Pharmacokinetic Modeling of Fer-de-Lance Envenomation

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Abstract

Bothrops asper is the most dangerous poisonous snake in Southern Mexico and Central America. Its venom is known to produce myonecrosis. The myotoxins present in the venom penetrate muscle cells altering ionic transport through the sarcoplasmic reticulum membrane causing an increase in the flow of calcium into the sarcoplasm resulting in a calcium overload. This calcium overload leads to phospholipases activation causing the lysis of the muscle cell, resulting in the release of intracellular muscle components into the circulation. Myoglobin is released from damaged muscle in parallel with creatine kinease. Myoglobin enters the renal circulation where it causes renal failure by the formation of casts in the tubules. This work presents a physiologically-based pharmacokinetic (PBPK) model for the distribution and metabolism of the *Bothrops-asper* venom in the human body. A three well-mixed compartment model well describes the experimental data. Mole balance equations for each compartment are developed. Experimental data from tests carried out into mice were used in order to estimate the rate parameters. The results are later extended to human by means of interspecies scaling.

Keywords: B.asper, myotoxin, physiologically-based pharmacokinetic model.