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ORIGINAL ARTICLE

Formulation and evaluation of lurasidone mouth dissolving film for management of psychosis

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ABSTRACT
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. 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 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: LMDF6>LMDF3 best formulations in terms of drug release and formulations LMDF5, LMDF2, LMDF4, LMDF1 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 super case II transport mechanism.
Keywords: *Formulation and evaluation, Lurasidone, Mouth dissolving film, Psychosis*

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INTRODUCTION

Psychosis is a common and functionally disruptive symptom of many psychiatric, neurodevelopmental, neurologic, and medical conditions and an important target of evaluation and treatment in neurologic and psychiatric practice. Psychosis is a clinical syndrome composed of several symptoms. [1] It is not a nosological entity. Symptoms of psychosis occur in a wide range of mental disorders and show a high degree of inter-individual variability between persons with different mental disorders, and a high degree of intra-individual variability over time. Symptoms of psychosis are usually embedded in the wider clinical picture of the mental disorder, which may include symptoms of mania and depression. [2]. The signs and symptoms for the prodromal stage of psychotic illness and the eventual psychotic experience may be different. [3]. Psychotherapy, also known as talk therapy, can also be recommended by the doctor for the treatment of psychosis [4-5] Mouth dissolving films have been described as an alternative approach to conventional dosage forms. They are a versatile platform that provides fast, local, or systemic effects. Additionally, these systems can be easily applied by themselves, especially for dysphagia patients, geriatric, pediatric, or bedridden patients, as well as patients who cannot easily access water. These drug delivery systems can be administered in various ways such as orally, buccally, sublingually, ocularly, and transdermally [6].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. Also, they must be nontoxic, biodegradable and biocompatible [7].

Oral route is one of the most preferred routes of drug administration due to its safety, ease of administration, and acceptability by patients. About 60 % of conventional dosage forms are available as the oral solid dosage forms. Orally dissolving strips and films are useful in patients such as pediatrics, geriatrics, bedridden, and emetic patients and conditions such as sudden episodes of allergic attacks or coughing. They can be used for local and systemic delivery. There is an increasing interest in the development of orally dissolving film and strips as an alternative to fast dissolving tablets, due to their faster dissolution rate, higher exibility, and better patient compliance [8]. Research on the potential of using orally dissolving films as carriers for the delivery of several active medicinal components has recently surfaced. Additionally, commercially available dissolving film items such as Listerine, Chloraseptic, Triaminic, and multivitamins are now accessible. An oral dissolving film's core is often composed of a plasticizer, a film-forming polymer, or a combination of polymers that give the film the required elasticity and shape [9].An excellent medication option for an oral dissolving film formulation is anti-psychotic. Anti-psychotic medication formulation as an orally dissolving strip, which must be applied to the patient's tongue without swallowing in order to administer the dose, would greatly simplify dosage administration and increase patient compliance. Therefore, the objective of this effort was to design, create, and describe anti-psychotic medication mouth dissolving films.

The oral route is the most often used method of drug delivery among all other routes since it has the benefit of simple administration. However, it also has potential downsides, such as poor bioavailability because of its first-pass impact and tendency to produce abruptly high and low plasma concentrations of the medication; as a result, patient noncompliance occurs [10].Despite the limitations, continuous intravenous infusion has been shown to maintain a constant and sustained medication concentration within the therapeutic range for an extended period of time. However, this method of administering drugs also has some disadvantages, such as needle discomfort and unintentional needlesticks. As a result, regular hospitalization throughout treatment is required, along with under medical supervision. Nowadays, the recommended method of administering drugs is through mouth dissolving film because of patient compliance [11].An atypical antipsychotic called lurasidone is used to treat bipolar I disorder-related depressive episodes and schizophrenia. In individuals ≥13 years old, lurasidone is approved for the treatment of schizophrenia.

It is also indicated as a monotherapy for the treatment of bipolar depression in patients ≥10 years old, or in combination with lithium or valproate for the treatment of bipolar depression in adults. Lurasidone is an atypical antipsychotic that is a D2 and 5-HT2A (mixed serotonin and dopamine activity) to improve cognition. It is thought that antagonism of serotonin receptors can improve negative symptoms of psychoses and reduce the extrapyramidal side effects that are often associated with typical antipsychotics [12-15].

