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FORMULATION AND CHARACTERIZATION OF ATENOLOL FAST DISSOLVING FILMS

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ABSTRACT

The aim of present work deals with formulation and characterization of atenolol fast dissolving films. Atenolol is a β – selective adrenergic antagonist used as antihypertensive agen. Films were formulated using film forming polymer like Hydroxypropylmethylcellulose (HPMC E5)(F1 – F8) and tween 80 is added to the formulation from F5 – F8 by solvent casting technique with the help of Polyethylene glycol (PEG 400) as a plasticizer and glycerine as a sweetening agent. FT-IR analysis was performed to study the interaction between the drug and polymer .The films were evaluated for weight variation, surface pH , folding endurance , drug content , dissolving time , disintegration time, in-vitro dissolution studies. Based on the evaluation parameters F4 containing Drug: Polymer (1:4) ratio showed optimum performance and marked increase in releasing of drug 92.34%, though F8 formulation has maxmimum drug release as it has less tensile strength. It can be concluded in the study that mouth dissolving film can be potential novel drug dosage form for poorly water soluble drugs.

Keywords: Atenolol, HPMC E5, Tween 80, FT-IR.

INTRODUCTION

From past few decades there is a fabulous change in designing various drug delivery systems to achieve rapid onset of action in order to treat sudden surprising disorders like hypertensive reactions. Travelling through various milestones from discovering a conventional tablet, capsule, modified release tablet and capsules, oral disintegrating tablets, wafers to achieve oral drug administration and now aspiring another milestone in novel era of formulating fast dissolving buccal films. Fast-dissolving buccal films with their unique nature of convenience in dosing and portability of thin films gained an quick acceptance in administering the drugs in young and geriatric patients effectively [1,2].

These fast dissolving films contain active ingredient embedded in matrix of film forming polymers that disintegrates quickly when taken orally in saliva, within a few seconds without need of water or chewing. Hence patient compliance is more in patients with difficulty in swallowing and chewing. And more than all these bioavailability of drug is significantly greater than the conventional tablet dosage form bypassing first pass metabolism. Apart from above fast dissolving buccal films can withstand friable nature when compared to oral dispersible tablets [3-5].

Atenolol drug was chosen because of its anti-hypertensive activity, unavailability of film dosage form in the market and in order to increase its solubility nature and to have a rapid onset of action for hypertensive patients. A fast dissolving film is prepared using hydrophilic polymers by solvent casting technique, using HPMC E-5 a known film forming polymer in combination with glycerine, PEG, TWEEN-80. Fast dissolving film was evaluated for the properties like weight variation, surface pH, folding endurance, dissolving time, drug content estimation, disintegration time, *in-vitro* drug dissolution studies [6]. Salient features of fast dissolving buccal film are easily administered by patients who are mentally ill, disabled and uncooperative. Administration of buccal film requires no water and it has a quick disintegration and dissolution of

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the dosage form. Un obstructive and can be designed to leave minimal or no residue in the mouth after administration and also provides a pleasant mouth feel. There is no risk of chocking [7-11]. Ideal characteristics of drug choosing for fast dissolving film includes drug should have pleasant taste. Drugs with smaller and moderate molecular weight are preferable. The drug should have good stability and solubility in water as well as in saliva. It should be partially unionized at the pH of oral cavity. It should have the ability to permeate oral mucosal tissue.

EXPERIMENTAL WORK

Materials

Atenolol was received as a gift sample from A – Z Pharmaceuticals (Chennai), HPMC E5 was received as a gift sample from A – Z Pharmaceuticals (Chennai). All other chemicals used in this study were of analytical grade.

Methods

Fourier Transformed Infra Red (FT-IR) spectroscopic analysis

FT-IR spectra of pure atenolol, HPMC E5, physical mixture of Atenolol with HPMC E5 and atenolol formulation were analysis. The peaks and patterns produced by pure drug were compared with physical mixture and formulation.

Preparation of atenolol fast dissolving film [12, 13]

Fast dissolving films of atenolol was prepared by solvent casting technique using film forming polymer HPMC E5 as given in table No. 1. Polymer was weighed accurately according to formulation and soaked in water for 1hr for the purpose of polymer swelling. Simultaneously atenolol was weighed accurately and dissolved in 5ml of distilled water. To this drug solution, polymer solutions and glycerin were added and mixed thoroughly with the help of magnetic stirrer and is sonicated for 20 min. for the removal of air bubbles. From this, 15ml of solution was transferred into petridish slowly drop by drop in order to get uniform spread of the solution and it is kept for 24hrs at room temperature for drying. After drying, these film s were removed from the petridish and cut into definite shapes and are packed.

