



New Technology of Thermoplastic Coating for Osmotic Pump Tablets: Study on in vitro Drug Release

Chunping Yuan^{1,2} Huimin Hou¹ Shuyun Ou² Shujing Zhao² Yongjian Gao² Qing Liu²

¹National Pharmaceutical Engineering Research Center, China State Institute of Pharmaceutical Industry, Shanghai, China

²Research and Development Center, Sinopharm Group Guangdong Medi-world Pharmaceutical Company Limited, Foshan, China

Address for correspondence Huimin Hou, PhD, National Pharmaceutical Engineering Research Center, China State Institute of Pharmaceutical Industry, 1111 Halley Road, Shanghai 201203, China (e-mail: houhm@nperc.com).

Pharmaceut Fronts 2019;1:e1–e10.

Abstract

Aim The in vitro drug release profiles of metformin hydrochloride thermoplastic coated tablets and nifedipine thermoplastic coated tablets were studied.

Methods By measuring the in vitro release profiles of the thermoplastic coated tablets of model drugs, the effects of membrane thickness, polyethylene glycol-1,500 (PEG1500) content, number of orifice, stirring speed, and release medium on the drug release were investigated, and the rule and mechanism of drug release were also analyzed by comparing with the osmotic pump tablets (OPTs).

Results Thermoplastic coated tablets with single- or double-chamber construction performed the same function of controlling the drug release, operated under the same release mechanism (osmotic pressure drove the drug release), and exhibited the same release characteristics (zero-order release, unaffected by release medium, and stirring speed) and release rule (release rate was inversely proportional to the membrane thickness but proportional to the PEG1500 content) as compared with OPTs prepared by the common spray coating technology.

Conclusion Thermoplastic coated tablets have the same release characteristics in vitro as OPTs. The new technology of thermoplastic coating can replace the spray coating technology of OPTs. This study provides theoretical basis and practical support for the industrialization and clinical application of thermoplastic coating technology.

Keywords

- ▶ thermoplastic coating
- ▶ spray coating
- ▶ metformin hydrochloride
- ▶ nifedipine
- ▶ osmotic pump tablet

Introduction

In the preceding reports, a new technology of thermoplastic coating was developed and the properties of the coating membrane (H membrane) were evaluated.^{1,2} This technology consists of following three steps: hot-melt extrusion for membrane, heat skin coating, and laser melt cutting (abbreviated as HHL; ▶ Fig. 1). Metformin hydrochloride thermoplastic coated tablets (HHL-METF) and nifedipine thermoplastic coated tablets (HHL-NIF) were prepared by this technology.

The traditional metformin hydrochloride osmotic pump tablets (METF-OPTs) such as Fortamet, and nifedipine osmotic pump tablets (NIF-OPTs) prepared by spraying cellulose acetate (CA) dissolved in acetone on the surface of tablets are available in the market.³ Water-soluble METF, an inexpensive oral hypoglycemic agent, widely used in type II diabetes, has

expanded usage due to its other beneficial effects. METF is mainly absorbed in the upper part of the small intestine after oral administration. It is taken two to four times a day with a half-life of 0.9 to 2.6 hours. In addition, it has a stimulating effect on the gastrointestinal tract. Therefore, METF-OPTs with fewer side effects are developed and marketed abroad.^{4–6} Water-insoluble NIF, a commonly used antihypertensive drug, should be taken thrice a day with a short half-life. Its large peak/trough ratio of blood concentration can cause significant blood pressure fluctuations, resulting in serious adverse effects. In clinical practice, NIF-OPTs have been widely used once daily to better control blood pressure.⁷

In this paper, in vitro drug release profiles of HHL-METF and HHL-NIF were studied and compared with those of OPTs prepared by the conventional spray coating. The effects of membrane thickness, polyethylene glycol-1,500 (PEG1500)



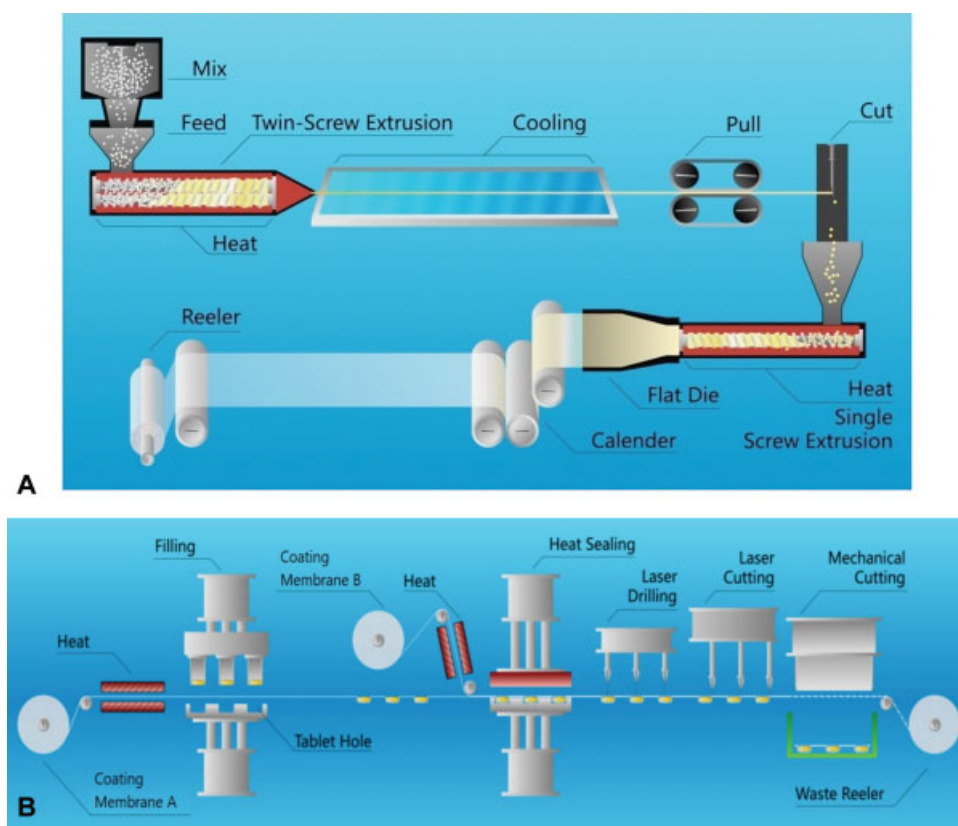


Fig. 1 (A) Schematic illustration of the H membrane preparation and (B) the process of thermoplastic coating.

content, number of orifice, stirring speed, and release medium on the drug release were investigated, and associated mechanisms of drug release were also explored.

