FORMULATION AND EVALUATION OF MIRABEGRON SUBLINGUAL TABLET

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ABSTRACT

Aim: This study aims to explore the potential of sublingual tablet of Mirabegron for the treatment of overactive bladder. Overactive problem is widely seen in geriatrics patients and Mirabegron can be alternative choice of drug to treat the syndrome.Materials and Methods: Mirabegron Sublingual Tablet formulated by direct compression method which is cost effective and quick process. Different polymers like mannitol, SSG, MCC PH 101, citric acid monohydrate, low substituted hydroxycellulose, talcum, aspartame, β-cyclodextrin, magnesium stearate used in different ratio.

Result and Discussion: All the prepared formulations showed acceptable pre-compression parameters, disintegration test, dissolution test, drug content, wettability test. After studying the evaluation parameters, the formulation F2 showed the good result in overall parameter due to perfect amount of SSG, MCC pH 101 and citric acid monohydrate.

Conclusion: The study was concluded that the Batch F2 showed good results compared to other batches. This shows that SSG, MCC pH 101 and Citric acid monohydrate play significant role in preparation of Sublingual tablet.

Key words: sublingual, mirabegron,overactive bladder, first pass effect

INTRODUCTION

Background

The first-pass metabolism creates difficulties for efficient oral drug delivery as it involves extensive metabolism of the drug in the gut and liver before reaching the bloodstream, causing low efficacy and bioavailability. To tackle this problem, various drug delivery methods have

been invented, such as rectal, buccal, and transdermal.Local drug delivery in the oral cavity can be targeted at various sites, including the buccal, sublingual, periodontal, tongue, and gum regions, as well as adjacent areas like the pharynx, larynx, adenoids, and tonsils. There are three categories of drug delivery via the membranes of the oral cavity: sublingual, buccal, and local delivery. Sublingual delivery involves placing the drug under the tongue, where it is rapidly absorbed into the bloodstream through the mucosal membranes lining the floor of the mouth.[1,2]Sublingual drug delivery system has many advantages like fast absorption, drug stability, avoidance of hepatic metabolism and so on. [3,4]Lipids which are present in the sublingual mucous membrane act as the main barrier for the permeability of hydrophilic drugs. However, well-hydrated connective tissues provide resistance to hydrophobic drug molecules.[5]. Various mathods are availalle for instance direct compression,mouth molding, spray drying, taste masking, freeze drying, mass extrusion and sublimation. Among them direct compression is easy,reliable and cost effective.[6] Sublingual tablets have become a highly favorable solution because of their convenience, rapid disintegration in the mouth, and immediate drug delivery, making them suitable for emergency treatment of health conditions [7]. Mirabegron is being developed as a new treatment for the management of overactive bladder (OAB). It is an orally active drug that works by activating the β3-adrenoceptor with a better safety profile than antimuscarinic drugs. However, long-term adverse effects are not yet completely investigated [8]. When the bladder is relaxed during the storage phase of micturition, 3-ARs are activated. The activation of adenylyl cyclase and subsequent production of cAMP is the widely acknowledged mechanism by which 3-ARs elicit direct detrusor relaxation in the majority of animals.Only a minor, if any, involvement for this route in bladder relaxation has been found in investigations using adenylyl cyclase or protein kinase A inhibitors. [9] Mirabegron is currently at phase I of clinical trials for the treatment of overactive bladder. [10] Overactive bladder (OAB) is a disorder of the filling phase of the bladder, characterized by symptoms of urgency, urinary frequency, and nocturia, with or without urgency incontinence in the absence of any other underlying pathology. It is a highly prevalent disorder estimated to affect 50–100 million people worldwide.[11]

MATERIALS AND METHOD

MATERIALS:

Mirabegron (active pharmaceutical ingredient), mannitol, citric acid monohydrate, sodium starch glycollate (SSG), microcrystalline cellulose pH 101 (MCC pH 101), low substituted

hydroxycellulose, aspartame, talcum, betacyclodextrin, magnesium stearate were obtained as gift from Time Pharmaceutical Pvt. Limited, Nepal. And all the necessary chemicals and reagents used were laboratory and analytical grade.

Equipments

From compression to evaluation, various instruments like HPLC (Shimadzu Prominence-I LC-2020C),Electronic balance (Wensar),pH Meter (Hana),UV Spectrophotometer (Shimadzu UV-1900i),Fourier Transform Infrared (FTIR, PerkinElmer UTAR Two),Dissolution apparatus (Lab India DS 1400),Hardness tester (Campbell Electronics),Friabilator (Aastha International),Disintegration apparatus (Veego),Compression machine (Shiv International) were used.

METHODS

Formulation of various Formulaion of Mirabegron Sublingual Tablets.

Five formulations will be prepared from F1 to F5 by direct compression technique. First of all, sieve all the ingredients through #40 (mesh size) and mix in separate pouch. In one pouch, mix mirabegron, microcrystalline cellulose pH 101, talcum and mannitol for 5 minutes. And in another pouch, mix the other excipients like sodium starch glycollate, citric acid monohydrate, low substituted hydroxycellulose, betacyclodextrin and aspartame for 5 minutes. After that mix the both pouches samples in one pouch and add magnesium stearate. Now sample is ready for compression.

The detail of composition of each formulation is given in Table 7.

Table 7: Composition of various formulation of Mirabegron Sublingual Tablet.