EVALUATION TESTS [14 - 20]

Weight variation

For weight variation three films of every formulation were taken weighed individually on digital balance then average weight was calculated.

Surface pH

The film to be tested was placed in a petridish and was moistened with 0.5 ml of distilled water and kept for 1hr. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and kept for 1 min to allow equilibrium condition.

Folding endurance

The folding endurance was determined by repeatedly folding one film at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance.

Dissolving time

The dissolving time was determined by placing the film in a beaker containing 50 ml of phosphate buffer (pH 6.8). Time required by the film to dissolve completely was noted.

Drug content estimation

A circular film of 2.5cm diameter was cut and placed in a beaker containing 100 ml of phosphate buffer pH 6.8 solutions. The contents were stirred in magnetic stirrer to dissolve the film and the contents were transferred to a 100ml volumetric flask. The absorbance of the solution was measured against the corresponding blank solution at 273 nm. As the absorbance noted above 1mcg/ml, 1ml of the stock was further diluted to 10ml of phosphate buffer solution (pH6.8) and absorbance was measured at 273nm.

Disintegration time

It was determined by using disintegration test apparatus. $5cm^2$ film was placed in the basket, raised and lowered it in such a manner that complete up and down movement at a rate to achieve equivalent to thirty times a minute. Time required by the film to achieve no trace of film remaining above the gauze was noted. All the above evaluation parameters are discussed in table no 2.

In-vitro drug dissolution studies

The dissolution studies were conducted using phosphate buffer pH 6.8 are shown in table 3. Each film strip (containing drug equivalent to 5 mg) was then submerged into the dissolution medium. The dissolution study was carried out using dissolution test apparatus USP type-II at 37^0C, at 50 rpm, using 900 ml phosphate buffer (pH 6.8) as dissolution medium. Test samples were withdrawn at different time intervals and analyzed spectrophotometrically at 273 nm. The absorbance values were transformed into concentration using standard graphic.

RESULTS AND DISCUSSION

IR spectroscopic interactions were conducted to determine possible drug: polymer interactions. IR spectra of pure drug atenolol and physical mixture of atenolol and HPMC E5 were obtained in Figure No. 1. The characteristics peaks of atenolol and polymer were present in the physical mixture, thus indicating no significant evidence of chemical interaction between drug and polymer which confirms the stability of drug. The major

peaks N – H stretching at 3346.85 cm^{-1} , C –N stretching at 1236.03 cm^{-1}, C=C stretching at 1513.85cm^{-1}, aromatic C – H stretching at 2961.91cm^{-1} which were present in pure drug atenolol were also found in physical mixture indicating that there is no interaction between drug and polymer.

All the prepared films (fig 2) were found to be non-tacky. Three films each of 1 cm^2 were cut at three different places from the casted film and weight variation was determined. Weight variation varies from 54mg to 64 mg. It was observed that *in-vitro* disintegration time varies from 12 to 18 sec for all the formulations. *In-vitro* disintegration time of the films was found to be increased with increase in the amount of the polymer.

Folding endurance of film was found to be in the range of 102 to 152. The prepared film formulations were assayed for drug content. Results of drug content showed the uniformity of the drug and less loss of drug content. The surface pH of the films was ranging from 6.71 to 6.81. The surface pH of the films was found to be neutral. The *in-vitro* drug release profiles of the formulations in phosphate buffer pH 6.8 show differences depending on their composition. A rapid dissolution of all the film preparations was observed by the dissolution test. The drug release order of atenolol fast dissolving films prepared by solvent casting technique are given as follows $F_8 > F_7 > F_6 > F_5 > F_4 > F_3 > F_2 > F_1$. F_5 to F_8 drug release was more rapid in films containing tween 80 because of the surfactants causing wetting of film.

