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FORMULATION AND EVALUATION OF ORAL DISPERSIBLE TABLET OF AN ANTI-COAGULANT DRUG

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Abstract: Apixaban is a new-generation anticoagulant drug that selectively inhibits coagulation factors Xa. It is used in thromboprophylaxis in patients following knee replacement surgery. It comes under the BCS class III drug and its permeation is its rate-limiting step with low oral bioavailability of 50%. To get the maximum therapeutic effect the bioavailability of the drug needs to be enhanced. The main purpose of this work is to enhance the bioavailability of the drug by using superdisintegrants. Nine formulations were prepared by direct compression method using varying concentrations and combinations of superdisintegrants namely Sodium starch glycolate, Croscarmellose sodium, and Dehydrated banana powder. The other excipients like Lactose, Microcrystalline cellulose were used as diluents, Magnesium stearate and talc were used as glidants, Sodium saccharine was used as a sweetening agent, Sodium lauryl sulphate was used as a solubilizing agent. FTIR study has revealed that there is no interaction between drug and excipients. The pre-compression parameters like bulk density, tapped density, angle of repose, Hausner's ratio, and Carr's index were found to be within the pharmacopoeial limits. Post-compression parameters like hardness, thickness, wetting time, *Invitro* disintegration time, *In-vivo* dispersion time, drug content, and *Invitro* drug release studies were performed.

Keywords: Oral dispersible tablets, Anticoagulant, Apixaban, Superdisintegrants, Croscarmellose sodium, Sodium starch glycolate, Dehydrated banana powder, Direct compression, Bioavailability, *Invitro* dispersion time, *Invitro* % drug release.

Introduction: Amongst the various routes of delivery of the drug, the oral route is the most preferred route of drug delivery by patients. And amongst all the oral administration dosage forms the tablet is the most preferred one, because of its ease of administration, compactness, and flexibility in manufacturing. Because of these reasons many attempts have been made to develop oral solid dosage forms for safe, effective, and reproducible plasma concentration after the administration. The main problems associated with the oral dosage forms are difficulty in swallowing, resulting in non-compliance, and ineffective therapy especially in geriatric, paediatric, and traveling patients who may not have access to water and are most in the need of easy swallowing of tablets. Hence, to overcome these problems, a solid dosage form has been developed which can quickly disintegrate or dissolve when taken orally even without water. The dosage form when comes in contact with saliva disintegrates immediately, and disintegration usually takes place within 30-50 seconds after administration. In these formulations after the disintegration of the drug in the oral cavity, the drug solution can be absorbed partially or completely absorbed in the sublingual mucosal blood vessels, or be absorbed from the gastrointestinal tract. The absorption from the oral mucosal cavity and pre-gastric absorption bypasses the first-pass metabolism of the liver and the bioavailability of the drugs may be increased.[1-6]

Advantages of oral dispersible tablets:[7-9]

- No need for water to swallow the tablet.
- The bioavailability of the drug is increased as partially the drug is absorbed from the mouth, pharynx, and oesophagus saliva passing down into the stomach.
- Cost-effective.
- No need to chew.
- Allows high drug loading.
- Avoids first-pass metabolism and thus reduces dose and side effects.
- Rapid drug therapy intervention.
- Allows rapid administration.
- Dissolution and absorption of the drug are fast, offering quick onset of action.
- Suitable for motion sickness, sudden allergic actions, or cough that requires quick onset.
- Accurate dosing as compared to liquids.
- Oral dispersible tablets can be easily administered to pediatrics, elderly, and mentally disabled patients.
- Conventional manufacturing equipment.
- The risk of choking and suffocation caused by swallowing of the conventional tablet by the disabled person is avoided.

Disadvantages of oral dispersible tablets:[10-11]

- Several oral dispersible tablets are hygroscopic in nature and cannot maintain physical integrity under normal conditions.
- Bad taste of the drugs is difficult to formulate as an oral dispersible tablet; special precautions should be taken before the formulation of such drugs.
- Dryness of the mouth due to decreased saliva production may not be a good candidate for these tablets.

Selection of drug candidates for oral dispersible tablets:[12-14]

- The drugs that have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage form.
- The drugs that produce a significant amount of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pre-gastric GIT.
- Drugs having the ability to diffuse and partition into the epithelium of the upper GIT (log P > 1, or preferable > 2), and those able to permeate oral mucosal tissue are considered ideal for ODT formulation.
- Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs.
- Patients with Sjogren's syndrome or dryness of the mouth due to decreased saliva production may not be a good candidate for ODT formulation.
- Drugs which are having a short half-life and need frequent dosing, which is very bitter or either have unacceptable taste whose taste masking cannot be achieved or which require controlled or sustained release are inappropriate for ODT formulation.

Thrombosi:[15]

Thrombosis describes the formation of a clot within a blood vessel that reduces blood flow and may cause infarction of tissues supplied by that vessel. The most common forms of occlusive thrombosis occur in arteries and lead to myocardial infarction and stroke. Deep vein thrombosis (DVT) mostly occurs in the legs and is associated with pulmonary embolism (PE); collectively, these are termed venous thromboembolism (VTE)

Anticoagulants:[16-17]

Anticoagulants also called blood thinners are drugs that are used to treat and prevent blood clots. They interrupt the process involved in the formation of blood clots and work by targeting the clotting factors such as thrombin, fibrin, and vitamin K. Anticoagulants work by interfering with blood protein to lengthen the time

it takes to form a blood clot. Anticoagulants interfere with various clotting factors in the coagulation process to slow down the process.

