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FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING FILM OF LEVOSALBUTAMOL SULPHATE

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ABSTRACT

Aim of the present study was to develop the Fast Dissolving Oral Films of levosalbutamolsulphate, a short-acting β2 adrenergic receptor agonist used in the treatment of Asthma and chronic obstructive pulmonary disease. Chemically, levosalbutamol is the active enantiomer of salbutamol. Fast dissolving oral films deliver drug directly in the vascular system and by passes the hepatic first pass metabolism so dose of the drug may also reduce significantly. Fast dissolving films were prepared using solvent casting method, hydrophilic polymers (HPMC K-15cps, HPMC E-15, HPMC K-100) were selected as film forming agents and propylene glycol was used as plasticizer to give flexibility to the films. In FT-IR study no interaction was observed between drug and the excipients. Blank films were prepared and evaluated. Concentration of polymer was optimized during preliminary studies. Three blank films were selected for the incorporation of drug. After characterization the drug loaded films and studying their disintegration time & In-Vitro drug release studies, among the formulations [F1 to F10] F3,F9toF10 was selected the best formulation as its disintegration and dissolution time was less and it release drug to a greater extent compared to other formulations with minimum time. As dose of the drug gets reduced from 5 mg to just 2 mg, therefore adverse effects of the drug may also get reduced. Therefore fast dissolving oral films can play an important role in oral drug delivery.

KEYWORDS: Orally disintegrating film, Levosalbutamol sulphate, HPMC, Solvent casting method, Drug release.

INTRODUCTION

Levosalbutamolor levalbuterolis a short-acting β2adrenergic receptor agonist used in the treatment ofasthma and chronic obstructive pulmonary disease (COPD).

Activation of β2 adrenergic receptors on airway smooth muscle leads to the activation of adenylatecyclaseand to an increase in the intracellular concentration of 3',5'-cyclic adenosine monophosphate (cyclic AMP). The increase in cyclic AMP is associated with the activation of protein kinase A, which in turn, inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation.

levosalbutamol is well tolerated. Common mild side-effects include an elevated heart rate, muscle cramps, and gastric upset (including heartburn and diarrhea).

Medicine to such patients i.e. pediatric, children, geriatrics etc. Fast-dissolving The fast dissolving drug delivery system is a new drug delivery technique to provide films have acquired great importance in the pharmaceutical industry due to their unique properties & advantages.[2,3] As the fast dissolving film utilizes sublingual route, rapid absorption of the drug is possible, which finally lead to quick onset of drug action. Difficulty in swallowing is a common problem of all age group, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Solid dosage form that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convience of easily swallowable dosage form. In case of allergic condition rapid action of drug is required. The fast dissolving films fulfill the requirement of potential solid dosage form for levosalbutamol in treating allergic conditions. It shows patient compliance, rapid on-set of action; increased bioavailability and good stability make this film popular as a dosage form of choice.

Prepared film were subjected to different evaluation parameters like physical properties, disintegration time, content uniformity and dissolution studies.

MATERIALS AND METHODS

Material

Table: 1 Material used with their source.

Sr No.	Material	property	Source
1	Levosalbutamol sulphate	Pure drug	Mecloieds pharmaceutical, Mumbai.
2	Hpmc, Hpmk-15,Hpmc k-100.	Film former	Zim laboratories, Nagpur.
3	Propylene glycol, PEG 400, PEG 6000, GLYCERINE.	platicizer	Lobachemie laboratory chemical ltd,Mumbai.
4	Sodium lauryl sulphate	surfactant	Vamapharma, Nagpur.
5	Aspartame	Sweetner agent	Mecloieds pharmaceuticals, Mumbai.
6	Citric acid	Saliva stimulating agent	Lobachemie laboratory chemical ltd,Mumbai.

Equipments used with their source

Table: 2 Equipments used with their source.

Sr No.	Equipment	Model no.	Make
1	Oven rotek	Or-203	Labindia
2	Disintegration apparatus	Da-40	Electrolab
3	Uv-spectrophotometer	Uv-1800	Shimadzu japan
4	Digital balance	Bl-22oh	Shimadzu japan
5	Ph meter	Pico+	Labindia
6	Magnetic stirrer	Lms-28oe	Labtop
7	Screw gauge	Sg-001	Electrolab
8	Sonicator	3-5 l 100h	Pci analytics

Preparation of Fast Dissolving Film

Oral fast dissolving film of containing of levosalbutamol sulphate was prepared by the solvent casting method. The polymers (HPMC K-15) and plasticizers (propylene glycol, PEG-400, glycerin) was dissolved in about sufficient quantity of distilled water in separate beaker to prevent the excessive air bubbles formation. In the second beaker levosalbutamol was add and stir both solution 30min. Then two solutions mixed together and specified amount of other excipients such as saliva stimulating agent, sweetening agent, flouring agent etc. was added to that mixture as well as sufficient quantity of remaining water & stirred for 1 hour. After stirring kept for 30 min for sonication to remove all air bubbles from final solution. Then the final solution was casted on petridish and it was dried in the oven at 45ºC for 12 hr. The film was carefully removed from the Petridish, and cut according to the size required for single dose and testing (Dose: 2 x 2 cm).

Table: 3 Formulation Details of Blank fast dissolving film.

Ingredient(mg)/ Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}
HPMC E 15	200	300	400	500	-	-	-	-	-	-
HPMC K 15	-	-	-	-	200	300	400	500	-	-
HPMC K 100	-	-	-	-	-	-	-	-	200	300
PROPYLENE GLYCOL	1	-	1	-	1	-	1	-	1	-
PEG 400	-	1	-	1	-	1	-	1	-	1
SLS	50	50	50	50	50	50	50	50	50	50
Citric Acid	50	50	50	50	50	50	50	50	50	50
Aspartame	55	55	55	55	55	55	55	55	55	55
AMARANTH	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
RESILT	+	+	++	+++	+	+	++	+++	+	+

+ -Poor + +-Average + + +-Excellent

Table: 4 Formulation Details of Blank Fast Dissolving Film.

