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DISSOLUTION ENHANCEMENT OF LAMOTRIGINE

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ABSTRACT

Enhancing the dissolution by formulating a Mouth Dissolving Film of Lamotrigine and *Invitro* evaluation of Mouth Dissolving Film, Comparative study of *Invitro* dissolution studies between the formulated Mouth Dissolving marketed immediate release tablet formulation. Formulation of mouth dissolving film by solvent casting method using Gellan gum as Film forming polymer, Glycerine as Plasticizer and Microcrystalline cellulose as Super disintegrant, Aspartame as Sweetening agent, Citric acid as Saliva stimulating agent. The formulated mouth dissolving films were evaluated for dissolution and disintegration studies and compared with conventional tablet formulations and gave satisfactory results of enhanced dissolution.

INTRODUTION

Oral dissolving film drug delivery systemwere first developed in late 1970s as based on the technology of the transdermal patch. An alternative to table capsule and syrups for paediatrics and geriatrics patients who experienced difficulties in swallowing traditional oral solid dosage form that dissolves or disintegrates quickly in the oral cavity, resulting in solution or suspension without need for the administration of water is known as mouth dissolving dosage form.

Lamotrigine is an anticonvulsant agent. It inhibits sodium channel, thereby stabilizing neuronal membrane and release of excitory and 200mg tablets and also available in chewable and dispersible tablet. It is efficiency used in a wide variety of seizure, lennax, gas-taut syndrome and also used for bipolar disorder. This article mainly helps in class-II drug by

developing and evaluating mouth dissolving film located with lamotrigine. the reason for selecting oral dissolving drug delivery system because of an its large surface area for drug absorption as it avoid first pass metabolism and there is a rapid onset of pharmacological action and ease of administration. It's a novel drug delivery system since lamotrigine was only available as tablet [chewable, disintegrating, extended release] and IV formulation.

MATERIAL AND METHODOLOGY: MATERIAL

Lamotrigine were purchased from MICRO LAB's. Gellan gum, microcrystalline cellulose and other excipients such as glycerine, ethanol, de-ionized water sucrose received from MICRO LAB's. All other chemicals and reagents were ofanalytical grade or better.

Plasticizer

These plasticizers are important for providing the mechanical properties to the FDF's. mechanical properties which are mainly improved by using these plasticizer are percentage elongation and tensile strength. Optimized amount of plasticizers are used to get a better FDF's. the commonly used plasticizers are polyethylene glycol [PEG 400, 4000, etc].

Flavoring Agent

Flavors are added to provide taste to the film. There are various flavor which are added to the film formation. Any flavor can be added intense mint, sour fruit flavor, or other sweet confectionary flavors are also added to the fast dissolving film formulation.

Coloring Agent

The coloring agents are added to the film formation to impact color to the FDF's. coloring agents should compatible with the drug and other ingredients.

Sweetening Agents

It is most important part of the oral pharmaceutical product. Sweetening agents helps in the taste masking of the bitter drugs. They are commonly used in the formulation as like as sucrose, dextrose, fructose, glucose etc. they are also polyhydric alcohols such as sorbitol, mannitol, and isomalt.

Saliva Stimulating Agent

Saliva stimulating agents are used to increase the rate of production of saliva that would aid the faster disintegration of ODF. Citric acid, malic acid lactic acid ascorbic acid and tartaric acid are the few examples of saliva stimulants.

METHODS

Solvent casting method

Water soluble ingredients are dissolved in water. API and other agents are dissolved in suitable solvent to form a clear viscous solution. Both the solution are mixed. Degassed under vacuum. Resulting solution is cast as a film.

Hot melting extrusion

The drug is mixed with carriers in solid form. Extruder having heater melts the mixture. Finally the melted mixture is shaped into film bythe dies.

