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OPTIMIZATION OF FORMULATION METHODOLOGY IN FAST DISSOLVING BUCCAL FILMS OF SALBUTAMOL SULPHATE

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ABSTRACT

The present study aimed at development and evaluation oral fast dissolving film of Salbutamol Sulphate utilizing HPMC and Chitosan as a film forming polymer and PEG 1000 as a plasticizer and cross povidone, cross carmellose sodium and sodium starch glycolate as a plasticizer. The film was prepared by two techniques i.e., solvent casting method and semisolid casting method. The objective of this study is to select an optimized formulation technique among these two techniques. In the formulation, concentration of film forming polymer, superdisintegrants are selected as independent variable and formulation technique and its impact on film characters are selected as dependent variable. The optimized formulation was evaluated for stability studies and the results were found to be desired. The accelerated stability study indicated the stability of the optimized formulation up to 3 month. Then it can be concluded that the fast disintegrating films of Salbutamol sulphate was a suitable alternate for the conventional film available in the market.

Key Words: Plasticizer, Oral Fast Dissolving Film, Salbutamol sulphate.

INTRODUCTION

Recently, fast-dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, which aim to enhance safety and efficacy of a drug molecule by formulating it into a convenient dosage form for administration and to achieve better patient compliance. Some companies introduced more robust forms of fast-dissolving drug delivery; for example Lavipharm Laboratories Inc. (Lavipharm), invented an ideal fast-dissolving drug delivery system, which satisfied the unmet needs of the market. In fast dissolving films, the bioavailability of the drug is significantly greater than that observed for conventional tablets [1].

Mouth dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It

Then rapidly disintegrates and dissolves to release the medication for oral mucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed [2].

Recently, fast-dissolving drug delivery systems have started gaining fame and acceptance as new drug delivery systems, which aim to enhance safety and efficacy of a drug molecule by formulating it into a conventional oral dosage form for administration and to achieve better patient compliance. Some companies introduced more robust forms of fast-dissolving drug delivery the film is placed on the top or the floor of the tongue. When put on the tongue, this film dissolves instantaneously, releasing the drug which dissolves in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such case is enhancing drug bioavailability, No risk of chocking, Provide good mouth feel. Fast dissolving drug delivery system to overcome this problem difficulty in swallowing tablets/capsules etc. This review article overview the advancement in the oral dosage forms, application,

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formulation consideration, method of preparation, evaluation, marketed product and patented technologies of oral fast disintegrating films [3].

MATERIALS AND METHODS

Salbutamol was obtained as a gift sample from Med zone laboratories, Pondicherry. And all solvents used in the formulation are selected as analytical grade solvents. Instrument like UV spectrophotometer (SCHIMADZU), FTIR are used for the Analytical evaluations.

1) Solvent casting method

In solvent casting method water soluble polymers are dissolved in water and the drug along with other Excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate and dried [4].

2) Semisolid Casting

In this method, solution of water soluble film forming polymer is mixed to solution of acid insoluble polymer to form homogenous viscous solution (e.g. cellulose acetate phthalate and cellulose acetate butyrate). After sonication, it is coated on non-treated casting film. On drying the thickness of the film should be about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4 [5].

Evaluation of fast-dissolving films

Thickness:

As the thickness of film is directly concern with drug content uniformity, it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital Vernier calipers at different strategic locations [6].

Drug content uniformity

A fast-dissolving film (25 cm^2) was transferred into a graduated flask containing 100 ml of distilled water. The flask was shaken for 4 h in a mechanical shaker. The solution was filtered and after suitable dilutions with distilled water, the absorbance value was measured at 276 nm using the placebo patch (patch without drug) solution as a blank, and the drug content was calculated [7].

Folding endurance

The folding endurance is expressed as the number of folds (number of times the film is folded at the same place) required to break the specimen or to develop visible cracks. This also gives an indication of brittleness of the film. A strip of 2.5 cm × 2.5 cm (6.25 cm2) was subjected to folding endurance by folding the patch at the same place repeatedly several times until a visible crack was observed, and the values were reported [8].

Surface pH

The film to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water and kept for 30 s. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min. The average of three determinations for each formulation was done [9].

Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross sectional area of the strip as given in the equation below [9].

$$\text{Tensile strength} = \frac{\text{Load at breakage}}{\text{Strip thickness} \times \text{Strip width}}$$

Disintegration time

Disintegration of orally fast dissolving films requires U.S.P. disintegration apparatus. The disintegration time limit is of 30 seconds or less for orally disintegrating film described in CDER. Guidance can be applied to fast dissolving oral strips. Disintegration time will vary depending on the formulation but typically the disintegration range from 5 to 30. seconds. Although, no official guidance is available for oral fast disintegrating films [10].

