Novel Spin Coating Technique for Development of Zolmitriptan Mouth Dissolving Film

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***Abstract*—**In present investigation first attempt was made to design & developed zolmitriptan mouth dissolving film prepared by novel spin coating technique. This technique was reported earlier in the field of electronics, physical science and for application of biomedical science. Dissolvable oral thin films are in the market since past few years for the application of pharmaceutical and medical, which was widely accepted by consumers for quick onset of action. Zolmitriptan was selected as model drug, which was widely used in the treatment of migraine containing mouth dissolving film formulation (F1-F9) were composed and optimized F8 formulation contained HPMC E-15 (400mg), propylene glycol (0.6ml), citric acid (1.5mg), Pine-apple flavor (0.1ml) & Neotame (1mg) were used as a film former, plasticizer, saliva stimulating agent, flavoring & sweetening agent respectively and further film was characterized by different evaluation parameters like disintegration time, dissolution time, tensile strength, percentage elongation & scanning electron microscopy etc. Film prepared by Spin coating Technique was found to be less disintegration time 11 Sec, good tensile strength 3.2 (N/mm^2), less thickness 0.01mm, maximum drug content 99.25 %, less weight variation and good folding endurance. From this study, it can be concluded that the spin coating technique has more potential and industrial applicability for development of fast acting dosage form.

***Keywords*—** Development of Zolmitriptan Mouth Dissolving Film.

I. Introduction

FAST-dissolving oral drug delivery systems are solid dosage forms, which dissolve as well as disintegrate within 1 min when placed in the mouth without chewing or drinking water. (1) Mouth dissolving films (MDF) as dosage forms have gained significance in the pharmaceutical field as patient friendly, novel and convenient products (2). These dosage forms possess certain specific advantages like no need of water for disintegration, rapid onset of action, ease of transportability, accurate dosing, ease of handling, improved patient compliance and pleasant taste. (3,4,5) They experience disintegration in the salivary fluids of the oral cavity within a second, where they release the active pharmaceutical agent. (6) MDF is ideal by patients when suffering from motion sickness, dysphasia and mental disorders while they are unable to consume large amount of water. The advantages of suitable dosing and portability of film have led to an extensive applicability of this dosage form in pediatrics as well as geriatric patients. (7,8) Also convenient for administration for disabled, bedridden patients and for travelers and busy people, who do not always have access to water. (9) In this research work, first time spin coater process was used in the field of pharmaceutical for the preparation of mouth dissolving film.

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II. Material & Method

Zolmitriptan was obtained as a gift sample from Cipla Ltd, F & D, Mumbai. Neotame was obtained as a gift sample from Kawarlal and Co. Chennai, India. All other chemicals and reagents used were of analytical grades and used as received.

A. Preparation of mouth dissolving film by spin coating technique:

Spin coating has been used for several decades for the application of thin films. A typical process involves depositing a small puddle of a fluid resin onto the center of a substrate and then spinning the substrate at low speed to high speed. Final film thickness and other properties will depend on the nature of the resin (viscosity, drying rate, percent solids, surface tension, etc.) and the parameters chosen for the spin process. Factors such as final rotational speed, acceleration, and fume exhaust contribute to how the properties of coated films. The Zolmitriptan MDF formulation (F1 to F9) prepared by a spin coating technique which is shown in (Table 1 & Fig.1). The amount water soluble polymer HPMC E-15 with other Excipients Propylene Glycol, Citric Acid, Pineapple flavor, Amaranth dies, Neotame are dissolved Beaker (A) and drug dissolved in Methanol Beaker (B). The solutions are mixed properly with the help of magnetic stirrer and these viscous solutions were sonicated up to the bubble free solution and finally depositing a small puddle of a viscous solution onto the center of (substrate) circular glass slide 3 x 3cm of spin coater and then

spinning the substrate at high speed (1500 rpm) for 20 sec and remove the coated substrate from spin coater and placed in hot air oven at 450C for two hours. After 2 hrs and pill out the film from the substrate and further evaluation of physical properties like thickness (10, 11), weight variation (12), content uniformity (13), disintegration Time (14 & 18) and tensile properties like tensile strength (15), percentage elongation (16), folding endurance (16) and In-vitro dissolution study of all MDFs were determined in auto-dissolution apparatus (Electrolab TDT-08l plus) following the USP paddle method. All tests were conducted in 250 ml pH 6.8 phosphate buffer. The dissolution medium was maintained at a temperature of 37 ± 0.5 0C with a paddle rotation speed at 50 RPM. Aliquots (5 ml) withdrawn at various time intervals were immediately filtered through Whitman filter paper and assayed for drug content spectrophotometrically (shimandzu- 1800) at 222.40 nm. The absorbance values were transformed into concentration by reference to a standard calibration curve obtained experimentally. (r2 = 0.9993). The in vitro dissolution test was performed in triplicate for each batch. (17)