Oral anticoagulants can be classified as follows:

1. Vitamin K antagonists: Inhibit the activation of the vitamin K-dependent clotting factors. The degree of depression of clotting factors is dose-dependent. The only vitamin K antagonist available in Hong Kong is warfarin.
2. Direct thrombin inhibitors (DTIs): Bind with thrombin which is the central effector of coagulation to inactivate thrombin. An example includes dabigatran etexilate.
3. Direct factor Xa inhibitors: Bind to clotting factor Xa specifically to block its activity. Examples include apixaban and rivaroxaban.

Table no 1: Formulation of oral dispersible tablet containing Apixaban

Ingredients	**Formulation**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Apixaban	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**
Lactose monohydrate	**89**	**89**	**89**	**89**	**89**	**89**	**89**	**89**	**89**
Microcrystalline cellulose	**57**	**57**	**57**	**57**	**57**	**57**	**57**	**57**	**57**
Sodium starch glycolate	**6.5**	**12.5**	**18.5**	**6.5**	**12.5**	**18.5**	**_**	**_**	**_**
Croscarmellose sodium	**18.5**	**12.5**	**6.5**	**_**	**_**	**_**	**6.5**	**12.5**	**18.5**
Banana powder	**_**	**_**	**_**	**18.5**	**12.5**	**6.5**	**18.5**	**12.5**	**6.5**
Magnesium stearate	**7**	**7**	**7**	**7**	**7**	**7**	**7**	**7**	**7**
Talc	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**
Sodium saccharine	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**
Sodium lauryl sulphate	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**

**** Total weight of each tablet is 200mg****

Evaluation of oral dispersible tablet

1. Precompression studies:

The flow properties of the powder blend (before compression) were characterized in terms of angle of repose, Carr's index and Hausner's ratio.

1.1 Angle of Repose (θ):[18]

The angle of repose (θ) is determined by the fixed funnel method. The height of the funnel has been adjusted in such a way that the tip of the funnel touches the top of the heap of the powder blend (Funnel was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above the powder surface). Allow the powder blend to flow freely to the surface through the funnel. The diameter & height of the powder cone was measured and angle of repose was calculated using the following equation,

$$\theta = tan^{-1} (h/r)$$

Where θ is the angle of repose, h is the height of cone in cm and r is the radius of the cone base in cm.

1.2 Bulk Density and Tapped Density:[19]

Bulk density is the ratio of total mass of powder to the bulk volume of powder. Tapped Density is the ratio of total mass of powder to the tapped volume of powder. It is expressed in gm/ml.

1.2.1 Bulk Density (ρb):

Bulk density was determined by pouring the powder blend into a graduated cylinder. Determine the bulk volume (Vb) and mass (m) of the powder blend. The bulk density was calculated by using the following formula,

Bulk density (ρb) = Mass of powder (m) / Bulk volume of powder (Vb)

1.2.2 Tapped Density (ρt):

The measuring cylinder containing known mass of powder blend was tapped 100 times for a fixed time. Measure the minimum volume occupied in the cylinder (Vt) and mass of the powder (m). The tapped density was measured by using the following formula,

Tapped density (ρt) = Mass of powder (m) / Tapped volume of powder (Vb)

1.2.3 Compressibility index [Carr's Index]:[20]

The compressibility index determines the flow property characteristics of powder blend. The percentage compressibility of powder blend is a direct measure of the potential powder arch and stability. The Carr's index can be calculated by the following formula,

% Carr's index = {(Tapped density – Bulk density) / Tapped density} x 100%

1.2.4 Hausner's Ratio:[21]

Hausner's ratio is used for the determination of flow properties of powder blend. The ratio can be calculated by the taking the ratio of tapped density to the ratio of bulk density.

Hausner's ratio = Tapped density / Bulk density

2. Method of Preparation – Direct Compression:[22]

Using superdisintegrants and the direct compression approach, ODTs of apixaban were prepared using the formula in table 3. The 5 mg of apixaban was prepared into 200 mg tablets. Lactose and MCC were used as diluents in each formulation. Prior to mixing, the required amount of apixaban and other excipients were carefully weighed and passed through a #40 mesh sieve. After being pulverised for 15 minutes, all the components were transfered to mortar in a geometric arrangement. The obtained powder mixture was further compacted into tablets using a Rotary tablet press with 12 stations by adding magnesium stearate and talc as a lubricant and glidant in the appropriate amounts.

3. Post-compression studies:

The prepared tablets were evaluated for post compression tests like weight variation, hardness, thickness, friability and drug content, wetting time, *In-vitro* disintegration time, *In-vitro* dispersion time and *In-vitro* dissolution studies.

3.1 Weight Variation:[23-24]

Twenty tablets were chosen at random and weighed one by one. Determine the tablet's average weight. To pass this test, none of the tablets of each formula deviated from the average weight by more or less than 7.5%. The average weight difference of the two tablets shall not exceed the specified percentage. The difference in any tablet should not exceed twice the percentage.

3.2 Hardness:[25]

Hardness or tablet crushing strength (the force required to break a tablet in a diametric compression) was measured using Pfizer tablet hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted. It is expressed in kg/cm2.

3.3 Tablet Thickness:[26]

Tablet thickness can be measured using a simple procedure. 5 tablets were randomly taken from each formulation and their thickness was measured using Vernier callipers and the average reading noted. The thickness is measured by placing the tablet between the two arms of a vernier calliper.