Materials and Methods

Materials

The standard substances of METF and NIF were purchased from the National Institute for Food and Drug Control (Beijing, China). The reference listed drug product, METF-OPTs (Fortamet, 500 mg), was purchased from Watson Laboratories of Florida (Florida, United States). CA was purchased from Eastman Chemical Company (Kingsport, Tennessee, United States). Triethyl citrate (TEC) was purchased from Fengyuan Tushan Pharmaceutical Company (Bengbu, China). PEG1500 was purchased from Nanjing Weier Chemical Company (Nanjing, China). Metformin hydrochloride tablets core (500 mg/core) and nifedipine double-layer tablets core (60 mg/core) were gifts from National Pharmaceutical Engineering Research Center (Shanghai, China). Sodium chloride (NaCl) and methanol were purchased from National Pharmaceutical Chemical Reagent Co., Ltd. (Beijing, China).

Preparation Method for Thermoplastic Coated Tablets

Preparation of Thermoplastic Coating Membrane

H membranes were prepared by the hot-melt extrusion process according to the preceding report.¹ The corresponding amounts of CA, TEC, and PEG1500 of the formulation

compositions from ▶Table 1 were weighed and mixed. The mixture was hot-melt extruded into a plastic strip at 180°C through a twin-screw extruder (Thermo Scientific Process 11, Thermo Fisher Scientific, United States). The plastic strip was cut into plastic granules using a plastic cutting machinery (15–80, Zhejiang Good Plastic Machinery Co., Ltd., Hangzhou, China). The plastic granules were further extruded through a single-screw extruder (Thermo Scientific HAAKE Rheomex 19/10 OS, Thermo Fisher Scientific, United States) at 190°C to obtain a sheet with thickness of approximately 1 mm. From which, membranes used for thermoplastic coating with thickness of 100, 80, and 60 μm were further calendered on a double-roller calender at 170°C.

Table 1 Membrane composition and thickness of HHL-METF

HHL-METF	Membrane composition (g)			Thickness (μm)
	CA	TEC	PEG1500	
M10-100	65	25	10	100
M10-80				80
M10-60				60
M10-60 (nonorifice)				60
M15-80	60	25	15	80
M5-80	70	25	5	80

Abbreviations: CA, cellulose acetate; HHL-METF, metformin hydrochloride thermoplastic coated tablets; PEG, polyethylene glycol; TEC, triethyl citrate.

Table 2 Membrane composition and thickness of HHL-NIF

HHL-NIF	Membrane composition (g)			Thickness (μm)
	CA	TEC	PEG1500	
N15-100	60	25	15	100
N10-100	65	25	10	100
N5-100	70	25	5	100

Abbreviations: CA, cellulose acetate; HHL-NIF, nifedipine thermoplastic coated tablets; PEG, polyethylene glycol; TEC, triethyl citrate.

Preparation of Coated Tablets

HHL-METF and HHL-NIF were prepared by the HHL method (refer to the preceding report¹) using different thermoplastic coating membranes with compositions shown in ►Tables 1 and 2. In (M10-100), M represented METF, 10 represented the 10% PEG1500 content in H membrane used for coating, and 100 represented 100 μm membrane thickness. In (N15-100), N represented NIF, 15 represented the 15% PEG1500 content in H membrane used for coating, and 100 represented 100 μm membrane thickness. All tablets listed in ►Tables 1 and 2 except (M10-60 nonorifice) were laser drilled with an orifice. Typical examples of thermoplastic coated tablets are shown in ►Fig. 2. As can be seen in ►Fig. 2, HHL-METF was a single-chamber thermoplastic coated tablet and HHL-NIF was a double-chamber thermoplastic coated tablet.

Determination of Release Profiles

Release Profiles of HHL-METF

The release experiments were performed according to the first method (basket method) of dissolution and release assay (0931) of Chinese Pharmacopoeia (volume IV, 2015 edition). The release medium in the automatic dissolution tester (6,300 type, Distek Company, United States) was 900 mL water or NaCl solution (0.9%, w/v) maintained at (37 ± 0.5)°

C. The stirring speed was 50 or 100 rpm. Each time, 5 mL of release medium was withdrawn at 1, 2, 4, 6, 8, 12, 16, 20, and 24 hours, respectively, and used as test samples. In addition, the standard substance of METF was accurately weighed, dissolved and diluted to approximately 30 μg/mL with water, and used as the standard solution. The test samples and the standard solution (0.5 μL each) were accurately injected into high-pressure liquid chromatograph (HPLC, H-class, Waters, United States). The column was Waters Acquity UPLC Bridged Ethylene Hybrid (BEH) C18 (2.1 × 50 mm, 1.7 μm, Waters) with the column temperature maintained at 30°C. A 0.05% sodium heptane sulfonate solution was first adjusted to pH 4.0 with 10% phosphoric acid and then the adjusted 0.05% sodium heptane sulfonate solution:acetonitrile (84:16) was used as the mobile phase at a flow rate of 0.4 mL/min.⁸ The detection wavelength was at 233 nm. According to the external standard method, the cumulative release percentages at different time points were calculated from recorded chromatograms by peak area. The corresponding release rates were then calculated.

