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Formulation and Evaluation of Oral Fast Dissolving Film of Glibenclamide

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Keywords: Orally disintegrating film, Glibenclamide, Solvent Casting Method, Drug Release, Fast Onset of Action.

ABSTRACT

The aim of the present study was to formulate fast dissolving films of Glibenclamide using HPMC K-15, HPMC E-15 HPMC K-100 polyethyleneglycolPEG (400) as a plasticizer, tween 80 as a surfactant, and citric acid as a salivary agent. Glibenclamide solid dispersion of PEG 6000 is dispersed in the polymer solution. Films were prepared by the solvent casting method and found to satisfy the mouth dissolving time and other film parameters. The film instantly gets wet by saliva, rapidly hydrates, adheres to a tongue and rapidly disintegrates and dissolves to release the drug for the oro–mucosal absorption or allow for gastrointestinal absorption to be achieved when swallowed. The formulated films exhibited acceptable film endurance. The time required for the film to dissolve and release 26 seconds and 2 minutes respectively. It can be concluded from the study that the oro–flash release film can be a potential novel drug dosage form for poorly water-soluble drugs.

INTRODUCTION:

The ultimate goal of any drug delivery system is the successful delivery of the drug, in which almost 90% of the drugs are administered to the body for the treatment of various disorders and diseases as it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. In this, the drug is dissolved or swallowed and then enters into the systemic circulation to produce the desired effect. Despite astounding advancement in drug delivery the oral route of drug administration is considered as the most important method of administration of drug for systemic effect because of self-medication, ease of administration and avoidance of pain compared to parenteral route.

Recently fast dissolving technology have been emerging out as a new drug delivery system that provides a very convenient means of taking medications and supplements.[2] Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms. The buccal cavity is an attractive route of administration for Systemic drug delivery. Oral mucosa has a rich vascularization and offers higher permeability to many drugs. It has been well known that after buccal and sublingual administration drug solutes are rapidly absorbed into the reticulated vein and are then drained into the systemic circulation [3].The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with a conventional mean of taking their medication. Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. [4]

Glibenclamide is an oral hypoglycemic agent belonging to the second generation of sulfonylurea's used in the treatment of type II non-insulin-dependent diabetes. Its hypoglycemic effect is due to stimulation of insulin release from pancreatic beta cells and sensitization of the peripheral tissues to insulin. Glibenclamide is highly lipophilic (logP = 4.7) and poorly soluble in aqueous media. According to the Biopharmaceutical Classification Scheme (BCS), Glibenclamide comes under Class II drug, poorly soluble but able to permeate gastrointestinal mucosa(6)

The fast-dissolving drug delivery system is a new drug delivery technique to provide films have acquired great importance in the pharmaceutical industry due to their unique properties

& advantages [7,8]. As the fast dissolving film utilizes sublingual route, rapid absorption of the drug is possible, which finally lead to quick onset of drug action. Difficulty in swallowing is a common problem of all age group, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Solid dosage form that can be disintegrated, dissolved or suspended by saliva in the mouth resulting easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convenience of easily swallowable dosage form. It shows patient compliance, rapid onset of action; increased bioavailability and good stability make this film popular as a dosage form of choice.

Prepared film was subjected to different evaluation parameters like physical properties, disintegration time, content uniformity and dissolution studies. The oral cavity as a site for drug delivery:

Anatomy & nature of oral cavity-

The oral cavity it may be divided into two regions, the outer oral vestibule, bounded by the lips and cheeks and the oral cavity itself the borders being and formed by the hard & soft palates, the floor of the mouth and tonsil.

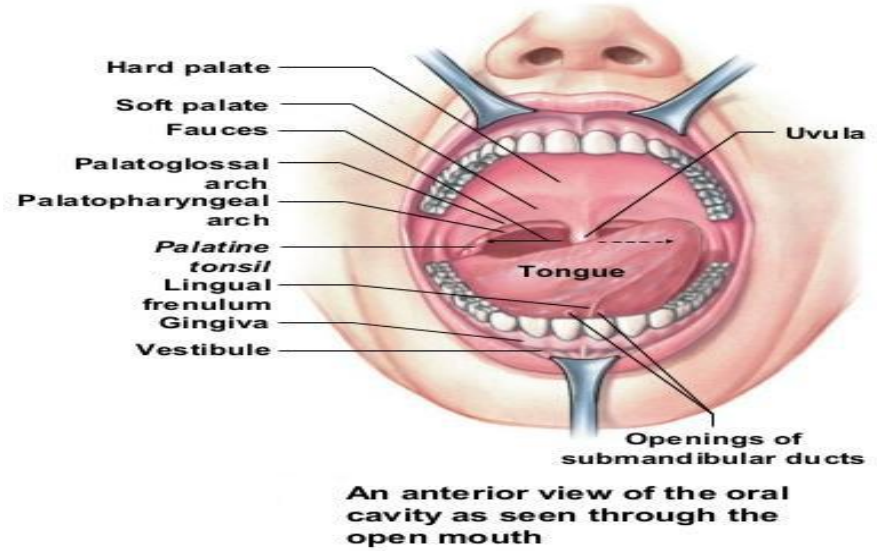

Fig. 1: Schematic representation of the "open" oral cavity.

Physical description of the oral cavity:

As given figure-1, the mucosa that lines the oral cavity may be divided into three types, classified according to their function as;

1. Masticator mucosa, which includes the mucosa around the teeth and on the hard palate and these regions have keratinized epithelium.

2. Lining mucosa, which covers the lips, cheeks, fornix, a base of the oral cavity, lower part of the tongue, buccal mucosa and the soft palate and these regions have non-keratinized epithelium.

3. Specialized mucosa, which covers the dorsum of the tongue with highly keratinized [13].

Regional variation in the composition of oral mucosa:

The difference in the structure thickness and blood flow depending on their location. The membrane that lines the oral cavity has a total area of 200 cm2 and shows keratinized and non-keratinized tissue occupies about 50% and 30% respectively.

Oral mucosa:

The oral mucosa is composed of an outermost layer of stratified squamous epithelium (about 40-50 layers thick), a lamina propria followed by the submucosa as the innermost layer (Fig.1).

The composition of the epithelium varies depending on the site in the oral cavity. The mucosa of the gingival and hard palate are keratinized similar to the epidermis contain neutral lipids like ceramides and acylceramides which are relatively impermeable to water. The mucosa of The soft palate, the sublingual, and the buccal regions, however, are not keratinized contain only small amount of ceramide.

The composition of mucus layer:

Mucus is a translucent and viscid secretion which forms a thin gel, mean thickness of this layer varies from about 50-450 μm in humans secreted by the global cells lining the epithelia or by special glands with mucus cell acini. It has the following general composition.

