



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Research Article

A Process Development and Validation of Mirabegron Extended Release 25 Mg and Silodosin 8mg Bilayer Tablet

Chandan Singh*, Dr. Rita Saini, Dr. Shivanand Patil

Department of Pharmacy, Shree Dev Bhoomi Institute of Education Science and Technology, (Affiliated from VMSB Uttarakhand Technical University) Dehradun, Uttarakhand-248011.

ARTICLE INFO

Published: 04 June 2025

Keywords:

Bilayer tablet; Mirabegron, silodosin, Process Validation, Overactive bladder (OAB) & Benign prostatic hyperplasia

DOI:

10.5281/zenodo.15593321

ABSTRACT

Mirabegron & silodosin, is used often in combination as bilayer tablets, are primarily used to treat the symptoms of overactive bladder (OAB) & benign prostatic hyperplasia (BPH). Mirabegron drug helps to relax bladder muscles by increasing urine storage capacity and reduction in urine urgency. The drug Silodosin helps to relax the muscles in the prostate and bladder neck by improving urinary flow and reducing BPH-related symptoms. The aim of the research study is to process validation (PV) of the formulation development of bilayer tablet of Mirabegron & silodosin drug. Process validation batches were manufactured for the demonstration of the process performance for reproducibility and consistency within its range of operation as per process design. Mirabegron to be manufactured in extended-release form for prolonged action and silodosin in immediate release form. Based on the results of the validation process, the observed results indicate that the process design for the manufacturing of the product, mirabegron and silodosin tablet 25mg & 8 mg is found to be robust enough for manufacturing of a quality drug product. These validated products give the specified quality attribute results & meet all the predetermined specification criteria. The PV study highlights the potential of a Mirabegron ER & Silodosin bilayer tablet approach, combining immediate release & Extended-release formulation, for creating an extended-release dosage form mirabegron & immediate release dosage form of silodosin.


INTRODUCTION

Bilayer tablets continue to represent a new era in which controlled delivery design can be effectively advanced laterally through a variety of

methods to provide an approach to an effective drug transport system (Han et al., 2022). Bi-layer tablets appear to be designed for the simultaneous release of two drugs, two discordant constituents,

*Corresponding Author: Chandan Singh

Address: Department of Pharmacy, Shree Dev Bhoomi Institute of Education Science and Technology, (Affiliated from VMSB Uttarakhand Technical University) Dehradun, Uttarakhand-248011.

Email : chandansinghph89@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



and then similarly for sustained release tablets, where the maintenance dose is the second layer and the immediate release is the first layer. Bilayer tablets continue to be an improved, advantageous way to overcome the shortcomings of single-layered tablets (Maddiboyina et al., 2020). The concept of validation has undergone constant development since it was originally introduced in the US in 1978. The idea of validation has grown over time to include a variety of tasks, from computerized systems for clinical trials to analytical techniques used for quality control of pharmacological ingredients and items. Because each process is so different, there is one-size-fits all method for validation and regulatory agencies like the FDA and EC have created broad optional standards (Ishitsubo et al., 2024). Nevertheless, validation is one component of quality assurance related to a specific process. The term validation simply implies "action of proving effectiveness" or "assessment of validity." Validation, as defined by the European Community for pharmaceutical products, is the "action of proving" that any procedure, process, requirement, material, activity, or system genuinely produces the desired results in line with GMP principles. A documented procedure that offers a high level of assurance that a particular process will reliably yield a product that satisfies its predefined specifications and quality attributes is known as process validation (Swetanshu et al., 2020). Mirabegron (Mrb), a β_3 -adrenoceptor agonist, was a new class of pharmaceutical treatment for OAB. The mechanism of action differences suggest that adding a β_3 -adrenoceptor agonist to an antimuscarinic agent could enhance efficacy in the treatment of OAB (Lee et al., 2019). The European urology association guideline recommends α -1-blockers for distal ureteric stones. Tamsulosin and silodosin are the most commonly used α -1-blockers in medical expulsive therapy. Silodosin has a 38-fold higher

selectivity for α -1A than tamsulosin. In a study by Gupta et al, tamsulosin and silodosin had expulsion rates of 58% and 82%, respectively. Silodosin was also associated with a shorter expulsion time compared to tamsulosin. In the opposite way of thinking, ureter relaxation may be helpful for easy F-URS procedure, and this can easily be achieved by administering silodosin preoperatively (Diab et al., 2024).

