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Research Article

FORMULATION AND EVALUATION OF FAST DISINTEGRATING ORAL THIN FILMS OF CINITAPRIDE HYDROGEN TARTARATE

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A B S T R A C T

Cintapride hydrogen tartarate is a gastro-prokinetic agent and antiulcer agent. It is a substituted benzamide which acts as 5HT1 & 5HT4 receptor agonist and 5HT2 receptor antagonist. In the present study, efforts were taken to develop Fast disintegrating oral thin films of Cinitapride hydrogen tartrate with an objective to achieve rapid disintegration, and further improving the bioavailability of the drug. Also, to resolve the swallowing problems (Dysphasia) in pediatric, geriatric patients by rapid disintegration in saliva and improve the patient compliance. Fast disintegrating oral thin films were prepared by solvent casting method using HPMC E 5, HPMC E 15 and PVP K90 as polymers. The prepared oral thin films were evaluated for thickness, Disintegration time, Dissolution time, Folding endurance, pH, Tensile strength of the film. Among the prepared formulations, the formulation (F1) showed better performance in terms of disintegration time and drug release when compared to other formulations.

INTRODUCTION

Orally fast dissolving films (OFDFs) have been introduced in the market recently as they provide convenience and ease of use over other dosage forms such as orally disintegrating tablets. This technology evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers, so OFDFs are gaining the interest of large number of pharmaceutical industries [1]. Fast dissolving oral thin film drug delivery system is solid dosage form which dissolves in a short period of time when placed in the mouth without drinking water or chewing. They undergo disintegration in the salivary fluids of the oral cavity within a minute, where they release the active pharmaceutical ingredient [2]. A film or strip can be defined as a dosage form that employs a water-dissolving polymer (generally a hydro colloid, which may be a bio adhesive polymer) [4], which allows the dosage form to quickly hydrate, adhere, and dissolve when placed on the tongue or in the oral cavity (i.e. buccal, palatal, gingival, lingual, or sublingual) to provide rapid local or systemic drug delivery [3].

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Oral thin films are useful in patients such a pediatric, geriatrics, bedridden, emetic patients diarrhoea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful whether local action desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething.[7] The oral thin-film technology is still in the beginning stages and has bright future ahead because it fulfils all the need of patients. Eventually, film formulations having drug/s will be commercially launched using the OTF technology [5].

Fast dissolving drug delivery system have acquired great importance in the pharmaceutical industry due to their unique properties and advantages like availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity, no need of water, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste and improved patient compliance especially for pediatric and geriatric.

MATERIALS AND METHODS

Cinitapride Hydrogen tartarate was obtained as gift sample from Symed Laboratories Pvt. Ltd, Hyderabad, Telangana. HPMC E15, HPMC E5, PVP k90, Citric Acid, Propylene Glycol and Aspartame were procured from Asian Scientifics, Hyderabad.

Preparation of standard curve for Cinitapride Hydrogen Tartarate

Standard curves for Cinitapride Hydrogen Tartarate was performed in water, 6.8 pH saline phosphate buffer. Aliquots of 0.5, 1, 1.5, 2, 2.5 and 3 mL of Cinitapride Hydrogen Tartarate standard solution of 100 mcg/mL (*stock solution-II*) was taken and diluted to obtain concentrations from 2 to 12 mcg/mL with appropriate media. The absorbances of solutions were determined at 260 nm against respective media as blank.

Solvent casting method: HPMC E5, HPMC E15 & PVP K90 were weighed in required ratios and they were then dissolved in water (Cold water) as solvent. Cinitapride hydrogen tartrate (31.4mg), Propylene glycol was added to the above dispersion under continuous stirring. 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.

Table 1 Formulations of Cinitapride hydrogen tartarate oral thin film

S.No	Ingredients	F1	F2	F3	F4	F5	F6
1	Drug(mg)	31.4	31.4	31.4	31.4	31.4	31.4
2	HPMC E 15 (mg)	300	450	---	---	---	---
3	HPMC E 5 (mg)	---	---	300	450	---	---
4	PVP K90	---	---	---	---	300	450
4	Propylene glycol(ml)	0.3	0.3	0.3	0.3	0.3	0.3
5	Citric Acid	0.1	0.1	0.1	0.1	0.1	0.1
6	Aspartame	0.1	0.1	0.1	0.1	0.1	0.1
6	Water	15ml	15ml	15ml	15ml	15ml	15ml

Evaluation

Fast disintegrating oral films are evaluated for the following parameters

- Color and Clarity
- Thickness of the film.
- Disintegration time.
- Dissolution time.
- Folding endurance.
- pH.
- Assay
- Tensile Strength
- FTIR

Thickness measurement

Thickness of the film is measured using a dial gauge tester. Thickness at different points is measured from which the average thickness of the fast dissolving oral films was determined [4].

