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Formulation And Evaluation Of Fast Dissolving Oral Film Of Meclizine

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ABSTRACT The main objective of present research work is formulation and evaluation of fast dissolving oral film of meclizine. Meclizine (MCZ) is a first-generation antihistamine of the piperazine class drug, used in the treatment of motion sickness (H1 receptor antagonist). MCZ is a white to light yellowish-white crystalline powder and practically insoluble in water. The preliminary study showed that Meclizine is white to slightly yellowish, crystalline powder. It has been observed that Meclizine was soluble in methanol, ethanol,chloroform and 0.1NHCl, slightly soluble in distilled water. Results of Loss on drying of Meclizine was found 2.86±1.48%. The Melting point of Meclizine was found 220-223°C. Identification of Meclizine was performed by UV/VIS Spectroscopy. The 10 µg/ml solutions of Meclizine was scanned in the range of 200-400nm to determine the λ_{max} for drug. The λ_{max} of Meclizine was found to be 232.0nm. From the respective stock solution (1mg/ml) different concentration of 10, 20, 30, 40 and 50µg/ml Meclizine was prepared and scanned inUV region.Their absorbances were noted at 232nm and calibration curve was plotted as absorbance vs concentration and their linearity range was determined. The thickness of the Meclizine OFDFs formulations F1 – F6, developed with HPMC and superdisintegrants (SSG, CCS and CP) were found ranging from 42±4 µm to 62±5µm. The formulations F1 – F6 developed with different concentrations of SSG, CCS and CP, disintegration time were found in the range of 1.45±0.14 sec to 2.45±0.32 sec. The formulations F8 prepared with CCS and CP having different concentrations were ranging from 1.45±0.14 sec. The data of disintegration time indicates that increasing the concentrations of polymer along with different viscosities tends to increase the disintegration time. The formulated OFDFs were evaluated and the % moisture content was calculated. A reduced % moisture content was observed with increase in polymer concentration varying from 1.25±0.25% to 1.58±0.65% w/w for Meclizine films. The Content uniformity was worked out on individual films of 12 samples. A film of size 2.5*2.5 cm^2 was cut and kept in10 ml of volumetric flask containing solvent. This was then shaken in a mechanical shaker till it was dissolved to get a homogeneous solution and then filtered. Concentrations the drug content was found in the range of 98.56±0.25-99.11±0.25%. Even though all the formulations drug content within the specification range, Cumulative % drug release was calculated on the basis of drug content of Meclizine present in the respective film.

KEYWORDS: Evaluation, Compliance, Dysphsia, Disintegration, Drug.

INTRODUCTION

Oral route is a most preferred route of drug administration for systemic effect due to its ease of administration, non-invasiveness, adaptability, patient compliance and acceptability. About 60% of all the formulations are solid dosage form. Tablet is the most preferred dosage form due to ease of manufacturing, transportation and more patient compliance. Generally geriatric, pediatric, nauseous, bedridden and non-compliance patients experience difficulties in swallowing the conventional oral dosage form and do not take their medicines as prescribed. It is estimated that 50 % of the population was affected by this problem, which finally results in a higher chance of non-compliance & ineffective therapy.

The elderly constitute a major portion of today's population mainly because of increased life expectancy of individuals. Dysphagia or difficulty in swallowing is common problem, the disorder of dysphagia is associated with many medical conditions including stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebralpalsy.The most common complaint with tablet is size, fear of chocking followed by surface form and taste. The problem of swallowing tablets is more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water.

To overcome this Oral fast disintegrating drug delivery systems were developed, these systems were first developed in the late 1970s as an alternative to tablets, capsules and syrups for pediatric & geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms. These dosage forms either dissolve or disintegrate generally within a 3 minute in mouth, without need of water. Oral fast Disintegrating dosage form have started gaining popularity & acceptance as new drug delivery system because they are easy to administer &lead to better patient compliance.