Semi solid casting

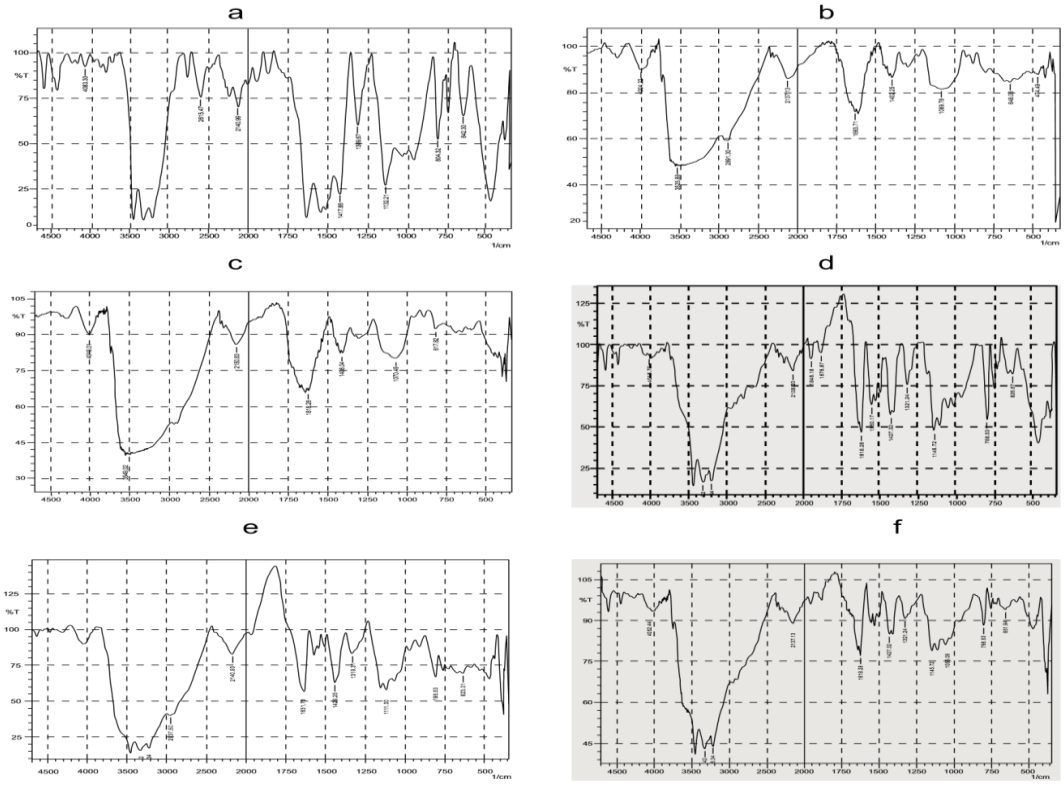
Solution of water soluble film forming polymer is prepared. Resulting solution added to a solution of acid insoluble polymer. Appropriate amount of plasticizer is added to that gel mass is obtained. Finally the gel is casted in to the film or ribbons using heat controlled drums.

Solid dispersion extrusion

Drug is dissolved in a suitable liquid solvent The solution is incorporated in to melt of polyethylene glycol obtained below 70*c. Finally the solid dispersion are shaped in to the films by means of dies.

Rolling method

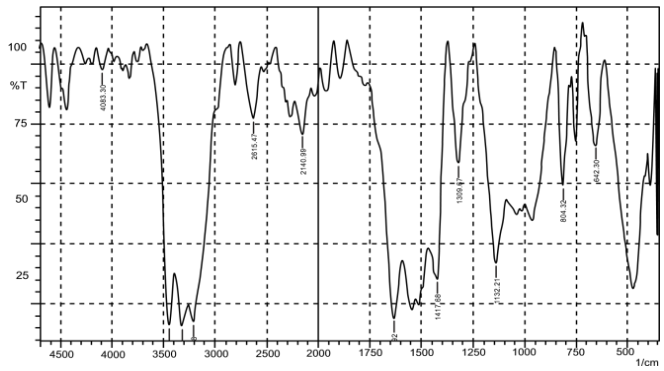
Prepare pre-mix with film forming polymer, polar solvent and other additives except a drug. Add premix to master batch feed tank. Fed it via first metering pumps control valve to either or both of the last and second mixer. Add required amount of drug to the desired mixer. Blend the drug with master batch premix to give a uniform matrix. Specific amount of uniform matrix is then fed to the pan through second metering pumps. The film is finally forced on thesubstrate and carried away via the support roller. The wet film is the dried using controlled bottom drying.



a) FTIR of lamotrigine; b) gellan gum; c) xanthen gum; d) gellam gum with laomotrigine; e) xanthen gum with lamotrigine; f) in situ gel formation.

Identification of drugs

FTIR spectroscopy



FTIR spectra of lamotrigine, gellan gum, drug with gellan gum, insitu gel formulation are shown in following graphs.

FITR spectrum of sample drug of lomotrigine

Solubility Studies

The pure drug is partially soluble in water and ethanol, & completely soluble in methanol, acetone, PBS pH-6.6.

Melting Point

The melting point of the drug is found to be 225-235*C and it accordance with the reference.

λ Max Of Lamotrigine With Methanol

The absorption maxima of lamotrigine in methanol is found to be 309 nm.

