

FABRICATION AND CHARACTERIZATION OF FAST DISSOLVING FILMS OF *ECLIPTA PROSTRATE* LEAVES EXTRACT TO TREAT MOUTH ULCERS

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ABSTRACT

Objective: This research focused on the design of fast dissolving herbal film of *Eclipta Prostrate* leaves extract for mouth ulcers.

Methods: The extract of *Eclipta Prostrata* leaves was formulated as films by solvent casting method using various polymers viz., HPMC E5, HPMC E15, sodium alginate and PVA. The films were designed by using propylene glycol as a plasticizer, SSG as super disintegrate and honey as a sweetener. Furthermore, the films were evaluated for thickness, folding endurance, weight variation, % elongation, surface pH, % moisture uptake, % moisture loss, disintegration and *in vitro* drug release study.

Results: The revealed that all the films were good in appearance and had a smooth texture. Out of all ten formulations, F3 and F5 disintegrated rapidly with a disintegration time of 27 and 32 seconds. The drug release studies revealed that all the formulations had a good release profile, but the F3 formulation showed rapid release i.e. 83.57% in 4 min. The stability studies revealed that the formulations F3 and F5 were found good with non-tackiness, easily separable and disintegrated at 29 and 33 sec respectively with no appearance and drug release.

Conclusion: The research revealed that *Eclipta prostrate* leaves extract can be formulated into oral films for the treatment of mouth ulcers with improved bioavailability and expected patient compliance.

Keywords: *Eclipta prostrate*, Extract, Oral films, Super disintegrants and mouth ulcer

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INTRODUCTION

Administration of dosage forms through the oral route is the most convenient and suitable route. Some classes of patients are facing difficulty to take oral formulations i.e. geriatric, pediatric and dysphagia patients due to difficulty of swallowing or chewing dosage forms [1, 2]. Fast dissolving films having the ability to dissolve and disintegrate quickly in a few seconds when placed on a patient's tongue or in oral mucosa and release the drug for oromucosal or intragastric absorption. Hence, they offer a number of advantages over other solid dosage forms viz., tablets and capsules by eliminating swallowing problems and maintaining water, which leads to more patient compliance. The rapid release of the drug from the films is due to the large surface area of the film, which is exposed to the moist oral area and causing quick disintegration and dissolution in oral cavity in seconds [3, 4]. The design of oral films with herbal extract is an interesting trend.

Ulcers are lesions on the surface of the skin or mucous membrane characterized by a superficial loss of tissue. There are many varieties of ulcers such as mouth ulcer, esophagus ulcer, peptic ulcer and genital ulcer [5]. Mouth ulcers/sores are common ailments that affect many people at some point in their life cycle. The sores appear on any of the soft tissues of the mouth including lips, cheeks, gums, tongue and floor and roof of the mouth. In the period of ulcer, eating increases the pain rather than relieves the pain. The other symptoms include nausea, vomiting and weight loss [6]. At present 75-80% of the world population using herbal medicine mainly in developing countries due to cultural acceptability, compatibility and lesser side effects. Preliminary phytochemical screening of the medicinal plant *Eclipta Prostrate* (Asteraceae) indicated the presence of important secondary metabolites like flavonoids and tannins, which are active principles for antiulcer activity. *Eclipta Prostrate* is used traditionally in the Indian system of medicine as hepatoprotective, anti-inflammatory, hypoglycemic, immunomodulator and in wound healing. The plant shows significant attenuation in lipid peroxidation, superoxide dismutase activity. The antisecretory activity of the plant is evidenced by significant reduction in gastric volume, acid output and an increase in gastric pH [7, 8].

The aim of the present investigation was to fabricate and characterize the fast dissolving film of *Eclipta Prostrate* leaves

extract by solvent casting method with a blend of polymers viz., HPMC E5, HPMC E15, sodium alginate and PVA [9].

MATERIALS AND METHODS

Materials

Leaves of the plant *Eclipta Prostrate* were collected directly from the plant in and around Guntur, Andhra Pradesh, India from March to August. The plant was authenticated as *Eclipta Prostrate* by Dr. Ammani (Voucher specimen V 2762), Head, Department of Botany, Acharya Nagarjuna University, Guntur, Andhra Pradesh, India. The plant was deposited at the biology department of the laboratory. HPMC E15, HPMC, PVA were procured from Merck Labs, Mumbai. Sodium alginate, propylene glycol, sodium starch glycolate was from Fisher Scientific, Mumbai. Sugar was purchased from the local market. All ingredients were of pure and analytical grade.

