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Short communication

Application of a novel Revolver apparatus for a biorelevant dissolution test of ropinirole sustained release tablets

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Introduction

Biorelevant dissolution tests of oral solid dosage forms open the gate to valid in vitro-in vivo predictions (IVIVP). A recently developed Revolver apparatus (Fig. 1) allows mimicking the acceptor fluid composition and flow as well as pH changes occurring in the human fasted intestine**.** This work presents and showcases the first application of the Revolver in dissolution testing of SR tablets with ropinirole hydrochloride (RH).

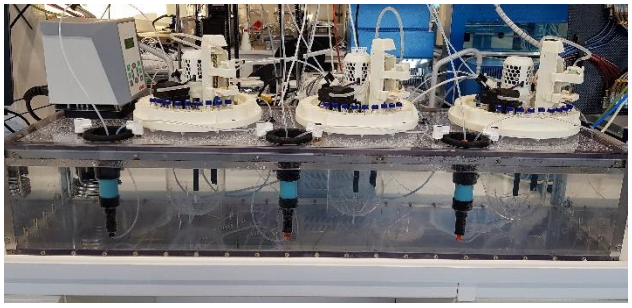

Fig. 1. The Revolver apparatus.

Materials and methods

RH secondary pharmaceutical standard (99.5 % pure) was purchased from Sigma-Aldrich (Poland). Polpix SR 2 mg tablets were purchased from a local pharmacy. All other chemicals were at the analytical grade.

Drug dissolution profiles from Polpix SR 2 mg tablets were obtained according to modified USP Ropinirole Extended-Release Tablets test 1 protocol by Revolver apparatus (Physiolution Polska Sp. z o.o., Poland). Tablets in JP sinkers were placed in a vessel of Revolver apparatus (Test Scenario A, Fig. 2). In the Test Scenario B, the tablets were positioned in the 3D printed flow through cells (Fig. 1 and 2). The paddle speed of Revolver was fixed at 100 rpm (Scenario A) and the flow rate of peristaltic pump was set at 8 ml/min (Scenario B). The tests were conducted in 900 mL of citric acid buffer pH=4.0 or 4 mM modified Hanks' buffer at 37 ± 0.5 °C for 24 h. The pH profiles in modified Hanks' buffer were simulated and controlled by integrated, 3-channel pHysio-grad® v. 2.2 (Physiolution Polska Sp. z o.o., Poland) which enables a dynamic adjustment and change of the media pH by introducing CO2 or an inert gas into the dissolution medium (Fig. 2). Samples (1 mL) were withdrawn at 1, 2, 4, 6, 8, 12, 16, 20 and 24 h and filtered through 1 µm UHMW PE cannula filters (Dissolution Accessories, The Netherlands).

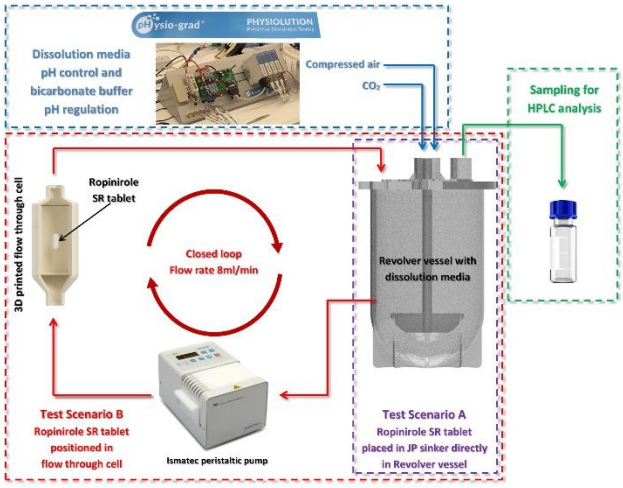

Fig. 2. Scheme of ropinirole dissolution test scenarios of Polpix SR 2 mg tablets in the Revolver apparatus.

