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CREATION AND ASSESSMENT OF A MOUTH DISSOLVING FILM CONTAINING LURASIDONE FOR THE TREATMENT OF PSYCHOSIS

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Abstract:
Because oral thin dissolving films or strips include water-soluble polymers, they dissolve or adhere to salivary mucosa in the mouth cavity or on the tongue in a matter of seconds, releasing the medication as fast as possible. The ideal thin film should have all the characteristics of a drug delivery system, including an acceptable formulation stability, a sufficient drug loading capacity, quick dispersion or dissolution, or extended application. Lurasidone must be formulated into buccal patches, and this medication is appropriate for this use. There are several uses for bioadhesive formulations in the therapy of illnesses, both locally and systemically. They must also be biocompatible, harmless, and biodegradable. nine fast-dissolving film formulations with varying polymer concentrations were created using lurasidone as a model drug candidate. Through the preparation of many oral dispersible film formulations, the impact of the polymer's nature was investigated. The release of the several formulations that included a blend of polymers was discovered to be in the following order: The optimal formulations for medication release and formulations are LMDF6>LMDF3. The most releases in less than an hour were discovered to be LMDF5, LMDF2, LMDF4, and LMDF1.The findings of the release kinetics investigation demonstrated that every formulation more closely followed the first order drug release profile, meaning that the release rate was dependent on the drug's starting concentration. The non-fickian or super case II transport mechanism was shown by the slope values of the Korsmeyer-Peppas plot.

Keywords: Formulation and evaluation, Lurasidone, Mouth dissolving film, Psychosis

Introduction:

In neurologic and psychiatric practice, psychosis is a prevalent and functionally disruptive symptom of many psychiatric, neurodevelopmental, neurologic, and medical diseases. It is a key focus for examination and therapy. A clinical condition made up of several symptoms is psychosis. [1] It is not a creature of nosology. Psychosis symptoms are present across a broad spectrum of mental diseases and exhibit significant inter- and intra-individual heterogeneity among individuals with various mental disorders as well as over time. Psychosis symptoms are often part of a larger clinical picture of the mental illness, which may also include depressive and manic symptoms. [2]. There may be differences between the prodromal stage of mental disease and the final psychotic episode in terms of signs and symptoms. [3]. The physician may also suggest psychotherapy, often referred to as talk therapy, as a treatment for psychosis. [4-5] It has been said that mouth dissolving

films provide an alternative to traditional dose forms. They provide rapid, local, or systemic effects and are a very flexible platform. Furthermore, patients with dysphagia, elderly, paediatric, or bedridden patients, as well as those who have difficulty accessing water, may simply use these devices on their own. There are many methods to provide these drug delivery systems, including transdermally, ocularly, buccally, sublingually, and orally [6].The ideal thin film should have all the characteristics of a drug delivery system, including an acceptable formulation stability, a sufficient drug loading capacity, quick dispersion or dissolution, or extended application. They must also be biocompatible, nontoxic, and biodegradable [7].
Because of its patient acceptance, safety, and convenience of administration, the oral route is one of the most used methods for administering drugs. Oral solid dose forms are available for around 60% of traditional dosage forms. For patients with illnesses including acute bouts of allergy reactions or coughing, as well as bedridden, emetic, paediatric, and elderly patients, oral dissolving strips and films are helpful. Both local and systemic delivery may make use of them. Because oral dissolving films and strips dissolve more quickly than fast-dissolving tablets and have greater exibility and better patient compliance, there is growing interest in their development [8].
Recently, there has been research on the possibility of employing oral dissolving films as carriers for the administration of many active pharmaceutical ingredients.Furthermore, over-the-counter dissolving film products including multivitamins, Listerine, Chloraseptic, and Triaminic are now obtainable. A plasticizer, a film-forming polymer, or a mixture of polymers that give the film the necessary elasticity and shape often make up the core of an oral dissolving film [9].Anti-psychotics are a great drug choice for an oral dissolving film formulation. A formulation of anti-psychotic drug in the form of an oral dissolving strip that would simplify dosage administration and improve patient compliance would require the patient to apply the medication to their tongue without swallowing. Thus, the aim of this endeavour was to design, produce, and delineate oral disintegrating films containing anti-psychotic medications.
Among all the medication delivery methods, the oral route is the most frequently used due to its ease of administration. It does, however, have some potential drawbacks, including reduced bioavailability due to its first-pass effect and a propensity to induce suddenly high and low plasma concentrations of the drug, which leads to patient noncompliance [10].Continuous intravenous infusion has been shown to provide a consistent and sustained medicine concentration within the therapeutic range for a considerable amount of time, despite its drawbacks. Nevertheless, there are several drawbacks to this mode of medication delivery, including painful needles and accidental punctures. As a consequence, continuous hospitalisation under medical care is necessary throughout the course of therapy.Due to patient compliance, mouth dissolving films are now the preferred route of medication administration [11].Lurasidone is an atypical antipsychotic used to treat schizophrenia and depressive episodes associated with bipolar I disorder.Lurasidone is authorised for the treatment of schizophrenia in people ≥13 years of age. It may also be used alone in individuals under the age of ten to treat bipolar depression, or in conjunction with valproate or lithium to treat bipolar depression in adults. Lurasidone is an atypical antipsychotic that enhances