3.4 Friability:[27-28]

The friability test is used to assess how friction and impact affect tablets, which typically cause them to chip, cap, or break. For this, Roche friabilator was employed. The apparatus uses a spinning plastic chamber that rotates at 25 rpm to thoroughly abrade and shock tablets. The tablets move in 6 inch rotations. Understanding the tablet's mechanical strength is crucial when handling it.

10 pre-weighed pills should be placed in the friabilator, which should be turned 100 times. They powdered the tablets and weighed them once more. Compressed tablet weight reduction shouldn't be more than 1%.

The friability (F) is calculated by the following formula,

$$F = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

3.5 Wetting time:[29-31]

A tiny petridish filled with 6 ml of phosphate buffer pH 6.8 was placed with a piece of tissue paper folded twice. Place the pills in a petridish at room temperature and place the tissue paper on top with care. The wetting time is the length of time it takes for water to completely wet the top surface of the tablets. The measurement was carried out three times (n = three) to test for repeatability. A timer is used to measure the wetting period. The shorter the wetting time, the more porous the tablet becomes.

3.6 Water absorption ratio:[29-31]

The weight of the tablet before keeping in the petridish containing water was noted (W_b) using digital balance. The wetted tablet from the petridish was taken and reweighed (W_a) using the same. The water absorption ratio R, is determined by the following formula:

$$W = \frac{Wa - Wb}{Wb} \times 100$$

Where, W_a = weight of tablet after water absorption & W_b = weight of tablet before water absorption.

3.7 *Invitro* Disintegration time:[32-33]

The disintegration time for all the formulations was carried out using tablet disintegration test apparatus. Six tablets were placed individually in each tube of disintegration test apparatus, and the basket rack is positioned such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. The basket containing the tablets is moved up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated discs on each tablet. Phosphate buffer of pH 6.8 is used as disintegration medium and was maintained at a temperature of 37º±0.5ºC, and time taken for the entire tablet to disintegrate completely was noted. This method records the physiological state of the oral cavity and can be used as a screening tool for ODT product development.

According to the test, the tablet must disintegrate and all particles must pass through the 10-mesh screen in the time specified. If any residue remains, it must have a soft mass. If one or two tablets fail to disintegrate the test is repeated using 12 tablets.

3.8 *Invitro* Dispersion time:[34-35]

In vitro dispersion time of prepared tablet was done by dropping the tablet in 10 ml measuring cylinder containing 6 ml of phosphate buffer of pH 6.8 which is maintained at a temperature of 37º±0.5ºC. Three tablets from each formulation were randomly selected and time required for complete dispersion of tablet was measured.

3.9 Drug content :[36]

Ten tablets were randomly selected from each formulation and pulverized to a fine powder. Weighed aliquots containing an amount of powder equivalent to a single dose were taken and dissolved in 100ml of phosphate buffer of pH 6.8, filtered,and assayed for the drug content utilizing a UV-VIS Spectrophotometer at 280 nm.

Drug content was estimated by the formula,

$$\textbf{Drug content} = \frac{\textbf{Concentration} \times \textbf{Dilution factor}}{\textbf{1000}}$$

$$\%\ \textbf{Drug Content} = \frac{\textbf{Practical yield}}{\textbf{Theoretical yield}} \times \textbf{100}$$

3.10 *Invitro* dissolution studies:[36-37]

Invitro dissolution studies for all the formulated tablets of Apixaban was carried out using USP II paddle method at 50 rpm in 500 ml of 0.1N HCl solution as a dissolution medium. The dissolution medium was maintained at 37±0.50ºC.

5ml of the sample was taken at various time intervals. To maintain the consistent volume throughout the experiment, 5ml of buffer was replaced. The samples were properly diluted, and a UV-visible spectrophotometer was used to quantify the proportion of drug released from each formulation at 280 nm.

Result and discussion:

In this study, the nine formulations (F1-F9) were prepared using natural and synthetic superdisintegration in the combination and other excipients by direct compression method.

The pre-compression studies such as Standardization and calibration curve, FTIR, Melting point, Bulk density, tapped density, angle of repose, % Compressibility and Hausner's ratio were evaluated.

The Post-compression studies like Weight variation, Hardness, Friability, Thickness, wetting time, Water absorption ratio, *Invitro* disintegration time, *Invitro* dispersion time, *Invitro* drug release studies, Drug release kinetics study were determined for all the nine formulations F1-F9, and the formulation which was found to be the most satisfactory and was further subjected to stability study.

Calibration curve of Apixaban

Determination of absorption maxima (λmax)

The highest wavelength of the Apixaban sample was found at 280nm when it was scanned in a UV-visible spectrophotometer between 400nm and 200nm in a solution of 100µg/ml in solvent Dimethyl sulfoxide and diluted with pH 6.8 buffer.