Oral fast disintegrating dosage form mainly consist of oral disintegrating tablets which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue but leave residues in mouth which causes feeling of grittiness in mouth.Even with fast dissolving tablets there is a fear of choking due to its tablet type appearance. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets. The most common complaint was tablet size, followed by surface form and taste. To overcome problems of mouth dissolving tablets, a new drug delivery system for the oral delivery of the drugs, was developed which is known as Fast dissolving films/mouth dissolving films/oral dispersible film/oral dissolving film/oral disintegrating film.

Fast dissolving oral films ($FDOF_s$) is a type of oral drug delivery system for the oral delivery of the drug which was developed based on the technology of the transdermal patches.This delivery system consists of a thin film of the size of a postage stamp, which is placed on the patient's tongue or mucosal tissue, where it instantly hydrates by absorbing saliva; the film then rapidly disintegrates and dissolves to release the drug for oral mucosal absorption. This fast dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment. Fast dissolving oral films were

initially introduced in the market as breath fresheners and personal care products such as dental care strips and soap strips. However, these dosage forms were introduced in the United States and European pharmaceutical markets for therapeutic benefits.

Special features of fast dissolving oral films

1. Thin elegant film
2. Available in various size and shapes
3. Unobstructive
4. Excellent mucoadhesion
5. Fast disintegration and dissolution
6. Rapid drug release
7. By passes first pass effect.

Advantage of fast dissolving oral films:

1. No need of water for administration.
2. Convenient for pediatric, geriatric and dysphasic patients having difficulty in swallowing.
3. Rapid disintegrating and dissolution in the oral cavity due to larger surface area of films.
4. Rapid onset of action with increased bioavailability due to by passing hepatic first pass effect.

MATERIALS AND METHODS

Formulation of oral film of Meclizine

Casting process of fast disintegrating oral film

Various methods are available for casting of oral films.This is fast disintegrating oral film hence on the laboratory scale solvent casting technique was adopted for formulation of films.

Solvent casting technique: Meclizine containing fast dissolving films was fabricated by the solvent casting method. The optimized amount of HPMC was dissolved in 5ml of water and stirrered continuously for 1 hour,optimized amount of plasticizer and drug were dissolved in 95% ethanol and then added to the polymeric solution, the optimized amount of drug was dissolved in 2ml of water and kept in sonicator for proper dispersion. Polymeric solution was stirred for 30 min using magnetic stirrer and was kept in undisturbed condition till the entrapped air bubbles were removed.The aqueous solution was casted in a glass moulds having 2.5x2.5cm^{2}10 films area and was dried at controlled room temperature (25°-30°C, 45 %RH) as well as at increased temperature (microwave oven).The film took approximately 48 hr to dry at controlled room temperature. The dried film was carefully removed from the glass plates and was cut into size required for testing. The films were stored in air tight plastic bags till further use.

Selection and optimization of film forming agents

Two film forming agents and one co-film forming agent 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. Concentration of film forming agent is optimized on the basis of thickness and appearance of film.

Optimization of formulations

Table 1: Selection and Optimization of Film Forming Agents

Name of ingredients (mg for 12 strips)	F1	F2	F3	F4	F5	F6
API Equivalent to 25mg (100 mg of physical mixture)	1200	1200	1200	1200	1200	1200
HPMC	400	600	800	400	600	800
Glycerin	-	-	-	-	-	-
PEG-400	100	100	100	100	100	100
SSG (mg)	100	150	200	-	-	-
CCS (mg)	-	-	-	100	150	200
Aspartame (mg)	25	25	25	25	25	25
Citricacid (mg)	50	50	50	50	50	50
DM water qs to (ml)	30	30	30	30	30	30

HPMC=Hydroxypropyl methylcellulose, PEG 400= Polyethylene glycol 400, SSG= Sodium starch glycolate, CCS =Croscarmellose sodium.

