CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND EVALUATION FAST DISSOLVING SUBLINGUAL FILMS OF TICAGRELOR

[1]Sweety Vishwakarma, [2]Dr. Shailendra Bindaiya, [3]Dr. Shailendra Lariya
[1]Radharaman College of Pharmacy (RCP), Bhopal (M.P.)

Article Received: May 2022 **Accepted:** June 2022 **Published:** June 2022

Abstract:
Ticagrelor is a P2Y12 platelet inhibitor used in patients with a history of myocardial infarction or with acute coronary syndrome (ACS) to prevent future myocardial infarction, stroke and cardiovascular death. Ticagrelor is used to prevent a serious or life-threatening heart attack or stroke, or death in people who have had a heart attack or who have acute coronary syndrome (ACS; blockage of blood flow to the heart). The objective of this work is to prepare and evaluate fast dissolving sublingual films containing Ticagrelor. Formulation F3 showed the least disintegration time of 8±1sec. Formulations containing only Sodium starch glycolate, Crospovidone and Cross carmellose sodium showed minimum disintegration time of 8±1sec sec select as optimized formulation. The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time.

Key words:*Ticagrelor, sublingual films, Formulation, Evaluation*

Corresponding author:
Sweety Vishwakarma
Radharaman College of Pharmacy (RCP), Bhopal (M.P.)
sweetyvish14@gmail.com

QR code

*Please cite this article in press*Sweety Vishwakarmaet al,***Formulation And Evaluation Fast Dissolving Sublingual Films Of Ticagrelor.,****Indo Am. J. P. Sci, 2022; 09(6).*

INTRODUCTION:

The Fast-Dissolving Drug Delivery Systems was an advancement that came into existence in the early 1970's and combats over the use of the tablets, syrups, capsules which are the other oral drug delivery systems. Fast Dissolving Drug Delivery Systems serves as a major benefit over the conventional dosage forms since the drug gets rapidly disintegrated & dissolves in the saliva without the use of water. [1]

It provides the direct entry into the systemic circulation thereby avoiding the hepatic first pass Effect and ease of administration. [2] This delivery system consists of a thin film, is simply place below the tongue, instantly wet by saliva; the film rapidly dissolves. Then it rapidly disintegrates and dissolves to release the medication for systemic absorption This fast-dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist sublingual environment. [3] FDFs are useful in patients such as paediatric, geriatrics, bedridden, emetic patients, diarrhoea, sudden episode of allergic, attacks, or coughing for those who have an active life style. [4]

However per-oral administration of drugs gives rise to some problems such as hepatic first pass metabolism and degradation within the GI tract. These problems can be overcome by administration through the sublingual mucosa. The sublingual route can produce a rapid onset of action within a short period of time due to high permeability and vascularization of the sublingual mucosa. Fast dissolving film is prepared using hydrophilic polymers that rapidly dissolves or disintegrates within few seconds. [5]

There has been increased demand for the novel dosage form to gain more patient compliance. Fast dissolving films recently have acquired great importance in the pharmaceutical industry due to their unique properties and specific advantages like no need of water for disintegration, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste and improved patient compliance. Fast dissolving film is a type of drug delivery system, which when placed in the oral cavity it rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption, without chewing and intake of water. This technology evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers.

Ticagrelor is a P2Y12 platelet inhibitor used in patients with a history of myocardial infarction or with acute coronary syndrome (ACS) to prevent future myocardial infarction, stroke and cardiovascular death. Ticagrelor is used to prevent a serious or life-threatening heart attack or stroke, or death in people who have had a heart attack or who have acute coronary syndrome (ACS; blockage of blood flow to the heart). The objective of this work is to prepare and evaluate fast dissolving sublingual films containing Ticagrelor.

MATERIAL AND METHODS:

Material:

Ticagrelor was obtained as a gift sample from Pharmaceutical Company. HPMC was procured from Qualikems fine chem Pvt Ltd Vadodhara. PEG400, sodium starch glycolate, croscarmellose sodium was obtained from S.D fine chemicals limited, Mumbai. Citric acid, ethanol was obtained from Loba Chemical Pvt Ltd (Mumbai, India). Hydrochloric acid, KH_2PO_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 analytical grade.

