

BIOCHEMICAL EFFECTS INDUCED BY DEOXYNIVALENOL INTOXICATION IN PIGLETS**

A. Dinischiotu^{1*}, D. Dinu¹, M. Rebedea¹, G. Stoian¹, I. Taranu²,
D. Marin², M. Costache¹

¹University of Bucharest, Biochemistry and Molecular Biology Research Center, Faculty of Biology, Romania

²Nutrition and Animal Biology Institute, Romania

* Corresponding author: dinischiotu@yahoo.com

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Abstract: Thirty-5 weeks-old pigs were fed corn-soybean diets containing 0.5 ppm and 1.5 ppm. deoxynivalenol. Sera samples were collected from ten piglets in each group at the end of 35 days of the trial to study the effect of certain serum biochemical parameters. Highly significant ($P < 0.05$) differences were observed for serum urea and gamma glutamyl transferase between control and mycotoxin treated groups. Mycotoxin treated groups did not reveal any significant difference for serum total protein, albumin, globulin, aspartate transferase and alanine transferase.

Key words: piglet, deoxynivalenol, serum biochemical parameters

Introduction and Literature Review

Trichothecene mycotoxins are a diverse group of sesquiterpenoid metabolites (Grove, 2000) that are produced by fungi encountered in food and the environment (Pestka and Smolinski, 2005). The most frequently encountered trichothecene, deoxynivalenol (DON or “vomitoxin”), is produced by various strains of fungi including *Fusarium* spp. This compound is a common contaminant of cereal grains (Rotter et al., 1996). DON is resistant to degradation during processing (Jackson and Bullerman, 1999) and, therefore, is often encountered in human and animal food (Peska and Smolinski, 2005).

DON has been reported to produce a variety of adverse health effects in farm animals, such as reduction of feed intake (Danicke et al., 2004) and

alteration of the immune system (*Bondy and Peska, 2000*). As the cellular level, the main toxic effects of DON is inhibition of protein synthesis via binding to ribosomes and interfering with peptidyltransferase (*Goyarts and al., 2006a*).

The effects of intermediate to high levels of DON on pigs are well known and include decreased feed intake, and alteration of the immune response. Effects of low levels of DON, which commonly detected in contaminated feed, remain unknown. The aim of this study was to investigate the effects of a diet contaminated with a low concentration of DON (0.5 mg/kg feed and 1.5 mg/kg feed) on same biochemical serum characteristics.

Materials and methods

Thirty-5 weeks-old, crossbred weanling piglets were housed in floored indoor pens. The piglets (15 females and 15 males) were randomly assigned among the treatments. Piglets were fed on a corn-soybean meal basal diet and randomly assigned to one of the three treatments: one control group without DON, a 0.5 ppm

DON feed group, and a 1.5 ppm DON feed group. On the 15 day of the experiment, blood samples aseptically collected by jugular venipuncture from each animal, were allowed to clot and centrifuged at 1500 rpm for 20 min and serum were collected. Serum total protein and albumin were estimated by Lowry (*Lowry et al., 1951*) and Dumas (*Doumas et al., 1971*) methods, respectively. Serum urea was measured by the kinetic method using glutamate dehydrogenase as coupled enzyme (*Sampson et al., 1980*). Aspartate transaminase (AST) and alanine transaminase (ALT) were assayed by spectrophotometric methods of *Reitman and Frankel (1970)* and gamma glutamyl transferase (GGT) by *Szasz (1976)* method.

All values were expressed as means \pm SEM. The differences between control and manganese-treated groups were compared by Student's *t*-test using standard statistical packages. The results were considered significant if the P value was less than 0.05.

Results of Investigations and Discussion

The effects of DON treatments on piglets serum total protein, albumin and urea in piglets normal fed and DON fed are presented in Table 1.

Comparison of means of serum total protein, albumin and globulin not reveal any significant differences between control and DON treated groups. Serum urea concentration was affected by DON administration in the food of piglets. Thus, at 0.5 ppm DON, the serum urea has increased by 43.1%, while 1.5 ppm DON administration the increase was 50.7%.

