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Pharmaceutical Sciences **Research Article……!!!**

"FORMULATION AND EVALUATION OF DEXLANSOPRAZOLE BUCCAL TABLET WITH DIFFERENT POLYMERS"

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KEYWORDS:

Dexlansoprazole, HPMCK4M, HPMCK15M, Carbopol.

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ABSTRACT

In the present study an attempt was made to formulate and evaluate a new Bucco adhesive tablets for buccal drug delivery of Dexlansoprazole in order to overcome bioavailability related problems, to reduce dose dependent side effects and frequency of administration. Different twelve formulations of mucoadhesive buccal tablets were prepared by using HPMCK4M, HPMC K15M and Carbopol 934 as mucoadhesive polymer in a different concentration by direct compression method. The prepared formulations were evaluated for pre compression and post compression parameters which revealed good flow properties of the blend and physical attributes of the prepared tablets were found to be practically within control limits. The swelling index was proportional to polymer content. The surface pH of all tablets was found to be satisfactory i.e. close to neutral pH hence, buccal cavity irritation should not occur with these tablets. Drug release and drug diffusion from the tablets were depended on the concentration and type of the polymer used in the formulation. *FT-IR* studies showed the compatibility of drug with excipient. From the *in-vitro* drug release study it was found that formulation F5 and F6 has good drug release (95.83%&92.84%) when compared to other formulations. The formulation F5 and F6 containing Dexlansoprazole, HPMCK15M as mucoadhesive polymer is the optimized formulation. The release data was treated with kinetic equation and it followed zero order release. The mechanism of drug release was found to be Fickians diffusion and followed anomalous release.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a chronic symptom of mucosal damage caused by stomach acid coming up from the stomach into the esophagus. GERD is caused by the changes in barrier between the stomach and the esophagus, including abnormal relaxation of the lower esophageal sphincter. The most common symptoms include heart burn and regurgitation fig-1. Medications such as proton pump inhibitors, H_2 receptor blockers and antacids are used in the treatment of GERD. DSP is a proton pump inhibitor drug used in the treatment of GERD. However, it is degraded in acidic stomach pH, thus lacking in pharmacological action of the drug.GERDis a common condition with a prevalence of 10–20% in the Western world and an annual incidence of 0.38–0.45%. The range of GERD prevalence estimate is 18.1–27.8% in North America and 8.8–25.9% in Europe. In the United States (US), 20% of the population experience GERD-related symptoms weekly and 7% daily. Several studies have demonstrated that patients with GERD have reduced health-related quality of life and work productivity. GERD is the most common outpatient gastroenterology diagnosis in the US with a concomitant significant economic burden.

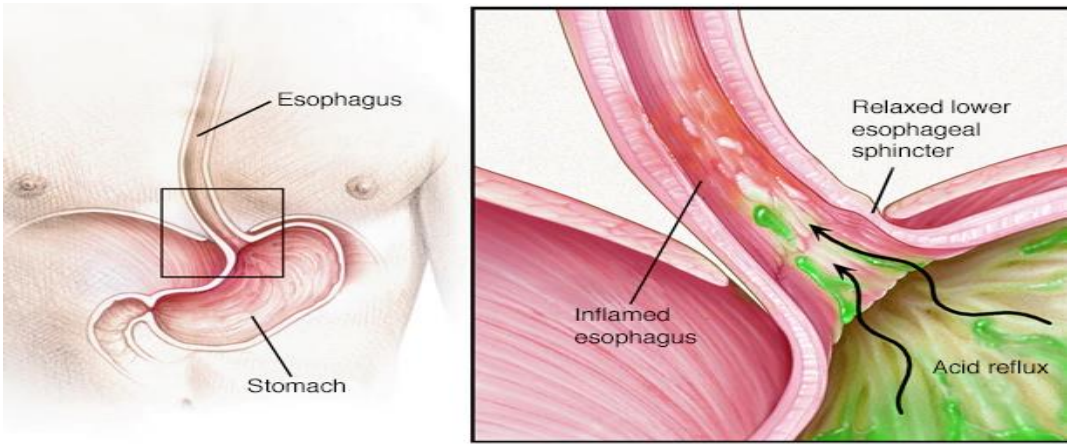


Fig1: Heart burn and GERD occur

II. DEXLANSOPRAZOLE

Dexlansoprazole, sold under the trade name Dexilant among others, is a medication which reduces stomach acid. It is used to treat gastroesophageal reflux disease. Effectiveness is similar to other proton pump inhibitors (PPIs).

Dexlansoprazole is a new generation PPI used for the management of symptoms associated with GERD and erosive esophagitis.

BUCCAL MUCOSA

1) Anatomy & Physiology of Oral Mucosa

i) The oral cavity is lined by thick dense & multi-layered mucous membrane of highly vascularized nature.

ii) Drug penetrating into the membrane passes through net of capillaries & arteries and reaches the systemic circulation.

