

Technical Bulletin

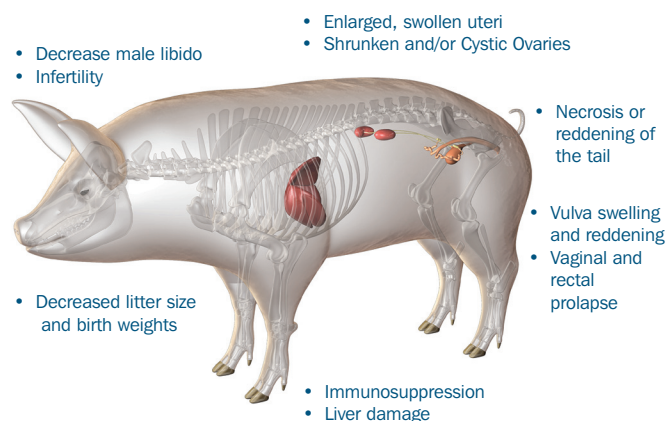
Zearalenone Toxicity, a Significant Factor in Reduced Swine Fertility and Reproduction

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The presence of zearalenone in feed is unavoidable and zearalenone toxicosis is hard to treat. The most practical way to treat zearalenone toxicosis is to use an enterosorbent to prevent the initial dietary absorption by the gut and subsequent conjugated zearalenone compounds from being reabsorbed via enterohepatic circulation. Due to its rapid absorption in the small intestine, the inactivation of zearalenone after ingestion becomes extremely critical in stopping toxicity. By understanding the absorption and metabolism of zearalenone, producers are able to select the right methods to control and treat zearalenone toxicosis more effectively and economically.

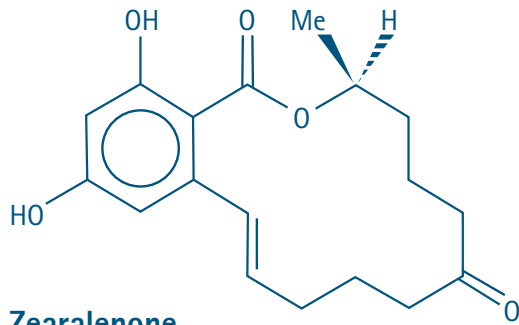
The appearance of a red and swollen vulva in gilts and increased abortions and stillbirths during gestation may indicate zearalenone contamination of the feed. The mycotoxin zearalenone is the greatest contributor to economic loss in swine reproduction.¹ It is produced by *Fusarium* fungi and commonly found in grains worldwide. Production, storage, and climate conditions all contribute to growth of these fungi.² Due to its similar chemical structure to estrogen, zearalenone causes estrogenic effects in swine,³ and affects all age groups including gilts and sows that are the most sensitive. Its clinical and subclinical symptoms are illustrated in Figure 1.

FIGURE 1. Clinical Effects of Zearalenone Toxicosis



Understanding zearalenone's biological effects and its metabolism can help swine producers manage mycotoxigenesis properly and prevent economic loss. The chemical structure of zearalenone is 6-(10-hydroxy-6-oxo-trans-1-undecenyl)- β -resorcyclic acid lactone (Figure 2). Its optically active isomer 1-form is isolated from the mycelia of *Fusarium graminearum*. It is a colorless crystalline solid with a melting point of 164-165° C, indicating that zearalenone is hard to destroy under normal feed processing. In fact, when zearalenone was present in ground corn no decomposition was seen after 44 h at 150° C.⁴ Zearalenone is slightly soluble in water and is more soluble in acetone, ether, benzene, alcohols and aqueous alkali. Due to its similarity to estrogen, zearalenone and its metabolites can bind to estrogen receptors, causing estrogenic effects in pigs.

FIGURE 2. Structure of Zearalenone



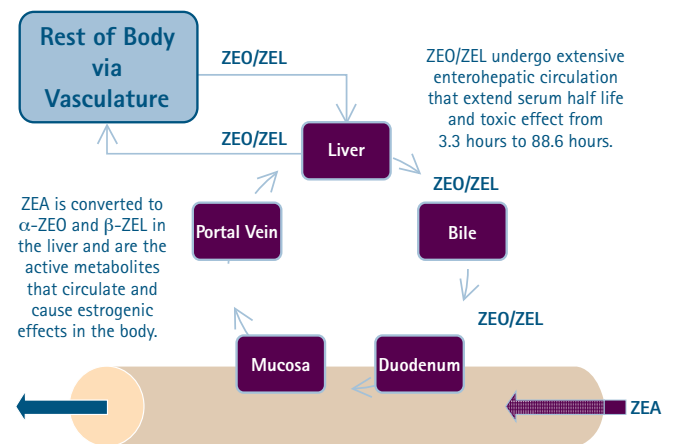
Gilts fed zearalenone contaminated feed can have prolonged estrus cycle intervals, decreased pregnancy rate, and improper fetal development. For instance, feeding 20 mg zearalenone/day for 5 days to gilts during mid or late stages of the estrus cycle significantly increased the length of inter-estrus intervals from 20 d (normal) to a 74 d (longest) interval.⁵ In a separate study, pseudo-pregnancy was increased 25%, 88%, and 88% after gilts were fed 3, 6, and 9 ppm zearalenone, respectively, prior to artificial insemination as compared to their control group.⁶