MATERIAL AND METHODS

Pre-formulation: The drug powder was determined for specific fundamental physical and chemical properties.

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) / Guragum (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: Ten milliliters of the casting solution were put into glass molds, and they were vacuum-dried for twenty-four hours at 40°C to evaporate the solvent. The films were peeled off and sliced into a square that measured 2.0 cm by 2.0 cm (4.0 cm2). It was let to dry at room temperature for a full day. The clear, bubble-free thin film was carefully removed from the petri dish, where fast-dissolving films were made using various polymers and ratios while keeping the plasticizer and sweetener concentrations constant.

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 number 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 thin films 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} x 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:
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 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 (LMDF6) 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 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.

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. 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. The partition coefficient of drug inn-octanol: pH 6.8 phosphate buffer was 3.8. 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. Oral thin films are ideal for many groups of patients including geriatrics, pediatrics, and psychiatrics as well as for those people who have difficulty in swallowing. Many drugs can be formulated in the form of fast dissolving films to provide the advantages of mouth dissolving drug delivery system. In the present study, lurasidone was used as a model drug candidate and nine fast-dissolving films formulations containing different polymer

concentrations were prepared. Mouth dissolving films of lurasidone were prepared by the solvent casting method on glass molds, using HPMC E15 Guargum, Sodium starch glycolate as disintegrating agent, glycerin as plasticizer and aspartame as sweetener and distilled water as a solvent. The effect of the nature of polymers was studied by preparing various formulations of oral dispersible films. The characterization and evaluation of prepared fast dissolving films were done for various parameters like thickness of the films, drug content uniformity, folding endurance of the films, disintegration time, In-vitro dissolution and stability studies. The Effect of polymer concentration was studied with different formulations prepared using HPMC E15, Guargum individually and in a combination of these polymers in different concentrations. 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. The drug release was found to be in the following order: LMDF6>LMDF3 best formulations in terms of drug release and formulations LMDF5, LMDF2, LMDF4, LMDF1 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. The stability study of optimized formulation LMDF6 oral mouth dissolving film was showed up to 2 years and followed accelerated stability study test as per ICH guideline at room temperature.

Table 1: Formulation casting solution of mouth dissolving films

F. Code	Lurasidone (mg)	HPMC E15 (mg)	Guargum (mg)	Sodium starch glycolate (mg)	Glycerol (ml)	Distilled Water qs (ml)
LMDF1	30	50	0	10	0.5	10
LMDF2	30	100	0	10	0.5	10
LMDF3	30	150	0	10	0.5	10
LMDF4	30	0	50	10	0.5	10
LMDF5	30	0	100	10	0.5	10
LMDF6	30	0	150	10	0.5	10

Table 2: Physical properties of oral mouth dissolving films (LMDF1 – LMDF6)

Formulation Code	Weight of film (mg)	Thickness of film (µm)	Folding endurance	Drug content (%)	Surface pH	Tensile strength (Mpa)	Water vapor transmission rate
LMDF1	35.11±1.2	103.1±1.2	98	98.19	6.26	3.19	19.01
LMDF2	36.11±1.3	103.2±1.1	96	99.03	6.22	4.01	18.19
LMDF3	38.12±1.1	103.2±1.1	97	94.01	6.02	2.11	22.18
LMDF4	37.12±1.3	102.3±1.3	99	99.48	6.14	3.02	21.01
LMDF5	38.11±1.1	103.1±1.2	104	97.71	6.25	2.21	24.16
LMDF6	38.12±1.2	104.2±1.3	99	98.91	6.35	3.27	28.12

Table 3: *In-vitro* drug release study of oral mouth dissolving films (LMDF1 – LMDF6)

Time (Min.)	LMDF1	LMDF2	LMDF3	LMDF4	LMDF5	LMDF6
0	0	0	0	0	0	0
10	47.65	42.42	31.23	46.21	40.21	29.03
20	75.60	53.03	41.34	71.13	50.21	42.21
30	84.34	67.22	53.37	78.23	66.21	54.02
40	87.87	75.21	61.76	83.21	72.21	66.13
50	91.23	81.11	65.78	89.12	79.13	70.11
60	93.23	85.22	71.48	93.11	83.24	77.23
70	98.32	93.21	77.45	97.91	91.25	83.12
80	99.12	98.22	81.47	99.12	96.24	87.21
90	99.87	99.78	87.32	99.71	99.16	94.11
100	99.99	99.99	97.02	99.99	99.67	99.34
110	99.99	99.99	99.99	99.99	99.99	99.99
120	99.99	99.99	99.99	99.99	99.99	99.99