Release Profiles of HHL-NIF

The experiment was performed according to the first method (basket method) of dissolution and release assay (0931) of Chinese Pharmacopoeia (volume IV, 2015 edition). The release medium in the automatic dissolution tester (6,300 type, Distek Company, United States) was 900 mL sodium dodecyl sulfate solution (1%, pH = 1.2) maintained at (37 ± 0.5)°C. The stirring speed was 100 rpm. Each time, 5 mL of release medium was withdrawn at 0.5, 1.5, 2, 2.5, 3, 4, 6, 8, 10, 16, and 24 hours, respectively, and used as test samples. In addition, the standard substance of NIF was accurately weighed, dissolved with methanol, and diluted to approximately 40 μg/mL with release medium, and used as the standard solution. The test sample and the standard solution (0.5 μL each) were accurately injected into high-pressure liquid chromatograph (HPLC, H-class, Waters,

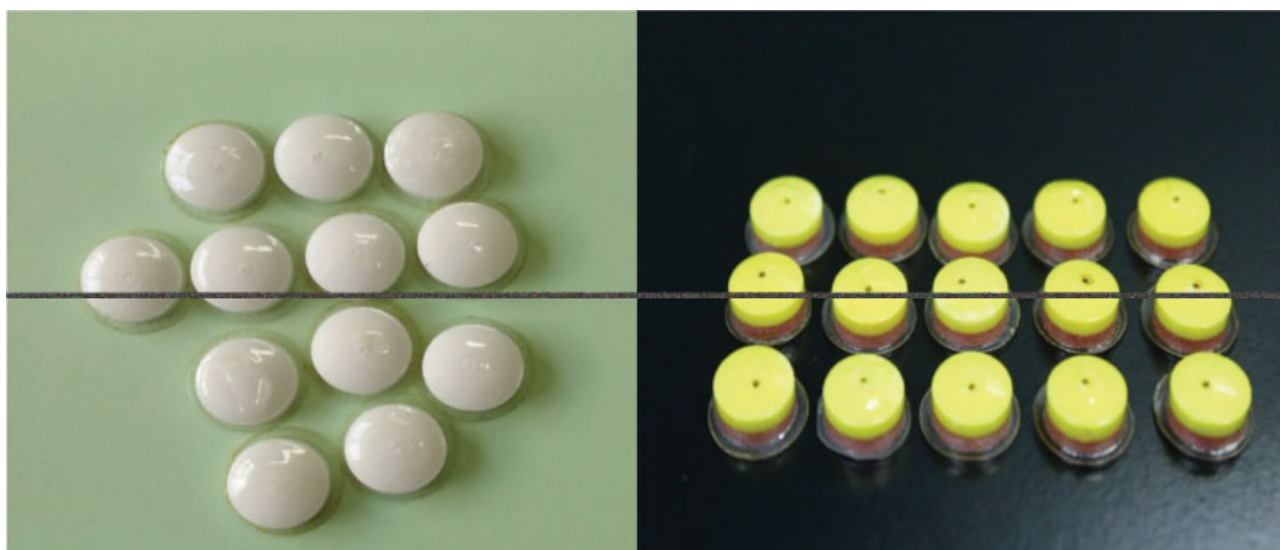


Fig. 2 Typical examples of thermoplastic coated tablets prepared by the HHL method: HHL-METF (white) and HHL-NIF (yellow). HHL, technology of thermoplastic coating; HHL-METF, metformin hydrochloride thermoplastic coated tablets; HHL-NIF, nifedipine thermoplastic coated tablets.

United States). The column was Thermo Hypersil BDS C18 (4.6 × 50 mm, 2.4 μm, Thermo) with the column temperature maintained at 30°C. Methanol:acetonitrile:water (25:25:50) was used as mobile phase at a flow rate of 1.0 mL/min.⁹ The detection wavelength was 235 nm. According to the external standard method, the cumulative release percentages at different time points were calculated from recorded chromatograms by peak area. The corresponding release rates were then calculated.

Comparison of Release Profiles

The “similarity factor” f_2 was used to compare the drug release profiles, which was calculated according to the following equation:

$$f_2 = 50 \times \lg \left\{ \left[1 + \left(\frac{1}{n} \right) \sum_{i=1}^n (R_i - T_i)^2 \right]^{-0.5} \times 100 \right\}$$

where n is the total number of sampling times; R_t and T_t are the cumulative drug release percentage at time point t for two different samples, respectively.¹⁰ If f_2 is larger than 50 (between 50 and 100), the two release profiles of tablets are considered to be similar.

Fitting of Drug Release Models

The release data of HHL-METF and HHL-NIF were fitted with drug release models by calculating the correlation coefficient R^2 ¹¹ of zero-order, first-order and the Higuchi square-root of time release equations, respectively.

Results and Discussion

Specificity Assay for Release Profile Determination

Specificity Assay of METF

The METF standard solution, the test samples of (M10–80) at different time points (1, 4, 8, and 16 hours) in water and the test sample of (M5–80) at 20-hour in NaCl solution (0.9%, w/

v) were assayed on the high-pressure liquid chromatograph, and the results are shown in ►Fig. 3. METF was baseline separated without interferences, and no new impurity peak was detected within 20 hours indicating that the specificity of the assay met the requirements.

Specificity Assay of NIF

The NIF standard solution and the test samples of (N10–100) at 1, 4, 8, and 16 hours were analyzed on the high-pressure liquid chromatograph. The results are shown in ►Fig. 4. NIF was baseline separated without interferences, and no new impurity peak was detected within 16 hours indicating that the specificity of the assay met the requirements.

Factors Affecting the Drug Release

Effect of Membrane Thickness on Drug Release

Based on the method, discussed in section “Release Profiles of HHL-METF,” HHL-METF coated with membranes of different thicknesses [100 μm (M10–100), 80 μm (M10–80), and 60 μm (M10–60)] were tested for METF release at a stirring speed of 50 rpm in water. The results are shown in ►Fig. 5. It was seen that, at any given time, the cumulative drug release percentage decreased as the coating membrane thickness increased.