Ingredient(mg)/ Formulation	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}	F_{16}	F_{17}	F_{18}	F_{19}	F_{20}
HPMC K 100	400	500	-	-	-	-	-	-	-	-
PVA	-	-	200	300	400	500	-	-	-	
CARBAPOL	-	-	-	-	-	-	200	300	400	500
PROPYLENE GLYCOL	1	-	1	-	1	-	1	-	1	-
PEG 400	-	1	-	1	-	1	-	1	-	1
SLS	50	50	50	50	50	50	50	50	50	50
Citric Acid	50	50	50	50	50	50	50	50	50	50
Aspartame	55	55	55	55	55	55	55	55	55	55
AMARANTH	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
RESILT	++	+++	+	+	++	+++	+	+	+	++

+ -Poor + +-Average + + +-Excellent

6.4 Formulation of levosalbutamol sulphate Film by Solvent Casting Method

From the preliminary physical observation of the films prepared the best compositions were used for the incorporation of levosalbutamol sulphate.

Calculated amount of levosalbutamol sulphate was dissolved in the polymeric solution, after complete dissolution of the drug; propylene glycol (plasticizer) was added and stirred to form a homogeneous solution. The solution was casted on petridishthen kept in hot air oven at 40ºC for 24 hours. The film thus formed was cut into size of 2X2 cm diameter. Each containing 2 mg levosalbutamol sulphate. The detailed compositions of the levosalbutamol sulphate fast dissolving film are given in table No: 3,4.

Table: 5 Formulation Details of Levosalbutamol sulphate Fast Dissolving Film.

Ingredient(mg/ml) Formulation	F_1	F_2	F_3	F_4	F_5
LVS	36	36	36	36	36
HPMC E 15	200	300	400	-	-
HPMC K15	-	-	-	200	300
HPMC K 100	-	-	-	-	-
PROPYLENE GLYCOL	1	1	1	1	1
SLS	50	50	50	50	50
Citric Acid	50	50	50	50	50
Aspartame	55	55	55	55	55
AMARANTH	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s

Table: 6 Formulation Details of Levosalbutamol sulphate Fast Dissolving Film.

Ingredient (mg/ml) Formulation	F6	F7	F8	F9	F10
LVS	36	36	36	36	36
HPMC E 15	-	-	-	-	-
HPMC K15	400	-	-	-	200
HPMC K 100	-	200	300	400	200
PROPYLENE GLYCOL	1	1	1	1	1
SLS	50	50	50	50	50
Citric Acid	50	50	50	50	50
Aspartame	55	55	55	55	55
AMARANTH	q.s	q.s	q.s	q.s	q.s
Water	q.s	q.s	q.s	q.s	q.s

EVALUATION PARAMETER OF FILMS

The prepared film was evaluated for following specifications.

Visual Inspection

Oral fast dissolving films were inspected manually for their transparency and air bubbles.

Weight

Oral fast dissolving film weighted on analytical balance.

Thickness

Film thickness was measured by using a micrometer screw gauge apparatus. A strip of 2 X 2cm was placed between the thickness rods and thickness was measured in five different positions.

Folding endurance

Folding endurance was measured by manually or practically for the prepared films. Take a 2X2cm films and folded repeatedly at the same place till it broke. The no times the film could be folded at the same place without breaking gave the exact valve of folding endurance.

PH

The PH was determined by dissolving a film in 1-2 ml of distilled water and then the PH of the obtained solution was measured by the PH meter.

Dissolution studies

The release rate of the levosalbutamol sulphate fast dissolving film was determined by the help of USP Dissolution Test Apparatus-II. The dissolution test was performed using 900ml Phosphate Buffer Solution PH 6.8, at 37 ±5ºC with 50 rpm of the paddle speed. Aliquot 5ml of the solution was collected from the dissolution apparatus at time interval of 1 min and at the same time add 5 ml or same amount of fresh dissolution medium. The Aliquot filtered through the whatman filter paper. The absorbance of the filtered solution was measured at 276 nm. The aliquot should be withdrawn at the zone between the surface of the dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. Cumulative percent drug release can be calculated by using the equation obtained from the standard curve or % drug release formula. (A = Con. Of Std. / Abs. of Std. X Abs. of sample X volume of dissolution apparatus X Dilution factor / 1000, B = A-Value/Label claim X 100).

RESULT AND DISCUSSION

UV Spectroscopy

The UV spectrum of levosalbutamol sulphate in Phosphate buffer solution PH 6.8 in the range of 400–200nm. The spectrum indicated that the observed λmax of levosalbutamol sulphate was 276 nm which is matched with pharmacopoeial value.

Preparation of standard Calibration curve of levosalbutamol

Levosalbutamol sulphate showed maximum absorption at wavelength 276 nm in PBS PH 6.8. Standard curve was plotted by taking absorption of diluted stock solutions (5, 10, 15, 20, 25, 30 µg/ml) at wavelength 276 nm.

