



***In vitro* permeability and solubility study of mefloquine hydrochloride according to the Biopharmaceutics Classification System (BCS) guidelines**

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Mefloquine is a novel compound for the treatment of malaria; however, absolute oral bioavailability is unknown since an IV dosage form is not available. This study intends to classify mefloquine according to the Biopharmaceutics Classification System (BCS) guidelines issued by the FDA. Studies of mefloquine to date have not conducted a thorough investigation of its BCS classification, and the conflicting results suggest class I, II, or IV, partially due to inconsistent measurements of in vitro absorption behavior. The results presented here will provide BCS-relevant evidence of the absorption and permeability of mefloquine. The permeability of mefloquine was assessed in vitro using uni-directional permeability assays and will be assessed using bi-directional permeability assays with and without a pH gradient in a Caco-2 cell monolayer system, which has been fully validated at Absorption Systems. Minoxidil, a high permeability internal standard, and atenolol, a reference for monolayer integrity, were included in the unidirectional permeability experiment. The apparent permeability coefficient (P_{app}) of mefloquine was lower than that of minoxidil, with and without an apical-to-basolateral (A-B) pH gradient. This suggests that mefloquine is a low permeability drug according to BCS classification. The recovery was approximately 50%, and there was no non-specific binding, indicating significant cell accumulation. In bidirectional testing, the efflux ratio ($P_{app} \text{ B-A} / P_{app} \text{ A-B}$) will be calculated to determine the role of active transport in permeation. Further, the aqueous solubility of mefloquine will be assessed using the shake-flask method at pH 1.0, 3.0, 5.0 and 7.5.

Biography

Absorption Systems, founded in 1996, assists pharmaceutical, biotechnology, and medical device companies in identifying and overcoming ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) barriers in the development of drugs, biologics, and medical devices. The company's mission is to continually develop innovative research tools that can be used to accurately predict human outcomes or to explain unanticipated outcomes when they occur. Absorption Systems has facilities near Philadelphia, PA, and in San Diego, CA, and serves customers throughout the world. For information on the company's comprehensive contract services and applied research programs, please visit www.absorption.com.