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FORMULATION AND EVALUATION OF IMEGLIMIN HYDROCHLORIDE IMMEDIATE RELEASE TABLET

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ABSTRACT

Imeglimin hydrochloride, an oral drug that really oversees type 2 diabetes, brings down blood glucose levels. Among other overabundance impacts, it additionally supports mitochondrial DNA and movement while diminishing the making of responsive oxygen species (ROS). Imeglimin tablets with a quick delivery recipe are presently being created and tried frequently.

Tests finished with super-disintegrants like Croscarmellose sodium, and how much PVPK-30 was changed to additionally limit the breaking down time. Microcrystalline. The diluent in the definition preliminaries was cellulose, the folio was polyvinylpyrrolidone (K-30), and the Glidant was colloidal silicon dioxide.

Using the USP Device II (Paddle) at a temperature of 37°C ± 0.5°C at a speed of 50 rpm, concentrates on in vitro drug discharge were led. Hydrochloric corrosive 0.1N was utilized as the dissolving specialist. For preliminaries F1 and F6, the level of the drug given at different times was determined utilizing UV innovation. The review' discoveries exhibited that Preliminary F6 was the best detailing. Every estimation was inside the reach permitted by the Pharmacopoeial Details. Different tablet actual properties, including hardness, thickness, weight variety, friability, % drug content, and in vitro drug discharge, were scrutinized.

KEYWORDS: Type 2 diabetes, Wet granulation, In vitro dissolution, Disintegration, and Pre-formulation, Imeglimin hydrochloride.

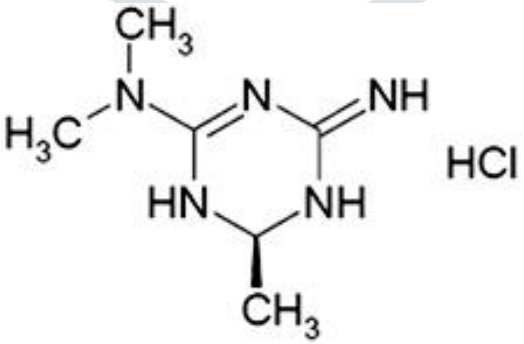
HIGHLIGHTS:

- Rapid therapeutic action of Imeglimin hydrochloride & Rapid on set of action.
- Introduce the effect of Imeglimin Hydrochloride Immediate Release Tablet for Type 2 diabetes (T2DM).
- Better option of drug to cure absolutely the type 2 diabetes.

ABBREVIATIONS

Cm	:	Centimeter
˚C	:	Degree centigrade
gm	:	Gram
IRL	:	Immediate release layer
Mm	:	Millimeter
Mg	:	Milligram
MCC	:	Micro-crystalline cellulose
Min	:	Minute
Ml	:	Milliliter
RPM	:	Revolution per minute
RH	:	Relative humidity
CCS	:	Croscarmellose Sodium
PVP K-30	:	Polyvinylpyrrolidone K-30
Sec	:	Seconds
t1/2	:	Half life
w/w	:	Weight by weight
w/v	:	Weight by volume
%	:	Percentage

QSAR/QSPR:



Chemical (CAS) Name:
(4R)-6-N,6-N,4-trimethyl-1,4-dihydro-1,3,5-triazine-2,6-diamine;hydrochloride

CAS Number: 775351-61-6

INTRODUCTION

Introduction on Imeglimin

Imeglimin, a major ingredient of the primary treatment in this novel class of oral anti-diabetic drugs known as "glimins," contains tetrahydrotriazine. Following a first in vivo phenotypic screen based on rodent anti-hyperglycemic effectiveness, it is produced by chemically changing a lead molecule. Figure 1 depicts the chemical composition that made identification simpler.

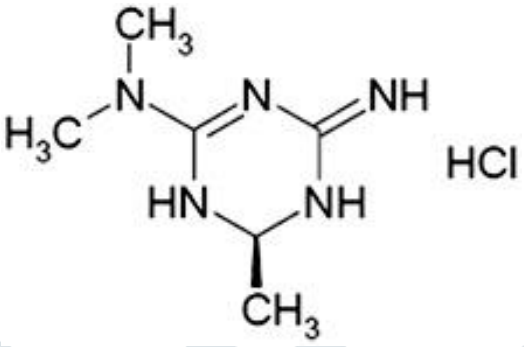


Figure 1 Imeglimin Hydrochloride

Imeglimin Hydrochloride, a member of the glimins class of drugs, is an original tetrahydrotriazine-containing oral anti-diabetic drug. Its molecular weight is 191.66 g/mol, and its organic name is (4R)-6-N,6-N,4-trimethyl-1,4,5-triazine-2,6-diamine hydrochloride. Imeglimin seems as a white, crystalline powder with a significant water solubility.

Imeglimin uses a different mode of action from other anti-hyperglycemic drugs, making it an avant-garde and first-in-class oral anti-diabetic medicine. It increases mitochondrial function and especially targets the bioener getics of mitochondria. Imeglimin controls the mitochondrial respiratory chain complex's functions while efficiently reducing the production of reactive oxygen species. By raising the quantity of insulin released in response to glucose and the responsiveness of the pancreatic beta cells, Imeglimin has been shown to normalise glucose tolerance in persons with type 2 diabetes. Additionally, it enhances insulin sensitivity in animal models of diabetes. According to a recent finding, Imeglimin is known to prevent the opening of the mitochondrial permeability transition pore, a known factor contributing to cell death, without affecting mitochondrial respiration. The study's findings

RATIONALE

Imeglimin can treat the three main pathophysiologic elements that cause type 2 diabetes: a slowing of beta-cell senescence, an increase in hepatic gluconeogenesis, and a decrease in muscle glucose uptake. It lowers haemoglobin A1c and fasting plasma glucose just as effectively as metformin and Sitagliptin.

Imeglimin is a therapy option for type 2 diabetes when diet and exercise alone are inadequate. Enhancing insulin activity is one of its odd and varied modes of action. It successfully lowers hepatic glucose creation while enhancing insulin signaling in the skeletal muscle and liver. Imeglimin also protects beta-cell mass and increases glucose-stimulated insulin secretion (GSIS). Imeglimin Hydrochloride is an effective diabetes medication because it particularly addresses mitochondrial bioenergetics. Additionally, Imeglimin Hydrochloride carries a low risk of hypoglycemia.

Despite the fact that there are other anti-diabetic medications accessible, Imeglimin hydrochloride seems to be a viable treatment for diabetes patients. It offers more safety, more power, and better tolerability than competing options.