	F_1(mg)	**F_2(mg)**	**F_3(mg)**	**F4(mg)**	**F5(mg)**
Mirabegron	25	25	25	25	25
Mannitol	30	30	30	30	30
Microcrystalline cellulose 101	27	24	23.5	28.5	25.5

Citric acid monohydrate	1	2.5	2.0	0.5	1.5
Sodium Starch Glycollate	6	7.5	8.5	5	7
Low substituted Hydroxycellulose	5	5	5	5	5
Talcum	2	2	2	2	2
Aspartame	0.5	0.5	0.5	0.5	0.5
Betacyclodextrin	13	13	13	13	13
Magnesium Stearate	0.5	0.5	0.5	0.5	0.5
Total	110	110	110	110	110

Pre-compression parameter:

Angle of Repose [12]

An angle of repose gives the measurement of the maximum possible angle between the surface of the pile of powder and the horizontal plane. An angle of repose is determined by the measurement of the maximum possible angle between the surface of the pile of powder and the horizontal plane. To determine the value a dried and cleaned funnel is used. Blended powder is slowly poured from the funnel and a pile of powder is formed. Now measure the horizontal pile (h) with radius (r) and calculate the value accordingly.

$$Angle\ of\ repose = \ tan - 1(h/r)$$

Table4: Indication of Angle of repose

Angle of repose	Flow character
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

Bulk density and Tapped density[13]

Bulk density is defined as the mass of powder divided by bulk volume. It is calculated according to the equation,

$$\text{Bulk density} = \frac{\text{Weight of the powder}}{\text{Volume of the packing}}$$

The tap bulk density (TBD) of the disintegrant was determined using a USP tap density tester at 100 taps. Disintegrant (10g) was poured into calibrated measuring cylinder (100 ml) and change in volume was noted before and after tapping. TBD was calculated using the following equation,

$$T\text{apped bulk density} = \frac{\text{Weight of the powder}}{\text{Tapped volume of the packing}}$$

Hausner's ratio[14]

Hausner's ratio is calculated by following formula:

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ density}$$

Table5: Indication of Hausner's ratio

Hausner's ratio	Flow properties
1.00-1.11	Excellent
1.12-1.18	Good
1.19-1.25	Fair
1.26-1.34	Passable
1.31.45	Poor
1.46-1.59	Very poor
>1.60	Very very poor

Carr's ratio[15]

It is also known as the Compressibility index (I) which illustrates about the properties of formulating powder. It is calculated by the following formula:

$$Carr's\ index = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} * 100$$

Table6: Carr's Index

5-15	Excellent

12-16	Good
18-21	Fair to possible
23-35	Poor
33-38	Very poor
>40	Very very poor

FTIR for drug-excipient compatability[16]

Drug and excipient interference analysis is carried out by using FTIR technique. The drug and excipients interference reaction is analysed by FTIR spectrometry (PerkinElmer UTAR Two).

Post-compression parameter

Shape and size

Visually observe the tablet description.

Uniformity of Weight[17]

Weigh individually 20 units selected at random or, for single dose preparations in individual containers, the contents of 20 units, and calculate the average weight. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the table and none deviate by more than twice that percentage.

Table8: Uniformity of Weight

Dosage form	Average weight	Percentage deviate
Uncoated and film coated tablets	80 mg or less More than 80 mg but less than 250 mg 250 mg or more	10 7.5 5
Capsules, granules and powders (single-dose)	Less than 300 mg	10

Hardness[18,19]

The H or the crushing tolerance of 6 tablets of each batch was measured using campbell electronics.

Disintegration(DT) [20,21]

A relatively simple method with rigorous conditions was developed to evaluate the DT of rapidly disintegrating tablets. Individual tablet was dropped into a 10-mL glass test tube (1.5-cm diameter) containing 2 mL distilled water, and the time required for complete tablet

disintegration was observed and recorded. The visual inspection was enhanced by gently rotating the test tube at a 45- angle, without agitation, to distribute any tablet particles that might mask any remaining undisintegrated portion of the tablets. As per USP 42, disintegration test for sublingual test carried out in 900 ml distilled water at $37^{o}C \pm 0.5^{o}C$. Limit is below 2 minutes.

Friability test [22,23]

Weight about 6.5 g sample and place in friabilator. It is rotated for 25 rpm for 4 minutes. After that discard dust and weigh again. Calculate the Friability in percent.

$$\%\text{Friability} = \frac{\text{Initial weight}}{\text{Final weight}} \text{X}100$$

Wetting time[24]

The wetting time of the tablets can be measured using a simple procedure. A filter paper of 10 cm diameter was placed in a Petridish with a 10 cm diameter. One milliliter of water containing eosin, a water soluble dye, was added to Petridish. A tablet was carefully placed on the surface of the filter paper. The time required for water to reach the upper surface of the tablet was noted as a wetting time using stopwatch.

Dissolution test[25,26]

The dissolution study of was carried out using USP Apparatus II Rotating Paddle (Lab India) apparatus at 37 ± 0.5°C and 50 rpm using 900 ml of simulated saliva pH 6.8 as dissolution medium. Samples were withdrawn at 30 min, filtered. analyzed spectrophotometrically against known concentration of standard. Standard concentration is 0.0027 mg/ml and 5 ml withdrawn samples are diluted to 50 ml dissolution medium. The dissolution test is performed in six tablets.

