An In Vitro Release Test for Ketoprofen in Semisolids using Immersion Cells with USP Apparatus 2

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INTRODUCTION

Semisolid drug products are used for topical and systemic delivery of Active Pharmaceutical Ingredients (API). As stated in USP 40, General Chapter <1724>, semisolids (creams, ointment, gels, lotions, etc.) “may be considered extended-release drug preparations, and their drug release depends largely on the formulation and manufacturing process.” As a consequence, different excipients with differing physicochemical properties, and different production processes allow semisolids to be designed to achieve optimal, and commercially reproducible drug release characteristics. In order to develop, formulate, and reproducibly manufacture semisolid drug products, drug product quality and performance tests are required. In vitro tests (IVRT) serve to characterize the rate of drug released from a semisolid product, and between different semisolids to discern differences in release rate or deviations from drug release specifications of an approved product suggestive of formulation and process changes, errors in manufacturing, change of manufacturing site, or physical and/or chemical instability of the drug product. IVRT are required to verify acceptability of a formulation change, batch scaling, and change in manufacturing site. IVRT do not measure systemic absorption, bioavailability, or bioequivalence though changes in measured release-rate could correlate with these in vivo parameters since, for example, skin absorption or permeation would depend upon the API released from the drug product in a solubilized form.

METHODS

Lipoderm® and pleuronic lecithin organogel (PLO) formulations containing 10%, 20%, and 30% ketoprofen were prepared as outlined in Table 1. For each comparative drug release test, samples of equivalent strength Lipoderm® and PLO formulations were loaded into three of the six immersion cells used (immersion cell prep and experimental details in Fig. 1 and Table 2). Ketoprofen concentrations in receiver media samples were determined by HPLC (Table 3). Cumulative ug ketoprofen per cm² released over six hours was plotted versus square root of time.

RESULTS

What Defines Acceptable IVRT Data?

1. MKT less than 30% of the sample API released at last sample point

2. Data is linear when plotted against V

3. Slopes are consistent

4. No significant lag time to linearity

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5. Slopes (flux) proportional to API concentration.

CONCLUSION

Preliminary evaluation of the described IVRT for Ketoprofen topical drug products suggest it may be suitable for determining differences in drug release from different formulations and identifying changes in drug release related to variability in manufacturing processes and materials. Under the conditions of test, ketoprofen is released from PLO at a faster rate than Lipoderm®-based formulations.