Table 2: Data obtained for λmax of Apixaban

TRIAL	WAVELENGTH (nm)	ABSORBANCE
1.	280	0.895
2.	280	0.943
3.	280	0.912

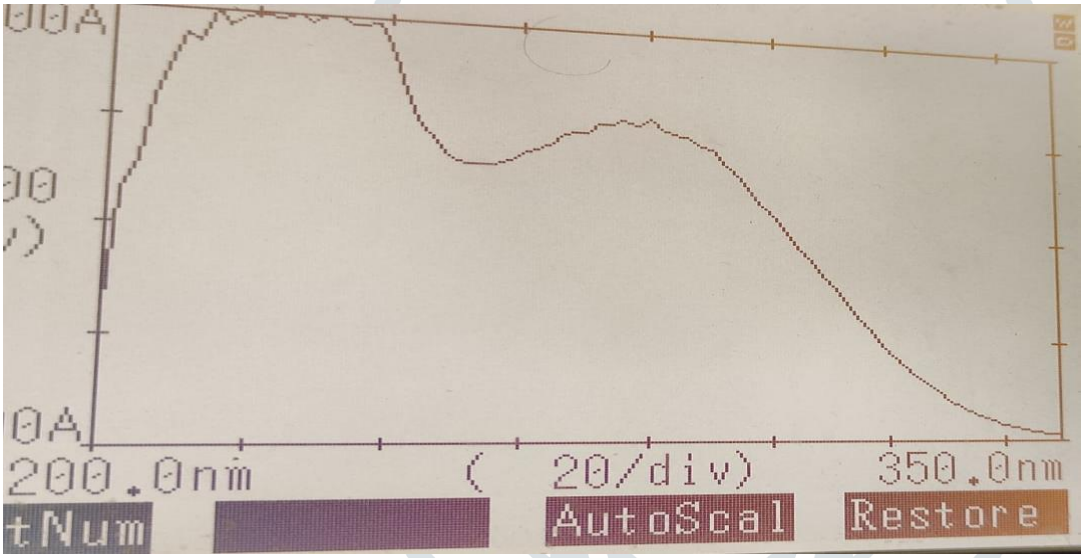


Figure no 1: UV-spectrum of Apixaban

Construction of calibration curve for Apixaban in phosphate buffer of pH 6.8:

When five solutions of different concentration 5, 10, 15, 20, 25 µg/ml of Apixaban were subjected to UV analysis at 280nm (λmax), the absorbance of each concentration was taken in UV spectrophotometer. The slope of the standard curve was found to be 0.0341 with the correlation (R^2) value of 0.9996.

Table no 3: Calibration curve data of Apixaban in phosphate buffer pH 6.8 at 280nm

S.NO	CONCENTRATION (µg/ml)	UV ABSORBANCE (Mean ± SD, n=3)
1.	0	0
2.	5	0.149±0.0036
3.	10	0.311±0.0355
4.	15	0.485333±0.0247
5.	20	0.667±0.0383
6.	25	0.866±0.0491

The data is presented in an average of mean ± SD, n=3

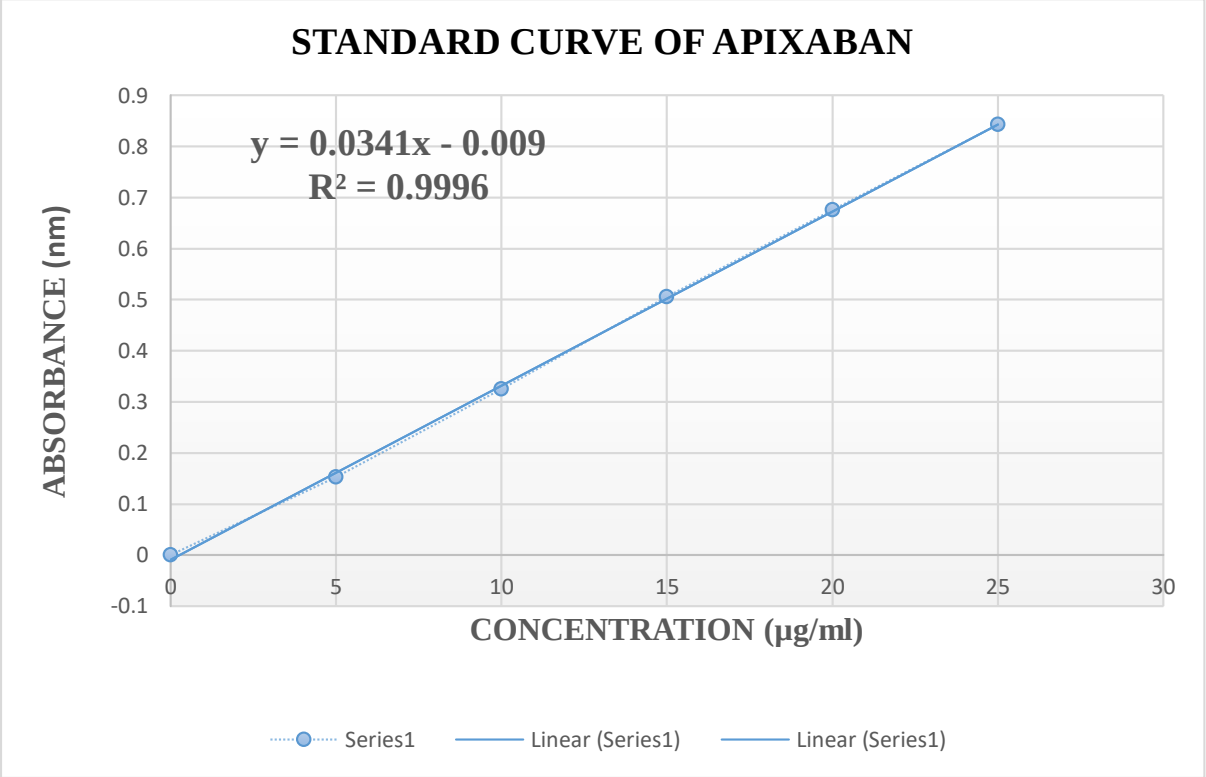


Figure no 2: Standard Calibration Curve of Apixaban

Melting Point of Apixaban:

The melting point of Apixaban was performed thrice using melting point apparatus and the average results are compared with the standard which is shown in Table.