Methods:

Formulation:

Drug (Ticagrelor) containing fast dissolving films were fabricated by the solvent casting method. Xanthan gum, Gelatin, Gum acacia, cross carmellose sodium, Aspartame by solvent casting technique with ice cold distilled water and sublingual films were prepared. Drug solution was sonicated for 30-45 min to solubilize the drug completely in the solvent. Drug solution was poured into polymeric solution and ethanol was added for alkaline hydrolysis. Both solutions are uniformly mixed to get a homogeneous solution on magnetic stirrer at 250-320 rpm. Then this solution was spread on film former by adjusting the desired temperature on glass moulds of 15cm*5 cm^2. Once the wafer sheet was ready, it was cut into desired size of 2.5*2.5 cm^2 cm was dried and The dried films were carefully removed from the glass plates and was cut into size required for testing. The films were stored in air tight plastic bags till further use. The composition of sublingual films is given in Table 1 [6].

Table 1: Selection and Optimization of Films Forming Agents

Name of ingredients (mg for 12 strips)	F1	F2	F3	F4	F5	F6	F7	F8	F9
API	720	720	720	720	720	720	720	720	720
Sodium starch glycolate	100	200	300	100	200	300	100	200	300
Crospovidone	25	50	100	25	50	100	-	-	-
Cross carmellose sodium	25	50	75	-	-	-	25	50	75
Gelatin	-	-	-	25	50	75	25	50	75
Methyl Paraben	20	20	20	20	20	20	20	20	20
Aspartame	20	20	20	20	20	20	20	20	20
Citric acid	50	50	50	50	50	50	50	50	50
DM water qs to (ml)	30	30	30	30	30	30	30	30	30

Evaluation of prepared Films:

Thickness:

Three random films were selected from each batch and the thickness was measured
at three different places using a vernier caliper [7].

Weight uniformity:

For each formulation, three randomly selected patches were used. For weight variation test, 10 films from each batch were weighed individually by digital electronic balance and the average weight and relative standard deviation was calculated [8].

Surface pH Determination:

The surface pH of fast dissolving films was determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the oral mucosa, it is important to keep the surface pH as close to neutral as possible. The wafer to be tested was placed in a Petri dish and was moistened with 0.2 ml of distilled water. The electrode of pH meter (Electronic india) was placed on the surface of wafer to determine the surface pH [8].

Folding Endurance:

This was determined by repeatedly folding one films at the same place until it broke. The number of times the films could be folded at the same place without breaking cracking gave the value of folding endurance.

Percentage of Moisture Content:

The films were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual films were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight [9].

$$\text{Percentage of Moisture Content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \text{x } 100$$

Drug Content Analysis:

The patches (n=3) of specified area were taken into a 10 ml volumetric flask and dissolved in methanol and volume was made up with 10 ml methanol. Subsequent dilutions were made and analyzed by UV spectrophotometer at 300nm.

Disintegrating time:

The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of polymers to minimizes the disintegrating time. In vitro disintegration time was determined by placing the wafer in a Petridis containing 10ml distilled water with swirling every 10 sec. The time at which the wafer disintegrated was noted.

***In vitro* dissolution study:**

The *in vitro* dissolution test was performed using the USPXXX dissolution apparatus II (Paddle type). The dissolution studies were carried out at 37±0.5°C; with stirring speed of 50 rpm in 900 ml phosphate buffer (pH 6.8). Films size required for dose delivery (2.5×2.5 cm^2) was used. Five ml aliquot of dissolution media was collected at time intervals of 1, 2, 5, 10 and 15 minutes and replaced with equal

volumes of phosphate buffer (pH 6.8). The collected samples were filtered through 0.45 µm membrane filter and the concentration of the dissolved Ticagrelor was determined using UV-Visible spectrophotometer at 300nm. The results were presented as an average of three such concentrations [9].

RESULTS AND DISCUSSION:

Drug content was analyzed by UV-Visible spectrophotometer at 300nm. The percentage drug content was between 96.65±0.16% and 99.65±0.18% as shown in Table 8.3, which proved uniform drug distribution within the Ticagrelor films.All preparations absorb moisture at a very fast rate and they disintegrate as soon as they come in contact with water. The formulated Ticagrelor films showed a disintegration time in the range of 7±1-22±4sec (as shown in Table 8.3). Formulation F3 showed the least disintegration time of 8±1sec. Formulations containing only Sodium starch glycolate, Crospovidone and Cross carmellose sodium showed minimum disintegration time of 8±1sec sec select as optimized formulation. The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agents were selected for this work.