Table 1: Composition of mucus layer

Water	**95%**
Mineral salt	1%
Glycoprotein's and lipids	0.5-3%
Free proteins	0.5-1.0%

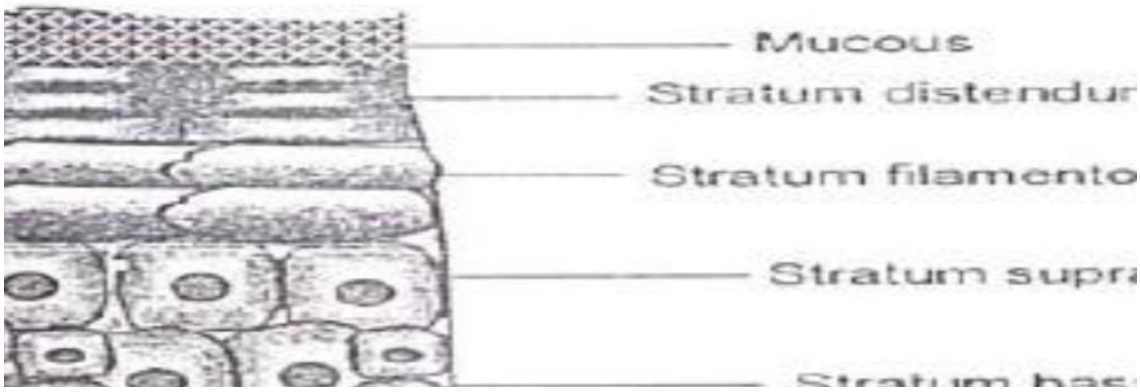

Fig. 2: Schematic diagram of cross-section of the oral mucosa

Functions of mucus layer:

1. Protective**:** Resulting particularly from its hydrophobicity.

2. Barrier: The role of the mucus layer as a barrier to tissue absorption of the drugs and influences the bioavailability.

3. Adhesion: Mucus has strong cohesion properties.

4. Lubrication: It is necessary to compensate for the removal of the mucus layer due to digestion, bacterial degradation, and solubilization of mucin molecules.

Salivary secretion:

There are mainly three glands which secrete saliva in the oral cavity such as parotid, sublingual, and submandibular.

MATERIALS AND METHODS:

MATERIAL:

Table-2: Material used with their source.

Sr. No.	Material	Property	Source
1	Glibenclamide	Pure drug	Flamingopharmaceutical, Mumbai.
2	HPMC E-15 HPMC K15 HPMC K100	Film former	Zim laboratories, Nagpur.
3	PEG (400) PEG (600) GLYCERINE.	Plasticizer	Loba Chemie laboratory chemical Ltd, Mumbai.
4	Tween (80)	Surfactant	Vamapharma, Nagpur.
5	Citric acid	Saliva stimulating agent	Loba Chemie laboratory chemical Ltd, Mumbai.

Equipment used with their source:

Table 3: Equipment used with their source

Sr. No.	Equipment	Model No.	Make
1	Oven rotek	OR-203	Labindia
2	Disintegration apparatus	DA-40	Electrolab
3	UV-spectrophotometer	UV-1800	Shimadzu japan
4	Digital balance	Bl-22oh	Shimadzu japan
5	pH meter	Pico+	Labindia
6	Magnetic stirrer	LMS-28oe	Labtop
7	Screw gauge	SG-001	Electrolab
8	Sonicator	3-5 l 100h	PCI analytics

Infrared Spectroscopy (IR):

A physical mixture of drug and excipients were prepared to study the compatibility. Drug-polymer compatibility studies were carried out using IR spectroscopy.

UV Spectroscopy:

The UV spectrum of Glibenclamide in PBS (pH 6.8) was scanned in the range 400-200 nm. The spectrum indicated that the observed λ_{max} of Glibenclamide was232 nm which was matched with pharmacopoeial value.

Preparation & Selection of Blank Film for Formulation:

Table 4: Formulation Details of blank fast dissolving film

Ingredient(mg) formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
HPMC K-15	200	250	300	-	-		-	-	-	
HPMC K-100	-	-	-	200	250	300	-	-	-	-
HPMC E-15	-	-	-	-	-	-	200	250	300	-
PVP										300
PEG(600)	1ml	1ml	1ml	1ml	-	-	-	-	-	-
Glycerine	-	-	-	-	-	-	-	0.3ml	0.3ml	0.3ml
SLS	-	-	-	-	-	-	-	50	50	50
PEG(400)	-	-	-	-	1ml	1ml	1ml	-	-	-
Citric acid	50	50	50	50	50	50	50	50	50	50
Tween (80)	1ml	1ml	1ml	1ml	1ml	1ml	1ml	-	-	-
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

+ -Poor + +-Average + + +-Excellent

Preparation of Fast Dissolving Film:-

The oral fast-dissolving film containing Glibenclamide was prepared by the solvent casting method. The polymers (HPMC K-15) and plasticizers (propylene glycol, PEG-400, Glycerine) were dissolved in over sufficient quantity of distilled water in the separate beaker to prevent the excessive air bubbles formation. In the second beaker, Glibenclamide was added and stirred both solutions 30 min. Then two solutions mixed together and specified amount of other excipients such as saliva stimulating agent, flouring agent etc. was added to that mixture as well as sufficient quantity of remaining water & stirred for 1 hour. After stirring kept for 30 min for sonication to remove all air bubbles from final solution. Then the

final solution was casted on Petri dish and it was dried in the oven at 45ºC for 12 hr. The film was carefully removed from the Petri dish and cut according to the size required for single dose and testing (Dose: 2 x 2 cm).

Table 5: Formulation Details of fast dissolving film of Drug

Ingredient (mg) formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9
Glibenclamide (mg)	80	80	80	80	80	80	80	80	80
HPMC E-15 (mg)	200	250	300	-	-	-	-	-	-
HPMC K-15 (mg)	-	-	-	200	250	300	-	-	-
HPMC k-100 (mg)	-	-	-	-	-	-	200	250	300
Citric acid (mg)	50	50	50	50	50	50	50	50	50
TWEEN(80) (ml)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
PEG (400) (ml)	1	1	1	1	1	1	1	1	1
Ethanol (ml)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Water (ml)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Evaluation Parameter of Films

The prepared film was evaluated to following specifications.

Visual Inspection:

Oral fast dissolving films were inspected manually for their transparency and air bubbles.

Weight:

Oral fast dissolving film weighted on the analytical balance.

Thickness:

Film thickness was measured by using a micrometer screw gauge apparatus. A strip of 2 X 2cm was placed between the thickness rods and thickness was measured in five different positions.

Folding endurance:

Folding endurance was measured by manually or practically for the prepared films. Take 2X2cm films and folded repeatedly at the same place till it broke. The no times the film could be folded at the same place without breaking gave the exact valve of folding endurance.

pH:

The pH was determined by dissolving a film in 1-2 ml of distilled water and then the PH of the obtained solution was measured by the pH meter.