Con.(mg/ml)	Abs.
5	0.251
10	0.516
15	0.803
20	1.062
25	1.270

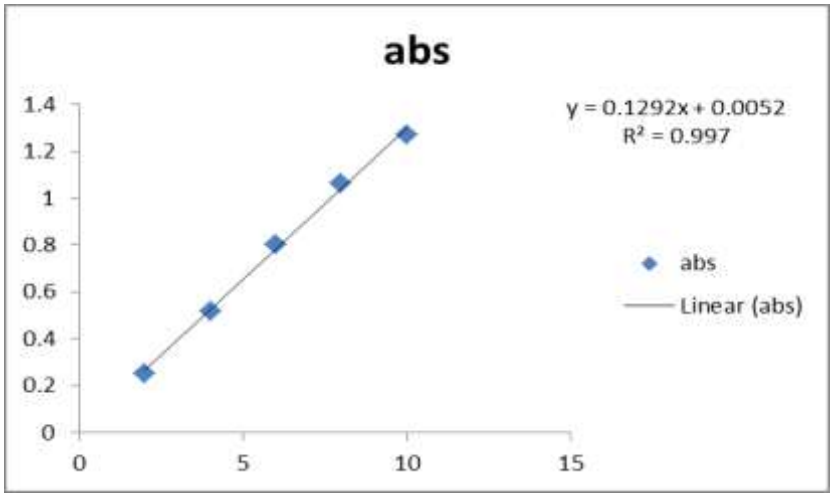


Fig: No3 Calibration curve of levosalbutamol sulphate.

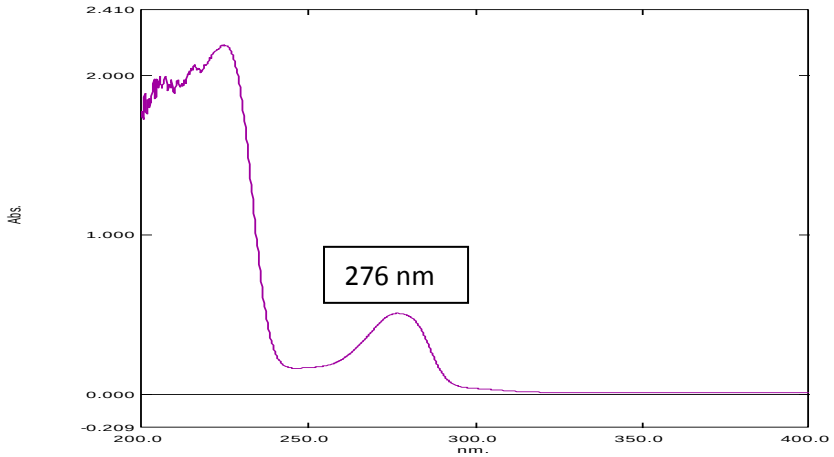
Standard Calibration Curve of Levosalbutamol Sulphate in Phosphate Buffer Ph 6.8 Solution

Standard Stock Solution

A stock solution containing 1 mg/ml of pure drug was prepared by dissolving 100 mg of Levosalbutamol in sufficient phosphate buffer pH 6.8 to produce 100 ml solution in a volumetric flask.

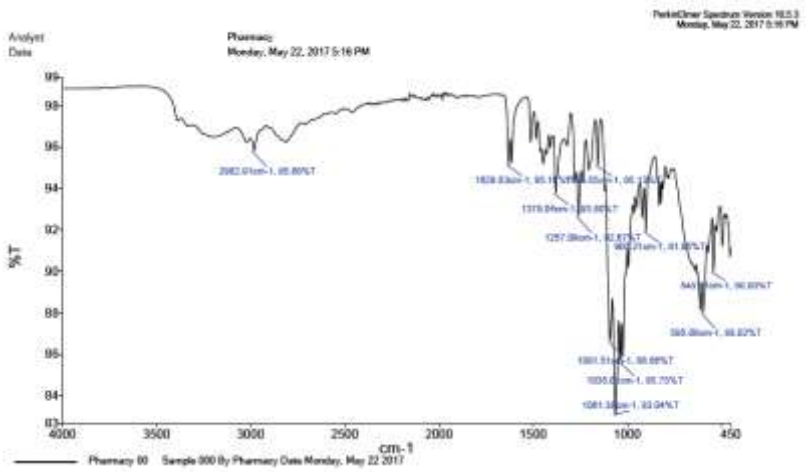
Stock Solution

From the standard stock solution, 5 ml of the stock solution was further diluted to 50 ml with phosphate buffer pH 6.8 into a 50 ml volumetric flask and diluted up to the mark with phosphate buffer pH 6.8. Aliquots of 0.2, 0.4, 0.6, 0.8, and 1 ml of stock solution were pipette out into 10ml volumetric flasks. The volume was made up to the mark with phosphate buffer pH 6.8. These dilutions give 2, 4, 6, 8 and 10 mg/ml concentration of Levosalbutamol sulphate respectively. The absorbance was measured in the UV-Visible spectrophotometer at 276 nm using distilled water as blank and graph of concentration versus absorbance was plotted.



Graph 4: U.V. absorption spectrum of Levosalbutamol sulphate in Phosphate buffer (pH 6.8).

FTIR: FTIR studies were carried out for detection of drug polymer interaction. In the present study the IR study of pure drug levosalbutamol sulphate, polymer HPMC K-15, drug with HPMC K-15, HPMC–K100, HPMC E-15 & sodium lauryl sulphate were carried out to study the compatibility between them.

