

*Research proves an isotonic protein solution can reduce PEDV shedding, with beneficial effects on the intestine and favorably modulates the intestinal immune response.*



# Efficacy of an isotonic protein solution against porcine epidemic diarrhea confirmed



**MATHIEU CORTYL\* presents a trial that confirms that an isotonic protein solution significantly reduced Porcine Epidemic Diarrhea Virus shedding, maintained intestinal tissue integrity, and modulated the immune response and tissue repair.**

## Background

Anecdotally the isotonic protein solution (IPS), known as Tonisity Px has been reported to be effective in supportive treatment of piglets with active porcine epidemic diarrhea virus (PEDV) infections. A 2024 peer-reviewed article in the *Veterinary Immunology and Immunopathology* journal, a leading international journal of comparative immunology, however, is the first report to show a beneficial impact on PEDV using a commercially available swine feed product – Tonisity Px.

Tonisity Px is unique in that it is delivered as a supplementary liquid drink that is consumed voluntarily by neonatal pigs who are still primarily dependent upon suckling the sow's

milk, at a moment when there is an opportunity to positively modulate intestinal development. Piglets of this age are the ones most commonly affected by PEDV, with mortality rates of 50-80%.

## Trial design

The study examined the effects of administering Tonisity Px (120 mL/pig/day of a 3% IPS) via the drinking water to 14-day-old PEDV-infected piglets. All 16 piglets in the IPS group consumed the product voluntarily and quickly each day, verified by visual confirmation of the empty drinking pans.

Outcomes were measured on indicators of intestinal integrity, ▷

immune response, tissue repair and virus shedding. Piglets were followed for 21 days, with samples taken at 1, 5, 14 and 21 days after infection.

### Biomarkers

Four key biomarkers, related to the pathologies of PEDV, and considered to be key indicators of cell adhesion and gut integrity, as well as immune response and gut remodeling were measured:

E-cadherin and fibronectin are structural proteins in the intestine. E-cadherin contributes to epithelial barrier formation by regulating the incorporation of claudins into tight junctions. E-cadherin is also important for clearance of pathogens, suggesting its importance in the intestinal immune system. Fibronectin plays an important role in the homeostasis of the barrier function of the intestinal mucosa. During a mucosal injury, fibronectin participates in the restoration of epithelial integrity.

Interferons (IFNs) - the body's first line of antiviral defence - are cytokines that are secreted by host cells in response to virus infection, and block virus replication at many levels. IFN-α may also exert an anti-inflammatory effect.

MMP-9 is a matrix metalloproteinase enzyme that aids in tissue remodeling, and also participates in the initiation of pro-inflammatory responses.

### Results

#### Biomarkers

##### 1. E-cadherin

E-cadherin did not change significantly over time in the IPS group. However, the E-cadherin content was significantly lower for the control group on days 14 and 21 post-infection compared to day 1 (Figure 1).

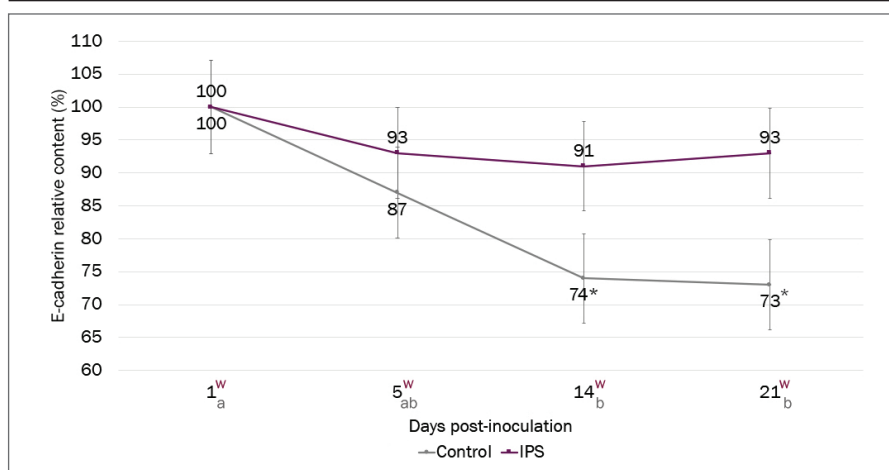
##### 2. Fibronectin

Fibronectin did not change significantly over time in the IPS group, and never reached lower than 90% of the baseline level. However, the fibronectin content was significantly lower for the control group on days 5, 14 and 21 post-infection compared to day 1 (Figure 2).