Imeglimin hydrochloride was shown in clinical tests to dramatically lower HbA1c levels when compared to a placebo while maintaining a similar safety profile. Imeglimin showed a respectable level of safety and acceptability when administered as a stand-alone medication.

Introduction on Immediate Release Tablet:

Conventional oral medication conveyance procedures, which have been utilized from now onward, indefinitely seemingly forever to treat intense and ongoing sicknesses, utilize a wide assortment of portion structures, including tablets, containers, pills, powders, arrangements, emulsions, suspensions, and vapor sprayers. These conventional definitions keep on being vital to the drug business. The circulatory system focus, then again, bit by bit ascends to a remedial level when a medication is taken as recommended, stays there for some time, and afterward at last tumbles to a sub-restorative level, delivering the solution pharmacologically inert.

Advantage of the tablet dosage form

- They feature a unit dosage form, variable lease content, and good dose accuracy..
- Oral dosage forms have the lowest cost.
- The least expensive and simplest items to package and strip; smaller, lighter, and easier to swallow.
- The coating process helps mask pungent odours and sharp tastes.
- Suitable for mass production.

Advantages of Immediate Release Drug Delivery System

- Increased adherence
- Improved stability and bioavailability
- Fit for controlled-release substances.
- Be able to offer liquid medicinal advantages in the form of a solid mixture; • Permit substantial medication loading; able can be adapted to be compatible with current processing and packaging equipment.
- More affordable
- Enhanced solubility of medicinal formulations

MATERIAL AND METHODS

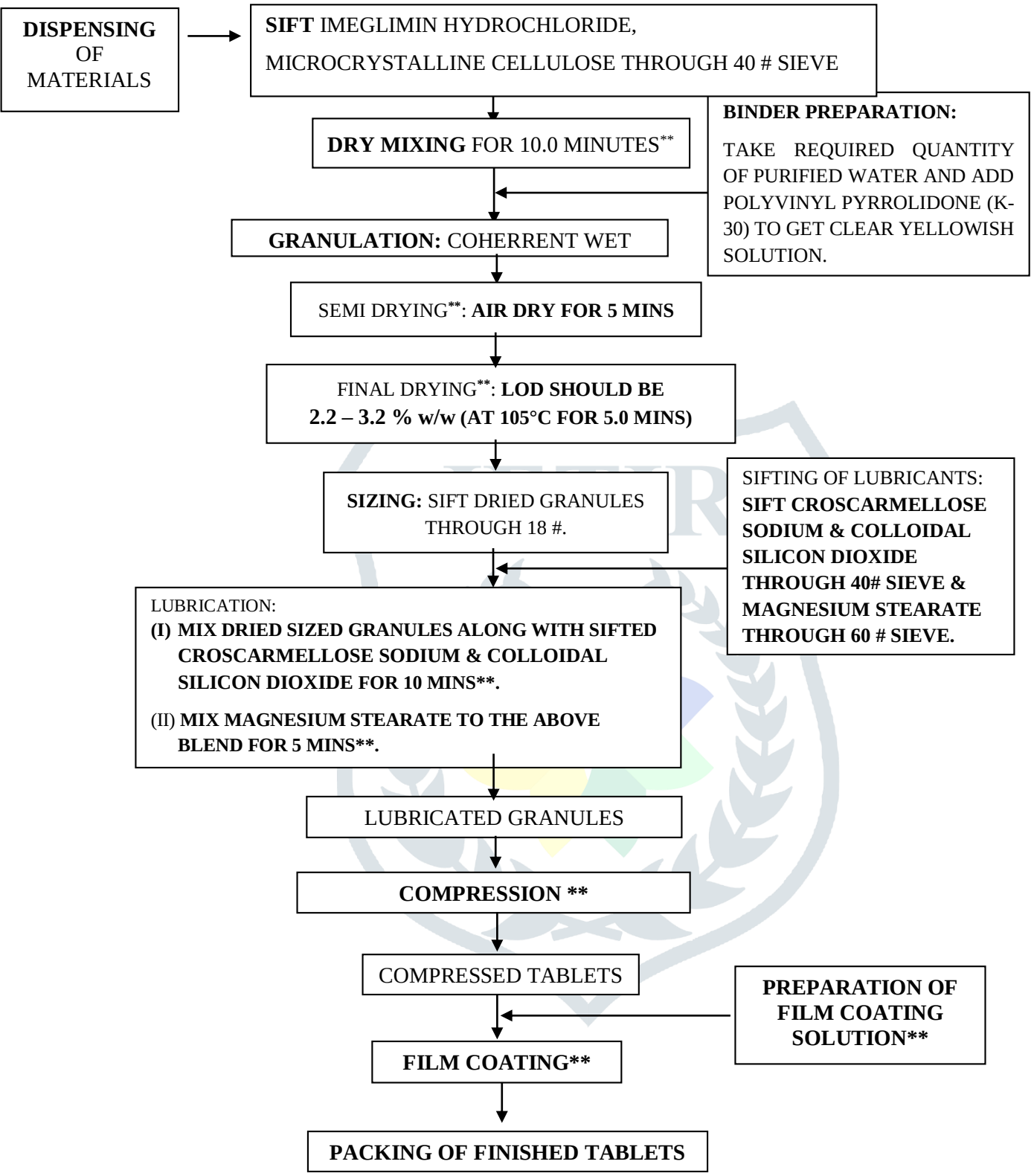
TABLE 1: LIST OF MATERIALS

S. No.	Ingredients	Company Name (from where material received)
1.	Imeglimin Hydrochloride	Windlas Biotech Ltd.
2.	Microcrystalline Cellulose	Windlas Biotech Ltd.
3.	Polyvinyl Pyrrolidone (K-30)	Windlas Biotech Ltd.
4.	Croscarmellose Sodium	Windlas Biotech Ltd.
5.	Colloidal Silicon Dioxide	Windlas Biotech Ltd.
6.	Magnesium Stearate	Windlas Biotech Ltd.
7.	H.P.M.C.	Windlas Biotech Ltd.
8.	PEG - 400	Windlas Biotech Ltd.
9.	Titanium Dioxide	Windlas Biotech Ltd.
10.	Purified Talc	Windlas Biotech Ltd.