2) There are mainly three functional zones of oral mucosa:

i) Masticatory mucosa: (25% of the total oral mucosa) covers the gingiva and hard palate. Keratinized epithelium

ii) Lining mucosa: (60% of the total oral mucosa) covers the lips, cheeks, soft palate, lower surface of the tongue and the floor of the oral cavity. Non-keratinized mucosa.

iii) The specialized mucosa: (15% of the total oral mucosa) is found on the dorsum of the tongue high selective keratinizationfig:4

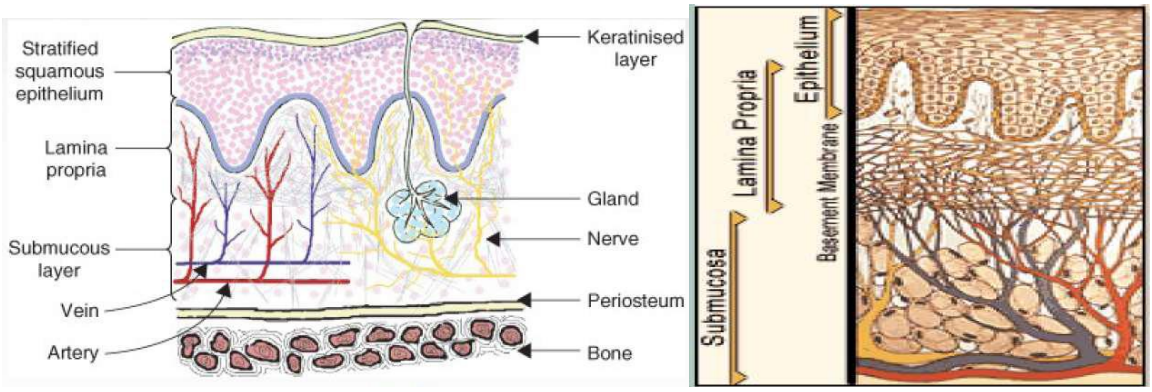


Fig:2 Oral moucosa

Mu**coadhesive drug delivery system.**

One such novel drug delivery system is that the mucoadhesive drug delivery system. Investigation regarding the mucoadhesive system began within the 1980's. Dosage forms designed for mucoadhesive drug delivery should be small and versatile enough to be acceptable for patients and will not cause irritation. Other desired characteristics of a mucoadhesive dosage form include high drug loading capacity, controlled drug release (preferably unidirectional release), good mucoadhesive properties, smooth surface, tastelessness, and convenient application. Bio-erodible formulations containing thermoplastic polymers are often beneficial because they are doing not require system retrieval at the top of desired dosing interval. Variety of relevant mucoadhesive dosage forms are developed for a spread of medicine. Several peptides, including TRH, Insulin, Octreotide, Leuprolide, and Oxytocin, are delivered via the mucosal route, albeit with relatively low bioavailability (0.1–5%), owing to their hydrophilicity and enormous relative molecular mass, also because the inherent permeation and enzymatic barriers of the mucoadhesion. The various sites available for mucoadhesion within the body are :

i) Ocular

ii) Oral

iii) GIT

iv) Buccal

v) Nasal

vi) Rectal

vii)Vaginal

Each site of mucoadhesion has its own advantages and drawbacks alongside the basic property of prolonged residence of dosage form at that specific site. In buccaland sublingual sites, there's a plus of fast onset alongside bypassing the first pass metabolism, but these sites suffer from inconvenience due to taste and intakeof food. In GIT, there's an opportunity for improved amount of absorption due tomicrovilli, but it's a drawback of acid instability and first-pass effects. Rectal andvaginal sites are the simplest ones for the local action of the drug but they suffer frominconvenience of administration. Nasal and ophthalmic routes have another drawback ofmucociliary drainage and clearance by tears, respectively, that might clear the dosageform from the location.

MATERIALS AND METHODS

MATERIALS

Dexlansoprazole giftsample obtained from Sri Krishna Pharma ltd, Carbopol934 balaji drug,HPMC and Magnesium stearate obtained from Yarrow Chem products Mumbai, Talc Centraldrug house (P) LTD.

Table: 1 Composition of Bucco adhesive tablets containing Dexlansoprazole

Ingredients (mg)	**Formulation code**											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Dexlansoprazole	30	30	30	30	30	30	30	30	30	30	30	30
HPMC K4M	30	60	90	120								
HPMC K15M					30	60	90	120				
Carbopol 934									30	60	90	120
Mannitol	136	106	76	46	136	106	76	46	136	106	76	46
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2

METHOD OF PREPARATION

Direct compression method was employed to prepare buccal tablets of Dexlansoprazole using HPMC K4, HPMC K15 and Carbopol 934 as polymers. All the ingredients including drug, polymer and excipients were weighed accurately according to the batch formula (Table:5) Then all the ingredients except lubricants were mixed in the order of ascending weights and blended for 10 min by triturating in a glass mortar & pestle. After uniform mixing of ingredients, lubricant was added and again mixed for 2 min. Final lubricated blend equivalent to the compressed in to tablets using 4 mm round flat punches on 10-station rotary tablet compression machine (Rimek). mucoadhesive tablet with a total weight of 200 mg/tablet.

EVALUATION OF BUCCAL TABLETS CONTAINING

Determination of angle of repose (θ)

A glass funnel is held in place with a clamp and place a graph paper below it. Approximately weighed quantity of powder is poured through the funnel keeping the orifice of the funnel blocked by the thumb. A gap of 6.4 mm is maintained between the bottom of the funnel stem and the top of the powder pile.

Again, the powder is poured through the funnel keeping the orifice of the funnel blocked by the thumb. The height of the heap is measured. The circumference of the heap is marked by pencil and diameter is determined with the help of scale and finally the radius is determined,and the angle of repose is calculated using the formula.

