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Formulation and Evaluation of Fast Dissolving Buccal Films Containing Bambuterol HCL

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ABSTRACT: The main objective of this research work is to formulate fast dissolving films to improve the patient compliance and bioavailability of Bambuterol HCl. Bambuterol HCl undergo first-pass metabolism, the development of fast dissolving buccal films of Bambuterol HCl release the drug in the buccal cavity and absorb through the buccal region. Hence first-pass metabolism of the drug could be avoided by developing into a fast-dissolving film of Bambuterol HCl. Fast dissolving Buccal films were prepared by solvent casting method using various polymers like HPMC E15, PVP K30, PVA and PEG600 as plasticizer and saccharin as a sweetening agent and vanillin as a flavoring agent and % Drug release is calculated using the calibration curve method. Dissolution profile as studied in a USP dissolution apparatus type 1 using a pH 6.8 simulated saliva. It was investigated how factors including release profile, concentration, and polymer type affected the results. The formulation was optimized on the basis of various evaluation parameters like the Folding endurance test, Weight uniformity test, Drug content, Stability test and *In-vitro* drug release. Formulation **F3** successfully fast the release of drug within 6 minutes. The IR spectra showed stable properties of Bambuterol HCl in mixture of polymers used and revealed the absence of interaction between drug and selected polymer, stability studies were as per ICH guidelines and result indicated that the selected formulation was stable.

KEY WORDS: Bambuterol Hcl, HPMC E15, PVP K-30, PVA.

INTRODUCTION

ASTHMA:

Asthma is a long-term inflammatory disease of the conducting airways that results in mucus overproduction, airway wall remodeling, airway narrowing, and bronchial hyper-reactivity (BHR), which is the tendency of smooth muscle cells in asthmatic individuals to react to nonspecific stimuli like cold air and exercise. These effects are caused by a combination of epithelial cells and many cells of the innate and adaptive immune systems.

This causes recurrent episodes of dyspnea, wheezing, and tightness in the chest in sensitive patients.The disease is very common in affluent societies, in which almost 1 in 10 children and 1 in 12 adults is affected, which results in substantial morbidity and annual healthcare expenditure. Worldwide, up to 300 million people are affected[1,2].

In 28 countries, the β2 adrenergic agonist terbutaline's biscarbamate ester prodrug, bambuterol has been authorized for the management of asthma.. It is available in 10 and 20mg (25 and 50 μmol) tablets as the hydrochloride salt. Bambuterol is stable to presystemic elimination and is The prodrug is hydrolyzed to terbutaline primarily by butyrylcholinesterase, and lung tissue is capable of this metabolic pathway. It is also oxidatively metabolized to products which can be hydrolyzed to terbutaline[3].

Oral administration of bambuterol to patients with asthma prolongs the broncho dilating effect produced by terbutaline, thus making once-daily dosing sufficient. Once daily bambuterol and twice daily sustained-release terbutaline appear to have similar clinical efficacies.

In a randomized, double-blind, cross-over trial, 28 individuals with nocturnal asthma received either bembuterol or a placebo. All patients were symptomatic despite taking inhaled β_2-agonists, inhaled corticosteroids (in 26 patients the median daily dose was 1500 μg) and oral corticosteroids (in eight patients the median daily dose was 10 mg).

Patients demonstrated ≥20% overnight fall in peak expiratory flow (PEF) for at least half of the 14-day run-in period. After that, they were divided into two 14-day treatment periods at which time placebo and bambuterol 20 mg nocte were administered in a random order. Compared to placebo, bambuterol produced a 16% improvement in mean PEF on waking and a 10% improvement

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in evening PEF measured 24 h after drug intake. Bambuterol significantly reduced frequency of nocturnal awakening from 1.1 to 0.7 per night and nocturnal β_2-agonist use from 2.7 to 2.1 puffs[4].

Other nocturnal symptoms: cough, wheeze was also significantly reduced during bambuterol treatment and patients'quality of sleep was improved[5]. Effects of the inhaled corticosteroid budesonide and the oral β-agonist bambuterol on the nocturnal worsening of asthma were studied in patients with allergic asthma. Both medications had a positive impact on nocturnal symptoms, yet budesonide's effects outweighed bambuterol. Our results show a correlation between the degree of airway responsiveness and the occurrence of nocturnal asthma symptoms, and they also show that budesonide and bambuterol diminish nocturnal airway responsiveness and asthma symptoms[6].

Comparison to oral mucosal drug delivery and gastro intestinal drug delivery

In gastrointestinal drug delivery the drug to be administered in the form of tablet, capsule, drug to be enter in to the systemic circulation it can require more time it not give a fast onset of action and to undergo fast pass metabolism large amount of drug to be loosed. Drug to be administered in intravenous it is not self-administered route[7].

For this reason the fast onset of action and drug to be directly enter into the systemic circulation drug can be delivery by a film form it can be administered by an oral mucosal route this region more blood supply the drug directly enter into the systemic circulation give a more patient compliance for symptoms of hypertension like vertigo and tiredness especially in elder people and prazosin hydrochloride drug can be administered in the treatment of prostatic hypertrophy and urinary retention it can require fast onset of action the drug administered in the oral mucosal route drug direct enter in to the blood circulation and reach the site of action at the faster rate and give faster relief of action to the painful and frequent urination in men urinary retention[8].

Drug absorption across the oral mucosa, two major routes of absorption is involved in oral mucosal drug permeation the Trans cellular or intracellular route (where drugs permeate directly through the cells) and the Para cellular or intercellular route (where drugs permeate by passive diffusion through the spaces between thecells)[9].