Extracting *Eclipta prostrate* leaves

The fresh leaves were collected in bulk from local areas. Then the debris was removed from the collected material and dried in shade. The dried leaves were coarsely grounded in a mixer. The coarse powder was successively extracted by the soxhlation process with water. Extract was concentrated by distilling the solvent and then dried [10]. The dried extract was collected and was stored in a desiccator for further use.

Phytochemical screening of the extract

The extract was tested for the presence of various active chemical constituents namely steroids, alkaloids, tannins, phenolic compounds, flavonoids, glycosides, diterpenes, triterpenes and saponins [11, 12]. The results of the phytochemical study were given in table 1.

Preparation of fast disintegrating films

Fast disintegrating films of *Eclipta Prostrate* extract were prepared by solvent casting method as per the formulae given in table 2 [13]. The films were formulated by using various polymers viz., HPMC, PVA, HPMC E15, and Sodium alginate. The required quantity of polymers and plasticizer (propylene glycol) was dissolved in double-

distilled water. This polymeric dispersion was stirred for 1 h using a magnetic stirrer and kept aside for deaeration. In another beaker plant extract, super disintegrate (sodium starch glycolate) and honey was dissolved in a specific proportion of distilled water. The resulting aqueous solution was added to polymeric dispersion and stirred for 1h. After deaeration of the blend, it was casted on the film former apparatus (VJ Instruments, Mumbai) and temperature was maintained at 30-50 °C. Dried film was carefully removed from the film-forming machine and trimmed into 3×3 cm² size. Trimmed films were stored in an airtight container and subjected for evaluation.

Evaluation tests

Standard calibration curve for *Eclipta prostrate* leaves extract

Accurately weighed amount of *Eclipta prostrate* (10 mg) extract was dissolved in a few ml of water and the volume was made up to 10 ml with water. From this stock solution aliquot of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml and 1.0 ml were pipetted out into a series of 10 ml volumetric flasks and makeup to mark with water in order to get a concentration within the Beer's range from 20-100µg/ml. The samples were analyzed by UV spectrophotometer [14]. The process was carried out in triplicate.

Antimicrobial activity

Biological screening of plant extracts was most frequently carried out to determine the antibacterial activity. These evaluations are done by means of standard *in vitro* assay (agar well diffusion) utilizing a broad spectrum of pathogenic and nonpathogenic bacteria. In the present study gram-positive (*S. Aureus*, *B. Subtilis*) and gram negative (*E. Coli*, *P. Aeruginosa*) bacterial strains were used. These organisms are responsible for various minor or major infections in humans [15, 16].

Morphological properties

The morphological properties such as homogenous nature of films, colour, transparency and surface texture were observed visually. All the formulations were stored at room temperature 25±30 °C in airtight containers.

Uniformity of film thickness

The thickness of the films was measured by using a screw gauge at 5 different strategic locations. This helps in determining the uniformity of thickness of oral fast disintegrating films, which directly relates to the accuracy of the dose [17].

Folding endurance

Folding endurance proved the information regarding the flexibility as well as the physical ability of the films. It was measured by firmly folding films repeatedly in the middle. The number of folds required to produce crack in the film was noted as the value of folding endurance [18].

Tensile strength

Three films from each formulation were taken and cut into 5 cm width and 10 cm length. The force required to break the films was determined using tensile strength apparatus (HIKS tensile strength apparatus THE-500) in triplicate. tensile strength is calculated by using the formula [19].

$$\text{Tensile strength} = \text{breaking force}/\text{area of cross - section}$$

Percentage elongation

Percentage elongation provides information regarding the mechanical property of the films. When the physical force was applied on the films, it stretches, referred to as a strain. Strain causes the deformation of films by changing the original dimension of the films. The percentage elongation value increases with an increase in the plasticizer concentration. It was calculated by using the following formula [20].

$$\text{Percentage elongation} = (L - L_0)/L_0 * 100$$

Where, L=final length, L₀= initial length

Percentage moisture loss

The percentage moisture loss studies were carried to check the film's physical stability. Initially weighed films of predetermined size (3×3

cm²) were placed in a desiccator containing anhydrous calcium chloride for three days. The films were removed and weighed again to calculate the percentage moisture loss by using the following formula [21].

$$\% \text{ Moisture loss} = ((\text{initial weight} - \text{final weight})/\text{initial weight}) * 100$$

Percentage moisture uptake

The weighted films were kept in a desiccator at room temperature for 24h. The films were collected and exposed to 84% relative humidity using a saturated solution of potassium chloride in desiccators until a constant weight was achieved. The % moisture uptake was calculated by using the formula [22]

$$\% \text{ Moisture uptake} = ((\text{initial weight} - \text{final weight})/\text{initial weight}) * 100$$

Surface pH

To measure the pH of the film, the film was cut into a square shape (3×3 cm²) and was placed in a dish and moistened with 1 ml of water and kept aside for 1 min. The surface pH of the films was measured by using a pH meter (ELICO-LI120). The process was carried out in triplicate [23].

