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Original Article

Comparative study of Cross povidone and Cross Carmellose Sodium to formulate Immediate Release Tablet of Theophylline

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ABSTRACT

Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablet and capsules. One important drawback of these dosage forms for some patients is the difficulty to swallow. Dysphagia or difficulty in swallowing is common among all age groups. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Fast disintegration tablets are not only preferable for people who have swallowing difficulties, but also are ideal for active people. In this study formulation of immediate release tablet with two different super disintegrants i.e. Cross Carmellose Sodium and Crosspovidone was carried out to study the disintegrating time of IRTs and various other parameters were also noted down.

Keywords: Fast dissolving tablet, immediate release tablet, Theophylline

INTRODUCTION

Fast dissolving drug delivery system (FDDDS) are a new generation of formulation which combine the advantages of both liquid and conventional tablet formulation and at the same time, offer added advantages over both the traditional dosage forms. They provide the convenience of a tablet formulation and also allow the ease of swallowing provided by a liquid formulation. FDDDS offer the luxury of much more accurate dosing than the primary alternative oral liquids. This segment of formulation is especially designed for dysphagic, geriatric, bed-ridden, travelling and psychotic patients who are unable to swallow or refuse to swallow conventional oral formulations.[2]

The FDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and/or quick disintegrating tablet. All FDTS approved by the food and drug administration (FDA) are classified as orally disintegrating tablets. Recently, the European pharmacopoeia adopted the term oro-dispersible tablet for a tablet that disperse or disintegrating in less than 1-2 min in the mouth before swallowing. Such a tablet disintegrates into smaller granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. The disintegrating time for good FDTs varies from several seconds to about a minute.

Need For Development of IRTs

Patient factors:

- patients who have difficulty in swallowing or chewing solid dosage forms
- patient's incompliance due to fear of choking
- very elderly patients of depression who may not be able to swallow the solid dosage forms
- an eight-year-old patient with allergies desires a more convenient dosage form than antihistamine syrup
- a middle-aged patient undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2- blocker
- a schizophrenic patient who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic
- a patient with persistent nausea, who may be journey, or has little or no access to water.

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Effectiveness Factor: Dispersion in saliva in oral cavity causes pre-gastric absorption of drug which dissolves. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. Any pre-gastric absorption avoids first pass hepatic metabolism which increase the bioavailability

MATERIAL AND METHOD

Material: Theophylline was taken as drug gifted sample from Cipla and other excipients like CCS and crosspovidone was purchased from Loba Chemicals.

Methods

Direct Compression Method: The drug and all excipients were mixed together to get uniform mixing of drug and excipients and sieve through sieve no 120 to get uniform particle size for enhancing flow as well as compression properties.

FORMULATION OF IRTs:

INGREDIENTS	IRT1	IRT2	IRT3	IRT4	IRT5	IRT6
Theophylline	50	50	50	50	50	50
CCS	5	10	15	-	-	-
Crosspovidone	-	-	-	5	10	15
Lactose	40	35	30	40	35	30
Mg stearate	3	3	3	3	3	3
Talc	2	2	2	2	2	2

COMPATIBILITY PARAMETERS OF IRTs: Compatibility studies include the compatibility of excipients with api present in the formulation. Compatibility studies include the four weeks study data in humidity chamber. The drug is mixed with all excipients in different vials using ratio mikxture of 1:1 to ensure proper mixing and incompatibilities. To accesses the incompatibilities fourier transmission infrared spectroscopy was performed. The incompatibility data is attached below:

