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Formulation and Evaluation of Fast Dissolving film of Granisetron Hydrochloride

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Abstract

The objective of present research work was to develop Fast Dissolving film of Granisetron Hydrochloride for treatment of emesis and to increase dissolution profile to get fast onset of action.In this present study various concentration of HPMC K-15 and Pullulan were selected on the basis of extensive literature survey. Various concentration of both film forming agents were prepared in ten batches as MOF-I to MOF-X. The optimization of film forming agents was done on basis of general appearance, thickness and weight. The optimized oral film shows good tensile strength, percentage elongation and folding endurance. The dissolution data revealed that all drugs release within 30 min and release were constant after 40 min which shows the fast release of the drug from films.On comparing the dissolution data of optimized batch with marketed Tablet Grandem- 2mg (aristo pharmaceuticals).

It was found that optimized film shows better on set of action and may show better bioavailability than tablet. Hence film can be used as alternative dosage form for treatment of emesis. .

Keywords: Emesis, Fast Dissolving Films, HPMC, Pullulan, Optimization

Introduction

Some patients have difficulties in swallowing or chewing solid dosage which forms risk or fear of chocking so this is a major problem in the use of tablets. Oral dissolving film is a new drug delivery system for oral delivery of drug. Oral film a type of film which is used in acute condition such as pain, antiemetic, anti-migraine, anti-hypertension, congestive heart failure, and Asthma etc. oral dissolving film has gained popularity due to its availability in various size and shape[(1)]. Oral dissolving films are intended to disintegrate or dissolve within seconds. They offer advantages such as administration without water, rapid onset of action and convenience of dosing. For fast dissolving active pharmaceutical ingredients absorption is possible through the oral mucosa and may improve bioavailability [(2)].

A variety of polymers are available for preparation of Oral solids. The polymers can be used alone or in combination to obtain the desired strip properties. The film obtained should be tough enough so that there won't be any damage while handling or during transportation. The robustness of the strip depends on the type of polymer and the amount in the formulation [(3)]. On the other hand, fastdissolving strip dosage form should have the property to disintegrate in seconds when placed in mouth and deliver the drug to the oral cavity instantaneously.

As the strip forming polymer (which forms the platform for the Oral solids) is the most essential and major component of the Oral solids, at least 45%w/w of polymer should generally be present based on the total weight of dry Oral solids.

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Of the various polymers available, pullulan, gelatin and hypromellose are most commonly used for preparation of Oral solids.

Plasticizer is a vital ingredient of the Oral solids formulation. It helps to improve the flexibility of the strip and reduces the brittleness of the strip. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of strip. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer [(4).] Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, Citrate derivatives such astributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients. Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The sweet taste in formulation is more important in case of pediatric population. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations. Suitable sweeteners include: (a) water soluble natural sweetener: xylose, ribose, glucose, sucrose, maltose, steviosideetc (b) water soluble artificial sweetener: sodium or calcium saccharin salts, cyclamate salts, acesulfame-k etc (c) Dipeptide based sweetener: aspartame (d) protein basedsweeteners:thaumatin I and II. The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol, isomalt and maltitol can be used in combination as they additionally provide good mouth-feel and cooling sensation [(5)]

Closed-angle glaucoma: In this kind, the iris-cornea angle becomes partially or totally closed, obstructing the flow of aqueous humour and raising IOP as a result.[12,16] There may or may not

Vomiting is to be differentiated from retching, regurgitation or rumination. Retching or dry heaves involves the same physiological mechanisms as vomiting, but occurs against a closed glottis; there is no expulsion of gastric contents. Regurgitation is the return of small amounts of food or secretions to the hypo pharynx in the context of mechanical obstruction of the esophagus, gastro esophageal reflux disease or esophageal motility disorders. Rumination is similar to regurgitation, except small amounts of completely swallowed food are returned to the hypo pharynx from the stomach and is often re-swallowed. Rumination is not associated with nausea [(6)]

Granisetron hydrochloride is a selective serotonin (5HT3) receptor antagonist and used in treatment of chemotherapy induced nausea and vomiting (CNIV), post operative nausea and vomiting and others. When given at doses of 2-4 mg per day. After single, 2 mg oral dose of Granisetron Hydrochloride and peak plasma concentration are achieved within 2-3 hr. the pharmacokinetics of Granisetron hydrochloride exhibit considerable inter individual variation and the elimination half life is reported to be around 3 to 4 hours in normal subjects and 9-12 hours in cancer patients.

