Formulation And Evaluation of Fast Disintegrating Tablet of Nicardipine

Janhavi .K. Bundele[1], Pratik .B. Bhanage[2], Dr. Megha.T. Salve[3]
[1, 2, 3] Dept of Pharmacy
[1, 2, 3] Shivajiroa Pawar college of Pharmacy, Pachegaon, Ahilyanagar - 413725

Abstract- *The aim of this study was to formulate and evaluate Nicardipine Fast Disintegrating Tablets (FDTs), which are designed to provide rapid onset of action, enhanced bioavailability, and improved patient compliance, especially in individuals with swallowing difficulties. Nicardipine, Calcium channel blocker, was selected as the model drug due to its potent analgesic and anti-inflammatory properties. The tablets were formulated using the direct compression method, which is cost-effective and efficient for mass production. Various excipients, including microcrystalline cellulose, crospovidone, sodium starch glycolate, and magnesium stearate, were utilized to optimize the disintegration, flowability, and compression characteristics of the formulation.*

Pre-compression studies were conducted to assess the powder blend's flowability and compressibility, using parameters such as bulk density, tapped density, Carr's index, angle of repose, and moisture content. These evaluations indicated that the powder blends had suitable flow properties for tablet compression. Post-compression testing, including hardness, friability, disintegration time, and dissolution, demonstrated that the prepared tablets met the desired criteria for fast disintegration and drug release. The disintegration time was found to be within the required limits for FDTs, ensuring rapid release of the drug upon contact with saliva.

A calibration curve for Nicardipine was developed using UV spectrophotometry to quantify drug content in dissolution studies. The dissolution profile showed rapid release of Nicardipine, which is characteristic of fast-dissolving tablets. Stability studies confirmed that the tablets were stable under standard storage conditions, with no significant changes in drug content or physical properties.

In conclusion, the formulated Nicardipine FDTs were successfully developed with satisfactory characteristics in terms of disintegration, dissolution, and stability. These tablets offer an efficient alternative for the delivery of Nicardipine, improving patient compliance and providing rapid therapeutic action. Further studies may explore the optimization of excipients and the effect of different formulation variables on the performance of the tablets.(FTIR) spectrum. The solid dispersions can be evaluated by in-vitro dissolution studies

Keywords- Nicardipine, Fast Dissolving, Tablet

I. INTRODUCTION

Oral drug delivery remains the most preferred route of drug administration due to its ease of use, patient compliance, and cost-effectiveness. However, conventional oral dosage forms such as tablets and capsules may not be suitable for all patient populations, especially pediatric, geriatric, and those with dysphagia (difficulty in swallowing). This limitation has led to the development of Fast Disintegrating Tablets (FDTs)—solid dosage forms that disintegrate rapidly in the oral cavity without the need for water.

FAST DISINTEGRATING TABLETS (FDT)

Fast Disintegrating Tablets (FDTs) are gaining significant attention in pharmaceutical research and industry due to their convenience, rapid onset of action, and potential to enhance bioavailability. These tablets dissolve or disintegrate in the mouth within seconds, releasing the active pharmaceutical ingredient (API) for immediate absorption and therapeutic effect.

Requirement of enhanced bioavailability, with quicker onset of action and subject compliance pave the way for novel oral dosage forms. Of them, fast disintegrating formulations using super disintegrates and hydrophilic ingredients are coming into picture.

These systems saw their innovation in late 1970‟s when the research was carried out for search of a substitute for the conventional dosage forms for elderly and paediatric who encounter problem in taking the standard oral solid-dosage form(Nehal Siddiqui MD et al., 2010).

Orally FDT is one of the recently developed delivery system for the oral drug delivery. Transdermal drug delivery system formed the basis of this advanced technology. These

systems on coming in contact with oral mucosal tissue gets hydrated by with saliva It thereby undergoes quick disintegration releasing the drug that undergoes instant absorption into systemic circulation via buccal mucosa.

Drinking water is the requisite for oral drug administration which leads to nuisance in swallowing bulky traditional dosage forms(Ashish et al., 2017).In order to avoid the dysphagia and perk up patient compliance, FDTs are introduced as These disintegration formulations are of diffeternt types

ADVANTAGES OF FAST DISSOLVING /DISINTEGRATING TABLETS

1. Improved Patient Compliance

One of the most significant advantages of Fast Disintegrating Tablets (FDTs) is their ability to enhance patient compliance, particularly in populations with difficulty swallowing solid dosage forms. This includes:

- Pediatric patients: Children often have trouble swallowing conventional tablets or capsules. FDTs, which dissolve or disintegrate rapidly in the mouth, can improve the ease of medication administration, thereby increasing the likelihood of adherence to prescribed therapies.
- Geriatric patients: Elderly individuals may experience difficulty swallowing tablets due to age-related conditions such as dysphagia or dry mouth. FDTs eliminate the need for water and provide an easier method of ingestion.
- Patients with medical conditions: Individuals suffering from conditions such as stroke, Parkinson's disease, or esophageal strictures may also face difficulties with swallowing solid dosage forms. FDTs can provide an alternative that is easy to administer.

2. Faster Onset of Action

FDTs are designed to disintegrate rapidly upon contact with saliva, allowing for immediate release of the active pharmaceutical ingredient (API). This rapid disintegration significantly improves the onset of action of the drug, which is especially advantageous for pain management, as seen in the case of Nicardipine. Faster disintegration and dissolution in the oral cavity enable the drug to be absorbed more quickly in the gastrointestinal tract, leading to a reduced time to therapeutic effect.

For Nicardipine, which is commonly used for pain and inflammation relief, a faster onset of action is crucial for the effective management of acute pain, such as postoperative pain or musculoskeletal injuries.

3. No Need for Water

Traditional tablets and capsules often require water for swallowing. For patients with swallowing difficulties or those who are not in a position to access water, this can be an obstacle to proper medication administration. FDTs eliminate the need for water, as they dissolve or disintegrate in the mouth when placed on the tongue. This feature makes them especially beneficial for patients who may not have easy access to water or who have difficulty swallowing large pills.

4. Enhanced Bioavailability

One of the primary challenges in oral drug formulation is the poor solubility and bioavailability of certain drugs, such as Nicardipine. When a drug is poorly soluble, its dissolution in the gastrointestinal tract becomes the rate-limiting step for absorption. FDTs can improve the bioavailability of poorly soluble drugs by enhancing their dissolution rate in the oral cavity, leading to better absorption and higher bioavailability.

