IJPSR (2021), Volume 12, Issue 2 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 12 February 2020; received in revised form, 13 May 2020; accepted, 22 May 2020; published 01 February 2021

FORMULATION AND EVALUATION OF SAGO STARCH FILM CONTAINING LEVOCETIRIZINE DIHYDROCHLORIDE

D. Pathak, S. Pahwa * and S. Singh

Lloyd Institute of Management and Technology (Pharm), Plot No.11, Knowledge Park-II, Greater Noida - 201306, Uttar Pradesh, India.

Keywords:

Anti-histamine, Starch, Mucoadhesive, Levocetirizine dihydrochloride

Correspondence to Author:
Dr. Shilpa Pahwa

Professor,
Lloyd Institute of Management and Technology (Pharm), Plot No.11, Knowledge Park-II, Greater Noida - 201306, Uttar Pradesh, India.

E-mail: shilpapahwa@yahoo.co.in

ABSTRACT: Levocetirizine dihydrochloride is an orally active, third-generation non-sedative antihistamine used in the symptomatic relief of seasonal and perennial allergic rhinitis. It competes with endogenous histamine for binding at peripheral H1-receptor sites on the effector cell surface. The present work aimed to prepare mucoadhesive buccal films to deliver the drug in a controlled manner with a longer duration of action, which is beneficial in managing severe conditions of allergies. The semisolid casting method was used to prepare the film using different conc. of sago starch and glycerol (plasticizer) with a variation of heating time and heating temperature. The study clearly indicated the influence of heating time and concentration of sago starch on drug release profile. It was noticed that the rate of drug release increased with increased heating time and slowed as the concentration of polymer increased. Prepared mucoadhesive films were evaluated for parameters such as thickness, surface pH, swelling properties, tensile strength, drug content *etc*.

INTRODUCTION: Amongst the various routes of administration available, the oral route is the most suited one. However, one major drawback of drugs given through oral route is that they are prone to hepatic fist-pass metabolism or metabolism in GI tract [1, 2]. Hence, an alternative to this is the delivery of drugs through mucosal surfaces such as nasal, rectal, vaginal, oral, *etc*. Such mucoadhesive drug delivery systems increase the bioavailability of the drug by bypassing first-pass metabolism or avoiding metabolism in the GI tract. Amongst the various sites available for mucoadhesive drug delivery, buccal mucosa is the best because of its good accessibility, robust epithelium, quick and easy removal of the dosage form in case of need, good drug absorption, reduction of the first-pass metabolism, and patient compliance [3, 4].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(2).1082-91

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(2).1082-91

Hence, attempts have been made to develop buccal mucoadhesive films over the existing tablets. Levocetirizine dihydrochloride is a third-generation non-sedative antihistaminic drug used to relieve allergy symptoms. This drug has more than 70% oral bioavailability; due to high bioavailability, its dose is very low (5 mg once daily), which is very much suitable for film formation, Hence, this drug was chosen as the model drug, and a film was prepared using sago starch. Indian sago (Cassava) starch is used as polymer, which is obtained from the root of the Cassava plant *Manihot esculanta*, Crantz (Fam. Euphorbiaceae).

MATERIALS AND METHODS: Levocetirizine dihydrochloride was a gift sample from Ancalima Lifescience Pvt. Ltd., Murthal, Haryana and Indian sago starch was obtained from the local market of Sonipat (Authenticated by PUSA, Delhi); other chemicals used were of analytical grade. The film was prepared by solvent casting method.

Preparation of Mucoadhesive film of Levocetirizine Dihydrochloride: Mucoadhesive films of Levocetirizine dihydrochloride were

prepared by solvent casting technique, employing a plastic sheet (placed on glass surface). A circular cast film was prepared with various formulations of mucoadhesive films with drug and sago starch in different ratios. 9 batches (L_1 to L_9) were prepared.

Drug and sago starch were added in the following ratio.1:6 for L_1-L_3, 1:9 for L_4-L_6, 1:12 for L_7-L_9. Glycerol was used in the concentration of 1.25% w/v, 1.87 w/v, 2.5% w/v for L_1-L_3, L_4-L_6, L_7-L_9, respectively. The calculated amounts of polymers were dispersed in a water drug solution.

The above dispersions were heated at 90 °C until the gelation of starch took place. Then the gelatinized starch was cast in the plastic laminated glass plate. It was kept overnight in an oven at 50 °C for drying of the film. These films were peeled off after drying and stored in a desiccator till further use **Table 1**.

TABLE 1: COMPOSITION OF SAGO STARCH BASED ORAL FILMS FOR LEVOCETIRIZINE DIHYDRO-CHLORIDE (DRUG CONCENTRATION 0.8% w/v)

Ingredients	L_1	L_2	L_3	L_4	L_5	L_6	L_7	L_8	L_9
Sago starch (gm)	2.5	2.5	2.5	3.75	3.75	3.75	5	5	5
Levocetirizine dihydrochloride (gm)	0.405	0.405	0.405	0.405	0.405	0.405	0.405	0.405	0.405
Glycerol (gm)	0.625	0.625	0.625	0.937	0.937	0.937	1.25	1.25	1.25
Saccharine sodium (gm)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Methyl paraben (gm)	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Propyl paraben (gm)	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Distilled water (ml)	50	50	50	50	50	50	50	50	50

Study of Physical Characteristics of the Formulations:

Weight Variation and Thickness: [5] Each formulation was prepared in triplicate (n = 3), and 5 films equivalent to 1 × 1 cm^2 area were cut from each batch. Their weight was measured using a digital balance (Shimadzu Corporation, Tokyo, Japan).

