# *In vitro* reduction of zearalenone to β-zearalenol by rainbow trout (*Oncorhynchus mykiss*) hepatic microsomal and post-mitochondrial subfractions

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## Summary

Mycoestrogen zearalenone (ZEA) is found in human foods and animal feeds. Its estrogenic potency mainly depends on its biotransformation fate. The hepatic biotransformation of ZEA in rainbow trout was investigated in this study. Various concentrations of ZEA were separately incubated with the hepatic microsomal and post-mitochondrial sub-fractions in the presence of NADPH, and the metabolites were determined by means of HPLC. Moreover, the rate of glucuronidation for ZEA and its reduced metabolites were estimated in the presence of uridine diphosphate glucuronic acid. β-zearalenol (β-ZOL) was found to be the major metabolite of ZEA by both sub-cellular fractions. The enzymatic kinetics analyses indicated that the α-ZOL and β-ZOL production by microsomal fraction were 8- and 2-fold higher than those by post-mitochondrial fraction, respectively. High percentages of ZEA and its metabolites are conjugated with glucuronic acid at the lower concentrations. Data suggest that the hepatic biotransformation of ZEA in rainbow trout resulted in its detoxification as the main metabolite tends to be β-ZOL with weak estrogenic property. Moreover, at certain concentrations, the produced metabolites are entirely conjugated with glucuronic acid, which may consequently cause a prolonged duration of action due to entero-hepatic cycle.

**Key words:** Zearalenone, Hepatic biotransformation, Subcellular fractions, Glucuronidation, Rainbow trout

## Introduction

Fish nutritionists use plant ingredients along with other sources of proteins for fish diet formulating. According to the United Nations Food and Agriculture Organization (FAO) reports and similar reports by individual scientific groups, it has become clear that plant ingredients including vegetable oil, soybean meal, corn gluten and wheat percentages in whole fish diet has been significantly elevated (Nizza and Piccolo, 2009). As there are increasing interests for using the vegetable sources in fish diet, it would be essential to consider the safety of diet including being free from mycotoxins, too. The occurrence of various mycotoxins including zearalenone in fish meal and different plant materials such as maize, wheat, rice, and soybean has been reported (Weidenbörner, 2007).

ZEA, 6-(10-hydroxy-6-oxo-trans-1-undecenyl)-β-resorcylic acid lactone, is produced as a secondary metabolite by *Fusarium* species including *F. culmorum* and *F. graminearum* (Hestbjerg *et al*., 2002). These molds contaminate crops such as maize, barley and wheat (Yamashita *et al*., 1995; Jiménez and Mateo, 1997). The concentration of ZEA in feed materials can vary from a few micrograms up to 276 mg/kg (Vrabcheva *et al*., 1996). ZEA is a stable compound and is not degraded by routine food and feed processing procedures. Since ZEA binds to estrogen receptors (ERs) after ingestion and acts as an estrogenic compound, it is referred as a mycoestrogen (Malekinejad *et al*., 2005). Animals exposed to ZEA or ZEA-contaminated feed, show symptoms of hyperestrogenism. In this regard, previous data indicated that pigs are the most sensitive species (Decasto *et al*.,