Determination of Bulk Density and Tapped Density

20 g of the mixed blend (W) was introduced into a 100 ml measuring cylinder, and the initial volume was observed. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals for 100 tapping. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated using the following formula.

Bulk density = W / VO

Tapped density = W / VF

Where, W = weight of the initial granules

VO = Initial volume of the granules

VF = Final volume of the granules.

Hausner's Ratio: It indicates the flow properties of the granules and is measured by the ratio of tapped density to the bulk density.

Hausner's Ratio = Tapped density/Bulk density

Compressibility index (Carr's Index): The flow ability of powder can be evaluated by comparing the bulk density and tapped density of powder and the rate at which it packed down. Compressibility index is calculated.

$$\text{Compressibility index (\%)} = \frac{\text{(Tapped density – bulk density)}}{\text{Tapped density}} \times 100$$

Post-compression Parameters

Appearance, colour, and odour of tablets

Organoleptic properties such as taste, colour, odour was evaluated. Ten tablets from each batch were randomly selected and taste tested, colour visually compared and odour checked.

Weight variation

All prepared Dexlansoprazole buccal tablets were evaluated for weight variations as per USP monograph. Twenty tablets were randomly selected from each batch and individually weighed using an electronic balance. The average weight was calculated, individual tablet weight was then compared with the average value to find out the deviation in weight and percent variation of each tablet was calculated. The weight variation of tolerances for uncoated tablet was given below:

Tablet hardness

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its strength or hardness. The hardness of ten randomly selected buccal tablets was measured by using Monsanto hardness tester which measures the pressure required to break diametrically placed tablets by applying pressure with coiled spring and expressed in Kg/cm^2.The mean and standard deviation values were calculated and reported.

Friability

Friability was performed by using Roche Friabilator to determine friability It is expressed in terms of percentage (%). For friability testing 10 tablets from each batch were randomly selected, initially weighed and transferred into Friabilator apparatus that revolves at 25 rpm for 4 minutes dropping the tablets through a distance of 6 inches with each revolution. At the end of test (after 100 revolution), tablets were dedusted, reweighed and percentage loss was determined.

% friability was then calculated by the following formula:

$$\text{\% Friability} = \frac{\text{Initial weight of tablets - final weight of tablet}}{\text{Initial weight of tablets}} \times 100\%$$

Percentage friability of tablets less than 1% was considered as acceptable.

Content Uniformity

Five tablets from each formulation were powdered individually and a quantity equivalent to 30 mg of Dexlansoprazole was accurately weighed and extracted with a suitable volume of 6.8 pH buffer. Each extract was suitably diluted and analysed spectrophotometrically at 285 nm.

Swelling study

The swelling behaviour of a dosage form was measured by studying its weight gain or water uptake. Buccal tablets were weighed (W_0) and placed separately in petri dishes with 5ml of phosphate buffer pH 6.8. At the interval of 1,2,3,4,5,6,7 and 8 hours, tablets were removed from the petri dish and excess surface water was removed carefully using filter paper. The swollen tablet was then reweighed (W_t) and the swelling index (SI) were measured in terms of percent weight gain, as given by the following formula:

$$SI = \frac{(Wt - W0)}{W0} X\ 100$$

Where, SI= Swelling index

W_0 =Initial weight of dosage form

W_t =Weight of dosage form at time t

Surface pH

The surface pH of the tablet was determined to investigate the effect of pH on the bioadhesion and possible side effects of the tablets in vivo. This was determined by allowing the tablet to swell in 10 ml of phosphate buffer (pH 6.8) for 2 hrs. A combined glass pH electrode was brought in contact of the swollen tablet and the pH was measured after 1 min equilibrium.

***Ex-vivo*mucoadhesion time**

Mucoadhesive strength of the tablets was measured on a modified two-arm physical balance. The sheep buccal mucosa was used as biological membrane for the studies. The sheep mucosa was obtained from the local slaughter house and stored in krebs buffer at 4^0C from the time of collection and used within 3 hrs of procurement. The membrane was washed with distilled water and then with phosphate buffer pH 6.8 at 37^0C. The buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece

of buccal mucosa was tied to the glass vial, which was filled with phosphate buffer. The glass vial was tightly fitted into a glass beaker (filled with phosphate buffer pH 6.8 at 37^0 C ± 0.5^0C), so that it just touches the mucosal surface. The buccal tablets were suck to lower side of a rubber stopper. The two side of the balance were made equal before the study, by keeping a 5 gms, was removed from the right-hand pan, which lowered the pan along with the tablet over the mucosa. The balance was kept in the position for 1 min contact time. Mucoadhesive strength was assessed in terms of weight (gm) required to detach the tablet from the membrane. The time for detach from the sheep buccal mucosa was recorded as the mucoadhesion time. Mucoadhesive strength which was measured as force of adhesion in Newton's formula.

Force of adhesion (N) = Mucoadhesive strength / 100 × 9.81

In-vitro drug release study

The USP type- II rotating paddle method was used to study the drug release from the tablet. The dissolution medium consisted of 900ml of sodium phosphate buffer pH 6.8. The release study was performed at 37± 0.5^0C, with a rotation speed of 50 rpm. The disk was placed at the bottom of the dissolution vessel. Aliquots (5ml each) were withdrawn at regular time intervals and replaced with fresh medium to maintain sink conditions. The samples were filtered, with appropriate dilutions with phosphate buffer pH 6.8 and were analysed spectrophotometrically at 285nm.