Advantages of the oral cavity as a site for drug delivery[10]

Accessibility the different sites in the oral cavity are easily accessible. This property increases patient convenience. Additionally, the delivery system can be precisely positioned at any spot within the oral cavity to target a particular membrane, differentiating the various routes of administration within the oral cavity. Because oral mucosal drug delivery devices are easily accessible, they are also simple to use.

1. **Buccal delivery:** is drug administration through the mucosal membranes lining the cheeks and the area between the gums and upper and lower lips to the systemic circulation.
2. **Sublingual delivery:** is systemic delivery of drugs through the mucosal membranes lining the floor of the mouth to the systemiccirculation. The oral mucosa's structure is a desirable location for medication delivery due to a number of its characteristics. Its surface area is around 200 cm^2.

It consists of 2 layers:

A thick, stratified squamous vascular epithelium, and an underlying, vascular layer of mesodermal origin. Its epithelium is approximately 40 to 50 cell layers thick oral squamous stratified epithelium can be divided into two, namely non-keratinized, keratinized epithelium.

MATERIALS & METHODS

Table No. 1: The list of Materials used

Sl. no.	Materials	Property	Source
1	Bambuterol HCl	Pure drug	Yarrow chem. Product, Mumbai
2	HPMC E15	Polymer	Yarrow chem. Product, Mumbai

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3	PVP K-30	Polymer	SD fine chem. Laboratories Pvt Ltd
4	PVA	Polymer	SD fine chem. Laboratories Pvt Ltd
5	Sodium hydroxide	Used in the preparation of saliva	SD fine chem. Laboratories Pvt Ltd
6	Di sodium hydrogen phosphate	Used in the preparation of saliva	SD fine chem. Laboratories Pvt Ltd
7	Potassium di hydrogen phosphate	Used in the preparation of saliva	SD fine chem. Laboratories Pvt Ltd
8	PEG 600	Lubricant	Yarrow chem. Product, Mumbai
9	Sodium saccharin	Sweetening agent	SD fine chem. Laboratories Pvt Ltd
10	Vanillin	Flavoring agent	SD fine chem. Laboratories Pvt Ltd.

Table No. 2: List of Instruments used

Sl. No	Name of instrument	Manufacturingcompany
1	Uv spectrophotometer	Shimadzu uv-1800
2	Hot air oven	Matri enterprises
3	FTIR spectroscopy	Agilent technologies cary 630 FTIR
4	Dissolution apparatus	Electrolab td t08l tablet dissolution apparatus
5	Digital balance	Sartorius & essaevibra
6	Magnetic stirrer	Remi equipment
7	Digital caliper	Remi equipment
8	Ph meter	Lt lutron
9	Micro pipettes	Accupipet & superfit xl^{+}
10	Glass moulds	Tarson product pvt ltd

EXPERIMENTAL METHODS

Melting Point:

Melting point of the drug was determined by open capillary method. This was compared with the literature melting point value of drug. The melting point of the pure drug was found to be 222^0 to 224^0C.

Preparation of simulated saliva solution (pH 6.8):

Dissolve 11.45gm of potassium di hydrogen orthophosphate and 28.20 gm of sodium dihydrogen orthophosphate in water and adjust the pH 6.8 with sodium hydroxide solution and dilute with water to produce 1000 ml.

Determination of λ max of Bambuterol Hcl using simulated saliva buffer pH 6.8

Accurately weighed quantity of 50mg of Bambuterol Hcl was taken in 50ml volumetric flask & made up to 50ml by using phosphate buffer of pH 6.8

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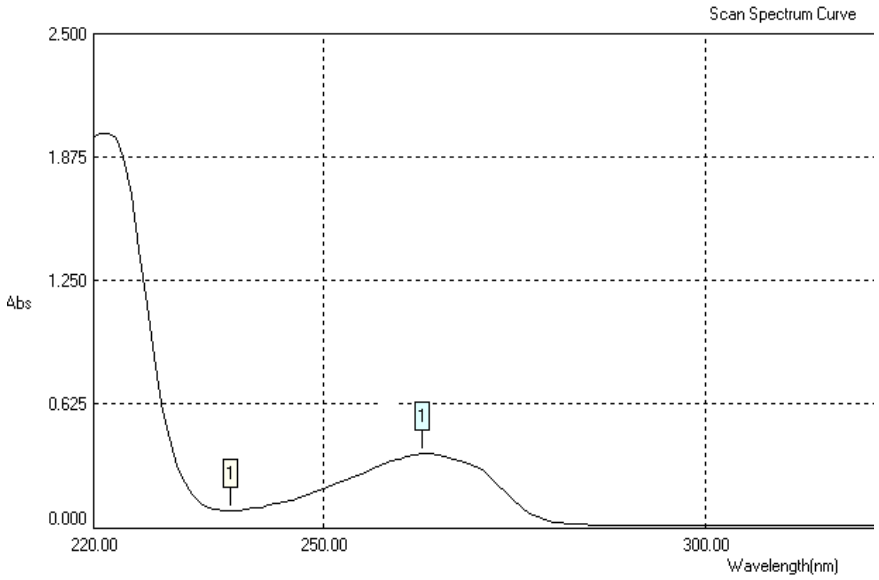
Scanning: From the above stock solution, 100µg/ml solution was prepared and scanned between 200-400nm by keeping buffer as blank. The lambda max of Bambuterol HCl was found to be 263nm.



λmax=263nm

Figure 1: Determination of λ max of Bambuterol Hcl using simulated saliva buffer pH 6.8

Preparation of calibration curve in using simulated saliva buffer pH 6.8

Accurately weighed quantity of 50 mg of Bambuterol Hcl was taken in 50 ml volumetric flask, make up to the volume with simulated saliva buffer pH 6.8 (stock I). Preparing aliquots from stock I , 0.5, 1,1.5,2,2.5,3,3.5 & 4 ml.