In the case of Nicardipine, an CALCIUM CHANNEL BLOCKER with relatively poor aqueous solubility, formulating it as an FDT can help overcome this limitation by allowing the drug to disintegrate and dissolve more rapidly in the gastrointestinal tract, improving the overall therapeutic effect.

5. Reduced Gastrointestinal Irritation

CALCIUM CHANNEL BLOCKERs like Nicardipine are known to cause gastrointestinal (GI) irritation, especially when taken over an extended period. Conventional tablets can irritate the stomach lining as the drug dissolves slowly and comes into direct contact with the gastric mucosa.

FDTs, on the other hand, disintegrate rapidly and have the potential to enhance the dissolution and absorption of the drug in the upper gastrointestinal tract. This could potentially reduce the amount of time the drug remains in contact with the gastric mucosa, potentially lowering the risk of irritation, ulcers, or bleeding.

Additionally, FDTs may allow for more precise dosing and faster absorption, reducing the overall exposure to

high drug concentrations at any given time, which can mitigate GI irritation.

6**. Easy to Manufacture**

FDTs are typically manufactured using direct compression, a simple and cost-effective method compared to other specialized tablet formulations like sustained-release or enteric-coated tablets. The use of superdisintegrants in the formulation allows for rapid disintegration, and the tablets can be produced without the need for expensive equipment or complex procedures.

This ease of manufacture not only reduces production costs but also makes FDTs a viable option for large-scale commercial production, benefiting both patients and pharmaceutical companies alike.

7. Stability

FDTs can be formulated to have good chemical and physical stability, as the disintegration process occurs only upon contact with moisture. As long as the tablets are stored in a moisture-controlled environment, they can retain their stability and potency for extended periods. In the case of Nicardipine, FDTs may help preserve the drug's stability by minimizing the need for excipients that could degrade the drug or its efficacy over time.

8. Versatility in Formulation

The FDT formulation can be customized with a variety of excipients to meet specific therapeutic needs. For example, Nicardipine FDTs can be designed with additional excipients that:

- Improve solubility: Using solubilizing agents like cyclodextrins to enhance the solubility of Nicardipine.
- Modify taste: Many drugs have a bitter taste, but FDTs allow for the inclusion of flavor-masking agents to improve palatability.
- Add active ingredients: FDTs can be used for combination therapy, where more thanone active ingredient is included to provide multidimensional therapeutic effects.

LIMITATIONS OF FDT

- Lower mechanical strength of tablets
- The formulations are highly porous and soft ,they are friable and brittle hence intricate to handle.
- Formulation badly tasting drugs into FDT is difficult as special flavouring agents are required to reach patient compliance
- Majority of FDT are hygroscopic hence require special packaging techniques for protection from humidity.
- Dryness in mouth is not favorable condition for FDT

SALIENT FEATURES OF FDTS

- Ease of administration for elderly, stroke victims, bedridden patients
- The dissolved drugs are absorbed from the mouth, pharynx and oesophagus while passage of saliva thus increasing bioavailability
- Pre-gastric absorption results in enhanced bioavailability thus reduction in dosage Enhanced clinical performance through a cutback of unwanted effects.
- Changes the perception of medication for pediatric patient.
- Avoids the risk of choking or suffocation hence improves safety.
- Advantageous for motion sickness, rapid occurrence of allergies
- Enhances the bioavailability, of insoluble and hydrophobic drugs by providing due to rapid dissolution of formulation and dissolution of drug
- Higher stability for as the drug is present in solid dosage form till consumption
- Permit higher drug loading and is cost effective.

II. LITERATURE SURVEY

Kumar(2014) Superdisintegrants play a crucial role in FDT formulations, as they ensure that the tablet disintegrates quickly upon contact with moisture. Crospovidone, croscarmellose sodium, and sodium starch glycolate are the most commonly used superdisintegrants. Crospovidone is a cross-linked polyvinylpyrrolidone that swells rapidly upon hydration, resulting in rapid tablet disintegration and enhanced dissolution rates

Madhavi and Reddy (2012) demonstrated that crospovidone and croscarmellose sodium could effectively reduce the disintegration time of tablets while maintaining mechanical strength. They observed that crospovidone exhibited superior performance in disintegration and drug release compared to other superdisintegrants.

Huang et al. (2014) noted that sodium starch glycolate, a natural polysaccharide, exhibited excellent disintegration properties, especially in dry and hydrophobic formulations.
The choice of superdisintegrant significantly impacts the drug release profile and overall performance of FDTs. Studies have shown that a combination of disintegrants often yields the best results in terms of both disintegration time and drug release rate.

Modasiya et al., 2009 formulated Piroxicam FDT using sodium starch glycollate, Ac-Di-Sol and hydoxy propyl methylcellulose. All the FDTs analysed for pre compression and post compression parameters.The powder blends subjected to direct compression technique. Bulk density of all tablets is between 0.415 to 0.455 g/cm^3 , tapped density ranging 0.501 to 0.543g/ cm^3. The Hausner's ratio value < 1.2 indicates enhanced flow property with compressibility index >10 and angle of repose < 40^0. The drug content ranged between 98.50 – 102.3% , hardness within 4.3 – 5.6 kg/cm^2 ,tensile strength between 9.54 to 12.93 .

Latha et al., 2015 prepared Ondansetron HCL rapid disintegration tablets by direct compression method comprising cross povidone, cross carmellose sodium and sodium starch glycolate, and analysed.The results indicate that all formulations exhibited uniform weight with acceptable weight variation (≤1.19%),hardness within 2.5 to 3.0 kg/cm3,and friability < 1% indicating superior mechanical strength.the formulations containing 6% sodium starch glycolate exhibited minimum disintegration time of 24 sec and maximum drug release of 98% in 30 mins.