Table no 4: Melting point of Apixaban

TRIAL	STANDARD MELTING POINT (ºC)	OBSERVED MELTING POINT (ºC)	AVERAGE MELTING POINT (ºC)
1.	235-240	237	238±1
2.		238	
3.		239	

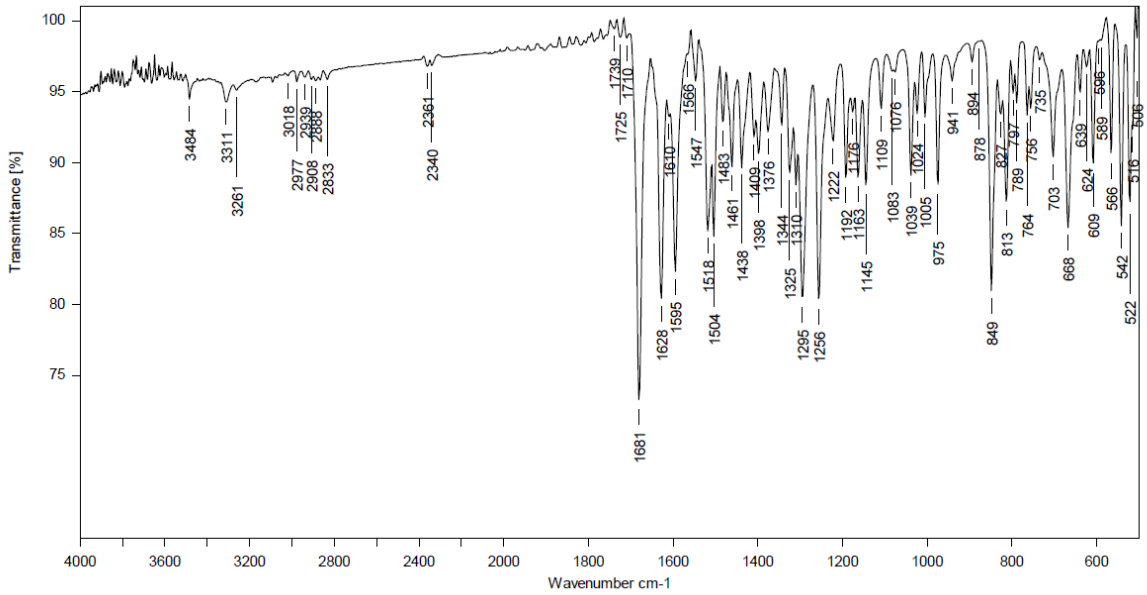


Figure no 3: IR BAND OF APIXABAN

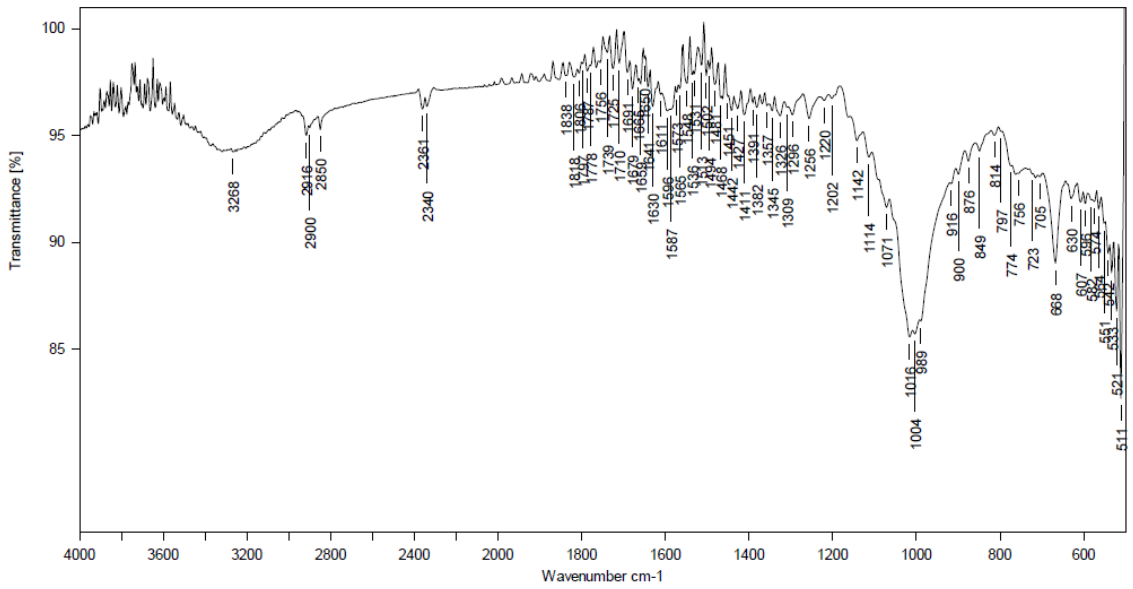


FIGURE 4: IR BAND OF MIXTURE 1 (Apixaban, Sodium starch glycolate, Croscarmellose sodium, Lactose monohydrate, Microcrystalline cellulose, Magnesium stearate, Talc, Sodium saccharine, Sodium lauryl sulphate)