Preparation of simulated saliva solution (pH 6.8):

Dissolve 11.45gm of potassium dihydrogen orthophosphate and 28.20 gm of sodium di hydrogen orthophosphate in water and adjust the pH 6.8 with sodium hydroxide solution and dilute with water to produce 1000 ml.

FORMULATION DESIGN

1. Formulation of blank polymeric fast dissolving oral strips:

The blank fast dissolving oral strips were prepared by using Hydroxy propyl methyl cellulose E 15, PVP K-30 and Polyvinyl alcohol by solvent casting technique, the detailed composition is given in table no 3.

Method:

Accurately weighed quantity of polymer was dissolved in water and polyethyleneglycol600 (plasticizer), was added gradually with continuous stirring. Then 10mL resultant mixture was poured into each smeared glass molds 6× 8 cm. Drying was carried out at 40ºC for 24 hours in hot air oven. Similarly, the same procedure was carried out for remaining polymers. (HPMCE15, PVP K-30 , PVA, PEG-600, sodium saccharine, citric acid and vanillin).

Table no 3: Formulation details of blank

Formulation	Polymer & its composition				PEG 600 (ml)	Water (ml)	Remarks
	HPMC E15	PVP K30	PVA	HPC			
1	200	---	---	---	0.1	**10**	+++
2	250	---	---	---	0.1	10	++++

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3	300	---	---	---	0.1	10	++++
4	350	---	---	---	0.1	10	++++
5	---	200	---	---	0.1	10	++
6	---	250	---	---	0.1	10	++++
7	---	300	---	---	0.1	10	++++
8	---	350	---	---	0.1	10	++++
9	---	---	200	---	0.1	10	+++
10	---	---	250	---	0.1	10	++++
11	---	---	300	---	0.1	10	++++
12	---	---	350	---	0.1	10	++++
13	---	---	---	200	0.1	10	++
14	---	---	---	250	0.1	10	++
15	---	---	---	300	0.1	10	+++
16	---	---	---	350	0.1	10	+++

++ Poor, +++ Average & ++++ Excellent

Above rating is given on the basis of appearance, smoothness, weight uniformity & thickness.

Based on the above observations, HPMC E15, PVP K-30, PVA shows good properties and the concentration range from 250-350mg.

Formulation of fast dissolving oral strips:

From the preliminary physical observation of the strips prepared the best compositions were used for the incorporation of Bambuterol Hcl by solvent casting technique. Bambuterol Hcl was dissolved, then polymers are added (PVA, PVP K-30 , HPMC E15), PEG-600 (plasticizer) was added and stirred to form a homogeneous solution. Finally Citric acid, vanillin and Sodium saccharin were added and stirred to form a homogeneous mixture. The mixture was poured into a 6 x 8 centimeter (length x width) mold. then stored for 24 hours at 40ºC in a hot air oven. The resulting film was then divided into strips of 2 by 2 centimeters. The prepared square thin orals strips were packed using single pouches, blister card with multiple units, multiple-unit dispenser, and continues roll dispenser aluminum pouch and stored in desiccator[11].

Table No. 4: Composition of different formulation of Bambuterol Hcl fast dissolving buccal films:

Formulation	ts composition (mg)				Plasticizer (mL) PEG600	Citric acid (mg)	Sodium saccharin (mg)	Vanillin (mg)	D.water (mL)
	BAM (Drug)	HPMC E15	PVP K30	PVA					
F1	120	250	---	---	0.1	2	2	2	10
F2	120	300	---	---	0.1	2	2	2	10
F3	120	350	---	---	0.1	2	2	2	10

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F4	120	---	250	---	0.1	2	2	2	10
F5	120	---	300	---	0.1	2	2	2	10
F6	120	---	350	---	0.1	2	2	2	10
F7	120	---	---	250	0.1	2	2	2	10
F8	120	---	---	300	0.1	2	2	2	10
F9	120	---	---	350	0.1	2	2	2	10

Evaluation of Bambuterol Hcl fast dissolving buccal films:

The Bambuterol Hcl fast dissolving buccal films were evaluated for the following properties:

1. **Physical properties**
   a. Physical appearance and surface texture
   b. Weight Uniformity
   c. Thickness uniformity
   d. Folding Endurance
2. **Evaluation of Bambuterol Hcl fast dissolving buccal films for**
   a. Drug-polymer interaction studies
   b. Drug content uniformity
   c. *In-vitro* drug release
   d. Permeation study

1. Physical properties:

a. Physical appearance and surface texture of strips[12]:

This parameter was checked simply with visual inspection of strips and evaluation of texture by feel or touch.

b. Weight uniformity ofstrips:

Three strips of the size 2×2 cm were weighed individually using digital balance and the average weights were calculated.

c. Thickness of strips:

Thickness of the strips was measured using screw gauge with a least count of 0.01mm at different spots of the strips.The thickness was measured at three different spots of the strips and average was taken.

d. Folding endurance of strips[13]:

Strips' flexibility can be statistically assessed using a concept called "folding endurance." Folding endurance of the strips was determined by repeatedly folding a small strip of the strips (approximately 2x2 cm) at the same place till it broke. The value of folding endurance is determined by how many times strips might be folded in the same direction without breaking.