A digital micrometer (Mituotoyo, Japan) was used for thickness measurement at five different places of film, and the mean was calculated.

Surface pH [5, 6] of Films: The surface pH of films was determined since an acidic or alkaline pH may cause irritation to the buccal mucosa. The surface pH was determined by taking a film from each formulation (L1-L9). The films were allowed to swell for 2 h on the surface of 2% agar plate; the surface pH was measured using a pH paper placed on the surface of the swollen film. A mean of 3 readings was recorded.

Swelling Percentage: [5, 6-9] A film from each formulation was weighed, and then phosphate buffer (pH 6.8) was poured into the petridish. In 15 mins intervals an increase in the weight of the film was noted for 60 min, and the weight was calculated.

The following formula was used to calculate swelling properties.

$$\text{Swelling percentage \% } S = (Xt - Xo) / Xo \times 100$$

Where, % S is swelling percentage, Xt is the weight of swollen film after time t, Xo is the weight of film at time zero.

Folding Endurance: [12] Films of size (1 × 1 cm) were cut by a sharp blade. Folding endurance was determined by repeatedly folding a small strip of film at the same place till it tore off.

Scanning Electron Microscopy (SEM): For the study of the surface topology of the films scanning electron microscopy of the formulated films was performed using a scanning electron microscope (ZEISS EVO 50).

Tensile Strength: [13] In this study, Tensile meter (Fibrotech electronics Roorkee) instrument equipped with 25 kg load cell was used to determine and evaluate the mechanical properties of the films. A Film strip was cut with the dimensions 1 × 1 cm^2 and without any visual defects and positioned between two clamps separated by a distance of 3 cm. The lower clamp was held stationary, and the strips were pulled apart by the upper clamp moving at a rate of 2 mm/sec until the strip broke. At the point when the strip broke, the applied force was recorded. The tensile strength values calculated by the following formula:

Tensile strength kg/cm^2 = Force to break (kg) / Initial cross sectional area of the sample (cm^2)

***Ex-vivo* Mucoadhesion:** [14, 15] Modified physical balance method was used to determine the *ex-vivo* mucoadhesive strength of the prepared films. As a model mucosal membrane, goat buccal mucosa was used. The tissue was obtained from the goat after slaughter and stored in a simulated artificial saliva solution. A pan balance was used. Stainless steel tissue holder was used in place of one pan of the balance. On the ground surface of the two tissue holders, two rectangular pieces of tissues were cut and glued with an adhesive. By placing an empty beaker on one pan and weights on the other, both sides of were balanced. Between the two tissue surfaces, 1 × 1 cm^2 of the film was placed. Water was added dropwise after 10 min to the empty beaker which is placed on the pan until both tissue holders detach. The water collected in the beaker was weighed and expressed as a weight (gram force) required for the detachment, using the following equation:

$$\text{Detachment stress (dyne/cm}^2) = m \times g/A$$

Where m is the weight of the water infused at the detachment, g the acceleration due to gravity considered as 980 cm/s^2, and A the area of tissue exposed (cm^2).

Drug Content: 1 × 1 cm^2 film from each batch was kept in 10 ml phosphate buffer (pH 6.2). The solution was filtered, and drug content was determined using UV- Visible spectrophotometer (UV-1700 pc). From each batch, three readings were taken.

***In-vitro* Drug Release using Modified Magnetic Stirrer Method:** [15] *In-vitro* release of drug from the mucoadhesive film was studied by modified magnetic stirrer assembly. Phosphate buffer solution (pH 6.2) 100ml was used as dissolution medium. 1 × 1 cm^2 film from each batch (L1-L9) was taken and placed inside in a test tube containing 2 ml of pH 6.2 phosphate buffer, and the test tube opening was tied with a cellophane membrane. The test tube was placed in an inverted position in the beaker containing the dissolution medium. The dissolution medium was stirred continuously at 50 rpm using a magnetic stirrer, and the temperature was maintained at 37 ± 5 °C. 2 ml samples were withdrawn at regular intervals, and the same was replaced by an equal volume of fresh buffer solution, samples were analyzed by using UV spectrophotometer.

***In-vitro* Drug Release using Franz Diffusion Cell:** In receptor compartment of Franz diffusion cell phosphate buffer pH 6.2 (15ml) was placed, 2 ml of the same medium was taken in donor compartment, and cellophane membrane was placed between the compartments. 1 ×1 cm^2 film from each batch (L1-L9) was placed in the donor compartment. The temperature was maintained at 37 °C. The samples (0.25ml) were withdrawn, and drugs were analyzed using UV spectrophotometer.

RESULTS AND DISCUSSION:

Weight Variation and Thickness: Weight variation of all the 9 batches (L1-L9) was checked by weighing 1 × 1 cm^2 of film from each batch, and it was observed that all the batches were uniform in weight **Table 2**.

The thickness of the formulated sago starch-based oral films was a measure in five different places to ensure the uniformity of the films. The average and standard deviation of all five readings were calculated in **Table 2**. The result obtained confirmed that all the films were uniform and did not have any significant difference in the thickness at different points. The thickness of the films was increasing as the concentration of starch increased.