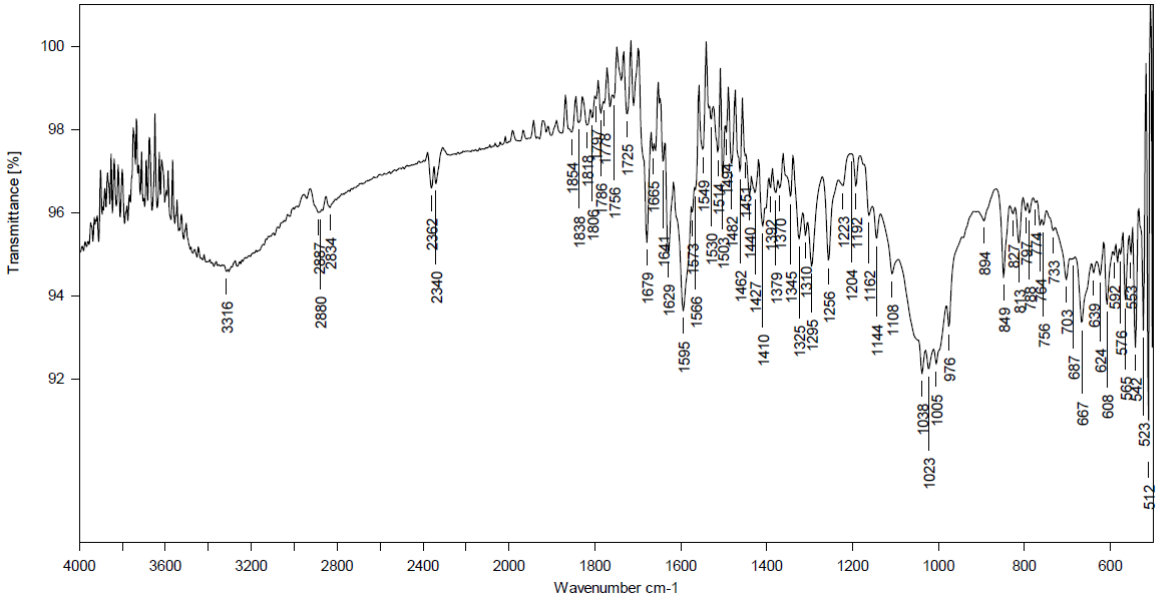


FIGURE 5: IR BAND OF MIXTURE 2 (Apixaban, Sodium starch glycolate, Banana powder, Lactose monohydrate, Microcrystalline cellulose, Magnesium stearate, Talc, Sodium saccharine, Sodium lauryl sulphate)

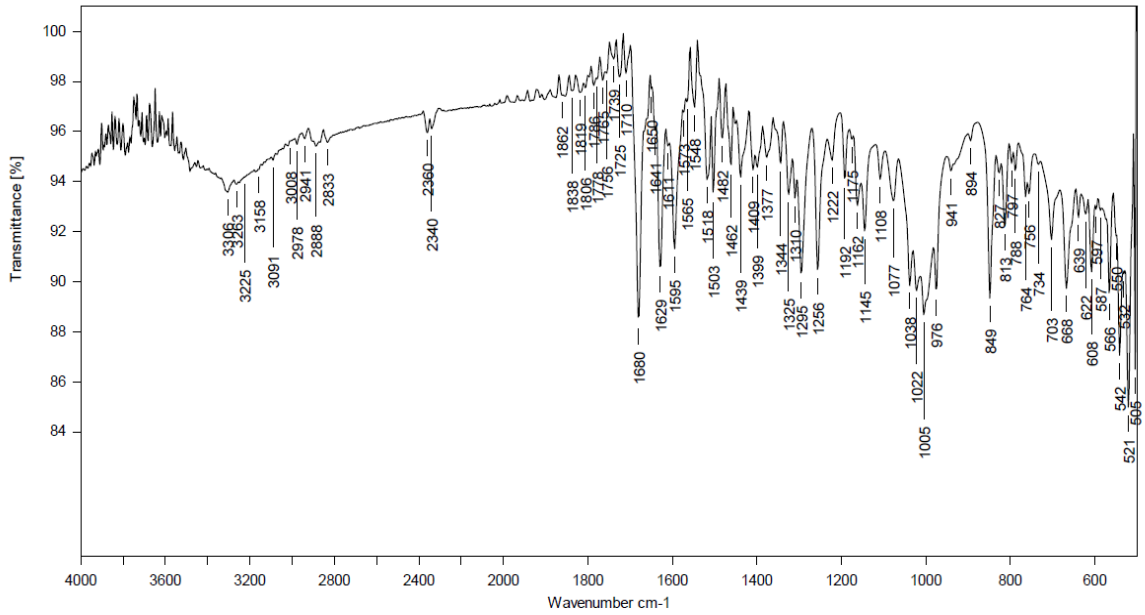


FIGURE 6: IR BAND OF MIXTURE 3 (Apixaban, Croscarmellose sodium, Banana powder, Lactose monohydrate, Microcrystalline cellulose, Magnesium stearate, Talc, Sodium saccharine, Sodium lauryl sulphate)

PRECOMPRESSION STUDIES:

Table no 5: Pre-compression study data of Formulation (F1 – F5)

PARAMETERS	**FORMULATION CODE**				
	F1	F2	F3	F4	F5
Angle of repose (Ɵ°)	25.96±0.493	25.26±0.251	25.366±0.351	19.123±0.798	19.513±0.373

Bulk density	0.454±0.079	0.356±0.033	0.496±0.025	0.7833±0.07	0.392±0.04
Tapped density	0.57±0.02	0.688±0.0899	0.47±0.0552	0.7613±0.064	0.357±0.0568
Compressibility	15.58±0.39	18.33±0.235	14.8±0.468	19.466±0.793	13.763±0.616
Hausner's ratio	1.466±0.187	1.78±0.288	1.165±0.18	1.5833±0.275	1.356±0.702

Table no 6: Pre-compression study data of Formulation (F6 – F9)