2. Evaluation of Bambuterol Hcl fast dissolving buccal films:

a. Drug-polymer interaction study of buccal films[13]:

Because of their close proximity, drug-polymer interactions could occur in any formulation. IR spectroscopy is the method used in this work to understand drug-polymer interactions. One of the most potent analytical methods that allows for chemical identification is infrared spectroscopy. Infra-red spectra of pure drug Bambuterol Hcl and formulations were scanned by using FTIR method.

b. Drug content uniformity of strips[14]:

The UV Spectrophotometric technique was used to examine the strips for uniform drug content. Strips of 2×2 cm size were cut from three different places from the casted strips. Each film was placed in 100 mL volumetric flask and dissolved in simulated saliva pH

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6.8 and 2 mL is taken and diluted with water up to 10 ml. The absorbance of the solution was measured at λ max 263 nm using UV/ visible spectrophotometer (Shimadzu, japan). The percentage drug content was determined.

c. *In-vitro* drug release[15]:

The release rate of Bambuterol Hcl fast dissolving oral strips was determined by using the USP paddle method. The RPM of the paddle was maintained at 50 RPM. The film with 2×2 cm was placed in the 300 mL of 6.8 pH simulated saliva as dissolution medium, and temperature was maintained at 37°C±0.5ºC. 5 mL of the sample solution were taken out of this dissolving medium at various times. The samples were filtered through Whatman filter paper and absorbance was determined 263nm using UV-Visible spectrophotometer.

d. *In-vitro* Disintegration study[14]:

Disintegration of strips was carried out by petri Dish method. In this method on strip at a time was placed in petri Dish containing a 5ml of distilled water and the time required to dissolve the strip completely was measured. Estimation was carried out in triplicate.

Permeation study[16]: The prepared fast dissolving Buccal strips are placed in the Franz diffusion cell on the upper membrane of the (donor compartment) and the receptor compartment contain a simulated saliva (22 ml) it can be contact with the permeation membrane washed and soaked with phosphate buffer 6.8 upper side of the donor compartment contain a film attach the film of length and width (2×2) cm it contains 1 mg of drug. And additionally, the receptor compartment has a magnetic bead and simulated saliva. When this diffusion compartment is positioned in a magnetic stirrer, the medication begins to permeate through the dialysis membrane and enter in to the receptor compartment the drug to be enter in the receptor compartment and this solution taken 2 ml every 5minutes up to 45 minutes and preserve the sink condition by adding another 2 milliliters of fake saliva to the receptor compartment. Samples are then taken at regular intervals and examined using a Shimadzu UV-visible spectrophotometer.

Stability studies[17]:

Stability testing is performed to give proof of how a drug's or product's quality changes over time under the impact of various environmental conditions. According to ICH recommendations, stability studies were conducted to evaluate the medication and formulation stability. The formulated fast dissolving oral strips were wrapped in aluminum foil and stored at 40 ± 0.5ºC for period of four weeks. After four weeks strips were tested for appearance, drug content and *in-vitro* drug release.

RESULTS

Pre-formulation Studies

Drugs-polymer interaction study by FT-IR spectrophotometer

An FT-IR spectroscopy study has been carried out separately to check the compatibility between the drug (Bambuterol Hcl) and the polymers (HPMC E15, PVP K-30 , PVA) used for the preparation of Drug and polymers. The FT-IR was performed for drug, polymers, and physical mixture of drug and polymers. The spectra obtained from FT-IR spectroscopy study at wave number from 4000 to 500 cm^{-1} are shown below.

