

FORMULATION AND EVALUATION OF ORAL DISINTEGRATING FILM OF ATENOLOL

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ABSTRACT

Objective: The main objective of the study was to formulate the oral disintegrating films loaded with atenolol by solvent-casting method and to carry out its evaluation studies.

Methods: The films were prepared using the film-forming hydrophilic polymer like hydroxypropyl methylcellulose (E-5) and super disintegrant like pectin in various proportions. The formulated oral films were characterized for Fourier transform infrared (FTIR) and morphological evaluations. Various physicochemical parameters such as weight variation, folding endurance, surface pH, *in vitro* disintegration, and *in vitro* dissolution studies were carried out.

Results: FTIR studies revealed that there was no drug-polymer interaction. The morphological evaluation of films showed that all the films were homogenous and transparent. The folding endurance test ensured that the films had sufficient brittleness and by weight variation test, it was inferred that all the films were within the deviation. The surface pH study showed the pH of the films was around neutral pH. The drug was well distributed in all the films. The films disintegrated within 120 s and the fastest being disintegrated in 30 s. Based on all the evaluation parameters, F6 had shown optimal performance and remarkable increase in drug release of 94.38% in 2 min.

Conclusion: Thus, formulated oral disintegrating films can be termed as an alternative approach to deliver atenolol.

Keywords: Atenolol, Oral disintegrating film, Hydroxypropyl methylcellulose, Pectin.

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INTRODUCTION

In modern era, the development of novel delivery system for oral route has grabbed a lot of attention due to its patient compliance [1]. Delivery through buccal route was considered as one of the important alternatives to administer the loaded drug through oral route, as it was considered as the most convenient, easiest, and the fastest route of drug absorption [2]. Stratified squamous epithelium which was separated by the wavy basement membrane, from the underlying tissue of lamina propria and submucosa was present in the surface of oral cavity which eases the delivery of administered drugs. Oral mucosa which is highly vascularized ensures better permeability of many drugs and thus the absorption of drugs is better at this site [3]. Therefore, bioavailability of drug can be improved by bypassing the first pass metabolism when administered through buccal cavity [4].

Among various formulations administered through buccal cavity oral films (OFs) have started to gain popularity and acceptance, due to their rapid disintegration or dissolution when placed under the tongue or buccal cavity, self-administration even without the use of water; the first kind of OFs were used for mouth freshening, sold as Listerine® pocket packs™ by the major pharmaceutical company Pfizer. First therapeutic oral thin films for the treatment of sore throat with benzocaine as loaded drug were Chloraseptic® [5]. Oral dissolving films (ODFs) are ultrathin in size with an active agent along with the pharmaceutical excipients. Drugs belonging to various classes such as antiulcers, antiasthmatics, antitussives, expectorants, antihistamines, and nonsteroidal anti-inflammatory drugs can also be loaded in ODFs [6]. For the preparation of any fast dissolving film, critical parameters that alter properties of film are choosing and optimizing the concentrations of excipients used in the formulation. OFs once administered into buccal cavity undergo rapid disintegration under the tongue, providing a quick onset of

action [7]. OFs contain large surface area, promoting rapid wetting in the moist oral environment. These films can be used to treat patients suffering from developmental and mental disorders, geriatrics, and pediatrics who have difficulty in swallowing [8]. The film should have sufficient elasticity and tensile strength. They should be non-sticky to the packaging materials and to fingers while administration [9,10].

Atenolol is an adrenergic β 1-antagonist, and it is widely prescribed to treat various cardiovascular diseases such as hypertension, angina pectoris, arrhythmias, and myocardial infarction [11]. The main objective of the current research is to improve the bioavailability of atenolol at the receptor site by formulating OFs. As the conventional dosage forms had shown decreased bioavailability.

MATERIALS AND METHODS

Materials

Atenolol was obtained from Vani Pharma Labs Ltd., Hyderabad, India. Ethanol (solvent) and Tween 80 (Surfactant) were obtained from Merck Specialities Pvt., Ltd., Mumbai, India. Hydroxypropyl methylcellulose (HPMC) (polymer) and pectin (super disintegrant) were obtained from Loba Chemie, Mumbai, India. Glycerine (Plasticizer) and mannitol (Cryoprotective) were obtained from Merck Specialities Pvt., Ltd., Mumbai, India. Citric acid (saliva stimulant), aspartame (sweetener), and methylparaben (preservative) were obtained from Ranbaxy, Fine Chemicals Ltd.

Methods

Preparation of oral disintegrating films of atenolol

The procedure employed in the preparation of OF was solvent-casting method. Polymer (HPMC) was soaked in distilled water (5 ml) for 1 h. Additives such as aspartame, glycerine, mannitol, and other ingredients

were dissolved in 95% ethanol (around 2 ml). Drug and solubilizer complex equivalent to 25 mg and super disintegrant were taken and added to the polymer solution. The gross mixture was stirred for 1 h at 1000 rpm and for the removal of entrapped air; the mixture was subjected to sonication for 10 min. This mixture was poured on an ointment slab and allowed to air dry. Then, films of 2 cm×2 cm² were cut and were encased in a butter paper, sheathed by aluminum foils, and stored in desiccator for further evaluation studies [12]. Different compositions employed to formulate OFs loaded with atenolol are depicted in Table 1.