Sunil et al., 2007 prepared fenoverine FDT using crospovidone, croscarmellose sodium, and sodium starch glycolate.The results indicate that disintegration time of optimized formulation is 15.9 sec in vitro and 37.16 sec in vivo. Hence they could successfully formulate fenoverine rapidly disintegrating tablets with pleasing taste, plenty mechanical strength, and shorter disintegrating time

Bhupathi et al., 2012 prepared and evaluated Terbutaline sulphate FDT for enhanced rest time and bioavailability. The drug excipients compatibility study by IR revealed the compatibility amongst both. The formulations prepared with crystalline cellulose and sodium starch glycolate and evaluated. The drug dissolution study indicates release of 95% and 96% for two formulations microcrystalline cellulose and sodium starch glycolate within 10 minutes. The formulations with maximum amount of sodium starch glycolate exhibited maximum release of 98%.

Chinnala et al., 2017 formulated Cinitapride hydrogen tartrate FDTs with crospovidone (CP), croscarmellose sodium (CCS), and sodium starch glycolate (SSG) in varying ratios . All the tablets evaluated for pre-compression parameters.The bulk and tapped densities ranged between ranged between 0.412–0.432 g/cc and 0.507–0.528 g/cc respectively. The weight and thickness of all tablets are ±9.5% and mean±5% respectively. Wetting time values lie between 19.76 to 39.53 sec. Water absorption ratio ranged from 57.30 to 78.82 %. The disintegration time varied between 17.43 - 38.61 seconds. The tablets prepared using crosspovidone have exhibited maximum drug release 96.94±0.47% in 30 min.

III. AIM AND OBJECTIVES

Aim:

To formulate and evaluate fast disintegrating tablets (FDTs) of **Nicardipine** using various superdisintegrants for rapid onset of action, enhanced patient compliance, and effective drug delivery.

Objectives:

1. To conduct preformulation studies of Nicardipine to assess physicochemical properties and compatibility with excipients.
2. To formulate fast disintegrating tablets of Nicardipine using different superdisintegrants (Crospovidone, Croscarmellose Sodium, Sodium Starch Glycolate) by direct compression technique.
3. To evaluate the pre-compression parameters such as bulk density, tapped density, compressibility index, Hausner's ratio, and angle of repose of the powder blends.
4. To evaluate the post-compression parameters of the tablets, including:
    - Weight variation
    - Hardness
    - Friability
    - Disintegration time
    - Wetting time
    - Water absorption ratio
    - Drug content uniformity
5. To perform in vitro drug release studies to assess the dissolution profile of the formulations.
6. To identify the optimized formulation based on disintegration time and drug release behavior.

4. Drug Profile

Attribute	Details
Generic Name	Nicardipine
Brand Names	Cardene, Cardene IV
Drug Class	Calcium Channel Blocker (Dihydropyridine class)
Mechanism of Action	Inhibits calcium ion influx into vascular smooth muscle and myocardium; causes arterial vasodilation and reduces blood pressure.
Indications	- Hypertension (especially emergency/acute cases)- Angina pectoris- Subarachnoid hemorrhage (for vasospasm prevention)
Route of Administration	Oral, Intravenous (IV)
Dosage Forms	- Capsules: 20 mg, 30 mg- IV solution: various concentrations
Typical Dosage	Oral: 20–40 mg three times dailyIV: Starting at 5 mg/hr, titrate as needed
Onset of Action	IV: Within minutesOral: 30–60 minutes
Half-Life	8–14 hours (oral); shorter with IV
Metabolism	Hepatic (extensively via CYP3A4)
Excretion	Primarily in urine

5. Materials Used

- Nicardipine (API)
- Superdisintegrants (Crospovidone, Croscarmellose Sodium, SSG)
- Excipients: MCC, mannitol, magnesium stearate, talc

S. No	Equipment Name	Source
1	Digital weighing machine	Contech Instruments Ltd. Mumbai, India
2	Tablet compression machine	Cemache, Ahmadabad
3	Monsanto hardness tester	Cintex Ind. Corporation, Mumbai
4	Friability tester	Electrolabpvt Ltd. India
5	Disintegration apparatus	Electrolabpvt Ltd. India
6	Infrared spectrophotometer	FTIR 8400 S, Shimadzu, Japan

7. Experimental Work

PREPARATION OF CALIBRATION CURVE FOR NICARDIPINE

The calibration curve recorded in 6.8 pH buffer comprising 2/10M sodium hydroxide and 2/10M potassium di hydrogen ortho phosphste).

Preparation of 0.2 M NaOH

8gm of NaOH dissolved in minimum water and made upto mark in 1000ml standard flask

Preparation of 0.2 M KH2PO4

27.218 gm potassium di hydrogen ortho phosphate dissolved in water and made upto mark in 1000ml standard flask.

Preparation of Nicardipine standard solution Preparation of stock I

0.01g drug dissolved in 6.8 pH buffer and made upto mark in 100 ml standard flask with to give 1000 mcg/ml concentration.

Preparation of stock II

0.01ml of above solution transferred to a 100 ml standard flask and made upto volume using buffer to get 100 mcg/ml concentration.

PLOTTING OF STANDARD CURVE FOR NICARDIPINE(Dixit and

Puthil,2009;Arya et al., 2014)

Aliquots of 0.2, 0.4, 0.6, 0.8, 1ml withdrawn for Stock II and made up to 10ml using 6.8pH buffer to obtain concentration of 2, 4, 6, 8, 10 mcg/ml solutions. All the samples analyzed spectrophotometrically at 369 nm.

PRELIMINARY SOLUBILITY STUDIES OF NICARDIPINE

The solubility of pure drug is measured according to the method published byHiguchi and Connors in 1965. Excess Nicardipine dissolved in 25ml solutions of water-soluble carriers like PEG 6000, Kollidon CL, PVPK-30, Soluplus, Aerosil 200, Poloxamer 127, HPMC and Urea. The samples mixed well for 24 hours at 25^0C followed by filtration through

Whatman filter paper no 1. The filtered diluted using CH_3OH and evaluated for drug concentration at 369 nm.