Table 4: Stability Studies of mouth dissolving film (LMDF6) at various temperature

S. No	Time Interval (days)	Drug Content (%)		
		2ºC ± 0.5ºC	25°C± 2ºc/60%	40ºC ± 2ºC/75%
1	0	99.05±0.14	99.25±0.11	99.05±0.11
2	30	98.72±0.11	98.12±0.11	98.02±0.12
3	60	98.16±0.12	97.16±0.17	97.06±0.12
4	90	98.01±0.13	96.91±0.12	96.11±0.11
5	180	97.27±0.11	96.07±0.11	95.11±0.11

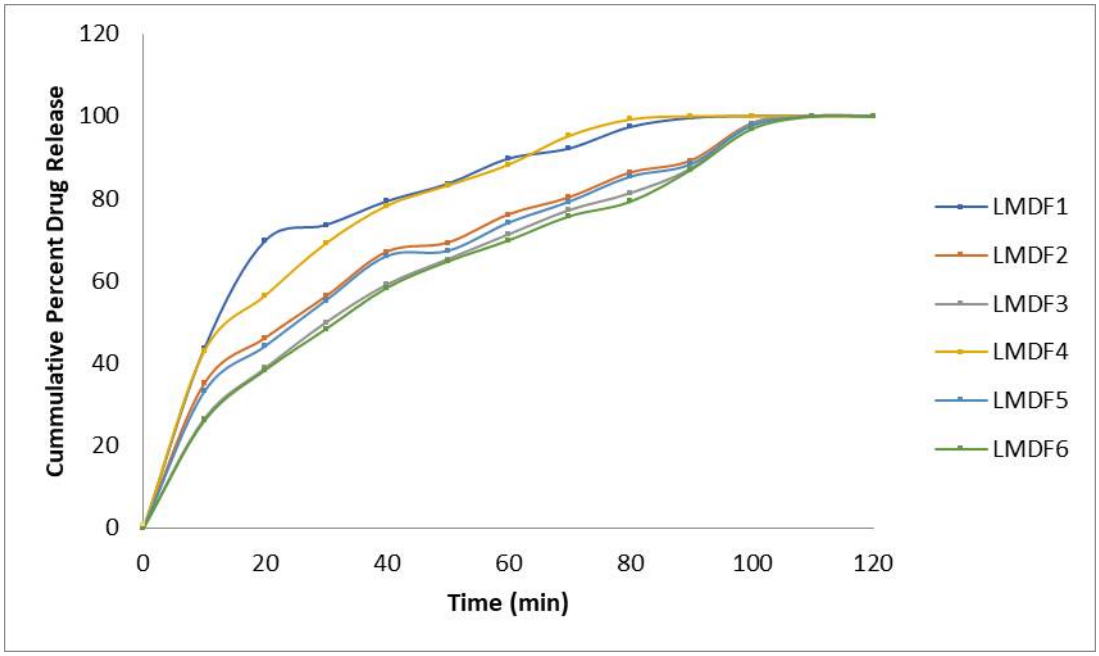

Figure 1: Zero-order plots of oral mouth dissolving films (LMDF1 – LMDF6)