Figure 1. IR spectra of atenolol and physical mixture of atenolol and HPMC E5

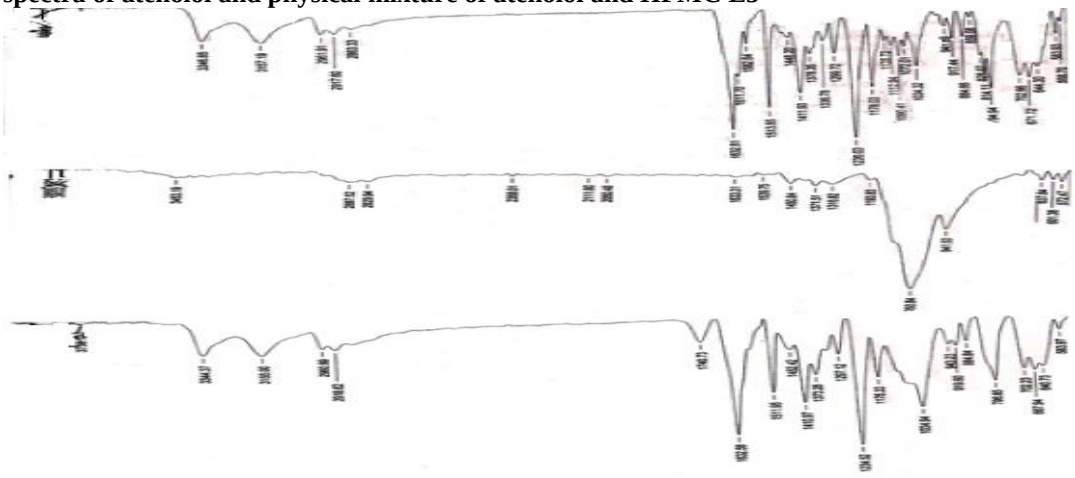
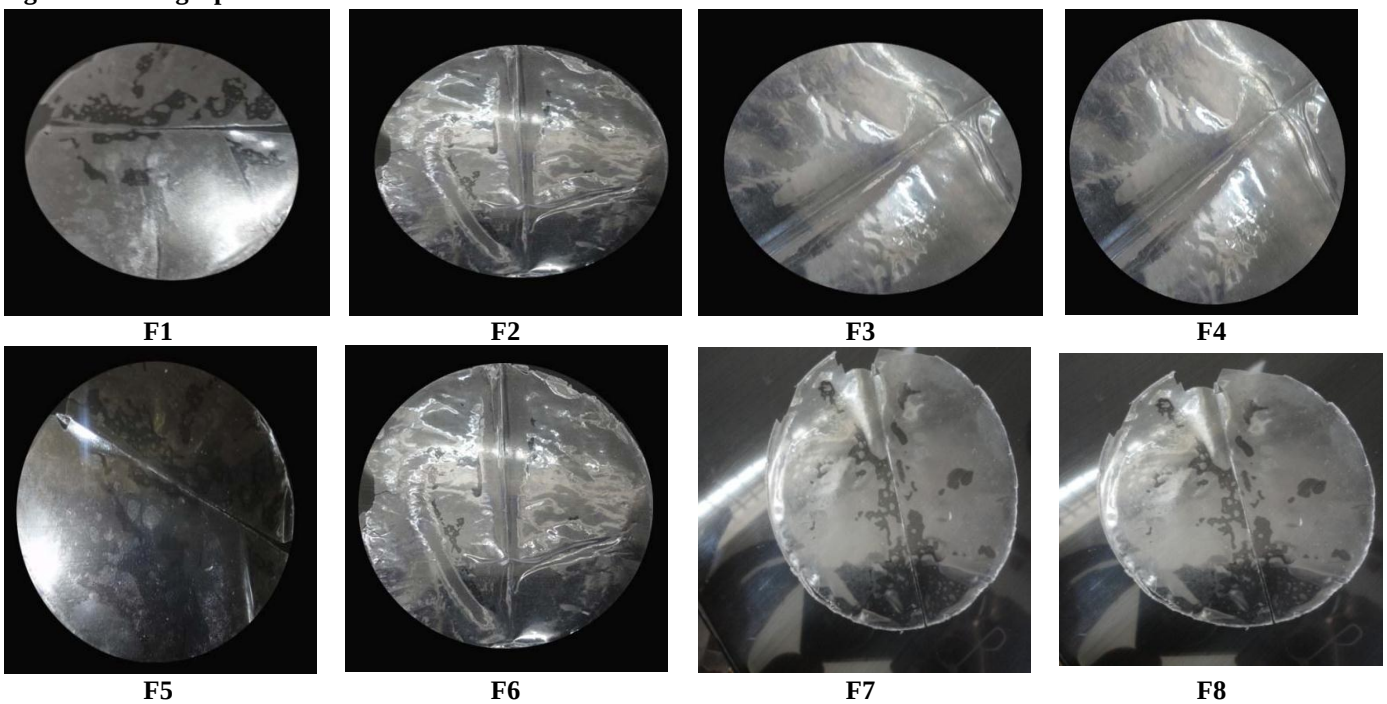