Dissolution calculation:

$$\frac{Absorbance\ of\ sample}{Absorbance\ of\ standard} \times \frac{Weight\ of\ standard}{100} \times \frac{1}{100} \times \frac{900}{25} \times \frac{50}{5} \times Assay\ of\ standard\% \times 100$$

Drug content (Assay)

Buffer solution: 1.36 g/l solution of Potassium dihydrogen phosphate in Mili-Q water, add 1 ml of triethylamine to it. Adjust the PH to 4.5 ±0.05 with orthophosphoric acid.

Mobile Phase preparation: Mix buffer solution and Acetonitril in 80:20 (v/v) ratio.

Diluent preparation: 50% methanol in Mili-Q water.

Standard stock preparation: Accurately weight about 50 mg of Mirabegron working standard and transfer into a 100 ml of volumetric flask. Add about 50 ml of diluent, sonicate to dissolve and dilute to volume with diluent. Shake well to mix.

Standard Preparation: Pipette out 5 ml of the standard stock solution into 50 ml of volumetric flask, dilute to volume with diluent and mix well.

Sample stock Preparation: Weigh about 240 mg òf sample powder (equivalent to 50 mg Mirabegron) in 100 ml volumetric flask. Add about 50 ml of diluent, sonicate to dissolve and dilute to volume with diluent. Shake well to mix.

Sample Preparation: Pipette out 5 ml of the standard stock solution into 50 ml of volumetric flask, dilute to volume with diluent and mix well.

Note: Standard 1 and Standard 2 shall be prepared as same manner as standard solution.

Table9: Chromatographic Condition for Assay

Column	**C18 (15cm*4.6 mm 5 µm), Shimadzu**
Flow rate	**1.0 ml/min**
Detector	**250 nm**
Run time	**1.5 times of Retention time**
Temperature	**45^{o}C**
Sample Temperature	**15^{o}C**

Procedure:

i. Inject Blank Solution.
ii. Inject Standard solution-1.
iii. Inject 5 replicate standard solution-2, test is not valid unless the tailing factor is not more than 2.0 and Relative standard deviation is not more than 2.0.
iv. Inject Blank solution.
v. Inject 2 consecutive sample solutions.
vi. Inject bracketing standard solution-2.

Calculation:

$$\frac{\text{Peak area of sample}}{\text{Peak area of standard}} \times \frac{\text{Weight of standard}}{100} \times \frac{5}{50} \times \frac{100}{\text{Weight of sample}} \times \frac{50}{5} \times \text{Assay of standard\%} \times 100$$

Analytical Method Development and validation:

Specificity[27]

Specificity is the ability to clearly assess the analyte in the presence of components, which may be expected to be present in the formulation. Typically these might include impurities, degradants, sample matrix, etc. In the working standard, the retention zone should be free of potential interference at the retention zone of the active ingredient. Prepare placebo solution, blank solution, standard solution and sample solution as prescribed in preparation of solution.The chromatogram/spectrum/printed data from potentiometer of all the above solutions are recorded and compared.

Accuracy[28]

The accuracy of an analytical procedure expresses the closeness of agreement between the value, which is accepted either as a conventional true value or an accepted reference value and the value found. The accuracy of an analytical method is expressed in terms of % recovery. Prepare placebo solution, standard solution corresponding to 100% concentration of the test solution using Working Standard. Pipette out equal amount of placebo solution in 9 different volumetric flasks and spike with the required amount of standard solution to attain the final concentration of 80%, 100% and 120% of the test solution.

Analyze all the samples and calculate the amount of drug present and calculate the % recovery.

Linearity and Range[29]

The linearity of an analytical procedure is its ability (within a given range) to obtain test results, which are directly proportional to the concentration (amount) of analyte in the sample. For assay, prepare sample solution normally from 80% to 120% of test concentration. Plot the calibration curve where concentration is plotted along the x-axis and reading of solution is plotted along y-axis in excel sheet. Determine the correlation coefficient, slope, y-intercept and residual sum of squares from the calibration curve.

Precision[30]

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed condition. Precision may be considered at two levels: repeatability and intermediate precision. The precision of an analytical procedure is

usually expressed as variance, standard deviation or coefficient of variation of a series of measurements.

Robustness[31,32]

The robustness of the analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameter and provides an indication of its reliability during normal usage. If measurements are susceptible to variation in analytical conditions should be suitably controlled or precautionary statements should be included in the procedure. One consequence of the evaluation of robustness should be that a series of system suitability parameter (e.g. resolution test) is established to ensure that the validity of analytical procedure is maintained whenever used. At least two variable method parameters should be considered for evaluation of Robustness.

RESULTS :

Pre-compression and post-compression analysis were carried out. Since the drug content (assay) method was not available in pharmacopoeia so assay method was validated.

Pre-compression Parameter

Angle of repose

Shortly, the angle of repose of different batches ranged from 31.733° to 33.133°. According to Table 10, all the trial formulation batches revealed the passable flow property of the powder blend as given in Table 10.

Bulk density and tapped density

As shown in Table 10, the bulk density and tapped density ranged from 0.388–0.435 g/ ml and 0.511–0.540 g/ml. After this, bulk density and tapped density were used to calculate Carr's index and Hausner's ratio.

Hausner's ratio

Hausner's ratio in trial batches ranges from 1.241 to 1.396. Trail batches ranges from F1 to F4 showed fair result where formulation F5 showed passable result which was depicted in Table 10.

Carr's index (I)

According to Table !0, Carr's index ranges from 19.34 to 28.34. Trial formulations F1 to F3 showed fair result whereas formulations F4 and F5 showed passable results.