Evaluation studies of the prepared OF

The prepared films were subjected to the fundamental evaluation tests. Films with any shortcomings, air entrapment, asymmetry in thickness, deviation in weight, or content uniformity were not taken into consideration for further studies. Physicochemical properties such as thickness, weight uniformity, folding endurance, surface pH, and drug content uniformity of the prepared films were determined.

Compatibility studies

Fourier transform-infrared (FTIR) studies were performed for pure drug, excipients, and the physical mixture to identify the compatibility between the drug and other excipients using KBr pellet method [13].

Physicochemical characteristics

Morphological studies (visual method)

Morphological studies were carried out to check color and transparency of films against a white and black background [13,14].

Folding endurance

Folding endurance indicates brittleness of film. It was determined by often folding the film at the same place until the film breaks [13,15].

Weight of films

Each OF was weighed, and the weight was recorded using weighing balance and variation in the weight was calculated [13].

Surface pH

The surface pH of the films was determined to inspect the possible secondary effects due to an *in vivo* pH change. The film to be examined was laid on a Petri dish and was wetted with 0.5 ml of distilled water and set aside for 1 h. The electrode of the pH meter was brought into contact with the surface of the film for 60 s, and the pH of the film was noted [13].

Drug content

2 cm×2 cm² film was taken into a 10 ml volumetric flask and dissolved in methanol (10 ml) and set aside for 2 h. Later, it was filtered through 0.45 µm membrane filter, and absorbance was checked at 224 nm [13,16].

In vitro disintegration studies

A strip of the formulated OF was placed in a Petri plate containing 25 ml of distilled water at 37°C. After placing the strip in Petri plate, it was swirled at every 10 s. After certain time, the film tends to disintegrate and that time was noted as disintegration time [13,17].

In vitro dissolution studies

The method used to perform *in vitro* studies for the formulated OF is beaker stirring method. This study was conducted using a 150 ml beaker, filled with 125 ml of 6.8 pH phosphate buffer which acts as dissolution media. Film was then placed on one side of the beaker using double-sided tape, and the medium was stirred at the speed of 200 rpm using magnetic stirrer. Sample volume of 5 ml was withdrawn at 15, 30, 45, 60, 90, and 120 s time intervals,

Table 1: Formulation chart for formulation of OF loaded with atenolol

Formulation	Drug (mg)	HPMC (mg)	Pectin (mg)	Surfactant (mg)	Glycerine (%)	Aspartame (mg)	Citricacid (mg)	Mannitol (mg)	Methylparaben (mg)
F1	25	50	10	0.2	2	3	1	10	1
F2	25	50	60	0.2	2	3	1	10	1
F3	25	75	10	0.2	2	3	1	10	1
F4	25	75	60	0.2	2	3	1	10	1
F5	25	50	10	0.2	4	3	1	10	1
F6	25	50	60	0.2	4	3	1	10	1
F7	25	75	10	0.2	4	3	1	10	1
F8	25	75	60	0.2	4	3	1	10	1

OF: Oral films, HPMC: Hydroxypropyl methylcellulose

and the sink condition was maintained. The withdrawn samples were analyzed at 224 nm using ultraviolet (UV) spectrometer (UV-1800, Shimadzu) [13].

RESULTS AND DISCUSSION

FTIR studies

The characteristic peaks of atenolol (pure), HPMC, and the physical mixture were depicted in Fig. 1a-c. From the graph, it was observed that there were no chemical interactions occurred between drug and polymer. Thus, from the figures, it can be inferred that the characteristic bands of pure drug were not affected by polymer and also not by the method used for preparation.

Physicochemical characteristics

Morphological properties

Homogeneity, color, and transparency of films were tested visually. All the films were found to be homogenous and transparent. The values were depicted in Table 2.

Folding endurance

Folding endurance of films was calculated and depicted in Table 2. From the results, it can be inferred that the formulated films have good brittleness.

Weight variation

Weight of 2 cm×2 cm² film from different batches was weighed, and variation was calculated using electronic weighing balance. From the results depicted in Table 2, it can be inferred that variation in the weight was in prescribed limits.

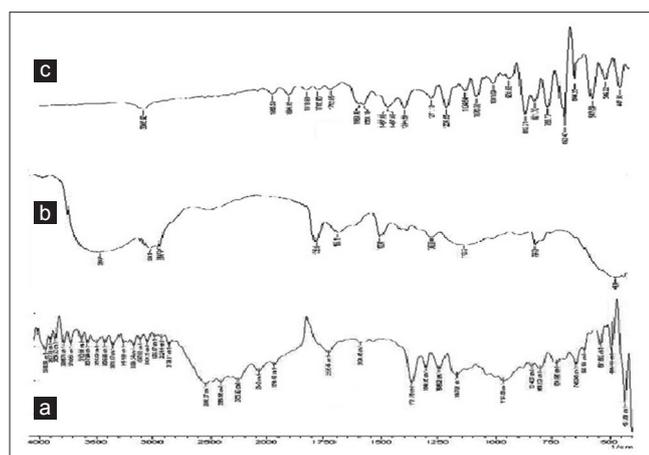


Fig. 1: Fourier transform-infrared spectrum of (a) atenolol, (b) hydroxypropyl methylcellulose, (c) physical mixture

Surface pH study

The film's surface pH was found to be in the range of 6.3–6.7. No irritation to the oral mucosa was seen, as surface pH of the films was around the neutral pH.