Table 1. Serum biochemical values of piglets after 15 days of DON treatment^a

<i>DON</i> (ppm)	<i>Total protein</i> (g/L)	<i>Albumin</i> (g/L)	<i>Globulin</i> (g/L)	<i>Urea</i> (g/L)
0	61.7 ± 5.3	29.7 ± 3.6	32.0 ± 3.9	20.9 ± 1.6
0.5	60.5 ± 4.1	31.9 ± 2.7	28.6 ± 1.9	29.9 ± 0.9*
1.5	62.4 ± 3.9	28.1 ± 2.4	34.3 ± 4.3	31.5 ± 3.2*

^a values are expressed as mean ± SEM/

* P < 0.05 vs. control+

Serum AST, ALT and GGT activity of piglets fed with DON are shown in Figure 1. The results, which are illustrated in Figure 1, indicate that the AST and ALT activities remained unaltered in serum after DON administration, while different results were noticed for GGT. Its activity level increased by 15.8% after 0.5 ppm DON treatment, and the increase was 2.5-fold higher after 1.5 ppm DON treatment, as compared to the control groups animals.

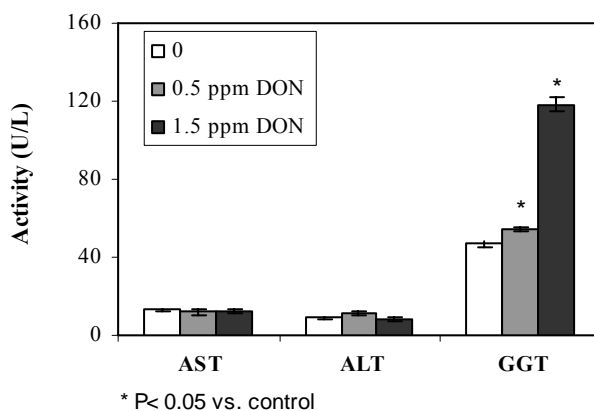


Figure 1. Effect of DON on serum enzyme of piglets

Trichothecenes, such as DON, are known to inhibit synthesis by binding

at the 60S subunit of eukaryotic ribosomes. Therefore, cells and tissues with high protein turnover, such as the liver, were suggested to react most sensitively to DON. This observation was not extensively investigated in pigs, the farm animals most susceptible to DON. A dose response study was carried out with piglets in order to examine the effects of increasing dietary DON-concentration on some clinical serum characteristics.

In the present study, we did not find any effect of DON on serum total protein, albumin and globulin (Table 2). These findings suggested that, 0.5 ppm and 1.5 ppm of DON administration in piglets food, has not an inhibitory effects on protein synthesis. No changes in serum total protein, albumin and globulin were also reported in pig for a subchronical diet containing 0.1 mg DON/kg (*Goyartss and al.*, 2006b). A significant increase in serum urea level was recorded ($P < 0.05$ vs. control). The increases in serum urea levels observed at both DON concentration suggested a progressive kidney damage induce by this mycotoxin. Our results were different from these of *Accenci et al.*, (2006), who showed that. low concentration of DON (between 280 and 840 $\mu\text{g}/\text{kg}$ food) did not modify 18 biochemical variables, including urea.

The serum transaminases, AST and ALT, were not affected by DON treatment, while the serum GGT activity was significant increase (Figure 2). The up-regulated of GGT, more than 2.5 fold, suggested alterations of the liver cells.

Conclusions

The results of this study showed specific changes in pigs serum parameters as a consequence of DON administration. The evaluation of serum urea level and GGT activity appeared to be suitable for distinguishing DON-related effects, while determination of serum protein concentrations seemed not to be an appropriate parameter.

BIOHEMIJSKI EFEKAT IZAZVAN INTOKSIKACIJOM PRASADI DEOKSINIVALENOLOM

*A. Dinischiotu, D. Dinu, M. Rebedea, G. Stoian, I. Taranu, D. Marin,
M. Costache*

Rezime

Deoksinivalenol (DON), mikotoksin koji proizvodi *Fusarium* spp., je čest kontaminant žitarica. Zbog ishrane koja je bogata žitaricama, svinje mogu biti izložene dejstvu ovog mikotoksina. Uticaj niskih do srednjih nivoa DON-a koji se obično otkrivaju u zagađenoj hrani, nisu na najbolji način objašnjeni. Cilj ovog istraživanja je bio ispitivanje uticaja obroka prirodno kontaminiranog sa dve koncentracije DON-a (0.5 ili 1.5 mg/kg hraniva) na neke biohemijske parametre.

Ukupno trideset odbijene prasadi, meleza u uzrastu od 5 nedelja je hranjeno sa obrokom koji je bio kontaminiran DON-om (0.5 ili 1.5 mg/kg hraniva) ili kontrolnim obrokom bez mikotoksina. Nakon 15 dana ishrane, uzimani su uzorci krvi, aseptički, radi separacije seruma. Parametri integriteta jetre i bubrega i iste odabrane metaboličke komponente metabolizma proteina su ispitivani.

