Research Article

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PREPARATION AND IN VITRO EVALUATION OF BUCLIZINE ORAL THIN FILM STRIPS

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Abstract

Buclizine is an antihistaminic water soluble drug. The objective of the present investigation was to improve bioavailablity of buclizine oral thin film strips by using solvent casting method with excipients. Water soluble synthetic polymer (Poly Vinyl Alcohol), plasticizer (PVP), solubilizer (PEG400), carbapol, sweetener (Mannitol) was used in the preparation of oral thin film strips of buclizine. The oral thin films of buclizine were prepared by solvent casting method using 1:1 and 1:2 ratios of drug and polymers. The influence of the proportion of polymer and several co-excipients on the release rate of the drug from formulations was studied.

Keywords: Antihistaminic, Buclizine, Oral thin film strips.

Introduction

Thin-film drug delivery uses a dissolving film or oral drug strip to administer drugs via absorption in the mouth (buccally or sublingually) and/or via the small intestines (enterically). A film is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic circulation via dissolution when contact with liquid is made. Oral films, also called oral wafers in the related literature, are a group of flat films which are administered into the oral cavity[1].

Buclizine

Buclizine is an antihistamine and anticholinergic of the piperazine derivative family. It is considered to be an antiemetic[4].

Thin-film drug delivery

Thin-film drug delivery uses a dissolving film or oral drug strip to administer drugs via absorption in the mouth (buccally or sublingually) and/or via the small intestines (enterically). A film is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic circulation via dissolution when contact with liquid is made[5].

Thin-film drug delivery has emerged as an advanced alternative to the traditional tablets, capsules and liquids often associated with prescription and OTC medications. Similar in size, shape and thickness to a postage stamp, thin-film strips are typically designed for oral administration,

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with the user placing the strip on or under the tongue (sublingual) or along the inside of the cheek (buccal). These drug delivery options allow the medication to bypass the first pass metabolism thereby making the medication more bioavailable. As the strip dissolves, the drug can enter the blood stream enterically, buccally or sublingually. Evaluating the systemic transmucosal drug delivery, the buccal mucosa is the preferred region as compared to the sublingual mucosa[2, 6].

Oral drug strip development

Strip forming polymers

The polymer employed should be non-toxic, non-irritant and devoid of leachable impurities. It should have good wetting and spreadability property. The polymer should exhibit sufficient peel, shear and tensile strengths. The polymer should be readily available and should not be very expensive. Film obtained should be tough enough so that there won't be any damage while handling or during transportation. Combination of microcrystalline cellulose and maltodextrin has been used to formulate Oral Strips of piroxicam made by hot melt extrusion technique. Pullulan has been the most widely used film former (used in Listerine PocketPak, Benadryl, etc.)

Plasticizer

Plasticizer is a vital ingredient of the OS formulation. It helps to improve the flexibility of the strip and reduces the brittleness of the strip. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutylphthalate, Citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients.

Active pharmaceutical ingredient

Since the size of the dosage form has limitation, high-dose molecules are difficult to be incorporated in OS. Generally 5% w/w to 30% w/w of active pharmaceutical ingredients can be incorporated in the OS[3].

Sweetening, flavouring and colouring agent

An important aspect of thin film drug technology is its taste and colour. The sweet taste in formulation is more important in case of pediatric population. Natural sweeteners as well as artificial sweeteners are used to improve the flavour of the mouth dissolving formulations for the flavours changes from individual to individual. A pigment such as titaniumdioxide is incorporated for colouring.

Stabilizing and thickening agents

The stabilizing and thickening agents are employed to improve the viscosity and consistency of dispersion or solution of the strip preparation solution or suspension before casting. Drug content uniformity is a requirement for all dosage forms, particularly those containing low dose highly potent drugs. To uniquely meet this requirement, thin film formulations contain uniform dispersions of drug throughout the whole manufacturing process[9].

