

A new solution for an old problem in pig production

Nearly a century has passed since the first scientific report about hyperoestrogenism in swine was published by researchers from Iowa State College in 1928. Even then, researchers were able to connect this severe condition to corn spoiled by above-average rainfall and frost damage. In 1965, the responsible substance was isolated from *Fusarium*-culture and called 'F2'-toxin. Nowadays, the commonly used term for this mycotoxin, which continuously challenges pig production, is zearalenone (ZEN).

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Despite knowledge gained since then, satisfying solutions to counteract ZEN are still rare. When farmers are confronted with highly contaminated feedstuffs or respective clinical symptoms, causative solutions have been limited until now.

Problems caused by ZEN

Pigs are the livestock species with the highest susceptibility to ZEN, with sexually immature gilts being especially sensitive. Due to its resemblance to oestrogen, ZEN interacts with oestrogen receptors and simulates oestrogenic effects. Some of the main effects of ZEN are related to hyperoestrogenism. It was

even debated whether 'myco-oestrogen' would have been a better term to describe ZEN and its effects, which include enlargement of the genital tract and disturbance of the reproductive cycle.

Nevertheless, ZEN also causes toxic effects, including impairment of the immune system which can increase its economic impact. Under field conditions, co-occurrence of ZEN and other mycotoxins like trichothecenes (for example deoxynivalenol (DON)) is common and can potentiate a negative impact.

One visible sign of hyperoestrogenism is the swelling and reddening of the vulva of female pigs (Fig. 1). But these visible signs of hyperoestrogenism are only the tip of the iceberg. ZEN fundamentally impairs the reproductive performance of pigs and therefore the economic success of the farm. Fig. 2 summarises some of the detrimental effects of ZEN in male and female pigs.

The new solution

To counteract ZEN, Biomin has developed ZENzyme. This unique, purified enzyme hydrolyses and therefore irreversibly detoxifies ZEN. The lack of oestrogenicity of the hydrolysed ZEN (HZEN) has been proven in the laboratory (in vitro) and in animal trials (in vivo).

For the in vitro trial, a well-established model for testing oestrogen-active substances was used. Oestrogen-sensitive cells were

Female pigs	Male pigs
• Delay of first oestrus and prolongation of weaning-to-oestrus interval. • Constant oestrus. • Pseudopregnancy. • Reddening of the vulva. • Enlargement of genital tract (vulva, uterus). • Impairment of development of follicles, oocyte maturation and embryo development. • Abortion, small litters, weak piglets. • Enlargement and reddening of the vulva of newborn piglets. • Splay leg in piglets.	• Feminisation: atrophy of testes, enlarged mammary gland. • Reduction of libido and testosterone level in plasma. • Reduction of sperm motility and head abnormalities of spermatozoa. • Impairment of viability of spermatozoa and sperm membrane functionality.

Fig. 2. Some of the most detrimental effects of ZEN in pigs.

stimulated with the substance of interest and any oestrogenic potency resulted in cell proliferation. As shown by the green line in Fig. 3, the cells were not stimulated to proliferate by the hydrolysed form of ZEN. After proving this principle of detoxification in vitro, the product Mycofix Plus 5.Z (MPL 5.Z), which contains ZENzyme was tested in vivo.

Measuring the effects in prepubertal piglets

The trial was carried out by SAMITEC (Analytical, Microbiological and Technological Solutions) in Brazil. A total of 24 female, prepubertal piglets with an average weight of 9.72kg were assigned to different treatment groups as shown in Table 1. Animals in the two ZEN treatment groups were exposed to a dose of

ZEN which considerably exceeded guidance levels from the European Commission for ZEN in final feed for gilts (0.1 ppm; EU regulation 2006/576/EG). A dose of 1.5ppm ZEN can cause effects in a short period of time. All trial animals were sacrificed after 21 days. To evaluate the effects of ZEN and the efficacy of treatment with MPL 5.Z, the following parameters were assessed:

- Vulvar volume at four different time points.
- Length and relative weight of the reproductive tract at the end of the trial (day 21), including macroscopic evaluation.
- Microscopic evaluation of the uterine horn (thickness of myometrium and endometrium).
- SAMITEC Index for Zearalenone (SIZ). This index was established by SAMITEC to evaluate the efficacy of products against the negative effects

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Fig. 1. Comparison of piglets consuming a control diet (left) and a ZEN-contaminated diet (right).