Table10: Results of Pre-compression Parameter

Formulation	Angle of repose(^{o})	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's ratio	Carr's index (I)

F1	32.400	0.435	0.540	1.241	19.34
F2	31.267	0.411	0.511	1.246	19.56
F3	33.133	0.429	0.534	1.248	19.65
F4	31.733	0.388	0.542	1.396	28.34
F5	32.867	0.395	0.532	1.348	25.70

Fourier Transform Infrared (FTIR) for drug-excipient compatability

Drug and excipient interference analysis carried out by using FTIR technique. FTIR of Mirabegron raw material compared with mixture of excipients (placebo) and there was no interference observed. Figure 2 showed that standard (red colour) and sample (brown colour) concordant to eachother. Sample was pure as compared to standard. In figure 3, mixture of excipients (greencolour) and mirabegron standard (red colour) showed different transmittance. Hence, there was no interference observed.

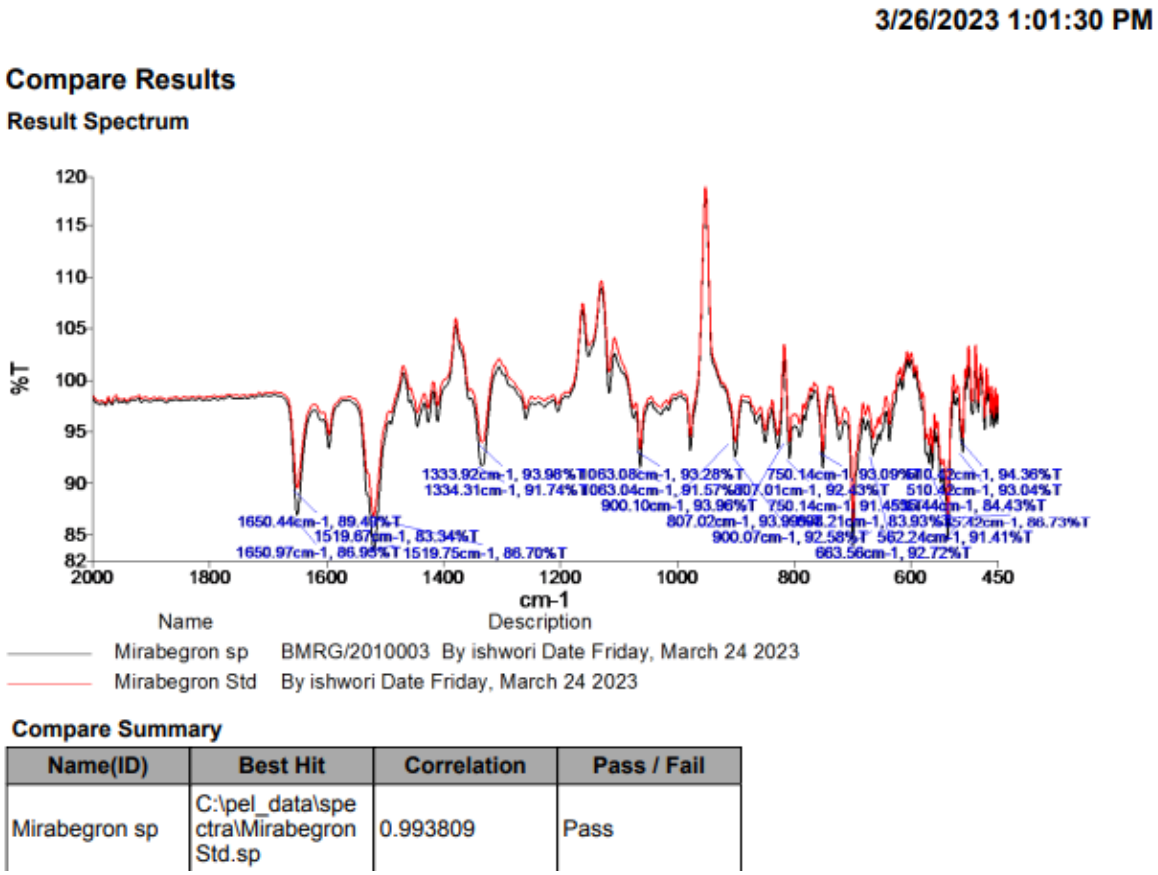

Figure2: FTIR of Mirabegron purity test with standard (Std)