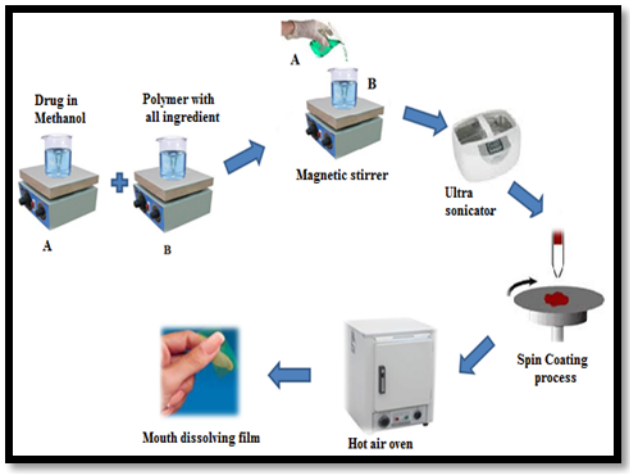

Fig.1: Spin coating technique

TABLE I
FORMULATION OF ZOLMITRIPTAN MDF BY SPIN COATING TECHNIQUE

Batch No.	Zolmitriptan (mg)	HPMC-E15 (mg)	Propylene Glycol (ml)	Citric Acid (mg)	Pineapple Flavour (ml)	Neotame (mg)	Methanol (ml)	Distilled Water (ml)
F1	40	200	0.2	1.5	0.1	1	0.5	2
F2	40	300	0.6	1.5	0.1	1	0.5	2
F3	40	400	0.4	1.5	0.1	1	0.5	2
F4	40	200	0.4	1.5	0.1	1	0.5	2
F5	40	300	0.2	1.5	0.1	1	0.5	2
F6	40	400	0.2	1.5	0.1	1	0.5	2
F7	40	200	0.6	1.5	0.1	1	0.5	2
F8	40	400	0.6	1.5	0.1	1	0.5	2
F9	40	300	0.4	1.5	0.1	1	0.5	2

III. RESULT & DISCUSSION

Before the formulation of mouth dissolving film, drug-excipient interaction study was carried out and characteristics peak were showed no interaction was found. The Zolmitriptan MDF formulation (F1 to F9) was prepared by a spin coating technique which is shown in (Table 1 & Fig.1). The amount water soluble polymer HPMC E-15 with other excipients were optimized and studied the effect concentration of propylene glycol and HPMC-E15 on disintegration time, tensile strength, pill out property and found to be increased concentration with increase the disintegration time, and thickness 0.01mm, In-vitro dissolution study (F8) shows 99.2587 drug release in 30 Sec. And other parameters like weight variation, content uniformity, percentage elongation, folding endurance found within limit, which is shown in (Table 2 & Fig. 2)

TABLE II
EVALUATION OF MDF FOR SPIN COATING TECHNIQUE

Batch No.	DT (sec)	Tensile Strength N/mm^2	Pill out	Thickness (mm)	% elongation (%)	Weight Variation (mg)	Folding Endurance	Drug Content %
F1	3	1.7	1	0.01	101.7	3.9	236	74.94386
F2	10	2.9	3	0.01	102.9	5.8	311	89.10987
F3	8	2.4	2	0.01	102.4	6.4	294	95.6754
F4	6	1.95	2	0.01	102.1	4.4	274	78.045
F5	4	1.8	1	0.01	101.8	5.1	249	83.09665
F6	5	1.93	1	0.01	101.9	6.3	263	92.832
F7	9	2.7	3	0.01	102.7	4.8	304	80.21365
F8	11	3.2	3	0.01	103.2	6.6	318	99.2587
F9	7	2.3	2	0.01	102.3	5.4	285	86.408