Effect of PEG1500 Content on Drug Release

Based on the method, discussed in section “Release Profiles of HHL-METF,” HHL-METF coated with membranes of different PEG1500 content [(15% (M15–80), 10% (M10–80), and 5% (M5–80))] was tested for METF release at a stirring speed of 50 rpm in water. The results are shown in ►Fig. 6. Similarly, based on the method, discussed in section “Release Profiles of HHL-NIF,” HHL-NIF coated with membranes of different PEG1500 content [15% (N15–100), 10% (N10–100), and 5% (N5–100)] was tested for NIF release at a stirring speed of 100 rpm in sodium dodecyl sulfate solution (1%, pH = 1.2).

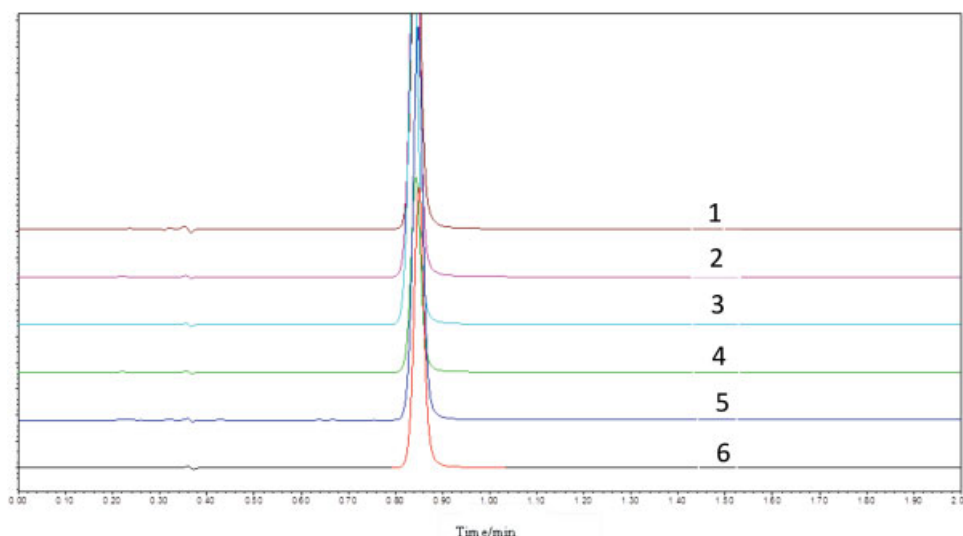


Fig. 3 High-pressure liquid chromatograms of METF standard solution and test samples of HHL-METF at different release time points. 1, METF standard solution; 2, M10–80 water medium–1-hour; 3, M10–80 water medium–4-hour; 4, M10–80 water medium–8-hour; 5, M10–80 water medium–16-hour; 6, M5–80 NaCl medium–20-hour. HHL-METF, metformin hydrochloride thermoplastic coated tablets; METF, metformin hydrochloride.

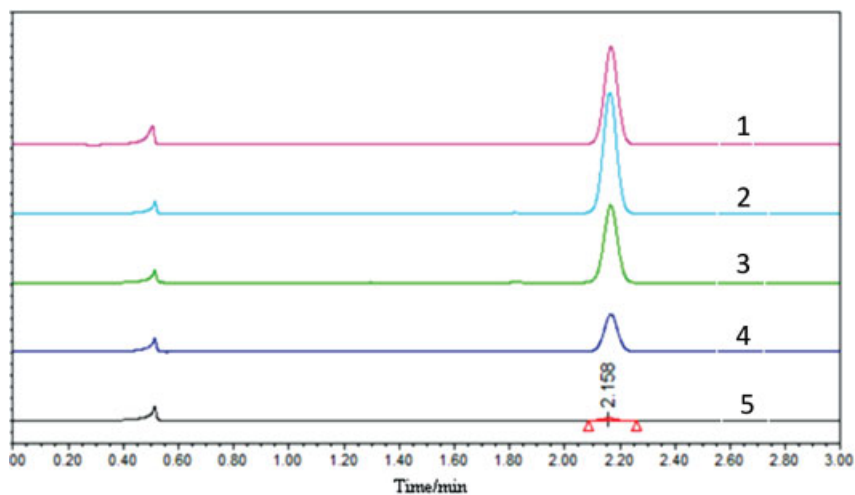


Fig. 4 High-pressure liquid chromatograms of NIF standard solution and test samples of HHL-NIF at different release time points. 1, N10-100-1-hour; 2, N10-100-4-hour; 3, N10-100-8-hour; 4, N10-100-16-hour; 5, NIF standard solution. HHL-NIF, nifedipine thermoplastic coated tablets; NIF, nifedipine.

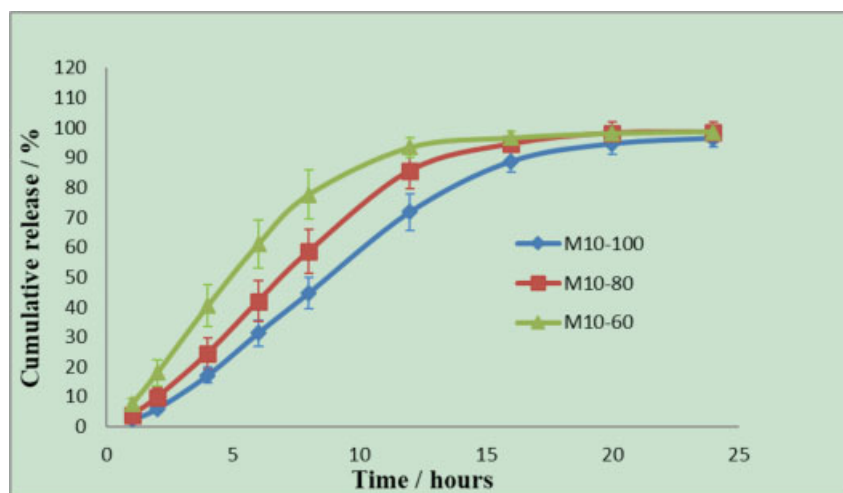


Fig. 5 Effect of membrane thickness on the release profiles of HHL-METF ($n = 6$). HHL-METF, metformin hydrochloride thermoplastic coated tablets.