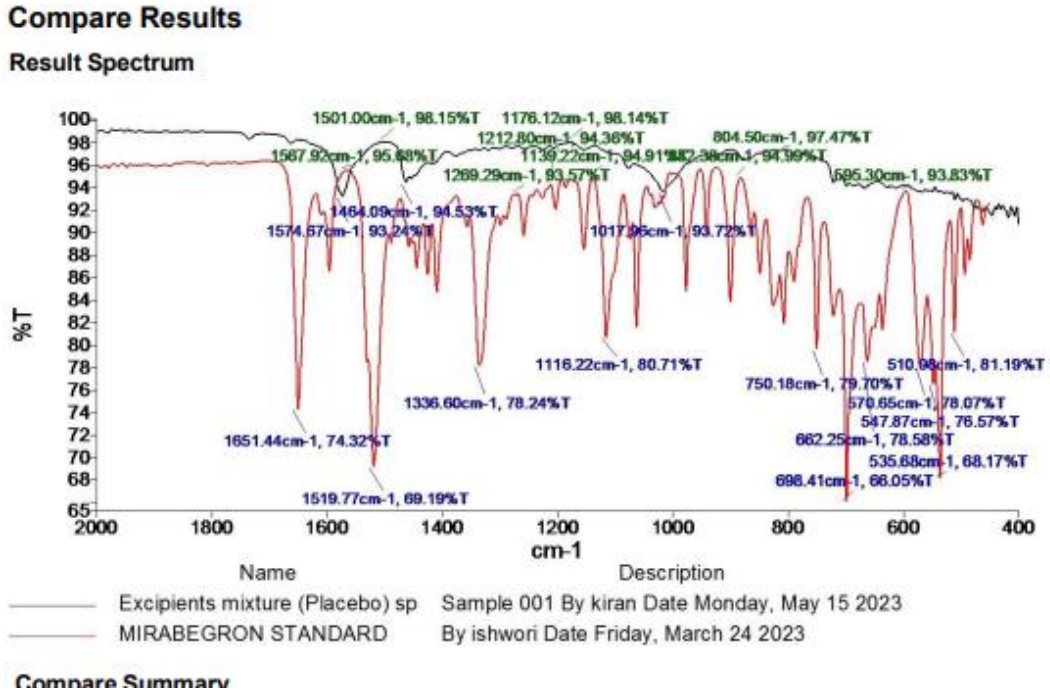

Figure3: FTIR of Mirabegron pure sample and mixture of excipients (placebo)

Post compression Parameter:

Shape and size:

Tablets formulated as round, uncoated tablet with break-line on side and smooth surface on other side.

Uniformity of Weight: The uniformity of weight is an essential parameter to ensure consistency in drug content across different tablets. The results indicate that all trial formulations have met the acceptance criteria for weight uniformity, falling within the range of 109.1 mg to 110.45 mg. This indicates that the manufacturing process was successful in achieving a consistent drug content in each tablet.

Hardness: Hardness is a critical parameter that determines the mechanical strength and robustness of the tablet. The observed hardness values ranged from 4.27 kg/cm^2 to 6.61 kg/cm^2. The influence of citric acid and SSG concentrations on tablet hardness is evident, with low amounts of citric acid monohydrate resulting in lower hardness. This suggests that optimizing the concentrations of these excipients could further enhance the mechanical strength of the tablets.

Disintegration Time: The disintegration time is an important factor for sublingual tablets, as rapid disintegration allows for the drug's prompt release and absorption through the sublingual mucosa. The disintegration times observed for all trial formulations ranged from 32 seconds to 59 seconds, well within the desired range of less than 2 minutes. Formulation F3 demonstrated

the minimum disintegration time, indicating its potential as a favorable candidate for rapid drug release.

Friability: Friability is a measure of tablet durability and resistance to abrasion during handling and transportation. The results show that all formulations have met the requirements specified in the Indian Pharmacopoeia, with friability values less than 1%. This indicates that the tablets have adequate strength to withstand mechanical stress without excessive breakage.

Wetting Time: Wetting time is crucial for sublingual tablets, as it determines the rate at which the tablet disperses upon contact with saliva. The wetting time ranged from 63 seconds to 86 seconds, indicating that an increase in SSG concentration led to decreased wetting time and improved tablet dispersibility in saliva.

Assay: The assay value of a drug product represents the percentage of the active pharmaceutical ingredient (API) present in the formulation. In this case, the assay results for the trial formulations of sublingual tablets containing Mirabegron ranged from 96.50% to 99.22%. Among these formulations, Formulation F2 exhibited a higher assay value of 99.22%, indicating a more significant amount of Mirabegron in the tablets compared to the other formulations.

The observation that Formulation F2 showed a higher assay value than other formulations could indeed be attributed to the concentration of citric acid monohydrate in the formulation. Citric acid is a common excipient used in pharmaceutical formulations due to its multifunctional properties, such as enhancing drug dissolution, improving wetting properties, and acting as a pH modifier.

Dissolution Test: Dissolution is a critical parameter that evaluates the drug release behavior from the tablet. The dissolution range observed in Table 11 varied from 60.87% to 97.19%. Formulations F2 and F3 showed the best dissolution results compared to other formulations. The dissolution behavior of these formulations could be attributed to the optimized concentration of citric acid and SSG, leading to enhanced drug release and dissolution.