RESULTS AND DISCUSSION

Results of Preformulation study

Physical evaluation

Table 2: Physical evaluation of drug

S. No.	Sensory Characters	Results of Physical evaluation
		Meclizine
1.	Colour	Slightly yellowish, crystalline powder
2.	Odor	Slight odor
3.	Taste	Tasteless

Results of Solubility:

Table 3: Solubility of Meclizine

Solvent used	Results of Solubility
Distilled Water	Sparingly soluble
0.1N Hydrochloric acid	Soluble
Ethanol	Soluble
Methanol	Soluble
Chloroform	Soluble
0.1NNaOH	Sparingly soluble
Phosphate buffer pH 6.8	Sparingly soluble

Results of Melting point:

Table 4: Melting point of Meclizine

S. No.	Melting Point of Meclizine
1.	220-223□

Identification test using FTIR Spectroscopy

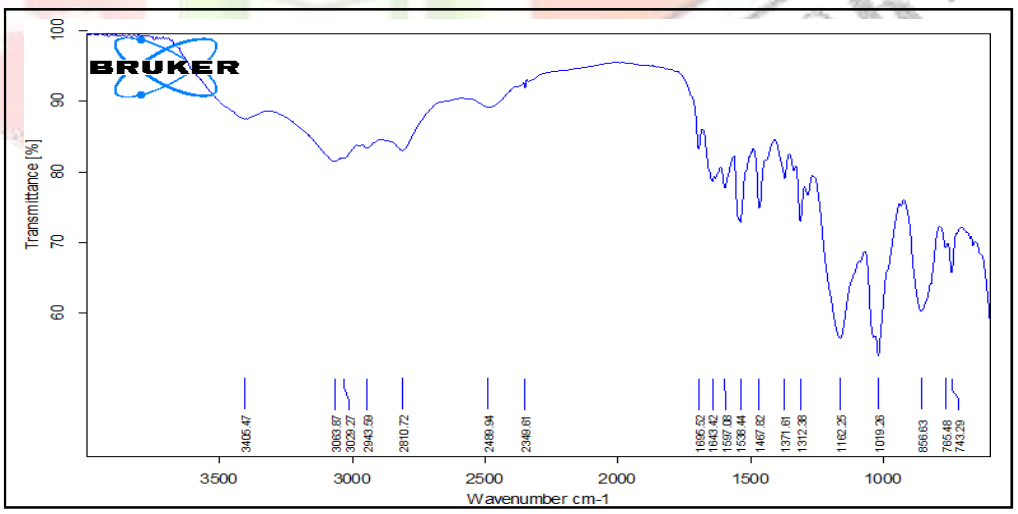

Figure 1:FT-IR Spectrum of Meclizine

A) Results of Loss on drying:

Table 5: Loss on drying of Meclizine

S. No.	Initial weight	Final weight after 15 minutes	% loss of drying	Avg. % loss Of drying
1.	5gm	4.87	2.5	2.76±1.38
2.	5gm	4.94	1.3	
3.	5gm	4.76	4.7	

(N=3,mean±SD)

