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Pharmacokinetic/Pharmacodynamic (PK/PD) modeling of anti-neoplastic agents

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Background: A disadvantage of static models as a means to select promising chemotherapeutic agents is its inability to mimic the pharmacokinetic profiles when assessing the pharmacodynamic response. We used a pharmacodynamic in vitro hollow fiber model of breast cancer to simulate the concentration time profile of (R)-roscovitine in humans in order to compare the cytotoxic activity of two proposed dosing regimens.

Methods: MCF-7 cultures were established in hollow fiber cartridges. Viability of undisturbed cells was determined by a fluorescence assay using resazurin. (R)-roscovitine concentration was controlled to simulate the administration of 800 mg BID and TID doses. The effect of the drug was assessed using flow cytometry to measure cell cycle distribution.

Results: The TID dosage regimen achieved a 15-20% decrease in growth that was not evident with the BID experiment. There was a statistically significant decrease of the proportion of S phase cells in both the TID (p=0.004) and BID (p=0.003) doses compared to the control and a statistically significant increase in G2 for the BID experiment.

Conclusion: The hollow fiber model is advantageous for pharmacodynamic characterization of proposed dosing regimens before translation to animal models or clinical trials.

Biography

Ayman M Noreddin received his Ph.D. University of the Pacific and research training at the Department of Medicine, Stanford University, CA. He had postdoctoral fellowship, University of Manitoba followed by an American College of Clinical Pharmacy fellowship. His research interest includes Pharmacoklinetic/Pharmacodynamic modeling of anti-infective therapy, clinical simulation and bacterial resistance in biofilm studies.

Noreddin has outstanding records of scientific and academic accomplishments with multiple research funding, numerous publications in highly prestigious journals and various presentations in both national and international conferences. He served as a scientific reviewer for the NIH as well as other national and international research institutions.

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