Figure 1: FTIR STUDY OF THEOPHYLLINE

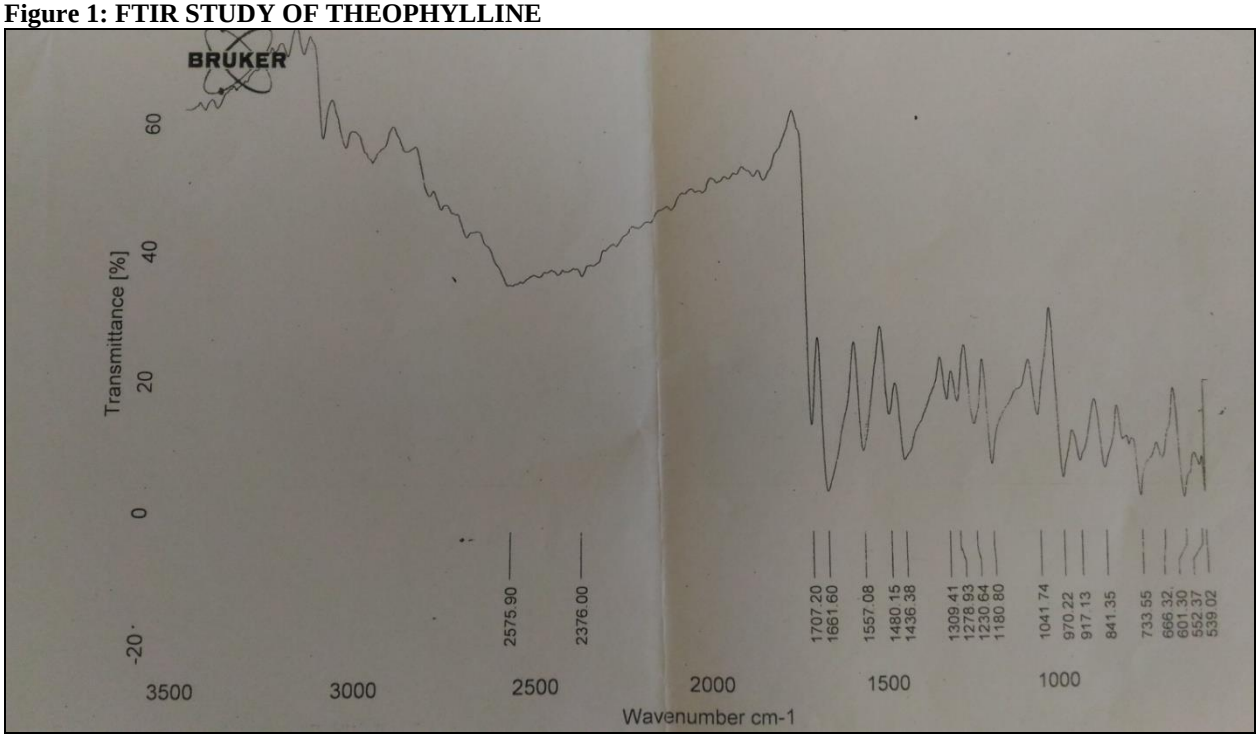


Figure 2: FTIR STUDY OF THEOPHYLLINE AND CROSSPOVIDONE

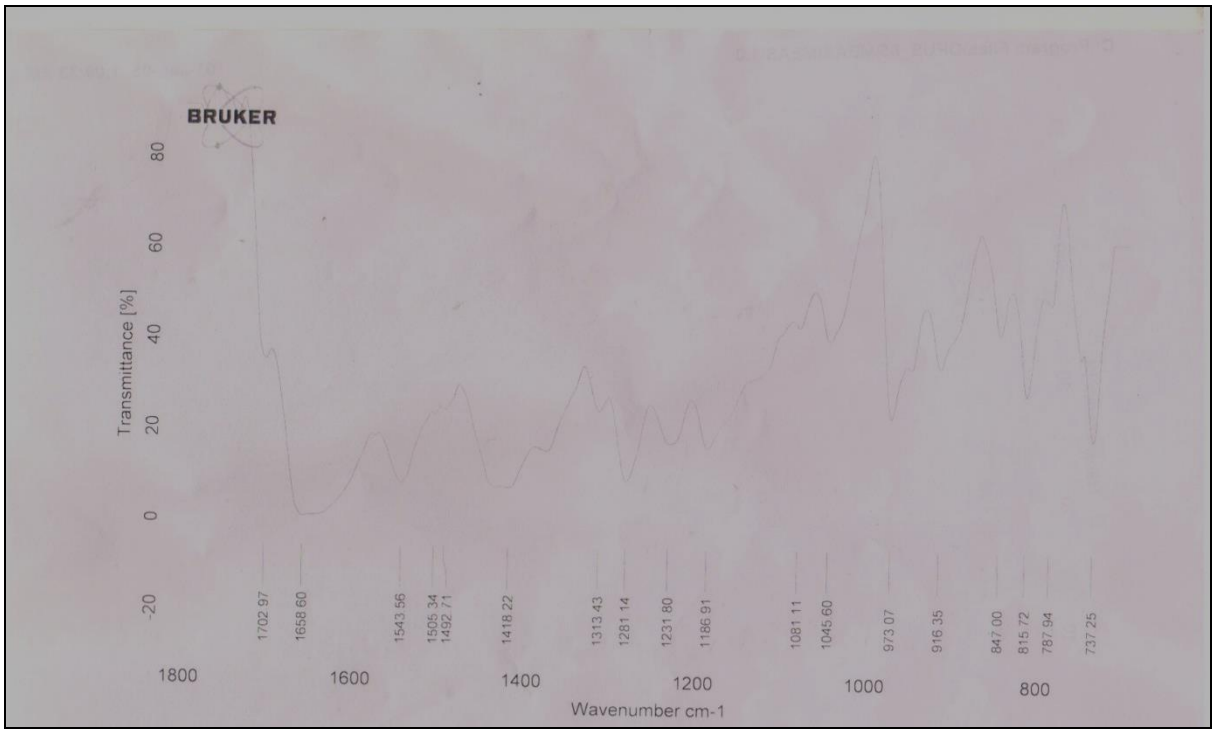


Figure 3: FTIR STUDY OF THEOPHYLLINE AND CCS

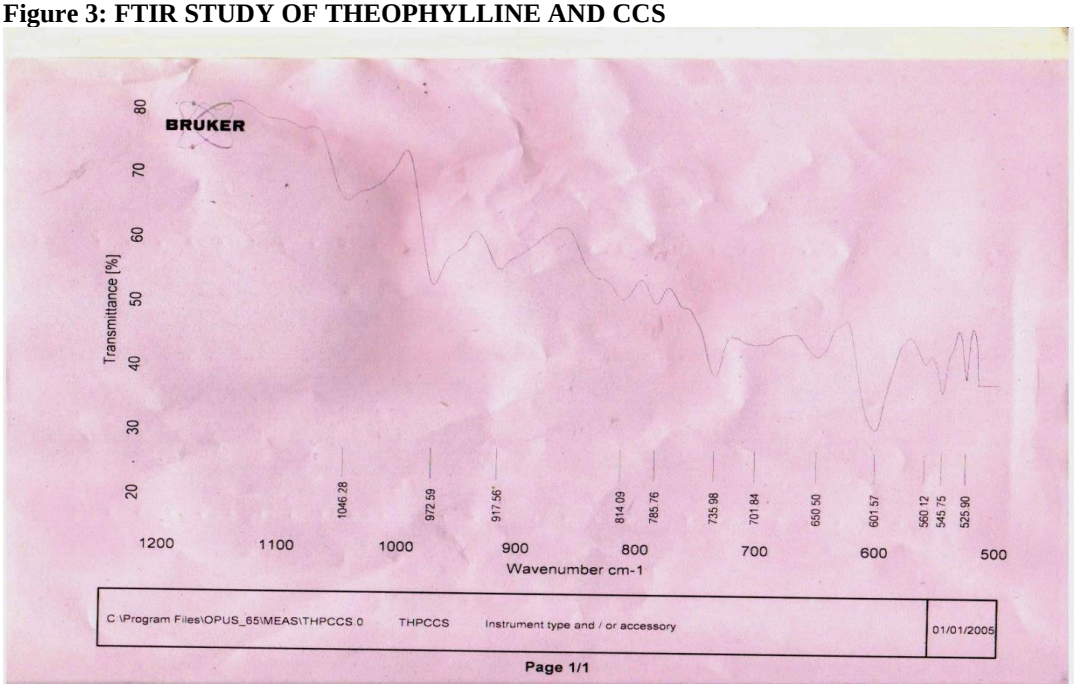


TABLE 1- PHYSICAL CHANGES AND PEAK OBSERBANCE IN FTIR

Mixture	Week 1 Physical Changes	Week 2 Physical Changes	Week 3 Physical Changes	Week 4 Physical Changes	IR Peaks (cm^{-1})	λ max (nm)
Drug	-	-	-	-	1705 1663 1084	271
Drug + Cross-povidone	-	-	-	-		271
Drug + CCS	-	-	-	-		271

EVALUATION PARAMETERS OF IRTs

POST COMPRESSION PARAMETERS OF IRT:

Thickness: Thickness of tablet is determined by the using digital micrometer.

Weight Variation: For weight variation test 20 intact tablets are weighed individualy to find out the intact weight of each tablet.

Friability: Friability test is done to know about the wear and tear losses during transport and handling of the tablets. Friablity test of tablet was done in the Roche type friabillator.

Hardness: Hardness parameter is determined for the disintegration time and various other parameters like solubility and bioavailability of the drug. Hardness parameter is done by the Pfizer type hardness tester.