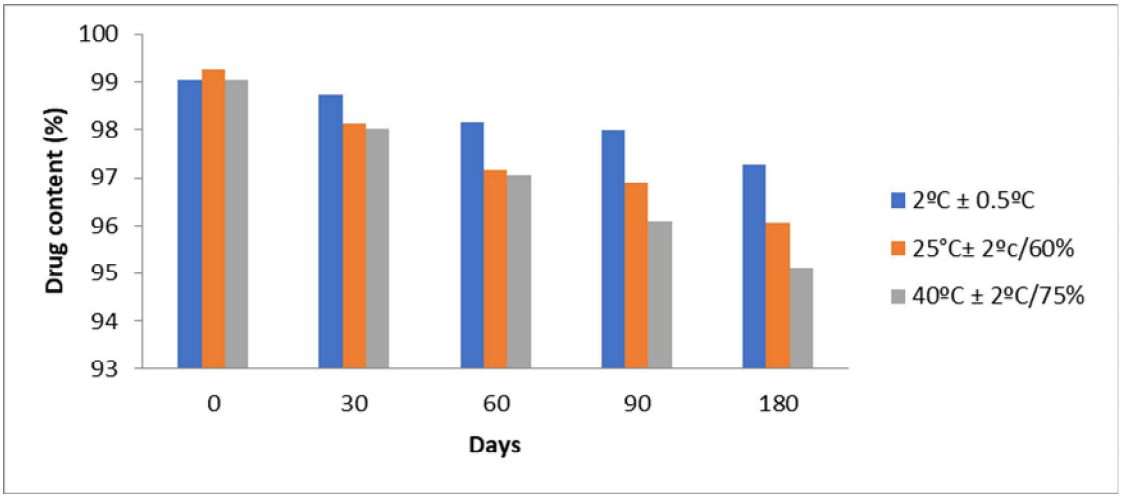

Figure2: Stability Studies of mouth dissolving film(LMDF6) at various temperature

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. 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

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REFERENCES

1. KinonBJ, Hill AL, Hong LS, KollackS. (2003). Olanzapine orally disintegrating tablets in the treatment of acutely ill noncompliant patients with schizophrenia. Int J Neuropsychopharmacol; 6:97-102.
2. Arya A, Chandra A, Sharma V,Pathak K. (2010). Fast dissolving oral films: an innovative drug delivery system and dosage form. Int J Chem Tech Res;2:576-83.
3. San L, Casillas M, Ciudad A, Gilaberte I. (2008). Olanzapine orally disintegrating tablet: a review of efficacy and compliance. CNS NeurosciTher;14:203-14.
4. Tamer MA, Hammid SN, Ahmed B. (2018). Formulation and in vitro evaluation ofbromocriptinemesylate as fast dissolving oral film. Int J Appl Pharm;10:7-20.
5. Bala R, Pawar P, Khanna S, Arora S. (2013). Orally dissolving strips: a new approach to oral drug delivery system. Int J PharmInvest;3:67-76.
6. LeeY, KimK, Kim M, Choi DH, Jeong SH.(2017). Orally disintegrating films focusing on the formulation, manufacturing process, and characterization. J Pharm Invest;47:183–201.
7. Meyer J, Loebel AD,Schweizer E. (2009). Lurasidone: a new drug in development for schizophrenia. ExprtOpin Invest Drugs;18:1715-26.
8. Franklin R, Zorowitz S, Corse AK, Widge AS, Deckersbach T. (2015). Lurasidone for the treatment of bipolar depression: an evidence-based review. NeuropsychiatrDisTreat;11:2143- 52.
9. Cruz MP. (2011). Lurasidone HCl (Latuda), an oralonce-daily atypical antipsychotic agent for the treatment of patients with schizophrenia. Pharm Ther;36:489-92.
10. Bawa R, Scarff JR. (2015). Lurasidone: a new treatment option for bipolar depression a review. InnovClin Neurosci;12:21-3.
11. Silva BM, Borges AF, Silva C, Coelho JF, Simoes S. (2015). Mucoadhesive oral films: the potential for unmet needs. Int J Pharm;494:537-51.
12. Shah S, Parmar B, Soniwala M, Chavda J.(2016). Design, optimization, and evaluation of lurasidone hydrochloride nanocrystals. AAPS PharmSciTech;17:1150-8.
13. Soni MM, Patel KR.(2016). Formulation and evaluation of fast dissolving films of lurasidone hydrochloride. Int J Pharm Res Bio Sci;5:101-23.
14. Mor J, Dubey V, Jalwal P. (2016). Formulation and evaluation of oral dissolving films of lisinopril. Int J Res Pharm Sci;1:34-8.
15. Hussain MW, Kushwaha P, Rahman MA, Akhtar J. (2017). Development and evaluation of fast dissolving film for orobuccal drug delivery of chlorpromazine. Int J Pharm Edu Res;51:539-47.