When diets contaminated with 15 or 30 ppm purified zearalenone were fed to post-mating gilts for 14 d, the number of live fetuses was reduced.⁷ In the same study, no embryonic development at all was observed in gilts fed 60 or 90 ppm dietary zearalenone. Young *et al.* (1981) reported swollen and red vulvas and reduced weight gain, feed consumption, and feed efficiency in gilts when dietary zearalenone concentrations were increased from 0 to 9 ppm.⁸ The same group reported that sows fed a diet with 10 ppm zearalenone showed an increased wean-to-estrus interval, reduction of litter size and fertility, and increased uterus weight and vaginal epithelium thickness.⁹

Yang *et al.* (2008) recently reported that feeding 1 to 3 ppm purified zearalenone to young female pigs, for 21 days, significantly increased vulva size and weight of other target organs, such as uterus, ovary, kidney and liver.¹⁰ The group also found that feeding 1 ppm of zearalenone decreased apparent crude protein and energy digestibility in postweaning female pigs and that the negative effects of zearalenone can be ameliorated by mixing a natural clay enterosorbent in the feed.¹¹

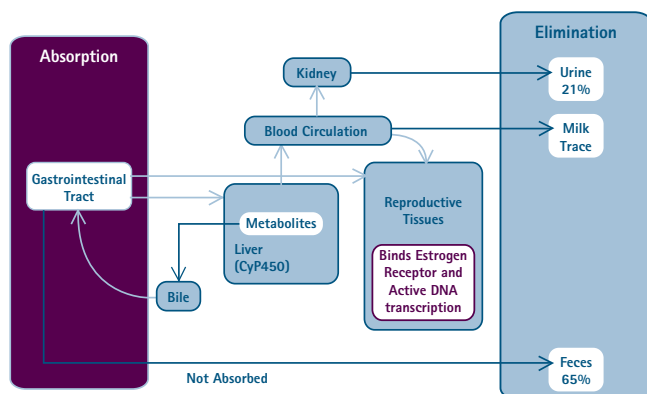
The absorption of zearalenone in the small intestine is very rapid. After a single oral dose of zearalenone in pigs, zearalenone and its metabolites can be found in the blood within few minutes, and over 85% of the zearalenone is absorbed by the intestinal lumen in less than 30 min.^{12,13} Zearalenone absorption follows first order kinetics with a K_a (kinetic constant) equal to 9.3/hr in a rat.¹⁴ Once it is absorbed into the body, enzymes such as CYP450 in the small intestine epithelial cells and the liver can quickly convert the zearalenone to α -zearalenol and β -zearalenol. The α -zearalenol has much greater estrogenic potency than its precursor in pigs. In the liver, zearalenone and its metabolites are conjugated with sugars and can be excreted into the small intestine through bile. Once conjugated zearalenone compounds travel into the small intestine, some of the compounds are excreted in feces and some are reabsorbed into the body through a cycle referred to as enterohepatic circulation (Figure 3).

FIGURE 3. Enterohepatic Circulation of Zearalenone



After zearalenone is absorbed into the body; literature suggests that there is no good treatment to reduce zearalenone toxicity in pigs. However, dietary enterosorbents may bind these conjugated zearalenone compounds, thus preventing the re-absorption via the enterohepatic circulation pathway. After a single intravenous injection of zearalenone in young pigs, zearalenone half-life in the blood was reported as 86.6 hours. However, when bile was prevented from entering the small intestine by cannulated bile duct (stopping the enterohepatic circulation), the half-life of zearalenone and its metabolites were significantly decreased to 3.3 hours.¹⁵ It suggests that the recovery rate from zearalenone toxicity can be accelerated by preventing the toxin 'recycling' in the body. Overall, about two-thirds of absorbed toxin is excreted into feces, mainly due to conjugated zearalenone compounds produced in the liver and released via bile. Water-soluble zearalenone metabolites are excreted in the urine and trace amounts of zearalenone and its metabolites are found in sow milk. The metabolism of zearalenone in sows is illustrated in Figure 4.

FIGURE 4. Zearalenone Metabolism in Sow



Preventing the initial ingestion of zearalenone absorption is key to productivity in your swine. Choosing a product that quickly binds the toxin becomes extremely critical in stopping zearalenone toxicity. By understanding the negative effects of zearalenone and how this problem can be mitigated, producers can make informed decisions on how to manage the problem.

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