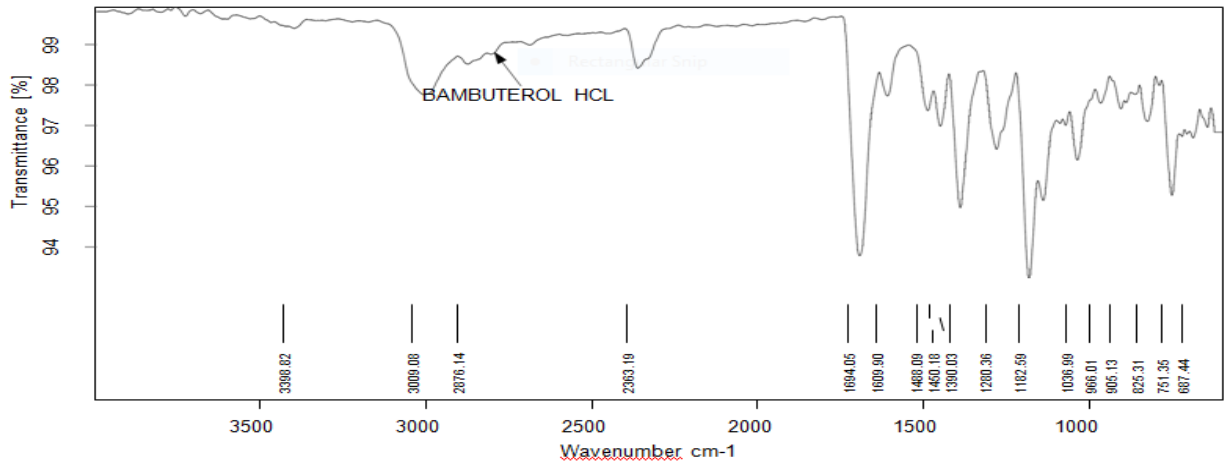

Figure 2: The FTIR spectrum of pure Bambuterol Hcl

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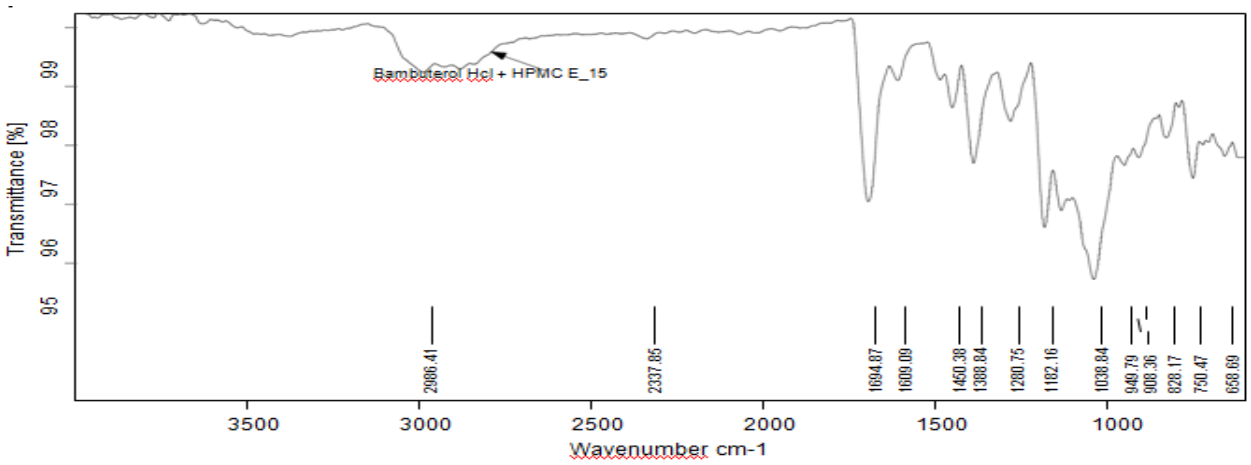

Figure 3: The FTIR spectrum of Bambuterol Hcl+HPMC E15

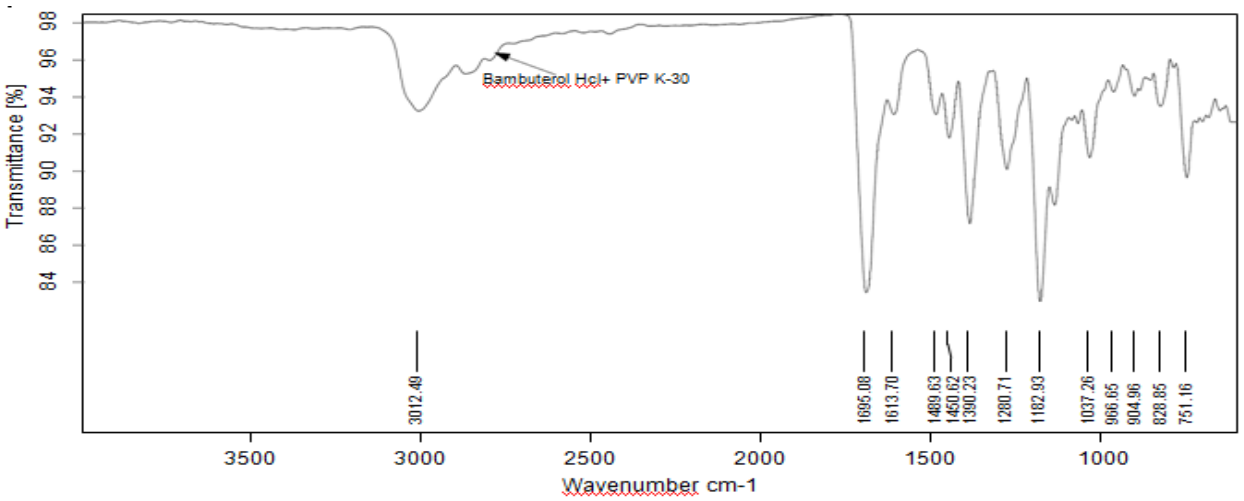

Figure 4: The FTIR spectrum of Bambuterol Hcl+PVP K-30

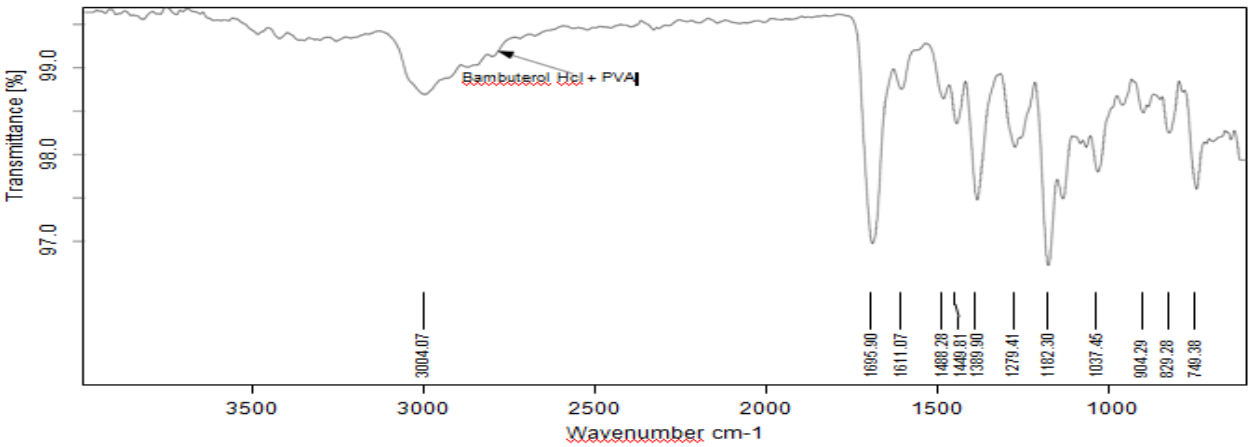

Figure 5: The FTIR spectrum of Bambuterol Hcl+PVA

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FTIR Interpretation

Table No 5: Interpretation of FTIR spectrum of above figures

Perusal to the above FTIR spectra, the characteristic peaks of Bambuterol Hcl of pure spectrum was retained in the FTIR spectra of physical mixture of drug with HPMC E15, PVA, PVP K30. Therefore, there was no drug polymer interaction is found. Hence, these polymers were used for the preparation of Buccal films.

