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Formulation, Development and Evaluation of Oro-Buccal Drug Delivery Films of Atypical Antipsychotic Drug

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ABSTRACT

Fast dissolving oral films (FDOFs) are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improve the efficacy of APIs by dissolving within minute in oral cavity after the contact with less saliva as compared to fast dissolving tablets, without chewing and no need of water for administration. Lurasidone is an atypical antipsychotic drug which is used for the treatment of schizophrenia. Schizophrenia is one of the psychotic mental disorders and characterized by symptoms of thought and social problem. It acts an antagonist at dopamine (D2) and serotonin (5HT2A and 5-HT7) receptors. Fast dissolving film of Lurasidone were prepared with the purpose of fast dissolving dosage form for very rapid onset of action, faster drug release and provide better patient compliance, which is beneficial in managing several condition like depression, sudden episodes, mentally ill and dysphasia. Developing dosage form was very convenient for the administration without the problem of swallowing and water. Oral fast dissolving films prepared by solvent casting method using HPMC E15/Xanthan gum/ Guar gum, sodium starch glycolate as disintegrating agent, glycerin as plasticizer and aspartame as sweetener and distilled water as a solvent. The prepared films were evaluated for the weight variation, thickness of films, folding endurance, drug content uniformity, surface ph, tensile strength, water vapor transmission rate, *in vitro* disintegration time, *in vitro* diffusion study, stability studies. The film weight was found to be in the range of 35mg to 40mg which ensured uniform distribution of drug in all the formulations. The thickness of LMDF1 to LMDF18 was found to be 98-110µm. From the results obtained for all formulations it can be concluded that the uniformity was achieved during the formulation. The folding endurance value of LMDF1 to LMDF18was found to be 48-110. From the results obtained from the above formulations, all formulations showed folding endurance value complies with in the limit 100- 150 except LMDF1 to LMDF18 fail to comply with the limit as per previous value. Percentage of drug content of LMDF7 was found to be 99.80% and was considered as best formulation compared to the other formulation. The formulations showed percentage drug content 86.12-99.80%. From the results obtained from the above formulations. The *in vitro* drug release was observed that in formulations containing a single polymer, the drug

release was found to be faster and films formed of HPMC E15 resulted in a fastest release of drug. Further, as the concentration of the polymer increased, the drug release was found to be decreased due to the increase in the time required for wetting and dissolving the drug molecules present in the polymer matrices. Among all, the formulation LMDF15 was found to be best formulation which releases 99.99 % of the drug within 1 hrs. The results of the release kinetics study showed that all the formulations obeyed first order drug release profile more closely, i.e., the release rate depended upon the initial concentration of drug**.** The slope values of the Korsmeyer-Peppas plot showed that the mechanism was non-fickian or supercase II transport mechanism. The stability study of optimized formulation LMDF15 oral mouth dissolving film was showed upto 2 years and followed accelerated stability study test as per ICH guideline at room temperature.

Keywords: Schizophrenia, Lurasidone, Fast dissolving films, Solvent casting method, *in vitro* drug release

Introduction

The oral solid dosage form accounting about 60% of all the dosage forms faces many problems which can be overcome by the development of other dosage forms such as fast dissolving oral films (FDOFs) devoid of such problems [1]. The concept of fast dissolving drug delivery system emerged from the desire to provide patient with a conventional mean of taking their medication [2]. It emerged out as a new drug delivery system as an alternative to conventional dosage forms for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms and that provides a very convenient means of taking medications and supplements [3]. FDOFs are thin films with an area of 5-20 cm2 containing an active pharmaceutical ingredient [4]. Buccal cavity is an attractive route of administration for systemic drug delivery of FDOFs among the various routes with their higher bioavailability, quick action and most patient compliance due to high blood flow and permeability of oral mucosa [3]. It is useful in patients such as paediatric-geriatrics with swallowing difficulties, bedridden, emetic patients, diarrhoea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful where local action is desired such as local anaesthetic for medications and supplements [3]. FDOFs are thin films with an area of 5-20 cm2 containing an active pharmaceutical ingredient [4]. Buccal cavity is an attractive route of administration for systemic drug delivery of FDOFs among the various routes with their higher bioavailability, quick action and most patient compliance due to high blood flow and permeability of oral mucosa [3]. It is useful in patients such as paediatric-geriatrics with swallowing difficulties, bedridden, emetic patients, diarrhoea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful where local action is desired such as local anaesthetic for toothaches, oral ulcers, cold sores or teething [5]. It remains as a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application, rapidly disintegrates and dissolves to rapidly release the medication for oromucosal absorption [6]. It also has an established shelf-life of 2-3 years depending on the active pharmaceutical ingredients [7] It is the