Table 2: Results of Evaluation of prepared Films

Formulation code	Thickness* in µm	Weight* mg	Folding endurance* (Times)	Surface pH Determination	Percentage of Moisture Content*	Drug content analysis (%)	Disintegrating time (Sec.)
F1	75±4	145±5	125±5	6.3±0.1	2.15±0.12	98.85±0.25	18±3
F2	79±6	149±4	136±4	6.5±0.2	2.05±0.15	98.12±0.12	13±2
F3	85±5	153±7	185±6	6.8±0.1	1.85±0.16	99.65±0.18	7±1
F4	78±3	141±8	145±5	6.3±0.1	2.36±0.17	97.45±0.13	22±4
F5	82±4	152±5	152±2	6.7±0.3	2.25±0.16	96.65±0.16	18±5
F6	89±2	163±4	163±4	6.5±0.2	2.36±0.15	97.78±0.17	15±2
F7	76±5	149±2	152±2	6.6±0.2	2.45±0.17	98.85±0.17	17±1
F8	85±6	153±4	164±3	6.7±0.2	2.14±0.16	98.65±0.23	15±6
F9	92±7	167±3	153±2	6.4±0.3	2.35±0.25	98.12±0.21	12±3

***Average of three determinations (N=3)**

Table 3: Results of *In-vitro* release study of optimized formulation F3

S. No.	Time (Sec.)	Percentage cumulative drug release
1.	60	55.65±0.25
2.	120	73.32±0.36
3.	180	88.98±0.14
4.	240	98.85±0.32
5.	300	99.12±0.18
6.	360	99.65±0.26

CONCLUSION:

The study conclusively demonstrated significant results for ticagrelor sublingual films. The sublingual films of ticagrelor are mostly helpful to the patients for the treatment of acute coronary syndrome, cardiac angina. The sublingual films of ticagrelor can be successfully prepared solvent casting method. Formulation F3 showed the least disintegration time of 8±1sec. Formulations containing only Sodium starch glycolate, Crospovidone and Cross carmellosesodium showed minimum disintegration time of 8±1sec sec select as optimized formulation. The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time.

REFERENCES:

1. Prabhu SC, Parsekar HD, Shetty A, Monteiro SS, Azharuddin M and Shabaraya AR. A Review

on Fast Dissolving Sublingual Films for Systemic Drug Delivery. Int J Pharm &Chem Sci 2014; 3(2): 482-496.
2. Dixit RP, Puthli S. Oral strip technology: Overview and future potential. J of Cont Rel 2009; 139: 94–107.
3. Thakur N, Bansal M, Sharma N, Yadav G and khare P. Overview A Novel Approach of Fast Dissolving Films and Their Patients. Adv in Bio Res 2013; 7(2): 50-58.
4. Kumar RK and Mercy SM. Fast Dissolving Film: A Unique Strategy for Drug Delivery Asian J. Pharm. Res 2014; 4(1): 47-55.
5. Patil SL, Mahaparale PR, Shivnikar MA, Tiwari SS, Pawar KV,Sane PN. Fast Dissolving Oral Films: An Innovative Drug Delivery System. Int J Res Rev Pharm App Sci 2014; 2(3): 482-496
6. Garsuch V, Breitkreutz J. Novel analytical methods for the characterization of oral wafers. Eur J Pharm Biopharm. 2009; 73:195–201.
7. Boateng JS, Matthews KH, Auffret AD, Humphrey MJ, Stevens HNE, Eccleston GM. In vitro drug release studies of polymeric freeze-dried wafers and solvent-cast films using paracetamol as model soluble drug. Int J Pharm. 2009; 378:66–72.
8. Boateng JS, Auffret AD, Matthews KH, Humphrey MJ, Stevens HNE, Eccleston GM. Characterisation of freeze-dried wafers and solvent evaporated films as potential drug delivery system to mucosal surfaces. Int J Pharm. 2010; 389:24–31.
9. Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, Piccerelle P. Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int J Pharm. 2005; 292:29–41.