PARAMETERS	**FORMULATION CODE**			
	F6	F7	F8	F9
Angle of repose (Ɵ°)	18.886±0.12	25.5±0.331	24.5±0.42	25.26±0.25
Bulk density	0.4483±0.025	0.5283±0.029	0.334±0.039	0.302±0.0166
Tapped density	0.447±0.04	0.553±0.061	0.331±0.0293	0.38±0.0937
Compressibility	14.656±0.498	9.856±0.335	15.796±0.527	18.62±0.506
Hausner's ratio	1.44±0.225	1.141±0.182	1.216±0.138	1.256±0.155

POST-COMPRESSION STUDIES

Table no 7: Post-compression study data of Formulation (F1 – F9)

FORMULATION	**Weight Variation(mg) ± SD (n=20)**	**Thickness (mm) ± SD n=5**	**Friability (%) ± SD n=10**	**Hardness (kg/cm^2) ± SD (n=3)**
F1	209.076±1.98	0.503±0.023	0.144±0.048	3.933±0.07
F2	201.26±1.28	0.5066±0.0115	0.177±0.05	3.3±0.1414
F3	199.53±0.82	0.486±0.0057	0.1553±0.0185	3.2667±0.275
F4	199.2±1.734	0.5±0.026	0.069±0.018	4.6±0.141
F5	195.67±1.026	0.52±0.06	0.4366±0.284	4.203±0.42
F6	201.566±1.167	0.55±0.01	0.127±0.033	3.9±0.353
F7	205.466±0.665	0.543±0.0115	0.206±0.0273	3.4±0.282
F8	210.29±1.296	0.5166±0.032	0.124±0.0168	3.46±0.353
F9	201.46±0.65	0.51±0.02	0.265±0.168	3.7±0.282

Table no 8: Post-compression study data of Formulation (F1 – F9)

Formulation	**Wetting time (sec) ± SD**	**Water absorption ratio (%) ± SD**	***Invitro* Disintegration time (sec) ± SD**	***Invitro* Dispersion time (sec) ± SD**	**Drug Content (%) ± SD**

F1	33.33±0.577	92.62±0.421	25.9±0.173	35.5±0.51	86.276±0.254
F2	22.33±0.577	97.069±0.078	19.43±0.4	25.866±0.321	96.796±0.195
F3	25.667±0.577	95.076±0.688	28.56±0.513	37.46±0.45	93.711±0.117
F4	34.6±0.577	93.23±0.225	38.66±0.65	42.16±0.288	89.406±0.178
F5	23±1	94.36±0.55	25.36±0.321	35.166±0.2886	93.363±0.176
F6	22.33±0.57	98.4±0.2	38.25±0.229	40.2±0.264	90.613±0.256
F7	29.5±0.5	92.06±0.305	21.53±0.5	30.46±0.503	91.576±0.551
F8	29.8±0.72	93.69±0.115	24.433±0.2	36.23±0.251	90.89±0.435
F9	29±1	96.6±0.458	20.5±0.5	39.1±0.1	94.546±0.579

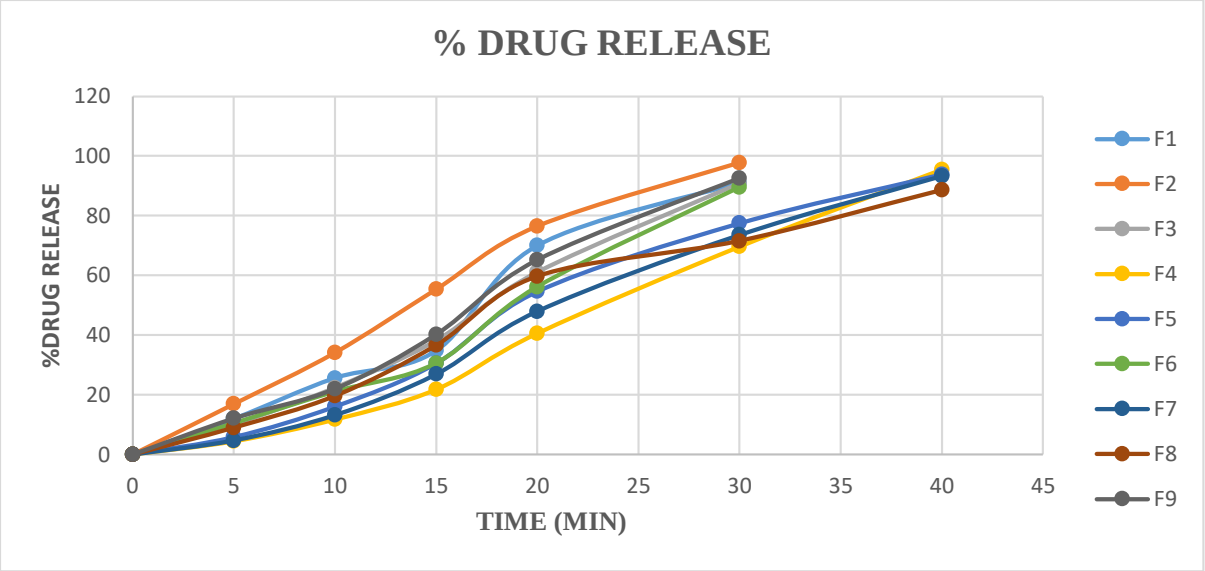
Table no 9: *Invitro* drug release data of Formulation (F1-F4)