Partition co-efficient of lamotrigine

the partition co-efficient of the lamotrigine drug is found to be 1.1. these indicating that the drug is practically insoluble in water and has high lipophilicity.

Composition of oral thin films

S. no.	Name of the recipients	Quantity
1.	Drug(lamotrigine)	5-30%
2.	Film forming polymer	40-50%
3.	Plasticizer	0-20%
4.	Saliva stimulating agent	2-6%
5.	Sweetening agent	3-6%
6.	Surfactant	Q.s
7.	Flavoring agent	Q.s
8.	Coloring agent	Q.s

Post formulation studies

3. Weight variation

An individual film was weighed on an electronic digital balance and the average weight was calculated. Then the average weight of film these substracted from the individual weight of the film. A large variation in weight is likely to have non- uniform drug content.

4. Surface pH

Surface PH of film should be close to that PH of baccal cavity that is PH 6.8. The mouth dissolving film was slightly moistened with the help of water. The surface PH was measured by bring the electrode in contact with the surface of mouth dissolving film.

5. Drug Content Uniformity

The drug content uniformity was determined by dissolving the film in 100ml of water with occasional shacking. Then 5ml of dissolved solution was taken and it is filtered through 0.45µm whatman filter paper. From that take 1ml filtered solution in 10ml volumetric flask and made upto 10ml of distilled water and shack well before

1. Visual Inspection Of Film

Clarity, transparency, oiliness, are the main parameters for visual inspection. The formed formed film show statisfactory result, so further evaluations carried out.

2. Thickness

The thickness of the film should be measured with the help of **micrometer screw gauge.** Film should be measured at centre of film and around the film and the mean thickness was calculated. In general, ideal film \films thickness should exhibit between 50 and 100 micrometres. going to UV analysis. Then the drug content was determined by using suitable UV spectroscopy.

6. Folding Endurance

Folding endurance was determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film was folded without breaking is computed as the folding endurance value.

7. Young's Modulus

Young's modulus or elastic modulus is measure of stiffness of film. It is represented as the ratio of young's modulus of applied stress over strain in region of elastic deformation as follows as

Young's modulus = Slope X 100 \ Film thickness X Cross head speed

Hard and brittle films demonstrates a high tensile strength and young's modulus with small elongation.

Invitro Dissolution

Invitro dissolution of mouth dissolving film was studied in phosphate buffer pH 6.8 which is used as dissolution medium. The rotation of the stirrer was adjusted to 50rpm. The temperature of the dissolution medium was maintained at 37°C± 0.5°C throughtout the experiment. The sample of 1ml of dissolution medium were withdrawn for 30 minutes at every 2 minutes intervals of time i.e., 2, 4, 6, 8, 10,12, 14, 16, 18, 20,…...30minutes and analysed for drug release by measuring the absorbance in UV spectroscopy. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. The invitro drug release data of oral marketed intermediate release tablet formulation was taken

from the article reference number and it was compared with invitro drug release ofoptimized formulation.

Dissolution apparatus

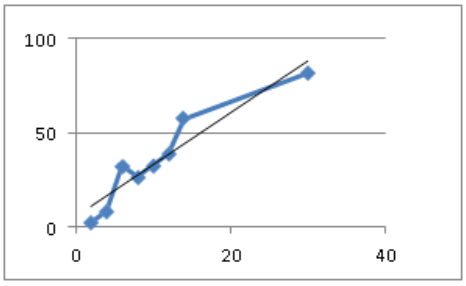
The invitro dissolution studies were conducted using 600ml of artificial saliva as dissolution medium with modified type 5 dissolution apparatus. A temperature of 37°C and 50rpm were used. Each film with dimension (2×2.5 cm^2) was placed on a watch glass covered with nylon wire mesh. The watch glass was then dropped into dissolution flask 5ml samples were withdrawn at 10,0,30,40,50, 60,70,80,90,100,120 sec time intervals and every time replaced with5ml of fresh dissolution medium.

The samples were analyzed by measuringabsorbance at 350nm.

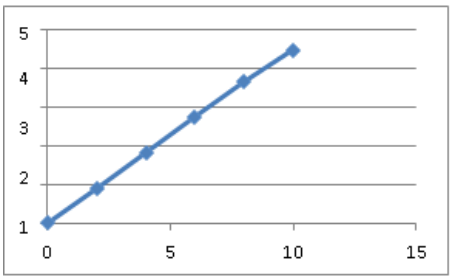
Invitro Dintergrating Time

Invitro disintegrating time is the time require to break the mouth dissolving film when brought incontact with saliva or water. Invitro disintegrating time was performed in the USP disintegrating time testing apparatus. Phosphate buffer pH 6.8 was used as medium. The film placed in the tube of the container and the disks were placed over it.