Percentage Moisture Loss (PML): All batches were kept at low humidity for three days, and percentage moisture loss was calculated. Results are shown in **Fig. 1**. Maximum PML was observed for batch L6 (37.5 ± 1.03%). **Table 2**, PML increased with heating time and decreased with an increase in polymer concentration.

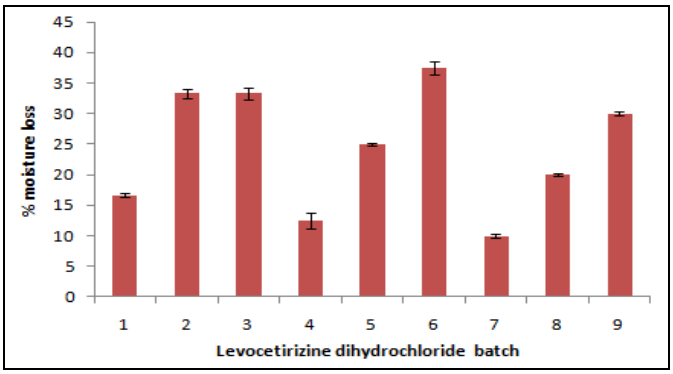

FIG. 1: PERCENTAGE MOISTURE LOSS OF FORMULATED STARCH FILMS

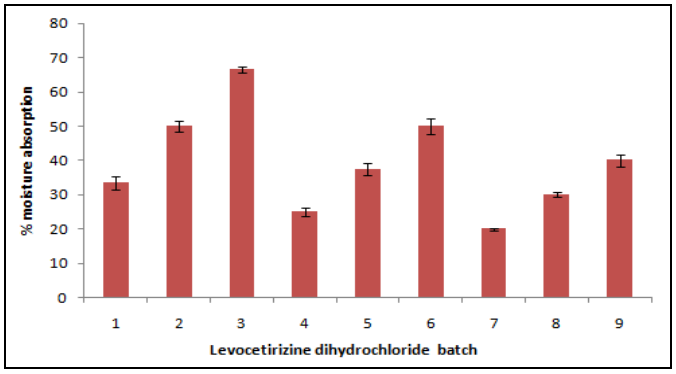

FIG. 2: PERCENTAGE MOISTURE ABSORPTION OF FORMULATED STARCH FILMS

Percentage Moisture Absorption (PMA): PMA of formulations was also determined by keeping them in high humidity conditions for three days. The results can be seen in **Table 2** (**Fig. 2**). The maximum value of PMA was in batch L3 (66.67 ± 0.92%).

Water Vapour Permeability (WVP): Water vapor permeability of starch films were evaluated in **Table 2**. Batch L_3 (26.67 ± 2.94 mg-mm/cm^2) exhibited maximum permeability for water vapours, while batch L_7 (15.15 ± 0.87 mg-mm/cm^2) showed minimum permeability. **Fig. 3** represents the graph of water vapor permeability of sago starch-based oral films.

TABLE 2: EVALUATION OF SAGO STARCH FILMS CONTAINING LEVOCETIRIZINE DIHYDROCHLORIDE

S. no.	Batch	Thickness* (mm)	Weight* (mg)	PMA#	PML#	WVP# (mg-mm/cm^2)
1	L_1	0.378±0.0098	64±5.48	33.33±1.93	16.67±0.36	19.26±1.67
2	L_2	0.371±0.0056	68±4.47	50±1.70	33.33±0.75	22.68±0.84
3	L_3	0.3738±0.0088	66±5.48	66.67±0.92	33.33±0.94	26.67±2.94
4	L_4	0.4216±0.0067	80±0	25±1.14	12.5±1.3	16.11±1.04
5	L_5	0.4402±0.0044	82±8.37	37.5±1.78	25±0.14	18.51±0.73
6	L_6	0.431±0.0068	82±8.37	50±2.42	37.5±1.03	24.71±0.63
7	L_7	0.5404±0.0042	106±5.48	20±0.34	10±0.37	15.15±0.87
8	L_8	0.5414±0.0043	104±5.48	30±0.73	20±0.26	16.55±0.62
9	L_9	0.5428±0.0032	104±5.48	40±1.87	30±0.36	22.13±0.73

* = readings are mean ± standard deviation (n=5); # = readings are mean ± standard deviation (n=3)

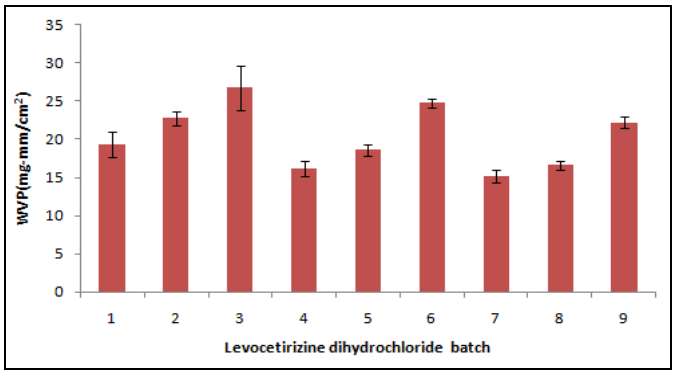

FIG. 3: WATER VAPOUR PERMEABILITY OF FORMULATED STARCH FILMS

Swelling Percentage: Swelling studies of films were performed using phosphate buffer pH 6.2 for 8 h. The results of which can be seen in **Table 3**. A graph was between percent swelling *vs*. time **Fig. 4**. It was observed that maximum swelling was observed between 4 to 6 h, after which the film weight decreased.