most advanced form of solid oral dosage form due to their flexibility plus comfort and improves the efficacy of APIs by getting dissolved within few sec in the oral cavity after coming in contact with saliva without chewing [8 ,9]. Some suitable drugs incorporated in FDOFs are selective serotonin reuptake inhibitors (Fluoxetine, Sertraline), Anti-emetics (Ondansetron, Granisetron), 5HT3 antagonists (Alosetron, Ondansetron, Granisetron, Palonosetron), Anti-epileptics (Carbamazepine, Clonazepam, Phenyloin), Anti-migrains (Almotriptan, Zolmitriptan), Dopamine D1 and D2 antagonists (Bromperidol, Domperidone) [10]. Bipolar depression is a serious, chronic psychiatric disorder with a lifetime prevalence of approximately 1% worldwide and major adverse consequences such as impairments in cognition, social functioning, and work capacity [11, 12]. Antipsychotic drugs are treatment of choice for both acute and longterm management of bipolar depression; the most distressing clinical signs and symptoms are managed with the long-term use of antipsychotic medication along with effective psychosocial interventions [13]. Lurasidone (3aR,4S,7R,7aS)-2-{(1R,2R)- 2-[4-(1,2-benzisothiazol-3-yl) piperazin-1-ylmethyl] cyclohexylmethyl} hexahydro-4,7-methano-2H isoindole-1,3-dione is an atypical antipsychotic and mediates its pharmacological action by blocking central dopamine D2 neuroreceptors [14, 15], Lurasidone has been approved by the US Food and Drug administration for treatment of bipolar depression alone or in combination with lithium in adults [16]. It is currently marketed under the trade name of LatudaTM and is a drug of choice since it causes minimal effects on body weight, has low potential of sedation, and does not cause significant changes across metabolic parameters [17]. The innovator concludes that Lurasidone absorption is influenced by food consumption and when administered with food the absorption of lurasidone showed a two fold increase; the maximum concentration (Cmax) alsom increased by threefold. The Tmax is shown to increase by 0.5-1.5 h with food. Considering the significant food effect on the bioavailability of lurasidone, it is recommended to be administered once daily with at least 350 cal of food (Latuda Prescribing Information accessed from www.latuda.com) [18]. Lurasidone has very low aqueous solubility (water 0.224 mg/ml) with the pKa value of 7.6 and LogP value of 5.6 in octanol/water (Australian Public Assessment Report for lurasidone accessed from www.tga.gov.au) [19]. This low aqueous solubility could be responsible for low bioavailability which is estimated to be about 9 to 19%. Moreover, as discussed earlier, Lurasidone has to be given with food for efficient absorption. However, for poorly soluble drugs, the presence of food interferes in the dissolution and uniform absorption of drugs [20]. Kesisoglou and co-authors have classically reviewed the food interaction with dissolution of poorly soluble drugs [21]. In this perspective, it is evident that the presence of food may interfere in the dissolution and uniform absorption of lurasidone from the gastrointestinal tract. Hence, improving the solubility and dissolution characteristics of lurasidone might allow uniform absorption of the drug from the gastrointestinal tract. The objective of the present research work was to develop fast dissolving oral films of Lurasidone. The formulation developed was simple, easy to prepare and economical with great applicability and also giving faster *in vitro* drug dissolution rate as compared to the commercially available immediate release tablets.

Materials and Methods

Materials

Lurasidone (pure) was received as a gift sample from Torrent Pharmaceuticals Ahmedabad Gujarat. India. HPMC K 15 was procured from Qualikems fine chem Pvt Ltd Vadodhara. Xanthan gum, Guar gum, sodium starch glycolate, was obtained from S.D fine chemicals limited, Mumbai. Citric acid, ethanol was obtained from Loba Chemical Pvt Ltd (Mumbai, India). Hydrochloric acid, KH_2 PO_4, NaoH was obtained from S. D. Fine Chem. Ltd., Mumbai. All other chemical were purchased from Hi Media, Mumbai. Double distilled water was prepared freshly and used whenever required. All the chemicals used in this work were of analyzical grade.

Preformulation

The drug powder was determined for specific fundamental physical and chemical properties. This first learning phase is known as preformulation. Before the formulation of drug substances into a dosage form, it should be chemically and physically characterized. The preformulation testing is the first step in the development of dosage forms of a drug substance. These investigations may confirm that there are no significant barriers to dosage form development.

Physical Appearance: Colour, odour, taste and appearance was notify by sensory organs and was found to be a yellow, odourless, crystalline powder

Melting Point: The required amount of drug will take in a capillary tube, and then the capillary tube will keep in a melting point apparatus.

Solubility Studies: The solubility study was done by incremental method of solvent. The fixed amount 10 mg of drug was kept in conical flask. Now the solvent was filled in burette upto desired scale. The solvent was continuously drop down into conical flask drop by drop with continuously stirrer and determined the amount of solvent need to dissolve the drug present in conical flask. Thus, we found the concentration of solution of solvent and drug to identify the solubility of drug.

Partition Co-efficient: The partition coefficient indicates the polar and non-polar nature of the drug. 10 mg of drug (lurasidone) was added in a mixture of distilled water (10 ml) and then n-octanol (10 ml) in a glass-stoppered test tube and shake for 2 hr. The aqueous phase will then separate using a separating funnel, and drug content was estimate by UV spectrophotometrically at 248 nm. The partition coefficient of drug calculated as follows

$$Po/w = Co/C_{pH6.8}$$

Where, Po/w = partition coefficient of drug, Co= concentration of drug in n-octanol, CpH6.8=concentration of drug in pH 6.8 phosphate buffer

FTIR of drug: KBr pellet technique will use for this study. In this, the sample and the KBr were taken in 1:300 ratios. The mixture of sample and KBr was triturated to make a fine powder and investigated the functional group wave number of drug and drug excipients mixture for determination of incompatibility study with FTIR

spectrophotometer. The drug-excipient compatibility study was carrying out for designing a chemically stable formulation for clinical and commercial development. The drug and the excipients was mix in the selected ratios using a mortar and pestle. The mixtures will transfer into glass vials and seal. The samples were kept at 40ºC±2ºC/75%±5% RH for four weeks. The samples was analyze for physical and chemical incompatibilities and also by FTIR spectrophotometer.