1. MATERIALS AND METHODS

1.1 Raw Materials

Mirabegron was purchased from MSN Laboratories Pvt. Ltd. (Telangana, India). Silodosin purchased from PRUDENCE PHARMA CHEM, Microcrystalline cellulose (Ankit pharma), lactose monohydrate (MODERN DAIRIES LIMITED), sodium starch glycolate (SUDEEP PHARMA PVT. LTD.), povidone (SUDEEP PHARMA PVT. LTD.), HPMC K4 M (Coloron India), polyethylene glycol 6000 (Vasudha chemicals, Mumbai, India), magnesium stearate (SKANT India), and colloidal silicon dioxide were purchased from (CABOT SANMAR LIMITED). Polyethylene oxide (Dupont India). and Opadry® coating agent (Opadry red 85G55308) were purchased from Coloron India.

1.2 Preparation of Bilayer Tablet

The formulations are designed for bilayer tablets combining IR (immediate release) and ER (Extended release) components in different ratios. Each drug layer has its separate granulation procedure. For the preparation of Immediate Release (IR) granules, Silodosin, microcrystalline cellulose, lactose monohydrate, and SSG (sodium starch glycolate) were mixed with an inactive binding solution, which is povidone-90 dissolved in purified water, using a high-speed mechanical stirrer. After mixing solutions in dry powder, the



wet granules were dried using an FBD. Dried granules were further sized using the 1.0 mm mesh and lubricated with magnesium stearate and Aerosil/colloidal silicon dioxide. For the preparation of SR granules, mirabegron, lactose, starch and HPMC K4 passed through the sieve and further binding done by using PVPK-90. The dry powder was mixed in RMG, and further binding has been done by the binding agent and dried by using FBD 120 kg. Dried granules sized by 1.0 mm mesh and mixed using Double cone Blender 185 ltr capacity. After mixing, the granules were lubricated with magnesium stearate (Jadiya et al.,

2024). The both layer granules were further compressed to form the bilayer tablets consisting of Immediate Release and Sustained release layers using an Cadpress IV compression machine using the round shape plain punches. The compaction pressure was set at 10 kN, to achieve the required hardness of tablets during the process of compression. The batch size was 2.0 lac tablets. After forming the bilayer tablets, the tablets were further coated with Opadry coating material using a solace auto coater 37" capacity. The detailed formulations are shown in table 1 and manufacturing scheme is shown as figure 2.

Table 1. Composition of formulations for bilayer tablet Mirabegron ER and Silodosin.

Sr. No.	Name of Raw Materials	Qty./Tablets (mg)	Qty./Batch (Kg)
Mirabegron Layer			
1.	Mirabegron	25.38	5.076
2.	Lactose	124.12	24.824
3.	Starch	33.75	6.750
4.	H.P.M.C. (K-4M)	32	6.400
5.	Isopropyl Alcohol	85 ml	17.000 Ltr
6.	Povidone K-90	3	0.600
7.	Colloidal Silicon Dioxide	2.25	0.450
8.	Magnesium Stearate	IP	0.900
Silodosin Part			
9.	Silodosin	8.44	1.688
10.	Lactose	70.85	14.17
11.	Microcrystalline Cellulose	32.53	6.506
12.	Sod starch glycollate	2.5	0.5
13.	Colour Iron Oxide Red	0.04	0.008
14.	Purified Water	25	5
15.	Povidone K-90	1.88	0.376
16.	Colloidal Silicon Dioxide	1.25	0.25
17.	H.P.M.C. E3	3.13	0.626
18.	Magnesium Stearate	1.88	0.376
19.	Sod starch glycollate	2.5	0.5
Coating materials			
20.	Opadry red	8.75	1.750
21.	Purified water	50	10 ltr

Selection of Manufacturing Equipment:

The equipment for the manufacturing of the products has been selected based on the equipment capacity & design. The equipment's used for the

manufacturing of bilayer products has been selected on the basis of manufacturing process design, product batch size, and available and required utility assessment criteria. The list of equipment has been approved based on the



manufacturing process of the product Mirabegron
Extended Release 25 Mg and Silodosin 8mg
Tablet (Bilayer Tablets).