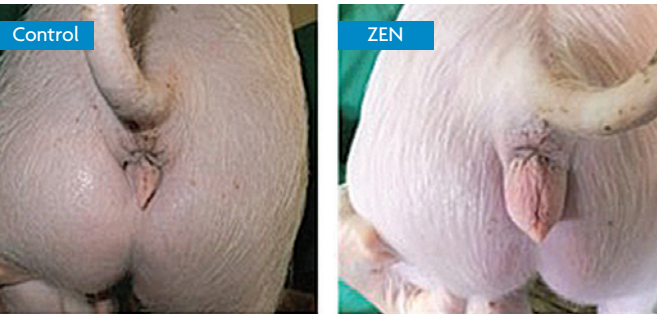


Table 1. Treatment groups.

Treatment	No. of piglets	ZEN	Mycofix Plus 5.Z
Control	6	No	No
MPL 5.Z	6	No	Yes
ZEN	6	yes (1.5ppm)	No
ZEN + MPL 5.Z	6	yes (1.5ppm)	Yes

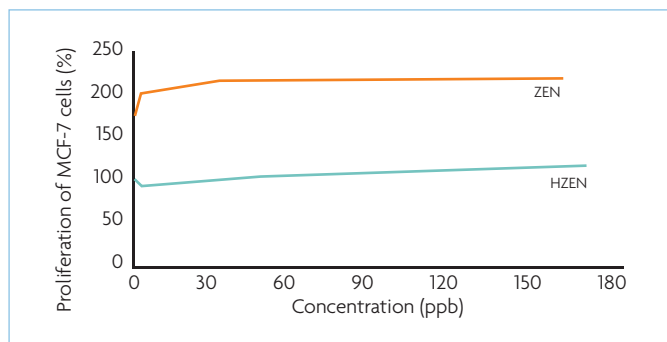


Fig. 3. Influence of ZEN and HZEN on proliferation of oestrogen-sensitive MCF-7 cells (Modified from Fruhauf et al. 2019).

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of ZEN. Calculation of the index includes vulvar volume, length and weight of the reproductive tract and development of body weight within the trial period. The higher the index, the more pronounced the effects of ZEN.

Counteracting ZEN

As expected, exposing gilts to 1.5ppm ZEN resulted in statistically significant higher average vulvar volumes (Fig. 4), an increase in the length (Fig. 5) and weight of reproductive tracts, enhanced thickness of myometrium and

endometrium, and a higher SIZ compared to the control group and the ZEN only group.

Mycofix Plus 5.Z efficiently counteracted the negative effects of ZEN in all parameters of interest (Figs. 4 and 5). Product safety was demonstrated by feeding one group of animals only Mycofix Plus 5.Z without ZEN, which did not result in any negative effects.

A new powerful tool against ZEN

The efficacy of ZENzyme was proven in the laboratory as well as in an animal trial performed in the most

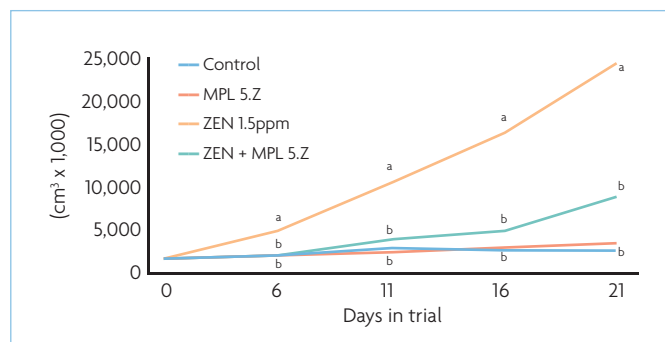


Fig. 4. Average vulvar volume (days 0, 6, 11, 16, 21; cm³ x 1,000). Different superscripts indicate statistically significant differences ($p < 0.05$).

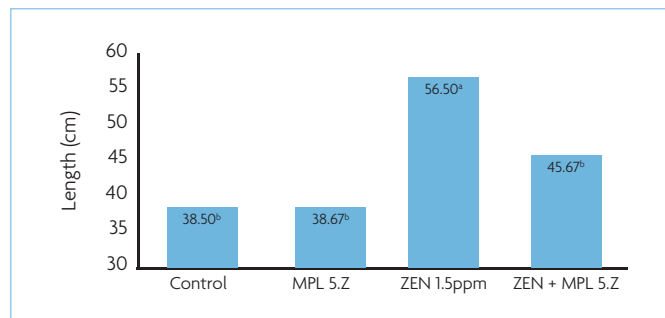


Fig. 5. Average reproductive tract length (day 21; cm). Different superscripts indicate statistically significant differences ($p < 0.05$).

sensitive group with high dosage of ZEN. Hence, a new powerful tool against the negative effects of ZEN

on pigs and other animal species is now available as part of Mycofix Plus 5.Z. ■