Determination of wavelength maxima (λmax): The UV spectrophotometric method was used to determine λmax of drug. The UV spectrophotometric method was used for structural validation of the drug. Drug lurasidone (50 mg) was accurately weighed and dissolved in 10ml of methanol and 40ml of PBS pH 6.8 in 50ml of a volumetric flask, and final volume was adjusted to 50ml. 10 ml of this solution was further diluted to 100ml to prepare a stock solution of 100µg/ml concentration. Further 1ml of stock solution was diluted up to 10ml PBS pH 6.8 to yield a theoretical concentration of 10µg/ml. The solution (10µg/ml) was scanned in the range 200-400 nm in a UV-Visible spectrophotometer (Shimadzu 1800, Japan) to determine the wavelength maxima

Preparation of Calibration Curve: Calibration curve will prepare spectrophotometrically based on UV absorption at λmax in PBS pH 6.8 for the quantitative estimation of the drug. Calibration curve was prepared spectrophotometrically based on UV absorption at λmax 248 nm in PBS pH 6.8 for the quantitative estimation of the drug. 50 mg drug was accurately weighed and placed in a 50 ml volumetric flask to prepare a 1 mg/ml solution in 10ml methanol and 40ml PBS pH 6.8.10 ml of this solution (1mg/ml) was added to 10 ml PBS pH 6.8 to yield atheoreticalconcentrationof100µg/ml.Diluentsof5to50µg/mlwereprepared and measured at λmax 248 nm. Calibration curve of drug lurasidone prepared was prepared using concentration vs absorbance data

Formulation of fast dissolving films: In the present study fast dissolving films of lurasidone was prepared by solvent casting technique. Flat, square-shaped, aluminum foil coated glass molds a will use for casting the films.

Preparation of casting solutions: Casting solutions was prepared by using selected polymers. The required weighed quantities of polymers HPMC E15/ Xanthan gum (XG) / Gura gum (GG) were separately or in combination kept for swelling overnight in 5 ml distilled water and dissolved. The drug and aspartame as sweetener were added to the polymeric solution directly as given in Table 1. Along with glycerol as a plasticizer and mixed thoroughly to form a homogenous mixture on magnetic stirrer. Finally polymer solution was added to Xanthan gum solution and volume made up to 10 ml with distilled water. The entrapped air bubbles were removed by applying sonication process.

Preparation of oral thin films: The casting solution (10 ml) was poured into glass molds and dried at40°C in a vacuum oven for 24 h for solvent evaporation. The films were removed by peeling and cut into a square dimension of 2.0 cm × 2.0 cm (4.0cm^2). It was dried for 24 hours at room temperature. The thin film was clear and bubble free and removed from the petri dish very carefully, where fast-dissolving films were prepared with different polymers and ratios by maintaining the concentration of the plasticizer and sweetener constant.

Table1: Formulation casting solution of mouth dissolving films

F. Code	Lurasidone (mg)	HPMC E15 (mg)	Xanthan gum (mg)	Guargum (mg)	Sodium starch glycolate (mg)	Citric acid (mg)	Aspartame (mg)	Glycerol (ml)	Distilled Water qs (ml)
LMDF1	30	50	0	0	10	5	20	0.5	10
LMDF2	30	100	0	0	10	5	20	0.5	10
LMDF3	30	150	0	0	10	5	20	0.5	10
LMDF4	30	0	50	0	10	5	20	0.5	10
LMDF5	30	0	100	0	10	5	20	0.5	10
LMDF6	30	0	150	0	10	5	20	0.5	10
LMDF7	30	0	0	50	10	5	20	0.5	10
LMDF8	30	0	0	100	10	5	20	0.5	10
LMDF9	30	0	0	150	10	5	20	0.5	10
LMDF10	30	25	25	0	10	5	20	0.5	10
LMDF11	30	50	50	0	10	5	20	0.5	10
LMDF12	30	75	75	0	10	5	20	0.5	10
LMDF13	30	0	25	25	10	5	20	0.5	10
LMDF14	30	0	50	50	10	5	20	0.5	10
LMDF15	30	0	75	75	10	5	20	0.5	10
LMDF16	30	25	0	25	10	5	20	0.5	10
LMDF17	30	50	0	50	10	5	20	0.5	10
LMDF18	30	75	0	75	10	5	20	0.5	10

Evaluation of mouth dissolving films

***Weight variation*:** Mouths dissolving oral films will weigh on digital balance and average weight will determine for each film. It is desirable that films should have nearly constant weight. It is useful to make sure that a film contains the required amount of excipients and drug.

***Thickness of films*:** By using micrometer screw gauge the thickness of the film was measured at 5 totally different places; an average of 3 values was calculated by using screw gauge. Folding endurance**:** The folding endurance was expressed as the number of folds (number of times the film is folded at the same place) requires to break the specimen or to develop visible cracks. This also gives an indication of brittleness of the film. A strip of 2.5 cm × 2.5 cm was subject to folding endurance by folding the film at the same place repeatedly several times until a visible crack was observed.

***Drug content uniformity*:** The prepared oral thinfilms were dissolved in 10ml methanol and 40ml PBS pH 6.8 mixtures. The mixture was filtered through whatman filter paper. After suitable dilutions, the concentration of the drug was determined by uv method at 248 nm.

***Surface pH*:** The film was placed in a petri dish and moistened with0.5 ml of distilled water and keep for 30 s. The pH of mixture was noticed by attaching the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min.