In vitro release studies

The release rate of the *Eclipta prostrate* extract from the fast-dissolving films was determined by the help of USP Dissolution Test Apparatus-II. The release study was performed in 900 ml phosphate buffer pH 6.8, at 37±5 °C with 50 rpm speed. Aliquot of the solution was collected and replaced with fresh medium at every 30 secs to maintain the sink conditions. The Aliquot was filtered through the Whatman's filter paper. The absorbance of the filtered solution was measured at 221 nm. The sample should be withdrawn at the zone between the surface of the dissolution medium and the top of the rotating paddle not less than 1 cm apart from the vessel wall. The cumulative amount of drug release was calculated by using the calibration data [24]. The process was carried out in triplicate.

Stability studies

The optimized formulation was evaluated for stability studies by storing at 40 °C and 75% RH for 3 mo. The samples were analyzed for physical appearance, disintegration time and preservative efficacy test [25].

RESULTS AND DISCUSSION

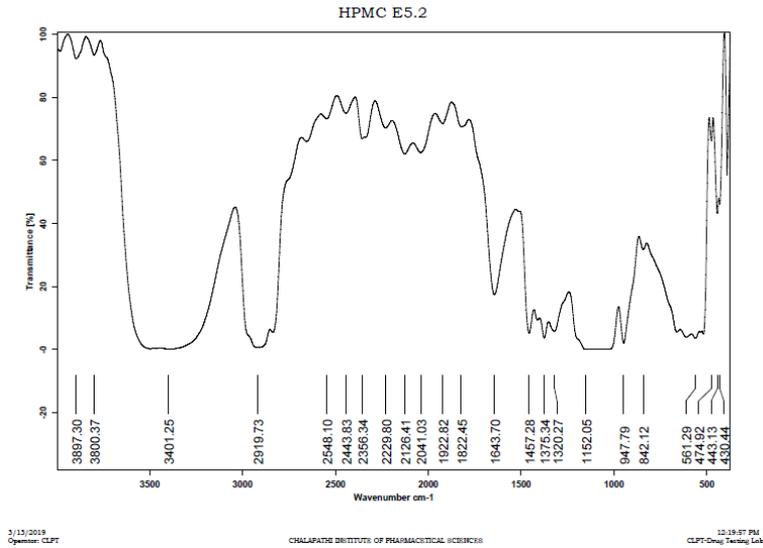
Eclipta prostrate known as bhringraj, is a famous herb widely used for hair growth, productive cough, ulcers, asthma and liver disorders. Hence, in the present investigation leaf extract of *Eclipta prostrate* was formulated into fast dissolving films to treat mouth ulcers [26]. The fresh leaves of *Eclipta prostrate* were collected in and around Guntur. They were dried by the air-drying process. The dried leaves of the *Eclipta prostrate* were extracted by the soxhlation process by using water as menstruum. The extract was dried and tested for phytochemical constituents. The results of the preliminary phytochemical screening revealed the presence of steroids, flavonoids, saponins, diterpenes. The data were given in table 1.

Table 1: Phytochemical constituent's data of *Eclipta prostrata* extract

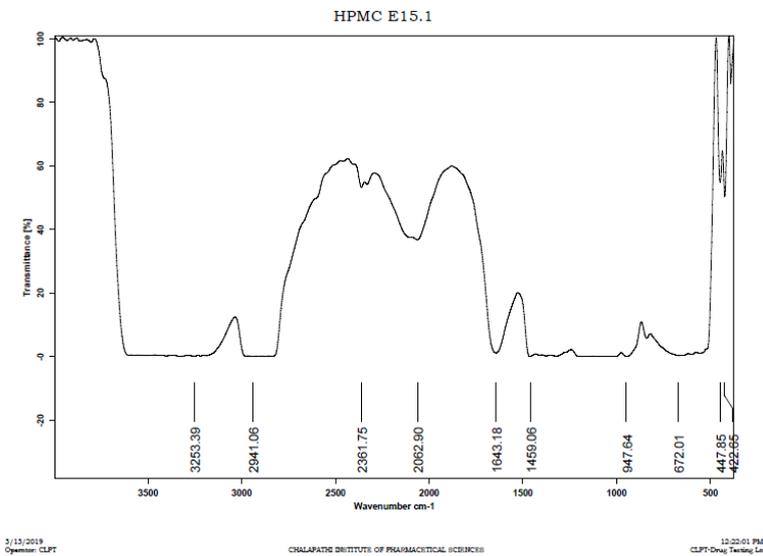
Active ingredient	Results*
Steroids	Present
Alkaloids	Absent
Phenolic compounds	Absent
Tannins	Present
Flavonoids	Present
Glycosides	Absent
Diterpenes	Present
Triterpenes	Present
Saponins	Present