The maximum swelling was observed in batch L3 (333.33 ± 3.57%), while batch L7 (180 ± 2.58%) exhibited minimum swelling.

TABLE 3: SWELLING OF STARCH FILMS CONTAINING LEVOCETIRIZINE DIHYDROCHLORIDE

Time (h)	Swelling (%) (mean ± SD) (n=3)								
	L1	L2	L3	L4	L5	L6	L7	L8	L9
0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
0.5	33.33 ±3.42	50 ±2.48	66.67 ±3.46	25 ±2.49	37.5 ±1.63	50 ±1.35	30 ±2.49	40 ±2.49	54.55 ±4.72
1	50 ±2.40	83.33 ±3.54	116.67 ±2.34	50 ±2.44	75 ±2.88	100 ±4.56	30 ±3.29	60 ±2.45	63.64 ±3.28
1.5	100 ±3.50	116.67 ±4.56	166.67 ±2.56	75 ±1.44	100 ±2.94	137.5 ±4.66	50 ±0.43	70 ±2.99	81.82 ±5.37
2	116.67 ±4.35	150 ±5.68	200 ±3.45	87.5 ±4.57	100 ±3.29	162.5 ±0.24	60 ±2.43	80 ±3.55	100 ±6.90
2.5	150 ±3.56	200 ±6.34	250 ±4.36	112.5 ±6.44	137.5 ±0.42	187.5 ±1.29	90 ±4.32	110 ±5.93	118.18 ±3.89

3	150 ±2.43	216.67 ±4.56	283.33 ±2.67	137.5 ±0.57	175 ±5.20	200 ±4.39	100 ±5.95	130 ±4.30	127.27 ±2.48
3.5	183.33 ±1.84	216.67 ±5.34	283.33 ±2.90	150 ±5.23	200 ±2.49	237.5 ±4.55	120 ±4.56	160 ±3.29	154.55 ±1.46
4	200 ±2.43	266.67 ±4.56	300 ±3.65	150 ±3.54	212.5 ±0.94	250 ±5.30	130 ±5.39	180 ±1.93	172.73 ±2.35
4.5	200 ±5.32	283.33 ±4.68	316.67 ±1.89	175 ±3.29	225 ±2.39	275 ±2.94	140 ±4.29	190 ±0.58	190.91 ±3.39
5	216.67 ±3.56	283.33 ±4.59	333.33 ±2.95	187.5 ±0.84	250 ±3.29	275 ±6.49	160 ±3.64	200 ±2.58	190.91 ±3.54
5.5	216.67 ±3.45	300 ±2.34	316.67 ±2.98	175 ±1.84	250 ±1.38	262.5 ±4.2	170 ±4.02	210 ±6.83	200 ±2.89
6	216.67 ±4.65	266.67 ±4.32	333.33 ±4.35	187.5 ±0.84	225 ±2.48	275 ±3.29	170 ±3.59	210 ±8.63	200 ±1.49
6.5	200 ±3.43	266.67 ±5.21	333.33 ±3.57	200 ±2.48	237.5 ±3.44	287.5 ±4.92	180 ±2.58	210 ±3.59	190.91 ±3.55
7	183.33 ±1.43	250 ±3.09	316.6 ±2.81	187.5 ±4.33	237.5 ±5.09	275 ±2.48	180 ±5.30	200 ±2.85	190.91 ±4.59
7.5	183.33 ±4.98	250 ±1.23	300 ±3.56	187.5 ±2.44	225 ±4.88	250 ±0.93	170 ±1.30	200 ±3.58	190.91 ±5.20
8	166.67 ±3.59	233.33 ±4.39	300 ±2.50	175 ±3.49	225 ±5.29	237.5 ±1.35	170 ±4.39	200 ±2.49	190.91 ±4.93

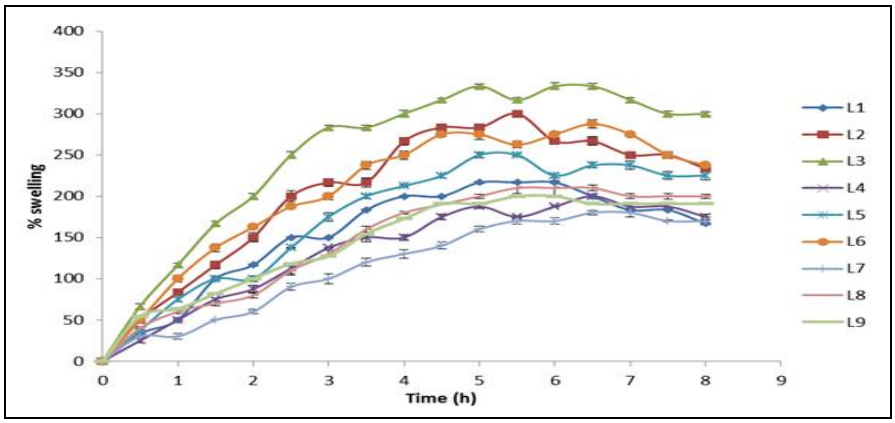

FIG. 4: SWELLING OF STARCH FILMS CONTAINING LEVOCETIRIZINE DIHYDROCHLORIDE

From the above results, it was observed that when the heating time of starch dispersion was increased the PML, PMA, WVP, and swelling of the films also increased. This may be that as we increase the heating time, the amount of starch getting solubilized in water increases, and the viscosity of starch dispersion decreases due to the solubilization of branched portion of starch *i.e.*, amylose. So, the structure of the film formulated is less compact, and film will be having more micro-cracks or pores from where the water can easily evaporate.