Dissolution studies:

The release rate of the Glibenclamide fast dissolving film was determined by the help of USP Dissolution Test Apparatus-II. The dissolution test was performed using 900 ml Phosphate buffer Solution pH 6.8, at 37 ±5ºC with 50 rpm of the paddle speed. Aliquot 5 ml of the solution was collected from the dissolution apparatus at a time interval of 1 min and at the same time add 5 ml or the same amount of fresh dissolution medium. The Aliquot filtered through the Whatman filter paper. The absorbance of the filtered solution was measured at 232 nm. The aliquot should be withdrawn at the zone between the surface of the dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. Cumulative percent drug release can be calculated by using the equation obtained from the standard curve or % drug release formula. (A = Con. of Std. / Abs. of Std. X Abs. of sample X volume of dissolution apparatus X Dilution factor / 1000, B = A-Value/Label claim X100

RESULT AND DISCUSSION:

UV Spectroscopy:

The UV spectrum of Glibenclamide in Phosphate buffer solution pH 6.8 in the range of 400 – 200 nm. The spectrum indicated that the observed λmax of Glibenclamide was 232 nm which is matched with pharmacopoeial value.

Preparation of standard Calibration curve of Glibenclamide:

Glibenclamide showed maximum absorption at wavelength 232nm in PBS pH 6.8. A standard curve was plotted by taking absorption of diluted stock solutions (5, 10, 15, 20, 25, 30 µg/ml) at wavelength 232 nm.

Con.(mg/ml)	Abs.
5	0.07
10	0.14
15	0.201
20	0.269
25	0.34

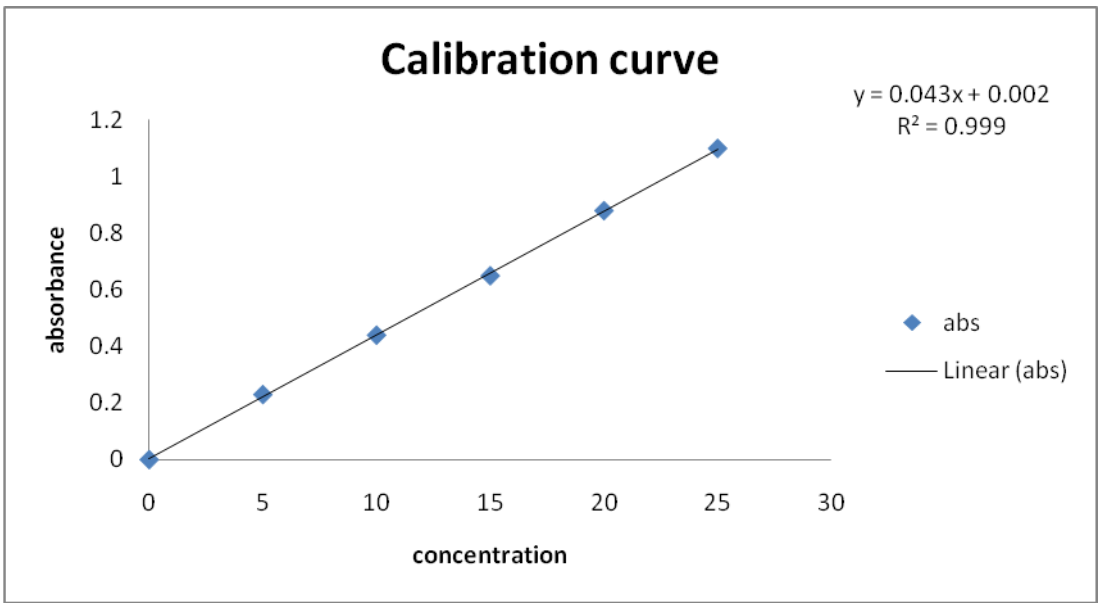

Fig. 3: Calibration curve of Glibenclamide

FTIR:

FTIR studies were carried out for detection of drug-polymer interaction. In the present study the IR study of pure drug Glibenclamide, polymer HPMC E-15, the drug with HPMC K-15, drug and HPMC–K100 drug were carried out to study the compatibility between them.

Observed frequencies	Assignment
1680-1800	C=0 Stretching
1395-1575	C-OH Stretching
1310-1360	C---N Stretching (Ter. Amine)
1020-1220	C-N Stretching (Amine)
1070-1150	-O- Stretching
460-600	C-H Stretching in aromatic ring

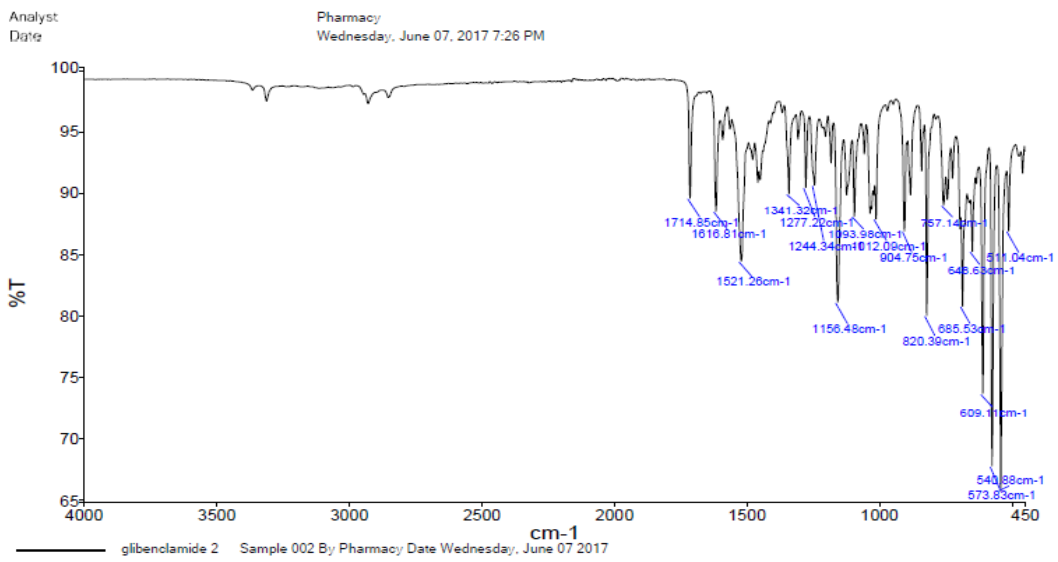

Fig. 4: FTIR Spectra of Glibenclamide with Interpretation data.