Table : Composition of Nicardipine

Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)
Nicardipine	8	8	8	8	8
Crospovidone	10	15	—	—	—
Croscarmellose Sodium	—	—	10	15	—
Sodium Starch Glycolate	—	—	—	—	15
Mannitol (diluent)	120	115	120	115	115
Microcrystalline Cellulose (MCC)	50	50	50	50	50
PVP K30 (binder)	5	5	5	5	5
Talc	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2
Total Weight	197	197	197	197	197

EVALUATION OF NICARDIPINE SD

Percentage practical yield(PPY)

The PPY of Nicardipine SD by collecting and weighing the samples using following formula (Lakshmi et al., 2012)

$$\% \text{ Practical Yield} = \frac{\text{Practical Mass (Solid dispersion)}}{\text{Theoretical Mass (Drug + Polymer + Surfactant)}} \times 100$$

Drug content

The drug content of Nicardipine SD analyzed by dissolving 0.02g of drug in carbinol, and made upto 100ml .The contents filtered and filtrate diluted and measured spectroscopically at 369 nm against blank.The actual drug content calculated using the equation(Patel et al., 2011).

Drug content (%) = Actual amount of Solid dispersion x 100 Theoretical amount of Solid dispersion

***In vitro* dissolution study of Nicardipine SD**

0.02 g of drug dispersed in dissolution medium surface comprising of 0.9 lit of phosphate buffer at pH 7.4 ,temperature of 37±0.5ºC, stirred at 50 rpm.The samples withdrawn at predetermined intervals, filtered and diluted with carbinol , analyzed at 369 nm in triplicate for drug contents (Mandal et al., 2010).

CHARACTERIZATION NICARDIPINE SOLID DISPERSION 5.6.1:FTIR studies

The IR spectra were recorded using an FTIR spectrophotometer (Shimadzu, Japan) with diffuse reflectance principle .The samples were scanned over the frequency range 4000–400-^{1}cm

.Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) studies were carried out using DSC 60, having TA60 software, Shimadzu, Japan. Samples were accurately weighed and heated in sealed aluminum pans at a rate of 10°C/ min between 40 and 350°C temperature rang under nitrogen atmosphere. Empty aluminum pan was used as a reference. (Nagamani et al., 2013)

PREPARATION AND EVALUATION OF NICARDIPINE FDT

Preparation of Nicardipine FDT

Step 1: Sifting

- Sift all the powders (Nicardipine, MCC, Mannitol, superdisintegrant, Aspartame) through sieve #40 to ensure uniform particle size.

Step 2: Dry Mixing

- Accurately weigh and mix the sifted powders in a mortar or blender for about 10–15 minutes to ensure uniform distribution of the drug and excipients.

Step 3: Addition of Lubricants

- Add magnesium stearate and talc (previously passed through sieve #60) to the powder blend. Mix gently for 3–5 minutes to avoid over-lubrication.

Step 4: Compression

- Compress the final blend into tablets using a tablet compression machine fitted with appropriate flat-faced punches (e.g., 6 mm or 8 mm).

EVALUATION OF NICARDIPINE FDT

Pre Compression Evaluation Tests

Angle of repose

Angle of repose signifies highest angle achievable between tablet surface and the horizontal plane. A rough and irregular surface exhibit larger angle of repose.

Weight accurately 100 gm of the blend and are cautiously poured through funnel with tip placed 2.5 cm height over the graph paper that is positioned on a horizontal surface. The powder is poured till apex of pile just reaches funnel tip. Angle of repose is calculated by the following formula

$\Theta = \mathbf{Tan^{-1}(h/r)}$

Where Θ = angle of repose, r= radius pf pile, h= height of the pile

Bulk density

Bulk density is powder mass divided by the bulk volume.It is analyzed by pouring the powder blend into graduated cylinder to determine volume (V*) and powder (M) .The bulk volume calculated as

b = M/V*

Tapped density

This is calculated by tapping a cylinder containing accurately weighed powder blend for about 250 times.
Tapped density is calculated as

$$*t = M/V_t$$

V_t –mimimum volume occupied
M-mass of the blend

Compressibility Index (Carr's Index)

Carr's index (CI) signifies the easiness with which a material can be encouraged to flow .CI value <10 indicates excellent powder flow while value between 26-31 indicates power flow

The CI calculated as follows
C.I(%) = Tapped density –Bulk density × 100
Tapped density

Hausner's Ratio

Hausner's ratio is an indicator of easiness of powder flow calculated as follows
Hausner'sratio=*dt/*db
Where *dt = tapped density,*db = bulk density

Post compression evaluation tests

Weight variations

20 random FDTs weighed and average weight determined. Then individual tablet weighed separately to obtain % deviation from the average. The accepted deviation for tablets with average weight ≤ 130mg is 10%, for ≥130mg is 7.5%.

Thickness

Thickness of tablet is crucial for patient acceptance and packaging hence to be controlled at± 5% deviation from standard value.Vernier Calipers used for measurement of thickness of 10 FDTs .the average and SD values recorded (Anroop N et al., 2007).

Hardness

Monsanto hardness tester was used for determination of hardness of randomly picked 10 tablets and average of measured values reported (Nerurkar J et al., 2005).

Friability

20 tablets randomly picked were weighed and subjected to friability test in Roche friabilator that rotated at 25 rpm for duration of 4min. the tablets were then reweighed after de-dusting (Ismat U, 2011) and following equation was used to calculate percent loss in weight due to impact and abrasion,
%Friability= (Loss in weight/ Initial weight) X 100.

Content uniformity

Randomly picked 20 tablets were powdered in a glass mortar after calculating their average weight and amount equal to 10 mg was dissolved in 100ml of phosphate buffer pH 6.8 and filtered followed by spectrometric determination of drug content at 369 nm (Nerurkar J et al., 2005).

In-vitro disintegration time (DT)

The DT of FDTs analyzed in USP device with six glass tubes measuring "3 long, open at the top, and held against 10" screen at lower end of the basket rack congregation. One tablet positioned in each tube with basket rack positioned in 1000ml beaker containing buffer at 37± 2 ^{0}C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.(Daniel and J. Axel, 2015)

7. Result and Discussion

UV CALIBRATION CURVE

The UV spectra of Nicardipine scanned between 200-400 nm denoted absorption maximum peak at 369 nm (figure 6.1). The calibration curve exhibited good linearity within concentration of 2-10 mcg/ml with correlation coefficient value of 0.999 (table 6.1 and figure 6.2).