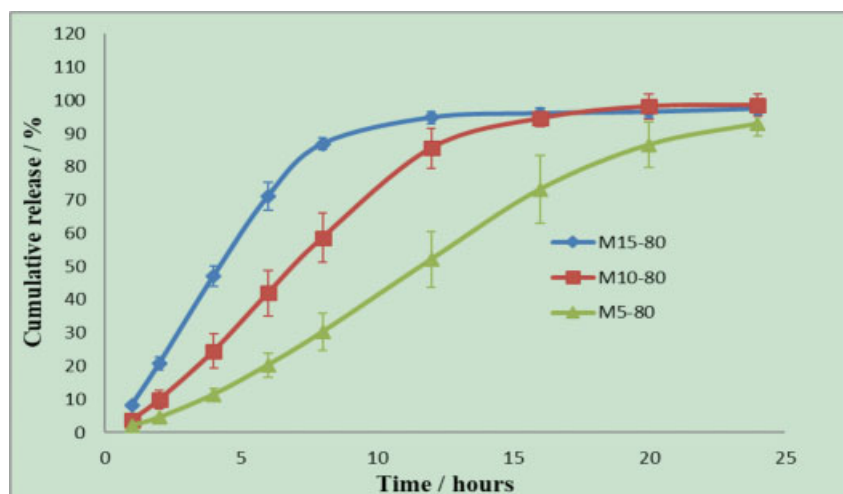


Fig. 6 Effect of PEG1500 content on the release profiles of HHL-METF ($n = 3$). HHL-METF, metformin hydrochloride thermoplastic coated tablets.

The results are reported in ►Fig. 7. In both cases, it was clear that at any given time, the cumulative drug release percentage increased with increasing PEG1500 content. This is consistent with the known effect of porogen content on drug release from traditional OPTs based on spray coating membranes.

Effect of Release Orifice (with or without) on Drug Release

Based on the method, discussed in section “Release Profiles of HHL-METF,” (M10-60) and (M10-60 nonorifice) were tested for the METF release in water at a stirring speed of 50 rpm. The results are shown in ►Fig. 8. The METF release profiles of both thermoplastic coated tablets with and without a laser-drilled orifice were indeed similar, as confirmed by a similarity factor f_2 of 75. This suggested that micropores in the membrane generated by the leaching of PEG1500 were large enough for releasing METF. Consistent with the preceding report,² in HHL-METF, water absorption was caused by the osmotic mechanism, and the release of water-soluble METF through micropores in the membrane was triggered by

diffusion mechanism due to high concentration of METF. The results showed that HHL-METF could control the drug release by adjusting the content of water-soluble PEG1500 in the membrane, similar to the ordinary microporous OPTs. The preparation process of microporous OPTs is relatively simple without the need for laser drilling. In addition, microporous OPTs can release drugs through multiple micropores distributed over the entire OPT surface in vivo, rather than pumping concentrated drug solution through one or two orifices, and, therefore, it should be safer with less adverse reactions than OPTs with orifices.¹²

Effect of Stirring Speed on Drug Release

Based on the method, discussed in “Release Profiles of HHL-METF,” METF release from (M15-80), (M10-80), and (M5-80) was determined in water at stirring speeds of 50 and 100 rpm, respectively. The results are shown in ►Fig. 9. Where it was seen that the stirring speeds studied had little effect on the METF release, as demonstrated by the similarity of release profiles from the three thermoplastic coated

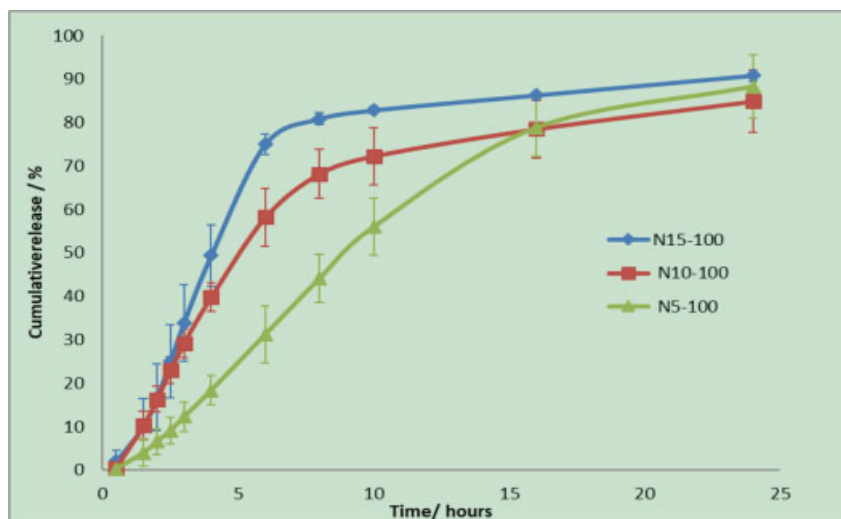


Fig. 7 Effect of PEG1500 content on the release profiles of HHL-NIF ($n = 3$). HHL-NIF, nifedipine thermoplastic coated tablets.

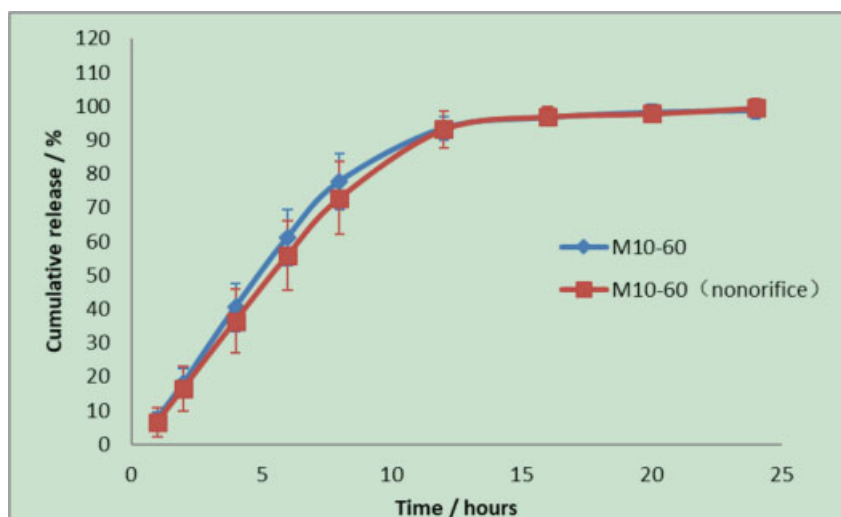


Fig. 8 Effect of release orifice (with or without) on the release profiles of M10-60 ($n = 6$).