Observed frequencies	Assignment
1395-1575	C-OH Stretching
1000-1250	C-0 Stretching (Amine)
680-880	C-H Stretching
600-680	C-Cl Stretching in aromatic ring
460-770	C-H Stretching in aromatic ring

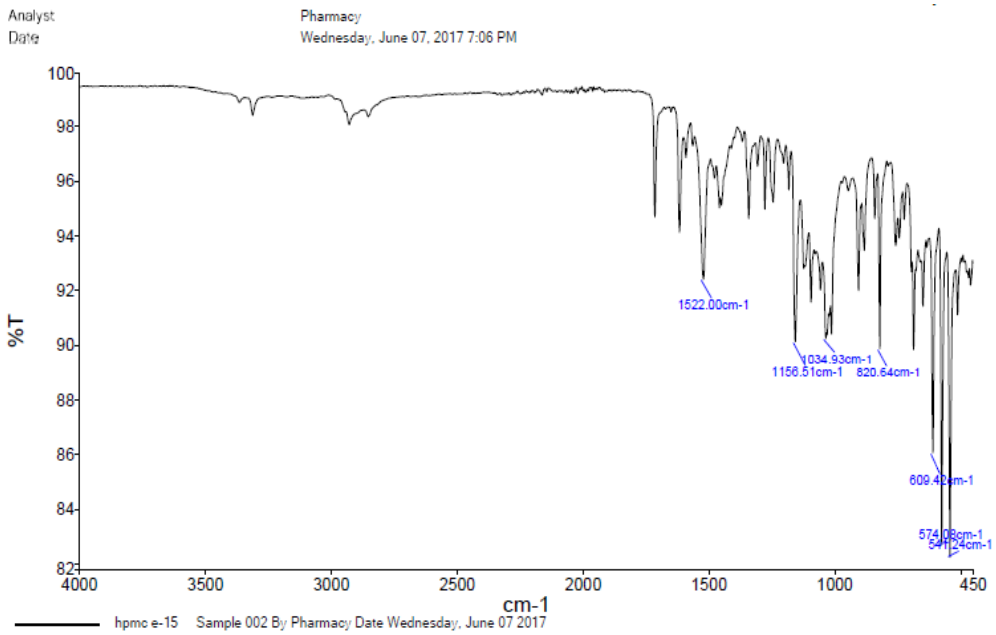

Fig. 5: FTIR Spectra of Glibenclamide+ HPMC E-15.

Observed frequencies	Assignment
1395-1575	C-OH Stretching
1000-1250	C-0 Stretching (Amine)
680-880	C-H Stretching
600-680	C-Cl Stretching in aromatic ring
460-770	C-H Stretching in aromatic ring

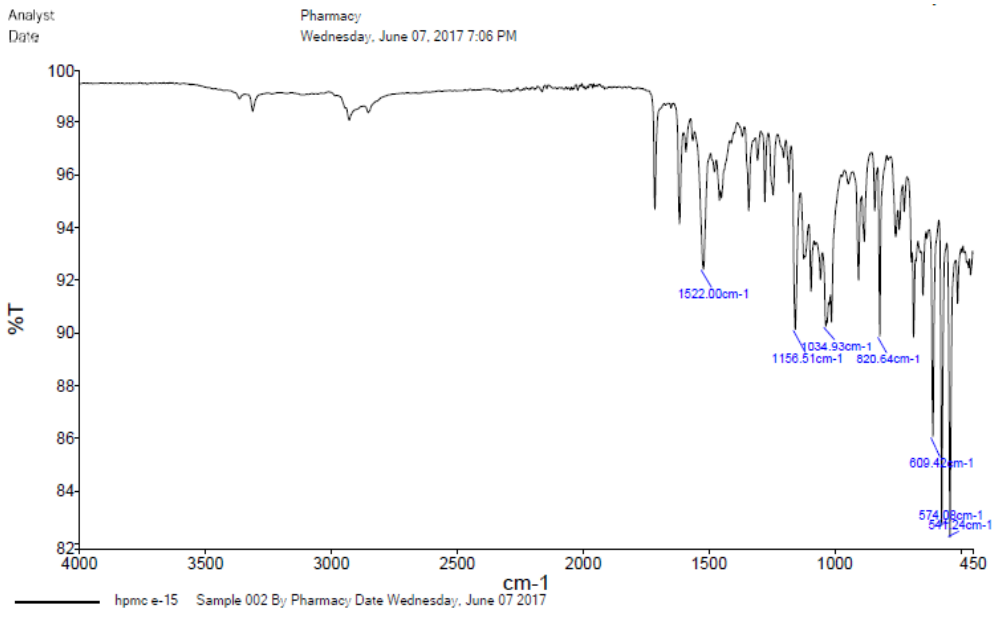

Fig. 6: FTIR Spectra of Glibenclamide + HPMC k-15.

Observed frequencies	Assignment
1680-1800	C=0 Stretching
1395-1575	C-OH Stretching
1310-1360	C---N Stretching (Ter. Amine)
1020-1220	C-N Stretching (Amine)
1070-1150	-O- Stretching
460-600	C-H Stretching in aromatic ring

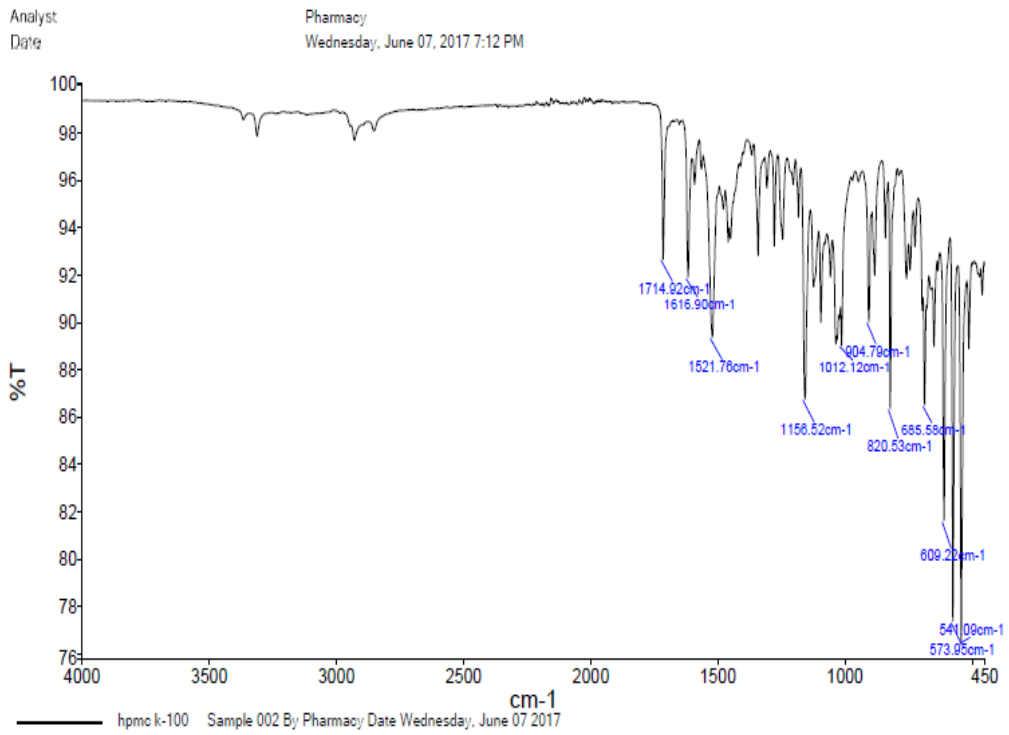

Fig. 7: FTIR Spectra of Glibenclamide + HPMC k-100.