Disintegration time

It is the time at which the film begins to break down when brought into contact with water. It can be determined by keeping a film of desired size in a Petri dish containing water and noting the time it takes to break down

Petri dish methods

2 mL of distilled water was placed in a Petri dish and one film was added on the surface of the water and the time measured until the oral film was dissolved completely.

Measurement of folding endurance

In order to carry out the endurance study, the strip of film is repeatedly folded at the same place until it breaks. The number of times the film is folded at the same place prior to breaking gives the folding endurance.

pH value [6]

The pH value was determined by dissolving one oral film in 2 ml distilled water and measuring the pH of the obtained solution. The pH was measured by using pH paper. Differences were expected because various polymers were used as well as the addition of API.

Assay [7]

The assay was performed to ensure the drug loading onto each film. This test was performed by dissolving the film in phosphate buffer with stirring. The resultant solution was filtered using a whatman filter paper, and the filtrate was diluted to 100 ml with the same buffer in a volumetric flask. Then 1 ml of the filtrate was further diluted to 10ml with buffer. This solution was analyzed using a spectrophotometer at 260 nm.

In vitro dissolution [7]

The *in vitro* drug release study of film was carried out using a rotating paddle dissolution test apparatus. 250ml of phosphate buffer (pH 6.8) was used, and maintained at 37±5°C while the basket was set at 50 rpm. A film sample of 4 $cm^2$was fixed onto the specially designed SS disk with the help of cyanoacrylate adhesive. The disk was put at the bottom of the dissolution vessel so that the patch remained on the upper side of the disk. Five milliliters of samples were taken at a interval of 60 sec., and the same amount was replaced with fresh buffer. The withdrawn samples were filtered through Whatmann filter paper and then 1ml of the filtered sample was further diluted to 10ml of the same medium and analyzed using a spectrophotometer at a wavelength of 260 nm. The cumulative percentage release for different formulations was calculated. The relationship between time and percentage release were plotted. The results of in- vitro dissolution studies of all formulations

Tensile strength

Tensile strength of the film is determined by using a tensile testing machine like the Instron tester. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below.

$$\text{Tensile strength} = \frac{\text{Load Failure} \times 100}{\text{Strip thickness X Strip width}}$$

Drug excipients interaction studies: FT-IR spectrum interpretation: IR spectral analysis was carried out using FT-IR by the KBr disc method. The sample and KBr were triturated and compressed to get the discs. The samples of pure drug, dummy formulation and optimized formulation were analyzed between wave numbers 4000.0 and 400.0 cm^{-1}.

RESULTS AND DISCUSSION

It was found that the estimation of Cinitapride Hydrogen tartarate 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, 2-12µg/ml.

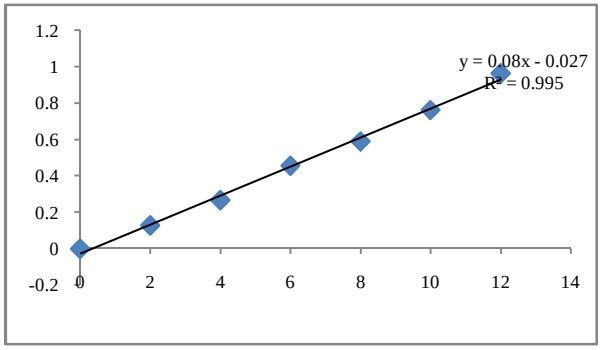

Fig 1 Standard graph of Cinitapride Hydrogen tartarate in pH 6.8 Phosphate buffer

Evaluation of Cinitapride Hydrogen tartarate oral thin films

Physical appearance: All the Oral thin films were visually inspected for colour and clarity.