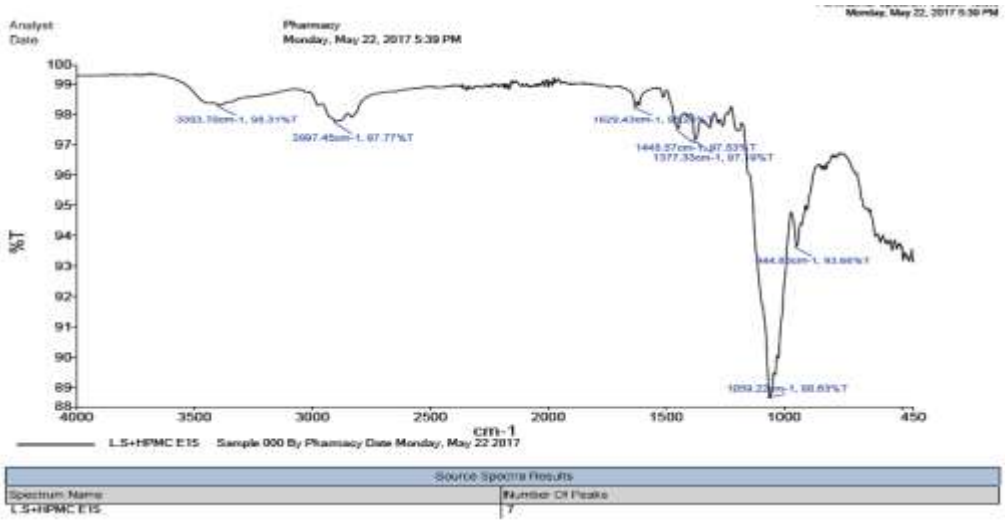


Source Spectra Results	
Spectrum Name	Number Of Peaks
Pharmacy 00	11

List of Peak Area/Height		
Peak Number	X (cm-1)	Y (%T)
1	2982.91	95.86
2	1629.03	95.16
3	1379.04	93.80
4	1257.09	92.67
5	1155.55	95.13
6	1091.51	86.66
7	1061.38	83.04
8	1035.81	85.73
9	900.21	91.95
10	595.09	88.02
11	540.03	90.00

Fig.No.5: FTIR Spectra of levosalbutamol sulphate with Interpretation data.

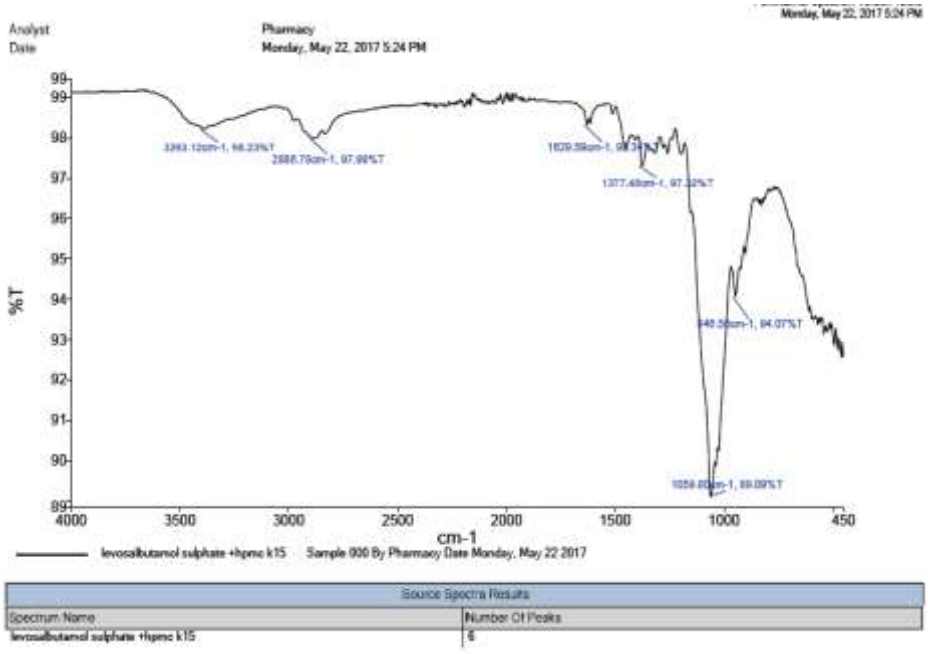
Values for IR spectrum of LVS Functional group	Reported Frequency (cm-1)	Obtained Frequency (cm-1)
C-H of 30carbon	1400-1375	1376.93
N-H bending of 20 amine	1640-1530	1627.63
C-O of phenol	1200-1240	1203.36
C-O of primary alcohol	1260-1000	1153.22
C-H stretching	3000-2840	2985.27



Source Spectra Results	
Spectrum Name	Number Of Peaks
LS+HPMC E15	7

List of Peak Area/Height		
Peak Number	X (cm-1)	Y (%T)
1	3393.70	98.31
2	2897.45	97.77
3	1629.43	98.26
4	1448.57	97.53
5	1377.33	97.19
6	1059.22	88.63
7	944.80	93.66

Fig.No.6: FTIR Spectra of levosalbutamol sulphate + hpmc k--100.



Source Spectra Results	
Spectrum Name	Number Of Peaks
levosalbutamol sulphate +hpmc k15	6

List of Peak Area/Height		
Peak Number	X (cm-1)	Y (%T)
1	3393.12	96.23
2	2886.78	97.99
3	1629.59	98.34
4	1377.48	97.32
5	1059.80	89.09
6	946.56	94.07

Fig.No.7: FTIR Spectra of levosalbutamol sulphate + hpmc k-15.

Differential scanning calorimatory (DSC)

DSC studies were carried out for detection of drug polymer interaction. In the present study the DSC study of pure drug levosalbutamol sulphate, polymer HPMC K-15, drug with HPMC K-15, HPMC K-100 & sodium lauryl sulphate were carried out to study the compatibility between them.