Nije registrovana razlika u koncentraciji ukupnog proteina, albumina i globulina između grupa. Koncentracija uree u serumu je bila pod uticajem davanja DON-a kroz obroke korišćene u ishrani prasadi, ali povećanje nivoa ove komponente krvi nije bilo zavisno od doze. Ova promena u nivou uree ukazuje na progresivno oštećenje bubrega koje izaziva ovaj mikotoksin.

Neki enzimi seruma, na primer aspartat aminotransferaza, nisu pokazivali nikakav sistematski uticaj..

Gama glutamil transferaza u serumu je bila pod uticajem DON-a. Ovaj enzim u serumu je povećan za više od 2.5 puta pri koncentraciji od 1.5 ppm DON-a u obroku za ishranu pilića. Povećanje gama glutamil transferaze bi moglo do ukase na uticaj tretmana DON-om na jetru.

Može se zaključiti da je određivanje uree u serumu i gama glutamil transferaze pogodno za razlikovanje uticaja koji su vezani za DON.

References

- ACCENSI, F., PINTON, P., CALLU, P., ABELLA_BOURGES, N., GUELFU, J.F., GROSIEAN, F., OSWALD, I.P. (2006): Ingestion of low doses of deoxynivalenol does not affect hematological, biochemical, or immune responses of piglets. *J. Anim. Sci.*, 84, 1935-1942.
- BONDI, G.S., PESKA, J.J. (2000): Immunomodulation by fungal toxins. *J. toxicol Environ Health B Crit. Rev.*, 3, 109-143.
- DANICKE, S., VALENTA, M., KLOBASA, F., DOLL, S., GANTER, M.,

- FLACHOWSKY, G. (2004): Effects of graded levels of Fusarium toxin contaminated wheat in diets for fattening pigs on growth performance, nutrient digestibility, deoxynivalenol balance and clinical serum characteristics. *Arch. Anim. Nutr.*, 58, 1-17.
- DOUMAS, B., WATSON BIGGS, H. (1971): Albumin standards and the measurement of serum albumin with bromocresol green. *Clin. Acta*, 31, 87-96.
- GOYARTS, T., DANICKE, S., TIEMANN, U., ROTHKOTTER, H.J. (2006a): Effect of the Fusarium toxin deoxynivalenol on IgA, IgM and IgG concentration and proliferation of porcine blood lymphocytes. *Toxicol. In Vitro*, 20, 858-867.
- GOYARTS, T., GROVE, N., DANICKE, S. (2006b): Effects of the Fusarium toxin deoxynivalenol from naturally contaminated wheat given subchronically or as one single dose on the in vivo protein synthesis of peripheral blood lymphocytes and plasma proteins in the pigs. *Food Chem. Toxicol.*, 44, 1953-1965.
- GROVE J. (2000): Non-macrocytic trichothecenes. Part 2. *Prog. Chem. Org. Nat. Prod.*, 68, 1-70.
- JACKSON L.S., BULLERMAN, L.B. (1999): Effects of processing on *Fusarium* mycotoxins. *Adv. Exp. Med. Biol.*, 459, 243-261.
- LOWRY, O.H., ROSEBROUGH, N.J., FARR, A.L., RANDALL, R.J. (1951): Protein measurement with the Folin phenol reagent. *J. Biol. Chem.*, 193, 265-275.
- PESKA, J.J., SMOLINSKI, A. (2005): Deoxynivalenol: Toxicology and potential effects on humans. *J. Toxicol. Environ. Health, Part B*, 8, 1-5.
- REITMAN, S., FRANKEL, S. (1970): Glutamate-oxaloacetate transaminase. In: Bergmeyer, H.U., (ed). *Methods of enzymatic analysis*. Chemie Verlag, Weinheim, Germany, pag. 723-727.
- REITMAN, S., FRANKEL, S. (1970): Glutamate-pyruvate transaminase. In: Bergmeyer, H.U., (ed). *Methods of enzymatic analysis*. Chemie Verlag, Weinheim, Germany, pag. 691- 685.
- ROTTER, B.A., PRELUSKI, D.B., PESKA, J.J. (1996): Toxicology of eoxynivalenol (vomitoxin): *J. Toxicol. Environ. Healt*, 40, 110-134.
- SAMPSON, E.J., BAIRD, M.A., BURTUS, C.A. (1980): A couplet-enzyme equilibrium method for measuring urea in serum. *Clin. Chem.*, 26, 816-826.
- SZASZ, G. (1976): Reaction rate method for gamma glutamyl transferase activity in serum. *Clin. Chem*, 22, 2051-2055.