Tensile strength: The tensile strength is determined by the apparatus which has two clamps, the upper one is fixed and the lower is movable. The film sample (0.5×3 cm) is clamped between the two clamps. The force at tearing and elongation is determined. The percent elongation (%E) is calculated using the following equation

$$\% E = \{(Ls-Lo) / Lo\} \times 100$$ Where, Lo = Original length

Ls = Length of the film after elongation

The modulus of elasticity of films was calculated from the equation

$$F/A = EM \{(Ls-Lo) / Lo\}$$

Where F = Breaking load (N), A = Cross- sectional area of the film, EM = Modulus of elasticity

Water vapor transmission rate: The water vapor transmission rate study, vials of equal diameter can be used as transmission cells. Cells are washed thoroughly and dried in an oven. One gm of calcium chloride is taken in the cell and the polymeric films (two cm2 area) are fixed over the brim with the help of an adhesive. The cells are accurately weighed and the initial weight is recorded. Films are then kept in a closed desiccator containing saturated solution of potassium chloride (80-90 % RH). The cells are taken out and weighed after 18, 36, 54 and 72 hours. From increase in weights, the amount of water vapor transmitted and the rate at which water vapor transmitted can be calculated by using the following formula:

$$\text{Water vapor transmission rate} = WL/S$$

Where, W = Water vapor transmitted in mg , L = Thickness of the film in mm, S = Exposed surface area in cm2

In vitro disintegration time: In vitro disintegration time is determined visually in a glass dish with 10 ml distilled water with swirling every 10 seconds. The disintegration time is the time when the film starts to break or disintegrate.

***In vitro diffusion study*:** In vitro diffusion study was carried out by using Franz-diffusion cell apparatus with PBS pH 6.8 as a dissolution medium. The temperature was maintained at 37±0.5°C with 50 rotations per minute. 1 ml of aliquots was withdrawn at different time intervals and same amount of fresh dissolution medium was added to maintain sink condition. The aliquots were analyzed for drug content at λ max 248 nm wavelength using UV-spectrophotometer. The cumulative percentage drug release was calculated and reported.

***Stability studies*:** The stability of the prepared mouth dissolving oral film (LMDF15) was evaluated as per the ICH guidelines. The shelf life of API drug was identified for drug decomposition during storage at different storage conditions at different temperatures. The degradation may result in environmental changes during storage of drug amount at LMDF15 due to chemical alteration or due to product instability. The prepared mouth dissolving oral film LMDF15 were stored at three different temperature and relative humidity conditions in covered polythyne bags and aluminium paper. The samples were stored at 2ºC ± 0.5ºC, 25°C/60% RH and 40°C/75% RH for 180 days in stability chambers. These samples were analyzed for drug content study was done. The shelf life of the formulations was calculated from the degradation rate constant at 25 ºC (k_{25}) by the following formula:

$$t_{10\%} = 0.104 / k_{25}$$

Results and Discussion

Identification studies showed that the drug supplied by Pharmaceutical companies matched with the reported official standards. The absorption maximum of lurasidone in PBS pH 6.8 was found to be 248 nm (Figure 1).

The λmax found to be very near the λmax reported in reference books. The data of calibration curves were linearly regressed, and the equation of the straight line for the standard curve as well as correlation coefficients was determined. The correlation coefficient for standard curves was found to be very near to one, which indicates an excellent co-linear correlation between concentration 5-50 µg/ml and absorbance (Figure 2). Hence, drugs are following the Beer-Lambert Law in the range of 5-50 µg/ml. The melting point of the drug was found to be similar to the published in reference books. The solubility profile of drug lurasidone showed its hydrophobic nature and was insoluble in chloroform and water but freely soluble in methanol. The partition coefficient was found according to their solubility profile that was indicating the hydrophobic nature of the drug (Table 2). The partition coefficient of drug inn-octanol: pH 6.8 phosphate buffer was 3.8(Table 4) and Drug excipient compatibility study for 4Weeks was done and there was no change in sample of drug and excipients (Table 4). Lurasidone was studied for compatibility with excipients in different environmental conditions. No drug interaction was observed during the time period of storage, showing their compatibility with all ingredients (Figure 3 -4). The Effect of polymer concentration was studied with different formulations (LMDF1 – LMDF18) prepared using HPMC E15, xanthan gum, guar gum individually and in a combination of these polymers in different concentrations. The weight variations in the films were found to be uniform in all the prepared batches. The film weight was found to be in the range of 35mg to 40mg which ensured uniform distribution of drug in all the formulations (Table 5). The thickness of LMDF1 to LMDF18 was found to be 98-110µm. From the results obtained for all formulations it can be concluded that the uniformity was achieved during the formulation (Table 6). The prepared oral films were studied for folding endurance by number of times; the film could be folded at the same place without breaking gave the value of folding endurance. The mean values of three readings were calculated. The folding endurance value of LMDF1 to LMDF18was found to be 48-110. From the results obtained from the above formulations, all formulations showed folding endurance value complies with in the limit 100-150 except LMDF1 to LMDF18 fail to complies with the limit as per previous value (Table 7). Percentage of drug content for different formulations was calculated and the results were shown in the Table 8. Percentage of drug content of LMDF7 was found to be 99.80% and was considered as best formulation compared to the other formulation. The formulations showed percentage drug content 86.12-99.80%. The pH of surface of oral films was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibrating for 1 min. The average of three determinations for each of the formulation was taken. Surface pH of all films was found to be within the limits 6-7 (Table 9). The tensile strength of oral thin films were be in the range of 2.04-4.01 (Mpa) and water vapor transmission of oral thin films were be in the range of 8.8-29.2(Table 10-11). The *invitro* drug release was observed that in formulations containing a single polymer, the drug release was found to be faster and films formed of HPMC E15 resulted in a fastest release of drug. Further, as the concentration of the polymer increased, the drug release was found to be decreased due to the increase in the time required for wetting and dissolving the drug molecules

present in the polymer matrices. The drug release was found to be in the following order: LMDF15>LMDF18>LMDF9best formulations in terms of drug release and formulationsLMDF6,LMDF3,LMDF14, LMDF11,LMDF17,LMDF8,LMDF5,LMDF2,LMDF13,LMDF10,LMDF16, LMDF7LMDF4LMDF1 were found to be the more release within 1 hr. (Table 12). The results of the release kinetics study showed that all the formulations obeyed first order drug release profile more closely, i.e., the release rate depended upon the initial concentration of drug (Figure 5-12). The slope values of the Korsmeyer-Peppas plot showed that the mechanism was non-fickian or supercase II transport mechanism. The stability study of optimized formulation LMDF15 oral mouth dissolving film was showed upto 2 years and followed accelerated stability study test as per ICH guideline at room temperature (Table 13-15).