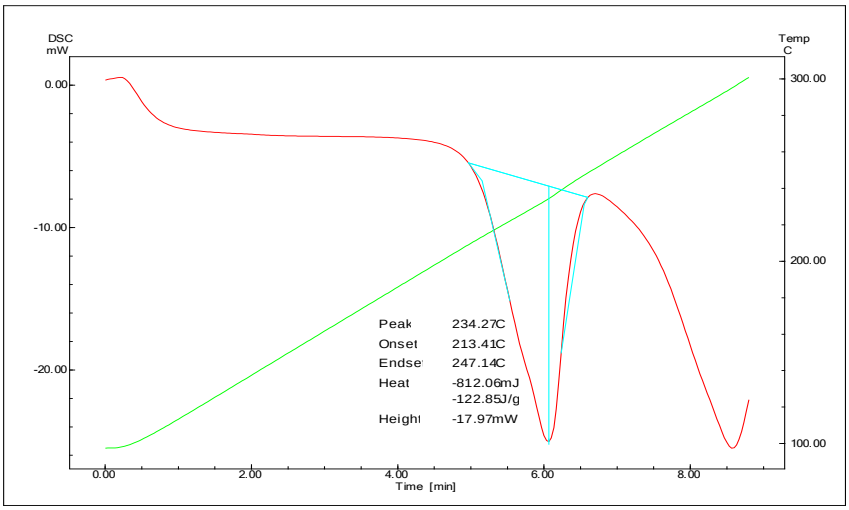


Fig: No8: Dsc of pure drug levosalbutamol sulphate

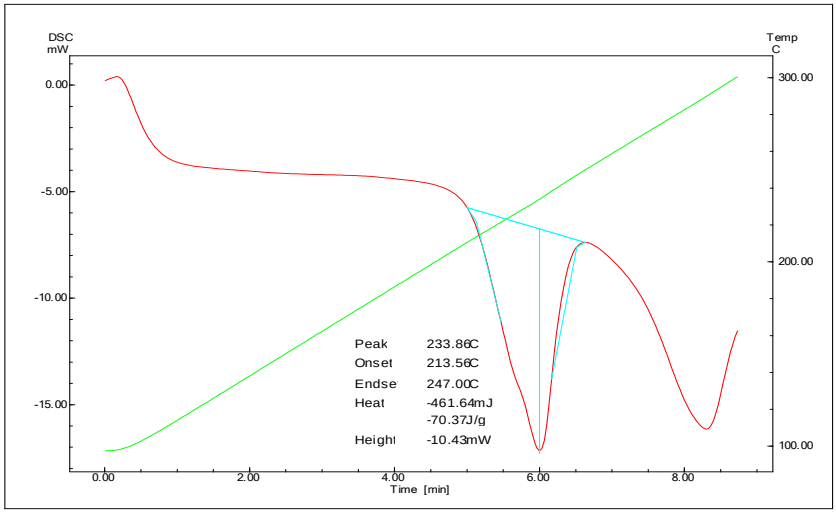


Fig.No9: Pure drug + excipient

In-Vitro dissolution studies

In present work, an attempt has been made to increase the % drug release of levosalbutamol sulphate with changes in concentration of polymers & plasticizers by solvent casting method.

Table no.7: In-Vitro dissolution study of levosalbutamol sulphate

Table no.7: In-vitro dissolution study of levosalbutamol sulphate [F1-F5].

Time(min)	% Drug release				
	F_1	F_2	F_3	F_4	F_5
1	37.90	51.77	25.76	27.50	37.90
2	43.31	58.99	32.84	31.12	39.84
3	48.75	64.52	36.49	34.76	41.80
4	52.49	68.34	40.16	41.88	45.49
5	56.24	72.18	55.98	49.05	49.21
6	63.48	74.31	61.49	52.78	52.95
7	67.29	78.18	75.69	61.74	56.70
8	71.13	82.07	83.04	81.14	86.48
9	74.98	87.71	121.63	91.99	121.62
10	82.31	108.98	134.43	95.95	127.48

All values expressed as mean ± SD (n=3), F = Formulation batch

Table no.8: In-vitro dissolution study/profile of levosalbutamol sulphate [F6-F10].

Time(min)	% Drug release				
	F_6	F_7	F_8	F_9	F_{10}
1	30.97	24.03	20.56	17.10	20.56
2	34.60	29.37	27.61	25.86	25.88
3	38.26	31.26	36.43	31.20	27.76
4	48.87	36.63	43.57	36.58	31.38
5	73.41	42.04	45.54	43.71	36.75
6	79.02	45.73	52.72	54.35	43.88
7	93.32	56.38	61.68	80.65	52.79
8	97.29	63.62	74.15	100.16	79.08
9	108.22	76.10	78.02	116.31	133.25
10	110.54	128.52	94.05	160.29	166.92

All values expressed as mean ± SD (n=3), F = Formulation batch

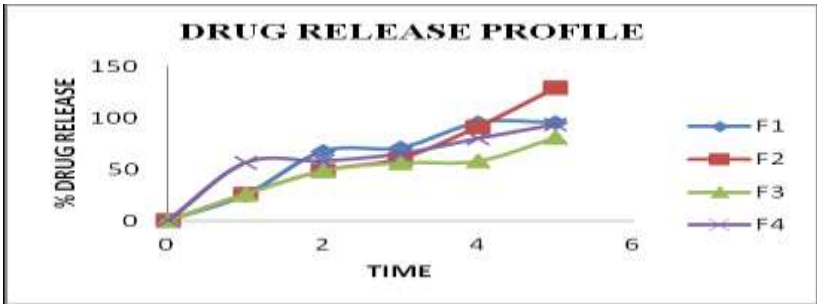


Fig. No.10: In-Vitro dissolution study/profile levosalbutamol sulphate of batches F1-F4.