TABLE 2: LIST OF EQUIPMENTS

Sr. No.	Machinery / Equipment
1.	Platform weighing balance (Digital)
2.	Multi Mill
3.	Vibro Sifter
4.	Double Cone Blender
5.	Compression Machine
6.	Hardness tester
7.	Weighing Balance
8.	Vernier Calipers Digital
9.	Disintegration Apparatus
10.	Friability Testing Apparatus
11.	Halogen Moisture Analyzer
12.	Rapid Mixer Granulator
13.	Tray Dryer
14.	Stirrer

Manufacturing Process Flow Chart



**** Critical process parameters.**

Manufacturing Process

Aim: To take a trial batch of Imeglimin Hydrochloride Tablets by wet granulation method.

Name of Product : Imeglimin Hydrochloride Tablets 500 mg

Description : White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.

Composition : Each film coated tablet contains:
Imeglimin Hydrochloride…….500 mg
Colour: Titanium Dioxide IP

Batch size : 100 Tablets

***Formula*:**
Table no. 10 Working Formula F1

BILL OF RAW MATERIALS

Sr. No.	Ingredients	Grade	Rational of use	Qty. / Tabs. [mg.]
1.	Imeglimin Hydrochloride	IH	API	500.00
2.	Microcrystalline Cellulose	IP	Diluent	85.50
3.	Polyvinyl Pyrrolidone (K-30)	IP	Binder	17.50
4.	Purified Water	IP	Binder vehicle	q.s.[@]
5.	Croscarmellose Sodium	IP	Disintegrant	12.50
6.	Colloidal Silicon Dioxide	IP	Glidant	5.00
7.	Magnesium Stearate	IP	Lubricant	9.50
	Total Weight			**630.00 mg**

[@] Not to be found in original product.

BILL OF FILM COATING MATERIALS

Sr. No.	Ingredients	Grade	Rational of use	Qty. / Tabs. [mg.]
1.	H.P.M.C (E-5)	IP	Film Forming material	9.02*
2.	P.E.G - 400	IP	Plasticizer	2.15*
3.	Titanium Dioxide	IP	Opacifier	2.86*
4.	Purified Talc	IP	Film Smoothening agent	0.28*
5.	Purified Water	IP	Coating Solvent	q.s.[@]

@Not to be found in original product.
*Include 10.0 % extra to compensate for film coating process loss.

Steps involved in the Working Formula (F1*) by Wet Granulation Method:

Sr. No.	Operation
1.0	**SIFTING:**
1.1	Check the intactness of sieve before & after use.
1.2	Sift Imeglimin Hydrochloride** and Microcrystalline Cellulose** through 40# sieve using a mechanical sifter. Collect it properly.
2.0	**BINDER PREPARATION:**
2.1	Dissolve Polyvinyl Pyrrolidone (K-30)** in Purified water** with continuous stirring for 5.0 minutes or until get a clear solution.
3.0	**GRANULATION:**
3.1	**DRY MIXING:** Transfer the sifted materials of step 1.2 to the RMG [Imeglimin Hydrochloride, Microcrystalline Cellulose]. Cover the mixer & run it for 10 minutes at slow impeller speed [for blend homogeneity] with chopper off.
3.2	**Addition of Binder solution:** Add the binder solution of step no. 2.1 steadily in RMG containing dry mix material. Rinse the binder vessel with Purified water**. Mix at slow impeller speed for 2 minutes. Then switch off the mixer & turn the mass manually with the help of scoops. Mix further for 2 minute at slow impeller speed with chopper ON (slow speed).
4.0	**SEMI DRYING:**
4.1	Transfer the wet granules of step no. 3.2 in Try dryer. Air-dry for 5 minutes.
4.2	**SIZING:** Pass the semi-dried mass of step no.4.1, through multi-mill using 6.0 mm perforated S.S. screen, knives forward direction at medium speed.
4.3	**FINAL DRYING:** Transfer the semidried sized granules of step 4.2 in Try dryer. Then dry the granules at 50 ± 5 °C.
4.4	**LOD DETERMINATION:** Check the Loss on drying (LOD) of granules at 105°C for 5.0 minutes, LOD should come in between 2.2 – 3.2 %. LOD should be checked by Halogen Moisture Analyzer.
4.5	Check the granules for proper drying & dry further if required. Note & record the Total time taken for drying when drying is complete.
4.6	Check the intactness of sieve before & after use.
4.7	Pass the dried granules of step no. 4.5 through 18 # S.S sieve sifted on a sifter.
4.8	If required pass the above 18 # over size granule through the multi-mill using 1.5mm S.S screen knives forward direction.
4.9	Re-dry if required & sift through 18 #.
4.10	Note down the weight of dried granules; store in polyethylene bag.
5.0	**LUBRICATION:**
5.1	Check the intactness of sieve before use.
5.2	Sift Croscarmellose Sodium** & Colloidal Silicon Dioxide** through 40 # sieve using a mechanical sifter.
5.3	Sift Magnesium Stearate** through 60 # sieve using a mechanical sifter.
5.4	Transfer the dried sized granules of step no. 4.10 & sifted material of step no. 5.2 to a blender. Mix for 10.0 minutes.
5.5	Add sifted Magnesium Stearate of step no. 5.3 to blend of step no. 5.4 in Blender and mix further for 5.0 minutes.
5.6	Collect the lubricated blend in polyethylene bags & keep tightly closed with proper labeling until taken for compression. Record wt. of the batch.

6.0 COMPRESSION OF TABLET

Type of punch: 'D' Tooling, _____ station.

6.1 Punch Description **16.0 mm X 8.0 mm**, capsule shape, standard concave
Upper Punch Break-line
Lower Punch Plain

6.2 Check the complete rotation of the turret by turning the wheel by hand followed by electric operation. Feed the granules and set the machine as per following specifications. Check tablet from one complete rotation.

6.3 Set RPM of Machine.

*Ensure that each die and punch set is clean and free from any defect.

****The amount of API and excipients should be taken as per Formula F1.**

TABLE. 3 IN PROCESS COMPRESSION PARAMETERS:

SR. NO.	PARAMETERS OBSERVED	LIMITS	FREQUENCY OF OBSERVATION
1.	Description	White to off white colored, elongated, biconvex, uncoated tablet, scored on one side & Plain on other side.	At the beginning of compression & throughout during process.
2.	Average Weight of tablets	630.00 mg ± 3.0%	Every 30 Minutes
3.	Group weight of 20 Tablets	12.600 gm ± 3.0%	Every 30 Minutes
4.	Uniformity of Tablet weight	630.0 mg ± 5.0%	Every 2 Hrs.
5.	Thickness	5.60 mm ± 0.30 mm	Every 30 Minutes
6.	Hardness	NLT 8.0 Kgf	Every 30 Minutes
7.	Disintegration Time:	NMT 15.0 minutes	Every 2 Hrs.
8.	Friability	NMT 1% w/w	Every 2 Hrs.
9.	Length	16.0 mm ± 0.20 mm	Every 2 Hrs.
	Width	8.0 mm ± 0.20 mm	

7.0 Record the yield & store the tablets in container (s) with lined polyethylene bags.

8.0 Before taking tablets for film coating, de-dust & Inspect the tablets for chipped, broken, spotted appearance. Segregate the rejection as reusable and to be destroyed, separately & note down the weights accordingly & store the tablets in polyethylene bag.