Table No.2 Evaluation of Oral thin films by physical methods

Formulation	Thickness (mm)	Folding endurance	Drug content (%)
F1	0.3569	20	45
F2	0.3520	25	65
F3	0.3470	27	57.5
F4	0.3496	24	60
F5	0.3460	30	67.5
F6	0.3517	32	92.5

The prepared Cinitapride Hydrogen tartarate Oral thin films were evaluated for Physical appearance, Weight variation, Thickness, Folding endurance, Drug content, and all the results were found to be within the pharmacopeial limits.

Tensile strength (F1)

The patches (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 1.63 gm/cm^2

FTIR Studies

Table No. 3 In-Vitro Drug Release

Time (Min)	F1	F2	F3	F4	F5	F6
5	24.6	18.2	21.7	17.7	16.2	14.8
10	39.7	29.7	34.3	26.4	31.6	23.4
15	56.3	37.3	51.2	34.8	48.4	31.2
20	72.4	49.8	67.7	44.5	56.7	40.1
25	84.1	61.3	79.6	56.7	69.2	51.7
30	97.2	87.8	89.9	79.2	83.9	69.2

The prepared Cinitapride Hydrogen tartarate oral thin films were evaluated for In-vitro drug release studies, Among all the 6 formulations F1 formulation which contain HPMC E 15 had shown 97.2% cumulative drug release with in 30 min.

Table No 4 Disintegration time

S.No	Disintegration Time (Sec)
F 1	39
F 2	47
F 3	43
F 4	56
F 5	59
F 6	68

CONCLUSION

In present study oral thin films of Cinitapride Hydrogen tartarate were developed to have a faster on set of action. The oral thin films were developed by using polymers HPMC E5, HPMC E 15 and PVP K90. 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 evaluated for various physical parameters Physical appearance, Weight variation, Thickness, Folding endurance, Tensile strength, Drug content, and all the results were found to be within the pharmacopeial limits, *in vitro* drug release studies by using dialysis membrane. Among all the 6 formulations F1 formulation which contain HPMC E15 300mg and shown 97.2% cumulative drug release within 30 min. And compared to HPMC E15, HPMC E5, and PVP K90, HPMC E 15 showed better drug release profile.