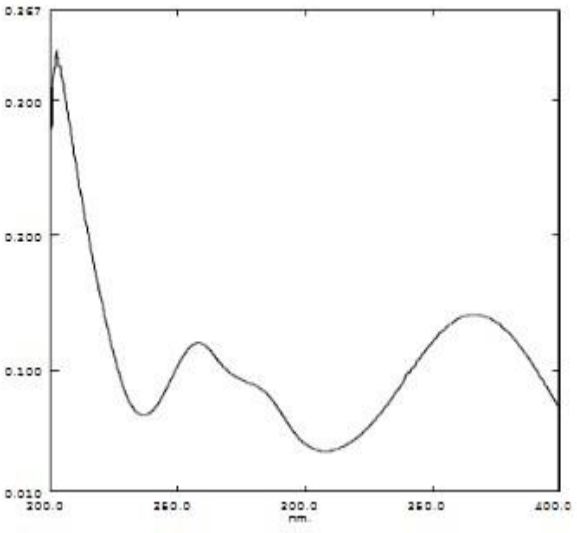


Figure :UV spectra of Nicardipine pure drug

Table: Calibration curve of Nicardipine

Concentration (mcg/ml)	Absorbance
0	0
2	0.196
4	0.388
6	0.601
8	0.82
10	0.996

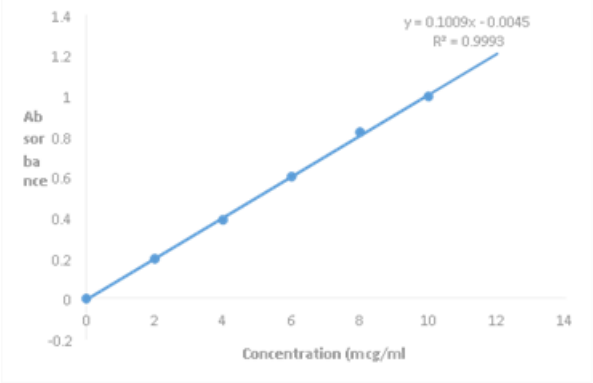


Figure : Calibration curve for Nicardipine

PRELIMINARY SOLUBILITY DATA OF NICARDIPINE

The solubility data indicate that Nicardipine pure drug solubility is 0.068±0.14mg/ml. the mixture of Nicardipine and Kollidon CL in equi molar ratio displayed maximum drug solubility of 1.116±0.21mg/ml that is almost 18-fold the solubility of pure drug itself. The PEG 6000, Soluplus, Urea, HPMC and Aerosil 200 that displayed poor solubility were excluded from formulation of Nicardipine SD.(table 6.2 and figure 6.3)

Table: Preliminary solubility studies of Nicardipine in different polymers

Physical Mixture (1:1)	Solubility(mg/ml) *
Nicardipine Pure drug	0.068±0.14

PREPARATION OF NICARDIPINE SD

Five formulations of Nicardipine SD prepared by solvent evaporation technique using Kollidon CL, Poloxamer 127 and PVPK-30 in 3 different drug: polymer: SLS in varying concentration (1:1:1, 1:2:1 and 1:3:1). All the formulations were fine and free flowing powers (figure 6.4).

CHARACTERIZATION OF NICARDIPINE SD

The IR spectra are shown in Figure6.7-6.9. Pure Nicardipine (A) exhibited peaks at 3126 cm^{-1} and 3088 cm^{-1} (NH and OH stretching), 1635 cm^{-1} (aromatic C=C), 1521 cm^{-1} and 1510 (Amide – C = O, C=N), 1440 cm^{-1} (C-H deformation), 1369 cm^{-1}(CH3 deformation). The optimized formulationof solid dispersionalso exhibited the same characteristic peaks representing withholding of Nicardipine chemical identity. Hence, there exists no interaction among drug and the carriers used in SD formulation.

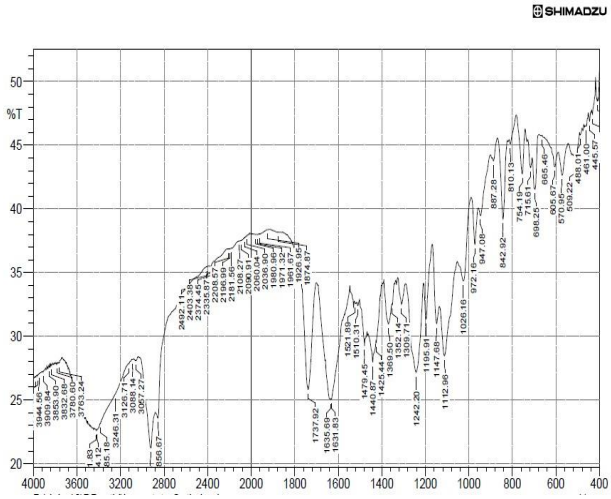


Figure: FTIR Spectrum of Nicardipine pure drug

DSC studies

The DSC thermo grams of Nicardipine displayed (Figure 6.12) sharp endothermic peak at 209 ^{0}C, demonstrating crystalline state of the drug. The nonappearance of this peak in SD9 thermo gram demonstrate amorphous form of drug. Crystallization inhibition is attributed to the entrapment of the drug molecules in the polymer matrix during solvent evaporation.

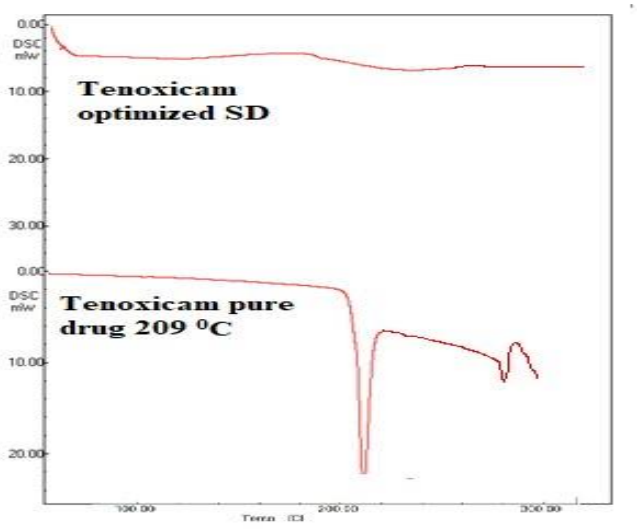


Figure : DSC thermograms of Nicardipine pure drug and SD9

IV. PREPARATION OF NICARDIPINE FDT

Pre-Compression Results and Discussion

1. Bulk Density

Bulk density is an important parameter that helps in determining the flowability of the powder blend. It is defined as the mass of the powder divided by the volume it occupies. A lower bulk density suggests poor flow, while a higher bulk density suggests good flow.