It was also observed that the PML, PMA, Water Vapour Permeability, and swelling decreased as the concentration of sago starch is increased. This may be due to the reason that as we increase the polymer concentration, the number of molecules within the same area are more and the structure of film will be more compact, and it will be having less pores from where water can escape or diffuse. Further, as we increase the concentration of starch the viscosity of solution also increased, which resulted in the slow movement of water in the film.

The value of all the four parameters was more in the case of sago starch films containing famotidine (water-insoluble drug), as compared to those of film containing Levocetirizine dihydrochloride (water-soluble drug). This is because the more number of microcracks present in the surface of films containing a water-insoluble drug, which was confirmed by the scanning electron microscopy of formulated films.

Surface pH of Films: The surface pH of the starch-based oral films was evaluated using 2% agar plates. The surface pH of all the formulations was observed between 6 to 7. The pH of the oral

cavity is around 6.2; hence surface pH of all the formulations was the same as that of oral cavity **Table 4.**

Folding Endurance: Folding endurance of the films was evaluated by repeatedly folding the film at the same place, at an angle of 180°. **Table 4** shows the folding endurance value of the levocetirizine dihydrochloride films. Folding endurance values of all 9 formulations were above 300, which show good folding-endurance. **Fig. 5** shows the folding endurance of films.

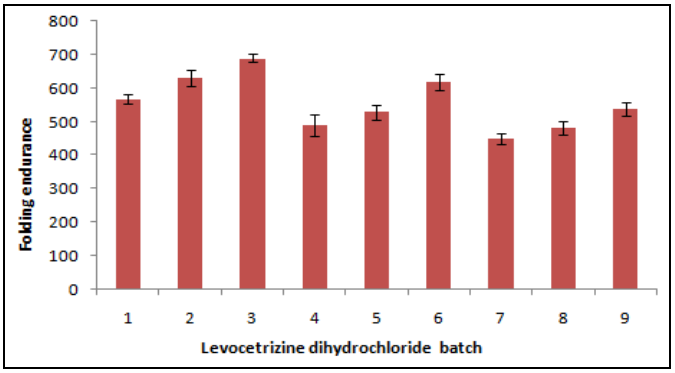

FIG. 5: FOLDING ENDURANCE OF FORMULATED STARCH FILMS

The value of folding endurance increases as we increase the heating time of starch dispersion, and the value decreased with an increase in starch concentration. The decrease in folding endurance with increased starch concentration may be because higher concentrations of amylose and amylopectin result in a more rigid structure.

Tensile Strength: Tensile strength of the formulations were determined, and results are shown in **Table 4**.

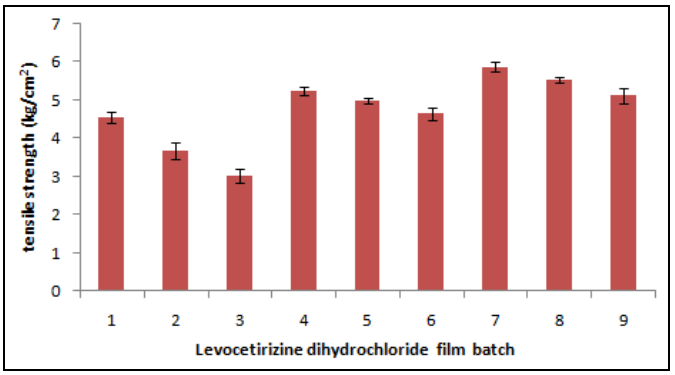

FIG. 6: TENSILE STRENGTH OF FORMULATED STARCH FILMS

Fig. 6 shows the tensile strength of starch films. The minimum tensile strength was observed in batch L_3 (3.036 ± 0.178 kg/cm^2) and batch L_7 (5.883 ± 0.123 kg/cm^2), showing the maximum tensile strength.

The tensile strength of films increases with an increase in starch concentration, and when the heating time of sago starch dispersion is increased the tensile strength of the films decreased. As the concentration of starch is increased, the viscosity of the starch dispersion increases; hence force required to break the films will be more and tensile strength will be higher.

On the other hand, when heating time is increased, the viscosity of solution decreased because of the more solubilization of amylose (gel-forming component of starch), and hence tensile strength of the films decreased.

***Ex-vivo* Mucoadhesion:** *Ex-vivo* mucoadhesion force was determined using goat buccal mucosa as model membrane and using modified physical balance method. The results were expressed as detachment stress (dynes/cm^2) and are shown in **Table 4**.

The maximum value of detachment stress was found in batch L_3 (11946.2 ± 198.93 dynes/cm^2), and the minimum values were found in the case of batch L_7 (2499 ± 185.89 dynes/cm^2). **Fig. 7** shows the detachment stress of formulations.