Table 2: Details of Equipment's Used for the Manufacturing of Batches

Sr. No.	Equipment Name	Capacity	Make
1	Vibro Sifter	30 Inches	Tapasya
2	RMG	120 ltrs.	Tapasya
3	Multi-mill	---	Avon
4	FBD	120 kg	Solace
5	Double Cone Blender	185 L	Tapasya
6	Tablet Compression Machine	45 Stations Bilayer	Cadmach IV
7	Metal Detector	NA	Technofour
8	Vibro DE duster	NA	Technofour
9	Auto coater	37"	Solace
10	Colloid mill	10 ltrs	Tapasya
11	Blister Packing Machine	40 - 60 cuts/min	Paam
12	Weighing Balance	200 g	Metler Toledo
13	Weighing Balance	150 Kg	Metler Toledo

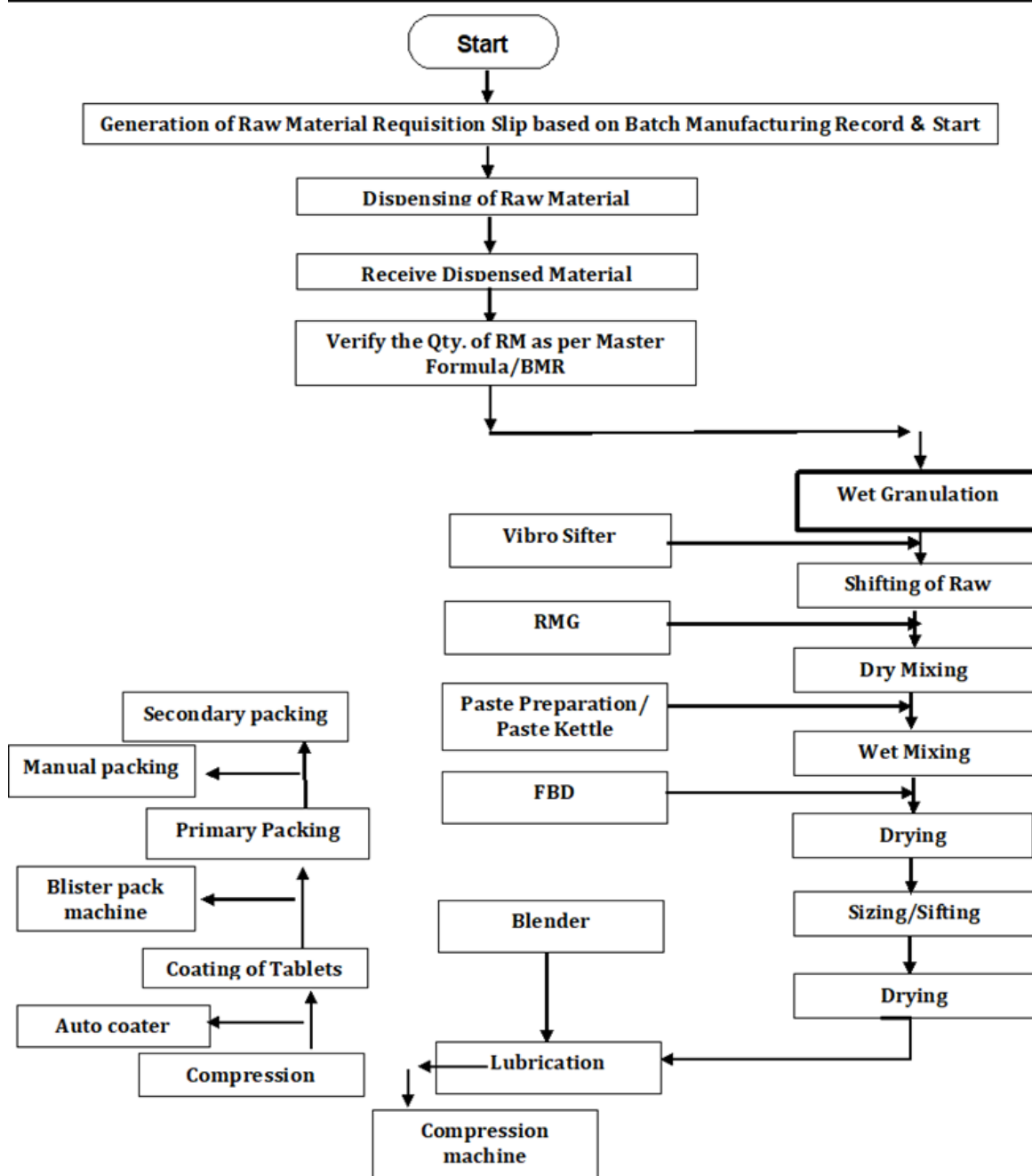


Figure 1: Flow chart of manufacturing & packaging process

2.4 Process Validation of Mirabegron (ER) and Silodosin Bilayer Tablet:

Various quality and control evaluation parameters were performed for the evaluation of bilayer table

formulation. Table 3 described in detail about manufacturing process, process variables and measuring controls.