*n=3

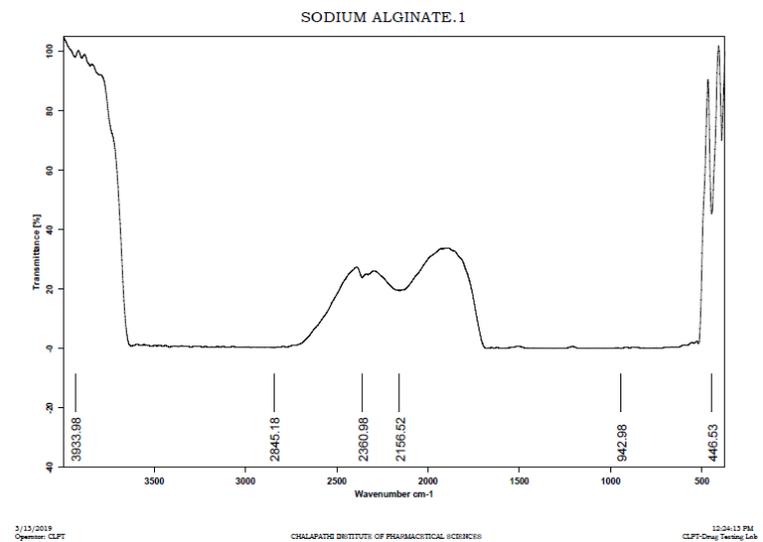
The compatibility of an extract with the polymers was studied by using IR spectroscopic methods. The spectra were shown in fig. 1 and 2. The spectra revealed that formulations having characteristic peaks same as that of the pure extract. It indicated that there was no interaction between drugs and excipients.



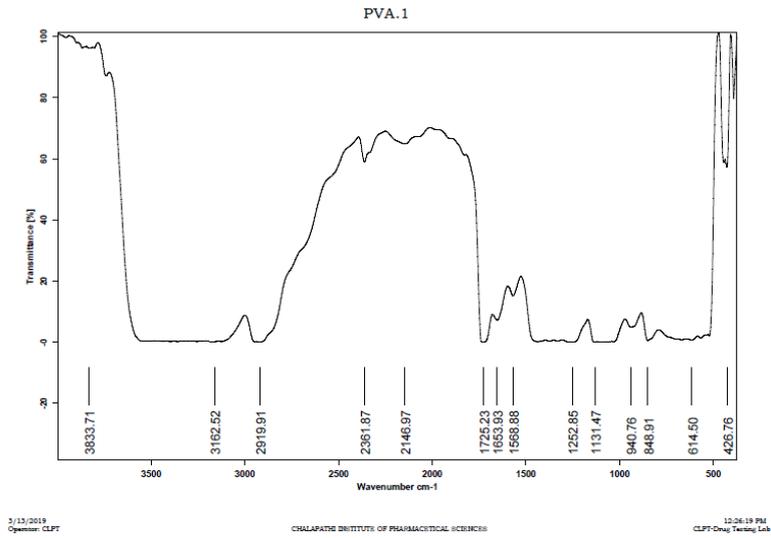
(a)



(b)