MODIFIED DISINTEGRATION METHOD FOR IRT:

Modified method: Disintegration of fast dissolving tablets is achieved in the mouth owing to the action of saliva, however amount of saliva in the mouth is limited and no tablet disintegration test was found in USP and IP to simulate *in vivo* conditions. A modified method was used to determine disintegration time of the tablets.

Parameters / Formulations	Thickness (mm)	Weight variation(mg)	Friability (%)	Hardness (kg/cm^2)
IRT 1	4.510±0.021	97.9±3.176	0.89±0.046	2.9±0.133
IRT2	4.258±0.034	99.2±2.923	0.85±0.045	2.7±0.113
IRT3	3.319±0.008	101.6±3.765	0.82±0.060	2.8±0.109
IRT4	3.385±0.016	96.4±3.874	0.91±0.057	2.5±0.165
IRT5	3.609±0.339	100.4±4.246	0.89±0.072	2.5±0.165
IRT6	3.523±0.028	101.9±3.876	0.85±0.029	2.6±0.146

Post compression parameters of IRT

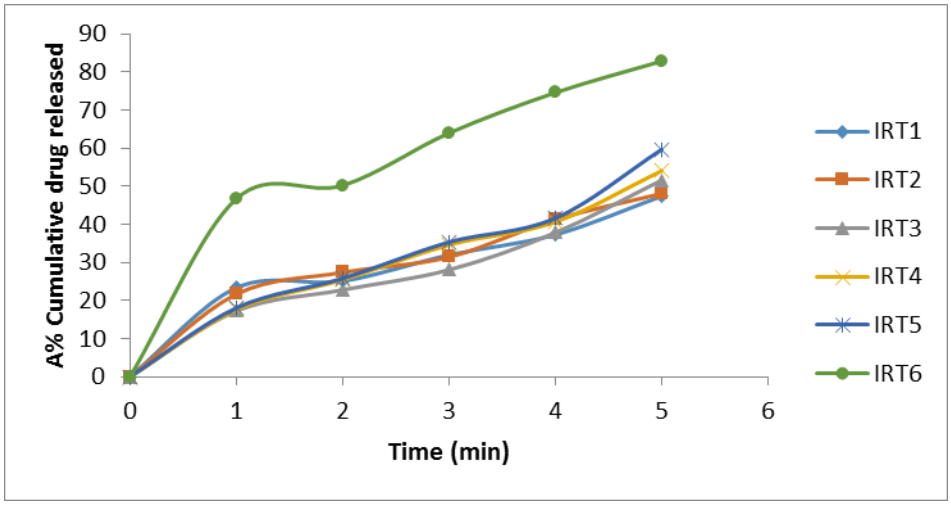
In phosphate buffer 6.8: A cylindrical vessel was used in which 10-meshscreen was placed in such way that only 2 ml of disintegrating or dissolution medium would be placed below the sieve. To determine disintegration time, 6 ml of phosphate buffer (pH 6.8), was placed inside the vessel in such way that 2 ml of the media was below the sieve and 4 ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. Six tablets were chosen randomly from the composite samples and the average value was determined.

DISSOLUTION STUDIES OF IRTs

Dissolution test is done in USP-2 apparatus according to US pharmacopoeia parameters.

Time (min)	% Cumulative drug released					
	IRT1	IRT2	IRT3	IRT4	IRT5	IRT6
0	0	0	0	0	0	0
1	23.34±0.124	21.66±1.37	17.28±0.875	17.64±0.236	18.06±2.67	46.68±3.96
2	25.10±0.320	27.38±1.569	22.8±0.396	25.45±2.34	25.82±3.68	50.21±1.269
3	31.9±0.163	31.43±0.346	28.06±1.96	34.60±3.214	35.32±1.69	63.94±2.968
4	37.28±0.621	41.30±2.39	37.81±2.96	40.64±1.96	41.60±0.569	74.57±0.987
5	47.4±0.984	48.07±0.962	51.59±2.386	54.07±3.5	59.65±0.1.86	82.82±3.01

GRAPHS FOR IRTs



Zero order release of IRTs

SUMMARY AND CONCLUSION:

In this study we found that IRT6 i.e formulation having higher amount of Crosspovidone posses higher dissolution rate than any other formulation. Crosspovidone act as super disintegrants leads to super bursting of tablet in media which increase the dissolution rate of tablet and prefound release of drug was seen in this case.

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