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R E S E A R C H A R T I C L E

Formulation and *In-vitro* Evaluation of Alosetron Oral Thin Films

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A B S T R A C T

Alosetron, is a 5-HT_3 antagonist used for the management of severe diarrhea-predominant irritable bowel syndrome. In present study oral thin films of Alosetron were developed to have a faster on set of action. The oralthin films were developed by using polymers Guar gum, Pullulan and PVP K30.Oral thin films were prepared by employing solvent casting method. Propylene glycol was selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F9, and all the formulations were evaluated for various physical parameters Physical appearance, Weight variation, Thickness, Folding endurance, Tensile strength, Drug content, Moisture uptake, Moisture content and all the results were found to be were found to be within the pharmacopeial limits, in-vitro drug release studies by using USP dissolution Apparatus Type II. Among all the 9 formulations F4 formulation which contain Pullulan 10mg and shown 97.06% cumulative drug release within 30 min. And compared to Guar gum, Pullulan and PVP K30, Pullulan showed better drug release profile.

Keywords: Alosetron, Guar gum, Pullulan and PVP K90.

A R T I C L E I N F O

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CONTENTS

1. Introduction

Oral disintegrating film or strip can be defined as, a dosage for that employs a water dissolving polymer which allows the dosage form to quickly hydrate by saliva, adhere to mucosa, and disintegrates, dissolves and releases medication for oromucosal absorption when placed on tongue or oral cavity.

2. Materials and Method

Alosetron, Guar gum, Pullulan , PVP K30, Propylene Glycol, Citric Acid, Aspartame all the chemicals were laboratory grade.

Formulation:

Development of Oral thin films: Oral thin films were prepared by solvent casting method.

Solvent casting method: Guar gum (mg) Pullulan (mg), PVP K30 (mg) were weighed in required ratios and they were then dissolved in water (Cold water) as solvent. Alosetron, Propylene glycol (ml), was added to the above dispersion under continuous stirring sweeteners like aspartame (mg), were also added to the above solution. Citric acid (mg) was also mixed with it. The uniform dispersion was poured in the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the thin films. After 24h, the dried thin film were taken out and stored in desiccator.

Evaluation of oral thin film:

Thickness of the film, Dissolution time, Folding endurance, Percentage of moisture uptake, Moisture content, Tensile strength of the film, Swelling property, Drug content, Weight variation.

Evaluation of Alosetron oral thin films:

Thickness of the film, Dissolution time, Folding endurance, Percentage of moisture uptake, Moisture content, Tensile strength of the film, Swelling property, Drug content, Weight variation.

3. Results and Discussion

Standard Calibration curve of Alosetron:

It was found that the estimation of Alosetron by UV spectrophotometric method at λ_{max}260 nm in 6.8 pH saline phosphate buffer and had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 0.5-3µg/ml.

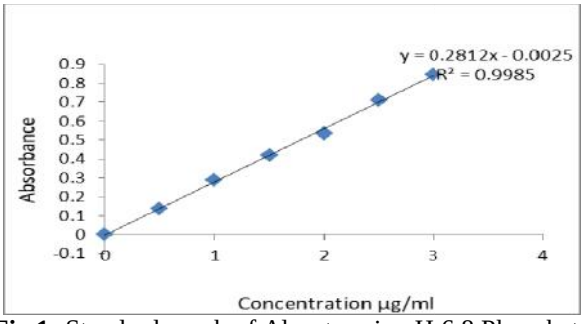

Fig 1: Standard graph of Alosetron in pH 6.8 Phosphate buffer

Flatness: All the Oral thin films were found to be flat without any foams.

The thickness of the films were found to be in the range from 0.3429 mm to 0.3632 mm, 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. The folding endurance of all the formulations was in the range of 105 to 122 results was given in, the drug content of all the films was in the range of 96.51to 99.05 suggesting that drug was uniformly dispersed throughout all films. The films showed weight variation between 28.42 to 32.51. The moisture uptake was found between 1.65% to 5.05% moisture content was found to be 2.17% to 3.23%.

Tensile strength (F4):

The films (10 samples of each) were dried at 60^0C for 24 hrs. Then they were placed in an isometric transducer and the force required for their rapture was measured by an oscillograph. The tensile strength of the patch was found to be **1.69gm/cm^2**

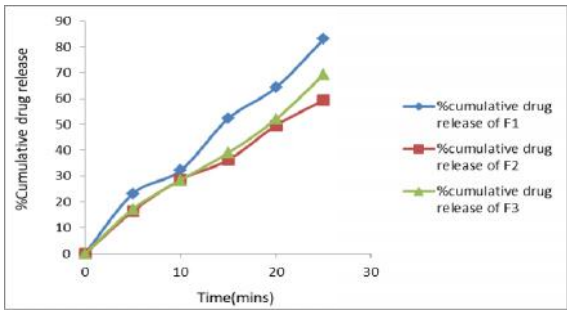

Fig 2: Dissolution graph of all formulations (F1-F3)