cognition via D2 and 5-HT2A (mixed serotonin and dopamine action). It is believed that blocking serotonin receptors might lessen the extrapyramidal side effects that are often connected to conventional antipsychotics and enhance the unfavourable symptoms of psychoses [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.

Casting solution preparation: Selected polymers were used to prepare the casting solution. The necessary weighted amounts of the polymers HPMC E15, Xanthan gum (XG), and gura gum (GG) were dissolved in 5 millilitres of distilled water and allowed to swell overnight, either individually or in combination. As shown in Table 1, the medication and aspartame, a sweetener, were added straight to the polymeric solution together with glycerol, a plasticizer, and thoroughly stirred to create a homogeneous mixture on a magnetic stirrer. After adding the polymer solution, the Xanthan gum solution was diluted to a level of 10 millilitres using distilled water. The sonication method was used to free the trapped air bubbles.

Oral thin film preparation included pouring ten millilitres of the casting solution into glass moulds and vacuum-drying them for twenty-four hours at 40°C to remove the solvent. After peeling off the films, a square measuring 2.0 cm by 2.0 cm (4.0 cm2) was cut. It was left to dry for a whole day at room temperature. From the petri plate, where fast-dissolving films were created using different polymers and ratios while maintaining consistent plasticizer and sweetener concentrations, the clear, bubble-free thin film was carefully removed.

Assessment of oral dissolving films Variation in weight: Oral film dissolver mouths will weigh on a digital scale, with the average weight for each film being determined. It is preferable if the weight of films is almost consistent. Verifying that a film has the appropriate quantity of medication and excipients is helpful.

Film Thickness: The film's thickness was measured using a micrometre screw gauge at five separate locations, and an average of three readings was determined.

Folding endurance: The amount of folds (the number of times the film is folded at the same location) needed to break the specimen or for visible fractures to appear is known as the folding endurance. This further indicates how fragile the film is. Folding endurance was tested on a 2.5 cm x 2.5 cm strip by folding the film at the same location many times until a fracture became noticeable.

Uniformity of drug content: 40ml of PBS pH 6.8 and 10ml of methanol were used to dissolve the oral thinfilms that had been made. Whatman filter paper was used to filter the mixture. Following appropriate dilutions, the drug's concentration was measured using the UV technique at 248 nm.

Surface pH: After putting the film on a petri dish and moistening it with 0.5 millilitres of distilled

water, it was left for 30 seconds. After permitting equilibration to occur for one minute, the pH of the combination was measured by placing the pH meter's electrode in contact with the formulation's surface.

Tensile strength: The device, which has two clamps—the lower one moveable and the upper one fixed—determines the tensile strength. A 0.5 x 3 cm film sample is clamped between the two clamps. It is established what the force is at elongation and ripping. The following formula is used to determine the percent elongation (%E).

% 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: Vials of the same diameter may be employed as transmission cells in the research of the water vapour transmission rate. After a thorough washing, cells are baked to dryness. One gramme of calcium chloride is added to the cell, and using an adhesive, the polymeric sheets (two centimetres in area) are adhered to the brim. The original weight of the cells is recorded once they are precisely weighed. After that, the films are stored in a closed desiccator with an 80–90% RH saturated potassium chloride solution. It is done to remove and weigh the cells after 18, 36, 54, and 72 hours. The following formula may be used to determine the quantity of water vapour transported and the pace at which it is transmitted based on weight increases:

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

PBS pH 6.8 was used as the dissolving media in an in vitro diffusion investigation that was conducted utilising a Franz-diffusion cell device. A constant temperature of 37±0.5°C was maintained at 50 rotations per minute. To maintain sink condition, 1 ml of aliquots was removed at various intervals and the same volume of new dissolving media was introduced. Using a UV spectrophotometer, the aliquots were examined for drug content at λ max 248 nm wavelengths. The drug release's cumulative percentage was computed and published.