Release kinetics

The results of *in-vitro* release profile obtained for optimized formulations were plotted in modes of data treatment as follows

1. Zero- order Kinetic model – Cumulative % drug released versus Time.

2. First- order Kinetic model – Log cumulative % drug remaining versus Time.

3. Higuchi's model- Cumulative percent drug released versus square root of time.

4. Korsmeyer equation / Peppa's model- Log cumulative percent drug released versus log time.

Stability study

In any rational drug design or evaluation of dosage forms for drugs, the stability of the active component must be major criteria in determining their acceptance or rejection. Stability can be

defined as the capacity of drug product to remain within specifications established to ensure its identity, strength, quality, and purity.

Purpose of stability studies

Stability studies are done to understand how to design a product and its packaging such that product has appropriate physical, chemical and microbiological properties during a defined shelf-life when stored and used.

The international Conference on Harmonization (ICH) guidelines titles "Stability Testing of New Drug substance and products" (Q A) describes the stability test requirements for drug registration application in the European Union, Japan and the United States of America. ICH species the length of study and storage conditions as given below:

Table:11 Drug substances intended for normal storage

Study type	Storage conditions	Periods
Long-term testing	25ºC ±2 ºC/60%RH±5%RH	12 Months
Accelerated testing	40 ºC±2 ºC/75%RH±5%RH	6 Months

RESULTS AND DISCUSSION

PREFORMULATION STUDIES

Drug description

Description of drug were showed on below Table no:2

Table no:2Description about drug

Drug	Dexlansoprazole
Nature	Solid
Colour	White
Odour	Odourless

Solubility Analysis

Solubility studies were carried out in different solvents and observations were showed Table no:3

Table no:3 Solubility profile of Dexlansoprazole

Solvent	Solubility
Methanol	Very soluble
0.1 N HCl	Very soluble
Phosphate buffer pH 6.8	Freely soluble
Water	Partially soluble

*All tests are done for three times

Solubility analysis is important because the drug has to dissolve in the solvents and also in the dissolution medium used. Dexlansoprazole was found to be very soluble in Methanol and0.1N HCL, freely soluble in Phosphate buffer pH 6.8 and partially soluble in water.

Melting Point determination: Melting point were carried out and observations were showed Table no: 4

Table no: 4 Melting point of Dexlansoprazole

Sample	**Melting point of sample in literature**	**Melting point of sample experimented determine***
Dexlansoprazole	140^{o}C	140^{o}C ± 1

- All readings are average of three determinations (n=3)

  Melting point of the obtained Dexlansoprazole was found to be 140^{o}C ± 1, that is within the standard range of 140^{o}C, which showed that the procured pure drug is Dexlansoprazole which is free from impurities.

  Drug and excipients compatibility studies by FT- IR Spectroscopy.

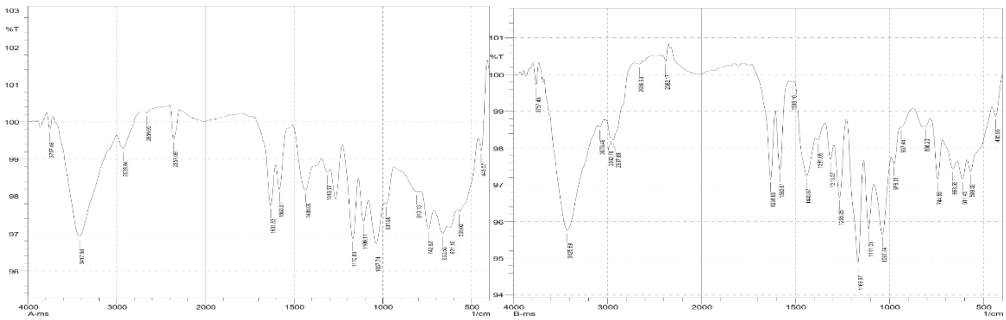


Fig: 3 FT-IR Spectrum of pure drug Dexlansoprazole**Fig:4 FT**-IR Spectrum of Dexlansoprazole +HPMC K4M

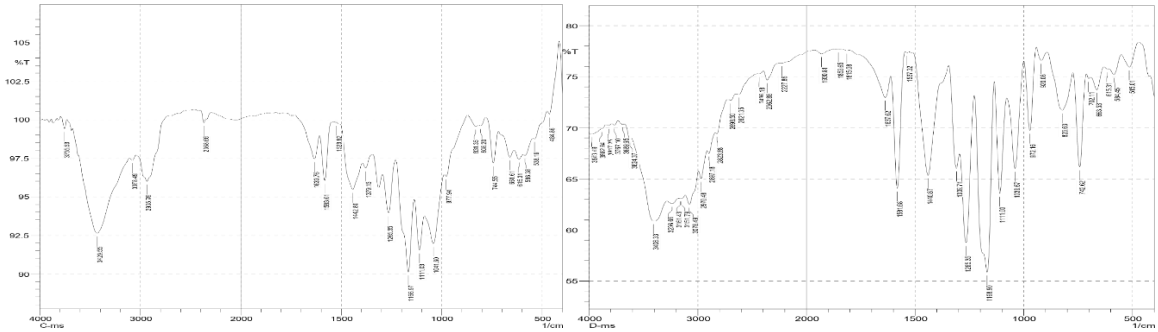


Fig:5 FT-IR Spectrum of Dexlansoprazole+HPMC K15M **Fig:6** FT-IR Spectrum of Dexlansoprazole +Carbopol 934

