McGill Global Health Programs

4th Annual McGill Global Health Conference

Dr. Kishor Wasan, R.PH, Ph.D.

Professor and Distinguished University Scholar, University of British Columbia and CIHR/iCo Therapeutics Research Chair in Drug Delivery for Neglected Global Diseases

Title of Talk:

Development and Evaluation of a Novel Oral Amphotericin B Formulation for the Treatment of Systemic Fungal Infections and Drug-Resistant Visceral Leishmaniasis (VL)

Abstract:

Our laboratory has made significant strides toward the development of a lipid-based amphotericin B formulation for oral administration. Initial data from both cell lines and in vivo research indicate that it is highly efficacious and exhibits low toxicity within the dosage range required in treating diseases such as systemic fungal infections and leishmaniasis.

Each year in the Indian subcontinent alone, over 500,000 individuals play host to Leishmania donovani, an insidious parasite that invades macrophages, rapidly infiltrates the vital organs and ultimately leads to severe infection of the visceral reticuloendothelial system. Visceral leishmaniasis, also known as Kala-azar, is most prevalent in the weak and the young within a population. Left untreated, almost all infected individuals will die. The therapeutic arsenal against Leishmania is limited to a small number of parenterally administered agents, with daily injections of pentavalent antimony compound for 28 days being the usual course of action. Due to increasing resistance, antimonial drugs can no longer be used in many areas, including northeastern India where the incidence of Kala-azar is highest. Amphotericin B is the current secondary treatment of choice against leishmaniasis and has a 97% cure rate with no reported resistance.

However, therapy with the first-generation formulation (FungizoneR) involves IV administration over a period of 30 to 40 days and is associated with infusion and drug-related side-effects (infection of the indwelling catheter, patient chills and shaking due to RBC haemolysis, dose-dependent renal toxicity, fever, bone pain, thrombophlebitis). Although lipid-based second-generation formulations exist (AbelcetR and AmBisomeR), which require a shorter course of therapy (3-5 days), are highly effective and exhibit lower toxicity when compared to FungizoneR, the cost of these formulations is a barrier to widespread use. Due to the difficult route of drug administration, toxicity issues and cost, amphotericin B is failing to reach the infected population and mortality rates continue to rise. The development of an inexpensive, safe and effective oral treatment is paramount in order to address both early and late stages of this deadly disease and drug-resistant forms of VL. This talk will highlight our current findings and future goals.