Approaches used for the formulation of oral thin films

- Conventional approaches
- Solvent casting method
- Hot-melt extrusion
- Semisolid casting

Solvent casting method[13]

In this method, firstly the water soluble polymers are dissolved in water at 1,000 rpm and can be heated up to 60°C. All the other excipients like colors, flavoring agent, sweetening agent, etc., are dissolved separately. Then both the solutions obtained are mixed thoroughly stirring at 1,000 rpm. The obtained solution is incorporated with the API dissolved in suitable solvent. The entrapped air is removed by vacuum. The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the desired size[11].

Materials & methods

Composition of buclizine oral thin film strips

Table No. 01: Formulation design of Buclizine oral thin film strips

Ingredients	B1	B2	B3	B4	B5	B6
Buclizine (mg)	4	4	4	4	4	4
PVA	4	8	12	4	8	12
PVP	23	58	23	58	23	58
PEG 400	4	8	12	4	8	12
Carbapol	32	16	8	32	16	8
Mannitol	16	16	16	16	16	16
Strip weight	98mg	98mg	98mg	98mg	98mg	98mg

Preparation of buclizine oral thin film strips by using solvent casting method

Aqueous solution 1:

Dissolved (PVA) polymer in 20 ml hot water with stirring to produce a clear solution and kept for 2 hr to remove air bubbles[14]. Carbapol 934P was first dissolved in water, neutralized with diethanolamine and then added to the cooled PVA solution.

Aqueous solution 2:

Dissolved pure drug, sweetener and plasticizer (PVP) in specified proportion of distilled water.

Aqueous solution 1 was mixed with aqueous solution 2 and stirred for 1 hr. The solution was cast on to 9 cm diameter petridish and was dried in the oven at 45^0c for 24 hr. The films were carefully removed from the petridish and checked for any imperfection and cut accurately to square films of 2 cm length, 2 cm width so that each film contained 4 mg of the drug the samples were stored in glass container maintained at temperature 30^0c and relative humidity 60% ± 5%until further analysis[7, 15].

Fig. No. 01: Buclizine Oral Thin Film Strip

Evaluation of oral thin film formulations

Tensile Strength

Tensile strength of the film was determined with digital tensile tester, which consists of two load cell grips. The lower one is fixed and the upper one is movable. The test film was placed between these two cell grips and force was gradually applied till the film breaks. It is calculated by formula

Tensile strength = force at break/ initial cross sectional area of film in mm^2

Percentage Elongation

The percentage elongation was carried out using Hounsfield universal testing machine. It consists of two load cell grips. The lower is fixed and upper is movable. The test film of specific 3inch x 10mm was fixed between these two cell grips and force was gradually applied till the film breaks. It is calculated by formula

$$\% \text{ Elongation} = \frac{\text{increase in length}}{\text{Original length}} * 100$$

Folding Endurance

The flexibility of films can be measured quantitatively in terms of Folding Endurance. Folding Endurance of the films was determined by repeatedly folding a small strip of the films (approximately 2x2cm) at the same place till it broke or visible cracks were observed. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

In vitro Disintegration Time

In vitro disintegration time is determined visually in a glass dish of 25ml distilled water with swirling every 10sec. The disintegration time is the time is the time when the film starts to break or disintegrates[10].

In vitro Dissolution Studies

The in vitro dissolution studies is carried out in simulated saliva solution pH 6.4 phosphate buffer using USP type-II paddle apparatus at 37±0.5ºC. Samples are withdrawn at regular time interval and analyzed by UV-Visible spectrophotometer at 230 nm[8, 12].