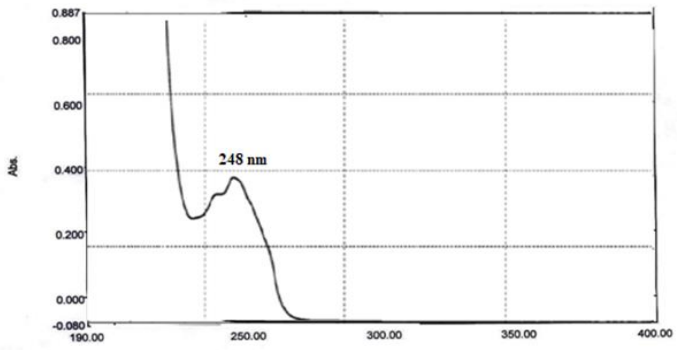


Figure 1: UV-Visible Scan of drug

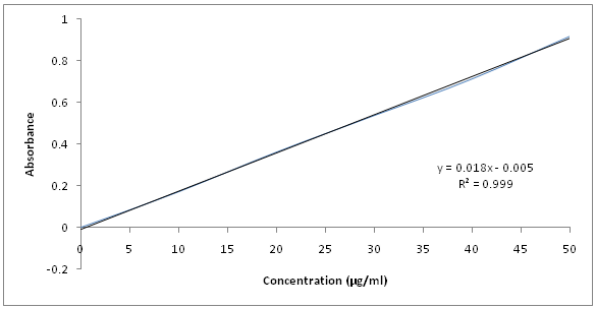


Figure 2: Calibration curve of drug in pH 6.8 phosphate buffer

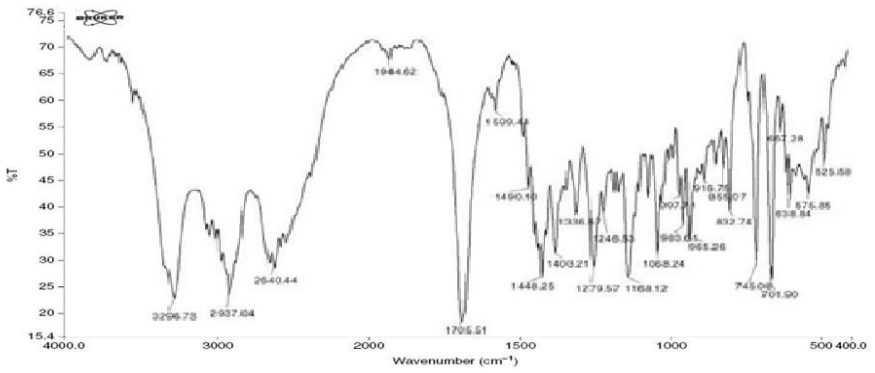


Figure 3: FTIR of drug

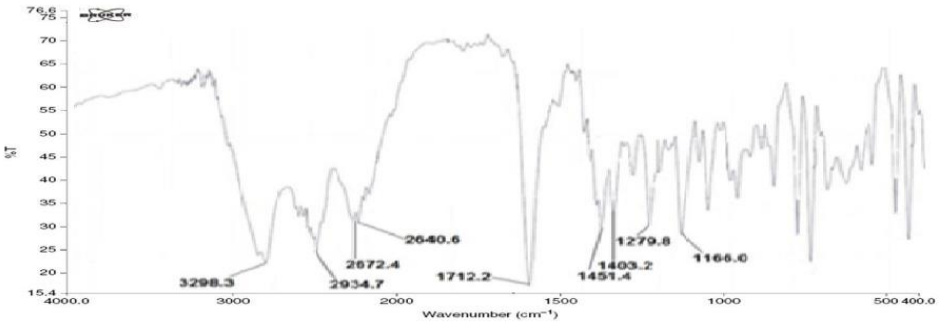


Figure 4: FTIR of drug and excipients

Table2: Solubility of Lurasidone in different solvent systems

S. No.	Solvents	Solubility (Lurasidone)
1	Distilled Water	Insoluble
2	Chloroform	Insoluble
3	0.1 N HCl	Sparingly Soluble
4	0.1 N NaOH	Soluble
5	PBS pH 6.8	Sparingly Soluble
6	Methanol	Soluble

Table3: Partition coefficient of drug in n-octanol: pH 6.8 phosphate buffer

Drug			Partition coefficient (Po/pH6.8)
	Aqueous Phase	pH 6.8 phosphate buffer	3.8
Lurasidone	2.08	7.92	

Table4: Drug excipients compatibility study for 4 Weeks

Materials	Test parameters			
	Initial Description	Refrigerator (2-8°C)	Room temperature	40°C±75%RH
Drug	Off White Powder	No Change	No Change	No Change
Drug + polymer + excipients	White Powder	No Change	No Change	No Change

Table 5: Weight variation of oral mouth dissolving films (LMDF1- LMDF18)