DSC:

DSC studies were carried out for detection of drug-polymer interaction. In the present study, the DSC study of pure drug Glibenclamide polymer HPMC K-15, drug with HPMC E-15, HPMC K-100 & sodium lauryl sulphate were carried out to study the compatibility between them.

DSC of pure drug Glibenclamide:

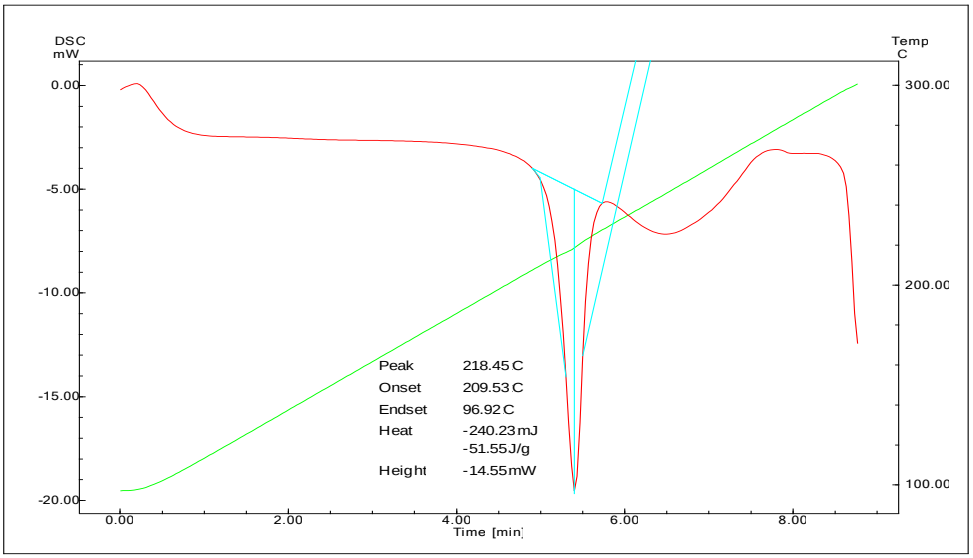

Fig. 8: DSC of Glibenclamide

DSC of EXCIPIENTS &Glibenclamide:

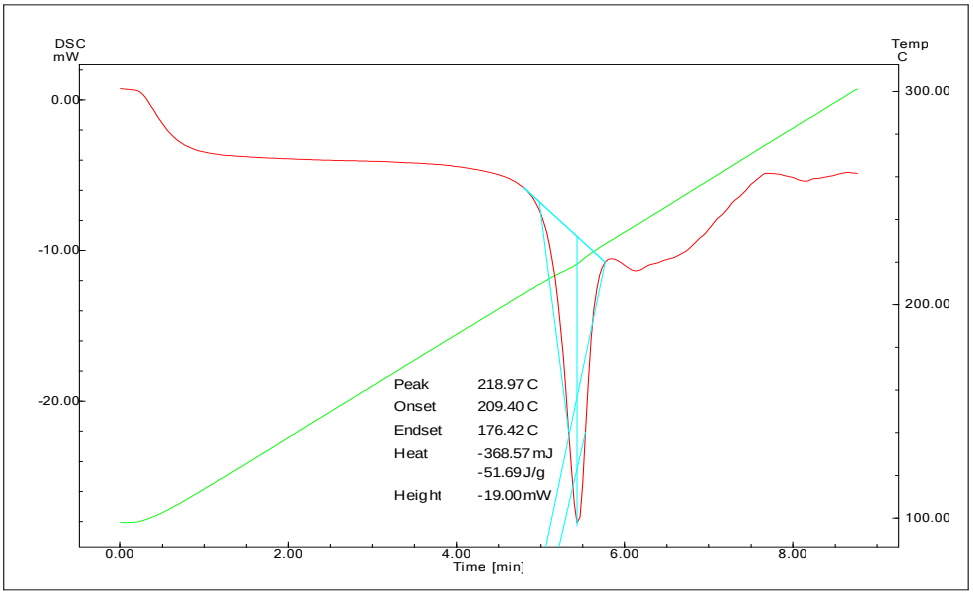

Fig. 9: DSC of Excipients &Glibenclamide

***In-vitro* dissolution studies:**

In present work, an attempt has been made to increase the % drug release of Glibenclamide with changes in the concentration of polymers & plasticizers by solvent casting method.

Table 6: *In-vitro* dissolution study of Glibenclamide

Time(min)	%Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	25.27	28.45	30.64	26.34	28.47	31.85	27.74	28.63	32.45
2	32.84	34.45	36.64	32.12	35.60	39.84	31.86	35.63	42.65
3	33.49	36.74	39.64	34.76	38.26	49.36	45.74	48.46	55.43
4	40.16	42.49	48.45	46.88	47.49	53.83	55.73	57.84	59.46
5	52.24	54.32	57.85	58.55	61.21	66.73	58.83	65.73	68.43
6	60.75	64.67	69.43	62.66	67.45	75.64	68.63	70.84	77.45
7	67.29	72.74	78.38	73.74	75.65	82.54	76.94	76.53	86.64
8	71.13	79.55	81.56	76.14	80.48	85.26	84.37	84.84	89.36
9	74.98	85.64	89.65	86.64	88.64	92.94	91.83	94.32	96.63
10	87.78	96.98	99.55	97.95	98.65	99.67	97.84	98.95	99.99

All values expressed as mean ± SD (n=3), F = Formulation batch.

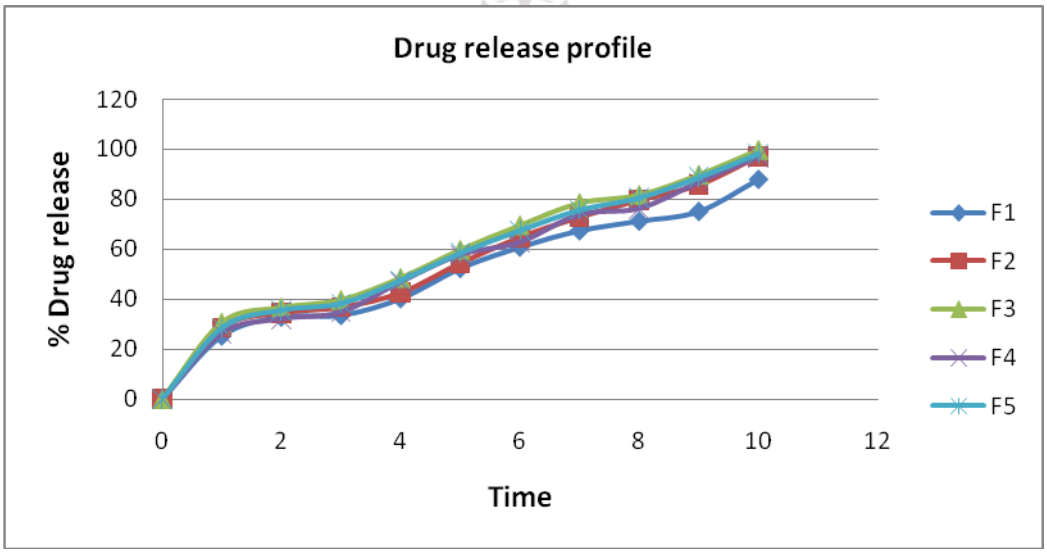

Fig. 10: *In-vitro* dissolution study/profile Glibenclamide of batches F1-F5.