TABLE. 8 PROCESS SHEET (FILM COATING OF TABLET)

SR. NO.	OPERATION
10.0	**PREPARATION OF FILM COATING SUSPENSION:**
10.1	Disperse H.P.M.C (E-5)** by sprinkling in Purified Water**, under constant mechanical stirring for 10.0 minutes, to get a whitish colored solution.
10.2	Add P.E.G 400** to step no. 10.1, under constant mechanical stirring.
10.3	Sift Titanium Dioxide** and Purified Talc** through 100 #.
10.4	Prepare slurry of step no. 10.3 with Purified Water**.
10.5	Pass the final prepared coating suspension (step no. 10.4) through Colloidal mill by '0' Adjustment gap for 10.0 minutes and add to above coating suspension into step no. 10.1.
10.6	Stir for 40-45 minutes to get suspension homogeneity.
10.7	Filter the coating suspension through pot sieve of 200 # & weigh.
10.8	**FILM COATING:**
10.9	Load the de-dusted & inspected uncoated tablets into a clean, dry coating pan and dry for 10 minutes at 0.5 rpm at 40°C - 50°C [Bed Temperature].
10.10	**Check the below mentioned film coating parameters:** **Auto-coater** Batch size is 100 Tablets. (As per formula F1) a) Pan Rpm: Initially 1 rpm and gradually increase upto 5 rpm. b) Pump rpm: 30 - 45 rpm c) Tablet bed to gun distance: 16 cm d) Inlet Air temperature: 50°C to 55°C e) Bed temperature: 30°C to 40°C f) Outlet Air temperature: 35°C to 40°C g) Atom air gauze: 2.0 kg/ cm^2 h) Fan air gauze: 2.0 kgs/cm^2 i) No. of guns: 1 Nos. j) Spray Gun Aperture size: 1.5 mm k) Coating Silicon Tube: 5mm ID/8mm OD l) Spray rate (gm/min): 45 to 70 gm/min m) Average weight of uncoated tablets: 630.00 mg (To be calculated based on average weight of the uncoated 500 tablets) n) Target Average weight of film coated tablets:643.00mg (To be calculated based on average weight of the film coated 500 tablets)
10.11	Switch on exhaust & apply the film coating suspension to the tablets using a clean spray gun assembly. (Ensure elegance) continue stirring of coating suspension during coating of tablet.
10.12	Dry the film coated tablets sufficiently after proper weight build up. (Approx.2.06%) Target average weight of film coated tablets = 643.00 mg.

****The amount of API and excipients should be taken as per Formula F1.**

TABLE. 4 FILM COATED TABLETS PARAMETERS:

SR. NO.	PARAMETERS OBSERVED	LIMITS
1.	Description	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.
2.	Average Weight of tablets	643.0 mg ± 3.0 %
3.	Group weight of 20 Tablets	12.86 gm ± 3.0 %
4.	Uniformity of Tablet weight	643.0 mg ± 5.0 %
5.	Thickness	5.70 mm ± 0.30 mm
6.	Disintegration Time	NMT 30.0 Minutes
7.	Length	16.10 mm ± 0.20 mm
8.	Width	8.10 mm ± 0.20 mm

11.0 Collect all the film-coated tablets in container or polyethylene bags.

12.0 Check and record net weight of the batch.

Formulation design for Wet Granulation/Trial 1 to Trial 5

Trial 1 Aim: Take a trial batch comparable to F1 in with increasing concentration of CCS. [F2$^{\$}$]

Trial 2 Aim: Take a trial batch comparable to F1 by adding more MCC and Magnesium Stearate as extra granular portion. [F3$^{\$}$]

Trial 3 Aim: Take a trial batch comparable to F2 by adding more Purified Water. [F4$^{\$}$]

Trial 4 Aim: Take a trial batch comparable to F1 in with increasing concentration of H.P.M.C (E-5) in coating stage. [F5$^{\$}$]

Trial 5 Aim: Take a trial batch comparable to F1 in with decreasing concentration of PVP K-30. [F6$^{\$}$]

Table 5: Formulation of immediate release tablet / Formulation design for Wet Granulation

Sr. No.	Ingredients	Grade	Qty. /Tabs [mg] F2$^{\$}$	Qty. /Tabs [mg] F3$^{\$}$	Qty. /Tabs [mg] F4$^{\$}$	Qty. /Tabs [mg] F5$^{\$}$	Qty. /Tabs [mg] F6$^{\$}$
1.	Imeglimin Hydrochloride	IH	500.00	500.00	500.00	500.00	500.00
2.	Microcrystalline Cellulose	IP	85.50	86.50	85.50	85.50	85.50
3.	Polyvinyl Pyrrolidone (K-30)	IP	17.50	15.50	17.00	17.50	15.00
4.	Purified Water	IP	q.s.$^{@}$	q.s.$^{@}$	q.s.$^{@}$	q.s.$^{@}$	q.s.$^{@}$
5.	Croscarmellose Sodium	IP	13.50	12.50	13.00	12.50	13.00
6.	Colloidal Silicon Dioxide	IP	4.00	5.00	5.00	5.00	6.00
7.	Magnesium Stearate	IP	9.50	10.50	9.50	9.50	10.50
8.	H.P.M.C (E-5)	IP	9.02*	9.02*	9.02*	10.05*	9.02*
9.	P.E.G - 400	IP	2.15*	2.15*	2.15*	1.10*	2.15*
10.	Titanium Dioxide	IP	2.86*	2.86*	2.86*	2.86*	2.86*
11.	Purified Talc	IP	0.28*	0.28*	0.28*	0.28*	0.28*
12.	Purified Water	IP	q.s.$^{@}$	q.s.$^{@}$	q.s.$^{@}$	q.s.$^{@}$	q.s.$^{@}$

@Not to be found in original product.

*Include 10.0 % extra to compensate for film coating process loss.

$^{\$}$Detailed Manufacturing Procedure followed and performed for all formulas given in above table by <u>Working Formula (F1).</u>

"Finally the Working Formula F1 considered as Final Formula because it full fill the complete requirements. And the final tablet manufactured by that formula found satisfactory".