Recent developments in the technology have presented viable dosage alternatives from oral route for pediatrics, geriatric, bedridden, nauseous or noncompliant patients. Buccal drug delivery has lately become an important route of drug administration. Various bioadhesive mucosal dosage forms have been developed, which includes adhesive tablets, gels, ointments, patches and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving films.

The objective of present research work was to develop Fast Dissolving film of Granisetron Hydrochloride for treatment of emesis and to increase dissolution profile to get fast onset of action.

Material and Methods

Materials

Granisetron Hydrochloride was obtained as gift samples Amneal Pharmaceutical. HPMC K-15, Pullulan, Cross Povidone, Cross Carmellose were obtained from Tirupati Balaji Pharmaceuticals. All other Chemicals used of Analytical grades and

all Solvents used for analysis were of HPLC grade.

Methods

Casting process of fast dissolving oral film:

Various methods are available for casting of oral films. Solvent casting technique on the laboratory scale was used for the preparation of fast dissolving oral film.

7.2.1.1 Solvent Casting Technique [7-8]

The method of solvent casting technique involves preparation of the film base which involves the mixing of suitable film forming excipients along with drug in a suitable solvent or solvent system. Once the solution is prepared, the film casting process is performed wherein a film of desired thickness is casted onto a moving inert substrate, where suitable rollers are employed for guiding the solution onto the substrate. The clearance or tolerance between the roller and the substrate determines the required thickness of the film; this process is used in large scale production wherein glass or teflon plates can be used as inert support material to cast a film at the laboratory scale. The formed strip is then subjected to drying process to remove the solvent.

The selection of solvent essentially depends on the API to be incorporated into the film. The physicochemical properties of the API like heat sensitivity, shear sensitivity, the polymorphic form of the API employed, compatibility of the API with solvent and film based excipients are to be critically studied. The predominant factors to be considered are liquid rheology, desired mass to be casted and uniformity of drug content. Solvent systems used in the preparation of solution or suspension should be selected carefully and more preferably from ICH Class 3 solvent list.

Heating processes can be used to assist the complete dissolution of materials. Mixing may cause formation of air bubbles and their entrapment during the solution preparation. Entrapped air tends to produce uneven films, deaeration step is imperative to get a uniform film which may be achieved by vacuum assisted machines.

Another important aspect is the moisture present in the solution. It is observed that moisture can cause changes in the mechanical properties of the films such as tensile strength, flexibility, folding endurance, young's modulus, elongation etc. Hence care should beexercised by using suitable humidity controls in the manufacturing production area. The solution is subjected to continuous mixing process in order to keep the viscosity and concentration unchanged. The solution or suspension may be kept under controlled temperature condition to achieve the desired viscosity of the material.

Table 1: List Various Ingredients used in preparation of films

S.NO.	NAME OF INGREDIENTS	Use in formulation
1	Granisetron Hydrochloride	API
2	HPMC K-15	Film Forming Agent
3	Pullulan	Film Forming Agent
4	Gum Acacia	Co-Film Forming Agent
5	Polyethylene Glycol-4000	Plasticizer
6	Glycerine	Plasticizer
7	Di-Butyl Pthalate	Co-Plasticizer
8	Sodium Starch Glycolate	Super Disintegrating Agent
9	Cross Povidone	Super Disintegrating Agent
10	Cross Carmellose	Super Disintegrating Agent
11	Sucralose	Sweetening Agent
12	Citric Acid	Saliva Stimulating Agent
13	FDA Approved Colorant (Yellow)	Colouring Agent
14	Demenralized Water	Solvent

Steps of preparation of films [9]

Weighing of all ingredients

The all solid material properly weighed by pre calibrated electronic balance (Citizen) and all liquid materials were also measured properly. Then all materials were properly labeled.

