Corelease™
Controlled Release Formulated Systems

Colorcon®

Development of Mirabegron Push-pull Osmotic Pump Tablet

Technical Data

Challenge

Extended-release matrix tablets are designed to prolong drug release, improving dosing convenience, plasma concentration stability, and patient compliance.

Mirabegron, a β_3-adrenergic receptor agonist for overactive bladder, is rapidly absorbed orally and formulated as an extended-release matrix to ensure steady absorption. As a weak base and BCS Class III drug, mirabegron has poor water solubility but dissolves better in acidic conditions, making its release rate sensitive to GI pH. Its bioavailability varies with dosage, gender, and diet.

A push-pull osmotic pump (PPOP) offers pH-independent, zero-order release, making it a promising alternative. This study aims to develop a PPOP formulation of mirabegron and compare its in-vitro release with the marketed matrix tablet (Myrbetriq™, Astellas Pharma) across different pH media.

Method

Two formulations of mirabegron PPOP tablet were designed to evaluate the influence of different drug layer (DL) and push layer (PL) ratio.

Table 1. Formulations of Mirabegron PPOP tablet

Materials	F1 (DL:PL=2:1)	F2 (DL:PL=1.6:1)
Mirabegron (D90=7.89µm)	55.0	55.0
Polyethylene oxide 200,000 MW	102.50	92.50
Silicon dioxide	0.75	0.75
Magnesium Stearate	1.50	1.50
Pull Layer total	159.75	149.75
Push Layer: Corelease OPL™	81.45	91.45
Total core tablet	241.20	241.20
Semi-permeable coating layer: Corelease CA™	24.12	24.12

Two manufacturing methods were used for the drug layer of the F1 formulation: direct compression (DC) and wet granulation (WG). In the DC method (F1-DC), mirabegron, polyethylene oxide, and silicon dioxide were blended, followed by magnesium stearate, and compressed with Corelease OPL™ to form bi-layer tablets.

In the WG method (F1-WG), the drug blend was granulated with a hydro-alcoholic solution (ethanol:water, 85:15), dried to <3% LOD, milled, and lubricated before compression with Corelease OPL.

F2-WG followed the same WG process but used a different drug:push layer ratio. Tablets were manually pressed using a rotary tablet press and tested for hardness. All bi-layer tablets were coated with Corelease CA™ in a perforated pan, and delivery orifices (1–3) were laser-drilled on the pull layer side of F1-WG.

Table 2. Corelease CA coating parameters

Parameters	Value
Pan load	800 g
Corelease CA Solid	6 %
Solvent (Acetone:water)	96:4
Inlet air volume	65 m^3/h
Spray rate	18 g/min
Product temperature	22-24℃
Pan speed	18-20 rpm
Atomization air	1.2 bar
Pattern air	1.5 bar
Coating weight gain	10% (theoretical)

Drug release profiles of both mirabegron osmotic tablets and marketed matrix tablets were measured in dissolution bath (VK7000, Varian, USA) using apparatus II (paddle method) with sinkers. The dissolution media were 1000 ml of pH1.2 HCl, DI water or pH 6.8 phosphate buffer (at 37±0.5℃) with paddle speed of 75 rpm. UV spectrophotometer was Cary 50 (Varian, USA) and test wavelength was 265 nm.

Results

Core tablet weight and tablet hardness of three formulations were measured, and the results are shown in table 3.

Table 3. Core tablet properties

	F1-DC	F1-WG	F2-WG
Tablet weight (mg)	238.2±2.3	240.0±0.5	240.1±0.4
Hardness (N)	64.2±5.2	89.8±3.8	87.7±0.6

Tablets manufactured by two different methods (DC and WG) on drug layer of F1 formulation had significant difference on drug release profile. Drug release rate of tablets produced by DC method was slower than WG method (figure 1). After 20 hours testing, some of white drug layer still could be seen inside of semi-permeable film (figure 2).

Figure 1. Effect of Manufacturing Method of Drug Layer

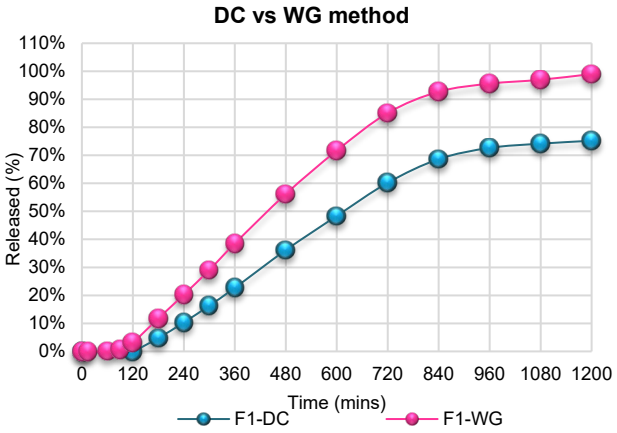
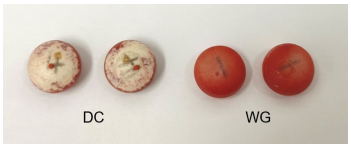
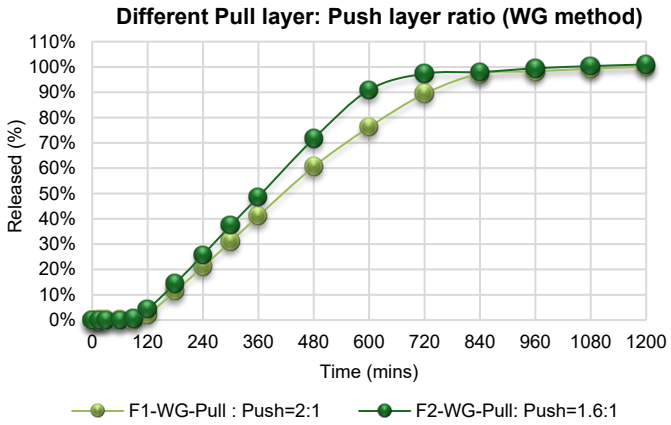