Sl no	Name of the compound	Range (cm^{-1})	Group	Observed range in the sample
1	Bambuterol Hcl	3300-3500	N-H	3398.82
		3000-3100	Aromatic rings	3009.08
		1690-1760	C=O	1694.05
		1080-1300	C-O	1280.36
2	Bam: HPMC E15	2850-2960	C-H	2986.41
		1690-1760	C=O	1694.87
		675-870	Aromatic rings	828.17
		1080-1300	C-O	280.75
3	Bam : PVP K-30	3000-3100	Aromatic rings	3012.49
		1690-1760	C=O	1695.08
		1350-1470	C-H	1450.62
		1080-1300	C-O	1280.71
4	Bam : PVA	3000-3100	Aromatic rings	3004.07
		1690-1760	C=O	1695.90
		1350-1470	C-H	1389.90
		1080-1300	C-O	1279.41

Preparation of standard graph of using Bambuterol Hcl in simulated salivary buffer 6.8

Table no 6: The concentrations of Bambuterol Hcl in simulated salivary buffer 6.8.

SL NO	CONCENTRATION (µg/ml)	Absorbance @ 263nm
1	50	0.06
2	100	0.11
3	150	0.16
4	200	0.22
5	250	0.27
6	300	0.32
7	350	0.37
8	400	0.42

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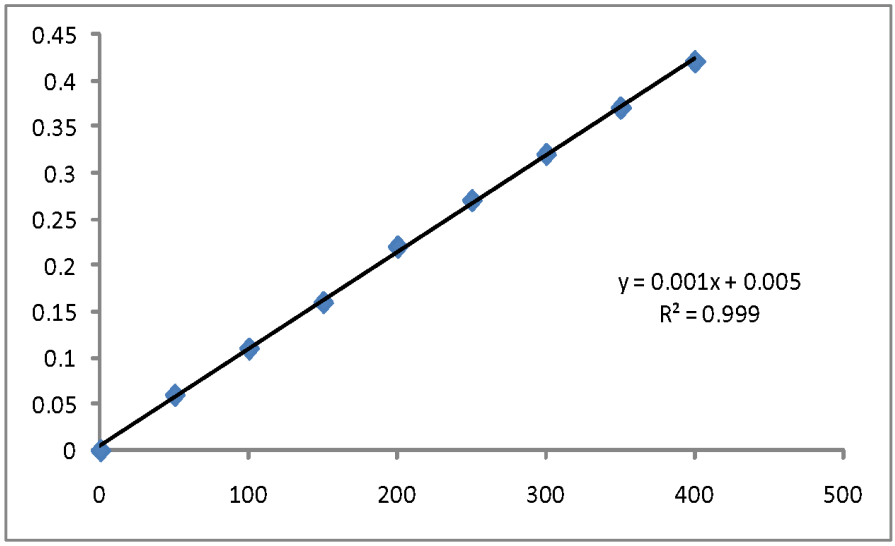

Figure 6: The Standard graph of Bambuterol Hcl using simulated salivary buffer of pH 6.8

Table no.7: Weight uniformity of various Bambuterol Hcl fast dissolving buccal films.

Formulation code	Weight of films(mg)			Average weight (mg)±SD
	I	II	III	
F1	30.67	31.66	30.82	31.05±0.53
F2	35.83	34.87	36.54	35.75±0.84
F3	38.79	37.45	38.93	38.39±0.82
F4	31.78	30.45	32.45	31.56±1.02
F5	34.98	36.73	35.43	35.71±0.91
F6	37.21	35.88	36.72	36.60±0.67
F7	31.49	32.36	30.79	31.55±0.79
F8	35.58	36.74	34.51	35.61±1.12
F9	38.45	37.43	36.72	37.53±0.87

Table no.8: Thickness uniformity of various Bambuterol Hcl fast dissolving buccal films.

Formulation code	Thickness of films(mm)			Average thickness (mm)±SD
	I	II	III	
F1	0.12	0.15	0.19	0.15±0.04
F2	0.18	0.14	0.21	0.18±0.04
F3	0.24	0.20	0.22	0.22±0.02
F4	0.23	0.27	0.29	0.26±0.03
F5	0.14	0.16	0.15	0.15±0.01
F6	0.12	0.17	0.14	0.14±0.03
F7	0.16	0.19	0.13	0.16±0.03
F8	0.21	0.20	0.24	0.22±0.02
F9	0.24	0.27	0.22	0.24±0.03

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Table no.9: Folding endurance of various Bambuterol Hcl fast dissolving buccal films.

Formulation code	Folding endurance of films			Average Folding endurance (num)±SD
	I	II	III	
F1	244	247	245	245.33±1.53
F2	220	218	215	217.67±2.52
F3	252	254	253	253.30±1.00
F4	218	224	219	219.33±1.53
F5	254	257	252	254.33±2.52
F6	250	254	259	252.00±2.65
F7	272	276	271	272.33±1.53
F8	223	227	221	223.33±2.52
F9	281	278	270	272.33±2.08

Table no.10: Disintegration study of various Bambuterol Hcl fast dissolving buccal films.

Formulations	Disintegration time (sec)			Average disintegration time(sec)±SD
	I	II	III	
F1	37	37	37	36.67±0.58
F2	44	41	43	42.67±1.53
F3	45	45	44	44.67±0.58
F4	38	39	42	39.67±2.08
F5	48	50	49	49.00±1.00
F6	54	57	53	54.67±2.08
F7	35	38	34	35.67±2.08
F8	50	50	48	49.33±1.15
F9	53	52	49	51.33±2.08

Table no.11: Drug content uniformity of various Bambuterol Hcl fast dissolving buccal films.

Formulation Code	% Drug Content
F1	99.68±0.64
F2	100.51±0.24
F3	101.76±0.24
F4	97.46±0.42
F5	98.01±0.24
F6	96.76±0.24
F7	95.93±0.24
F8	98.43±0.24
F9	100.10±0.64

n=3±SD

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Table no.12: *In-vitro* release data of various Bambuterol Hcl fast dissolving buccal films(F1-F5).