IMAGES OF TABLETS AFTER FINAL COMPRESSION AND COATING:

Figure 2 Y-Axis of Coated Tablet

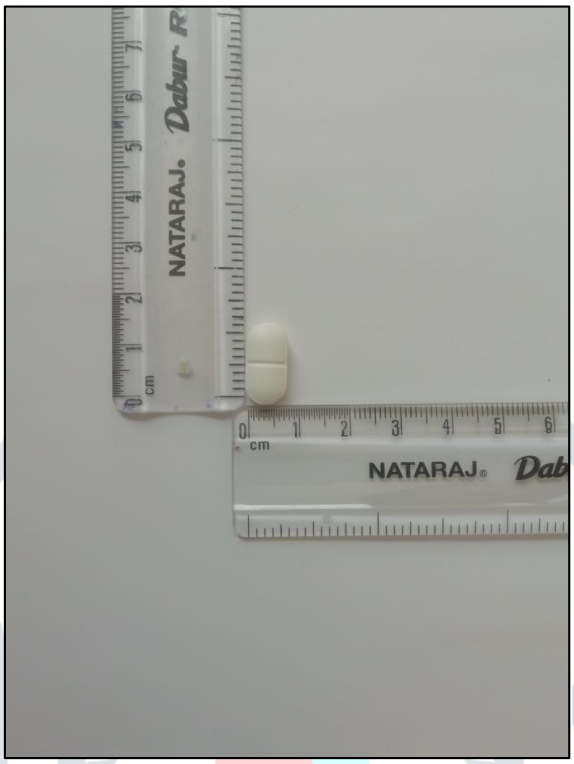
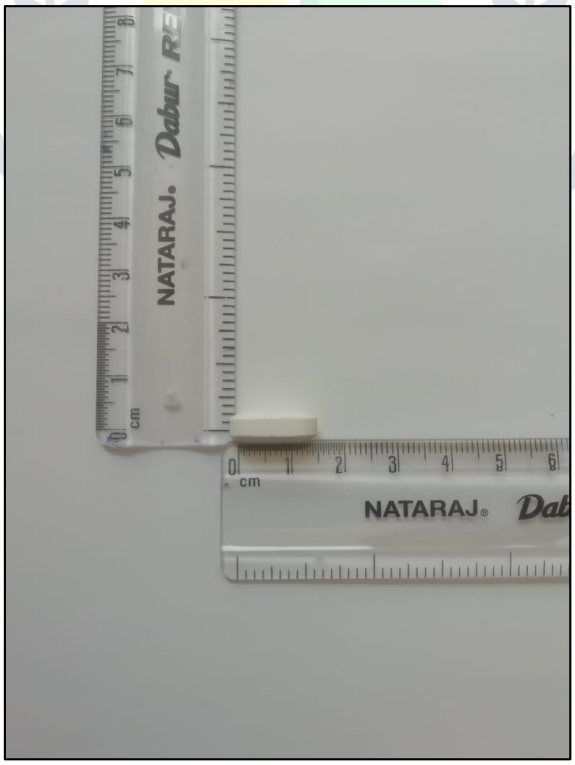


Figure 3 X-Axis of Coated Tablet



RESULTS

Final results of formulation are concluded in this section. Results of observation parameters for film-coated tablet are enclosed in this section.

Following parameters are evaluated for film-coated tablet:

- Description
- Length
- Width
- Thickness
- Disintegration time
- Average weight
- Uniformity of weight
- Weight variation
- Hardness
- Friability
- Dissolution Studies
- Stability Studies

Table 6: FINAL EVALUATION PARAMETERS OF FILM COATED TABLETS:

SR. NO.	TESTS	LIMITS	F1 RESULTS	F2 RESULTS	F3 RESULTS	F4 RESULTS	F5 RESULTS	F6 RESULTS
1.	Description	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.
2.	Average Weight of tablets	643.0 mg ± 3.0 %	643.81	643.99	642.88	645.08	644.78	642.20
3.	Uniformity of Tablet weight	643.0 mg ± 5.0 %	636.74-648.35	636.84-648.16	636.47-648.06	636.22-648.47	636.01-648.98	636.44-648.46
4.	Thickness	5.70 mm ± 0.30 mm	5.71-5.80	5.74-5.78	5.71-5.73	5.69-5.74	5.72-5.76	5.72-5.78
5.	Disintegration Time	NMT 30.0 Minutes	12-13 min	11-13 min	12-14 min	11-14 min	12-14 min	12-13 min
6.	Length	16.10 mm ± 0.20 mm	16.14-16.19	16.16-16.22	16.11-16.15	16.12-16.18	16.16-16.21	16.18-16.21
7.	Width	8.10 mm ± 0.20 mm	8.16-8.22	8.13-8.17	8.12-8.21	8.11-8.18	8.13-8.21	8.15-8.18
8.	Dissolution	Not less than 75 %	Min: 97 % Max: 102 % Avg.: 100 %	Min: 99% Max: 103 % Avg.: 101%	Min: 99 % Max: 102 % Avg.: 100 %	Min: 97 % Max: 101 % Avg.: 100 %	Min: 98 % Max: 103 % Avg.: 100 %	Min: 98 % Max: 101 % Avg.: 100 %
9.	% Drug content	90.0 % to 110.0 %	100.2 %	100.5 %	99.4 %	199.9 %	99.8 %	99.8%

IN-VITRO DISSOLUTION STUDY:

Dissolution Condition:

Dissolution in 0.1 N HCI (Official Media)

Dissolution Media	0.1 N hydrochloric acid
Apparatus	Paddle (USP-II)
Volume	900 ml
Temperature	Temperature 37°C ± 0.5°C
Rotation Speed	50 rpm
Time Point	10, 15, 20, 30, 45, 60 and 90 minutes
Units	12 Tablets

Dissolution in pH 4.5 Acetate Buffer:

Dissolution Media	pH 4. 5 Acetate Buffer
Apparatus	Paddle(USP-II)
Volume	900 ml
Temperature	37°C ± 0.5°C
Rotation Speed	50 rpm
Time Point	10, 15, 20, 30, 45, 60 and 90 minutes
Units	12 Tablets

Dissolution in pH 6.8 Phosphate (Potassium Dihydrogen Phosphate) Buffer:

Dissolution Media	pH 6.8 Phosphate (Potassium Dihydrogen Phosphate) Buffer
Apparatus	Paddle(USP-II)
Volume	900 ml
Temperature	37°C ± 0.5°C
Rotation Speed	50 rpm
Time Point	10, 15, 20, 30, 45, 60 and 90 minutes
Units	12 Tablets