In vitro drug release

Dissolution studies of films are performed by U.S.P. XXIII type II apparatus in 6.8 phosphate buffer (500ml) and 0.1N Hcl (500ml). The temperature required is 37±0.5°C and the rotation speed should generally 50 rpm. The samples are needed to withdrawn at various time intervals and should analyze spectrophotometrically [11,12].

RESULTS AND DISCUSSION

Fast dissolving films of Salbutamol can be considered suitable for clinical use in the treatment of asthma and other conditions of allergies closed to pulmonary system, where a quicker onset of action for a dosage form is desirable along with the convenience of administration. The prepared film met the standard evaluation parameters with a slight deviation within the prescribed limits. The short term stability studies carried out were confirmative of the drug stability in the film during the present study. The Disintegration studies revealed that the film prepared with Crosspovidone with semisolid casting method show faster disintegration as compared to film prepared with Crosscarmellose sodium and Sodium starch glycolate by solvent casting method. Even the dissolution studies confirmed that film prepared with Crosspovidone show faster drug release as compared to film prepared with Crosscarmellose sodium and Sodium starch glycolate. i.e., 102% of drug release in 15^{th} minutes itself. The results are shown in Table no 2-3 and Figure no:1.

Table 1. Composition of fast dissolving buccal films

Ingredient	F 1	F 2	F 3	F 4	F5	F6
	Solvent casting method			Semisolid casting method		
Salbutamol sulphate	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Chitosan	1:1	1:1	1:1	1:1	1:1	1:1
Cross carmellose sodium	5%	-	-	5%	-	-
S odium starch glycolate	-	5%	-	-	5%	-
Crosspovidone	-	-	5%	-	-	5%

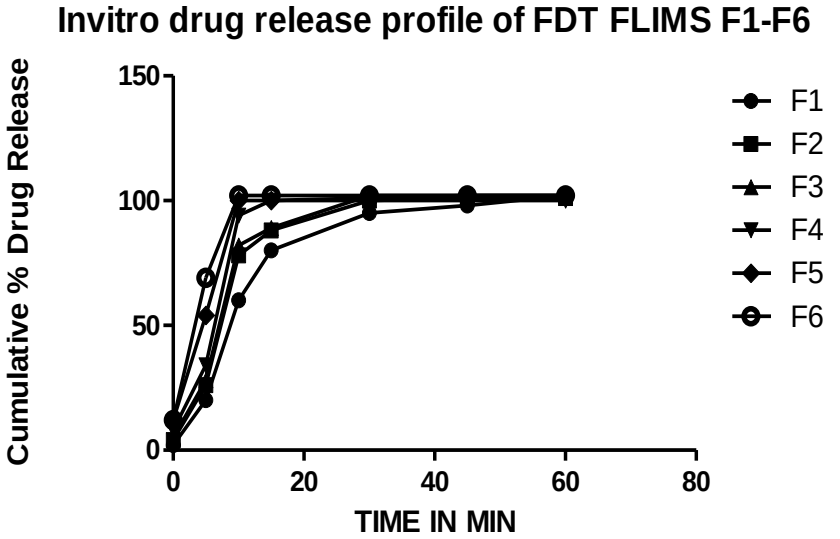
Table 2. Physical properties of fast dissolving buccal films

Formulation code	Uniformity of Thickness (mm)	Weight Variation (mg)	Wetting Time (in Sec)	Water absorption Ratio	In-vitro Disintegration time (in 60 Sec)	Drug Content in %
F 1	0.34±0.031	0.163±3.106	23.67±0.356	70.85±0.991	25.43±0.556	96.81±1.332
F 2	0.32±0.044	0.175±3.106	21.83±0.450	72.40±1.720	24.47±0.640	97.98±1.323
F 3	0.37±0.015	0.131±3.710	31.67±0.381	68.54±1.465	28.78±0.345	97.55±1.342
F 4	0.37±0.034	0.167±3.070	24.71±0.377	68.85±0.987	34.40±0.543	98.12±1.432
F 5	0.32±0.042	0.175±3.107	22.86±0.470	74.40±1.730	26.46±0.655	97.56±1.456
F 6	0.38±0.017	0.134±3.730	32.70±0.392	67.57±1.465	36.87±0.370	99.00±1.321

Table 3. Stability studies for optimized formulation F6 of fast dissolving buccal films

Time (Days)	Color & Appearance	Drug Content (%)	In-vitro Disintegration Time (Sec)
30	off-White colored, uniform thickness, good flexibility with folding endurance	98.00	20
60	off-White colored, uniform thickness, good flexibility with folding endurance	97.56	21
90	off-White colored, uniform thickness, good flexibility with folding endurance	96.78	17

Figure 1.



CONCLUSION

From the present results, it can concluded that the fast disintegrating film of Salbutamol prepared with Crosspovidone show a better disintegration time and the Dissolution profile**.** And from the results it can be concluded that semisolid casting method was a better formulation technique when compared to solvent casting technique. Further it is advised that the same work should be confirmed for its therapeutic efficacy with the Experimental and Clinical trials.

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