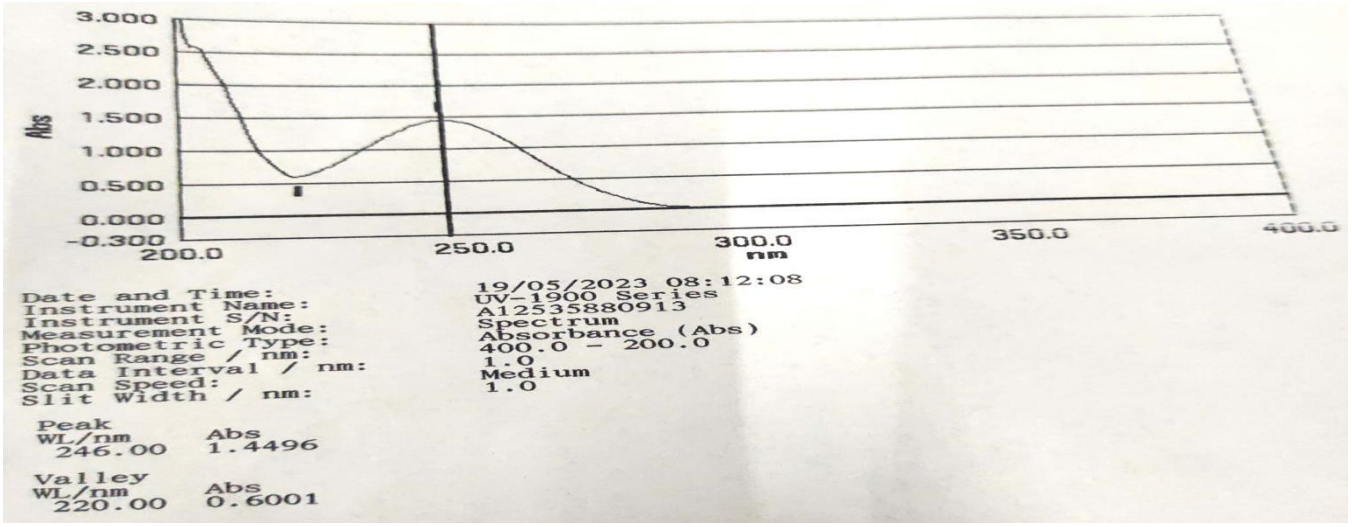

Figure4: Spectrum of Dissolution test for maximum wavelengh

Table11: Results of Pre-compression Parameter

Formulation	Unifromity of weight (mg±SD)	Hardness (Kg/cm^2 ±SD)	Disintegration time (Sec±SD)	Friability (%±SD)	Wetting time (Sec±SD)	Dissolution (%±SD)	Assay (%±SD)
F1	109.1±1.91	4.58±0.25	40±2.52	0.22±0.07	76 ±3.06	81.81±1.08	96.50±1.61
F2	110.15±1.18	4.36±0.15	32±1.53	0.18±0.08	65 ±1.53	92.63±1.97	99.22±0.50
F3	110.45±1.39	5.76±0.43	33±1.53	0.15±0.14	63 ±1.15	97.19±2.94	99.11±1.08
F4	110.30±1.81	6.61±0.09	65±1.00	0.35±0.03	96±2.65	60.87±2.13	98.38±1.36
F5	110.20±2.28	4.27±0.24	37±1.00	0.23±0.08	74 ±2.08	82.95±1.22	98.23±0.44