Results & discussion

Wavelength detection of Buclizine in phosphate buffer pH 6.4

Table No. 02: Wavelength detection of Buclizine in phosphate buffer pH 6.4

Wavelength	Absorbance
220	0.234
230	0.253
240	0.248
250	0.237
260	0.214
280	0.197
300	0.172
320	0.157
340	0.131
360	0.124
380	0.104

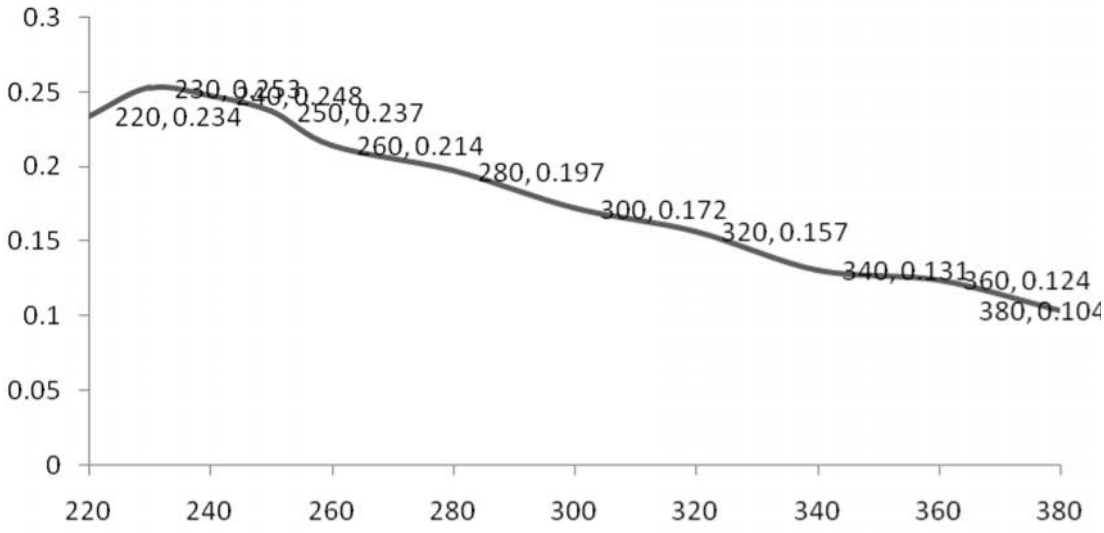

Fig. No. 02: wavelength detection of Buclizine in phosphate buffer pH 6.4

Construction of Calibration graph in 900ml phosphate buffer,ph 6.4: (λmax=230 nm)

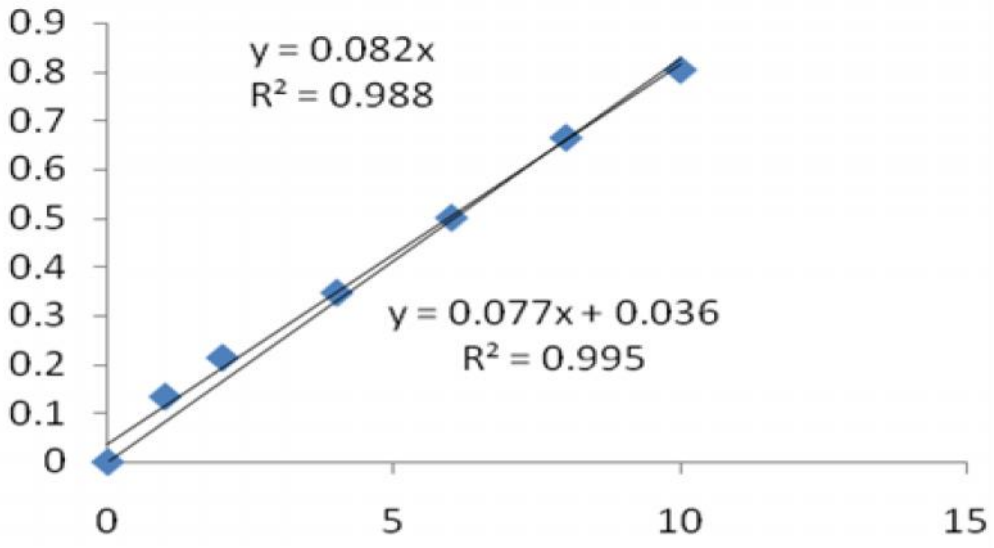

Fig. No. 03: Calibration graph of buclizine using 6.4 phosphate buffer

Calibration graph of buclizine using 6.4 phosphate buffer

Table No. 03: Calibration graph of buclizine using 6.4 phosphate buffer

Concentration µg/ ml	Absorbance Trial 1
0	0
1	0.134
2	0.214
4	0.347
6	0.501
8	0.665
10	0.804