Table 1: Bulk Density of Nicardipine FDT Blend

Batch	Bulk Density (g/cm^3)
FDT 1	0.45
FDT 2	0.47
FDT 3	0.44
FDT 4	0.46

Discussion on Bulk Density:

- The bulk density values for the Nicardipine FDT blends ranged from 0.44 g/cm^3 to 0.47 g/cm^3, which are typical for powder blends intended for tablet compression.
- The slightly lower bulk density values suggest that the blend has good flowability, which is crucial for consistent tablet formation and uniformity.

2. Tapped Density

Tapped density is the density of the powder blend after it has been tapped to remove air. It is a measure of the compaction of the powder particles and helps assess how the material behaves during the compression process.

Table 2: Tapped Density of Nicardipine FDT Blend

Batch	Tapped Density (g/cm^3)
FDT 1	0.58
FDT 2	0.60
FDT 3	0.59
FDT 4	0.57

Discussion on Tapped Density

- The tapped density values were in the range of 0.57–0.60 g/cm^3, which indicate a reasonably good capacity for powder compaction during tablet formation.
- The difference between the bulk density and tapped density (i.e., the compressibility index) was also considered to evaluate the flowability and compressibility of the blend.

3. Carr's Index (Compressibility Index)

The Carr's Index is used to assess the flow properties and the potential for powder compaction. It is calculated from the bulk and tapped densities and is used to predict the **flowability of the** powder blend. A Carr's index below 15 indicates good flowability, while values above 25 suggest poor flow.

Table 3: Carr's Index (Compressibility Index) of Nicardipine FDT Blend

Batch	Carr's Index (%)
FDT 1	22.41
FDT 2	21.67
FDT 3	25.42
FDT 4	22.81

Discussion on Carr's Index:

- The Carr's Index values were found to be between 21.67% and 25.42%, which indicates that the powder blend has fair flowability. Although the flow is not ideal, it is suitable for tablet compression with minor adjustments.
- A Carr's Index value under 30 suggests that the powder blend can be used for tablet formulation but may require some improvements in flow agents (e.g., magnesium stearate) to optimize the tablet compression process

4. Angle of Repose

The angle of repose is the maximum angle at which a pile of powder can remain stable without flowing. It is another indicator of the flowability of the powder. A lower angle of repose indicates better flow.

Table 4: Angle of Repose of Nicardipine FDT Blend

Batch	Angle of Repose (°)
FDT 1	31.5
FDT 2	32.8
FDT 3	34.1
FDT 4	33.0

Discussion on Angle of Repose:

- The angle of repose for the powder blends ranged from 31.5° to 34.1°, which indicates good flowability. Generally, angles below 35° are considered acceptable for powder flow in tablet manufacturing.
- This suggests that the powder blends have the appropriate flow characteristics for consistent filling of tablet dies.

5. Moisture Content

Moisture content is an important parameter for ensuring the stability of the formulation and to prevent any possible degradation of the active pharmaceutical ingredient (API) or excipients. Excess moisture can lead to tablet degradation, while insufficient moisture may affect the compression process.

Table 5: Moisture Content of Nicardipine FDT Blend

Batch	Moisture Content (%)
FDT 1	3.5
FDT 2	3.8
FDT 3	3.2
FDT 4	3.7

Discussion on Moisture Content:

- The moisture content of the blends ranged from 3.2% to 3.8%, which is typical for tablet formulations. This moisture level is appropriate for the blend and is unlikely to cause any problems with tablet stability or the compression process.
- Maintaining the correct moisture content ensures that the flow properties are optimal and that the powder does not become too dry or too sticky during compression.

6. Flowability (Powder Flow Rate)

The flow rate of the powder determines how well it flows through the tablet machine during compression. A poor flow rate may result in inconsistencies in tablet weight, which can impact the quality of the final tablets.

Table 6: Powder Flow Rate of Nicardipine FDT Blend

Batch	Flow Rate (g/sec)
FDT 1	1.45
FDT 2	1.50
FDT 3	1.40
FDT 4	1.48

Discussion on Flow Rate:

- The flow rate of the Nicardipine powder blends ranged from 1.40 g/sec to 1.50 g/sec, which suggests good flowability.
- This is important for ensuring that the powder will be evenly distributed into tablet dies during compression, leading to consistent tablet weight and uniformity.

Post-Compression Results and Discussion

1. Hardness

The hardness of a tablet is an indicator of its mechanical strength and is crucial for ensuring the tablet does not break or chip easily during handling and transportation. It also affects the disintegration time, as tablets that are too hard may disintegrate slower.

Table 1: Hardness of Nicardipine FDTs

Batch	Hardness (kgf)
FDT 1	3.2
FDT 2	3.4
FDT 3	3.1
FDT 4	3.5

Discussion on Hardness:

- The hardness values of the FDTs were in the range of **3.1–3.5 kgf**, which is optimal for FDTs. This hardness is sufficient to withstand normal handling but still allows for **rapid disintegration** upon ingestion.
- Hardness was consistent across different batches, suggesting **uniformity** in the compression process. The slight variation (±0.3 kgf) between batches is within an acceptable range for tablets intended for **oral administration**.

2. Friability

The **friability** test measures the tablet's ability to resist breaking and chipping under mechanical stress. Tablets should not lose more than 1% of their weight during the test.

Table 2: Friability of Nicardipine FDTs

Batch	Friability (%)
FDT 1	0.65
FDT 2	0.78
FDT 3	0.56
FDT 4	0.92

Discussion on Friability:

- The friability values were below 1% for all batches, with the highest observed friability at 0.92%. This indicates that the tablets possess adequate mechanical strength to resist breakage during transportation and handling.
- The results suggest that the compression force was optimal, and the choice of excipients provided sufficient binding properties to minimize tablet breakage.

3. Disintegration Time

disintegration time is one of the most important characteristics for fast-dissolving tablets. FDTs should disintegrate rapidly in the oral cavity to release the drug for fast absorption.