Stability Studies: In accordance with ICH requirements, the produced mouth dissolving oral film (LMDF6) was subjected to a stability assessment. The drug degradation during storage at several temperatures and storage conditions was used to determine the shelf life of API drugs. The samples were kept in stability chambers for 180 days at 2ºC ± 0.5ºC, 25°C/60% RH, and 40°C/75% RH. These samples were examined in order to determine the drug content.

Results and Discussion

Identification investigations revealed that the medication provided by pharmaceutical businesses was in compliance with the officially declared norms. In PBS pH 6.8, lurasidone's maximum absorption was measured at 248 nm. The medication lurasidone's solubility profile revealed that it

was hydrophobic and that it was easily soluble in methanol but insoluble in water and chloroform. The drug's hydrophobic nature was shown by the partition coefficient, which was determined based on their solubility profile. The drug inn-octanol's partition coefficient in a pH 6.8 phosphate buffer was 3.8. The compatibility of lurasidone with excipients under various environmental circumstances was investigated. Throughout the storage term, no medication interactions were noticed, demonstrating their compatibility with all constituents. Oral thin films are perfect for a variety of patient populations, such as those with swallowing difficulties and those in the paediatric, psychiatric, and geriatric categories. Fast-dissolving films are a convenient way to provide many medications the benefits of a mouth-dispensing drug delivery method.Using lurasidone as a model drug candidate, nine fast-dissolving film formulations with varying polymer concentrations were created for this investigation. With the use of HPMC E15 Guargum, sodium starch glycolate as a disintegration agent, glycerin as a plasticizer, aspartame as a sweetener, and distilled water as a solvent, mouth-dissolving lurasidone films were created using the solvent casting technique on glass moulds. Through the preparation of many oral dispersible film formulations, the impact of the polymer's nature was investigated. The produced fast-dissolving films were characterised and assessed for a number of characteristics, including thickness, drug content homogeneity, folding endurance, disintegration time, and stability and in vitro dissolution investigations. A variety of formulations made using HPMC E15, Guargum both alone and in combination with these polymers at varying concentrations were used to examine the effects of polymer concentration. In vitro drug release analysis revealed that single-polymer formulations exhibited the quickest drug release, with HPMC E15 films exhibiting the fastest drug release. Furthermore, it was discovered that the longer it took to wet and dissolve the drug molecules contained in the polymer matrix, the lower the drug release was as the polymer concentration grew. It was discovered that the medication released in the following order: The formulations LMDF6, LMDF2, LMDF4, and LMDF1 were shown to release the medication more quickly than LMDF3 in a one-hour period.The findings of the release kinetics investigation demonstrated that every formulation more closely followed the first order drug release profile, meaning that the release rate was dependent on the drug's starting concentration. The non-fickian or supercase II transport mechanism was shown by the slope values of the Korsmeyer-Peppas plot. The accelerated stability study test, conducted at room temperature in accordance with ICH guidelines, was used to examine the stability of the optimised formulation of LMDF6 oral mouth dissolving film for up to two years.

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 oforal 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	Drug Content (%)

