TOXICOKINETICS OF AFLATOXIN B1

AFB1 absorption, distribution and elimination is rapid in all animal species. Animal studies have shown that under normal conditions, 50-80% of the orally administered dose of AFB_1 is quickly absorbed from the duodenal region of the small intestine of non-ruminant animals (AFSSA, 2009). In ruminants, it passes rapidly through the rumen wall. After absorption toxin enters the liver through the hepatic portal blood supply, where it is metabolised in several derivatives. It is also metabolised in other tissues such as kidney, the intestinal tract and lung, but to a lesser degree (Leong et al., 2012). The flora and fauna in the gastrointestinal tract can also metabolise aflatoxins (Upadhaya et al., 2009).

The susceptibility of an animal to AFB_1 toxicity and carcinogenicity is to a large extent dependent on the rate of metabolism and the type of metabolites that are produced. In most animals, AFB1 is metabolised to AFP_1, AFM_1, AFQ_1 and AFB_1-8,9-epoxide (Guengerich, 2003; Kamdem et al., 2006). The major route of excretion of AFB_1 and its metabolites is the biliary pathway, followed by the urinary pathway (Gratz, 2007).

The parent compound can also be excreted in faeces. In cows, pigs and sheep, AFM1 is the main unconjugated metabolite in urine. In mammals, the exposure-based biomarker AFM1 can be detected in milk within 12 h after the ingestion of AFB1 (Battacone et al., 2012). The carry-over of AFB1 in feed metabolised into AFM1 in milk for dairy cows is usually 1–2% for low-yielding cows (<30 kg milk yield/day) and up to 6% for high-yielding cows (Veldman et al., 1992).

AFB1, AFM1 and AFP1 can form nucleic acid adducts or undergo conjugation to glutathione (GSH), conversion to dihydrodiols, or binding to serum proteins or other macromolecules (mechanism-based biomarkers). The binding of AFB1 metabolites to proteins and nucleic acids occurs soon after absorption. Both the DNA and the protein adducts have proven useful as both exposure and mechanism-based biomarkers in humans and animals (Guarisco et al., 2008). Around 80% of the depurinated adducts of AFB1 to nucleic acid are excreted within 48 hours of dosing. The correlation between dietary intake and adducts in urine and serum is more variable (IARC, 2002) compared to the close correlation between the levels of adducts in urine and levels in liver (IARC, 1993). Some metabolites bound to nucleic acids can persist in tissues for relatively long periods of time. The urinary DNA adduct reflects recent exposure, as excretion occurs over 24-48 hours, whereas the serum albumin adduct reflects accumulated longer term exposure (2-3 months).

Aflatoxins cause characteristic histopathology of the liver and these lesions are a [effect-based] biomarker of aflatoxicosis (Coppock et al., 2012). The lesions induced by aflatoxins vary with the level and duration of exposure (Coppock et al., 1989). The histopathology observed includes bile duct proliferation (hyperplasia), hepatocyte necrosis, and early fibrosis of the liver (Newberne and Butler, 1969). Species differences occur in the specific histopathology of aflatoxins. Hyperplasia of the bile duct cells occurs rapidly in ducklings and may be present in horses, dogs and chickens, and mild bile duct hyperplasia may be seen in cattle and pigs (Coppock et al., 1989).

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