##### 3. IFN-α

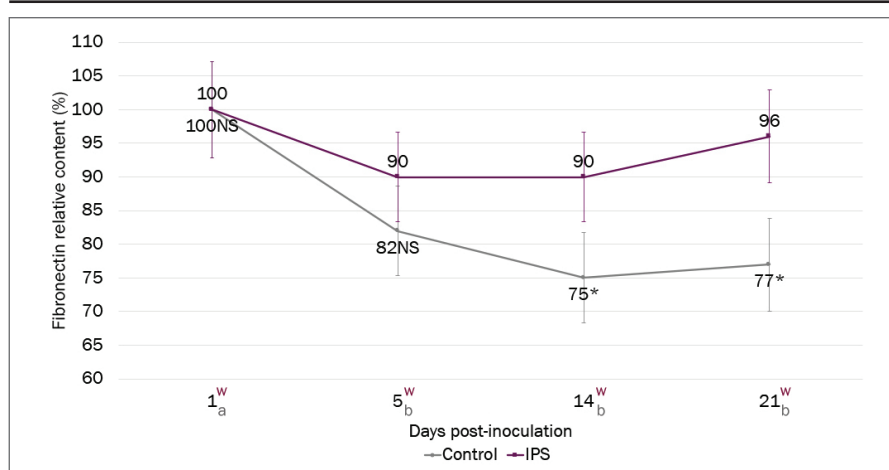
Compared to the control group, the IFN-α content was significantly

**Figure 1: Relative content (%; LS means and 95% confidence interval) of E-cadherin in the duodenum of PEDV-infected piglets (n = 4 piglets/treatment/sampling day).**



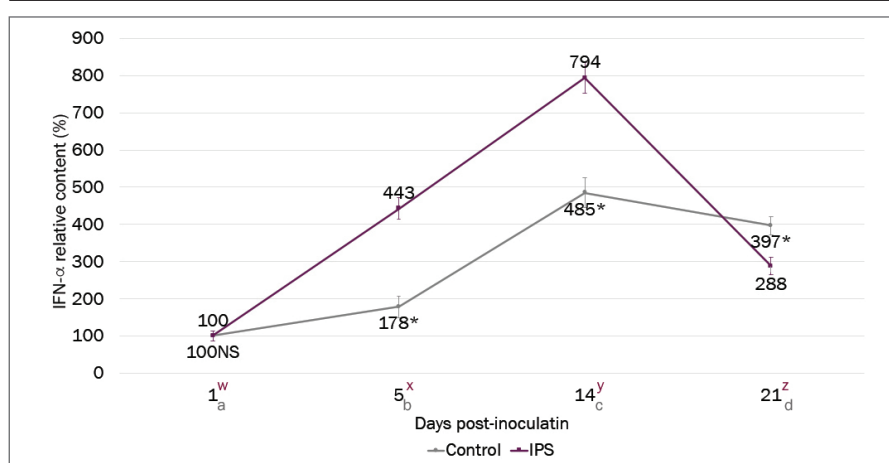
\*( $p \leq 0.05$ ); NS ( $p > 0.05$ ) indicate differences between treatment groups at the same time point; Different superscripts indicate differences between dpi, separately for each of the treatment groups (a,b,c,d Control; w,x,y,z IPS).

**Figure 2: Relative content (%; LS means and 95% confidence interval) of fibronectin in the duodenum of PEDV-infected piglets (n = 4 piglets/treatment/sampling day).**



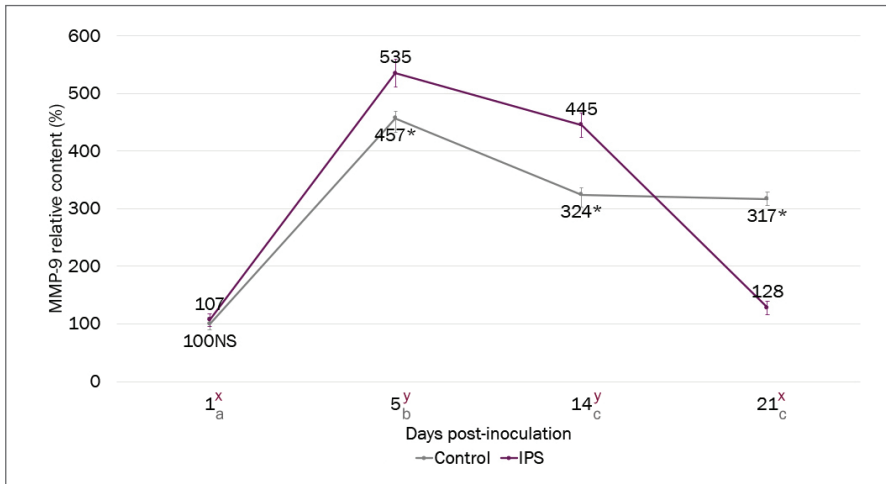
\*( $p \leq 0.05$ ); NS ( $p > 0.05$ ) indicate differences between treatment groups at the same time point; Different superscripts indicate differences between dpi, separately for each of the treatment groups (a,b,c,d Control; w,x,y,z IPS).