Preparation of Dissolution Medium:

TABLE RESULTS OF F6 IN DIFFERENT DISSOLUTION MEDIUM:

Imeglimin Hydrochloride Tablets 500 mg Dissolution result for (n=l 2)

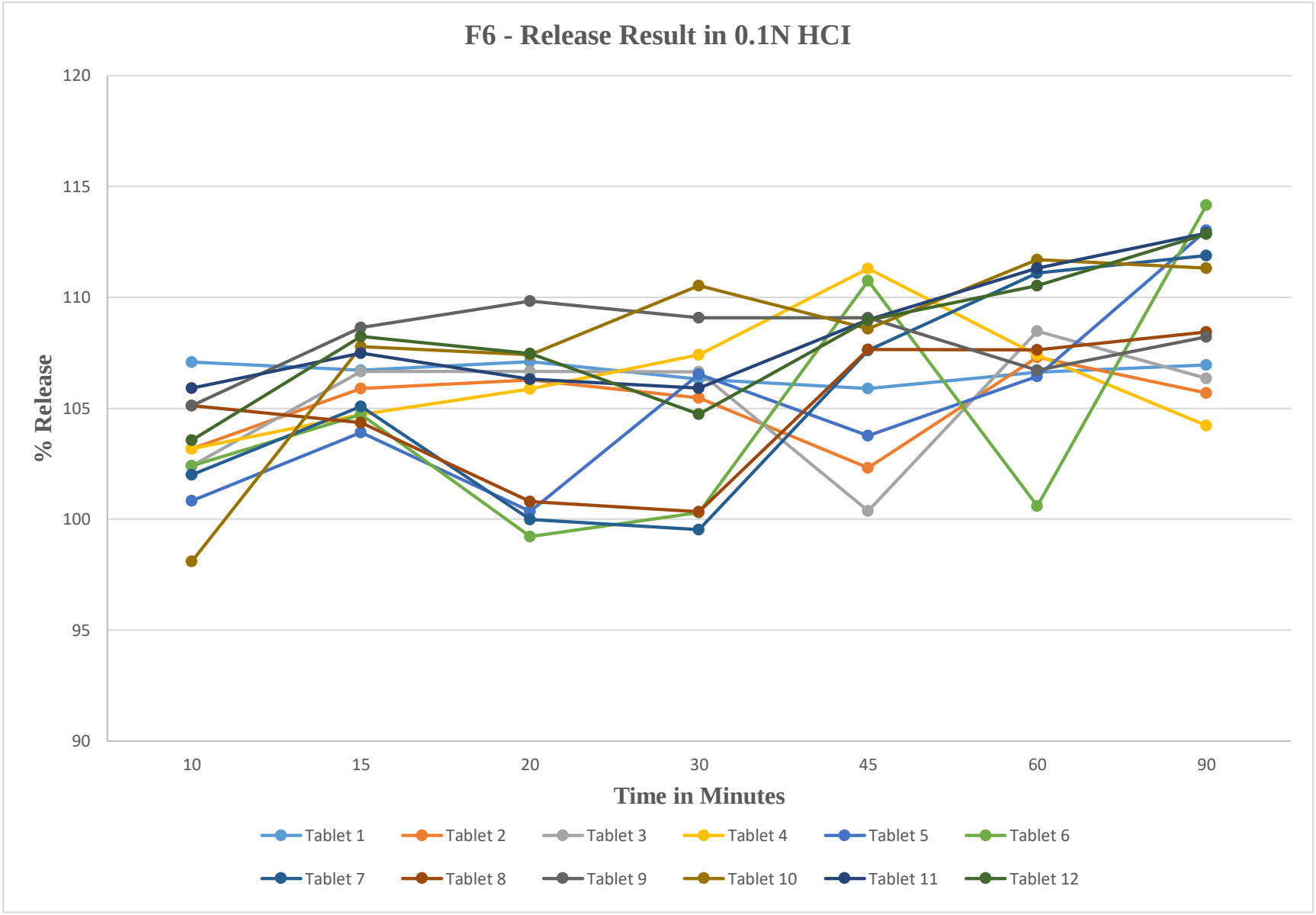
i) Release Result in 0.1N HCI

Product Name: Imeglimin Hydrochloride Tablets 500 mg

Batch: F6

No. of Tablets	10 Minutes	15 Minutes	20 Minutes	30 Minutes	45 Minutes	60 Minutes	90 Minutes
1	107.09	106.71	107.10	106.31	105.89	106.63	106.96
2	103.18	105.89	106.27	105.47	102.31	107.3	105 .69
3	102.40	106.66	106.66	106.65	100.37	108.47	106.36
4	103.18	104.72	105.87	107.41	111.30	107.40	104.23
5	100.83	103:91	100.36	106.53	103.77	106.44	113.03
6	102.4	104.71	99.21	100.29	110.75	100.59	114.16
7	102.01	105.09	99.99	99.52	107.62	111.11	111.89
8	105.13	104.35	100.80	100.33	107.66	107.64	108.44
9	105.13	108.65	109.84	109.08	109.08	106.72	108.23
10	98.10	107.79	107.41	110.53	108.59	111.70	111.32
11	105.91	107.48	106.32	105.91	109.00	111.33	112.90
12	103.57	108.24	107.47	104.73	108.98	110.53	112.87
Mean	103.24	106.18	104.77	105.23	107.11	107.98	109.45
Minimum	98.10	103.91	99.21	99.52	100.37	100.59	103.36
Maximum	107.09	108.65	109.84	110.53	111.30	111.70	114.16
% RSD	2.418	1.629	3.615	3.494	3.379	3.058	3.749