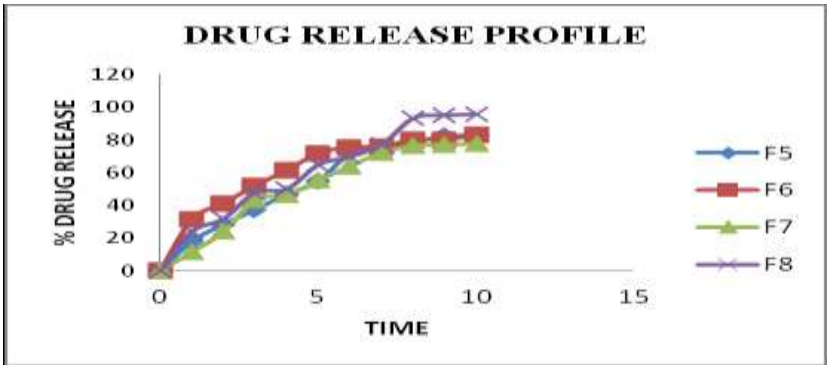


Fig. No.11: In-Vitro dissolution study levosalbutamol sulphate of batches F6-F8.

TABLE NO.9: Curve fitting analysis for different formulations.

FORMULATION	ZERO ORDER (R)	FIRST ORDER (R)	MATRIX (R)	HIXCROW (R)	PEPPAS (R)	BEST MODEL FIT
F1	0.7251	0.9522	0.9784	0.9095	0.9790	PEPPAS
F2	0.5789	0.9236	0.9346	0.7553	0.9364	PEPPAS
F3	0.9667	0.9113	0.8878	0.7718	0.9348	ZERO ORDER
F4	0.9652	0.8784	0.9442	0.9362	0.9389	ZERO ORDER
F5	0.9104	0.9211	0.8605	0.7502	0.8111	FIRST ORDER
F6	0.9683	0.9415	0.9628	0.8797	0.9552	ZERO ORDER
F7	0.9093	0.9122	0.8364	0.6448	0.8902	FIRST ORDER
F8	0.9747	0.8843	0.9596	0.9470	0.9828	PEPPAS
F9	0.9495	0.9224	0.8306	0.8167	0.9483	ZERO ORDER
F10	0.8805	0.9147	0.7506	0.7161	0.8617	FIRST ORDER

All values are expressed as mean ±SD, n=3, F=Formulation codes

IN-VITRO DISSOLUTION PROFILE OF MARKETED TABLETS

- **LEVOLIN**

Table No.17: Dissolution test protocol

Name of drug	LEVOLIN
Dissolution apparatus	USP TYPE II
00Temperature	37 ± 0.5 ^{0}C
Basket speed	50 rpm
Tablet strength	5 mg
Dissolution medium	PBS P^{h} 6.8
Volume of dissolution medium	900 ml
Detection	276 nm
Volume of sample removed	5 ml
Sampling profile	1 – 5 min

Dissolution profile of Marketed tablet & Formulation Batch-F9

Table No.10: Dissolution profile of marketed product levolin

Time (min)	% Drug release	
	LEVOLIN	F9
1	4	17.10
2	14	25.86
3	24	31.20
4	28	36.58
5	36	43.71
6	40	54.35
7	46	80.65
8	53	100.16
9	59	116.31
10	64	160.29

All values expressed as mean ± SD (n=3), F = Formulation batch

Table No.11: % Drug release of marketed productLEVOLINVs. Formulation F10.

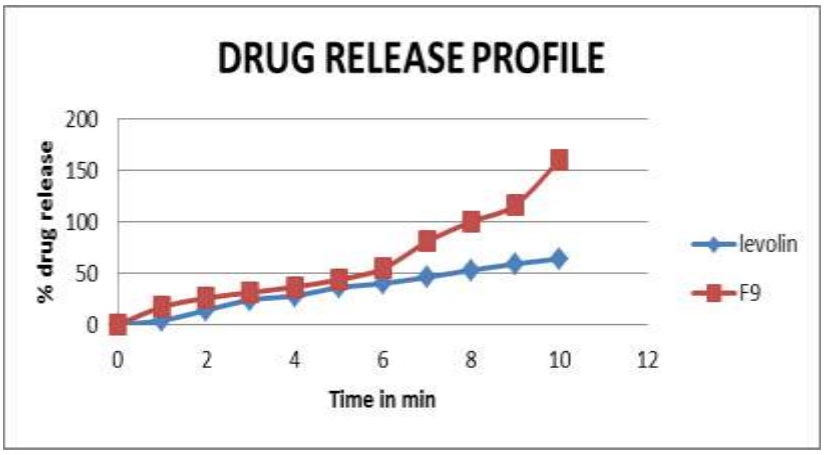


Fig.No.12: Dissolution profile comparison study of Marketed product with Formulation batch F9 (Comparative study).

Table no.12: Evaluation taste carried out on F1 to F10 formulations respectively.