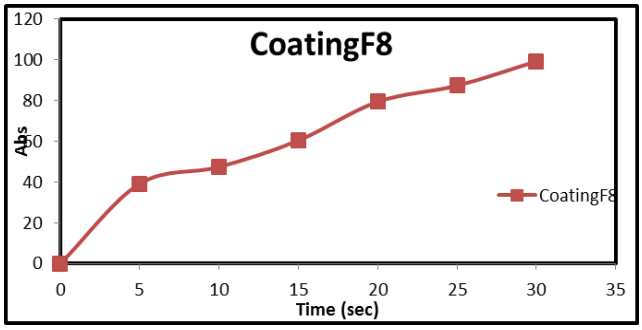

Fig. 2: In-vitro dissolution study

For morphological study the image of oral MDF was taken by scanning electron microscopy with 50000 x magnification values at 5 µm lengths. The image was scanned from both upper surface (A) and lower surface (B). Resulted film containing Zolmitriptan oral MDF was clear and colorless in nature were shown in (fig. 3) The lower surface (B) is shown smooth as compared to the upper surface (A) because of during formulation glass slide smoother surface. Scanned image also shows a clear image, therefore it should be conclude total drug and excipients was dissolved and uniformly distributed within the formulation.

Spin coating Technique

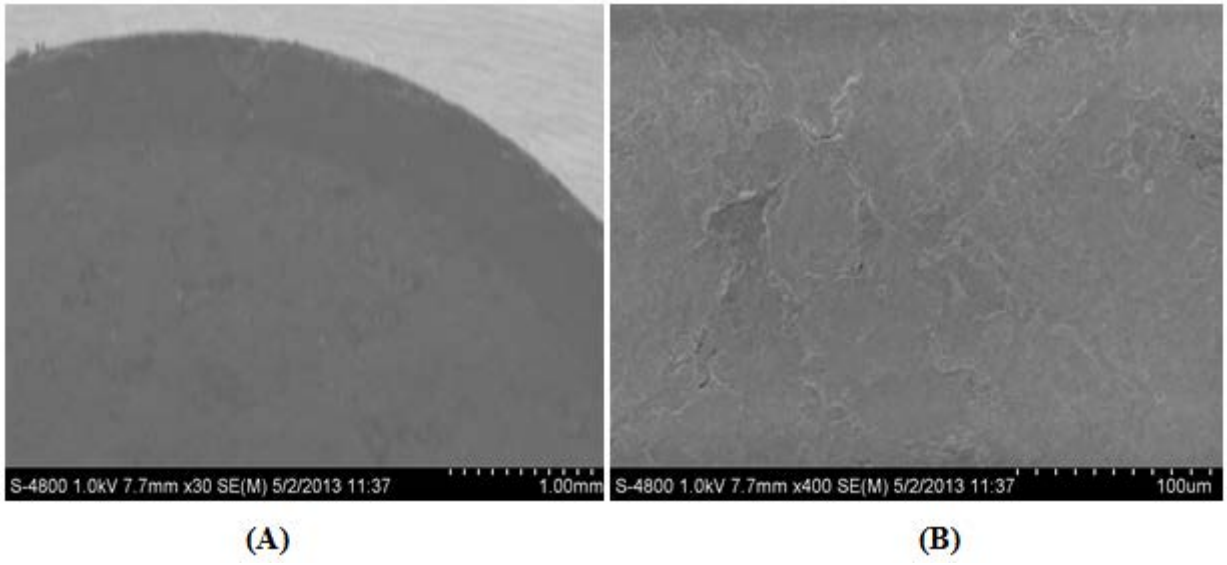

Fig. 3: SEM of Zolmitriptan mouth dissolving films

IV. CONCLUSION

In present study Zolmitriptan containing mouth dissolving films were prepared from F1-F9 formulation by spin coating technique for the treatment of migraine disease and formulation F8 was optimized containing concentration of HPMC-E15 400mg, propylene glycol 0.6ml, Pine-apple flavor

0.1ml & Neotame 1mg, citric acid 1.5mg. and further evaluated. Film prepared by Spin coating Technique was found to be less disintegration time 11 Sec, good tensile strength 3.2 (N/mm2), less thickness 0.01mm, maximum drug content 99.25 %, less weight variation and good folding endurance. From this study, it can be concluded that the spin coating technique has more potential and industrial applicability for development of fast acting dosage form.

ACKNOWLEDGEMENT

Authors are very thankful to management, HRPIPER, Department of Physics, R.C. Patel Arts Science & Commerce college, Shirpur and University Institute of Chemical Technology, North Maharashtra University, Jalgaon, 425 001, Maharashtra for providing technical support, necessary facility, equipment, material and facility for completion of this research work.

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