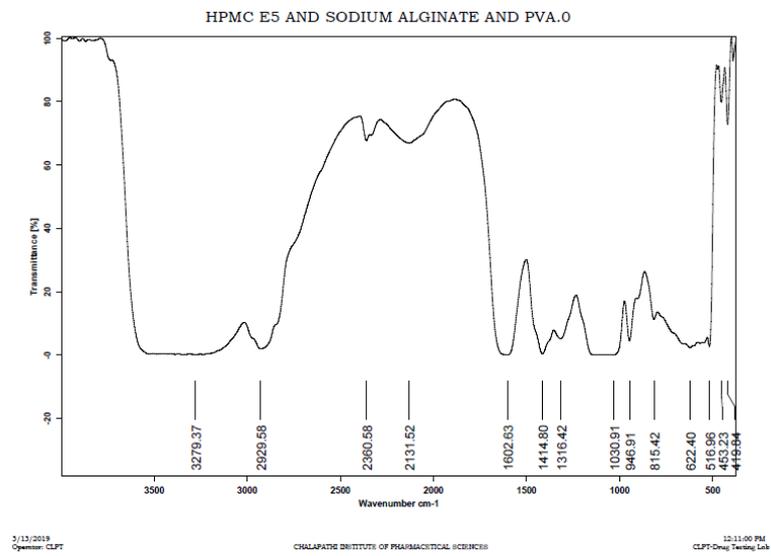


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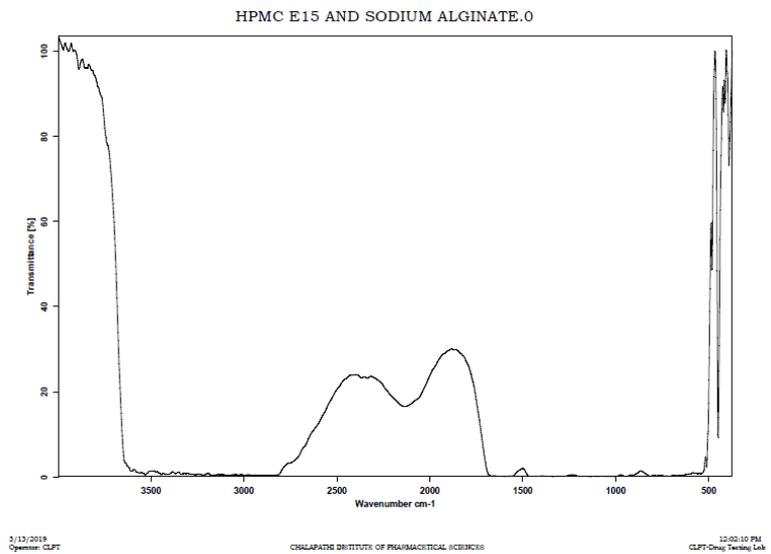


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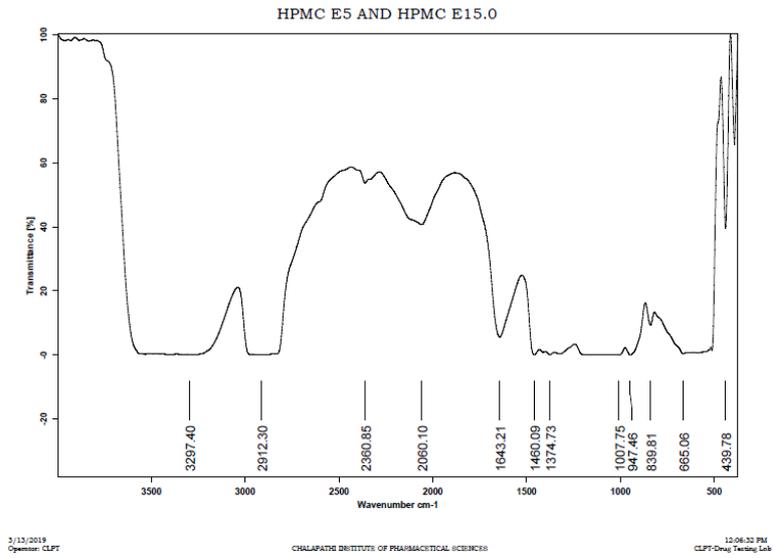
Fig. 1: FTIR spectra of a) F1 b) F2 c) F3 d) F4



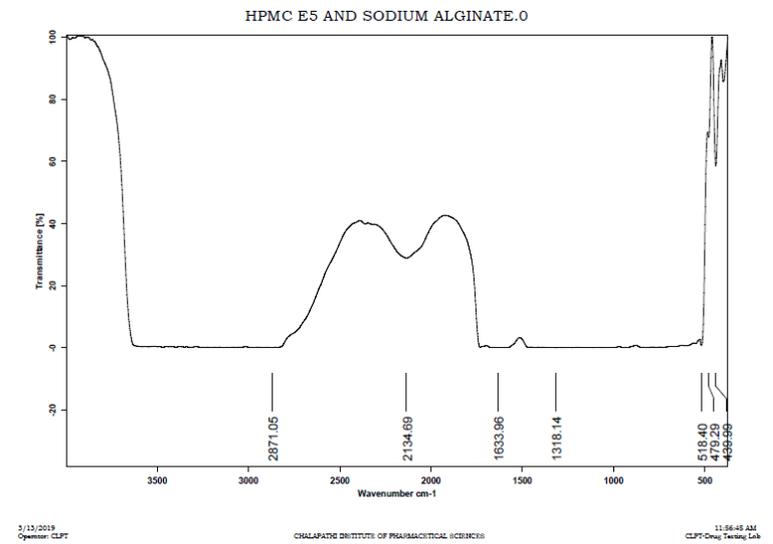
(e)