Formulations	Tack Test	Appearance	Weight (mg)	Thickness (mm)	Folding endurance	D.T (sec)	Surface PH	Con.uniformity
F1	Non tacky	Transparent	20	1	110	25	6-7	2
F2	Non tacky	Transparent	24	0.6	128	20	6-7	2.01
F3	Non tacky	Transparent	26	0.8	136	28	6-7	2
F4	Non tacky	Transparent	28	1.5	142	19	6-7	2.02
F5	Non tacky	Transparent	19	0.6	91	22	6-7	2
F6	Non tacky	Transparent	21	1.2	115	26	6-7	2
F7	Non tacky	Transparent	26	1	117	30	6-7	2.04
F8	Non tacky	Transparent	28	0.6	125	19	6-7	2
F9	Non tacky	Transparent	37	1	85	21	6-7	2
F10	Non tacky	Transparent	42	0.8	27	20	6-7	2.05

Table No.13: Stability parameter (Evaluation) of Fast dissolving films

Formulations	Tack Test	Appearance	Weight (mg)	Thickness (mm)	Folding endurance	D.T (sec)	Surface P^H	Con.uniformity (mg)
F3	Non tacky	Transparent	19	0.6	105	15	6-7	2.51
F5	Non tacky	Transparent	24	0.6	114	14	6-7	2.5
F7	Non tacky	Transparent	19	1.2	105	20	6-7	2.49
F9	Non tacky	Transparent	27	1	148	18	6-7	2.52
F10	Non tacky	Transparent	28	0.8	131	20	6-7	2.5

All values expressed as mean ± SD (n=3), F = Formulation batch

Table no.14: In-vitro %release data of stability (Formulation No. F3, F9 & F10).

Time/Formulation (min)	F3	F9	F10
1	25.76	17.10	20.56
2	32.84	25.86	25.88
3	36.49	31.20	27.76
4	40.16	36.58	31.38
5	55.98	43.71	36.75
6	61.49	54.35	43.88
7	75.69	80.65	52.79
8	83.04	100.16	79.08
9	121.63	116.31	133.25
10	134.43	160.29	166.92

All values expressed as mean ± SD (n=3), F = Formulation batch

Fig.No.13: 2X2 cm formulation No. F1, F2, F3, F4, F5

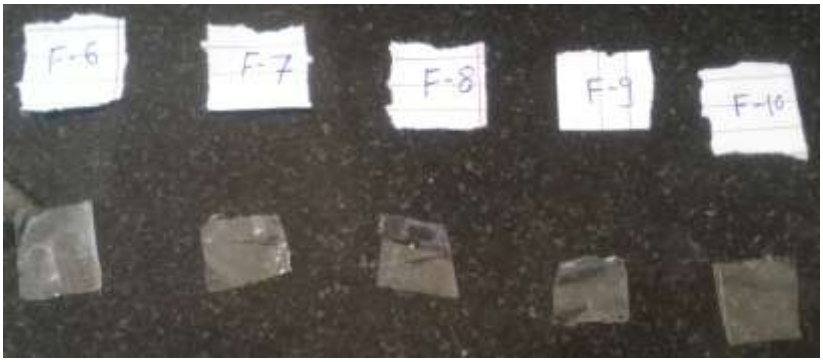


Fig.No.14: 2X2 cm Formulation No. F6, F7, F8, F9, F10.

STABILITY STUDY

The stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation & the drug release. Short term stability studies were performed in a Stability chamber over a period of 3 weeks (21 days) on the promising Fast Dissolving Film formulations F1,F2,F3,F4,F5,F6,F7,F8,F9 & F10 . Sufficient number of films formulation were packed in stability container and kept in a Stability chamber at Temperature 45ºc & RH 75%. Samples were taken on 21st day for drug content estimation; also the thickness, weight, folding endurance and In-Vitro disintegration studies were performed to determine the drug release profile

DISCUSSION

In the present research work Design and characterization of polymeric Fast dissolving film for oral film of levosalbutamol sulphate were prepared to improve efficacy of levosalbutamol sulphate by improving its bioavailability also by reducing its dose unlike in concentration. Levosalbutamol sulphate Fast dissolving film were prepared using , HPMC K-15,HPMC E-15 and HPMC K-100 in different concentrations by solvent casting technique, the prepared fast dissolving film were evaluated for various parameters and the results of these parameters were given in Table No. 12 and they are discussed in detail in the following section of this chapter.

Physical appearance and surface texture of fast dissolving film

These parameters were checked simply with visual infection of Fast dissolving film and by feel or touch. The observation suggests that the Fast dissolving film are having smooth surface and they are elegant enough to see.

Weight uniformity of fast dissolving film

The weight of Fast dissolving film was determined using digital balance and the average weight of all Fast dissolving film were given in table No-12 Fast dissolving film prepared with HPMC K15 in the concentration 300-450 mg and also in combination of PEG & Glycerol of 50 mg were weighed about 19-28 mg (n=3) respectively. The Fast dissolving film prepared using HPMC K-100 in concentration 200-400 mg in combination of PEG-400, PEG-6000, SLS, and also with Tween 80 having concentration of 150-200, 45, 200, 35 mg & q.s were weighed about 25-70 mg respectively.

Thickness of fast dissolving film

The thickness of the fast dissolving film were measured using screw gauge and the average thickness of all Fast dissolving film was given in table No-12 The thickness of the Fast dissolving film prepared with HPMC K-15 in the concentration 300-450 mg and also in combination of PEG & Glycerol of 50 mg the thickness of the Fast dissolving film prepared respectively are 70-100 mm respectively. The thickness of the Fast dissolving film prepared with HPMC K-100 in the concentration200-400 mg in combination of PEG-400 , PEG-6000, SLS and also with Tween 80 having concentration of 150-200, 45, 200, 35 mg & q.s was 50-170 mm (n=3) respectively.

Folding Endurance of Fast dissolving film

The folding endurance of the Fast dissolving film was determined by repeatedly folding a small strip of the Fast dissolving film at the same place till it broke and the average folding endurance of all Fast dissolving film was given in table No-12 The folding endurance of the fast dissolving film prepared with HPMC K-15 in the concentration 300-450 mg and also in combination of PEG & Glycerol of 50 mg was 91-142 (n=3) respectively. The folding endurance of the fast dissolving film prepared using HPMC K-100 in concentration 200-400 mg in combination of PEG-400 , PEG-6000, SLS, and also with Tween 80 having concentration of 150-200, 45, 200, 35 mg & q.s was 4-120 (n=3) respectively.