Mixing and stirring of contents

The all pre weighed material were mix properly on mechanical stirrer at controlled speed. The all material was added in solvent and then liquid material was added during stirring. The stirring speed of stirrer was kept at 200-500 RPM and temperature was set at 25-30^{0}C.The mixing was

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continued till clear, transparent solution was obtained.

Sonication of solution

After complete mixing of all ingredients the clear solution was sonicated to remove dissolved air which may appear during mixing process. The sonication was done by using bath sonicator. Three cycle of sonication of 5-10 sec was performed for complete removal of air.

Transfer of solution to glass reservoir

A 20.0 x 8.0 cm^2 sized film casting glass reservoir was fabricated having depth of 0.5cm. This sized film casting glass reservoir will produce 2.0 x 2.0 cm^2 size films. Before transferring the solution to glass reservoir the oil is spread over surface of glass reservoir to ensure proper removal of film after drying. Then the solution was carefully poured in to glass reservoir uniformly to ensure uniform thickness of film.

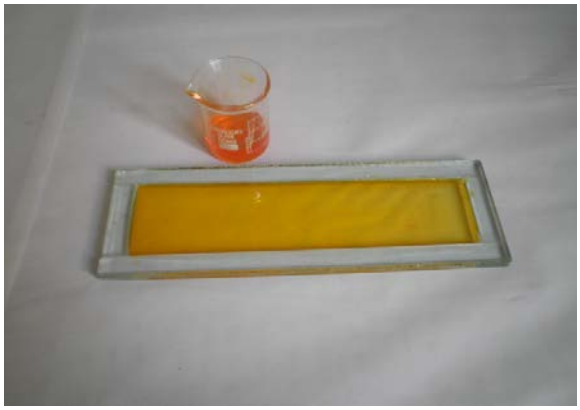

Figure 1: Transfer of Solution in to glass reservoir

Drying of film

Preliminary study suggests that 40 ± 1.0^{0}C for 12 hrs adequately dry the film. The drying was done in oven at constant temperature. The drying of film was done under controlled evaporation to assure no air entrapped during the drying process.

Removal of film from glass reservoir

After complete drying of film, the film was carefully removed from glass reservoir. The removal was easily performed as already food grade oil was used for lubrication. After complete removal of film it was ready to cut in appropriate size.

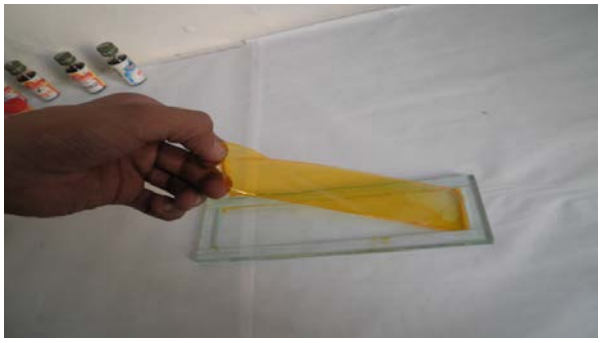

Figure 2: Removal of film from glass reservoir

Figure 3: Film ready to cut in appropriate size

Sizing of films.

After complete removal of films it was cut in to appropriate size for administration in oral cavity. The films were cut in to 2 X 2 cm^2.

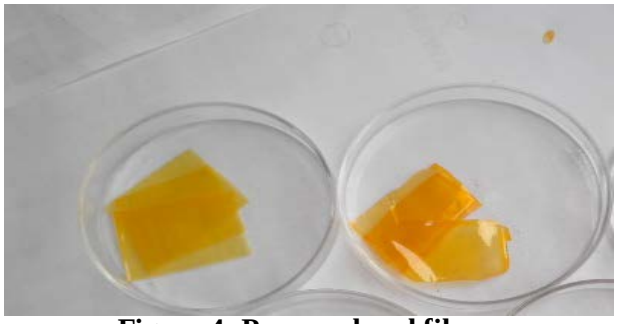

Figure 4: Prepared oral films

Optimization of films 108

The optimization is basic step for research. The optimization was performed by EVOP (Evolutionary Operation) method. This method is widely used in research and industry. This method evolves around one basic formula, this evaluation done by carefully planning and repetition. In this type of optimization the factors are optimized one by one. The advantage of this method is that it avoids excess preparation of batches and hence it

is cost effective, requires less time and usage of fewer chemicals.