B) Determination of λ_{max} of Meclizine

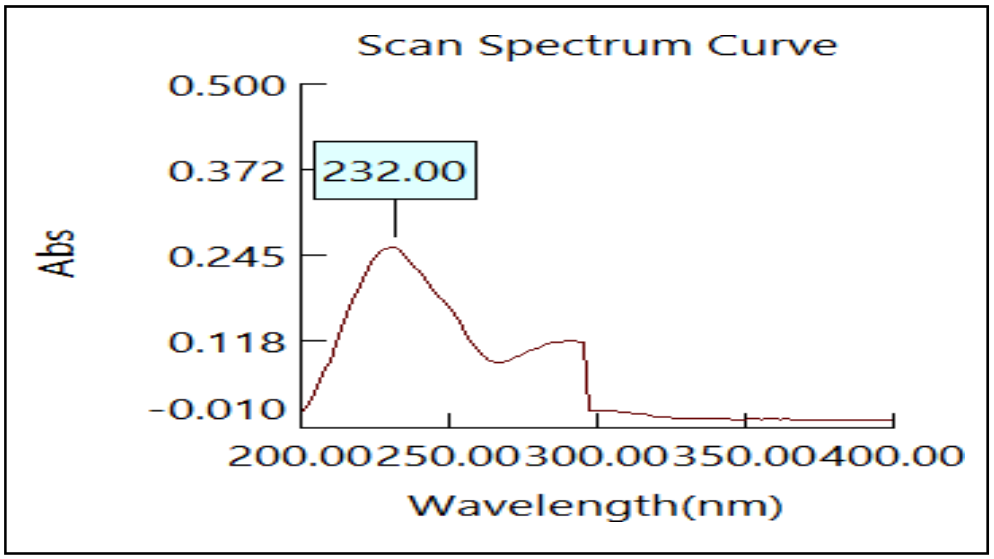

Figure 2: Determination of λ_{max} of Meclizine

Table 6: Readings for Calibration curve of Meclizine hydrochloride

S. No.	Concentration (µg/ml)	Absorbance
1.	5	0.373
2.	10	0.596
3.	15	0.815
4.	20	1.022
5.	25	1.174

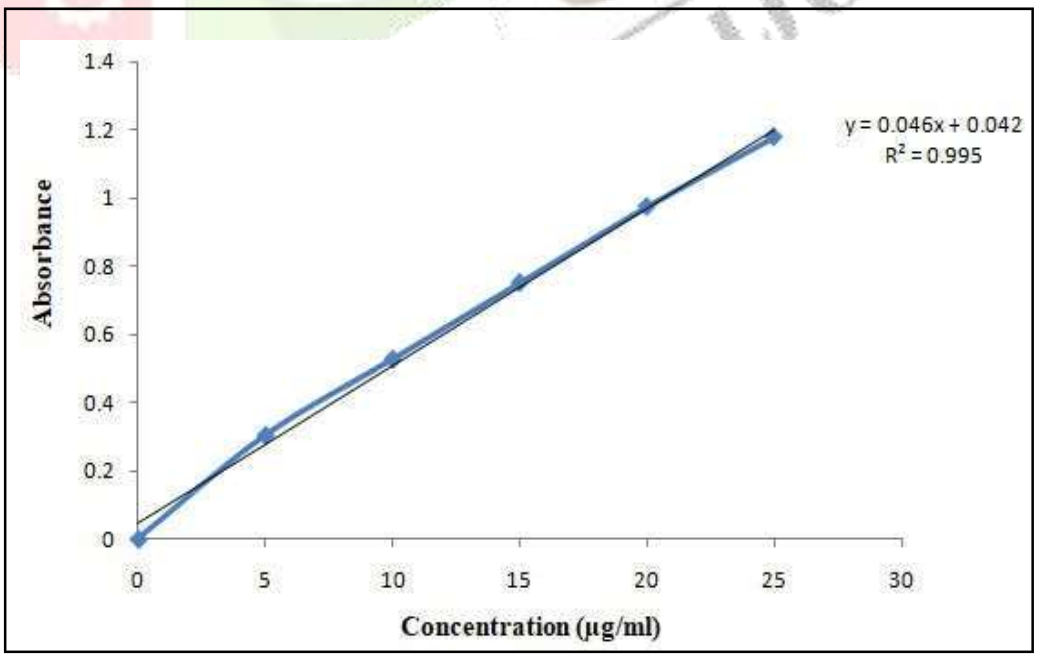

Figure 3: Graph of calibration curve of Meclizine at 232 nm

Evaluation of solid dispersions

Table 7: Percentage cumulative drug release of physical mixture

S. No.	Time interval (min.)	Percentage cumulative drug release of physical mixture*			
1	**0**	**1:1**	**1:2**	**1:3**	**Pure Drug**
2	30	25.56	29.98	35.65	9.45
3	60	36.65	38.85	42.23	11.23
4	120	45.58	52.23	59.98	14.45
5	240	55.54	63.45	69.94	16.65
6	360	62.23	71.15	73.36	18.89
7	480	65.25	73.32	76.45	20.41