Table 3: Product Critical Quality Attributes, Risk & control evaluation:

Manufacturing Process	Process Variables	Process Measuring Controls
Initial & Final Sifting	Granules size	Sieve Integrity

Dry Granulation & Wet Granulation	RMG Occupancy Rpm Impeller Rpm Chopper Amperage Mixing Time	Content Uniformity
Semi Drying/ Final Drying	Inlet Temperature Outlet Temperature Bed Temperature Drying Time	Drying Time Lod Of Granules
Lubrication	Rpm Time	Assay Bulk Density Particle Size Distribution
Compression	Machine Rpm Hopper Level Lubrication Of Machines Compaction Force	Tablet Appearance Uniformity Of Weight Disintegration Time Hardness Of Tab Thickness Of Tab Friability % % Assay Cu
Coating	Spray Rate Coating Pan Rpm Bed Temperature Inlet Temperature Bed Temperature	Tablet Description % Weight Gain Physical Parameter Assay
Packing	Forming & Sealing Temperature Machine Rpm	Leak Test Knurling Finished Product Quality Attribute

RESULTS AND DISCUSSION

As per the process validation protocol, sampling of products has been carried out in different stages of manufacturing, i.e. granulation, compression, coating & finished stage. The samples are further analyzed as per the specification of evaluation parameters of formulation process of bilayer tablet. The sampling plan of product was mentioned in the approved validation protocol accordingly sampling has been done. The analytical result of the product gives assurance that manufacturing processes are well-validated. Product sampling and analytical results of all the validation batches discussed in the below sections.

Pre-Formulation and Evaluation of Bilayer Tablet:

The analytical results of the formulation development process of bilayer tablet Mirabegron (ER) 25 mg and Silodosin 08 mg were observed in dry mixing stage. Sample was collected from three stages of the mixer i.e. top, middle and bottom. Detailed analytical reports of the samples were shown in table 4 & 5.

Table 4: Analytical Results of Mirabegron (ER) in dry Mixing Stage.

Sampling Point	Parameters	Acceptance Criteria	Observed Results		
			Trial 1	Trial 2	Trial 3



Top (L1)	Description	white coloured granular powder.	Complies	Complies	Complies
	Mirabegron EP 25 mg	98.0 % to 110.0% of labeled amount	103.2%	98.8%	102.3%
Middle (L2)	Description	white coloured granular powder.	Complies	Complies	Complies
	Mirabegron EP 25 mg	98.0 % to 110.0% of labeled amount	100.3%	102.5%	101.0%
Bottom (L3)	Description	white coloured granular powder.	Complies	Complies	Complies
	Mirabegron EP 25 mg	98.0 % to 110.0% of labeled amount	103.5%	101.7%	98.1%
Composite	Description	white coloured granular powder.	Complies	Complies	Complies
	Mirabegron EP 25 mg	98.0 % to 110.0% of labeled amount	98.9%	104.7%	100.6%

Table 5: Analytical Results of Silodosin in dry Mixing Stage.

Sampling Point	Parameters	Acceptance Criteria	Observed Results		
			Trial 1	Trial 2	Trial 3
Top (L1)	Description	light pink coloured granular powder	Complies	Complies	Complies
	Silodosin JP 08 mg	98.0 % to 110.0% of labeled amount	103.2%	101.8%	105.5%
Middle (L2)	Description	light pink coloured granular powder	Complies	Complies	Complies
	Silodosin JP 08 mg	98.0 % to 110.0% of labeled amount	100.3%	98.6%	98.8%
Bottom (L3)	Description	light pink coloured granular powder	Complies	Complies	Complies
	Silodosin JP 08 mg	98.0 % to 110.0% of labeled amount	103.5%	98.5%	98.4%
Composite	Description	light pink coloured granular powder	Complies	Complies	Complies
	Silodosin JP 08 mg	98.0 % to 110.0% of labeled amount	102.3%	105.8%	98.6%

Formulation and Evaluation of Coated Tablet:

Evaluation process was done for the final coated bilayer tablet of Mirabegron 25 mg and Silodosin

08 mg through various parameters like description, identification, average weight, uniformity of weight and dissolution. The detailed evaluation values of the all parameters are show in table 6.