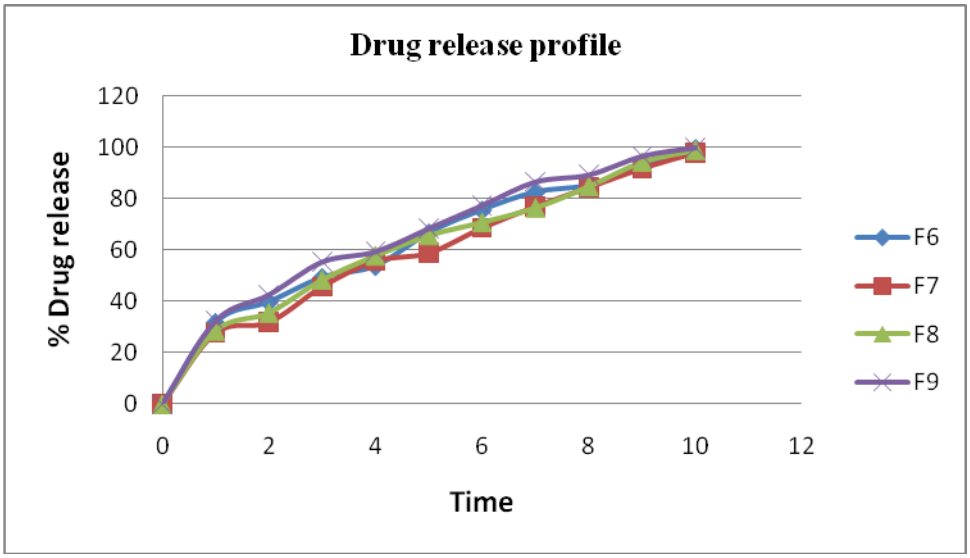

Fig. 11: *In-vitro* dissolution study/profile Glibenclamide of batches F6-F9

Marketed product testing:

The marketed product was tested for a different parameter as shown below.

Table No.7: Marketed product details of GLINIL-5

Parameter to be studied	**Result**
Brand name	Glinil
Strength	5 mg
Marketed by	Cipla Limited
Manufactured by	PGEAD03
Batch No.	05/2017
MFG Date	05/2019
Expiry date	Pack in a strip
Pack Size	White to off-white in round size
Description of dosage form	5 mg
Individual weight of tablet	Titanium Dioxide

Table 8: Dissolution test protocol: GLINIL-5

Name of drug	Glinil
Dissolution apparatus	USP TYPE II
00Temperature	37 ± 0.5 0C
Basket speed	50 rpm
Tablet strength	5 mg
Dissolution medium	PBS Ph 6.8
Volume of dissolution medium	900 ml
Detection	232nm
Volume of sample removed	5 ml
Sampling profile	1 – 5 min

Table 9: Dissolution profile of Marketed tablet GlinilVs Formulation Batch-F9

Time (min)	**% Drug release**	
	GLINIL	F9
1	10.62	32.45
2	15.46	42.65
3	23.85	55.43
4	31.57	59.46
5	46.11	68.43
6	59.21	77.45
7	73.72	86.64
8	85.47	89.36
9	96.89	96.63
10	98.89	99.99

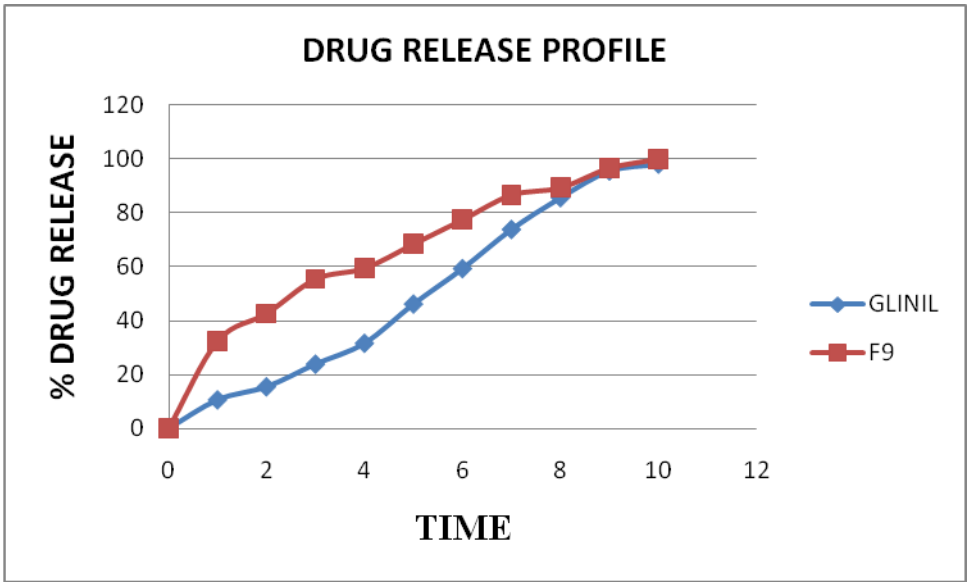

Fig. 12: Dissolution profile comparison study of Marketed product with Formulation batch F9 (Comparative study)

STABILITY STUDY:

The stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation & the drug release. Short term stability studies were performed in a Stability chamber over a period of 3 weeks (21 days) on the promising Fast Dissolving Film formulations F1, F2, F3, F4, F5, F6, F7, and F8&F9. Sufficient number of films formulation were packed in stability container and kept in a Stability chamber at Temperature 450c & RH 75%. Samples were taken on 21st day for drug content estimation; also the thickness, weight, folding endurance and *in-vitro* disintegration studies were performed to determine the drug release profile

Table 10: Evaluation parameter of Fast dissolving film

Formulations	Tack Test	Appearance	Weight mean (mg)	Thickness mean (mm)	Folding Endurance mean	D.T. mean (sec)	Surface P^H	Cont.uniformity%
F1	Non tacky	Transparent	19	1	210	25	6-7	95
F2	tacky	Transparent	25	0.6	228	20	6-7	97
F3	Non tacky	Transparent	28	0.9	236	28	6-7	99.45
F4	Non tacky	Transparent	22	0.8	215	19	6-7	96.34
F5	Non tacky	Transparent	18	0.6	104	22	6-7	97.43
F6	Non tacky	Transparent	29	1.2	232	26	6-7	99.96
F7	Non tacky	Transparent	18	1	217	22	6-7	98.65
F8	Non tacky	Transparent	22	0.8	225	19	6-7	99.54
F9	Non tacky	Transparent	30	1	256	32	6-7	99.75

All values expressed as mean ± SD (n=3), F = Formulation batch, TH = Thickness, Wt. =Weight.