Physical Evaluation of Thin film strips

Table No. 04: Physical Evaluation of Thin film strips

S. No	Formulations	*Tensile strength	*Percentage elongation	*Folding endurance (no. of folds)	*In-vitro disintegration time(sec)
1	**B1**	2.07±0.82	24.19±0.21	85.05±0.031	21.44±1.21
2	**B2**	2.42±0.02	20.18±0.13	89.14±0.110	17.86±1.57
3	**B3**	3.12±0.05	26.11±0.51	86.33±0.024	14.05±1.42
4	**B4**	1.54±0.04	18.16±0.07	92.24±0.022	21.26±0.81
5	**B5**	2.24±0.04	22.32±0.31	94.07±0.036	19.50±0.52
6	**B6**	3.05±0.03	19.05±0.11	96.03±0.016	16.42±1.05

Percentage Cumulative drug release of films B-1 to B-6

Table No. 05: Percentage Cumulative drug release of films B-1 to B-6

Time in SEC's	B1	B2	B3	B4	B5	B6
0	0.00	0.00	0.00	0.00	0.00	0.00
30	16.64	25.13	20.04	26.66	24.96	33.45
60	31.51	40.70	34.75	55.21	56.13	65.16
90	42.21	66.90	60.93	78.77	76.29	**100.15**
120	**59.08**	**80.28**	**76.38**	**99.92**	**94.37**	**100.18**

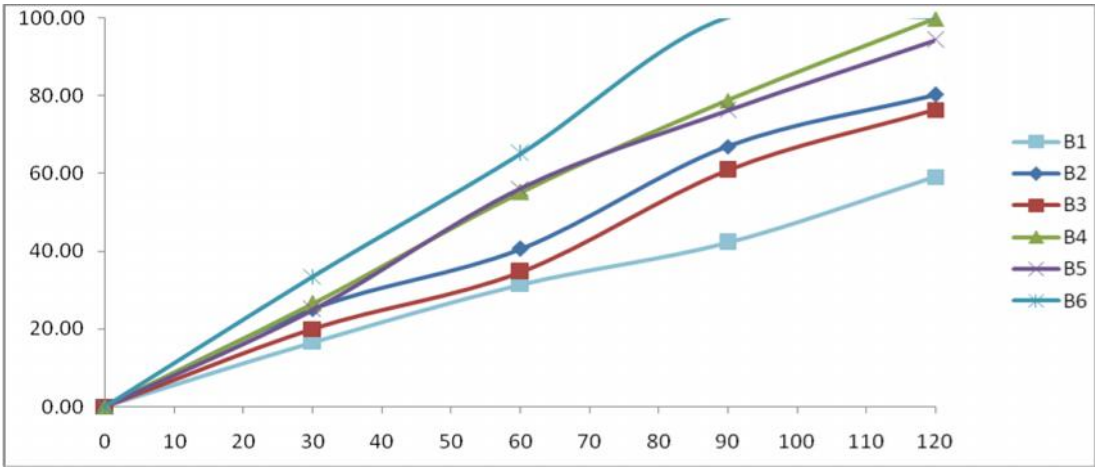

Fig. No. 04: Percentage Cumulative drug release of films B1 to B6
(Time on x-axis and % drug release on y-axis)

Summary and conclusion

The fast dissolving films containing Buclizine were prepared with an aim to have rapid onset of action and increased bioavailability in allergic conditions. Various cellulose derivatives were employed for their film forming properties of which PEG and PVA showed promising physicochemical properties as compare to all other grades therefore, it was selected for further studies. Prepared films were transparent with smooth surface and

acceptable mechanical properties. It can be concluded that Oral thin strip of Buclizine can be prepared using the polymer combinations of B4 and B5. Depending on physical evaluation and drug release it was concluded that B4 is optimized among all the formulations.

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