	(days)	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

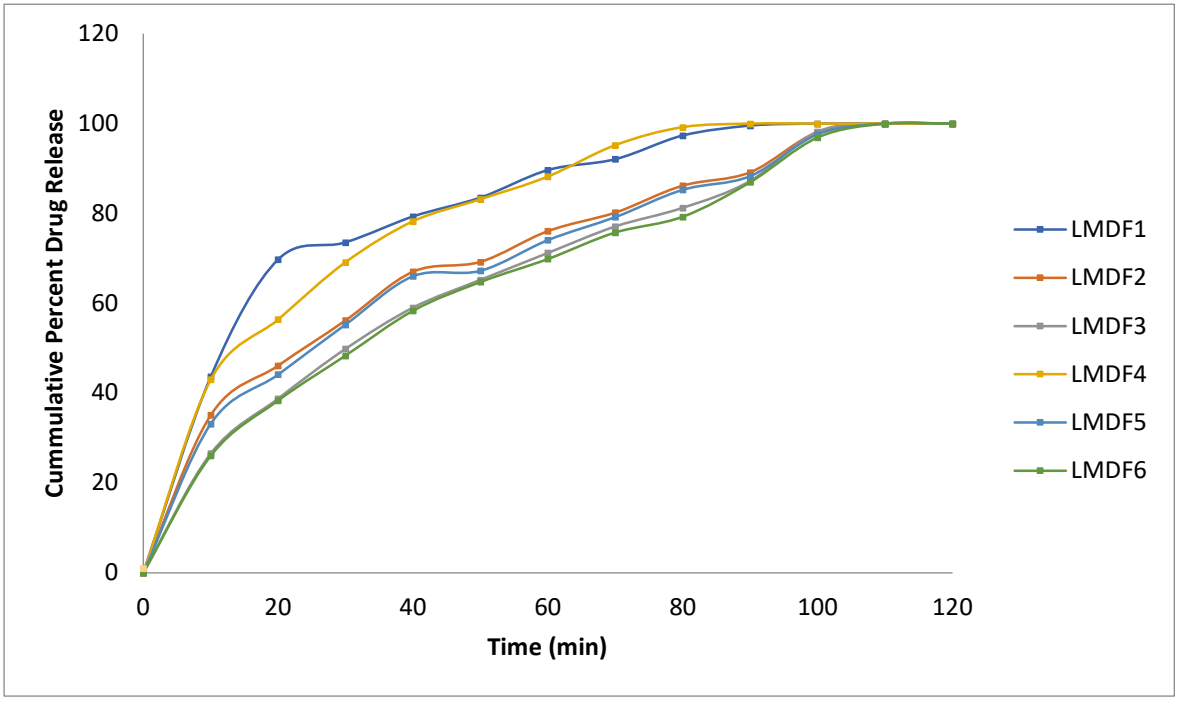

Figure 1: Zero-order plots oforal mouth dissolving films(LMDF1 – LMDF6)

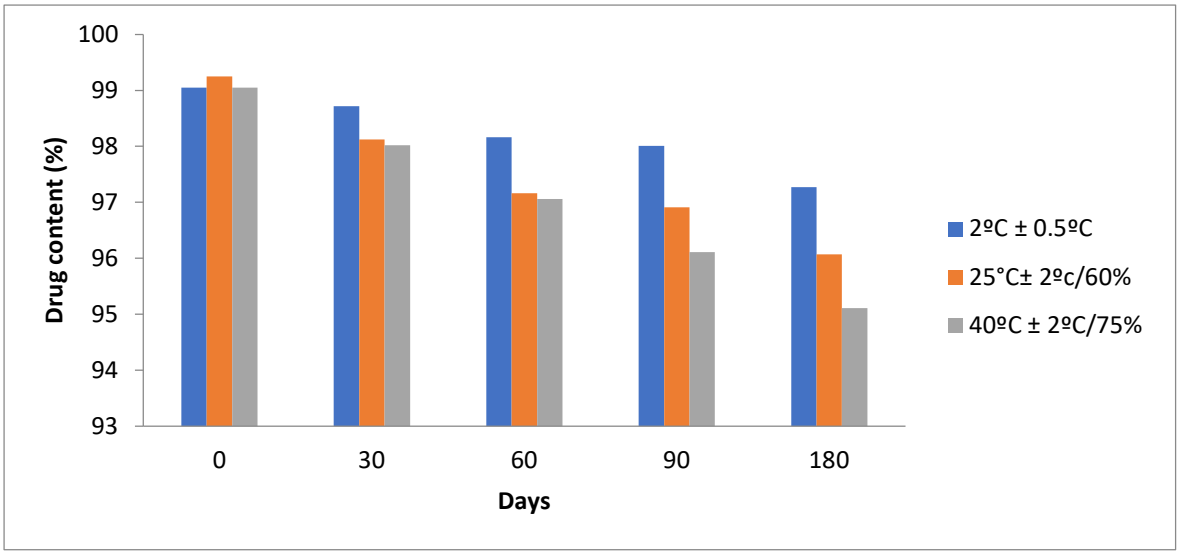

Figure 2: Stability Studies of mouth dissolving film(LMDF6) at various temperature

Summary and Conclusion:

Because oral thin dissolving films or strips include water-soluble polymers, they dissolve or adhere to salivary mucosa in the mouth cavity or on the tongue in a matter of seconds, releasing the medication as fast as possible. The ideal thin film should have all the characteristics of a drug delivery system, including an acceptable formulation stability, a sufficient drug loading capacity, quick dispersion or dissolution, or extended application. Lurasidone must be formulated into buccal patches, and this medication is appropriate for this use. There are several uses for bioadhesive formulations in the therapy of illnesses, both locally and systemically. They must also be biocompatible, harmless, and biodegradable. nine fast-dissolving film formulations with varying polymer concentrations were created using lurasidone as a model drug candidate. Through the preparation of many oral dispersible film formulations, the impact of the polymer's nature was investigated. The release of the several formulations that included a blend of polymers was discovered to be in the following order: The optimal formulations for medication release and formulations are LMDF6>LMDF3. The most releases in less than an hour were discovered to be LMDF5, LMDF2, LMDF4, and LMDF1.The findings of the release kinetics investigation demonstrated that every formulation more closely followed the first order drug release profile, meaning that the release rate was dependent on the drug's starting concentration. The non-fickian or super case II transport mechanism was shown by the slope values of the Korsmeyer-Peppas plot.

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