In another method the disintegration time can be visually determined by dipping the film in 25ml water in a beaker. The beaker should be shaken gently and the time was noted when the film starts to breaks or disintegrates.



a) *Invitro* drug release of optimizedformulation.



b) *Invitro* drug release of oral marketedtablet formulation.

CONCLUSION

From the present work it can be conclude that fast dissolving film formulation can be on innovative and promising approach for the delivery of drug with improved bioavailability in enhanced dissolution rate test masking, with better patient complaints as an effective therapy for the treatment. oral thin films are used as a good tool to increase the life cycle of the existing product by getting patent for same product as fast dissolving oral films. It is proven that the fast dissolving film provide the beneficial activity of rapid onset of action incase of epilepsy, mood stabilizer, bipolar disorder.

REFERENCES

1. Wallace, H; Shorvon, S; Tallis, R. Age- specific incidence and prevalence rates of treated epilepsy in an unselected population of 2,052,922 and age-specific fertility rates of women with epilepsy. Lancet, 1998; 352(9145): 1970-1973. [http://dx.doi.org/10.1016/S0140- 6736(98)04512-7].
2. Watts, P.; Smith, A. Pecsys: *In Situ* gelling system for optimized nasal drug delivery. Expert *Opin Drug Deliv., 2009*; 6(5): 543-552. [http://dx.doi.org/10.1517/174252 40902939135].
3. Umesh, G.H.; Kumar, H.; Mishra, G.; Sharma, A.K,; Gothwal, A.; Keshwari, P. Intranasal drug delivery: A noninvasive approach for the better delivery of neurotherapeutics. *Pharma. Nanotechnol., 2*017; 5(4): 1-12.
4. Vinayan, K.P.; Solomon, L.M. Neonatal seizures and epilepsies. *Int. J Epilepsy.,*2014; 1. [http://dx.doi.org/10.1016/j.ijep. 2014.08.001]
5. Sandeep saini, Arun Nanda, Monika Hooda and Komal, J.Dhari – Formulation and evaluation of mouth disosolving Anti- allergic tablets of levocetrizine dihydrochloride: journal ofchemical and pharmaceutical research, 2011; 3(5): 450-455.
6. Ms.Mital S.Panchal, Mr.giren Patel, Mrs. Arthi bagada, Dr. K.R. Vadalia – Formulation and evaluation of mouth dissolving film of Ropinirole hydrochloride by using Pullulan Polymer: International journal ofpharmaceutical research & Allied Sciences, 2012; 60-72.
7. P. Bhatt, M. Patel – Formulation and Evaluation of Fast Dissolving Film Rizatriptan Benzoate: International Journal of Medipharm Research, 2015; 1: 58-77.
8. Ravi Kumar K and Mercy Sulochana M– Formulation and Evaluation of Fast Dissolving Film of Lercanidipine Hydrochloride: International Journal of Innovative Drug Discovery, 2014; 4: 46-53.
9. Raosaheb S Shendge, Kishore S Salunkhe, Kashid Girish – Formulation and Evaluation

of Fast dissolving Sublingual Film of Antihistamine Drug: European Journal of Molecular & Clinical Medicine, 2020; 7: 2134-2143.

10. Peter Small, Harold Kim-Allergic Rhinitis Asthma And Clinical Immunology, 2011; 7: 1-8.
11. Poonam A. Padamwar, Poonam P. Phasate 1- Formulation and Evaluation of Fast Dissolving Oral Film of Bisprolol Fumarate: International Journal of Pharma Science and Research, 2015; 6: 135-162.
12. Smita V. Pawar, M.S.Junagade –Formulation and Evaluation of MouthDissolving Film of Risperidone: International Journal of PharmaTechResearch, 2015; 8: 218-230.
13. Sujith s. Nair, Roopith Padamanathan and Sreena K – Development and Evaluation of Fast Dissolving Oral Thin Film Containing Prochloroperazine Maleate: Europen Journal of Pharmaceutical and Medical Research, 2015; 1(3): 58-77.
14. Rushiraj Jani, Dasharath Patel –Hot Melt Extrusion: An Industrially Feasible Approach for Casting OrodispersibleFilm: Asian Journal of Pharmaceutical Sciences, 2015; 1-27.
15. Radha Bhati, Raja K Nagarajan-A Detailed Review on Oral Mucosal Drug Delivery System: International Journal of Pharmaceutical Science and Research, 2012; 3: 659-682.