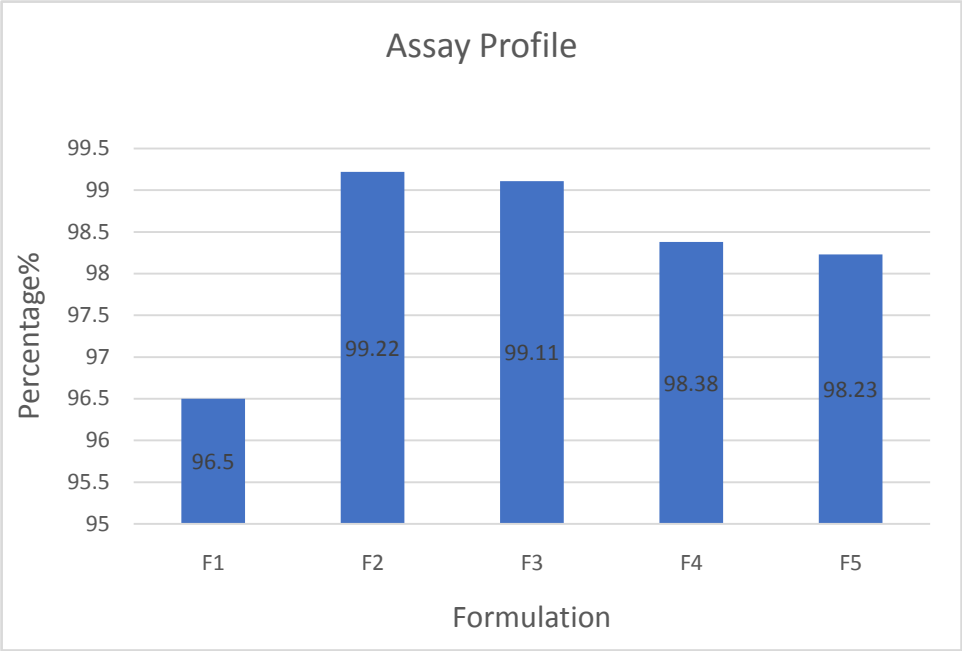

Figure 5: Diagram of Assay test

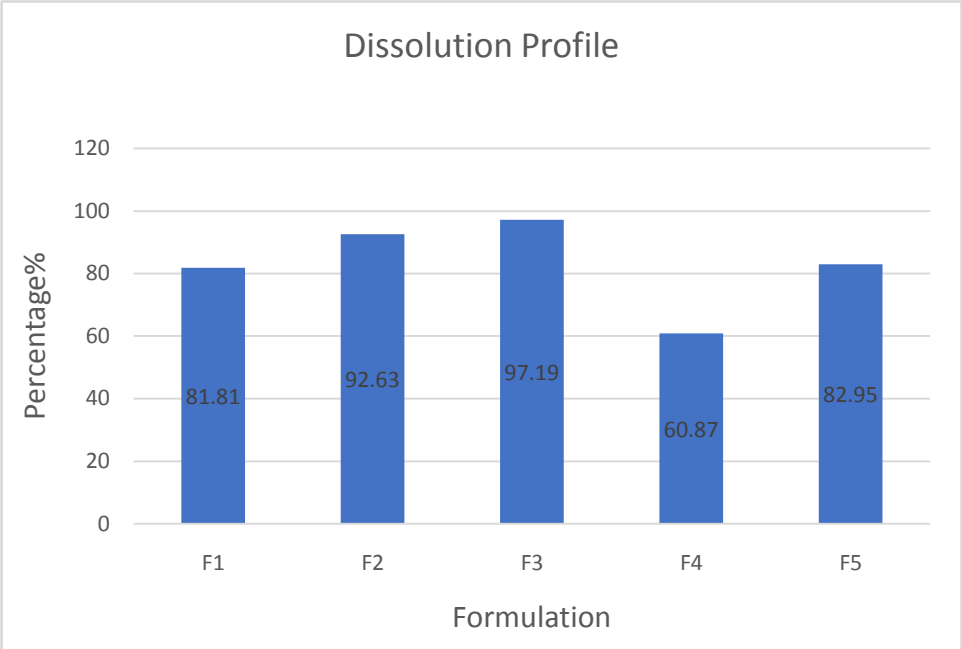

Figure 6: Diagram of dissolution test

Analytical Method Validation

Specificity

In specificity parameter; Blank, Placebo, standard and sample were injected simultaneously and interference was observed. Since there was no any interference seen with drug and excipients figure 4 illustrated below.

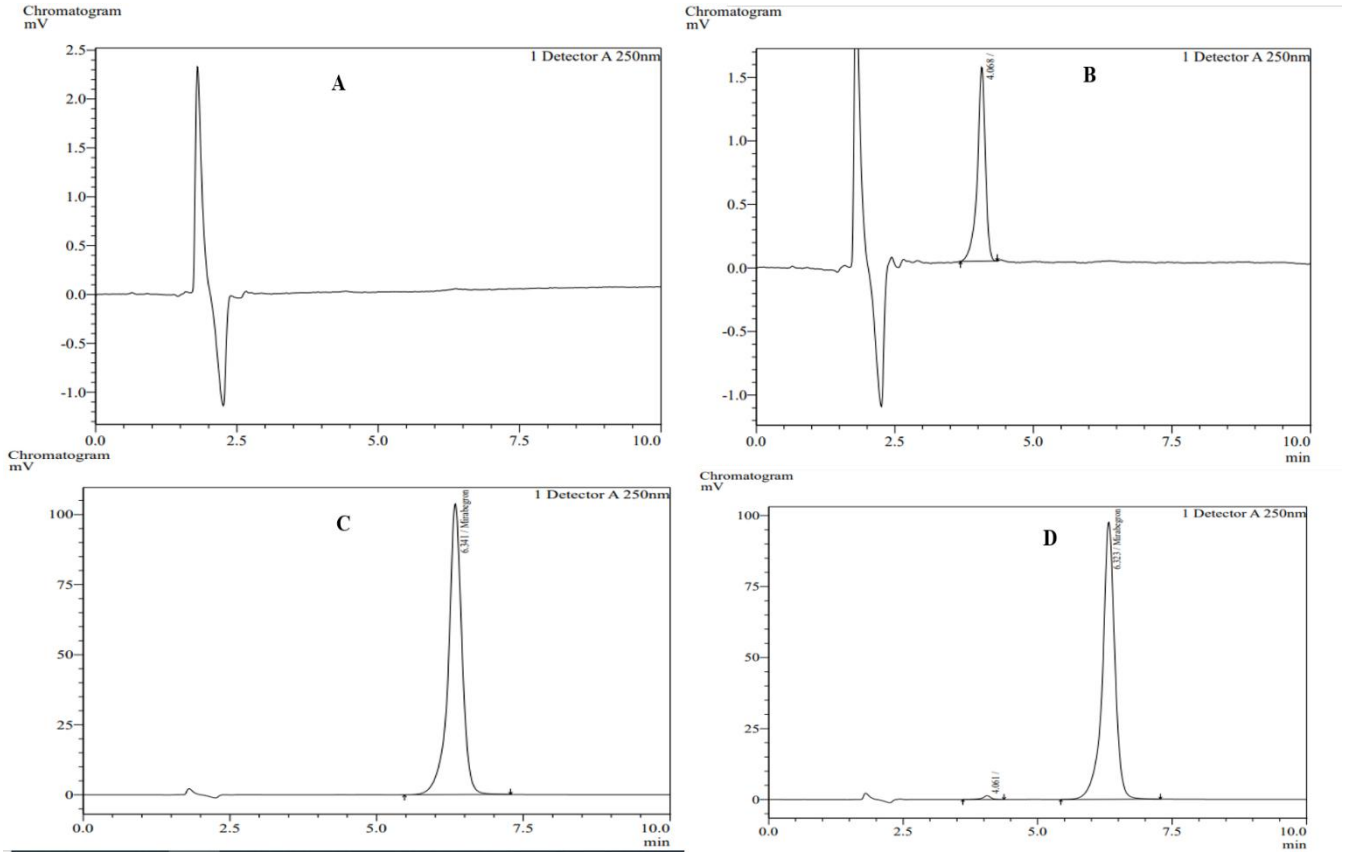

Figure 6: A: Chromatogram of Blank B: Chromatogram of Placebo C: Chromatogram of Stanadrd D: Chromatogram of Sample (Sublingual Tablet)

Accuracy

Triplicate samples of 80% (0.04 mg/ml) ,100% (0.5 mg/ml) and 120% (0.06 mg/ml) were prepared and injected in HPLC. Results showed assay method is accurate. Accuracy is 99.51% which is within limit of 98% to 102%.