Figure 2. Tablets after 20 hours Dissolution testing



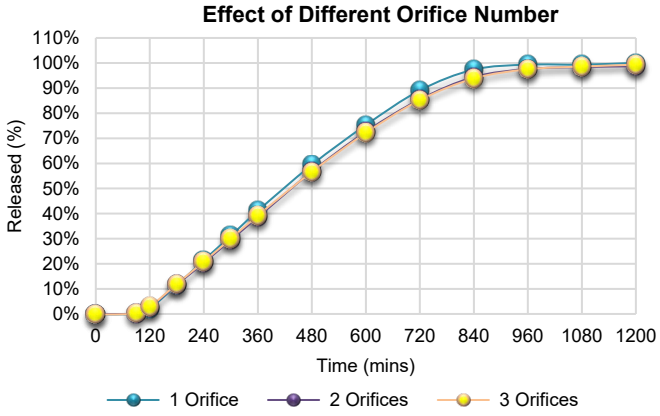
Additionally, formulations with different pull layer and push layer had different drug release profiles. The formulation of pull layer:push layer (1.6:1) had faster drug release than the formulation of pull layer:push layer (2:1), see figure 3.

Figure 3. Effect of Different Pull Layer and Push Layer ratio



Although, there were different number of orifices drilled on the side of drug layer of mirabegron PPOP tablets (F1-WG), drug release from different tablets exhibited very close release profiles (figure 4).

Figure 4. Effect of Different Number of Laser-Drilled Orifice



Tablet dissolutions (F1-WG) were assessed across various pH media. The marketed matrix tablets showed pH-dependent release due to mirabegron's weak base properties, with faster release in pH 1.2 HCl (figure 5).

In contrast, push-pull osmotic pump systems demonstrated consistent release profiles across all pH levels (figure 6), highlighting the robustness and reliability of osmotic technology for drugs like mirabegron.

Figure 5. Release Profiles of Marketed Matrix Tablets in Different pH Media

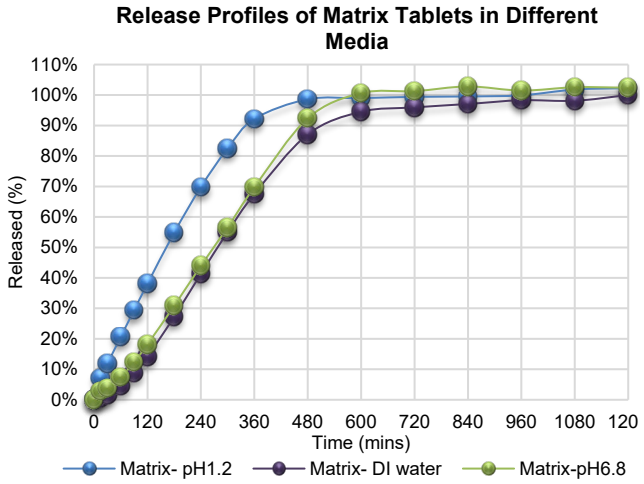
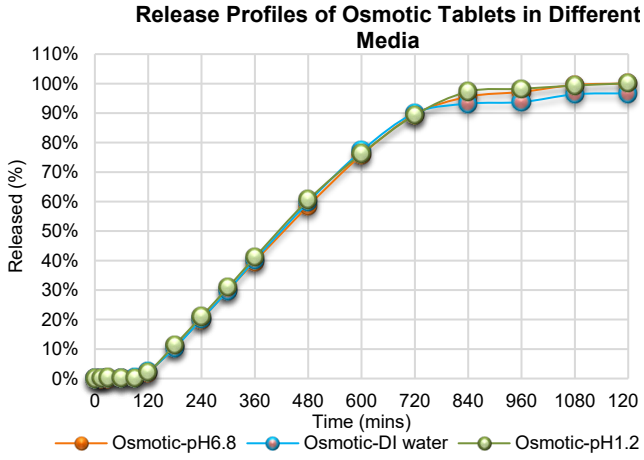


Figure 6. Release Profiles of PPOP Tablets in Different pH Media



Conclusion

A mirabegron PPOP tablet was successfully developed using Corelease OPL™ and Corelease CA™ from Colorcon.

Drug layer manufactured by wet granulation compared to direct compression exhibited a faster drug release profile and complete drug release. A 1.6:1 pull-to-push layer ratio provided faster release than 2:1. Orifice number had no impact on release.

Unlike matrix tablets, which showed pH-dependent profiles due to mirabegron's weak base nature, the PPOP tablets delivered consistent release across pH media, demonstrating the robustness of osmotic technology.

References

1. Chandra Prakash Sunuwar, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 4859-4865

2. Herma, S., Parmar, R., Dudhat, K., Shah, S., Soniwala, M., Dudhrejiya, A., Chothani, D., Pashavan, C., & Mori, D. (2024). Preparation and characterization of novel mirabegron salts for sustaining dissolution and improving diffusion/permeability. Journal of Drug Delivery Science and Technology, 92, 105363.

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