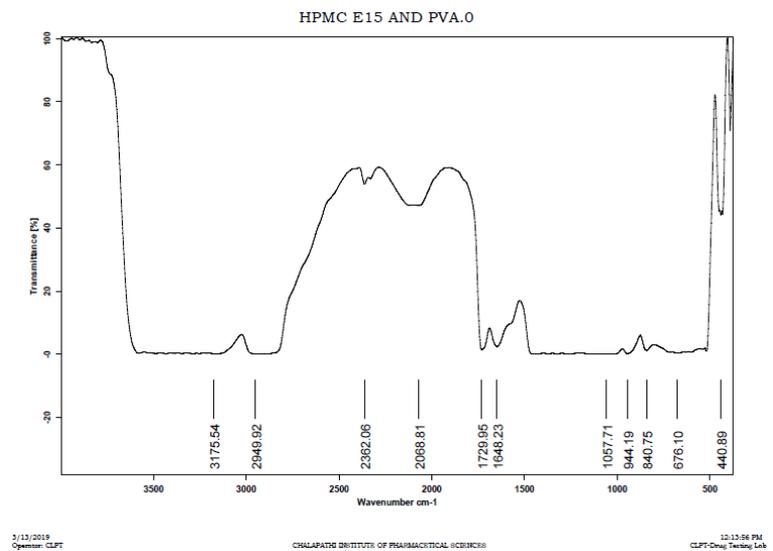
(f)



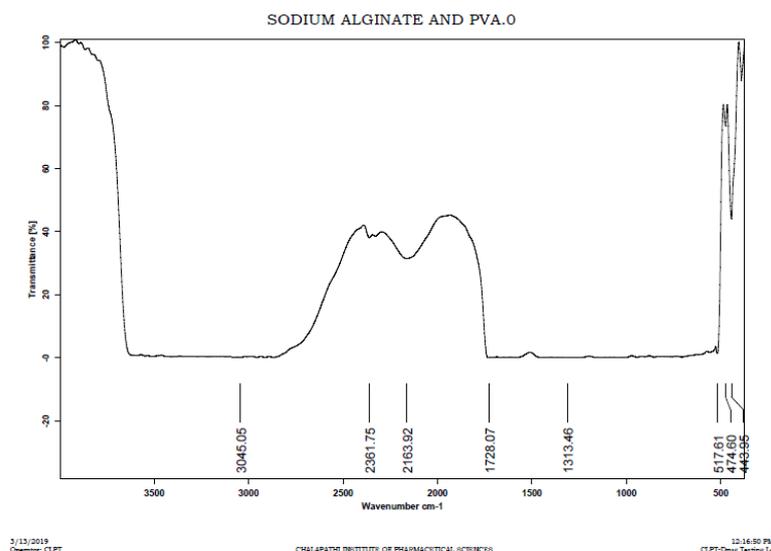
(g)



(h)



(i)



(j)

Fig. 2: FTIR spectra of formulation containing (e) F5 (f) F6 (g) F7 (h) F8 i) F9 (j) F10

The antibacterial activity of crude aqueous extract of *eclipta prostrata* against the pathogenic and nonpathogenic organisms was studied by agar well diffusion method. The activity was carried out at 500 μ g/ml concentrations and by measuring the zone of inhibition

[27]. The highest antibacterial activity was exhibited against *E. Coli* (16 mm) and moderate activity against *S. aureus* (13 mm), the data was given in table 2. The results indicated that the extract had good antimicrobial activity.

Table 2: Antibacterial activity data of aqueous extract of *Eclipta prostrata*

Name of the organism	Zone of inhibition in mm	
	Aqueousextract 500 μ g/ml	Amoxicillin 100 μ g/ml
<i>S. aureus</i>	15 \pm 0.14	24 \pm 0.54
<i>B. subtilis</i>	13 \pm 0.13	17 \pm 0.19
<i>E. Coli</i>	16 \pm 0.74	23 \pm 0.87
<i>P. aeruginosa</i>	13 \pm 0.27	19 \pm 0.35

*values are expressed as mean \pm sd, n= 3

The extract was formulated into fast dissolving films by solvent casting method with various polymers such as HPMC E5, HPMC E15, sodium alginate and PVA. Sodium starch glycolate was used as a

disintegrant, propylene glycol as plasticizer and honey as a sweetening agent [28]. The films were designed as per the formulae given in table 3.