Percentage drug content

Table 8: Results of drug content

Label claim	Amount found*	Label claim (%)	S.D.	%RSD
25 mg	24.95	99.80	0.045	0.038

***Average of three determination (n=3)

Differential scanning calorimetry (DSC)

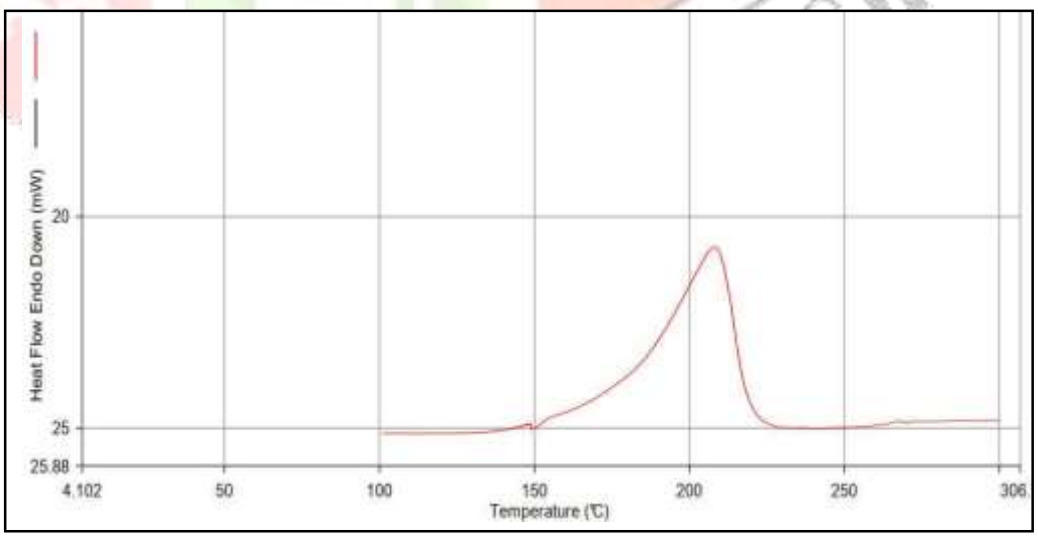

Figure 4: DSC analysis of pure Meclizine

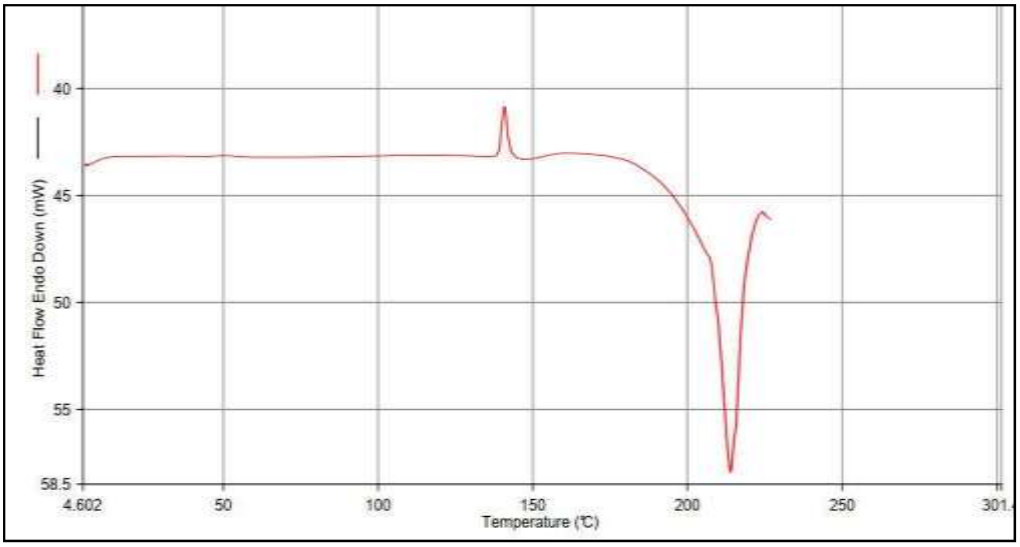

Figure 5: DSC analysis of optimized batch (MCZ+ PEG 4000)

Results of Evaluation of prepared Film

Table 9: Results of Evaluation of prepared Film

Formulation code	General Appearance	Thickness (µm)*	Weight (mg)*
F1	Translucent	62±5	165±3
F2	Translucent	58±6	160±4
F3	Translucent	55±5	155±5
F4	Translucent	48±4	145±6
F5	Translucent	45±5	125±7
F6	Translucent	42±4	120±3

***(N=3,mean±SD)**

Table 10: Result of folding endurance, disintegration time, tensile strength moisture content and assay

Formulation code	Folding endurance	Disintegration time (min.) *	Tensile strength (kg/cm^2)*	Moisture Content (%)*	Assay (%)*
F1	145±3	2.36±0.25	0.65±0.05	1.45±0.32	98.85±0.36
F2	156±4	2.25±0.36	0.47±0.03	1.52±0.25	98.56±0.25