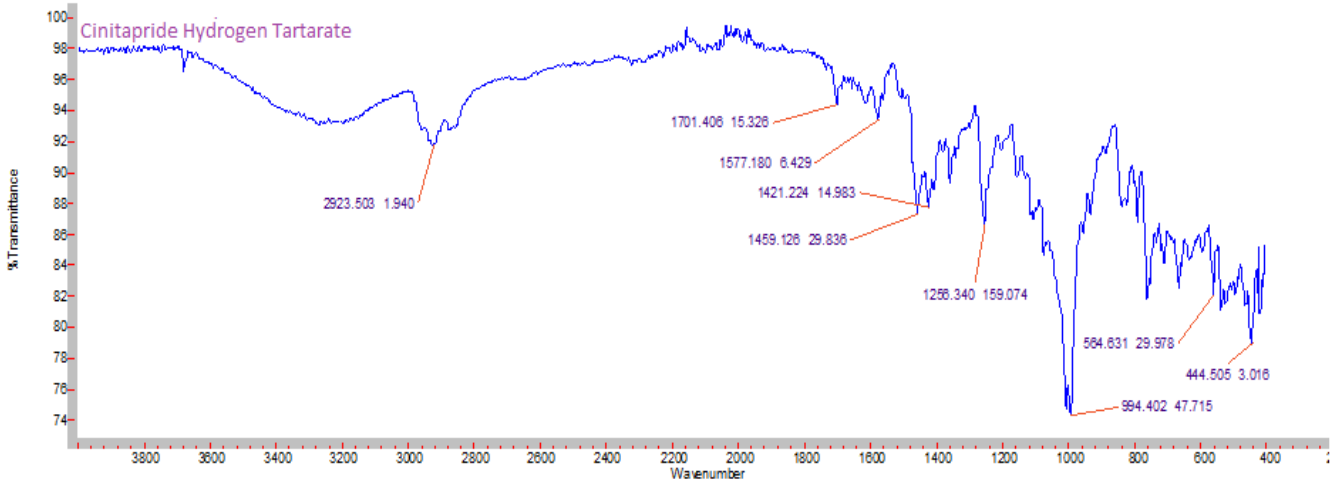

Figure No 2 FTIR of Pure Cinitapride Hydrogen Tartarate

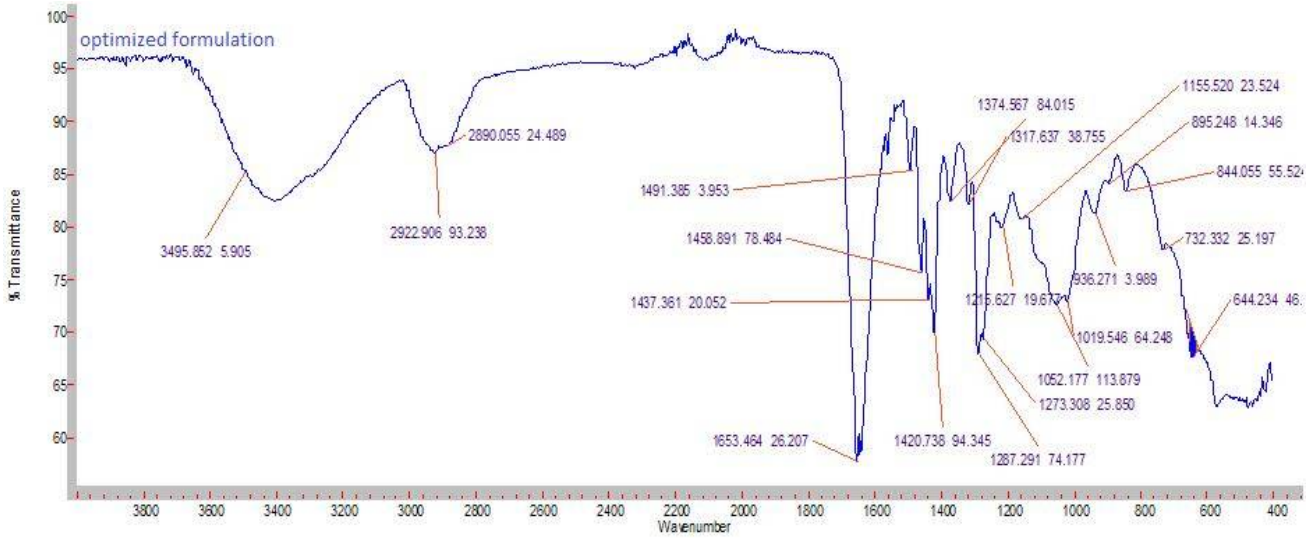

Figure No 3 FTIR of Optimized formulation F1

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References

1. PK Joshi, H Patel, V Patel, R Panchal. Formulation development and evaluation of mouth dissolving film of Domperidone. *Journal of Pharm Bioallied Sciences* 2012; 4:108-95.
2. A Dinge, M Nagarsenkar. Formulation and evaluation of fast dissolving films for the delivery of Triclosan to the oral cavity. *AAPS Pharm SciTech* 2008; 9 (2):349-56.
3. PV Shelke, AS Dumbare, MV Gadhave, SL Jadhav, AA, DD Sonawanne, Gaikwad. Formulation and evaluation of rapidly disintegrating film of Amlodipine Besylate. *Journal of drug delivery & Therapeutics* 2012;2(2):72-5.
4. A Doaa, S Nevine. Formulation of a novel Tianeptine sodium orodispersible film. *AAPS Pharm SciTech* 2010; 11(3):1018-25.
5. C Francesco, EC Irma, M Paola, B Susanna, S Francesca, GM Chiara, M.Lusia Nicotine fast dissolving films made of Maltodextrins:A feasibility study. *AAPS Pharm SciTech Dec* 2010; 2(4):1511-17.
6. B.W.Barry, Lipid-protein-partitioning theory of Skin Penetration Enhancement; *J. Control, Rel. 1991; 15:237-248*
7. SS Agrawal Permeation studies of atenolol and metoprolol tartarate form three different polymer matrices for Transdermal delivery. *Ind J Pharm Sci. 2007: 535-9.*
8. B W Barry "Dermatological Formulations: Percutaneous Absorption", Drugs and pharmaceutical sciences, *MARCEL DEKKER, INC. 1983; 18:1-39.*
9. M Saxena, Formulation and evaluation of Transdermal patches of metoclopramide hydrochloride. Indian drugs. 2006; 43(9):740-5.

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