Surface pH of fast dissolving film

Surface pH was determined by the fast dissolving film were allowed in contact with 1ml of distilled water. The surface pH was noted by pH meter near the surface of fast dissolving film and allowing to equilibrate for 1 min and the surface pH of all fast dissolving film was given in table No-12 The surface pH of the fast dissolving film prepared with HPMC K-15,HPMC E-15 and HPMC K-100 was found to in-between 6-7 PH (n=3).

Drug-Polymers interaction studies of fast dissolving film

Spectrum No1.Pure drug

The infrared spectrum of levosalbutamol sulphate recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No2.HPMC K-15

The infrared spectrum of HPMC K-15 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No4.Levosalbutamol + HPMC K-15

The infrared spectrum of pure drug &hydroxy propyl methyl cellulose K-15 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No5.Levosalbutamol + HPMC E-15

The infrared spectrum of pure drug &hydroxy propyl methyl cellulose E-15 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No6.Levosalbutamol + HPMC K-100

The infrared spectrum of pure drug &hydroxy propyl methyl cellulose K-100 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No7.levosalbutamol + SLS

The infrared spectrum of levosalbutamol sulphate& sodium lauryl sulphate recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No8.levosalbutamol + TWEEN-80

The infrared spectrum of levosalbutamol sulphate& tween -80 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Drug Content uniformity of fast dissolving film

Levosalbutamol sulphate fast dissolving films prepared with HPMC K-15,HPMC E-15 and HPMC K-100 in various concentrations and were subjected to the uniform dispersion of drug throughout the patch. In each case three Fast dissolving film were used and the average drug content was calculated, the results were shown in table no. the drug was dispersed in the range of 2-2.09 (n=3). Suggesting that drug was uniformly dispersed in all fast dissolving

film. The S.D. value calculated for such formulation is very less which suggest that the results are reproducible and accuracy in the method used to prepare the fast dissolving film.

***In-vitro* Drug Release of fast dissolving film**

All the Fast dissolving film of levosalbutamol sulphate prepared were subjected to *In-vitro* drug release studies for a period of 1-10 min.

The formulation F1, F2, F3, F4, F5, F6, F7, F8, F9 & F10.which are prepared using with HPMC K-15,HPMC E-15, in the concentration 200-400 mg and also in combination of PEG & Glycerol of 50 MG released 82.31%, 108.98%, 134.43%, 95.95%, 127.48%, 110.54%, 128.52%, 94.05%,160.29%,& 166.92% at the end of 10 min respectively. The detail *In-vitro* released data were shown in table No-7 and drug release profile fig. no.7, 8.

Stability study

The stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation & the drug release. Short term stability studies were performed in a Stability chamber over a periodof 3 weeks (21 days) on the promising Fast Dissolving Film formulations F3, F9 & F10. Sufficient number of films formulation were packed in stability container and kept in a Stability chamber at Temperature 45^{o}c & RH 75%. Samples were taken on 21st day for drug content estimation; also the thickness, weight, folding endurance and In-Vitro disintegration studies were performed to determine the drug release profile. The detail *In-Vitro*% drug release stability data were shown in table No-19and Stability parameter (Evaluation) of Fast dissolving films shown in table No-14.

CONCLUSION

From the present research work that is development and evaluation of levosalbutamol sulphate fast dissolving film for buccal drug delivery, the following points can be concluded:

1. In the beginning, blank polymeric fast dissolving film were prepared using HPMC K-15, HPMC K-100, HPMC E- 15, SLS, Chitosan, Eudragit L100, Sodium alginate, Lacroate, SSG, MSS, SLS, CSS and Cross povidone. The concentration of polymer was varied and the best were chosen for further work.
2. The prepared fast dissolving film were evaluated for number of parameters like physical appearance and surface texture, weight uniformity, thickness of fast dissolving film, folding endurance, surface pH, *In-vitro* residence time, drug excipients interaction studies, drug uniformity and *In-vitro* drug release.

3. The fast dissolving film prepared was checked visually for its appearance & surface texture. All the prepared fast dissolving film was of smooth surface & elegant texture.
4. All the prepared fast dissolving film using different concentration of various polymers are weighing in between 19.333 ±0.996 to 70.66 ±1.993 mg.
5. The fast dissolving film showed folding endurance values in between 5.666 ±4.3204to 142±3.2449.
6. Similarly surface pH of all the fast dissolving film prepared is ranging in between6-7pH.
7. The IR studies indicate that levosalbutamol sulphate showed complete entrapment within the polymer carrier bonding is suggested and there were no chemical interaction. Spectrophotometer. From the Infrared frequencies & the respective assignments given FTIR spectrum such as levosalbutamol sulphate + Polymer are compatible.
8. Similarly, the fast dissolving film are also subjected to drug content uniformity study and it lies in between 2-2.09 mg (n=3) which suggest that uniform dispersion throughout the fast dissolving film.
9. A good % drug release was observed for formulation F3, F9& F10.in time 1-10 min.
10. The *In-vitro* drug release study was carried out for all the fast dissolving film and release profile were subjected to various kinetic equations like Highuchi diffusion equation, First order equation, Zero order equation and Peppas exponential equation. The regression coefficient values of this kinetic equation are very nearer to one(1) suggesting that plots are fairly linear and slope values is (>1) more than one in all the cases suggest that drug was released by diffusion mechanism following super case-II transport. From the above results it can be concluded that levosalbutamol sulphate can be delivered in the form of fast dissolving film. Release pattern of drug from these fast dissolving films can be altered by using different formulation variables.
11. Finally the stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation & the drug release.

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