Formulation Code	Weight of film (mg)
LMDF1	37.24±1.1
LMDF2	39.22±1.2
LMDF3	40.8±2.1
LMDF4	38.25±1.1
LMDF5	38.90±1.2
LMDF6	40.01±1.1
LMDF7	37.16±1.7
LMDF8	38.13±1.8
LMDF9	36.11±1.3
LMDF10	37.05±1.2
LMDF11	34.91±1.1
LMDF12	39.01±1.3
LMDF13	35.11±1.2

LMDF14	36.11±1.3
LMDF15	38.12±1.1
LMDF16	37.12±1.3
LMDF17	38.11±1.1
LMDF18	38.12±1.2

Table 6: Thickness of oral mouth dissolving films (LMDF1-LMDF18)

Formulation Code	Thickness of film (µm)
LMDF1	98.1±1.1
LMDF2	100.2±1.2
LMDF3	102.1±1.6
LMDF4	101.3±1.4
LMDF5	105.2±1.2
LMDF6	109.2±1.3
LMDF7	99.3±1.2
LMDF8	106.3±1.1
LMDF9	110.2±1.1
LMDF10	102.1±1.3
LMDF11	101.1±1.1
LMDF12	103.2±1.1
LMDF13	103.1±1.2
LMDF14	103.2±1.1
LMDF15	103.2±1.1
LMDF16	102.3±1.3
LMDF17	103.1±1.2
LMDF18	104.2±1.3

Table 7: Folding endurance of oral mouth dissolving films (LMDF1- LMDF18)

Formulation Code	Folding endurance
LMDF1	98
LMDF2	99
LMDF3	93
LMDF4	105
LMDF5	92
LMDF6	94
LMDF7	112
LMDF8	101
LMDF9	98
LMDF10	95
LMDF11	99
LMDF12	96
LMDF13	98
LMDF14	96
LMDF15	97
LMDF16	99
LMDF17	104
LMDF18	99

Table 8: Percent drug content of oral mouth dissolving films (LMDF1- LMDF18)

Formulation code	Drug content (%)
LMDF1	86.11
LMDF2	90.41
LMDF3	93.12
LMDF4	94.17
LMDF5	91.17
LMDF6	93.21
LMDF7	99.80
LMDF8	97.22
LMDF9	99.51
LMDF10	94.91
LMDF11	96.05
LMDF12	97.19
LMDF13	98.19
LMDF14	99.03
LMDF15	94.01
LMDF16	99.48
LMDF17	97.71
LMDF18	98.91

Table 9: Surface pH of oral mouth dissolving films (LMDF1 – LMDF18)

Formulation code	Surface pH
LMDF1	6.28
LMDF2	6.34
LMDF3	6.25
LMDF4	6.51
LMDF5	6.44
LMDF6	6.67
LMDF7	6.71
LMDF8	6.72
LMDF9	6.81
LMDF10	6.16
LMDF11	6.17
LMDF12	6.19
LMDF13	6.26
LMDF14	6.22
LMDF15	6.02
LMDF16	6.14
LMDF17	6.25
LMDF18	6.35

Table 10: Tensile strength of oral mouth dissolving films (LMDF1-LMDF18)

Formulation code	Tensile strength (Mpa)
LMDF1	2.04
LMDF2	2.37

LMDF3	2.12
LMDF4	3.21
LMDF5	2.03
LMDF6	2.29
LMDF7	3.29
LMDF8	3.21
LMDF9	3.19
LMDF10	3.31
LMDF11	3.29
LMDF12	3.08
LMDF13	3.19
LMDF14	4.01
LMDF15	2.11
LMDF16	3.02
LMDF17	2.21
LMDF18	3.27

Table 11: Water vapor transmission rate of oral mouth dissolving films (LMDF1 – LMDF18)

Formulation Code	Water vapor transmission rate
LMDF1	18.18
LMDF2	12.14
LMDF3	22.22
LMDF4	21.18
LMDF5	28.14
LMDF6	29.21
LMDF7	21.22
LMDF8	19.31
LMDF9	23.11
LMDF10	18.22
LMDF11	21.14
LMDF12	24.92
LMDF13	19.01
LMDF14	18.19
LMDF15	22.18
LMDF16	21.01
LMDF17	24.16
LMDF18	28.12

Table 12: in-vitro drug release study oforal mouth dissolving films (LMDF15)

Time (Min.)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	0.000	0	0.000	0.000	100.000	2.000
10	3.162	1.000	26.06	2.606	0.416	97.394	1.989
20	4.472	1.141	38.34	3.834	0.584	96.166	1.983
30	5.477	1.215	48.34	4.834	0.684	95.166	1.978
40	6.325	1.266	58.34	5.834	0.766	94.166	1.974

50	7.071	1.303	64.74	6.474	0.811	93.526	1.971
60	7.746	1.333	69.87	6.987	0.844	93.013	1.969
70	8.367	1.358	75.74	7.574	0.879	92.426	1.966
80	8.944	1.380	79.26	7.926	0.899	92.074	1.964
90	9.487	1.398	86.99	8.699	0.939	91.301	1.960
100	10.000	1.414	96.92	9.692	0.986	90.308	1.956
110	10.488	1.429	99.99	9.999	1.000	90.001	1.954
120	10.954	1.442	99.99	9.999	1.000	90.001	1.954