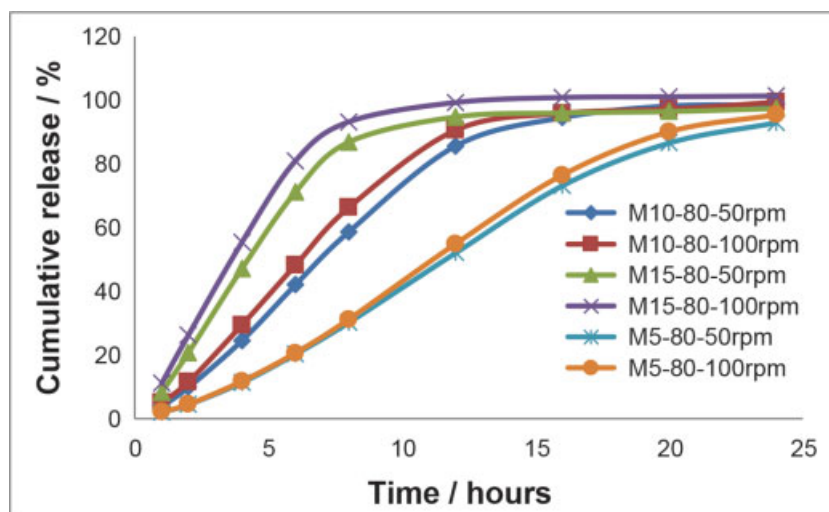


Fig. 9 Effect of stirring speed on the release profiles of various HHL-METF ($n = 3$). HHL-METF, metformin hydrochloride thermoplastic coated tablets.

tablets at the two stirring speeds, confirmed by their similarity factor f_2 being 60, 68, and 83, respectively (all > 50). It was, therefore, confirmed that the drug release from thermoplastic coated tablets was not affected by the stirring speed.

Effect of Release Medium on Drug Release

Based on the method, discussed in “Release Profiles of HHL-METF,” METF release from (M15-80) and (M5-80) was determined at a stirring speed of 50 rpm in 900 mL water and NaCl solution (0.9%, w/v), respectively. The results are summarized in ►Fig. 10. The effect of release medium on the release profile of (M15-80) membrane was not significant with a calculated f_2 of 59. The reason was that, although the osmotic pressure difference in the release medium of NaCl solution (0.9%, w/v) was reduced compared with the osmotic pressure difference in water, the change of osmotic pressure difference in NaCl solution (0.9%, w/v) was not large enough to affect the rate of water influx into the (M15-80) core. The effect of release medium on the release curve of (M5-80) was slightly significant and the cumulative drug release slightly slowed down in NaCl solution (0.9%, w/v). Nevertheless, the

release profiles of (M5-80) in water and NaCl solution (0.9%, w/v) were still similar ($f_2 = 53$).

NaCl solution (0.9%, w/v) does not significantly affect drug release because the ion-molar concentration of NaCl solution (0.9%, w/v) is 0.3077 mol/L. The solubility of METF is 346 mg/mL. Its ion-molar concentration is 4.178 mol/L, which is much larger than the ion-molar concentration of NaCl solution (0.9%, w/v). Therefore, basing on the Van't Hoff equation, the osmotic pressure difference is barely changed in the presence of NaCl solution (0.9%, w/v), indicating that the influence of NaCl solution (0.9%, w/v) on the osmotic pressure difference would be small enough to be ignored.

Comparison with Reference Listed Drug Product

According to the method, discussed in section “Release Profiles of HHL-METF,” METF release from (M10-100) and (M10-80), (M10-60 nonorifice), and reference listed drug product Fortamet was determined at a stirring speed of 100 rpm in water. The results are shown in ►Fig. 11. The similarity factor (f_2) between (M10-80) and Fortamet was 61, indicating the release profiles of these two tablets were similar.

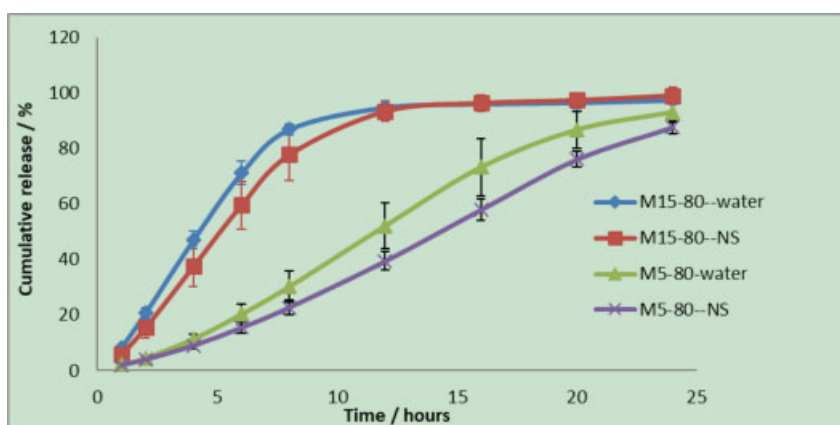


Fig. 10 Effect of different release medium on the release profiles of HHL-METF ($n = 3$). HHL-METF, metformin hydrochloride thermoplastic coated tablets. NS, NaCl solution (0.9%, w/v)