DISCUSSION

In present research work, Design and characterization of polymeric Fast dissolving film for the oral film of Glibenclamide were prepared to improve the efficacy of Glibenclamide by improving its bioavailability also by reducing its dose unlike in concentration. Glibenclamide Fast dissolving film was prepared using HPMC E15, HPMC K-15 and HPMC K-100 in different concentrations by solvent casting technique, the prepared fast dissolving film were evaluated for various parameters and the results of these parameters were given in Table 5 and they are discussed in detail in the following section of this chapter.

Physical appearance and surface texture of fast dissolving film:

These parameters were checked simply with visual infection of Fast dissolving film and by feel or touch. The observation suggests that the Fast dissolving films are having the smooth surface and they are elegant enough to see.

Weight uniformity of fast dissolving film:

The weight of Fast dissolving film was determined using digital balance and the average weight of all Fast dissolving film was given in table 10 Fast dissolving film prepared with HPMC in the concentration 200-300 mg and also in combination of PEG & Tween(80) of 1ml were weighed about 19-28 mg (n=3) respectively. The Fast dissolving film prepared using HPMC K-15 in concentration 200-300mg in the combination of PEG-400, PEG-6000, SLS, and also with Tween 80 having a concentration of 1ml,0.3ml &q.s were weighed about 25-70 mg respectively.

The thickness of fast dissolving film:

The thickness of the fast dissolving film were measured using screw gauge and the average thickness of all Fast dissolving film was given in table 10 The thickness of the Fast dissolving film prepared with HPMC K-15 in the concentration 200-300 mg and also in combination of PEG 1ml and Glycerol of 0.2ml mg the thickness of the Fast dissolving film prepared respectively are 70-100 mm respectively. The thickness of the Fast dissolving film prepared with HPMC K-100 in the concentration200-300 mg in a combination of PEG-400, PEG-6000, SLS and also with Tween 80 having a concentration of 200-300, 50, 200, 50 mg1ml&q.s was 50-170 mm (n=3) respectively.

Folding Endurance of Fast dissolving film:

The folding endurance of the Fast dissolving film was determined by repeatedly folding a small strip of the Fast dissolving film at the same place till it broke and the average folding endurance of all Fast dissolving film was given in table 10 The folding endurance of the fast dissolving film prepared with HPMC K-15 in the concentration200-300 mg and also in combination of PEG & Glycerol of 50 mg 1ml, 0.3ml was 91-142 (n=3) respectively. The folding endurance of the fast dissolving film prepared using HPMC K-100 in concentration 200-300 mg in a combination of PEG-400, PEG-6000, SLS, and also with Tween 80 having a concentration of 200-300, 50, 200, 1ml,0.3ml mg and q.s was 4-120 (n=3) respectively.

Surface pH of fast dissolving film:

Surface pH was determined by the fast dissolving film were allowed in contact with 1ml of distilled water. The surface pH was noted by pH meter near the surface of fast dissolving film

and allowing to equilibrate for 1 min and the surface pH of all fast dissolving film was given in table 10 The surface pH of the fast dissolving film prepared with HPMC K-15 and HPMC K-100 HPMC E-15 was found to in-between 6-7 PH (n=3).

Drug-Polymers interaction studies of fast dissolving film:

Spectrum No. 1. **Pure drug**:

The infrared spectrum of Glibenclamide recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No. 2. **HPMC K-15**:

The infrared spectrum of HPMC K-15 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No. 3. **DRUG + HPMC E-15**:

The infrared spectrum of pure drug &hydroxy propyl methyl cellulose E-15 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No. 4. **DRUG + HPMC K-100**:

The infrared spectrum of Glibenclamide&HPMC K-100 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Spectrum No. 5. **DRUG + TWEEN-80**:

The infrared spectrum of Glibenclamide& tween -80 recorded in a KBr pellet on Perkin Elmer Infrared Spectrophotometer. From the Infrared frequencies & the respective assignments given drug are compatible.

Drug Content uniformity of fast dissolving film:

Glibenclamide fast dissolving films prepared with HPMC K-15 and HPMC K-100 HPMC E-15 in various concentrations and were subjected to the uniform dispersion of drug throughout the patch. In each case, three Fast dissolving film was used and the average drug content was calculated, the results were shown in table 8. The drug was dispersed in the range of 2-2.09 (n=3). Suggesting that drug was uniformly dispersed in all fast dissolving film. The S.D. value calculated for such formulation is very less which suggest that the results are reproducible and accuracy in the method used to prepare the fast dissolving film.

***In-vitro* Drug Release of fast dissolving film:**

All the Fast dissolving film of Glibenclamide prepared was subjected to *In-vitro* drug release studies for a period of 1-10 min.

The formulation F1, F2, F3, F4, F5, F6, F7 , F8& F9 which are prepared using with HPMC K-15 in the concentration 200-300 mg and also in combination of PEG & Glycerol of 1ml 0.3ml released 87.78, 96.98, 99.55, 97.95, 98.65, 99.67, 97.84, 98.95 & 99.99 at the end of 10 min respectively. The detail *In-vitro* released data were shown in table 6 and drug release profile figure 10,11.

Stability study:

The stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation & the drug release. Short term stability studies were performed in a Stability chamber over a period of 3 weeks (21 days) on the promising Fast Dissolving Film formulations F3, F5, F6, F8 & F9. Sufficient number of films formulation were packed in stability container and kept in a Stability chamber at Temperature 45^{o}c & RH 75%. Samples were taken on 21st day for drug content estimation; also the thickness, weight, folding endurance and *In-vitro* disintegration studies were performed to determine the drug release profile. The detail *In-vitro* % drug release stability data were shown in table 6 and Stability parameter (Evaluation) of Fast dissolving films shown in table 6.