The manufacturing of films depends on many factors such as type and concentration of film formers, type and concentration of plasticizers, type and concentration of super disintegrating agents, type of methods employed in manufacturing and type of solvent system etc. Out of all factors, following three important factors were selected for optimization processSelection of Film Forming Agents

2. Selection of Plasticizers
3. Selection of Super disintegrating agents

The optimization of films was firstly done without drugs. The optimizations of all factors were done on the basis of general appearance, thickness, folding endurance, tensile strength, and percentage elongation and disintegration time.

Selection and optimization of film forming agents:

Two film forming agents and one co-film forming were selected for this research work. The concentration of film forming was important to form a proper thickness for appropriate packaging and handling of oral films. The two film forming agents like HPMC K15 and Pullulan at different concentration were taken. [235,236]

Concentration of film forming agent is optimized on the basis of thickness and appearance of film.

Table 2: Optimization of Film forming agents with their formulation code

Name of Ingredients	Formulation codes with weight of ingredients									
	MOF-I	MOF-II	MOF-III	MOF-IV	MOF-V	MOF-VI	MOF-VII	MOF-VIII	MOF-IX	MOF-X
API	-	-	-	-	-	-	-	-	-	-
HPMC K15	2400	3000	3600	4200	4800	-	-	-	-	-
Pullulan	-	-	-	-	-	2400	3000	3600	4200	4800
Gum Acacia	200	200	200	200	200	200	200	200	200	200
Glycerine	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml
PEG-4000	150	150	150	150	150	150	150	150	150	150
DBP	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml
SSG	200	200	200	200	200	200	200	200	200	200
Sucralose	120	120	120	120	120	120	120	120	120	120
Citric Acid	120	120	120	120	120	120	120	120	120	120
DM Water Qs	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32mL	32mL	32mL	32mL

Selection and optimization of plasticizer:

Two film plasticizer and one co- plasticizer were selected for this research work. The concentration of plasticizer was important for tensile strength percentage elongation and folding endurance of film.

Concentration of plasticizer optimized on the basis of tensile strength percentage elongation and folding endurance of film.

Table 3 : Optimization of Plasticizers with their formulation code

Name Of Ingredients	MOF-XI	MOF-XII	MOF-XIII	MOF-X IV	MOF-XV	MOF-XVI	MOF-XVII	MOF-XVIII	MOF-XIX	MOF-XX
API	-	-	-	-	-	-	-	-	-	-
HPMC K15	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600
Gum Acacia	200	200	200	200	200	200	200	200	200	200
GLYCERIN	-	-	-	-	1.0ml	1.2ml	1.4ml	1.6ml	1.6ml	2.0ml
PEG-4000	75	100	125	150	-	-	-	-	-	-
DBP	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml
SGS	200	200	200	200	200	200	200	200	200	200
Sucralose	120	120	120	120	120	120	120	120	120	120
Citric Acid	120	120	120	120	120	120	120	120	120	120
DM Water Qs To	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml

The tensile testing gives an indication of the strength and elasticity of the film, reflected by the parameters - tensile strength, elastic modulus, percentage strain, and load at yield.

Selection and optimization of super disintegrants

The most important criteria of present dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work.

Selection of proper super disintegrating agent or combination of two super disintegrating agents with their ratio were optimized by preparation of following batches.

Table 4: Optimization of Superdisintegrants with their formulation code

Name Of Ingredients	MOF-XXI	MOF-XXII	MOF-XXIII	MOF-XXIV	MOF-XXV	MOF-XXVI	MOFXXVII	MOF-XXVIII	MOF-XXIX	MOF-XXX	MOF-XXXI
API	-	-	-	-	-	-	-	-	-	-	
HPMC K15	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600	3600
GUM ACACIA	200	200	200	200	200	200	200	200	200	200	200
PEG-4000	125	125	125	125	125	125	125	125	125	125	125
DBP	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1ml	0.1 ml
SGS	200	300					150	150		250	250
CS	-	-	200	300	-	-	150	-	150	50	
CP	-	-	-	-	200	300	-	150	150	-	50
SUCRALOSE	120	120	120	120	120	120	120	120	120	120	120