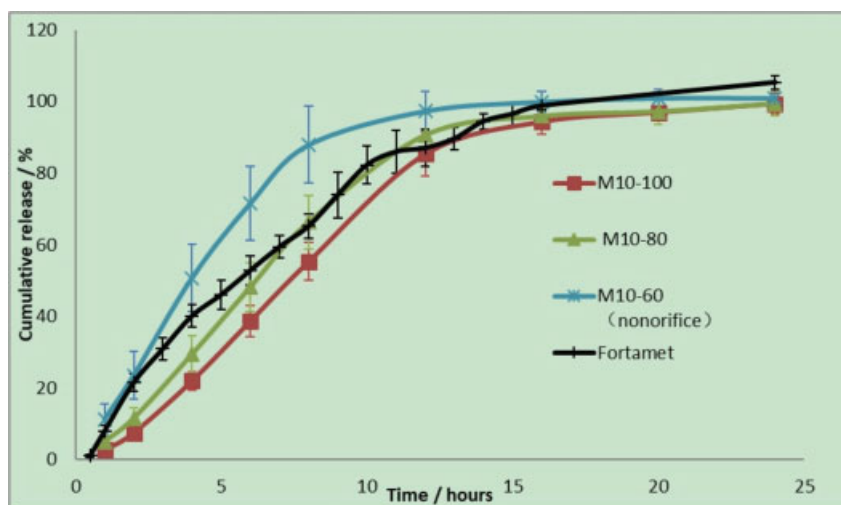


Fig. 11 Comparison of the release profiles between HHL-METF and Fortamet ($n = 3$). HHL-METF, metformin hydrochloride thermoplastic coated tablets.

Visualization of Drug Release

Photographs of (N5-100) at 0, 8, and 24 hours during release test are shown in ►**Fig. 12**. The push layer of the HHL-NIF expanded during the release process and facilitated the NIF release from the orifice. After 24 hours, the volume of HHL-NIF increased slightly due to the softness and ductility of the H membrane. Its release profile was consistent with that of the conventional push and pull OPTs.¹³

Mechanism of Drug Release

Fitting of Drug Release Models

The release data of HHL-METF and HHL-NIF were fitted with drug release models of zero-order, first-order, and the Higuchi square-root of time release equations. The results are shown in ►**Tables 3** and **4**. Based on 24-hour fitting, the releases of Fortamet, (M5-80), and (N5-100) were nearly zero-order. Whereas for 12-hour fitting, the releases of Fortamet, (M10-100), (M10-80), (M5-80), (M10-60),

(N5-100), and (N10-100) were nearly zero-order. Thus, tablets coated by the HHL method could achieve zero-order in vitro drug release by adjusting the content of the membrane thickness and PEG1500.

Mechanism of Drug Release

The release rate of common OPTs or microporous OPTs is calculated according to **Eq. (1)**¹⁴⁻¹⁶:

$$dm/dt = A K \pi c/h \quad (1)$$

where dm/dt is the quantity of drug released over time, A is the surface area of the coating, K is the permeability value of membrane, π is the osmotic pressure difference between the tablet core and the surrounding solution, c is the drug concentration pumped out of the tablet core, and h is the thickness of the tablet coating. According to Eq. 1, the release rate is inversely proportional to the membrane thickness and proportional to the membrane permeability.

The release rates of METF coated tablets and NIF coated tablets are shown in ►**Figs. 13** and **14**, where the following three aspects were noted:

(1) the release rate of (M10-80) was slower than that of (M10-60) but faster than that of (M10-100), indicating the release rate was inversely proportional to the membrane thickness.

(2) The release rate of (N10-100) was slower than that of (N15-100) but faster than that of (N5-100), indicating that the release rate was proportional to the PEG1500 content in membrane. In the above equation, K represents the permeability value of the osmotic membrane which encompasses the influence by the PEG1500 content of the membrane. The higher the PEG1500 content of membrane was, the larger the K value, the faster the release rate.

(3) For (N5-100), the release rate from 1.5 to 16 hours was constant at 3.26 ± 0.64 mg/h, and the cumulative drug release percentage of nifedipine reached 78.8% within 14.5 hours. For (M5-80), the release rate was constant at

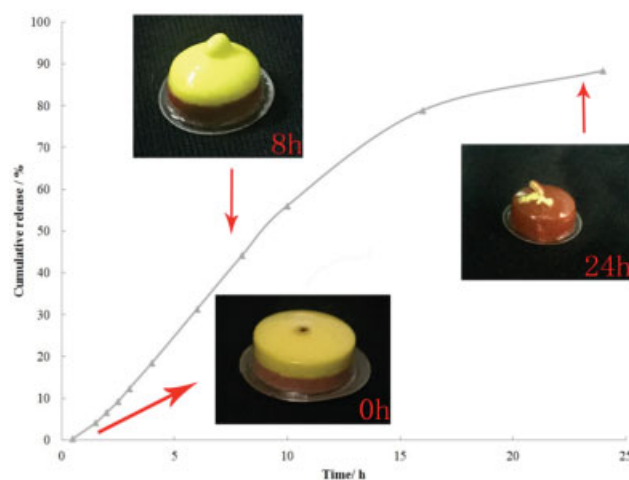


Fig. 12 Photographs of N5-100 at 0, 8, and 24 hours during release test.

Table 3 Correlation coefficient R^2 of fitting drug release from HHL-METF to various models

Tablets	Zero-order		First-order		Higuchi's model	
	24-hour	12-hour	24-hour	12-hour	24-hour	12-hour
Fortamet	0.956	0.978	0.907	0.972	0.993	0.995
M10-100	0.938	0.996	0.979	0.952	0.972	0.951
M10-80	0.883	0.997	0.979	0.943	0.956	0.972
M10-60	0.779	0.956	0.976	0.978	0.904	0.991
M15-80	0.694	0.904	0.907	0.989	0.840	0.968
M5-80	0.985	0.988	0.955	0.957	0.965	0.925
M10-60 (nonorifice)	0.710	0.913	0.967	0.980	0.854	0.975

Abbreviation: HHL-METF, metformin hydrochloride thermoplastic coated tablets.