Table 3: Formulae of herbal film

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Plant extract (%)	2	2	2	2	2	2	2	2	2	2
HPMC E5 (%)	4	-	-	-	2	-	2	2	-	-
HPMC E15 (%)	-	4	-	-	-	2	2	-	2	-
Sodium alginate (%)	-	-	4	-	-	2	-	2	-	2
PVA (ml)	-	-	-	4	2	-	-	-	2	2
PG (ml)	2	2	2	-	-	2	2	2	-	-
SSG (mg)	3	3	3	3	3	3	3	3	3	3
Honey (ml)	2	2	2	2	2	2	2	2	2	2
Water (ml)	10	10	10	10	10	10	10	10	10	10

The prepared films were evaluated for various parameters such as morphological and physicochemical parameters. All the formulated films had the uniform thickness and were transparent in nature. The films had smooth surfaces and they were elegant enough to appear. The thickness of the oral fast disintegrating films was measured by using a screw gauge and was varied from 0.127 \pm 0.012 mm to 0.163 \pm 0.052 mm. The visual appearance data of the films were given in table 4.

The surface pH of all the formulations was in the range of 5.42 \pm 0.320 to 6.85 \pm 0.521, these values were nearer to pH of the

saliva. It indicated that the films were not causing any irritation in the oral cavity. Percentage moisture uptake by the films gives information about the stability of the films. All the formulations showed the moisture uptake value less than 2.5%, it indicated that the formulations were stable. The films were subjected to the percentage moisture loss studies in order to know the amount of moisture present in the films after complete drying, which alters the stability of films. The results revealed that the loss of moisture was less and were not fragile in nature. Tensile strength indicates the ability of film to withstand rupture. The data of the study revealed that the values were between 1.45 \pm 0.01 to 2.35 \pm 0.42 cm². It

indicated that the films have enough tensile strength and can withstand its structure during transportation [29, 30]. The percentage elongation study reveals the elasticity and plasticity of the polymer and the data of the films was in the range of 1.5 to 7.6%. The data revealed that by changing the polymer type and concentration the values were changing. Folding endurance gives an

indication of the brittleness of the film. The brittleness of the film depends upon the concentration of hydrophilic polymer and plasticizer. The films exhibited the folding endurance values were above 250; it revealed that the films were non-brittle. The physicochemical evaluation data of the films was given in table 5 and 6.

Table 4: Morphological properties of herbal films

S. No.	Formulation	Visual appearance*	Surface*	Film forming capacity*	Tackiness*
1	F1	Homogenous, transparent	Smooth	Very good	Non tacky
2	F2	Homogenous, transparent	Smooth	Average	Tacky
3	F3	Homogenous, transparent	Smooth	Very Good	Non tacky
4	F4	Homogenous, transparent	Smooth	Very good	Non-tacky
5	F5	Homogenous, transparent	Smooth	Best	Non tacky
6	F6	Homogenous, transparent	Smooth	Average	Non tacky
7	F7	Homogenous, transparent	Smooth	Very good	Non tacky
8	F8	Homogenous, transparent	Smooth	Best	Tacky
9	F9	Homogenous, transparent	Smooth	Best	Non tacky
10	F10	Homogenous, transparent	Smooth	Average	Tacky

*values are expressed as mean±sd, n= 3

Table 5: Physico-mechanical properties of films

S. No.	Formulation	Thickness (mm±SD)*	%elongation (%±SD)*	Folding endurance*	Weight uniformity*	Tensile strength *	Surfaces pH*
1	F1	0.127±0.012	1.5±0.011	>200	3.52±0.041	1.45±0.012	5.32±0.051
2	F2	0.132±0.021	2.3±0.015	>250	3.54±0.041	1.63±0.018	5.69±0.064
3	F3	0.129±0.018	1.8±0.013	>270	3.55±0.042	1.85±0.021	5.88±0.075
4	F4	0.153±0.032	4.5±0.022	>200	3.57±0.042	2.15±0.041	5.54±0.031
5	F5	0.123±0.010	1.2±0.009	>280	3.63±0.046	2.42±0.062	6.08±0.090
6	F6	0.134±0.024	2.4±0.016	>230	3.65±0.046	1.34±0.009	6.25±0.092
7	F7	0.182±0.051	5.2±0.028	>270	3.73±0.050	2.35±0.055	5.90±0.082
8	F8	0.193±0.058	6.8±0.039	>250	3.81±0.051	1.92±0.032	6.32±0.95
9	F9	0.183±0.052	5.9±0.030	>250	3.83±0.052	2.35±0.055	6.55±0.125
10	F10	0.195±0.060	6.9±0.040	>230	3.85±0.052	1.36±0.009	6.58±0.127