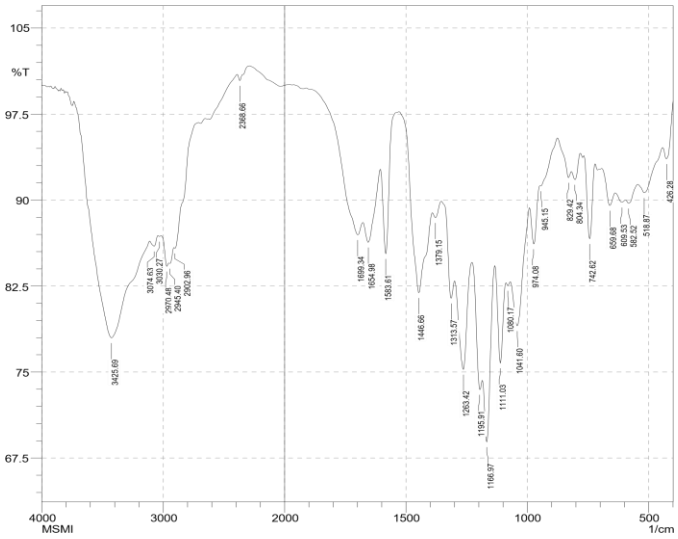


Fig:7 FT-IR Spectrum of Dexlansoprazole +All polymers

FTIR peaks of Dexlansoprazole is same as that of Drug and polymers are found there is no interaction.

The λmax in phosphate buffer pH 6.8

The λmax of Dexlansoprazole in phosphate buffer pH 6.8 was found to be 285nm.

Standard Calibration Curve

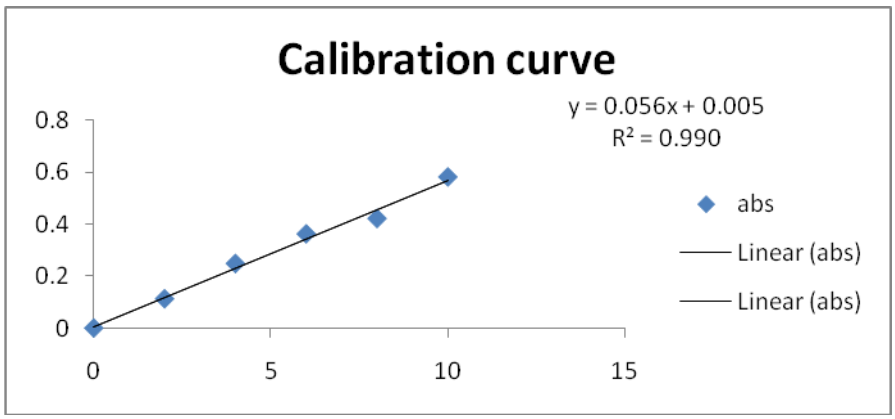


Fig:8 Calibration curve of Dexlansoprazole in phosphate buffer pH 6.8

Precompression evaluation parameters for powder mixture

The results are showed in table no:7

Table no: 7 Precompression parameters results for formulation F1-F12.

Formulation code	Formulation Code				
	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Angle of repose (˚)	Carr's index%	Hausner's ratio
F1	0.55	0.62	26.56	11.24	1.12
F2	0.58	0.66	27.47	12.12	1.13
F3	0.52	0.58	23.45	10.34	1.11
F4	0.55	0.62	27.01	11.29	1. 12
F5	0.55	0.62	24.17	11.29	1.12
F6	0.58	0.66	26.64	12.12	1.13
F7	0.62	0.71	26.56	12.67	1.07
F8	0.66	0.71	27.47	12.67	1.14
F9	0.62	0.66	29.98	6.06	1.06
F10	0.62	0.66	25.70	6.06	1.06
F11	0.66	0.71	26.56	12.67	1.07
F12	0.58	0.66	28.23	12.12	1.37

All readings are average of three determinations (n=3)

Post compression evaluation parameters: The results of post compressional evaluation parameters are shown in table no:8

Table no:8 Post compression parameters results for formulation F1-F12

Formulation code	Formulation Code					
	Thickness(mm)	Hardness (kg/cm^2)	%Friability	Weight variation (mg)	Drug content (%)	Surface pH
F1	3.7	3.8	0.25	201	85.33	5.22
F2	4.2	4.2	0.3	201	83.41	5.43
F3	4.0	4.1	0.5	200	85.17	5.60
F4	3.9	4.2	0.5	200	80.82	5.9
F5	4.0	4.0	0.25	201	98.12	6.21
F6	3.8	4.1	0.15	201	97.88	6.47
F7	3.7	4.2	0.75	200	93.0	6.10
F8	4.7	4.2	0.65	201	88.65	6.17
F9	4.2	4.0	0.25	200	86.92	6.42
F10	3.9	4.1	0.5	201	89.87	5.7
F11	3.9	4.0	0.4	200	83.83	5.65
F12	4.1	4.2	0.35	200	79.85	6.51