Table 4 Correlation coefficient R^2 of fitting drug release from HHL-NIF to various models

Tablets	Zero-order		First-order		Higuchi's model	
	24-hour	12-hour	24-hour	12-hour	24-hour	12-hour
N15-100	0.675	0.878	0.833	0.940	0.841	0.941
N10-100	0.757	0.924	0.897	0.976	0.906	0.976
N5-100	0.925	0.998	0.990	0.977	0.970	0.955

Abbreviation: HHL-NIF, nifedipine thermoplastic coated tablets.

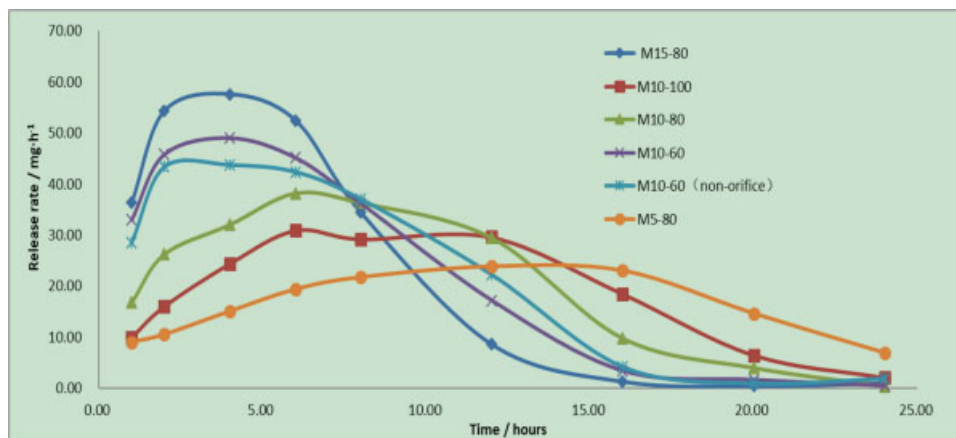


Fig. 13 Release rate-time profiles of HHL-METF. HHL-METF, metformin hydrochloride thermoplastic coated tablets.

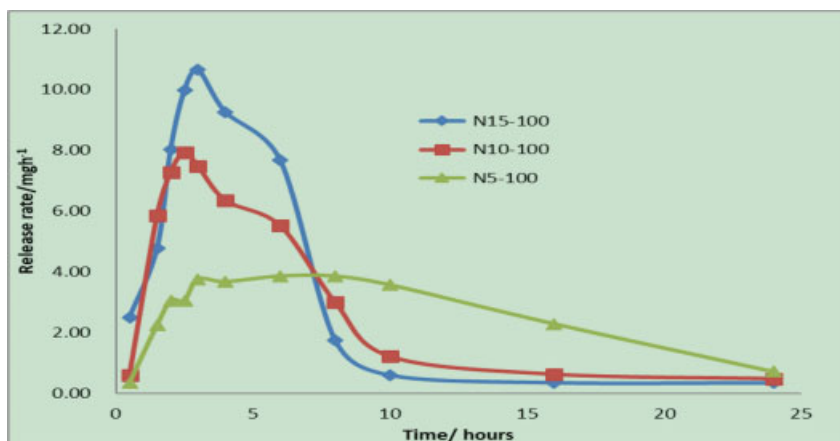


Fig. 14 Release rate-time profiles of HHL-NIF. HHL-NIF, nifedipine thermoplastic coated tablets.

22.03 ± 1.95 mg/h from 6 to 16 hours, and maintained a constant release during 10 hours, indicating that the release rates of both tablets were zero-order at certain time. It could be summarized that the drug release rule of the H membrane coated tablets, followed the above equation (Eq. 1), and was consistent with that of conventional spray coating OPTs and microporous OPTs. The prepared thermoplastic coating membrane of this study is a semipermeable membrane. The drug solubility, membrane thickness, and the PEG1500 content are all key factors affecting the constant release of the drug.

One of the key factors affecting the release of OPTs relates to the coating membrane. In the HHL method, the properties of the coated membrane are easily controlled by the PEG1500 content and membrane thickness. It is easy to control these factors by precisely weighing the amount of PEG1500 and adjusting the distance of the calender roller to obtain the desired thickness, irrespective whether it is the laboratory-scale or larger-scale production. However, the traditionally spray coating osmotic tablets have the disadvantages of needing to sample coated tablets from time to time and peel-off the coated membrane to measure the thickness which is cumbersome to operate. In addition, in the proposed thermoplastic coating, the membrane thickness can be maintained uniform in large-scale production using plastic industry's calendaring film process. Therefore, the HHL method with good reproducibility is easier to produce an ideal controlled release membrane for further thermoplastic coating than the conventional spray coating of OPTs.

Spray coating, which is generally used for OPTs coating, has many problems, such as using a large amount of organic solvent, environment pollution, safety risk, dust generation, and complicated operation, etc. The HHL method described here is not only free from organic solvents and dust generation, but also avoids the drug instability caused by solvent migration into the core during spray coating.

Conclusion

Thermoplastic coating is a new coating technology for OPTs. The thermoplastic coated tablets (HHL-METF and HHL-NIF) exhibited properties of controlling drug release and displayed the same release mechanism (osmotic pressure acted as the release power), the release characteristics (zero-order release, unaffected by release medium, and stirring speed), and release rule (e.g., release rate was inversely proportional to the membrane thickness but proportional to the content of PEG1500) similar to those of conventional OPTs prepared by common spray coating. The technology of thermoplastic coating could also prepare microporous OPTs.

The new technology of thermoplastic coating can replace the spray coating technology of OPTs. The technology is an integrated innovation with advantages of being scientific and reasonable, environmentally friendly, and economically beneficial. This study provides theoretical basis and practical

support for the industrialization and clinical application of thermoplastic coating technology.

Conflict of Interest

The authors declare no conflicts of interest.

Acknowledgments

This research work was supported by National Pharmaceutical Engineering Research Center and R&D Center of China Traditional Chinese Medicine Holding Co., Ltd. and our deepest gratitude goes to Prof. Ping I. Lee from University of Toronto for his careful work and thoughtful suggestion that have helped improve this paper substantially.

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