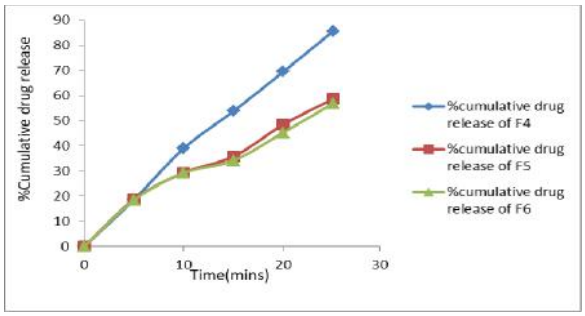

Fig 3: Dissolution graph of all formulations (F4-F6)

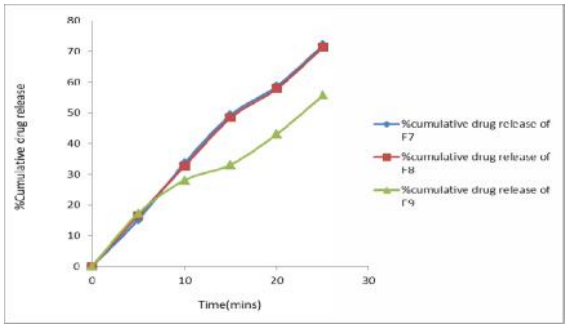

Fig 4: Dissolution graph of all formulations (F7-F9)

The prepared Alosetron oral thin films were evaluated for In-vitro drug release studies, among all the 9 formulations F4 formulation which contain pullulan had shown 97.06% cumulative drug release within 30 min.

4. Conclusion

In present study oral thin films of Alosetronwere developed to have a faster on set of action. The oralthin films were developed by using polymers Guar gum, Pullulan and PVP K30.Oral thin films were prepared by employing solvent

casting method. Propylene glycol was selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F9, and all the formulations were evaluated for various physical parameters Physical appearance, The thickness of the films were found to be in the range from 0.3429 mm to 0.3632 mm, 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. the folding endurance of all the formulations was in the range of 105 to 122 results was given in, the drug content of all the films was in the range of 96.51to 98.76 suggesting that drug was uniformly dispersed throughout all films. The films showed weight variation between 28.42 to 32.51.The moisture uptake was found between 1.65% to 5.05% moisture content was found to be 2.17% to 3.23%, invitro drug release studies by using dissolution apparatus USP Type II. Among all the 9 formulations F4 formulation which contain Pullulan 10mg and shown 97.06.% cumulative drug release within 30 min, and compared to Guar gum,Pullulan and PVP K30. Pullulan showed better drug release profile.

Table 1: Formulations of Alosetron oral thin film

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Drug(mg)	8	8	8	8	8	8	8	8	8
2	Guar gum (mg)”	10	15	20	---	---	---	---	---	---
3	“Pullulan (mg)	--“	---“	---	10	15	20	---	---	---
4	PVP K30” (mg)	---	---	---	---	---	---	10	15	20
5	Propylene glycol(ml)	1	1	1	1	1	1	1	1	1
6	“Citric Acid(mg)	“5	“5	“5	“5	“5	“5	“5	“5	“5
7	Aspartame(mg)	2	2	2	2	2	2	2	2	2
8	Water	QS	QS	QS	QS	QS	QS	QS	QS	QS

Table 2: Concentration and absorbance obtained for calibration curve of Alosetron in (pH 6.8)

S. No.	**Concentration (µg/ml)**	**Absorbance* (at 260 nm)**
1	0	0
2	0.5	0.135
3	1	0.287
4	1.5	0.421
5	2	0.535
6	2.5	0.712
7	3	0.845

Table 3: Evaluation of Oral thin films by physical methods

Formulation	Thickness (mm)	Folding endurance	Drug content (%)	Moisture uptake (%)	Moisture content (%)	Weight variation
F1	0.3465	110	98.67	2.98	2.17	28.42
F2	0.3498	119	99.06	3.05	1.89	30.89
F3	0.3632	105	97.64	5.05	3.23	31.51
F4	0.3541	117	98.51	3.09	3.18	30.52
F5	0.3519	121	97.34	2.93	2.43	31.54
F6	0.3429	114	98.76	2.63	2.19	31.09
F7	0.3467	120	96.51	1.73	3.17	29.25
F8	0.3569	122	98.52	1.65	2.23	32.51
F9	0.3612	106	99.05	2.16	3.19	30.09

Table 4: *In-Vitro* Drug Release

Time (Min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
5	23.19	16.45	17.23	18.65	18.72	18.45	15.21	16.58	17.23
10	32.18	28.61	28.47	39.05	29.41	29.23	33.61	32.61	28.04
15	52.31	36.29	39.01	53.84	35.81	34.24	49.27	48.37	33.13
20	64.29	49.62	52.06	69.51	48.51	45.35	58.72	57.92	43.11

25	83.08	59.43	69.32	85.62	58.72	56.93	72.05	71.43	55.71
30	89.21	72.48	84.05	97.06	73.21	69.23	81.94	80.66	69.23

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