*values are expressed as mean±sd, n= 3

Table 6: Physico-chemical properties of formulated films

S. No.	Formulation	%Moisture uptake*	%Moisture loss*	Disintegration time (sec)*	Drug content*
1	F1	2.041±0.056	1.136±0.014	61.2±0.132	89.1±0.03
2	F2	2.145±0.071	1.269±0.015	57.3±0.128	94.4±0.55
3	F3	2.052±0.074	1.146±0.018	27.3±0.140	95.3±0.01
4	F4	2.183±0.074	1.312±0.016	60.9±0.131	93.6±0.007
5	F5	2.207±0.075	1.450±0.017	32.4±0.147	92.9±0.03
6	F6	2.144±0.071	1.132±0.013	53.4±0.125	93.1±0.01
7	F7	2.166±0.073	1.045±0.010	53.3±0.125	92.4±0.06
8	F8	2.088±0.058	1.430±0.016	62.4±0.132	88.2±0.01
9	F9	2.114±0.062	1.224±0.015	67.3±0.137	90.1±0.03
10	F10	2.106±0.060	1.515±0.020	69.8±0.138	95.4±0.02

*values are expressed as mean±sd, n= 3

The disintegration time of the films was measured by using a disintegration rate testing apparatus. The data revealed that all the films were disintegrated within the time range of 27.3-69.8 sec. It indicated that all the films disintegrated very quickly. Drug Content of all the films was measured by standard assay method by taking 10 individual samples as per the test procedure. A film of size 2×2 cm² was cut and kept in 100 ml of the volumetric flask containing solvent. This was then shaken in a mechanical shaker till it was

dissolved to get a homogeneous solution and then filtered. The drug content was determined spectroscopically after appropriate dilution of the sample by measuring the absorbance at 221 nm. The drug release study of the films was carried out by using a paddle-type dissolution rate testing apparatus. The drug release study was carried out at 50 rpm for a period of 5 min. The release data from the films revealed that the release was in an immediate manner. The dissolution profile of all the formulations was depicted in fig. 3.

Table 7: Stability studies of *Eclipta Prostrate*

S. No.	Physical appearance*	Tackiness*	Film separation*	Disintegration*
F3	Very good	Non Tacky	Separates	29.32±0.27
F4	Average	Non Tacky	Separates	33.15±0.29
F6	Good	Tacky	Difficult to separates	NA

*values are expressed as mean±sd, n= 3

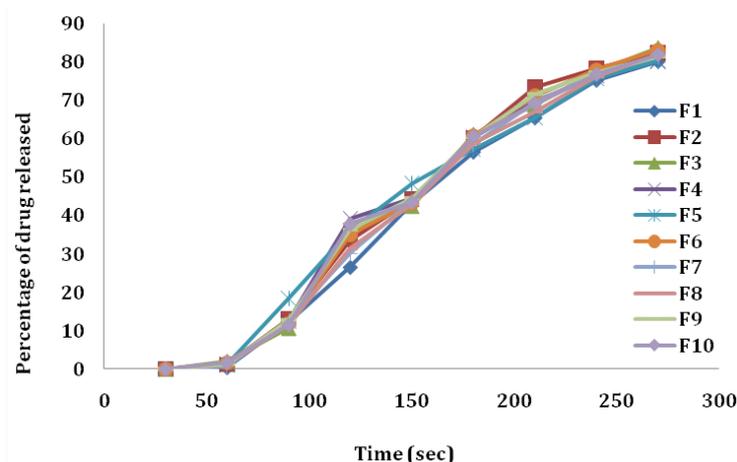


Fig. 3: *In vitro* release profile of fast dissolving films

The formulations were subjected to stability studies by storing them at 40 ± 2 °C and $75 \pm 5\%$ RH for a period of 3 mo. The formulations were tested for various parameters after the test period. The data revealed that formulation F3 was stable throughout the period. The data were given in table 7.

CONCLUSION

The objective of the present study was to fabricate and characterize the fast-dissolving herbal film of *Eclipta Prostrate* leaf extract for ulcer treatment. The aqueous extract of the leaves was collected by the soxhlation process. The phytoconstituents study of the extract revealed the presence of flavonoids, tannins and saponins which have anti-ulcer and antibacterial activity. The extract was formulated into films by solvent casting method with various polymers such as HPMC E5, HPMC E15, sodium alginate and PVA. The formulated films were subjected to physicochemical evaluation such as thickness, folding endurance, percentage elongation, moisture uptake, moisture loss, surface pH and drug release. All the formulations were good in appearance with smooth texture. The study revealed that out of the ten formulations F3 formulation showed fast disintegration, release, good appearance and stability. Based on the study results it can be concluded that *Eclipta prostrate* leaves extract can be effectively formulated in the form of oral films with expected patient compliance.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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