The amount of released RH was determined using a validated RP-HPLC-UV method using a Kinetex® XB-C18 column (2.6 µm, 100 Å, 3 x 50 mm, Phenomenex,

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United States). The mobile phase was composed of acetate buffer pH=2.5, ACN and MeOH (800:140:60, v/v/v). Injections of 8 µL were made and HPLC oven and PDA detector temperatures were 35 and 40 °C, respectively.

Results and discussion

RH dissolution profiles from Polpix SR 2 mg tablets in the conditions of Test Scenario A and B are shown in the Fig. 3A and 3B, respectively. The fastest dissolution kinetics of RH was demonstrated when Polpix SR tablets were placed in JP sinkers directly in Revolver vessel with a paddle (Fig. 3A). Slightly slower and incomplete dissolution of RH was observed when tablets were positioned in the 3D printed flow through cells (Fig. 3B). We do not observed the influence of media type on RH dissolution in both scenarios (f2 > 50).

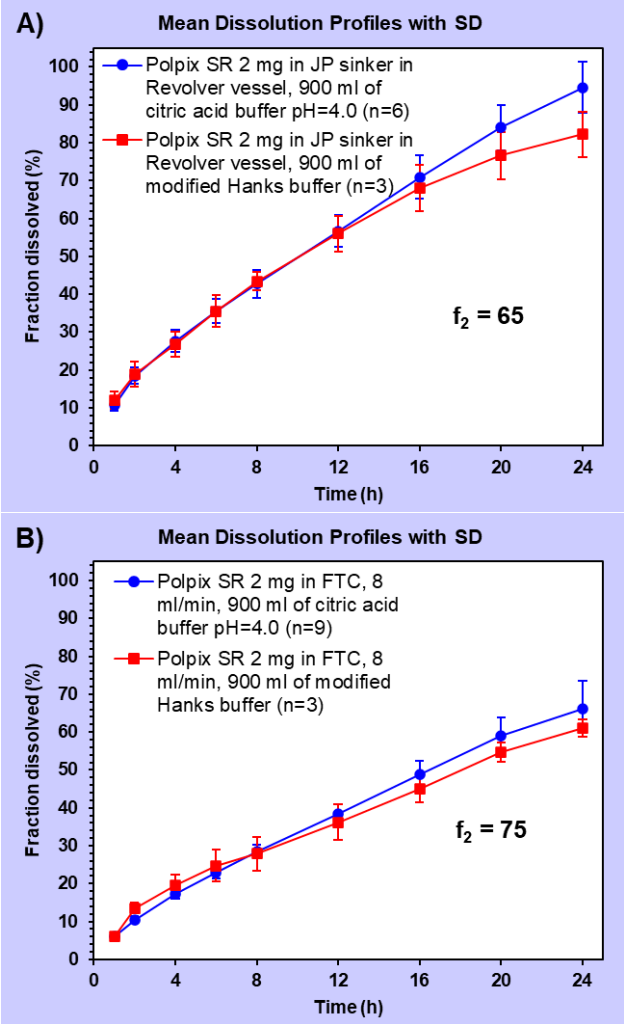

Fig. 3. The RH dissolution profiles from Polpix SR 2 mg tablets in the Revolver apparatus under: A) Test Scenario A, and B) Test Scenario B. The f2 values were calculated to compare the release profiles in various media.

Conclusion

The innovative Revolver device provides various hydrodynamic conditions and enables a dynamic adjustment and change of the bicarbonate buffers media pH to evaluate the dissolution efficiency of a sustained release dosage form. It can reflect the hydrodynamic conditions of the USP dissolution apparatus 2 (paddle) or 4 (flow-through cell). Each station is an independent unit, which can work flexibly with different dissolution test conditions and parameters. Moreover, it is cheap and thus can be a useful tool in pharmaceutical R&D labs for development of new products and to compare products properties under bio-relevant test conditions.

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