	Time (min)	Cumulative % Drug release(n=3±SD)				
		F1	F2	F3	F4	F5
	2	63.9±0.6	79.90±0.46	88.4±0.75	26±0.75	28.7±0.92
	4	74.32±0.47	89.47±0.47	99.63±0.63	41.58±0.93	44.33±1.15
	6	87.33±0.47	99.23±0.77	101.67±0.6	53.17±1.07	56.83±0.77
	8	92.42±0.30	102.48±0.61	-	69.03±0.47	76.45±2.48
	10	98.92±0.18	-	-	81.84±1.23	84.28±0.77
	12	-	-	-	89.87±1.38	101.67±1.0
	14	-	-	-	96.99±0.81	-

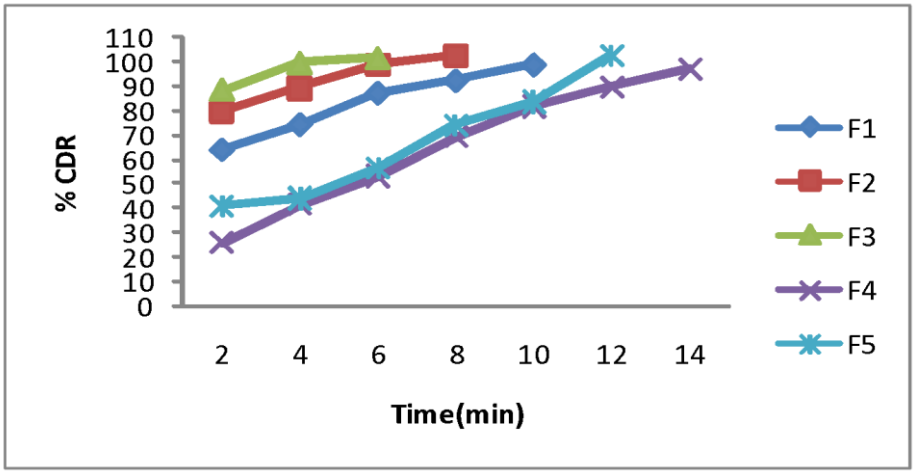

Figure no.7: *In-vitro* drug release profile of formulationsF1-F5

Table no.13: *In-vitro* release data of various Bambuterol Hcl fast dissolving buccalfilms.

	Time (min)	% Cumulative drug release			
		F6	F7	F8	F9
	2	41.1±0.6	53.10±1.20	58.7±0.96	64.70±0.75
	4	44.23±1.10	62.12±0.93	68.32±1.10	82.76±0.77
	6	56.63±0.77	71.88±0.93	82.35±1.10	93.13±0.47

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	8	74.01±0.77	84.28±0.77	74.22±0.93	102.28±1.07
	10	83.67±1.07	87.13±1.07	98.72±0.88	-
	12	102.48±0.81	96.99±1.10	-	-
	14	-	-	-	-

n=3±SD

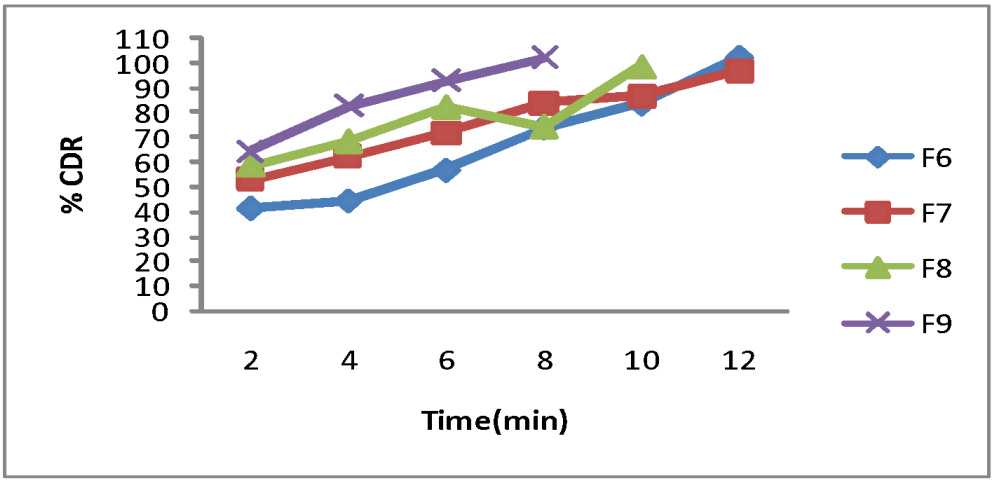

Figure no.8: *In-vitro* drug release profile of formulationsF6-F9

Table no.14: Drug *permeation* study data of various Bambuterol Hcl fast dissolving buccal films.

Time (min)	Permeation study				
	F1	F2	F3	F4	F5
5	43.78	26.84	43.78	54.34	53.02
10	52.32	42.48	52.32	63.60	64.32
15	68.64	48.48	68.64	78.48	70.80
20	72.48	57.60	72.48	82.08	73.68
25	84.72	69.84	84.72	83.76	89.52
30	91.20	71.52	91.20	85.20	92.64
35	94.32	96.72	99.12	95.76	97.68
40	-	-	-	-	-
45	-	-	-	-	-

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Table no.15: Drug permeation study data of various Bambuterol Hcl fast dissolving buccal films.