Table 6: Analytical results of coated tablets.

Parameters	Acceptance criteria	Trial 1	Trial 2	Trial 3
Description	Brick red coloured, round, biconvex, bilayered, film coated tablets, plain on both sides.	Complies	Complies	Complies

Identification	The retention time of the major peak in the chromatogram of test solution should be corresponds to that the standard solution obtained as directed in the assay.	Complies	Complies	Complies	
Average Weight	346.29 to 367.71 mg	359.39 mg	357.75 mg	354.23 mg	
Uniformity of weight	Not more than 2 tablets in 20 deviates from the average weight by more than 5.0%. No tablet deviates from the average weight by more than 10.0%.	Deviation - 3.79 to +1.59%	Deviation -1.70 to +2.17%	Deviation -2.37 to +4.04 %	
Dissolution					
1st hour Mirabegron EP	Not more than 30.0% of Labeled amount	Minimum	8.5%	12.5%	18.4%
		Maximum	12.2%	15.7%	22.5%
		Average	11.1%	14.0%	20.4%
3rd hour Mirabegron EP	25.0 to 65.0% of labeled amount	Minimum	32.3%	38.1%	42.1%
		Maximum	38.9%	44.4%	47.0%
		Average	35.1%	40.4%	45.9%
10 hour	Not less than 75.0% of labeled amount	Minimum	80.0%	85.7%	90.5%
		Maximum	98.8%	96.2%	98.8%
		Average	90.7%	90.6%	93.8%
Silodosin JP	Not less than 70% (Q) of Labeled amount in 45 minutes	Minimum	85.3%	92.3%	92.2%
		Maximum	95.3%	95.6%	99.1%
		Average	90.3%	93.9%	96.3%
Uniformity of Dosage units (By content Uniformity)					
Mirabegron EP	Acceptance value should be less than 15	9.10	11.2	5.50	
Silodosin JP	Acceptance value should be less than 15	10.30	13.0	5.49	
Assay: Each Film coated tablet contains:					
Mirabegron EP (as extended release form)25 mg	90.0 to 110.0% of labeled amount	103.0%	103.4%	102.5%	
Silodosin JP...8 mg	90.0 to 110.0% of labeled amount	98.4%	98.1%	98.3%	

Formulation and Evaluation of Final Bilayer Tablet:

Formulation of the bilayer tablet of Mirabegron 25 mg and Silodosin 08 mg was done with the help of

standard operating procedure. The evaluation of the formulation process was done for the final compressed bilayer tablet of Mirabegron 25 mg and Silodosin 08 mg compositions. The detailed



evaluation values of the all parameters are show in table 7.

Table 7: Analytical results of final bilayer tablet.

Parameters	Acceptance criteria	Trial 1	Trial 2	Trial 3	
Description	Brick red coloured, round, biconvex, bilayered, film coated tablets, plain on both sides.	Complies	Complies	Complies	
Identification	The retention time of the major peak in the chromatogram of test solution should be corresponds to that the standard solution obtained as directed in the assy.	Complies	Complies	Complies	
Average Weight	346.29 mg to 367.71 mg	357.65 mg	356.72 mg	355.06 mg	
Uniformity of weight	Not more than 2 tablets in 20 deviates from the average weight by more than 5.0%. No tablet deviates from the average weight by more than 10.0%.	Deviation -2.64 to +2.92%	Deviation -1.98 to +2.51 %	Deviation -1.61 to +2.64%	
Dissolution					
1 st hour Mirabegron EP	N ot more than 30.0% of labeled amount	Minimum	8.5%	12.5%	1 st hour Mirabegron EP
		Maximum	12.2%	15.7%	22.5%
		Optimum	11.1%	14.0%	20.4%
3 rd hour Mirabegron EP	25.0 to 65.0% of labeled amount	Minimum	32.3%	38.1%	3 rd hour Mirabegron EP
		Maximum	38.9%	44.4%	47.0%
		Optimum	35.1%	40.4%	45.9%
10 hour Mirabegron EP	Not less than 75.0% of labeled amount	Minimum	80.0%	85.7%	10 hour Mirabegron EP
		Maximum	98.8%	96.2%	98.8%
		Optimum	90.7%	90.6%	93.8%
Silodosin JP	Not less than 70% (Q) of Labeled amount in 45 minutes	Minimum	85.3%	92.3%	Silodosin JP
		Maximum	95.3%	95.6%	99.1%
		Optimum	90.3%	93.9%	96.3%
Uniformity of Dosage units (By content Uniformity)					
Mirabegron EP	Acceptance value should be less than 15	9.10	11.2	5.50	
Silodosin JP	Acceptance value should be less than 15	10.30	13.0	5.49	
Assay: Each Film coated Bilayer tablet contains:					
Mirabegron EP (as extended-release form) 50 mg	90.0 to 110.0% of labelled amount	103.0%	103.4%	102.5%	

