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Formulation and evaluation of salbutamol Sulphate Buccal patches

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Abstract

The objective of present study was to develop Buccal therapeutic systems of Salbutamol sulphate using various such as Eudragit, Sodium alginate polymers as matrix formers. Results revealed that prepared patches showed good physical characteristics, no drug-polymer interaction was observed. The *in vitro* release study revealed that F2 formulation showed maximum release in 6hrs. Formulation F2 was subjected for accelerated stability studies. The F2 formulation was found to be stable as there was no drastic change in the Physico-chemical properties of the patches, which was also confirmed by FTIR. Thus conclusion can be made that stable Buccal patches of Salbutamol sulphate has been developed. F2 formulation showed highest cumulative percentage drug release of 96.89 % were obtained during *in vitro* drug release studies after 6 hrs. The release of Salbutamol sulphate appears to be dependent on lipophilicity of the matrix. Hydrophilic matrices showed best release. The predominant release mechanism of drug through the fabricated was believed to be by diffusion mechanism. Based upon the *in vitro* dissolution data the F2 formulation was concluded as optimized formulation.

Keywords: Salbutamol sulphate, Eudragit, sodium alginate, FTIR studies, solvent casting technique, *in vitro* drug release studies

1. Introduction

The unique environment of the oral cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach, or which are extensively metabolized in the liver (first pass effect) [1]. The total area of the oral cavity is about 100 cm^2. Out of this about one third is the buccal surface, which is lined with an epithelium of about 0.5 mm thickness. The oral mucosal surface is constantly washed by the saliva [2] (daily turn out is about 0.5 to 2 liters). The continuous secretion of saliva results in rapid removal of released drug. Conversely, the thin mucin film, which exists on the surface of the oral mucosa, may provide an opportunity to retain a drug delivery system in contact with the mucosa for prolonged periods if it is designed to be mucoadhesive [2]. Such systems ensure a close contact with absorbing membrane, thus optimizing the drug concentration gradient across the biological membrane and reducing the differential pathway. Therefore, the buccal (oral) mucosa may be a potential site for controlled or sustained drug delivery [3]. Drug delivery via the membranes of the oral cavity is traditionally divided into three categories, Buccal delivery, which infers drug administration through the lining of the cheek to the systemic circulation. These sites for delivery differ in both structure and composition as well as in degree of permeability and therefore, also vary in their ability to retain a delivery for a desired length of time [4, 5]. Buccal route of drug delivery is a good alternative, amongst the various routes of drug delivery. Buccal drug delivery is most advantageous because it abundant blood supply in buccal mucosa, bypassing the hepatic first pass effect and accessibility. The purpose of this study was to develop formulations and systematically evaluate *in-vitro* diffusion studies of buccal films of salbutamol sulphate using various polymers. Salbutamol is used to treat wheezing and shortness of breath caused by breathing problems [6].

It works in the airways by opening breathing passages and relaxing muscles. To Prepare buccal therapeutic systems of salbutamol sulphate using various polymers as matrix formers. Formulated films were characterized for physicochemical properties. These salbutamol sulphate buccal patches is used to treat wheezing and shortness of breath caused by breathing problems (Such as asthma, chronic obstructive pulmonary disease). Albuterol belongs to a class of drugs known as bronchodilators.

2. Materials and Method

2.1. Materials

Salbutamol sulphate was collected as a gift sample from Aurobindo Laboratories Ltd, Hyderabad, polymers, were purchased from Vijaya chemicals Pvt. Ltd, HYD.

2.2. Methodology

Drug- excipient compatibility study

The compatibility of drug and formulation components is important prerequisite for formulation development. It is therefore necessary to confirm that the drug does not interact with excipients under experimental conditions and affect the shelf life of product or any other unwanted effects on the formulation [7].

Goal of excipient compatibility studies are: To identify excipients that are compatible with the active ingredient which do not have any impact on the stability of active ingredient. To assign relative risk level to each excipient within a functional class. To expect a stabilizer to interpose at these points of contact on a random basis is rather simplistic. Because solid state reactions are generally heterogeneous reactions which occur only at points of contact between drug and excipients [8].