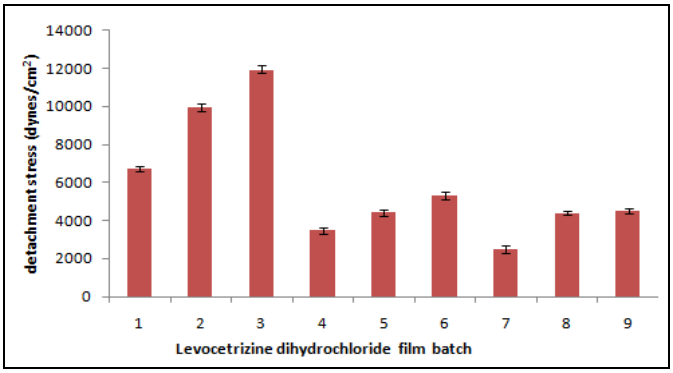

FIG. 7: *EX-VIVO* MUCOADHESION OF FORMULATED STARCH FILMS

Drug Content: The drug content of all formulations was determined using a UV spectrophotometer, and it was found that the drugs were uniformly distributed throughout the films as the standard deviation of all the batches is very less and within the limits **Table 4**.

% Drug Content = Actual Amount / Theoretical Amount × 100

TABLE 4: EVALUATION OF SAGO STARCH FILMS CONTAINING LEVOCETIRIZINE DIHYDROCHLORIDE

S. no.	Batch	Folding endurance[#]	Surface pH	Drug content[#] (mg/cm^2)	Detachment stress[#] (dynes/cm^2)	Tensile strength[#] (kg/cm^2)
1	L_1	567±15	6-7	5.0173±0.0116	6713±120.29	4.543±0.154
2	L_2	630±23	6-7	4.9707±0.3055	9956±201.09	3.678±0.231
3	L_3	689±12	6-7	4.9907±0.0116	11946.2±198.93	3.036±0.178
4	L_4	490±32	6-7	4.964±0.04	3469.2±175.089	5.239±0.098
5	L_5	529±22	6-7	4.9707±0.0306	4410±153.92	4.984±0.076
6	L_6	620±24	6-7	5.024±0.04	5292±193.93	4.652±0.167
7	L_7	449±15	6-7	4.9907±0.0231	2499±185.89	5.883±0.123
8	L_8	483±20	6-7	5.0107±0.0231	4400.2±120.28	5.549±0.077
9	L_9	538±19	6-7	4.9573±0.0231	4498.2±123.52	5.127±0.201

[#] = readings are mean ± standard deviation (n=3)

Scanning Electron Microscopy (SEM): From the study of SEM images, it was observed that the film surface containing Levocetirizine dihydrochloride is smooth and has very few cracks and pores.

***In-vitro* Drug Release using Modified Magnetic Stirrer Method:** *In-vitro* release studies of sago starch-based oral films were carried out using modified magnetic stirrer assembly. Phosphate buffer pH 6.2 was used as dissolution media at 37 ± 2 °C. The dissolution medium was continuously stirred at a speed of 50 rpm using a teflon coated magnetic bead. The release studies were carried out for 8 h. The results for release studies are shown in **Table 5; Fig. 8** shows the *in-vitro* drug release profile from films.

TABLE 5: *IN-VITRO* RELEASE OF LEVOCETIRIZINE DIHYDROCHLORIDE FROM SAGO STARCH FILMS USING MODIFIED MAGNETIC STIRRER ASSEMBLY

Time (h)	Cumulative drug release (%) (mean ± sd) (n=3)								
	L_1	L_2	L_3	L_4	L_5	L_6	L_7	L_8	L_9
0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
0.5	14.65 ±0.23	18.81 ±0.87	25.15 ±1.03	10.49 ±0.99	14.85 ±0.95	19.80 ±0.92	5.34 ± 0.80	10.89 ±0.94	15.05 ±0.45
1	30.92 ±0.78	34.10 ±0.87	38.47 ±0.34	20.02 ±0.2	24.78 ±0.86	31.13 ±1.89	14.86 ±1.82	21.41 ±0.85	26.96 ±0.33
1.5	40.26 ±0.53	45.82 ±0.82	50.58 ±1.39	30.93 ±0.54	35.30 ±0.85	43.04 ±0.42	24.78 ±0.58	29.35 ±0.48	35.50 ±1.24
2	52.37 ±0.54	56.74 ±0.64	64.08 ±0.63	38.88 ±0.31	46.61 ±0.93	52.97 ±1.34	31.73 ±0.60	36.30 ±0.24	44.63 ±0.42
2.5	60.11 ±0.44	64.29 ±0.29	72.82 ±0.55	48.40 ±0.54	53.77 ±0.85	60.12 ±0.98	38.88 ±0.56	44.24 ±0.87	52.77 ±0.90
3	67.07 ±0.32	72.03 ±0.19	78.18 ±0.63	58.52 ±0.64	66.46 ±0.37	72.41 ±0.86	48.80 ±0.65	54.44 ±0.11	64.67 ±0.95
3.5	76.19 ±1.06	82.14 ±1.1	91.27 ±0.34	68.85 ±0.3	74.41 ±0.65	82.34 ±0.84	57.73 ±0.67	62.30 ±0.24	69.25 ±0.74
4	81.96 ±0.32	85.93 ±0.37	98.23 ±0.43	75.21 ±0.45	78.58 ±0.74	90.68 ±0.86	65.87 ±0.77	70.44 ±0.42	77.19 ±0.85
4.5	86.13 ±1.02	91.68 ±0.73	98.84 ±0.35	82.15 ±0.53	85.72 ±0.47	93.47 ±0.47	75.40 ±0.75	78.18 ±0.85	83.94 ±0.87
5	90.49 ±0.62	93.87 ±0.35	99.04 ±1.06	86.33 ±0.65	91.68 ±0.75	95.66 ±0.90	81.95 ±0.68	86.11 ±0.62	90.29 ±0.97
5.5	94.07 ±1.29	96.06 ±0.87	99.23 ±0.34	90.89 ±0.34	93.48 ±0.58	96.26 ±0.85	90.68 ±0.93	91.68 ±0.53	93.08 ±0.59
6	95.26 ±0.9	96.65 ±0.83	99.43 ±1.20	92.88 ±0.64	95.06 ±0.56	97.25 ±0.63	94.46 ±0.45	94.66 ±0.3	95.66 ±0.35
6.5	95.86 ±0.48	97.25 ±1.30	99.63 ±0.35	94.87 ±0.24	96.85 ±0.06	97.45 ±0.59	97.24 ±0.56	96.65 ±0.42	96.85 ±0.75
7	96.26 ±0.39	97.45 ±0.39	99.65 ±0.54	96.45 ±0.64	97.25 ±0.76	97.45 ±0.75	97.84 ±1.56	97.05 ±0.97	98.04 ±0.9
7.5	96.85 ±0.44	97.65 ±0.83	99.83 ±0.47	97.45 ±0.6	97.45 ±0.39	97.85 ±0.89	98.24 ±1.63	97.45 ±0.89	98.64 ±0.80
8	97.25 ±0.45	97.65 ±0.94	99.83 ±0.63	98.04 ±0.69	97.85 ±0.94	98.24 ±0.54	99.03 ±0.36	98.64 ±0.68	99.83 ±0.99