Silodosin JP 8 mg	90.0 to 110.0% of labelled amount	98.4%	98.1%	98.3%
-------------------	-----------------------------------	-------	-------	-------

CONCLUSION:

Based on summary report and observed result at different stage, it is concluded that process validation of Mirabegron 25 mg (ER) & Silodosin 8 mg Tablets was carried out as per respective protocol and observed results of critical process parameters and critical quality attributes were found within the specified limit. Finished product results of batch were found within the specified limit.

REFERENCES

- Diab, T., El-Shaer, W., Ibrahim, S., El-Barky, E., & Elezz, A. A. (2024). Does preoperative silodosin administration facilitate ureteral dilatation during flexible ureterorenoscopy? A randomized clinical trial. *International Urology and Nephrology*, 56(3). <https://doi.org/10.1007/s11255-023-03824-6>
- Han, J. K., Kim, J. Y., Choi, D. H., & Park, E. S. (2022). A formulation development strategy for dual-release bilayer tablets: An integrated approach of quality by design and a placebo layer. *International Journal of Pharmaceutics*, 618. <https://doi.org/10.1016/j.ijpharm.2022.121659>
- Ishitsubo, N., Oguro, S., Shimahashi, H., Kawanishi, M., Adachi, T., Mitsuda, K., & Ishibashi, N. (2024). Development, Physicochemical Characteristics and Pharmacokinetics of a New Sustained-Release Bilayer Tablet Formulation of Tramadol with an Immediate-Release Component for Twice-Daily Administration. *European Journal of Drug Metabolism and Pharmacokinetics*, 49(1). <https://doi.org/10.1007/s13318-023-00865-1>
- Jadiya, S., Upmanyu, N., Sathiyarayanan, A., Jain, V., Dubey, R., & Buwade, P. (2024). Formulation and Development of Novel Sulfasalazine Bilayer Tablets for The Treatment of Arthritis Associated With IBD: In-vitro and In-vivo Investigations. *Journal of Pharmaceutical Sciences*, 113(7). <https://doi.org/10.1016/j.xphs.2024.02.019>
- Lee, H. G., Park, Y. S., Jeong, J. H., Kwon, Y. Bin, Shin, D. H., Kim, J. Y., Rhee, Y. S., Park, E. S., Kim, D. W., & Park, C. W. (2019). Physicochemical properties and drug-release mechanisms of dual-release bilayer tablet containing mirabegron and fesoterodine fumarate. *Drug Design, Development and Therapy*, 13. <https://doi.org/10.2147/DDDT.S212520>
- Maddiboyina, B., Hanumanaik, M., Nakkala, R. K., Jhawar, V., Rawat, P., Alam, A., Foudah, A. I., Alrobaian, M. M., Shukla, R., Singh, S., & Kesharwani, P. (2020). Formulation and evaluation of gastro-retentive floating bilayer tablet for the treatment of hypertension. *Heliyon*, 6(11). <https://doi.org/10.1016/j.heliyon.2020.e05459>
- Swetanshu, Bansal, M., & Kaushik, D. (2020). Optimization & Validation Of Bilayer Tablet Fabricated By Antihypertensive Drugs. *International Journal of Medical and Biomedical Studies*, 4(7). <https://doi.org/10.32553/ijmbs.v4i7.1262>

HOW TO CITE: Chandan Singh*, Dr. Rita Saini, Dr. Shivanand Patil, A Process Development and Validation of Mirabegron Extended Release 25 Mg and Silodosin 8mg Bilayer Tablet, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 6, 634-643. <https://doi.org/10.5281/zenodo.15593321>