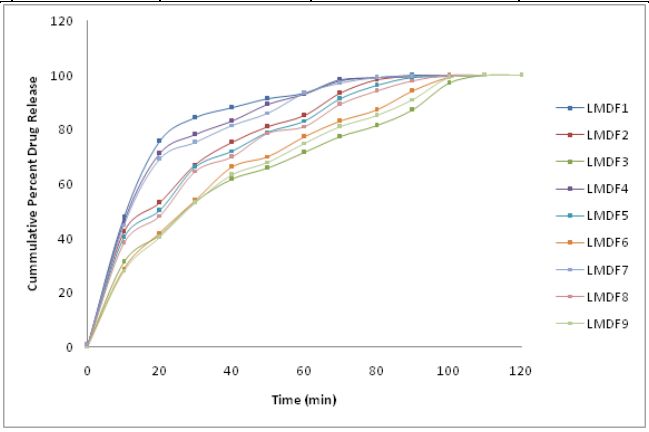


Figure 5: Zero-order plots of oral mouth dissolving films (LMDF1-LMDF9)

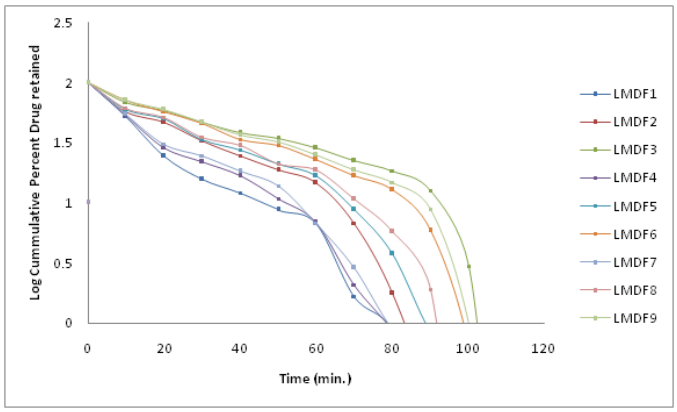
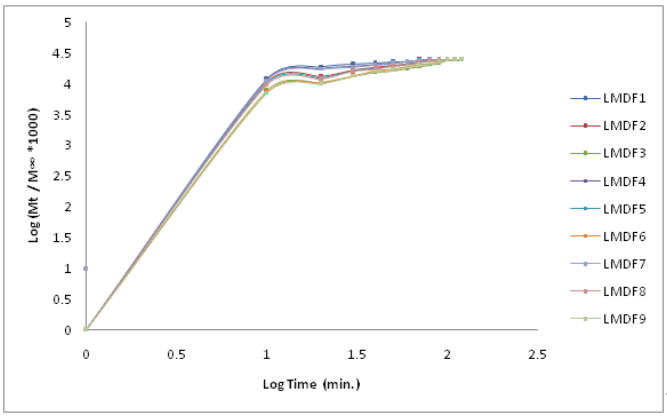


Figure 6: First-order plots of oral mouth dissolving films (LMDF1- LMDF9 Figure



)

Figure 7: Korsmeyer's-Peppas plot f oral mouth dissolving films (LMDF1-LMDF9)

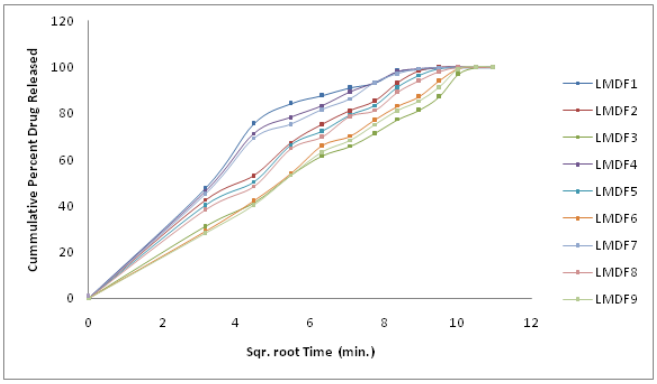


Figure 8: Higuchi kinetic plot of oral mouth dissolving films (LMDF1-LMDF9)

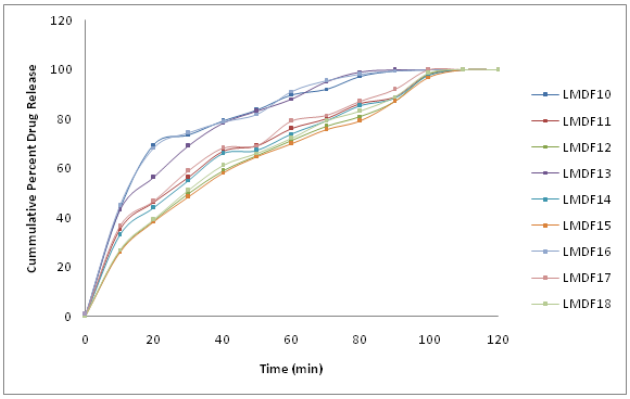


Figure 9: Zero-order plots of oral mouth dissolving films (LMDF10 – LMDF18)

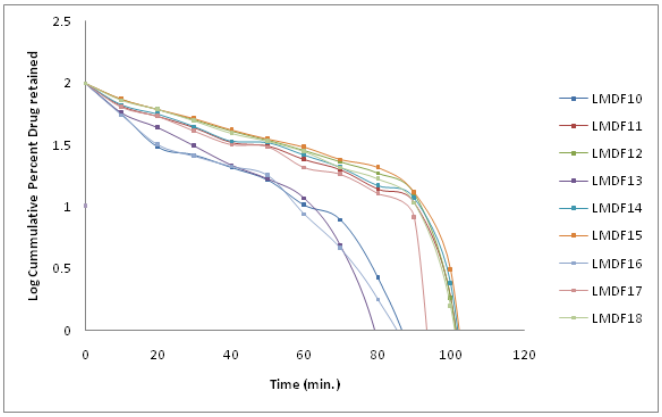


Figure 10: First-order plots oforal mouth dissolving films (LMDF10 – LMDF18)

