In Vitro Drug Release of Metronidazole 2% Topical Hydrogel (EctoSeal P2G) and Poloxamer Gel

Introduction:

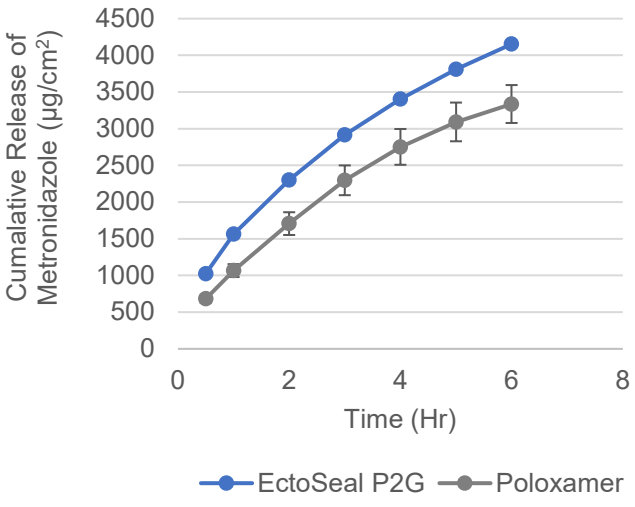
The *in vitro* drug release is a performance test for topical drug products used to measure the release rate of active pharmaceutical ingredients (APIs) from semisolid dosage forms. It is important to test the *in vitro* drug release of newly developed products (e.g., EctoSeal P2G) to ensure performance and comparability to a product of reference (e.g., Poloxamer Gel). This test is not intended though to predict *in vivo* performance, as opposed to the skin percutaneous absorption studies, since the primary factor that impacts bioavailability and clinical performance is skin permeation. However, this test can detect *in vitro* changes, as a result of formulation differences, that may correspond to altered *in vivo* performance of the dosage form. For this reason, its main purpose and use is comparison testing in which any difference in delivery rate is undesirable. This test is required by the FDA to determine the acceptability of minor processes and/or formulation changes in commercially approved semisolid dosage forms. The Unites States Pharmacopoeia (USP) recognizes different apparatus for the *in vitro* drug release test in the monograph <1724> Semisolid Drug Products – Performance Tests. The aim of this study was to evaluate and compare the *in vitro* drug release of Metronidazole 2% Topical Hydrogel (EctoSeal P2G) (PCCA Formula 14774) and Metronidazole 2% in Poloxamer 407 22% Gel. Poloxamer Gel is a well-established and referenced base used in wound management therapy, whereas PCCA EctoSeal P2G is a newly developed base with superior properties.

Methodology:

The *in vitro* drug release test was performed using the Franz Diffusion System (PermeGear, Inc.) using vertical diffusion cells (VDC) composed of 6-cell units. Each VDC cell assembly consisted of two chambers (donor and receptor chambers) separated by a membrane and held together by a clamp. The test samples (600 mg) sat on a synthetic, inert, highly permeable support membrane, intended to keep the test samples and receptor medium separate. A heating water circulator was used to maintain the temperature controlled at 37°C ± 1.00°C. The 6-cell units operated together at one time (i.e., single run). The receptor medium samples were collected at 0.5, 1, 2, 3, 4, 5 and 6 hours (Hr) by stopping the stirrer, withdrawing 1 mL of sample, and replacing the same volume with stock receptor medium.

Results and Discussion:

For each cell unit, the amount of metronidazole released (µg/cm^2) was determined at each sampling time, and the cumulative amount of metronidazole released was plotted *versus* time (Hr). Metronidazole 2% exhibited a similar *in vitro* release profile from both Topical Hydrogel (EctoSeal P2G) and Poloxamer Gel throughout the study period of 6 hours. The amount released from Topical Hydrogel (EctoSeal P2G) was slightly higher at all time points in comparison to Poloxamer Gel. By the end of the study, a total of 7,350.70 ± 49.88 µg/cm^2 (61.26%) and 5,905.56 ± 457.17 µg/cm^2 (49.21%) of metronidazole had been released from Topical Hydrogel (EctoSeal P2G) and Poloxamer Gel, respectively.



This comparative study was not designed to evaluate any statistical differences between the two bases. Instead, it is able to provide qualitative insights on the drug release performance of the bases.

In conclusion, the *in vitro* drug release test has demonstrated that metronidazole 2% has comparable release profiles when incorporated in the well-established Poloxamer Gel *versus* the newly developed PCCA EctoSeal P2G.