CITRIC ACID	120	120	120	120	120	120	120	120	120	120	120
DM WATER QS TO	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml	32 ml

Characterization of films

Determination of thickness

Thickness of film was most important parameter because uniformity of thickness determines content uniformity of BFDOF. The thickness of film was determined by Vernier Calipers at stage when film is removed from the fabricated glass reservoir. The thicknesses of one batch were determined in nine different places to assured the uniformity. For this study variation in thickness were kept ±2.5%, if variation was more than this batch is discarded.

Size of film

On area of the of tongue, film can be placed is about 2.5 x2.0 cm^2, to provide sufficient space for dissolving in oral cavity by putting film on tongue and hydrating with saliva, size 2.0 x 2.0 cm^2 were concluded as unit dose of drug.

Folding Endurance

Folding endurance was determined by repeating folding of the oral dissolving films at same point

Drug Content and Content Uniformity

As per pharmacopeial assay method the drug content and content uniformity were determined for API during optimization and during final batches of different combinations. Content uniformity was determined by selecting three samples of film.

Dissolution Test

A modified shaking water bath dissolution method was employed to determining the drug release profile of the film. The shaking water bath apparatus (100 strokes per minute) consist of a water bath, thermostatically controlled at 37±0.5 ^oC and a mechanical shaker platform onto which bottle holder plate were positioned. Glass bottles (125ml), the secured holders of holder plate. 100 ml of Phosphate Buffer, pH 6.5 equilibrated to 37±0.5 ^oC were used for dissolution medium. A specified time intervals, 2.0 ml aliquots of samples were taken out from each vessel (Three) using a syringe and filtered through 0.45 µ Millipore filter. An equal amount of fresh Phosphate Buffer, pH 6.5 was used to maintain the sink condition.

All dissolution samples were analyzed at predetermined specific wavelengths for API.

Results and Discussion

Optimization of films

Selection and optimization of film forming agents:

Most commonly used film formers are cellulose derivatives such as sodium carboxymethyl cellulose or hydroxypropyl methyl cellulose. In this study HPMC-K15 and pullulan were used. pullulan is a linear homopolysaccharide of glucose. Every third glucose units are α-(1→6) linked forming a maltotriose substructure. Pullulan is secreted by the fungus *Aureobasidium pullulans* and is used as a food ingredient. The enzyme pullulanase specifically hydrolyzes the α-(1→6) linkages in pullulan and converts the polysaccharide almost quantitatively to maltotriose. Pullulan is a highly hydrophilic polymer generally regarded as safe and dissolves rapidly in water. Pullulan was also selected as film forming agents.

In this present study various concentration of HPMC K-15 and pullulan were selected on the basis of extensive literature survey. Various concentration of both film forming agents were prepared in ten batches as MOF-I to MOF-X

The optimizations of film forming agents were done on basis of general appearance, thickness and weight. The results of different batches were given in following table.

Batch MOF-III produces desired thickness. Weight of individual film was around 120 mg and its appearance was found transparent.

The thickness of all Batches lies between 62±2 to 118±6 µm. The result shows that as the concentration of film forming polymer increases, the thickness of films also increases. When thickness of films is less than the required thickness it fails the folding endurance and the film are not transparent when the thickness is

higher, so the MOF- III was selected as optimized formula.

Table 5: Optimization of Film forming agents

Evaluation parameters	MOF-I	MOF-II	MOF-III	MOF-IV	MOF-V	MOF-VI	MOF-VII	MOF-VIII	MOF-IX	MOF-X
General appearance	TP	TP	TP	TP	TL	TP	TP	TL	TL	TL
Thickness in µm	62±2	66±3	71±5	79±3	81±6	68±3	77±4	95±5	105±3	118±6
Weight in mg	83±3	102±4	119±3	132±4	148±3	81±3	98±4	113±3	130±4	147±3

All values are expressed as mean ±SD , n= 3
TP- Transparent, TL- Translucent

Selection and optimization of plasticizer:

In general pharmaceutical excipients are regarded as "inactive" and therefore safe for human use, but this may not always be the case. Substances which are nontoxic for adults can be harmful for the hypertensive patient and are only usable with age or dose restrictions. A variety of adverse effects resulting from "inactive" ingredients have been described in the literature. Such problems with pharmaceutical excipients have been reported for gum acacia as co film forming agents which swells and helps to produce consistency to film, polyethylene glycol (4000) and glycerin as plasticizer along with DBP as co-plasticizer. Concentration of plasticizer optimized on the basis of tensile strength percentage elongation and folding endurance of film. Further ten more batches were formulated prepared to select the concentration of plasticizer and co-plasticizer. These batches were optimized on basis of folding endurance.

Table 6: Optimization of Plasticizers

Evaluation Parameters.	MOF-XI	MOF-XII	MOF-XIII	MOF-XIV	MOF-XV	MOF-XVI	MOF-XVII	MOF-XVIII	MOF-XIX	MOF-XX
Folding endurance	2	3	4	3	4	3	2	ND	ND	ND

All values are expressed as mean ±SD, n= 3; ND- Not dried properly

Hence batch MOF-XIII were optimized with selection of PEG-4000 due to better folding endurance.

Selection and optimization of super disintegrants

The most important criteria of present work were to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work.

Selection of appropriate super disintegrating agent or combination of two super disintegrating agents with their ratio was optimized by preparation of eleven batches.

The concentrations of super disintegrating agent/s were optimized on the basis of disintegration time.

Table 7: Optimization of Super Disintegrants

Name Of Ingredients	MOF-XXI	MOF-XXII	MOF-XXIII	MOF-XXIV	MOF-XXV	MOF-XXVI	MOF-XXVII	MOF-XXVIII	MOF-XXIX	MOF-XXX	MOF-XXXI
Disintegration Time in Seconds	46±2	35±1	42±2	41±3	44±2	41±1	38±1	36±1	45±3	27±1	39±1

All values are expressed as mean ±SD, n= 3

The disintegration time was found out in range of 27±1 to 46±2. The disintegration time decreases as concentration of super disintegrants increases. The batch having least disintegration time was selected so as to get less dissolution time of drugs. A combination of SSG (250 mg) and croscarmellose sodium (50 mg) were able to disintegrate oral film within 27 seconds, Hence MOF-XXX were selected for further study.

Optimized batch of film

Table 8: Optimized composition of Fast Dissolving film

S.No.	Name of Ingredients	Composition
1	Granisetron Hydrochloride	80 mg
2	HPMC K15	3600 mg
3	Gum acacia	200 mg
4	PEG-4000	125 mg
5	DBP	0.1ml
6	SSG	250 mg
7	CCS	50 mg
8	Sucralose	120 mg
9	Citric acid	120 mg
10	Colorant (Yellow)	QS
11	Flavour (Yellow)	QS
12	DM water	32 ml

The optimized batch of Granisetron Hydrochloride 2 mg/dose were prepared. The film was able to disintegrate within 26 seconds with thickness of 79±5 µm. This oral film was showing appropriate folding endurance The weight of each film were 125±2 mg.

Characterization of Optimized films

Determination of thickness

The thickness of films with drug was determined from three different positions.

The thickness of Optimized batche was found out to be 79±5 µm.

Disintegration Time

The disintegration time of all single layer films of each drug was determined.

The disintegration time was found out in range of 26±2 to 32±1 sec. The disintegration time is sufficient to get less dissolution time of drugs.

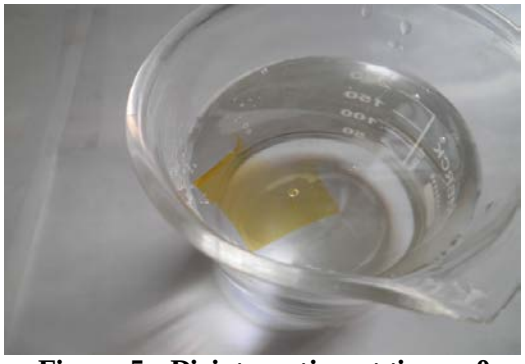

Figure 5 : Disintegration at time = 0

Figure 6: Disintegration at time = 60 Sec

Drug Content

The drug content of optimized batch was determined from three different positions.