Drug content

The percentage drug content in all the formulations varied between 95 and 99.50, as depicted in Table 2. Results suggested that there is a uniform distribution of atenolol in the formulated films with complete solubilization.

In vitro disintegration time

Disintegration time of all the batches of OD strips was within the range of 30–54 s, as depicted in Table 2. Results suggested that as the concentration of the polymer increases, there is an increase in the thickness of the film leading to higher disintegration time. Among all prepared formulations, F6 with low polymer concentration and high disintegrant concentration was found to disintegrate quickly in 30 s.

In vitro drug release

The study of drug release from the formulated films was carried out for 5 min at a time interval of 30 s. The drug release profile for all the oral disintegrating film formulations was shown in Fig. 2. Results suggested that as the concentration of super disintegrant increases there was remarkable increase in the drug release. However, with the increase in the concentration of polymer used, the results were found to be contrary. The F6 batch containing 50 mg of HPMC and 60 mg of super disintegrant has shown the drug release of 94.38% in 2 min.

CONCLUSION

Oral disintegration films loaded with atenolol were formulated successfully by solvent-casting method. FTIR studies suggested that characteristic bands of atenolol were not affected by polymer and method used for formulation. Formulated OFs were homogenous and transparent with a neutral surface pH. OFs containing high amount of super disintegrant and low amount of polymer, i.e., formulation F6 had shown optimum disintegration and *in vitro* release, when compared with other formulations. From the results, it can be concluded that formulated OFs release the drug into systemic circulation rapidly from the site of administration providing an alternative approach to treat hypertension.

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AUTHOR'S CONTRIBUTIONS

Author is a faculty in division of pharmaceuticals and the work contributed on faculty development program in the institution.

Table 2: Results of evaluation studies

Formulation	Appearance	Folding endurance	Weight of films (mg)	Surface pH	Drug content	<i>In vitro</i> disintegration (s)
F1	Homogenous and colorless	61	119.3	6.4	98.57±1.02	54.00
F2	Homogenous and colorless	65	123.5	6.5	99.36±0.21	49.00
F3	Homogenous and colorless	59	125.4	6.4	99.20±1.63	43.00
F4	Homogenous and colorless	63	118.6	6.7	97.85±1.44	39.00
F5	Homogenous and colorless	55	117.1	6.5	95.00±0.92	40.00
F6	Homogenous and colorless	57	121.9	6.6	99.40±0.86	30.00
F7	Homogenous and colorless	60	120.5	6.3	98.53±0.37	45.00
F8	Homogenous and colorless	59	118.2	6.4	99.20±0.56	36.00

*SD: Standard deviation, n=3

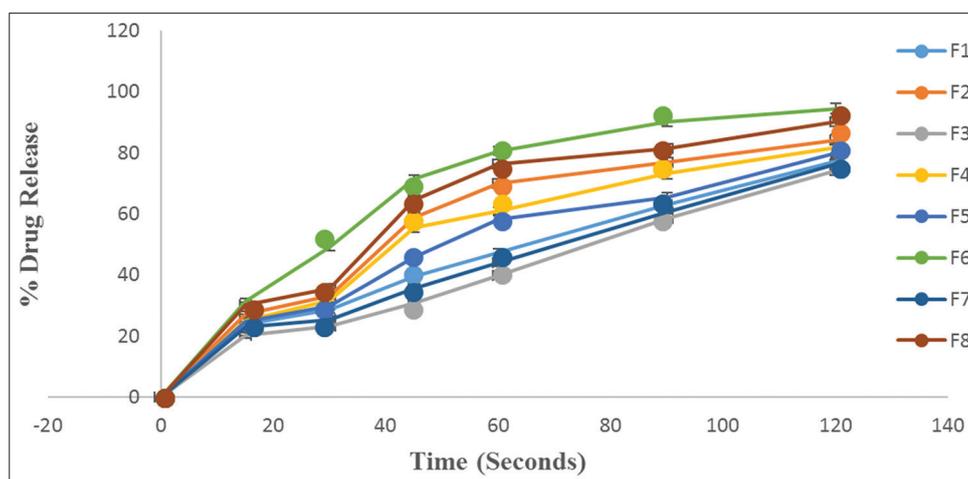


Fig. 2: *In vitro* drug release profile of the films loaded with atenolol

CONFLICTS OF INTEREST

The author confirms that this article content has no conflicts of interest.

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