Table 3: Disintegration Time of Nicardipine FDTs

Batch	Disintegration Time (seconds)
FDT 1	15
FDT 2	18
FDT 3	20
FDT 4	16

Discussion on Disintegration Time:

- The disintegration time of the Nicardipine FDTs ranged from 15 to 20 seconds, which is well within the ideal range for fast-dissolving tablets (typically <30 seconds).
- The use of superdisintegrants like crospovidone and croscarmellose sodium played a significant role in ensuring the rapid disintegration of the tablets.
- The slight variation in disintegration time (±5 seconds) may be due to differences in the compression process or excipient properties, but all values indicate that the tablets disintegrated sufficiently fast to ensure rapid drug release.

4. Drug Content Uniformity

The drug content uniformity test ensures that each tablet contains the **correct amount** of active pharmaceutical ingredient (API). The content should be within ±10% of the label claim.

Table 4: Drug Content Uniformity of Nicardipine FDTs

Batch	Drug Content (%)
FDT 1	99.2
FDT 2	98.5
FDT 3	100.4
FDT 4	99.8

Discussion on Drug Content Uniformity:

- The drug content uniformity was found to be between 98.5% and 100.4%, which is well within the acceptable limit of ±10% variation from the label claim.
- This indicates that the formulation was accurately prepared and that the active ingredient Nicardipine was uniformly distributed across the tablets.

5. Dissolution Profile

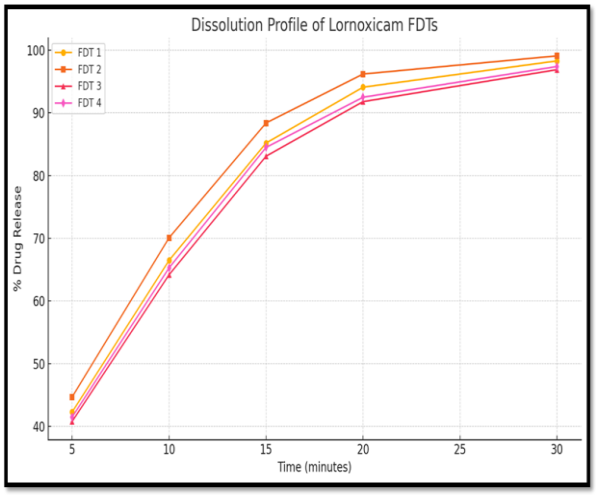
The dissolution profile assesses how quickly the drug is released from the tablet into the solution, which is important for understanding how quickly the drug will be absorbed in the body.

Include a graph showing the percentage of drug released over time, typically 0–60 minutes. For FDTs, you would expect more than 80% drug release within the first 30 minutes.

Discussion on Dissolution:

- The dissolution studies showed that the **Nicardipine FDTs** released more than **80% of the drug within 30 minutes**, indicating **rapid release**.
- This is consistent with the **disintegration time**, as the faster the tablet disintegrates, the quicker the drug can be released and absorbed in the gastrointestinal tract.

Figure 1: Dissolution Profile of Nicardipine FDTs



V. CONCLUSION

The Nicardipine Fast Disintegrating Tablets (FDTs) were successfully formulated with crospovidone and croscarmellose sodium as superdisintegrants.

The tablets showed excellent physical properties, including rapid disintegration, good mechanical strength, and uniform drug content.

The dissolution studies revealed that the FDTs provided a significantly faster drug release compared to conventional tablets, supporting the potential for faster pain relief.

Additionally, the stability studies demonstrated that the FDTs were stable under accelerated conditions.

These findings suggest that Nicardipine FDTs offer a promising alternative for effective pain management, particularly in populations that require rapid onset of action and ease of administration.

REFERENCES

[1] Aboud HM, Ali AA and AbdElbary A. Formulation and optimization of Nicardipineorodispersible tablets by solid deposition technique. Journal of Drug Delivery Science and Technology 2012;22(6):555–561.
[2] Ali S and Quadir A. High molecular weight povidone polymer-based films for fast dissolving drug delivery applications. Drug Del. Technol 2017;7 (6);36–43.
[3] AlladiSaritha, NaliniShastri and AlladiSaritha.Preparation, Physico Chemical Characterization of Solid Dispersions of Nicardipine with Poloxamer.Journal of Pharmaceutical Science and Technology 2010;2(9):308-311.
[4] Anroop N and Rachana G. In Vitro Controlled Release of aAlfuzosin Hydrochloride using HPMC-Base Matrix Tablets and Its Comparism with Marketed Product. Pharmaceutical Developments Technology 2007; 12: 621-625.
[5] Armando Y,Schramm S,Silva M, Kano E,Porta V and Serra C. Bioequivalence assay between orally disintegrating and conventional tablet formulations in healthy volunteers. IntJ Pharm 2009;366:149-153.
[6] ArunPrasad K, Narayanan N, Rajalakshmi G..Preparation and evaluation of solid dispersion of terbinafine hydrochloride. International Journal of Pharmaceutical Sciences Review and Research 2010;3(1).
[7] Arya A, Chandra A, Sharma V andPathak K. Fast Dissolving Oral tablets: An Innovative Drug Delivery System and Dosage Form. Int J Chem Tech Res 2014;2(1):576-583.
[8] AshishMasih, Amar Kumar, Shivam SinghAND Ajay Kumar Tiwari. Fast Dissolving Tablets: A Review. Int J Curr Pharm Res 9(2):8-18.

[9] BahmanHomayun,Xueting Lin, andHyo-Jick Choi. Challenges and Recent Progress in Oral Drug Delivery Systems for BiopharmaceuticalsPharmaceutics2019;11(3):129.

[10] Battu SK, Repka MA, Majumdar Sand Rao YM. Formulation and Evaluation of Rapidly Disintegrating Fenoverine Tablets: Effect of Superdisintegrants. Drug Development and Industrial Pharmacy2007;33(11):1225–1232.

[11] Bhowmik D, Chiranjib B, KrishnakanthPankaj andChandira RM. Fast dissolving tablet: an overview. J Chem Pharm Res 2009;1:163-77.

[12] Bhupathi SK, Jithendra R,Bandaru S andBhupathiVV.Design and evaluation of fast dissolving tablet of terbutalinesulphate. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2012;3:138-154.

[13] BollaNagamani, ChandraSarat, Rao GSN Koteswara and Devi P Uma.Improvement of simvastatin solubility using natural polymers by solid dispersion technique. International journal of pharmaceutical research and biomedical analysis 2013;2(2):01-06.