Figure 2. Photographs of films



F1 **F2** **F3** **F4**

F5 **F6** **F7** **F8**

Table 1. Formulation of atenolol fast dissolving films

S No.	Formulations	Atenolol (mg)	HPMC E_5(mg)	PEG (ml)	Tween 80(ml)	Glycerin (ml)	Distilled water (ml)
1	F_1	100	100	0.4	-	0.2	10
2	F_2	100	200	0.4	-	0.2	10
3	F3	100	300	0.4	-	0.2	10
4	F_4	100	400	0.4	-	0.2	10
5	F_5	100	100	0.4	0.5	0.2	10
6	F_6	100	200	0.4	0.5	0.2	10
7	F7	100	300	0.4	0.5	0.2	10
8	F8	100	400	0.4	0.5	0.2	10

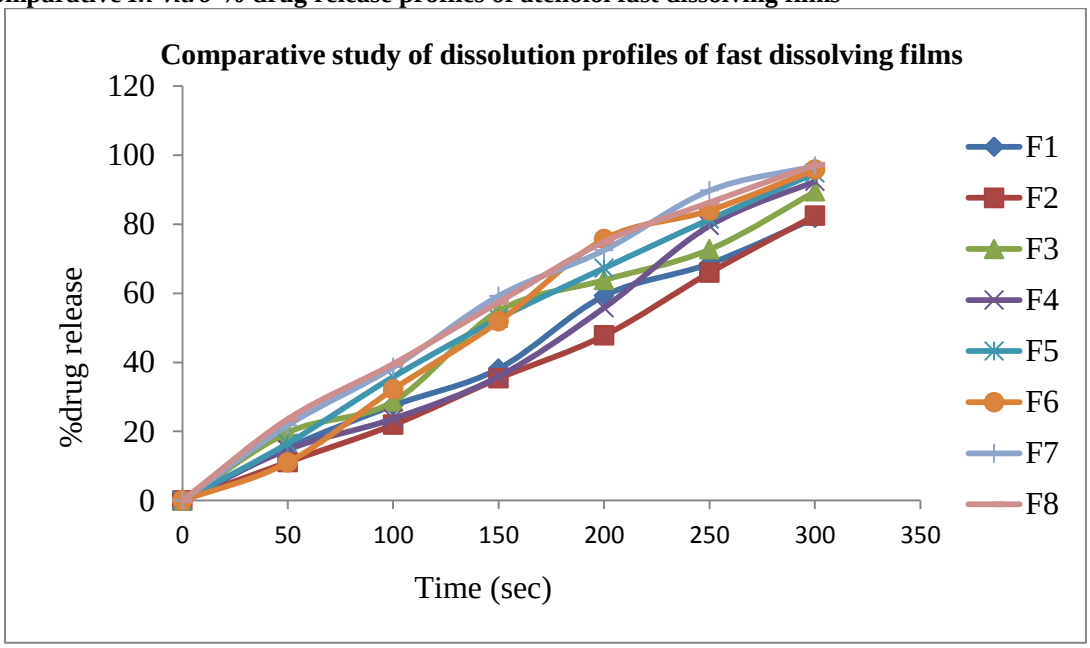
Table 2. Evaluation tests for atenolol fast dissolving films

S No.	Evaluation parameters	Formulations							
		F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	Weight variation (%)	55	58	62	64	54	56	64	59
2	Surface pH	6.73	6.81	6.79	6.78	6.76	6.74	6.73	6.71
3	Folding endurance test	128	134	147	152	103	106	104	102
4	Drug content (%)	71.24	70.8	68.48	87.20	54.4	58.62	68.65	69.47
5	Dissolving time (sec)	53	47	48	38	36	34	46	49
6	Disintegration time (sec)	15	17	18	18	14	12	16	16

Table 3. *In-vitro* drug release profiles of fast dissolving films:

S.NO	Time (sec)	% Drug release							
		F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	0	0	0	0	0	0	0	0	0
2	50	15.3	11.13	19.71	14.76	16.55	11.02	21.78	23.59
3	100	27.5	21.9	28.65	23.67	35.78	32.17	38.58	39.56
4	150	38.16	35.35	54.88	35.92	52.67	51.83	59.23	57.39
5	200	59.25	47.75	63.82	55.78	67.27	75.67	72.45	74.92
6	250	68.56	65.94	72.67	79.54	81.39	83.97	89.72	86.27
7	300	81.78	82.48	89.45	92.34	94.74	95.78	96.85	97.21