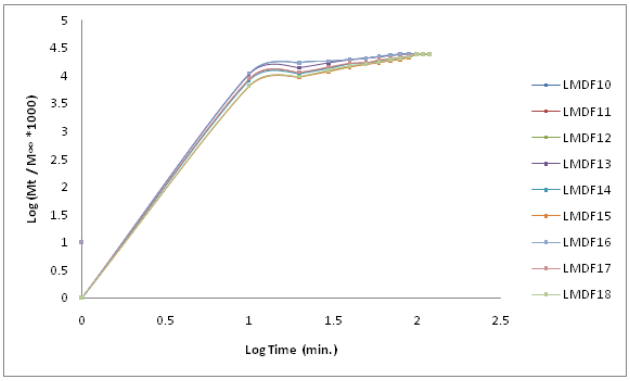


Figure 11: Korsmeyer's-Peppas plot of oral mouth dissolving films (LMDF10 – LMDF18)

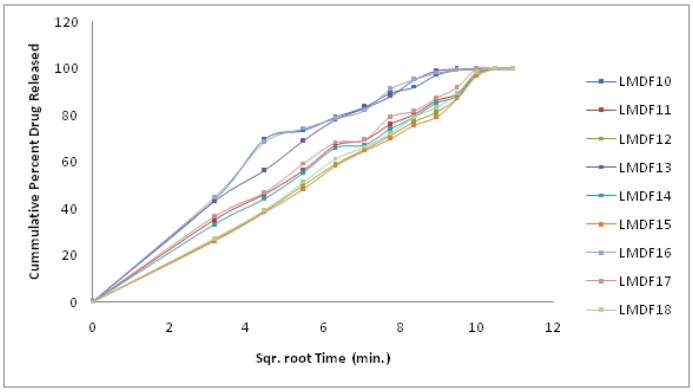


Figure 12: Higuchi kinetic plot of oral mouth dissolving films (LMDF10 – LMDF18)

Table 13: Stability Studies of mouth dissolving film(LMDF15) at 2ºC ± 0.5ºC

S. No	Time Interval (days)	Drug Content (%)
1	0	99.05±0.14
2	30	98.72±0.11
3	60	98.16±0.12
4	90	98.01±0.13
5	180	97.27±0.11

Table 14: Stability Studies of mouth dissolving film(LMDF15)at 25°C± 2ºc/60% ± 5% RH

S. No	Time Interval (days)	Drug Content (%)
1	0	99.25±0.11
2	30	98.12±0.11
3	60	97.16±0.17
4	90	96.91±0.12
5	180	96.07±0.11

Table 15: Stability Studies of mouth dissolving film(LMDF15) at 40ºC ± 2ºC/75% ± 5% RH

S. No	Time Interval (days)	Drug Content (%)
1	0	99.05±0.11
2	30	98.02±0.12
3	60	97.06±0.12
4	90	96.11±0.11
5	180	95.11±0.11

Conclusion

Oral thin dissolving films or strips is based on as quickly releasing the drug by dissolving or adhering in the mucosa with saliva within a few seconds due to it contains water-soluble polymers when it placed in the mouth cavity or on the tongue. Ideal thin films should possess the desired properties of a drug delivery system, such as a suitable drug loading capacity, rapid dispersion/dissolution, or prolonged application and reasonable formulation stability. Bioadhesive formulations have a wide scope of applications, for both systemic and local effects. The mucosa is relatively permeable with a rich blood supply. The oral transmucosal drug delivery bypasses first pass effect and avoids pre-systemic elimination in the GI tract. These factors make the oral mucosa a very attractive and feasible site for systemic drug delivery. A few drugs have been successfully administered via buccal route. The buccal region offers an attractive route of administration for systemic drug delivery. Lurasidone, has a need to formulate into buccal patches and the drug is suitable for it. Bioadhesive formulations have a wide scope of applications, for both systemic and local effect for management of diseases. Also, they must be nontoxic, biodegradable and biocompatible**.** Lurasidone is rapidly absorbed through oral administration and able to increase oral bioavailability by using hydroxyl propyl methyl cellulose, thickening agent as natural polysacharide material with using super disintegrating agents. Lurasidone drug will be use for developing a dosage form for a very quick onset of action, which is beneficial in managing severe conditions of allergies, aiding in the enhancement of bioavailability, and is very convenient for administration, without the problem of swallowing and using water. In the present study, Lurasidone was used as a model drug candidate and nine fast-dissolving films formulations containing different polymer concentrations were prepared. The effect of the nature of polymers was studied by preparing various formulations of oral dispersible films. The various formulations containing a combination of polymers, release was found to be in the following order: LMDF15>LMDF18>LMDF9best formulations in terms of drug release and formulations LMDF6, LMDF3, LMDF14, LMDF11,LMDF17,LMDF8,LMDF5,LMDF2,LMDF13,LMDF10,LMDF16, LMDF7LMDF4LMDF1 were found to be the more release within 1 hr. The results of the release kinetics study showed that all the formulations obeyed first order drug release profile more closely, i.e., the release rate depended upon the initial concentration of drug. The slope values of the Korsmeyer-Peppas plot showed that the mechanism was non-fickian or supercase II transport mechanism. Thus the oral thin films of lurasidone prepared by the solvent casting method on glass molds, using HPMC E15 and Xanthan gum, guar gum in combinational study with Sodium starch glycolate as disintegrating agent, glycerin as plasticizer and aspartame as sweetener and distilled water as a solvent was valuable dosage form for the future aspects in the field of pharmaceutical sciences.

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