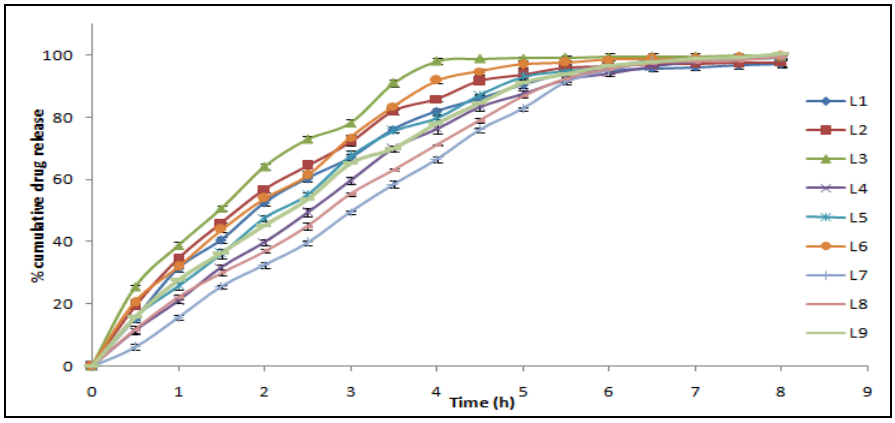

FIG. 8: *IN-VITRO* RELEASE PROFILE OF LEVOCETIRIZINE DIHYDROCHLORIDE FROM SAGO STARCH FILMS USING MODIFIED MAGNETIC STIRRER ASSEMBLY

From the results, it was found that most of the drug was released around 4-5 h. The maximum drug release after 4 hrs was from batch L_3 (98.23 ± 0.43%) and batch F_3 (97.64 ± 0.39%), while the minimum values were found in the case of batch L_7 (65.87 ± 0.77%) and batch F_7 (71.43 ± 0.89%).

***In-vitro* Drug Release using Franz Diffusion Cell:** *In-vitro* drug release of the sago starch-based oral films was also evaluated using Franz diffusion cell. 15 ml of phosphate buffer pH 6.2 was taken in the receptor compartment, while 2 ml of phosphate buffer pH 6.2 was taken in the donor compartment. The release study was performed for 8 h at 37±2 °C. The results for release studies are shown in

Table 6 and **Fig. 9** shows the *in-vitro* drug release profile from starch films containing Levocetirizine dihydrochloride.

From the results, it was found that most of the drug released around 4-5 h. The maximum drug release after 4 h was from batch L_3 (98.03 ± 0.89%), while the minimum values were found in batch L_7 (66.62 ± 0.97%).