**Figure 3: Relative content (%; LS means and 95% confidence interval) of IFN-α in the duodenum of PEDV-infected piglets (n = 4 piglets/treatment/sampling day).**



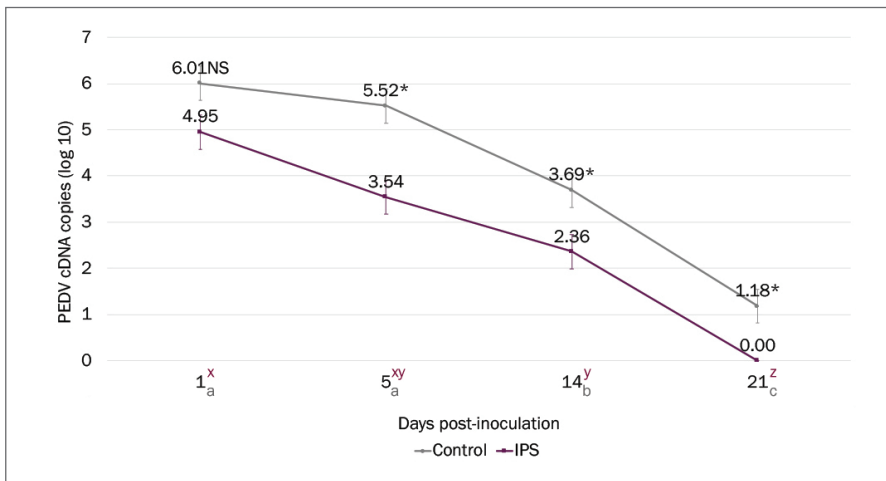
\*( $p \leq 0.05$ ); NS ( $p > 0.05$ ) indicate differences between treatment groups at the same time point; Different superscripts indicate differences between dpi, separately for each of the treatment groups (a,b,c,d Control; w,x,y,z IPS).

**Figure 4: Relative content (%; LS means and 95% confidence interval) of MMP-9 in the duodenum of PEDV-infected piglets (n = 4 piglets/treatment/sampling day).**



\*( $p \leq 0.05$ ); NS ( $p > 0.05$ ) indicate differences between treatment groups at the same time point; Different superscripts indicate differences between dpi, separately for each of the treatment groups (a,b,c,d Control; w,x,y,z IPS).

**Figure 5: PEDV content dynamics in the feces of PEDV-infected piglets (n = 4 piglets/treatment /sampling day).**



\*( $p \leq 0.05$ ); NS ( $p > 0.05$ ) indicate differences between treatment groups at the same time point; Different superscripts indicate differences between dpi, separately for each of the treatment groups (a,b,c,d Control; w,x,y,z IPS).

higher in the IPS group at day 5 and 14 and significantly lower on day 21 (Figure 3). The fact that both  $IFN-\alpha$  (and MMP-9, Figure 4) were lower in the IPS group on day 21 is a beneficial effect. Since both these markers are involved in tissue remodelling, the day 21 levels suggest that a return to a "normal" homeostatic state occurred more quickly in the IPS group.

#### 4. MMP-9 activity

Compared to controls, the active form of MMP-9 (80 kD protein) was significantly higher on days 5 and 14 and significantly lower on day 21 in the IPS group (Figure 4).

#### Virus shedding

Both groups had statistically similar

levels of PEDV at day 1. IPS pigs had a significantly lower PEDV load at all subsequent time points, with no detectable PEDV at day 21 (Figure 5).

#### Summary

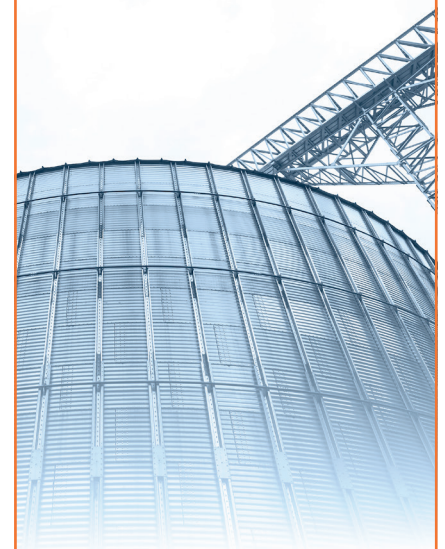
The piglets who consumed Tonisity Px shed less PED virus on days 5 and 14 post-infection and had cleared the virus by day 21 post-infection. This outcome was in contrast with the control group which had detectable virus excretion up to the end of the study (day 21 post-infection).

At the intestinal level, the Tonisity Px piglets had better intestinal tissue integrity than control piglets. This study is the first report of this panel

of biomarkers in the face of live pigs with PEDV infection, which also makes the study important on an immunological level. *Ap*

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