FIGURE 4: F6 - Release Result in 0.1N HCI



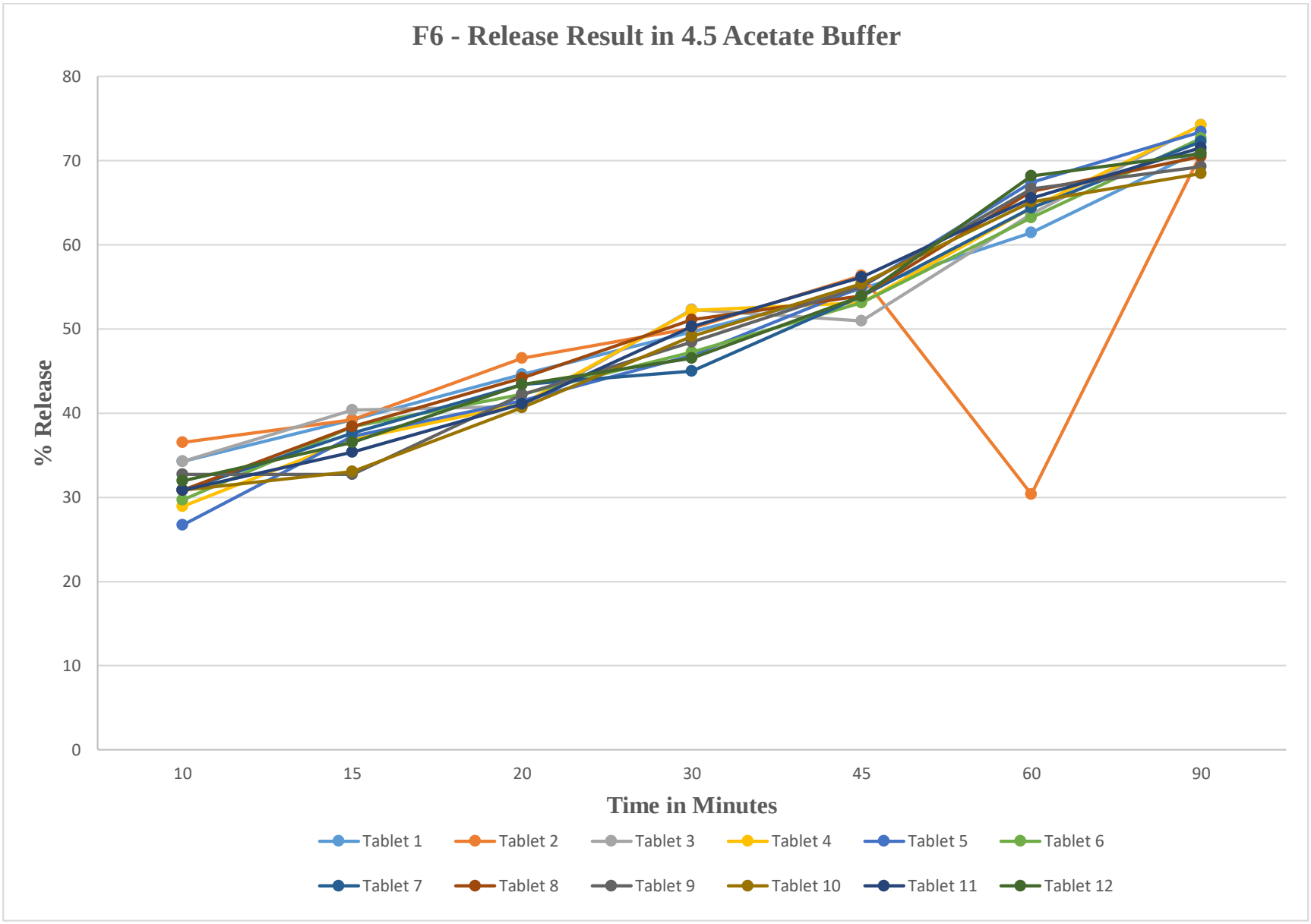
ii) Release Result in 4.5 Acetate Buffer

Product Name: Imeglimin Hydrochloride Tablets 500 mg

Batch: F6

No. of Tablets	10 Minutes	15 Minutes	20 Minutes	30 Minutes	45 Minutes	60 Minutes	90 Minutes
1	34.26	39.21	44.59	49.64	54.75	61.43	71.22
2	36.54	39.23	46.52	50.07	56.32	30.35	70.89
3	34.26	40.35	40.79	52.28	50.94	63.67	74.25
4	28.93	36.86	41.08	52.19	53.13	64.36	74.19
5	26.69	37.25	41.47	46.87	54.99	67 .39	73.44
6	29.69	38.40	42.24	47.27	53.12	63.20	72.64
7	30.83	37.65	43.39	45.01	53.87	64.35	72.27
8	30.83	38.41	44.16	51.12	53.95	66.34	70.47
9	32.74	32.72	42.22	48.44	55.04	66.64	69.26
10	30.83	33.08	40.68	49.11	55.36	65.09	68.45
11	30.83	35.36	41.08	50.29	56.16	65.52	71.55
12	31.97	36.52	43.39	46.53	53.89	68.17	70.81
Mean	31.78	37.08	42.63	49.09	54.29	64.70	71.62
Minimum	28.93	32.72	40.68	45.01	50.94	63.35	68.45
Maximum	36.54	40.35	46.52	52.28	56.32	68.17	74.25
% RSD	7.12	6.4	1.812	2.299	1.488	2.33	1.823