Formulation Development

Buccal patches containing Salbutamol were prepared by the solvent casting evaporation technique. The drug Salbutamol was dissolved in methanol. Polymers Sodium Alginate, and ER L100 were taken in a boiling tube, to this add Salbutamol drug which was previously dissolved in methanol. About 30ml of solvent mixture of dichloromethane: methanol (1:1) was added and vortexed. Sufficient care was taken to prevent the formation of lumps. The boiling tube was set aside for 4 hours to allow the polymer to swell. PEG was taken as a plasticizer and added to the mixture and mixed well. It was set aside for 2 hours to exclude any entrapped air and was then transferred into a previously cleaned petri plate (40cm^2), drying of patches was carried out in vacuum oven at room temperature. Dried patches were packed in aluminum foil and stored in a desiccator for further evaluation [9].

Table 1: Formulation Design of Salbutamol sulphate buccal Patches

Formulation Code	Drug (mg)	Eudragit	Sodium Alginate	DMSO	PEG
F1	10	50	-	0.1 ml	1ml
F2	10	100	-	0.1 ml	1ml
F3	10	-	50	0.1 ml	1ml
F4	10	-	100	0.1 ml	1ml

Characterization of Buccal formulation [9, 10, 11]

Physico- chemical evaluation

Physical appearance

All the formulated Salbutamol sulphate films were observed for color, clarity, flexibility, and smoothness.

Folding endurance

Buccal patches folding endurance was estimated by frequently double over at the same place till it broke. The number of times the film could be folded at the same place without breaking is the folding endurance. This was restate on all the films for three times and the mean values plus standard deviation was calculated.

Thickness of the film

The thickness of each film was measured by using screw gauze. Buccal patches thickness was estimated at various sites on each patch and the average thickness of the Buccal patch was capture as the thickness of the patch.

Weight uniformity

The formulated Buccal patches are to be dried at 60 ^{0}C for 6 hours before trial. A identify the area of 4.52 cm^2 of film is to be cut in different parts of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights.

Drug content

The formulated Buccal patch were assayed for drug content in each case. Patches from each formulation were assayed for content of drug. Each formulation was casted in triplicate and one patch from each was taken and assayed for content of drug.

The Buccal films (4.52 cm^2) were added to conical flask containing 100 ml of phosphate buffer pH 7.4 contain 0.5% SLS. This was then stirred with magnetic bead at 400 rpm for 2 hrs. The contents were filtered and the filtrate was analyzed spectrophotometrically. Similarly, a blank was prepared from Buccal films without drug.

Moisture absorption studies

The buccal patches were weighed exactly and placed in a desiccator containing aluminum chloride to maintain 79.50% RH. After 3 days, the films were taken out and weighed. The percentage of moisture uptake was calculated using the following formula.

$$\text{Perentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture loss studies

Three patches were weighed separately and kept in a desiccator contains calcium chloride at 37^{0}C for 24 hours. Then the last weight was noted when there was no further change in the weight of the patch. The percentage of moisture loss was calculated using the following formula [12].

$$\text{Percentage moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

Swelling study

Three buccal patch were weighed individually (W1) and

placed separately in 3% agar gel plates and incubated at 37 ± 1°C. After every 15min time interval until 1 h, the patches were removed from the Petri dish and excess surface water was removed carefully with blotting paper. The swollen patch was then reweighed (W2) and the swelling index (SI) were calculated using the formula given in equation [13].

[Swelling Index = [(W2-W1) ÷ W1] × 100,

Where W1 = initial weight of the patchW2 = final weight of the patch

***In vitro* release study [14]**

The release rate of the drug was determined by using Franz diffusion cell apparatus temperature maintained at 37 ± 0.5 ^{0}C and stirred at a rate of 200 rpm. Sink conditions was maintained all over the study. The vessel containing 10ml of phosphate buffer pH 6.8 phosphate buffer solution. Aliquots of 1ml of samples were withdrawn at various time meanwhile and then analyzed using a UV Spectrophotometer at 256 nm against blank.

% release rate of drug was determined using the following formula.

$$\text{Perentage drug release} = \frac{\text{Da}}{\text{Dt}} \times 100$$

Where, Dt = Total amount of the drug in the film
Da = The amount of drug released

Stability studies

Optimized medicated buccal films were subjected to short term stability testing. The Buccal films were sealed in aluminium foils and kept in a humidity chamber maintained at 40±2 ^{0}C and 75±5% RH for 3 months as per ICH guidelines [15].

3. Results and Discussion

Buccal patch of Salbutamol sulphate were prepared and evaluated.