TIME (MIN)	**% DRUG RELEASE ± SD**			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
5	11.98±0.5197	16.91±0.3332	10.11±0.5961	4.414±0.345
10	25.63±1.037	34.12±0.2948	22.42±0.195	11.71±0.6764
15	34.76±0.65	55.33±0.5663	38.21±0.57	21.77±0.606
20	69.98±1.6663	76.47±0.6061	61.12±0.2821	40.56±0.6835
30	91±0.7005	97.766±0.6735	90.846±0.2762	69.616±0.6206
40	-	-	-	95.41±0.4007

Table no 10: *Invitro* drug release data of Formulation (F5-F9)

TIME (MIN)	**% DRUG RELEASE ± SD**				
	F5	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0
5	5.821±0.7151	10.55±0.6724	4.71±0.378	9±0.173	12.09±0.11
10	16.05±0.177	21.1±0.67	13.22±0.391	19.64±0.448	22±0.494
15	30.51±0.8047	30.62±0.6184	26.91±0.459	36.6±0.436	40.23±0.38
20	54.66±0.5181	56.21±0.4314	47.97±0.321	59.69±0.376	65.21±0.543
30	77.473±0.5437	89.533±0.5701	73.54±0.395	71.54±0.33	92.633±0.338
40	93.87±0.7375	-	93.295±0.241	88.566±0.401	-

Figure no 7: Graph representing Percentage drug release of the Formulations (F1 – F9)



Melting point:

A melting point study of the Apixaban sample was done thrice and it was found to be 238°C which was within the normal range (235°C -240°C)

Baseline curve of Apixaban:

The wavelength maxima for the sample of Apixaban was found to be 280nm which was within the standard value. The obtained value confirmed the drug to be Apixaban as well as confirmed the λmax for further study of the sample.

Standard calibration curve of Apixaban:

Five different concentrations of 5, 10, 15, 20 and 25 µg/ml of Apixaban were prepared and the absorbance of each concentration was taken in a UV spectrophotometer at 280nm. The slope of the standard curve was found to be 0.0341 with a correlation coefficient (R2) value of 0.9996

FT-IR study:

All of the obtained spectra were analysed and contrasted to confirm the presence of the standard peaks. No evidence of a drug-excipient interaction was found, according to the interpretation report.

Pre-formulation studies

Angle of repose:

The results of angle of repose for all 9 formulations ranged between 18.886±0.12 to 25.96±0.493 which indicate excellent & good flow properties.

Bulk density and Tapped density:

The bulk density of all 9 formulations ranged from 0.302±0.0166 to 0.7833±0.07g/ml, and tapped density ranged from 0.331±0.0293 to 0.7613±0.064g/ml.

Compressibility and Hausner's ratio:

The compressibility index and Hausner's ratio for all the formulations ranged between 9.856±0.335 to 19.466±0.793 and 1.141±0.182 to 1.78±0.288 respectively which indicates good flow properties.

Post compression studies

Tablet thickness:

The thickness of the developed formulations ranged between 0.486±0.0057mm to 0.55±0.01mm.

Weight variation:

All the formulations were subjected to a weight variation test where all 9 formulations have shown weight from 195.67±1.026 mg to 209.076±1.98 mg. As the weight of tablets was 200 mg, and the acceptable weight variation range was between 185 mg and 215 mg (±7.5%), It was observed that all the 9 tablet formulations were within the pharmacopoeial limits.

Tablet hardness:

The hardness of all the 9 formulations developed varied from 3.2667±0.275 kg/cm^2 to 4.6±0.141 kg/cm^2.

Friability:

The loss in total weight of the tablets due to friability was in the range of 0.069±0.018% to 0.4366±0.284% in all the formulations and the friability value is less than 1% which meets the USP requirements and ensures that formulated tablets were mechanically stable.

Wetting Time:

The wetting time of the formulations was determined, and all the formulations (F1-F9) showed a wetting time of 22.33±0.577 to 34.6±0.577 seconds.

Water absorption ratio:

The water absorption ratio of all the formulations (F1-F9) was calculated using the equation, and all the formulations showed a good water absorption ratio from to 92.06±0.305 to 98.4±0.2%**.**

***Invitro* Disintegration time:**

In vitro disintegration time of formulations, F1 to F9 was determined, and all the formulations showed disintegration time of 19.43±0.4 to 38.66±0.65 .

***Invitro* Dispersion time:**

Invitro dispersion time of all the formulations of oral dispersible tablets (F1-F9) was determined and was found to be 30.46±0.503 to 42.16±0.288 seconds.

Drug content:

The drug content of prepared oral dispersible tablets was determined and was found to be in the range of 86.276±0.254% to 96.796±0.195.

***In-vitro* dissolution study:**

The % cumulative drug releases of Apixaban was done for 40 min for formulations F1 to F9 and the results were found to be in the range of 69.616±0.6206% to 97.766±0.6735% at 30 min. It shows that the percentage drug release of all the formulations was good, especially in the case of F2 containing 6.25% Sodium starch glycolate and 6.25% Croscarmellose sodium which gave %CDR of 97.766±0.6735% within 30 minutes, moreover, the wetting time of F2 was 22.33±0.577seconds and disintegration time was found to be 19.43±0.4 seconds, therefore, F2 was selected and proceeded towards further experiments.

Conclusion:

Apixaban fast-dissolving tablets were successfully formulated by the direct compression method. Nine such formulations were prepared by using different superdisintegrants and were subjected to evaluation parameters such as thickness, weight variation, hardness, friability, wetting time, uniformity of drug content, disintegration time, *in-vitro* dissolution study and stability study.

Even though all the formulations showed good results, Formulation F2 was identified as the best and ideal formulation based on wetting time, *In-vitro* disintegration time, *In-vitro* dispersion time and *In-vitro* % drug release.

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