CONCLUSION

In present study Glibenclamide, fast dissolving film for buccal drug delivery prepared and evaluated. In the beginning, blank polymeric fast dissolving film was prepared using HPMC

E-15 HPMC K-15, HPMC K-100, SLS, Sodium alginate, PVP, and Cross povidone. The concentration of polymer was varied and the best were chosen for further work. The prepared fast dissolving film was evaluated for a number of parameters like physical appearance and surface texture, weight uniformity, the thickness of fast dissolving film, folding endurance, surface pH, *in-vitro* residence time, drug excipients interaction studies, drug uniformity and *in-vitro* drug release. The fast-dissolving film prepared was checked visually for its appearance & surface texture. All the prepared fast dissolving film was of smooth surface & elegant texture. All the prepared fast dissolving film using a different concentration of various polymers is weighing in between 19.333 ±0.996 to 70.66 ±1.993 mg.

The fast-dissolving film showed folding endurance values in between 5.666 ±4.3204to 142±3.2449. Similarly, surface pH of all the fast dissolving film prepared is ranging in between 6-7pH. The IR studies indicate that Glibenclamide showed complete entrapment within the polymer carrier bonding is suggested and there was no chemical interaction and all excipients are compatible. Similarly, the fast dissolving film was also subjected to drug content uniformity study and it lies in between 2-2.09 mg (n=3) which suggest that uniform dispersion throughout the fast dissolving film. A good % drug release was observed for formulation F3, F5, F6, F8& F9 in 1-10 min. The *In-vitro* drug release study was carried out for all the fast dissolving film and release profile was subjected to various kinetic equations like Higuchi diffusion equation, First order equation, Zero order equation and Peppas exponential equation. The regression coefficient values of this kinetic equation are very nearer to one(1) suggesting that plots are fairly linear and slope values are (>1) more than one in all the cases suggest that drug was released by diffusion mechanism following super case-II transport. From the above results, it can be concluded that Glibenclamide can be delivered in the form of fast dissolving film. Release pattern of the drug from these fast dissolving films can be altered by using different formulation variables. Finally, the stability study was conducted by ICH guideline. It showed no significant change in properties of the optimized formulation and the drug release.

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REFERENCES

1. http://en.wikipedia.org.
2. Biradar SS. Bhagvati ST, Kuppasad IJ. Fast dissolving drug delivery systems; a brief review.Internet J Pharmacol. 2006; 4(2)
3. J.D. Smart, Buccal drug delivery, Expert Opin. Drug Deliv. 2 (2005) 507–517.
4. Lindgren S, Janzon L. Prevalence of swallowing complaints and clinical findings among 50-79-year-old men and women in an urban population. Dysphagia. 1991; 6: 187-192.
5. Sweetman, SC. Martindale: The complete drug reference. 36th ed. London: Pharmaceutical Press; 2009. p. 441.
6. Suresh D. Kumavat, Yogesh Chaudhary, PallaviDuvvuri, JigarDesaiand Franklin Quadras. Preparation and characterization of glibenclamide plasdone S630 solid dispersion by spray drying technique. Der Pharmacia Littre, 2013; 5 (4):310319
7. Liang AC, Chen LH. Fast dissolving intraoral drug delivery systems. Exp Open There Patents.2001; 11: 981–986. http://dx.doi.org/10.1517/13543776.11.6.981
8. Borsadia S, O'Halloran D, Osborne JL. Quick dissolving films-A novel approach to drug delivery. Drug Deliv Technol. 2003; 3: 63–66.
9. M. Carnaby, and M. Crary, 2005, Vol 13, pp970–1975.
10. T. Morita, 2003, Vol 123, pp665–671.
11. Y.Wu, C. Weller, L. Hamouz, F. Cuppett, and M. Schnepf, 2002, Vol 44, pp347–394.
12. A. Hambleton, F. T. Karbowiak, and A. Voilley, 2008, Vol 9, pp1058 1063.
13. Frey. 2006, pp92–93.
14. Omprakash G. Bhusnure, Parvez Kazi, Sachin B. Gholve, Sanjay S. Thonte, Jaiprakash N. Sangshetti. Formulation and Evaluation of Fast Disintegrating Tables of Nifedipine by QbD Approach. IJPPR. Human, 2015; Vol. 4 (3): 198-229.
15. Omprakash G. Bhusnure, MohiteYogita, Sachin S. Gholve, Giram P. Sidram, Thonte S.S. Formulation and Evaluation of Poorly Aqueous Soluble Drug by Solid Dispersion Method. Journal of Pharmacy Research 2016,10(1),33-40
16. BhusnureOmprkash G*, Kawale Prasad, GholveSachin B, and GiramPadmaja S. Formulation and *In-Vitro* Evaluation of Sustained Release Matrix Tablet of Desvenlafaxine Succinate by Interpolyelectrolyte Complex (IPEC) Formation Technique. RJPBCS. 2016;7(2);108-12
17. Amir H. Shojaei. Buccal mucosa as a route for systemic drug delivery: Are view; J. Pharmceut Sci.1998.1. (1) 15-30.
18. Amir H. Shojaei. Buccal mucosa as a route for systemic drug delivery: A review; J. Pharmceut Sci. .1998.1. (1) 15-30.
19. Tora-ToraDerrikson principles of anatomy and physiology 2nd edition edited by Bonnie Roech, Published by John wily & sons Inc. 2007, 902-908
20. Ross &Wilson. Anatomy and physiology in health and illness 9th edition edited by Anne Waugh & Alison Graw Published by Churchill Livingstone, Edinburgh;2001. 289-293
21. Chatter jee C. C. Human anatomy and physiology 10th edition Published by medical allied agency, Calcutta 1985. 427-435
22. Kharenko E. A, Larionova N. I, and Demina N.B. Mucoadhesive drug delivery system (Review). Pharmaceutical Chemistry Journal., 2009, 43 (4): 200-209.
23. Mashru RC, Sutariya VB, Sankalia MG, Parikh PP. Development and Evaluation of Fast Dissolving Film of Salbutamol Sulphate. Drug DevIndPharma 2005;1:25-34.
24. Chan SY, Chen LL, Chetty D, inventors. Orally Dissolving Films. US patent 20060198873A1. 2006 Sep 7.
25. Umekar MJ, Yeole PG. Research Paper: Characterization and evaluation of natural copal gum-resin as film-forming materialist J Green Pharma 2008;2:37-42.

26. Dixit RP, Puthli SP. Review Oral strip technology: Overview and future potential. J Controlled Release 2009; 139:94-107.
27. Garsuch VI. Preparation and characterization of Fast Dissolving Oral Films for paediatric use. Inaugural Dissertation to Heinrich Heine University, Dusseldorf, Germany 2009; 3.
28. Indian Pharmacopoeia. Govt. Of India. Ministry of Health and Family Welfare, Published by The Indian Pharmacopoeia Commission, Ghaziabad 2007 (2); 672-674(b).
29. Aggarwal V, Kothari B, Moe DV. Drug Delivery: Fast Dissolve System. In, Swarbrick J. (ed) Encyclopedia of Pharmaceutical Technology. 3rd ed. New York: Informa Healthcare 2007; 2:1104-1114.