Table 12: Results of Validation paramters:

S. No.	Validation Parameter	Result Obtained		Acceptance criteria	Status of compliance
	Specificity	No any interference obtained		Resolution: NLT 1.5 Placebo interference: NMT 2% Blank interference: NMT 1%	Complies
	Accuracy	99.51%		% Recovery : 98% to 102%	Complies
	Precision:				
	Repeatability Instrument precision Method precision	0.03 1.1043		% RSD is ≤ 2%	Complies
	Intermediate Precision	0.514		% RSD is ≤ 3%.	Complies
	Linearity				
	Correlation Coefficient; (r^2)	0.9995		r2 ≥ 0.99	Complies
	Deviation of y-intercept at 100%	0.99%		Y-intercept: ≤ 2% of target concentration response	Complies
	Robustness:				
	Deliberate change				
		Assay %			
	Change in flow rate (± 0.2 ml/min)	1.2 ml/min 98.26%	0.8 ml/min 98.26 %	Changes should be within the limits that produce acceptable chromatography.	Complies
	Range	1.00		Correlation Coefficient ; (r2) ≥ 0.99	Complies
	System Suitability				
	Number of theoretical plates	3496.2		NLT 2000	Complies
	Tailing factor	0.056		NMT 2	Complies
	% RSD	0.9974		NMT 2 %	Complies

Linearity and Range

For Linearity and range, 5 replicate standards of 80% (0.04 mg/ml) ,90% (0.045 mg/ml) ,100% (0.05 mg/ml) ,110% (0.055 mg/ml) and 120% (0.06 mg/ml) were injected in HPLC against

standard solution (0.05 mg/ml). Co-relation coefficient was 0.9995 as shown in Figure of Linearit and Range.

Table13: Linearity and Range (Mirabegron)

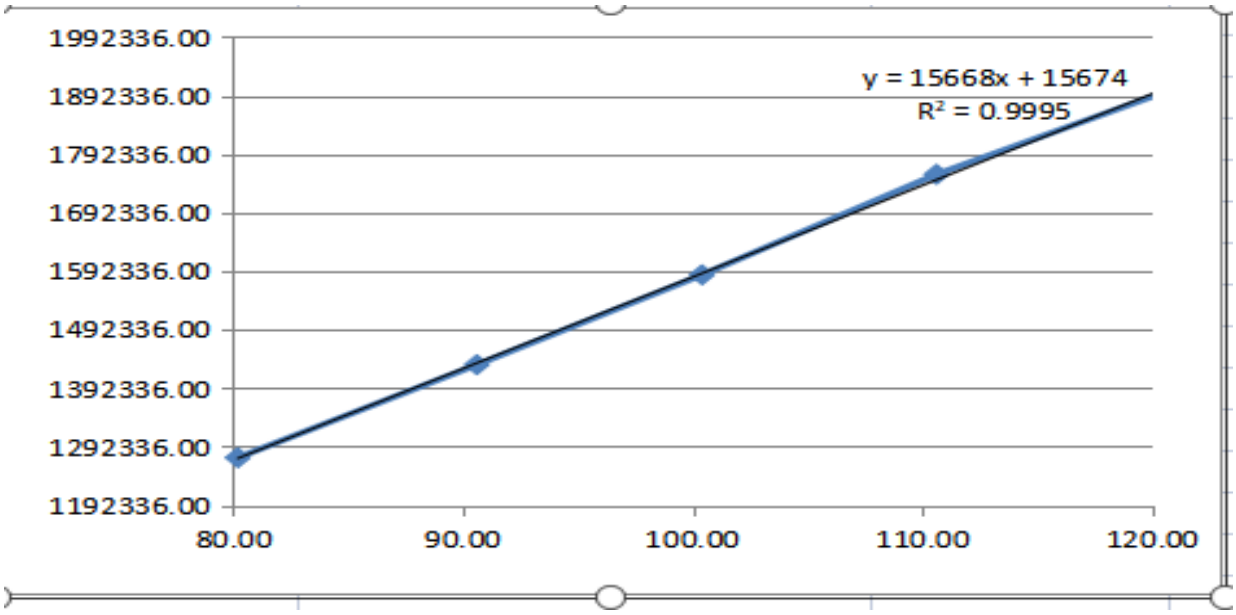

Figure7: Linearity and Range

Precision

Repeatability and Intermediate Precision was carried out. In repeatability method precision along with system precision was done and for Intermediate precision intra-day and inter-day analysis was carried with two different analysts.

Robustness

Small but unaffected parameters like flow rate (±0.2ml/min) and change in column (Peerless) parameters were changed and results were just like as normal results. Table 12 depicted that there was no significant change in assay value.

DISCUSSION

The post-compression parameters for the trial formulations of sublingual tablets containing Mirabegron demonstrated favorable outcomes. The tablets exhibited uniformity of weight, appropriate hardness, rapid disintegration, low friability, and optimal dissolution behavior. These results highlight the importance of excipient selection and their concentrations in achieving desired tablet properties and drug release characteristics. Formulations F2 and F3, in particular, showed promising results and could be considered for further development and optimization in pursuit of an efficient sublingual drug delivery system for Mirabegron.

CONCLUSION

Total 5 formulations had been formulated using different concentration of excipients. Different concentration of SSG, MCC pH 101 and citric acid monohydrate were used in the formulations. Formulation F2 showed good results compared to other batches. However, pre-compression and post-compression parameters of all trial formulations showed good results except formulation F4.

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