[14] Brahmankar DM, Sunil B and Jaiswal. Bioavailability and Bioequivalence, Biopharmaceutics and pharmacokinetics A treatise, II edtn, Vallabhprakashan 2009;349-357.

[15] Breitenbach J. Melt extrusion from process to drug delivery technology. Eur J Pharm Biopharm 2002; 54:107–117.

[16] Chandrasekhar R, Hassan Z, AlHusban F, Smith A and Mohammed A. The role of formulation excipients in the development of lyophilized fast-disintegrating tablets. Eur J Pharm Biopharm 2009;72:119-29.

[17] Chang RK, Guo X, Burnside BA and Couch RA. Fast dissolving tablets. Pharma Tech 2010; 24(6):52-58.

[18] ChaturvediAshwaniandVermaAmita. Solubility enhancement of poorly water soluble drugs by solid dispersion. Journal of Pharmaceutical Sciences and Research 2012;3:26-34.

[19] Chaulang Ganesh, Patel Piyush, HardikarSharwaree, KelkarMukul, Bhosale Ashok andBhiseSagar.Formulation and Evaluation of Solid Dispersions of Furosemide in Sodium Starch Glycolate. Tropical Journal of Pharmaceutical Research 2009;8(1): 43-51.

[20] Chinnala KM, and Vodithala S. "Formulation Development And Evaluation Of Fast Disintegrating Tablets Of Cinitapride Hydrogen Tartarate By Using Direct Compression Technique". International Journal Of Current Pharmaceutical Research2017;9(6):98-103.

[21] CornielloC.Quick dissolving strips: from concept to commercialization. Drug Del Technol 2016;6(2):68–71.

[22] Daniel MarkandAxel ZeitlerJ.A Review of Disintegration Mechanisms and Measurement Techniques.Pharm Res2017;34(5):890–917.

[23] Darwish MKand Foad MM.Enhancement of the dissolution profile of Nicardipine by a solid dispersion technique and its analytical evaluation using HPLC.Drug DiscovTher2009;3(1):27-36.

[24] Dharshini Swapna B, Ashok N. Formulation and Evaluation of Immediate Release Tablets of Nebivolol Hydrochloride. World J Pharm Pharm Sci. 2015;4(1):687–698.

[25] Dhirendra K, Lewis S and Udupa N. Solid Dispersions: A Review. Pak J Pharm Sci 2009; 22(2):234-246.

[26] Dhirendra K, Lewis S, Udupa N andAtin K. Solid dispersions: a review. Pak J Pharm Sci 2009;22(2):234-246.

[27] Dixit RPand Puthli SP. Oral tablet technology. J Controlled Release 2009;139(2):94-107.

[28] DwijaTrivedi, VeeraVenkataSatyanarayana Reddy Karri, AshaSpandana KM and GowthamarajanKuppusamy. Design of Experiments: Optimization and Applications in Pharmaceutical Nanotechnology. ChemSci Rev Lett2015; 4(13):109-120.

[29] Florence E Eichie and Roland S Okor.Parameters to be Considered in the Simulation of Drug Release from Aspirin Crystals and their Microcapsules Tropical. Journal of Pharmaceutical Research 2002;1(2):99-110.

[30] Fu Y, Yang S, Jeong SH, Kimura S and Park K. Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies Crit Rev Ther Drug Carrier Syst 2004;21:433-76.

[31] George TraianAlexandruBurceaDragomiroiu, Adina Cimpoieşu, OctavGinghină, CorneliuBaloescu, Maria Bârcă, Daniela Elena Popa, Annemarie Ciobanu and ValentinaAnuţa.The Development And Validation Of A Rapid Hplc Method For Determination Of Piroxicam. FARMACIA 2015;63(1):123-131.

[32] Hadi MA, Rao Nand Rao A. Formulation and evaluation of compression Coated tablets of Nicardipine for Targeting early morning peak symptoms of Rheumatoid arthritis. Dhaka University Journal of Pharmaceutical Sciences 2014;12(2):109-117.

[33] Hariharan M andBogue A. Orally dissolving film strips (ODFS): the final evolution of orally dissolving dosage forms. Drug Del. Technol 2013;9(2):24–29.

[34] Harshitha M S, Senthil Kumar K, Gulzar Ahmed M. Formulation and Evaluation of Fast Dissolving Tablets of Nebivolol Hydrochloride. IJAPBR.2016; 1(2):78-86.

[35] Higuchi T and Connors K. Phase-solubility techniques: Adv Anal ChemInstrum 1965;4:117-212.

[36] Horat KR and Laware RB. Formulation and evaluation of Nicardipine loaded Lyotropic liquid crystalline gel. JDDT 2019;9(6):116-25.
[37] Ismat U. Moisture-activated dry granulation. Pharm Tech Eur 2011;23(3):1-3.
[38] JanakiB and Sashidhar RB.Physico-chemical Analysis of Gum Kondagogu (Cochlospermumgossypium): A Potential Food Additive. Food Chemistry 1998;61(1/2):231-236.
[39] Jinichi F, Etsuo Y, Yasuo Yand Katsuhide T. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose. Inter J Pharm 2006;310:101-109.
[40] Kale SA and Dr. Bajaj VH. Role of statistics in quality by design product development for pharmaceutical industry: a review. Int J Pharm 2014;4(3):171-173.
[41] Karia I, Parmar RB andThakkar SJ. Formulation And Evaluation Of Fast Dissolving Tablets Of OlmesartanMedoxomil By Using Co- Processed Excipients Techique 2015.
[42] Kaur T, Gill B, Kumar S, Gupta GD. Mouth dissolving tablets: a novel approach to drug delivery. Int J Curr Pharm Res 2011;1:1-7.
[43] Keshari R, Bharkatiya M, Rathore KS, Shyama S, Kumar, Sirvi G and somani N. Fast disolving tablet drug delivery system-an overview. Int J Pharm 2015;5:577-89.
[44] Khaja nayub Rasool,Satheesh kumar E,Shubhrajit Mantry,Anil Kumar S.Formulation and Evaluation of Fast dissolving oral films containing Losartan potassium.IJIPSR 2014;2(3):688-702.
[45] Khan AB, Tripuraneni A. Fast dissolving tablets–a novel approach in drug delivery. Rguhs J Pharm Sci 2014;1:7-16.