discussion:

There was no interaction between the medication and -CD, as shown in the FT-IR graph above.

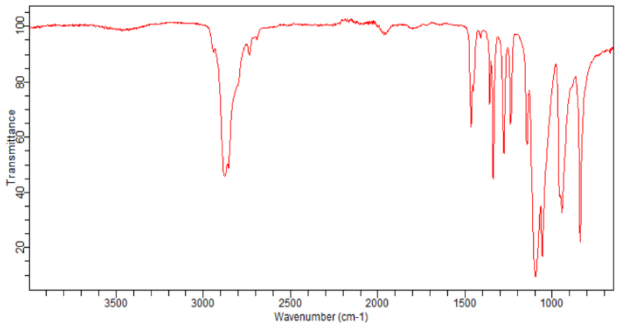

Fig. .10. FTIR spectra of PEG 4000

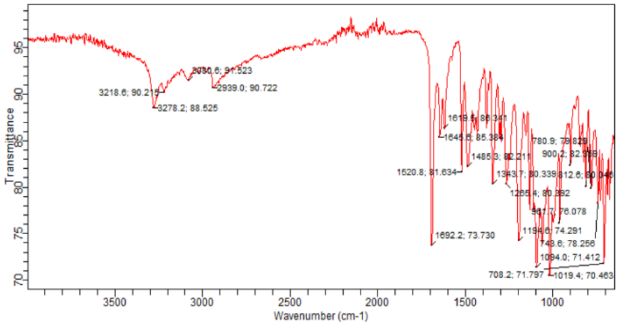

Fig. 11. FTIR spectra of cilnidipine + PEG 4000

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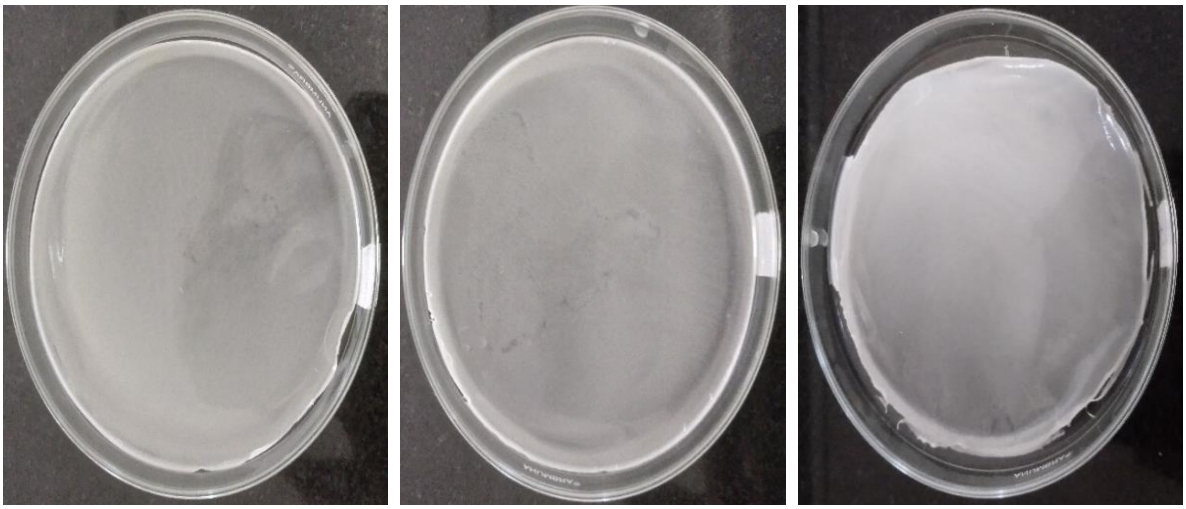
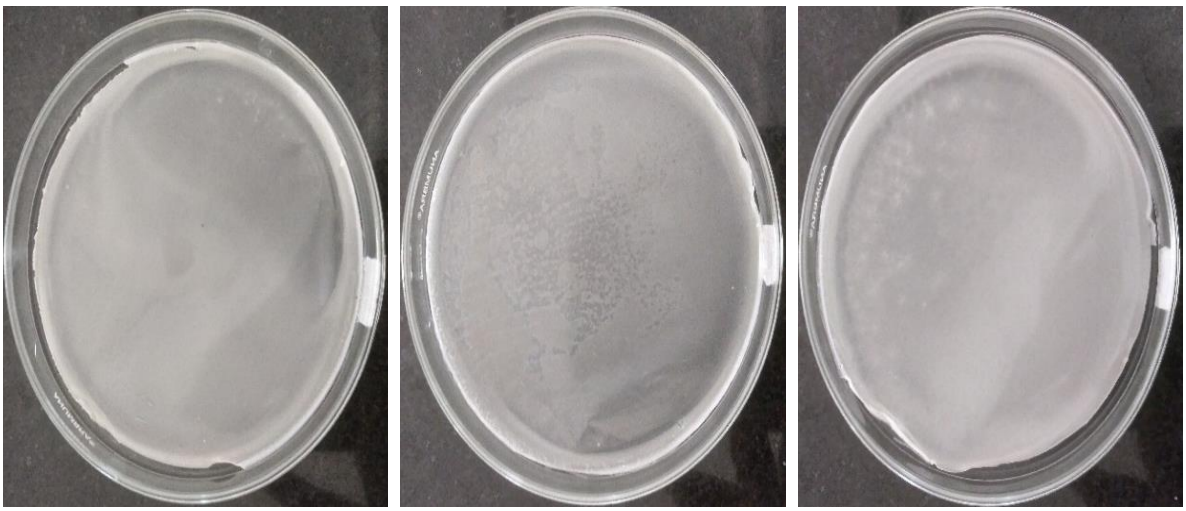
Evaluation parameter of instant dissolving film of Factorial batches:

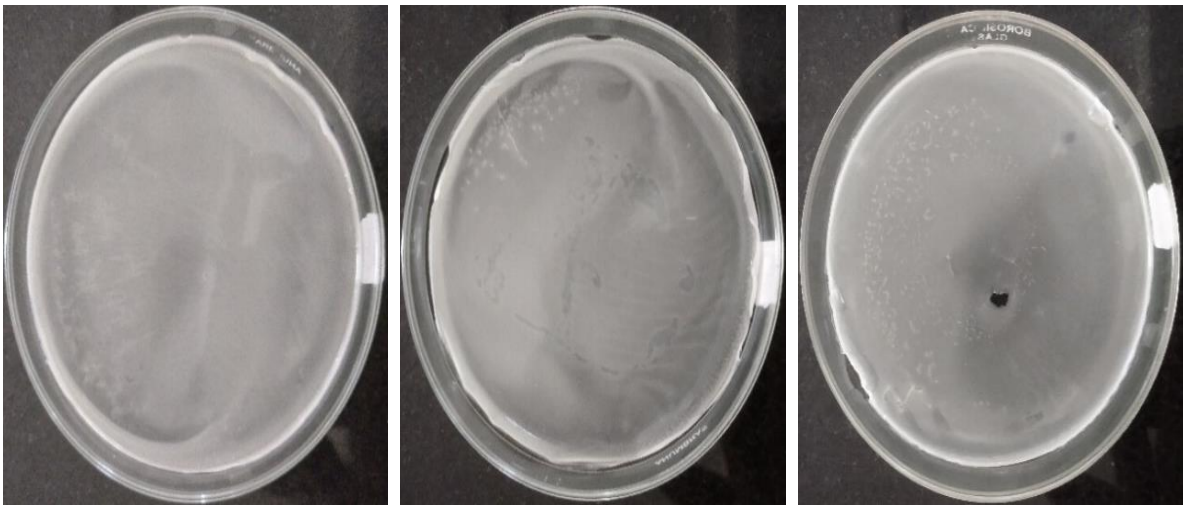
Physical appearance:



F-1 F-2 F-3



F-4 F-5 F-6



F-7 F-8 F-9

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Table No. 7 Physical appearance of prepared film

Formulation	Smoothness	Transparency	Stickiness	Intact/Broken
F-1	Smooth	Semi Transparent	Non-sticky	Intact
F-2	Smooth	Semi Transparent	Non-sticky	Intact
F-3	Smooth	Semi Transparent	Non-sticky	Intact
F-4	Smooth	Semi Transparent	Non-sticky	Intact
F-5	Smooth	Semi Transparent	Non-sticky	Intact
F-6	Not smooth	Semi Transparent	Non-sticky	Intact
F-7	Smooth	Semi Transparent	Non-sticky	Intact
F-8	Not smooth	Semi Transparent	Non-sticky	Broken
F-9	Not smooth	Semi Transparent	Non-sticky	Broken

Table No.8 .Mechanical properties of prepared film

Formulation	Force at break (gm)	Tensile strength (MPa)	Surface pH
F-1	2674	8.745	7.0
F-2	1925	6.294	6.9
F-3	1727	4.983	6.9
F-4	2588	7.934	6.7
F-5	1870	5.732	6.8
F-6	1710	4.659	6.9
F-7	2575	7.894	7.1
F-8	1787	5.478	6.9
F-9	1628	4.435	6.8

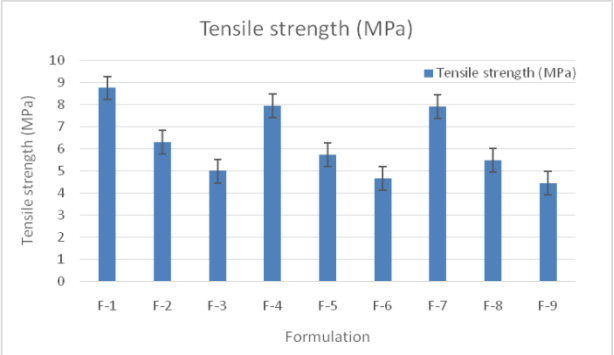

Figure No. 12: Comparison of Tensile Strength of film (F-1 to F-9)

IV. DISCUSSION

In the absence of plasticizers or at low concentrations of plasticizers, the formed film had a high tensile strength value. For the fast-dissolving film to be well tolerated by the oral mucosa, its surface pH must be close to neutral.

V. CONCLUSION

The solubility of the drug was improved prior to the preparation of the rapid dissolving film of cilnidipine that was carried out in this study. Physicochemically suited for the creation of an immediate dissolving film of cilnidipine for the control of hypertension since the drug cilnidipine is a BCS class II drug with poor solubility and high permeability. According to the combination Drug give improved drug release or better solubility by formed inclusion complex with -cyclodextrin, the dose of cilnidipine that was taken was 5 milligrammes per dose. In order to investigate the impact that PEG 400 and propylene glycol have on the formulation, a design called a factorial was utilised. Utilizing 32 different full factorial designs allowed for the completion of the instant film dissolving optimization process. It was discovered that the tensile strength of the formulations and the percentage of drug release both rose as the concentration of PEG 400 and propylene glycol were reduced, respectively. According to the results of the stability tests, the improved formulation likewise exhibited good stability.

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COMPETING INTERESTS

The authors declare that there are no commercial or financial relationships that could constitute as potential conflicts of interest in the conduct of the research.

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