TABLE 6: *IN-VITRO* RELEASE OF LEVOCETIRIZINE DIHYDROCHLORIDE FROM SAGO STARCH FILMS USING FRANZ DIFFUSION CELL

Time (h)	Cumulative drug release (%) (mean ± sd) (n=3)								
	L_1	L_2	L_3	L_4	L_5	L_6	L_7	L_8	L_9
0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
0.5	15.21 ±1.32	19.28 ±0.72	25.46 ±0.84	11.35 ±0.88	15.66 ±0.76	20.57 ±0.79	6.21 ±1.09	11.67 ±1.16	15.76 ±0.96
1	31.33 ±0.72	34.48 ±0.18	38.83 ±1.11	20.95 ±0.77	25.73 ±1.32	32.09 ±0.57	15.67 ±0.60	22.19 ±0.77	27.72 ±1.11
1.5	40.66 ±1.35	6.12 ±0.03	50.82 ±0.75	31.89 ±0.65	36.29 ±1.55	44.04 ±0.89	25.57 ±0.64	30.16 ±0.98	36.29 ±0.84
2	52.59 ±1.36	56.93 ±1.17	64.15 ±1.06	39.92 ±0.94	47.64 ±0.99	54.04 ±0.67	32.56 ±0.94	37.11 ±0.75	45.40 ±0.96
2.5	60.32 ±0.93	64.45 ±1.70	72.87 ±0.95	49.46 ±1.32	54.88 ±1.08	61.27 ±0.56	39.69 ±0.82	45.02 ±0.98	53.54 ±0.90
3	67.21 ±0.61	72.10 ±1.35	78.23 ±1.08	59.62 ±1.18	67.55 ±1.64	73.54 ±0.90	49.55 ±0.67	55.29 ±0.67	65.37 ±1.11
3.5	76.20 ±1.00	82.08 ±1.02	91.06 ±1.14	69.99 ±1.01	75.61 ±0.55	83.55 ±0.99	58.48 ±1.07	63.06 ±0.40	70.05 ±0.68
4	81.95 ±1.04	85.91 ±0.81	98.03 ±0.89	76.43 ±1.56	79.86 ±0.59	91.95 ±0.78	66.62 ±0.97	71.18 ±0.28	77.92 ±0.61
4.5	86.10 ±0.88	91.57 ±0.58	98.73 ±0.19	83.40 ±1.16	86.99 ±0.69	94.83 ±0.98	76.11 ±0.76	78.92 ±0.78	84.68 ±0.91
5	90.42 ±1.24	93.79 ±1.28	98.93 ±0.67	87.63 ±0.87	92.99 ±0.94	97.04 ±0.92	82.70 ±0.54	86.84 ±0.5.	91.03 ±0.44
5.5	93.97 ±1.34	95.95 ±1.00	99.13 ±0.81	92.21 ±0.68	94.85 ±0.93	97.66 ±0.54	91.38 ±0.89	92.43 ±0.89	93.86 ±0.19
6	95.18	96.57	99.32	94.25	96.45	98.65	95.23	95.44	96.44

	±0.77	±0.40	±1.14	±0.95	±0.64	±0.39	±0.56	±0.94	±0.97
6.5	95.78	97.16	99.52	96.24	98.24	98.86	98.02	97.44	97.65
	±0.8	±0.74	±1.18	±0.35	±0.49	±0.44	±0.34	±0.97	±1.02
7	96.18	97.36	99.52	97.84	98.66	98.87	98.65	97.86	98.84
	±0.98	±0.81	±1.11	±1.07	±0.90	±0.90	±0.99	±0.83	±0.77
7.5	96.76	97.56	99.72	98.85	98.86	99.26	99.05	98.26	99.44
	±0.93	±0.26	±0.69	±0.87	±0.48	±1.05	±0.77	±0.90	±0.62
8	97.16	97.56	99.72	99.45	99.26	99.66	99.84	99.43	100.62
	±0.61	±1.16	±0.61	±1.09	±0.63	±0.88	±0.56	±1.08	±0.87

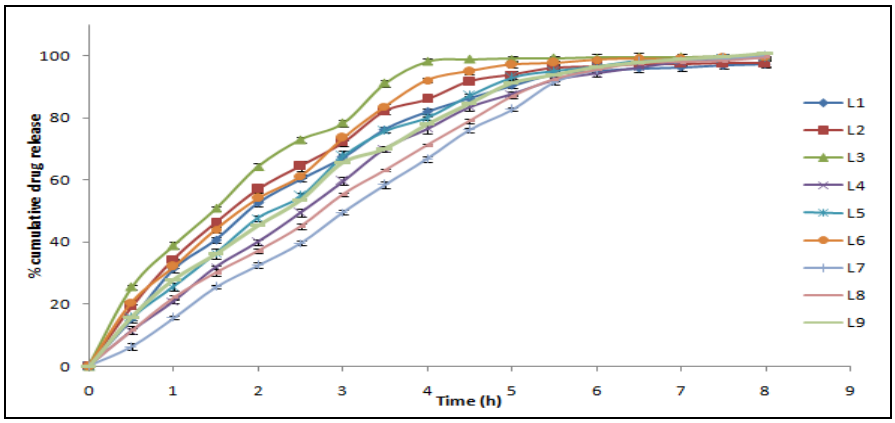

FIG. 9: *IN-VITRO* RELEASE PROFILE OF LEVOCETIRIZINE DIHYDROCHLORIDE FROM SAGO STARCH FILMS USING FRANZ DIFFUSION CELL

There was no significant difference in *in-vitro* drug release profiles obtained from both the above-mentioned methods.

CONCLUSION: Mucoadhesive buccal films were successfully formulated and evaluated to deliver the drug in a controlled manner. From the results, it was concluded that the sago starch could be a very useful platform for drug delivery in the oral cavity. The time of drug release can be controlled by varying concentrations of sago starch, as well as heating time.

Buccal drug delivery is a promising area for continued research with the aim of systemic delivery of orally inefficient drugs as well as a feasible attractive alternative for noninvasive delivery of potent peptide and protein drug molecules. However, the need for safe and effective buccal permeation enhancers is a crucial component for a prospective future in the area of buccal drug delivery.

ACKNOWLEDGEMENT: The author thanks Ancalima Lifescience Pvt. Ltd., for providing materials as gift samples for this work. The authors are also grateful to Coral Drugs (India) for their technical assistance.

CONFLICTS OF INTEREST: Nil

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How to cite this article:
Pathak D, Pahwa S and Singh S: Formulation and evaluation of sago starch film containing Levocetirizine dihydrochloride. Int J Pharm Sci & Res 2021; 12(2): 1082-91. doi: 10.13040/IJPSR.0975-8232.12(2).1082-91.