F3	165±3	2.45±0.32	0.58±0.02	1.58±0.65	98.78±0.14
F4	155±2	2.11±0.25	0.63±0.04	1.47±0.14	98.85±0.36
F5	185±4	1.45±0.14	0.74±0.06	1.25±0.25	99.11±0.25
F6	136±5	2.36±0.25	0.62±0.05	1.36±0.36	98.96±0.32

***(N=3, mean±SD)**

Results of optimized formulation

Table 11: Results of Optimized formulationF5

Name of Ingredients	Composition (mg) Per Strip
API	1200
HPMC K15	600
PEG-400	-
SSG	100
CCS	-
Aspartame	150
Citric acid	25
DM water qs to (ml)	30

Results of in-vitro release study of optimized formulation F5

Table 12: Results of in-vitro release study of optimized formulation F5

S. No.	Time (Min.)	Cumulative % Drug release*
1.	1	25.58±0.45
2.	2	45.65±0.25
3.	5	69.98±0.36
4.	10	78.85±0.25
5.	15	98.85±0.23

*(N=3,mean±SD)

Results of stability studies: Minor difference was found between evaluated parameters before and after ageing/storage and all was in acceptable limits. Therefore formulation remains stable for sufficient time.

Table 13: Characterization of stability study of Optimized Film (F5)

Characteristic	Time (Month)			
	Initial	**1Month**	**2Month**	**3Month**
% Assay*	99.45	99.25	98.85	98.25