In the present study 4 formulations with variable concentration of polymer were prepared and evaluated for physic-chemical parameters, *in vitro* release studies and stability studies.

Drug - excipient compatibility studies (FT-IR)

The compatibility between the drug and excipients was evaluated using FTIR peak matching method. There was no appearance or disappearance of peaks in the drug-excipients mixture, which confirmed the absence of any chemical interaction between the drug excipients, and other chemicals.

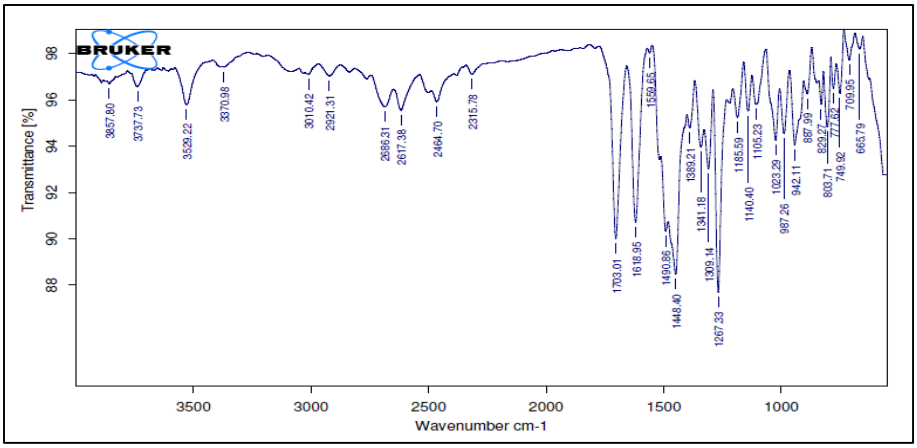

Fig 1: FT-IR Sample for Salbutamol

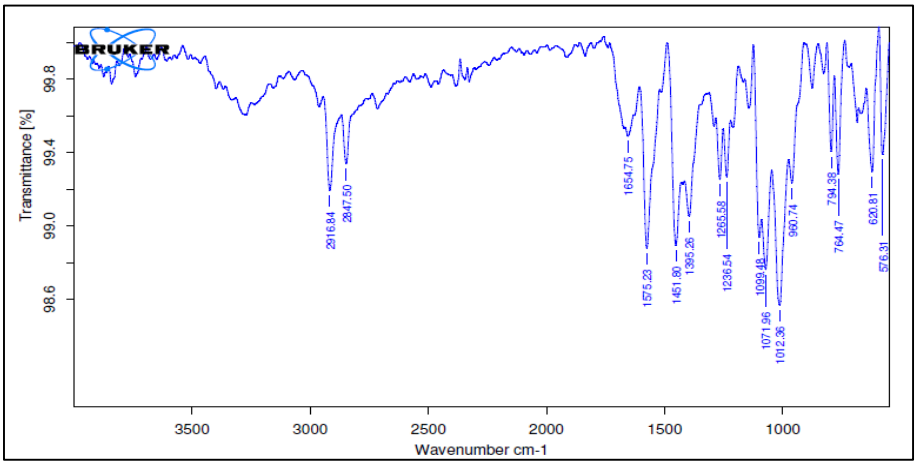

Fig 2: FT-IR Sample for Optimized Formulation

Physical appearance and surface texture of buccal patches

These parameters were checked simply with visual inspection of patches and by feel or touch. The observation reveals that the patches are having smooth surface and they are elegant in appearance.

Weight uniformity of buccal patches
The weight of the patches was determined using digital balance and the average weight of all patches

Thickness of buccal patches
The thickness of the patches was measured using screw gauge and the average thickness of all patches.

Folding endurance of buccal patches
The folding endurance gives the idea of flexible nature of patches. The folding endurance was measured manually, patches were folded repeatedly till it broke, and it was considered as the end point. The folding endurance was found optimum and the patches exhibited good physical and mechanical properties and the average folding endurance of all patches.

Drug content uniformity of buccal patches
Timolol maleate buccal patches prepared with various polymers were subjected to the valuation for uniform dispersion of drug throughout the patch. In each case three patches were used and the average drug content was calculated.

% moisture loss
The moisture content in the buccal patches ranged from 4.264 to 4.745%. The moisture content in the formulations was found to be increased by increase in the concentration of polymers.

