DBG5180010

Pharmacokinetics of antimicrobial agent used in shrimp aquaculture

Executive Summary

The time course of drug distribution/elimination is always modeled by multi-compartments, mostly 2. In the beginning of pharmacokinetic studies of shrimp, several investigators borrowed human pharmacokinetic models to describe their data sometimes with success. As the physiology and anatomy of Penaeidae are totally different from advanced vertebrates, for instances the differences in their circulatory system (open *vs.* closed) and tissues/organs responsible for the drug metabolism/elimination, the models used to explain the pharmacokinetics in Penaeid shrimps should be different from those of humans. Recently, an appropriate pharmacokinetic model for oxytetracycline antibiotics has been developed that explains more accurately the behavior of the antibiotic in adult *P. vannamei.* There is now evidence that the drug does not accumulate in the edible muscle. Also that there should be a peripheral compartment that eliminates the drug instead of a process linked directly to the central compartment. This elimination or disposal compartment was related to the physiological tissues/organ namely the hepatopancreas. Further studies need to be carried out to further investigate this role of the hepatopancreas in eliminating the antibiotic as well as their distribution and accumulation in the shrimp shell.

The pharmacokinetics of an orally administered oxytetracycline antibiotics in Penaeid shrimps can be assessed with respect to both the extent and rate of absorption. The bioavailability and absorption rate constants that correspond to the extent and rate of absorption, respectively, have been commonly reported. The method to determine the former is model-independent but not the latter. As a result the obtained absorption rate parameter

depends very much on the pharmacokinetic model. Most of the studies adopted the pharmacokinetic models used for humans which might not be appropriate in cases of the application to Penaeid shrimps and have problems of validity for the estimates of the absorption rate parameter. Faroongsarng et al (2007) developed the 3-compartment "first pass" model with absorption via the hepatopancreatic compartment and successfully fitted their data with an estimate of the valid absorption kinetic parameter. In addition, it has been demonstrated that the fraction unabsorbed *vs*. time plot and the method of deconvolution could alternatively result in determining an apparent absorption rate constant with regard to the pharmacokinetic model utilized.

Toxicokinetics, a kinetic study of the drug from an extreme dose level, did exhibit signs of abnormal processes in the distribution and elimination of the drug before causing damage to tissues/organs. As there have been very few antibiotics permitted for use in shrimp farms, there is very little information available in the literature on the toxicity of these drugs except for oxytetracycline. Recently we have carried out a kinetic study of OTC in extreme dose levels. It was found that the pharmacokinetics of OTC in shrimp was altered after only a single exposure. There is now evidence that these high levels can induce damage to the shrimp hepetopancreas that effect changes to the distribution/elimination of the drug in several tissues. In addition, the abnormally high oxytetracycline levels present in the muscle and shell has to be considered when deciding safe wash-out periods.