All readings are Average of three determinations (n=3)

Swelling index

The swelling indices of the various buccal formulations are table no:9

Table:9 Swelling index of the Dexlansoprazole buccal tablets

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	25.0	20.0	17.5	10.0	30.0	28.5	20.0	15.0	17.5	7.5	8.5	10.0
2	35.0	27.5	25.0	23.5	45.5	46.0	29.5	28.5	25.5	20.0	17.5	23.5
3	45.0	35.0	35.0	31.0	51.5	55.5	37.5	35.0	36.5	35.0	25.0	37.5
4	50.0	42.5	43.5	43.5	60.0	62.5	45.0	43.5	46.0	45.0	39.0	45.0
5	65.0	50.0	51.5	46.0	74.5	73.5	57.5	63.5	56.5	54.5	45.0	58.5
6	75.0	60.0	64.01	52.5	83.0	84.5	65.0	76.0	65.0	64.5	55.5	62.5
7	88.5	77.5	70.01	60.0	92.0	91.5	75.0	84.0	69.0	68.5	69.5	70.5
8	92.0	87.5	82.5	75.0	98.0	95.0	91.5	87.0	76.0	80.0	77.5	84.5

***Ex-vivo* Mucoadhesive strength, Force and Retention Time Table no:10**

Formulations	Mucoadhesive strength	Mucoadhesive force	Retention Time
F1	30.20	2.90	45min
F2	32.14	3.15	1.13min
F3	34.18	3.35	1.35min
F4	29.14	2.85	1.55min
F5	32.17	3.15	3.45min
F6	36.14	3.54	3.30min
F7	31.05	2.94	3.10min
F8	28.65	2.81	2.50min
F9	30.94	3.03	2.20min
F10	33.27	3.26	2.10min
F11	35.45	3.47	2.30min
F12	22.47	3.18	3.10min