Time (min)	Permeation study			
	F6	F7	F8	F9
5	36.96	39.60	41.58	44
10	47.76	53.52	55.20	63.60
15	59.52	64.56	68.64	78.96
20	60.48	70.32	71.28	81.12
25	66.48	72.96	77.28	88.08
30	74.40	82.80	83.52	89.04
35	88.56	91.68	94.80	96.72
40	96.72	98.64	97.92	-
45	-	-	-	-

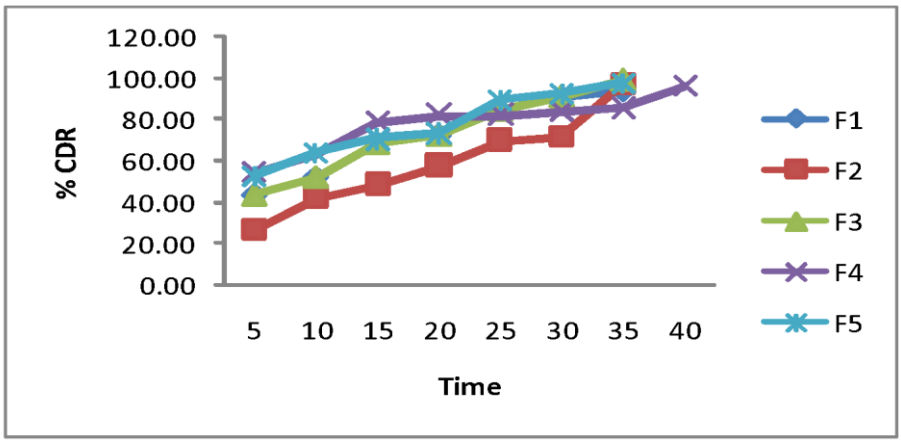

Figure no.9: *In-vitro* permeation profiles of F1-F5

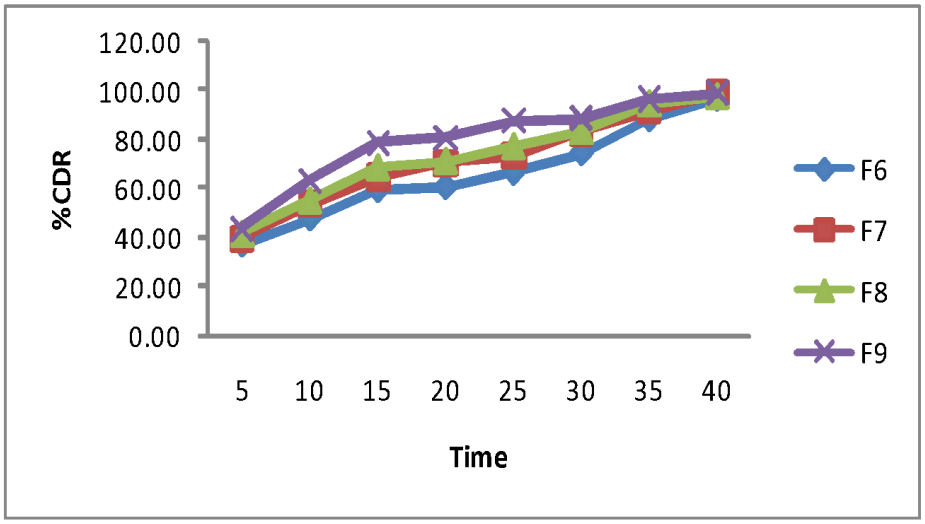

Figure no.10: *In-vitro* permeation profiles of F6-F9

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Stability studies:

Finally based on the thickness uniformity, weight uniformity, drug content uniformity, disintegration study, permeation study and *in-vitro* drug release study confirmed that F3 was the best formulation. For this films drug content uniformity and stability studies were carried out. The formulated films F3 were stored at 40 ± 0.5 ºC in hot air oven, over period of four weeks. At the end of four weeks films were tested for drug content and *in-vitro* release profiles. The ICH guidelines were followed for conducting stability studies. Samples were taken at 30 days for drug content and *in-vitro* release estimation. The drug content and *in-vitro* release results were suggesting that there was no significant change in drug content and *in-vitro* drug release.

Table no.16: Drug content data of stability study of formulation F3

SL.NO	Trial no.	1st day	After 4 weeks
1	I	100.79	97.88
2	II	100.38	98.71
3	III	100.79	99.54
4	Mean	100.65±0.24	98.71±0.83

n=3±SD

Table no.17: *In-vitro* release data of stability study F3

Time (min)	% cumulative drug release	
	1st Day	After 4weeks
2	64.6±0.75	72.69±0.46
4	87.03±0.93	81.54±0.47
6	98.92±0.77	98.62±0.93

n=3±SD

CONCLUSION

From the present research work that is "Formulation and evaluation of Bambuterol Hcl fast dissolving oral strips" for Anti-asthamatic the following point were concluded

- In the beginning blank polymeric strips were prepared by solvent casting technique using HPMC E15, PVP K-30, PVA, the concentration of polymer was varied and the best formulations were chosen for incorporating the drug.
- The prepared strips were evaluated for following parameters like physical appearance and surface texture, weight uniformity, thickness of strips, folding endurance and drug content uniformity, disintegration, permeation study, drug excipients interaction studies, *in-vitro* drug release and short-term stability studies.
- All the formulation showed acceptable quality control property formulation F3 having polymer concentration HPMC E15 350mg gave better drug release rate over period of 6 minutes for Bambuterol Hcl thus formulation F3 was found to be the most promising formulation on the basis of acceptable evaluation property and the *in-vitro* drug release rate. Based on the FTIR studies appear to be no possibility of interaction between the Bambuterol Hcl and polymers of other excipients used in the strips.
- Stability studies were conducted for the optimized formulation as per ICH guidelines for a period of 30 days which revealed that the formulation was stable. The result suggests that the developed fast release strips of Bambuterol Hcl could perform the better than conventional dosage form leading to improved efficacy and better patient compliance.

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