FIGURE 5: F6 - Release Result in 4.5 Acetate Buffer



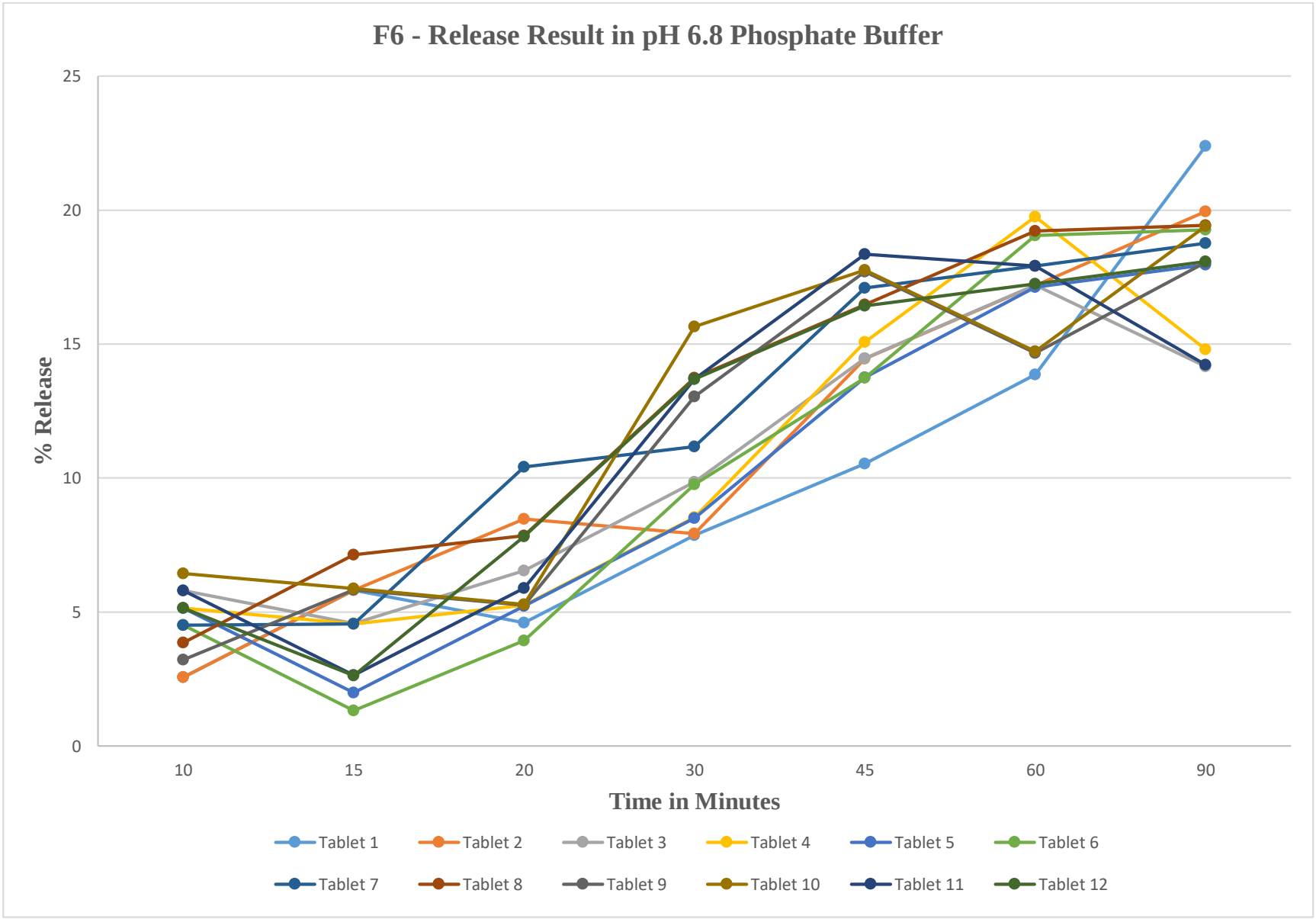
iii) Release Result in pH 6.8 Phosphate Buffer

Product Name: Imeglimin Hydrochloride Tablets 500 mg

Batch: F6

No. of Tablets	10 Minutes	15 Minutes	20 Minutes	30 Minutes	45 Minutes	60 Minutes	90 Minutes
1	2.57	5.82	4.60	7.87	10.54	13.87	22.40
2	2.57	5.82	8.47	7.92	14.45	17.18	19.95
3	5.80	4.57	6.55	9.85	14.47	17.20	14. 17
4	5.15	4.56	5.26	8.54	15.08	19.75	14.81
5	5.15	1.99	5.23	8.51	13.76	17.13	17.96
6	4.51	1.33	3.93	9.77	13.74	19.05	19.26
7	4.51	4.56	10.41	11.17	17.09	17.92	18.76
8	3.86	7.13	7.85	13.74	16.47	19.22	19.43
9	3.22	5.83	5.25	13.04	17.70	14.67	18.05
10	6.44	5.87	5.29	15 .66	17.76	14.73	19.40
11	5.8	2.64	5.89	13.69	18.35	17.91	14.23
12	5.15	2.63	7.82	13.70	16.43	17.25	18.08
Mean	4.56	4.39	6.37	11.12	15.48	17.15	18.04
Minimum	2.57	1.33	3.93	7.87	10.54	13.87	14.17
Maximum	6.44	7.13	10.41	15.66	18.35	19.75	22.40
% RSD	27.93	41.89	29.67	24.56	14.50	10.92	2.49

FIGURE 06: F6 - Release Result in pH 6.8 Phosphate Buffer



Stability Studies:

Table 7: Stability data

SR. NO.	TESTS	LIMITS	1 month	2 month	3 month
1.	Description	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.	White colored, elongated, biconvex, film coated tablet, scored on one side & Plain on other side.
2.	Hardness	NLT 8.0 Kgf	8.6	8.2	9.1
3.	Friability	NMT 1% w/w	0.01	0.03	0.01
4.	Disintegration Time	NMT 30.0 Minutes	12-13 min	11-12 min	12-14 min
5.	Dissolution	Not less than 75 %	Min: 99 % Max: 101 % Avg.: 100 %	Min: 98% Max: 103 % Ave: 101%	Min: 99 % Max: 101 % Ava: 100 %
6.	% Drug content	90.0 % to 110.0 %	99.1 %	100.2 %	99.8 %

For three months, the formulation was kept at 40°C and 75% RH as a part of an experiment into the short-term stability of the film-coated tablets. The stability research results showed no significant changes in any of the physical characteristics, drug content, or in vitro drug release rate.

DISCUSSIONS

In the continuous audit, Imeglimin hydrochloride second release pills were made and evaluated. Considering the dissolving profile examination of various plans, the best specifying, F6, was made freely and used to make the last tablet.

A stable Imeglimin hydrochloride prompt delivery tablet that can keep up with consistent restorative levels of the medication was the objective of the ongoing examination. Wet granulation was utilized to make the fast delivery tablet, which was produced with super-disintegrants like Croscarmellose sodium and polymers like H.P.M.C (E-5) and P.E.G - 400.

By including super-disintegrants like Croscarmellose sodium and changing the amount PVP K-30, I had the choice to truncate the time that our definition took to disintegrate in a couple of assessments. The arrangement focuses on used Microcrystalline Cellulose, Polyvinyl Pyrrolidone (K-30), and colloidal silicon dioxide as diluents, clasp, and Glidant.

The prescription release rate was insufficient when the powerful medication fixing (Programming connection point) was added directly to the definition, which provoked the development of movie covered rapid conveyance tablets.

Imeglimin hydrochloride pills can be isolated with 0.1N hydrochloric destructive. The results showed that 0.1N HCl is a preferable dissolvable over various solvents for Imeglimin hydrochloride. Right when a 0.1N hydrochloric destructive plan was used, the absorbance furthest reaches of Imeglimin hydrochloride was seen as at 245 nm.

By including super-disintegrants like Croscarmellose sodium and changing the amount PVP K-30, we had the choice to curtail the time that our definition brought to separate in a couple of preliminaries. The arrangement focuses on used Microcrystalline Cellulose, Polyvinyl Pyrrolidone (K-30), and colloidal silicon dioxide as diluents, clasp, and Glidant.

The prescription release rate was inadequate with regards to when the unique medication fixing (Programming connection point) was added directly to the specifying, which provoked the development of movie covered quick conveyance tablets.

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