***Average of three determination (n=3)**

SUMMARY AND CONCLUSION

Meclizine (MCZ) is a first-generation antihistamine of the piperazine class drug, used in the treatment of motion sickness (H1 receptor antagonist). MCZ is a white to light yellowish-white crystalline powder and practically insoluble in water. The preliminary study showed that Meclizine is white to slightly yellowish, crystalline powder. It has been observed that Meclizine was soluble in methanol, ethanol, chloroform and 0.1NHCl, slightly soluble in distilled water. Results of Loss on drying of Meclizine was found 2.86±1.48%. The Melting point of Meclizine was found 220-223°C. Identification of Meclizine was performed by UV/VIS Spectroscopy. The 10 µg/ml solutions of Meclizine was scanned in the range of 200-400nm to determine the λ_{max} for drug. The λ_{max} of Meclizine was found to be 232.0nm. From the respective stock solution (1mg/ml) different concentration of 10, 20, 30, 40 and 50µg/ml Meclizine was prepared and scanned in UV region.Their absorbances were noted at 232nm and calibration curve was plotted as absorbance vs concentration and their linearity range was determined. From the DSC data of the drug and drug plus excipient (physical mixture) obviously functionalities of drug have stayed unaltered including melting point of the peak. This proposes amid the procedure drug and excipient has not responded with the drug to offer ascent to reactant items. So there is no interaction between them which is in favor to proceed for formulation of tablets. Preformulation studies reported that the formulation of fast dissolving tablets of Meclizine can be prepared with appropriate methods. This thesis deals with the investigations carried out on the preparation and characterization of fast dissolving tablets containing Meclizine with increase its bioavailability. The enhancement of solubility was done in different amount PEG 4000, On the basis of percentage cumulative drug release study it was concluded that solid dispersion is better option in spite of pure drug. The study revealed that physical mixture shows a sudden bursting effect and erratic pattern in their release mechanism therefore the solid dispersion was best alternate. In solid dispersion it was found that in1:1 and 1:2 ratio there was also a bursting effect and at higher polymer ratio i.e. at 1:3 the drug release was truly delayed which can further optimized to get better results. Therefore 1:3 ratios were found to be superior and were used for further evaluation purpose. Different formulation of Meclizine oral fast dissolving films were prepared and evaluated for Thickness, Weight, folding endurance, disintegration time, tensile strength moisture content and assay. The thickness of the Meclizine OFDFs formulations F1 – F6, developed with HPMC and superdisintegrants (SSG, CCS and CP) were found ranging from 42±4 µm to 62±5µm. From the obtained thickness data it was observed that the thickness of the film was increased by increasing in the concentration of the film former. Hence, the thickness of the film was directly proportional to its film former concentration. The average weight of the films was measured in triplicate for each film and found in the range from 125±7–165±3mg. Formulations F1-F6 folding endurance was in the range of 136±5-185±4. The observed folding endurance data of the films developed with various viscosities and concentrations of film formers indicated that the increase in viscosities and concentrations of the film lead to increase in the folding endurance of the films. The formulations F1 – F6 developed with different concentrations of SSG, CCS and CP, disintegration time were found in the range of 1.45±0.14 sec to 2.45±0.32 sec. The formulations F8 prepared with CCS and CP having different concentrations were ranging from 1.45±0.14 sec. The data of disintegration time indicates that increasing the concentrations of

polymer along with different viscosities tends to increase the disintegration time. The formulated OFDFs were evaluated and the % moisture content was calculated. A reduced % moisture content was observed with increase in polymer concentration varying from 1.25±0.25% to 1.58±0.65% w/w for Meclizine films. The Content uniformity was worked out on individual films of 12 samples. A film of size 2.5*2.5 cm^2 was cut and kept in10 ml of volumetric flask containing solvent. This was then shaken in a mechanical shaker till it was dissolved to get a homogeneous solution and then filtered. Concentrations the drug content was found in the range of 98.56±0.25-99.11±0.25%. Even though all the formulations drug content within the specification range, Cumulative % drug release was calculated on the basis of drug content of Meclizine present in the respective film.