***In-vitro* drug release study:**

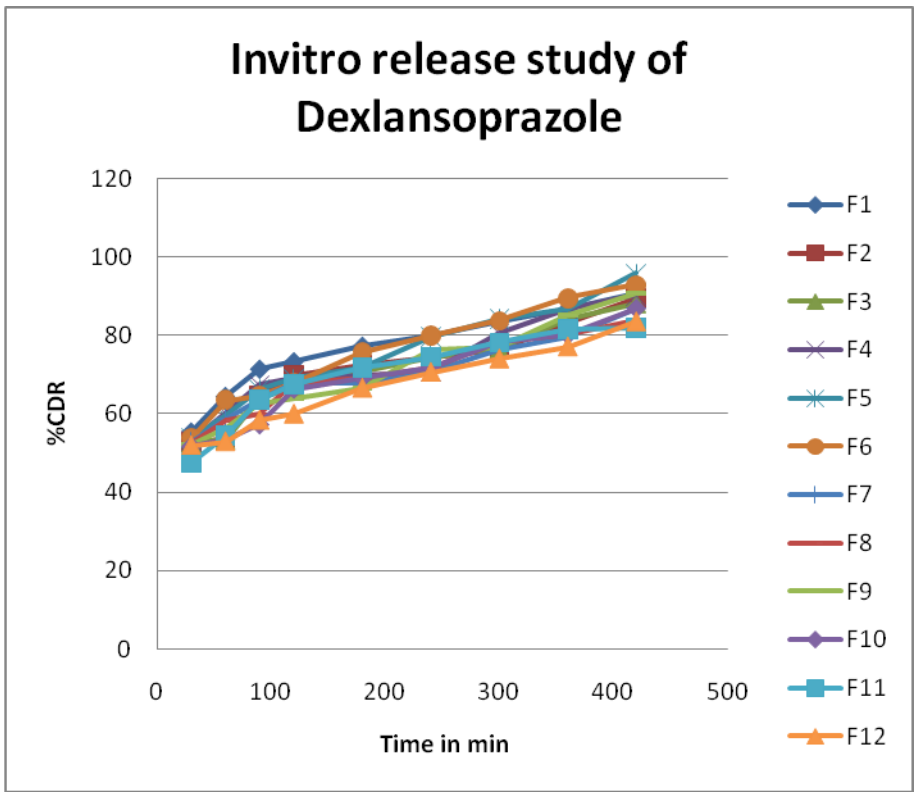


Fig:9 In vitro drug release study of all formulations in phosphate buffer pH 6.8

Kinetics of drug release

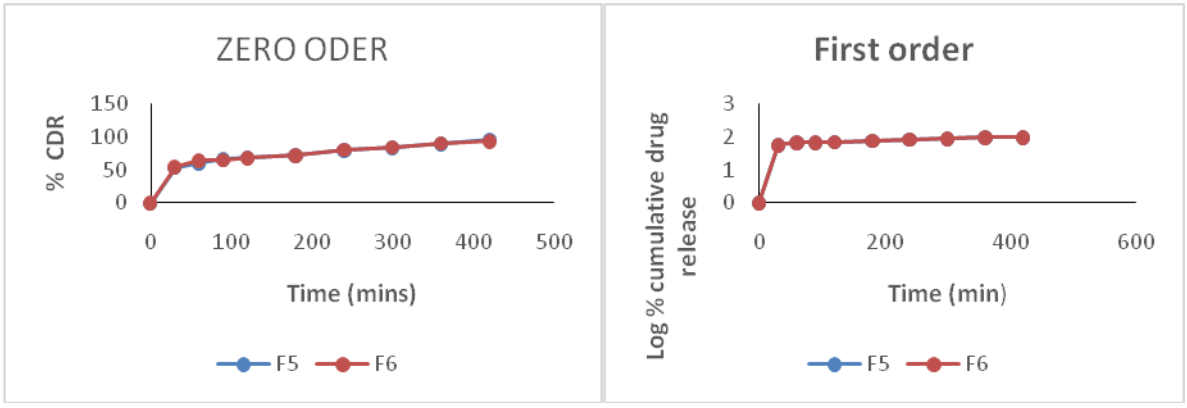
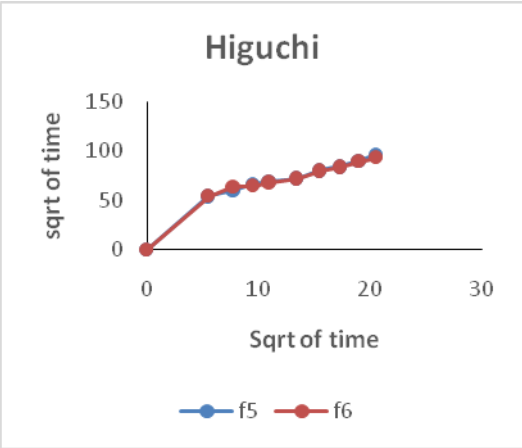


Fig: 10Zero order kineticsFig:11 First order



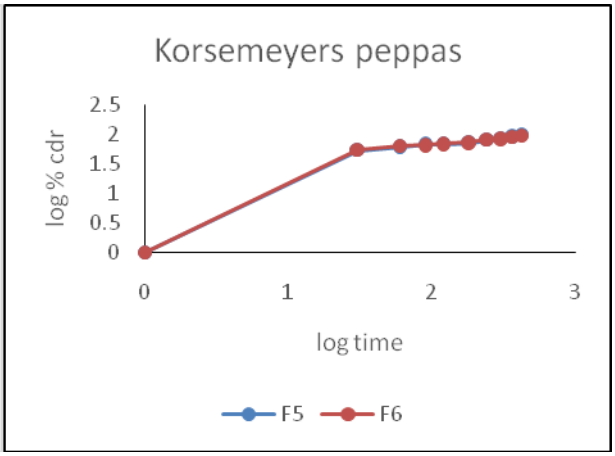


Fig:12 HiguchiFig:13 Korsmeyerpeppas

Table:11 Kinetics modelling data

Formulation	KINETIC DRUG RELEASE		MECHANISM OF RELEASE		
	ZERO ORDER	FIRST ORDER	HIGUCHI	KORSEMEYER PEPPAS	
	Correlation coefficient (r^2)	Correlation coefficient (r^2)	Correlation coefficient (r^2)	Correlation coefficient (r^2	Slope 'n' value
F5	0.67175	0.44925	0.89735	0.7845	0.4252
F6	0.6614	0.43752	0.89695	0.7965	0.4159

STABILITY STUDIES RESULTS

Three months of stability study for best formulations were carried out as per procedure Formulation F5& F6 was analysed for organoleptic properties and other various post compression study.

Table: **12** Stability data of selected F5 & F6 formulation stored at 40°C ± 2°C and 75 ± 5% RH.

No of Days	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	pH	Swelling index	%Drug Content	% CDR
0	4.0	4.1	0. 25	6.25	98.0	98.0	95.00
30	4.1	4.0	0.26	6.30	98.12	97.95	94.85
60	4.12	4.1	0.26	6.45	98.3	97.90	94.70
0	3.8	4.1	0.15	6.47	95.0	97.88	92.84
30	4.0	4.12	0.17	6.30	95.11	97.0	92.0
60	4.11	4.1	0.18	6.12	95.2	96.86	91.89

DISCUSSION

• Melting point is within the standard range of 140˚C which shows pure drug Dexlansoprazole is free from impurities.

• No considerable change in the FT-IR peak of Dexlansoprazole when mixed with excipient compared to pure Dexlansoprazole.

Pre compression studies of powder blend: The results of the preformulation studies are represented in table no. The bulk density and tapped density for core granules were found to be 0.55 to 0.58 g/cc and 0.62to 0.66g/cc respectively.

Hausner's ratio values were found in the range of 1.12 to 1.13 indicates good/free flow. The Carr's index values found in the range of 11.29 to 12.12 % which indicate that powder formulation has fair flow properties and powder bed is compressible. The angle of repose was found in the range of 24.17˚-25.64˚ indicating excellent flow property of the powder.

Pre compression studies of Dexlansoprazole buccal tablets

Thickness of tablets

All the formulations were evaluated for their thickness using Vernier callipers as per procedure and results . The range of all formulations was found to be 3.7to 4.17 mm. The average thickness for all the formulations were found to be within the allowed limit of deviation i.e.5% of the standard value.

Hardness

All the tablets formulations were evaluated for their hardness as per procedure in methodology and results. All the formulations have an average hardness in between 3.8 to 4.2 kg/cm2 which was found to be acceptable.

Friability

Friability is determined to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting. All the tablets formulations were evaluated for their percentage friability as per the procedure and results. The average percentage friability for all the formulations were in the range of 0.15% to 0.75%, which was considered acceptable.