%moisture absorption
The moisture absorption in the buccal patches ranged from 7.315 to 8.956 %.

Swelling index
The swelling index in the buccal patches ranged from 14.58 to 15.98 %.

Table 2: Physicochemical evaluation of Salbutamol sulphate patches

Formulation code	Weight (mg)	Thickness (µm)	Folding endurance	Swelling index	Drug content (%)
F1	234	247	236	15.98	94.12
F2	236	265	294	15.85	97.96
F3	231	272	268	14.58	95.26
F4	242	268	253	15.25	94.54

Table 3: Physicochemical evaluation of Salbutamol sulphate patches

Formulation code	Moisture loss	Moisture Absorption
F1	4.554	8.865
F2	4.344	8.956
F3	4.264	7.264
F4	4.745	7.315

***In vitro* release study**
Phosphate buffer 6.8 was used as medium for the release studies. The drug release profiles of Salbutamol sulphate patches containing different ratios of polymers tragacanth, chitosan and sodium alginate. It was cleared from the release profiles of formulations, that the drug release was governed by polymer nature and content. The formulations F1, F2, F3 and F4 showed the maximum release when comparing with other formulations due to the high concentration of polymer. The release was decreased as the concentration of hydrophobic polymer increase.

Table 4: *In vitro* drug release profiles of Salbutamol sulphate transdermal patch (F1-F4)

Time (Hrs)	F1	F2	F3	F4
0	0	0	0	0
30	23.45	21.24	20.89	24.24
1	35.29	34.52	31.28	30.19
2	49.62	44.29	45.22	40.17
3	63.59	62.29	61.2	60.28
4	72.54	71.22	70.19	73.45
5	81.49	79.32	78.45	80.46
6	92.35	96.89	93.18	94.15

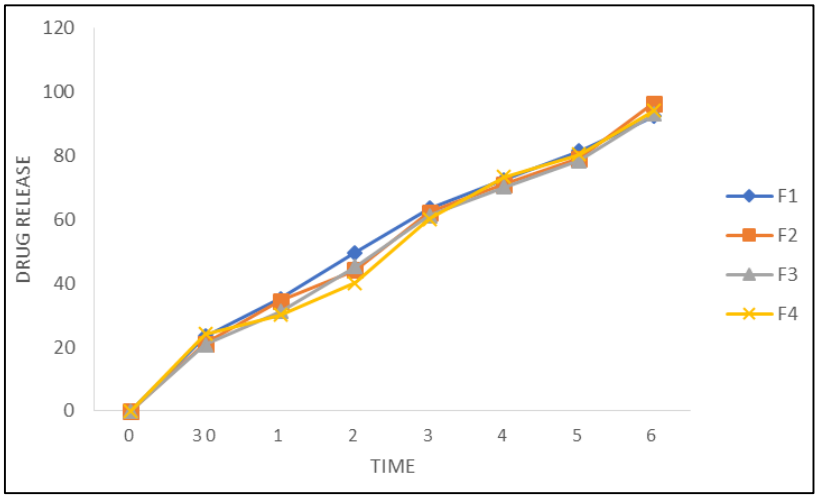

Fig 3: Drug release formulations

Stability studies

Optimized formulations F2 was selected for accelerated stability studies as per ICH guidelines.

Table 5: Stability study of Optimized Formulation

Formulation Code	Initial	1st Month
F2	96.44	95.55
F2	96.44	95.54
F2	96.44	95.58

4. Conclusion

From the obtained results, it can be concluded that. Buccal patches of Salbutamol sulphate were formulated by solvent casting technique. The I.R spectra let out that, there was no interaction between polymers and drug. All the polymers used were compatible with the drug. Characterization parameters like thickness, tensile strength, folding endurance, percentage moisture loss and swelling index indicates that patches were mechanically stable. Percentage weight variation and content uniformity were found to be uniform in all the patches. *In-vitro* drug release showed an abrupt release in the first day. There after the release profile was controlled and extended till the end of static release study, and the concentration was found to be above the minimum inhibitory concentration, which is an encouraging observation. Among the four formulations, the formulated patch F_2 showed 96.89% of release. Throughout the *in-vitro* release studies, the patches remained intact without any disintegration. All the patches were found to be stable over the storage period and conditions tested. Overall study suggests that among the patches prepared F_2 was found to show the best results. Hence it was considered as optimized formulation.

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