The drug content of optimized batch was found to be in range of 98.6 ±0.6 to 99.8 ±0.4 which shows good content uniformity throughout the film.

***In Vitro* Dissolution Studies:**

A modified shaking water bath dissolution method was employed to determining the drug release profile of the film. The shaking water bath apparatus (100 strokes per minute) consist of a water bath, thermostatically controlled at 37±0.5 ^{o}C and a mechanical shaker platform onto which bottle holder plate were positioned. Glass bottles (125ml), the secured holders of holder plate. 100 ml of Phosphate Buffer, pH 6.5 equilibrated to 37±0.5 ^{o}C were used for dissolution medium. A specified time intervals, 2.0 ml aliquots of samples were taken out from each vessel (Three) using a syringe and filtered through 0.45 µ Millipore filter. An equal amount of fresh Phosphate Buffer, pH 6.5 was used to maintain the sink condition.

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All dissolution samples were analyzed as predetermined specific wavelength.

Table 9 : % Cumulative release profile of optimized batch

S.No	Time in minutes	% Cumulative drug release films
1	0	0.0
2	5	31.43±0.6
3	10	76.55±0.8
4	15	91.23±1.2
5	20	94.87±0.9
6	25	94.96±0.8
7	30	95.54±0.9
8	40	96.54±1.1
9	50	97.55±0.8
10	60	98.55±0.7

Values are expressed as mean ±SD, n= 3

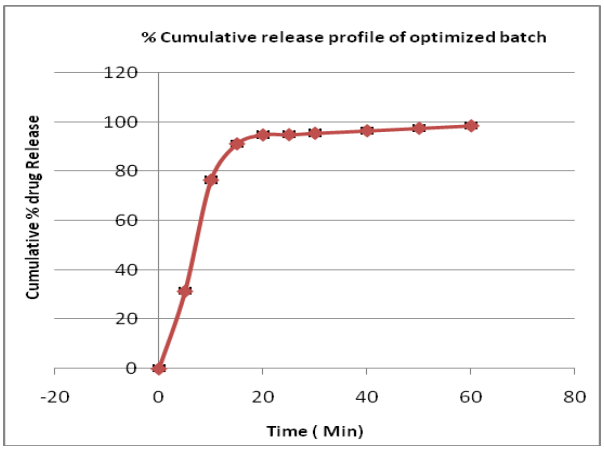

Figure 7: Drug Release profile of optimized batch

The dissolution data revealed that all drugs release within 30 min and release were constant after 40 min which shows the fast release of the drug from film.

Comparison with marketed formulation:

The dissolution data is compared with Marketed Tablet Grandem- 2mg (aristo pharmaceuticals). The dose of both formulations i.e. optimized film and marketed tablet was same. The data of release was given in following figure:

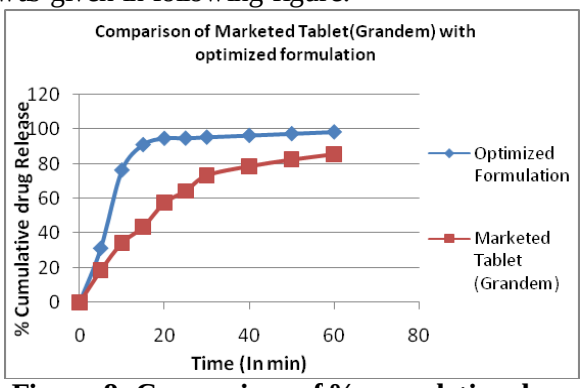

Figure 8: Comparison of % cumulative drug Release of optimized batch with Marketed Tablet

Conclusion

The optimized oral film shows good tensile strength, percentage elongation and folding endurance. The dissolution data revealed that all drugs release within 30 min and release were constant after 40 min which shows the fast release of the drug from films.

On comparing the dissolution data of optimized batch with marketed Tablet Grandem- 2mg (aristo pharmaceuticals),It was found that optimized film shows better on set of action and may show better bioavailability than tablet. Hence film can be used as alternative dosage form for treatment of emesis.

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