Weight Variation

All the tablets formulations were evaluated for their uniformity of weight according to the procedure and the results. The maximum weight was 202 and the minimum observed was 200. Thus, all the formulations were found to be complying with the standards given in IP.

Drug Content uniformity

Good drug content uniformity in all the tablet formulation was observed among the different bathes of the tablets and the percent drug content was found to be in the range of 79.85 to 98.12. This ensures that all the formulations contain stated or labelled amount of Dexlansoprazole in the tablets.

Surface PH

The surface PH of different batches of tablets was found in the acceptable range of 5.22 to 6.51. Hence it will not produce any local irritation to the mucosa.

Swelling index

Swelling index is an important parameter in judging the mucoadhesion property, at least in the initial stages, since water uptake is important for the polymers to uncoil and interact with the mucin. For uniform drug release and for effective mucoadhesion a good swelling behaviour of buccal tablet system is an appropriate and essential property. The formulation F1, F2, F3 & F4 containing HPMCK4M showed 40-50% swelling within 2 hrs and was found to be gradually increasing with time this is because HPMCK4M is swellable in water. The formulation F5, F6, F7 & F8 exhibit 60-80% swelling within 2 hrs and showed gradual increase in swelling with time as HPMCK15M is sparingly soluble in water. It is evident from the data that, as time and concentration of polymers increases the swelling index was increased because weight gained by tablet was increased proportionally with the rate of hydration. The formulation F9, F10, F11& F12 containing Carbopol934 showed maximum swelling within two hrs because in cold or hot water guar gum disperses and swells almost immediately to form a highly viscous thixotropic solution.

Ex-vivo Mucoadhesive strength, Force and Retention Time

All the tablets formulations were evaluated for their ex-vivo residence time as per procedure and the results. The formulation F5& F6 containing 30mg & 60mg of HPMCK15M showed higher residence time when compared to other formulations as HPMCK15M is sparingly soluble in water and hence remain attached to the mucous membrane for longer duration of time. As the concentration of mucoadhesive polymer increased in formulations, the residence time also increased. HPMCK4M showed less residence time because in cold or hot water it disperses and swells almost immediately to form a viscous thixotropic solution and hence erode and detach faster compared to other formulations.

In- vitro drug release study

The results of in-vitro drug release are represented. From the results given in the table 21-24 it was evident that HPMCK4M in the concentration of 30 mg (F1), is showing better result 90.75% drug release in 6 hrs when compared with other three formulations (F2, F3 and F4). And that of HPMCK15M results given in table 25-28 it was evident that HPMCK15M in the concentration of

30&60 mg (F5and F6), is showing better result 95.83% and 92.84 drug release in 6 hrs when compared with other two ratios (F7 and F8). In-vitro release of Carbopol934 results given in table 29-32 it was evident that Carbopol934 in the concentration of 30mg (F9), is showing better result 90.60% drug release in 6 hrs when compared with other three concentrations (F10, F11 & F12).

Kinetic studies

The in vitro drug release showed highest regression value for the zero-order kinetics and release data was best fit with Higuchi model kinetics because the value of 1-2 was greater in this model. The formulation follows the diffusion-controlled mechanism for drug release. The 'n' value was found to be F5 is 0.42 & F6 is 0.41 indicating that the drug release mechanism was diffusion and fickian release.

Stability studies

The stability studies for best formulations were carried out as per procedure& results. There was no change in color and shape. There were no significant changes in drug content and %CDR. Two months of stability studies revealed that; there was no any significant degradation of the drug.

CONCLUSION

Dexlansoprazole is a Gastroesophageal reflux disease (GERD) is a chronic symptom of mucosal damage caused by stomach acid coming up from the stomach into the esophagus.

The aim of this work was to develop a mucoadhesive buccal tablet for the buccal delivery of the Dexlansoprazole via buccal mucosa.

In present study an attempt was made to design mucoadhesive buccal tablets of Dexlansoprazole by direct compression method. Twelve formulations were designed by varying the concentration of polymers. All the formulations were evaluated for hardness, thickness, friability, weight variation, drug content estimation, surface pH determination, swelling index, in-vitro drug release, ex-vivo mucoadhesive strength, mucoadhesive force and residence time and short-term stability study.

FTIR studies revealed no interaction between the drug and excipients. The prepared formulations were evaluated for precompression and post compression parameters which revealed good flow properties of the blend and physical attributes of the prepared tablets were found to be practically within control limits. The swelling index was proportional to polymer content. The surface pH of all tablets was found to be satisfactory i.e. close to neutral pH. The details of results are given in chapter-5.

The in-vitro drug release study of majority of formulation showed more than 50% of drug release in 6 hrs. As the concentration of polymer increases the retarding of drug release also increased. The in-vitro drug release study of formulation F5&F10 containing Dexlansoprazole, HPMCK15M(30mg&60mg) as mucoadhesive polymer has good drug release (95.83% and 92.845) when compared to other formulations and was considered as optimized formulation.

Stability studies carried out for about 8 weeks for formulation F5 under 40 ± 2°C and 75 ± 5% RH. No significant change in physical appearance, pH, swelling index, ex-vivo residence time, drug content and % cumulative drug release indicates that the formulation F5 were stable and justify there was no degradation of drug during storage period.

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