BIBLIOGRAPHY

1. Liang CA, Chen HL. Fast dissolving intra oral drug delivery systems. Expert Opin. Ther. Patents. 2001; 11(6): 981-986.
2. Habib W, Pritchard JF, Bozigian HP, Gooding AE, Griffin RH, Mitchell R, Bjurstrom T, Panella TL, Huang AT, Hansen LA. Fast-dissolve drug delivery system. Crit. Rev. Ther. Drug Carrier Syst.2000; 17: 61–72.
3. Siddiqui MD, Garg G, Sharma PA. Short review on: A novel approach in oral fast dissolving drug delivery system and their patents. Adv. Bio. Res. 2011; 5(6): 291-303.
4. Brniak W, Jachowicz R, Pelka Przemyslaw. The practical approach to the evaluation of methods used to determine the disintegration time of orally disintegrating tablets. Saudi Pharm. J. 2015; 23:437-443.
5. Gisel EG. Oral motor skills following sensor imotor intervention the moderately eating impaired child with cerebral palsy. Dysphagia. 1994; 9: 180–192.
6. Avery SW, Dellarosa DM. Approaches to treating dysphagia patients with brain injury. Am. J. Occup. Ther. 1994; 48(3): 235–239.
7. Chauhan NS, Tomar A, Sharma K, Mittal A, Bajaj U. Formulation and evaluation of fast dissolving oral film of dicyclomine as potential route of buccal delivery. Int. J. Drug Dev. Res.2012; 4 (2): 408-417.
8. PatelA, Shaikh S, Khan G J, Molvi KI, Patel H. Review Article: various aspects of oral fast disintegrating dosage form. Int. J. Pharmacy Pharm. Res. 2016; 6(4):689-701.
9. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J. Control. Release.2009; 139(2): 94-107.
10. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: Aninnovative drug delivery system and dosage form. Int. J. Chem Tech. Res. 2010; 2(1):576-583.
11. Goel H, Rai P, RanaV, Tiwary AK. Orally Disintegration systems:Innovations in formulation and Technology. Recent Pat. Drug Deliv.Form. 2008; 2(3): 258- 274.
12. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Margret CR. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research. 2009; 1(1): 163-177.
13. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films: Innovations in formulation and

technology. Int. J. Pharm. Sci. Rev. Res. 2011; 9(2): 50–57.

14. Bala R, Pravin pawar, sushil khanna, sandeep arora. Orally dissolving strips: A new approach to oral drug delivery system. Int. J. Pharm. Invest. 2013; 3(2): 67– 76.
15. Choudhary DR, Patel VA, Chhalotiya UK, Patel HV, Kundawala AJ. Development and characterization of pharmacokinetic parameters of fast- dissolving films containing levocetirizine. Sci. Pharm. 2012; 80:779–787.
16. Zhang H, Zhang J, Streisand JB. Oral mucosal drug delivery: clinical pharmacokinetics and therapeutic applications. Clin. Pharmacokinetic. 2002;41(9): 661-680.
17. Jangra PK, Sharma S, Bala R. Fast dissolving oral films: Novel way for oral drug delivery.Int. J. Uni. Pharm. Bio. Sci. 2014; 3(1): 6-27.
18. Mali RR, Gupta S, Goel V. Novel study in fast dissolving drug delivery system: a review. Indian J. Pharm. Biol. Res. 2015; 3(1):93-107.
19. Heer D, Aggarwal G, Kumar SLH. Recent trends of fast dissolving drug delivery system-A novel review of formulation technology. Pharmacophore. 2013;4(1):1-9.
20. Mashru RC, Sutariya BC, Parikh PP. Development and evaluation of fast dissolving films of salbutamol sulphate. Drug Dev. Ind. Pharm. 2005; 31:25-34.
21. Gohel MC, Sharma R, Soniwala MM. Development of taste masked film of Valdecoxib for oral use. Ind.J. Pharm. Sci. 2007; 69:318-320.
22. Koland M, Charyulu N. Fast dissolving sublingual films of ondansetron hydrochloride: Effect of additives on in vitro drug release and mucousal permeation. J. Young Pharm. 2010; 2: 216-221.
23. Singh S, Gangwar S. Formulation and evaluation of rapidly disintegrating film of levocetrizine hydrochloride. Der Pharmacia Lettre. 2010; 2(2): 434-439.
24. Kulkarni N, Kumar LD, Sorg A. Fast dissolving orally consumable films containing an antitussive and a mucosa coating agent. U.S. Patent 2003; 206942.