Figure 3. Comparative *In-vitro* % drug release profiles of atenolol fast dissolving films



CONCLUSION

The drug release order of atenolol fast dissolving films prepared by solvent casting technique are given as follows $F_8 > F_7 > F_6 > F_5 > F_4 > F_3 > F_2 > F_1$. F_5 to F_8 drug release was more rapid in films containing tween 80 because of the surfactants causing wetting of film. From the characterization studies like *in-vitro* dissolution studies, folding endurance test, it can be concluded that F4 is optimum formulation and also be concluded that presence of tween 80 increses the rapid release of atenolol.

REFERENCES

1. Pankaj Shukla, Panchaxari M Dandagi, Rini Thomas, Sharath Chandra P. Effect of various superdisintegrants on the drug release profile and disintegration time of metaproterenol sulfate orally disintegrating tablets. *International Journal of Biological & Pharmaceutical Research*, 3(1), 2012, 169-176.
2. Habib W et al. Fast-dissolve drug delivery system. *Crit. Rev. Ther. Drug Carrier Syst*, 2000, 17, 61–72.
3. Liang CA, Chen HL. Fast dissolving intraoral drug delivery systems. *Expert Opin. Ther. Patents*, 11, 2001, 981-986.
4. Anderson O, Zweidorff OK, Hjelde T, Rodland EA, Problems when swallowing tablets. *Tidsskr NorLaegeforen*, 115, 1995, 947-949.
5. Joseph F Standing, Catherine Tuleu, Paediatric formulations-Getting to the heart of the problem. *International Journal of Pharmaceutics*, 300, 2005, 56–66.
6. Apoorva Mahajan et al. Formulation and Characterization of Fast Dissolving Buccal Films: A Review. *Scholars Research Library*, 3(1), 2011, 152-165.
7. Reddy LH, Ghose B, Rajneesh. *Indian J.Pharma. Sci*, 64(4), 2002, 331-336.
8. Kuchekar BS, Arumugam V. *Indian J. Pharm. Edu*, 35, 2001, 150.
9. Bhaskaran S, Narmada GV. *Indian Pharmacist*, 1(2), 2002, 9-12.
10. Indurwade NH, Rajyaguru TH, Nakhat PD. *Indian Drugs*, 39(8), 2002, 405-09.
11. Devrajan PV, Gore SP. *Express Pharma Pulse*, 7(1), 2000, 16.
12. Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Sugiyama T, Itoh Y. In vitro and in vivo characteristics of prochlorperazine oral disintegrating film. *International Journal of Pharmaceutical Scienses*, 368(2), 2009, 98–102.
13. Shimoda H, Taniguchi K. Preparation of fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. *European Journal of Pharmaceutics and Biopharmaceutics*, 73, 2009, 361-365.
14. Kulkarni N, Kumar LD, Sorg A. Fast dissolving orally consumable films containing an antitussive and a mucosa coating agent. U.S. Patent 2003, 206942.
15. Juliano C, Cossu M. Preparation, In Vitro Characterization and Preliminary In Vivo Evaluation of Buccal Polymeric Films Containing Chlorhexidine. *AAPS PharmSciTech*, 9, 2008, 1153-1159.
16. Anonymous. American Standard of Testing and Materials, ASTM D1004 - 08Standard Test Method for Tear Resistance (Graves Tear) of Plastic film and Sheeting.
17. Deshmane SV, Joshi UM, Channawar MA. Design and characterization of Carbopol-HPMC based buccal compact containing Propranolol hydrochloride. *Indian Journal of Pharmaceutical Education and Research*, 44(3), 2010, 67-78.
18. Khairnar Amit, Jain Parridhi, Baviskar Rowe Dheeraj, Development of mucosdhsive buccal patch containing aceclofenac: in vitro evaluation. *Internationl Journal of PharmTech Res*, 1(4), 2009, 34-42.
19. Barnhart S. Thin film oral dosage forms, in: Modified release drug delivery technology, Rathborne M, Hadgraft J, Roberts M, Lane M, 2nd edition, *Drugs and the pharmaceutical sciences*, 2000, p. 209 - 216.
20. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. *Journal of Controlled Release*, 139, 2009, 94–97.