



PATENTE HERBA[®]
PLUS

**ADVANCED NATURAL PIG
GUT HEALTH ENHANCER**

**Persistent enteric
pig diseases
experts in prevention**



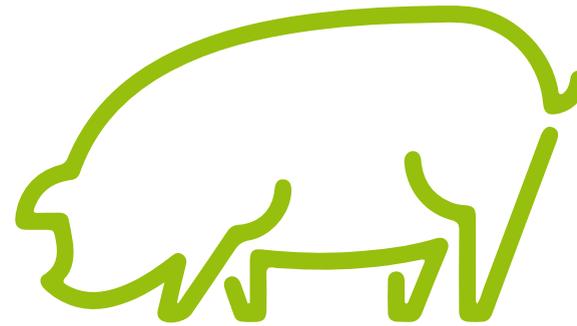
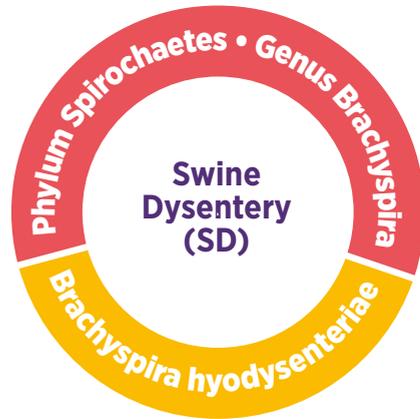
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persistent enteric pig diseases

the worldwide problems

Pig enteric diseases are a significant economic factor in pig production management due to the negative impact on performance and the increased expenses of treatment and preventative measures. **Two of the most commonly present enteric diseases worldwide are porcine proliferative enteritis (PPE), caused by *Lawsonia intracellularis* and swine dysentery (SD), caused by *Brachyspira hyodysenteriae*.**

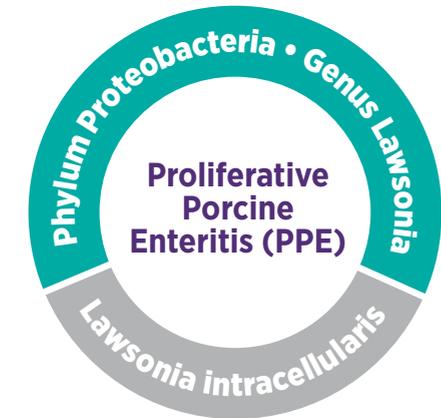


Antibiotic Growth Promoters (AGP) are used as a regular additive in pig nutrition to control pig enteric diseases such as swine dysentery and post-weaning diarrhea.

Antibiotic resistance has been caused by misusing antibiotics as a feed additive in a preventive dosage. Constant use of AGP has led to high antibiotic residues in animal products

The ban of AGP in 2006 in Europe and the trend of using it less on other continents, although fully justified due to increased bacterial resistance in humans and animals, has led to the following consequences: increased morbidity and mortality due to enteric infections, decreased weight gain, and increased therapeutic application of antibiotics. The ban has as a result also increased the problems in pigs' diarrhea and chronic infections due to *L. intracellularis* and *B. hyodysenteriae*.

Maintaining a Healthy Pig Gut is imperative in sustainable and cost-effective pig production. Guts are the largest organ of the immune system, whose function is influenced by multiple factors, such as: probiotic and pathogen microbiome interactions, quality of the nutrition, efficacy of digestion and absorption and production management-animal welfare.



The serology testing has revealed that 48-100% of pig farms are infected with *L. intracellularis* world wide.

Public pressure to decrease the use of antibiotics in controlling *L. intracellularis* related disease due to antibiotic resistance has led to the global demand to find suitable Natural Growth Promoters (NGP).

The lack of adequate veterinary-sanitary measures makes the incidence of SD up to 90% and mortality up to 50%.

Dramatically increasing resistance to several antibiotics that can be used in controlling SD requires more research to be conducted on developing new preventive measures.

CHALLENGES OF VETERINARIANS AND FARMERS



Reduction of weight gain



Increased feed conversion ratio



Increased mortality and morbidity



Decreased slaughter weight



Increased space utilization



Increased medical treatment expenses



Increased expenses of vaccination against PPE



Increased expenses of biosecurity improvement



Increased occurrence of diarrhea



Decreased animal-welfare

GLOBAL DEMAND FOR A NATURAL PIG GUT HEALTH ENHANCER

factsheets about SD and PE

—Etiology and Pathogenesis

L. intracellularis is a Gram-negative, microaerophilic, obligate intracellular, non-spore-forming, curved or S-shaped bacillus.

L. intracellularis invades the intestinal epithelial cells of mainly ileum and it is located in the apical membrane. Host reaction to the presence of bacteria is epithelial cell hyperplasia, crypt elongation, degeneration and necrosis of enterocytes, fewer goblet cells, and an inflammatory response. Less common acute form of PPE is characterized with increased congestion and hemorrhage of mucosal vasculature.

—Clinical signs

There are 2 main forms of Porcine Proliferative Enteropathy (PPE) caused by *L. intracellularis*:

1. CHRONIC

a) Subclinical form of PPE, common

- No clinical signs, except financial losses due to low production performance

b) Pig Intestinal Adenomatosis (PIA), common

- 6-20 week old pigs with low performance and occasional moderate remittent diarrhea, without change in the feces color
- low mortality

c) Necrotic Enteritis (NE), less common

- Secondary infection in pigs with the PIA form of intestinal disease

d) Regional Ileitis (RI), less common

- Recovery form of NE

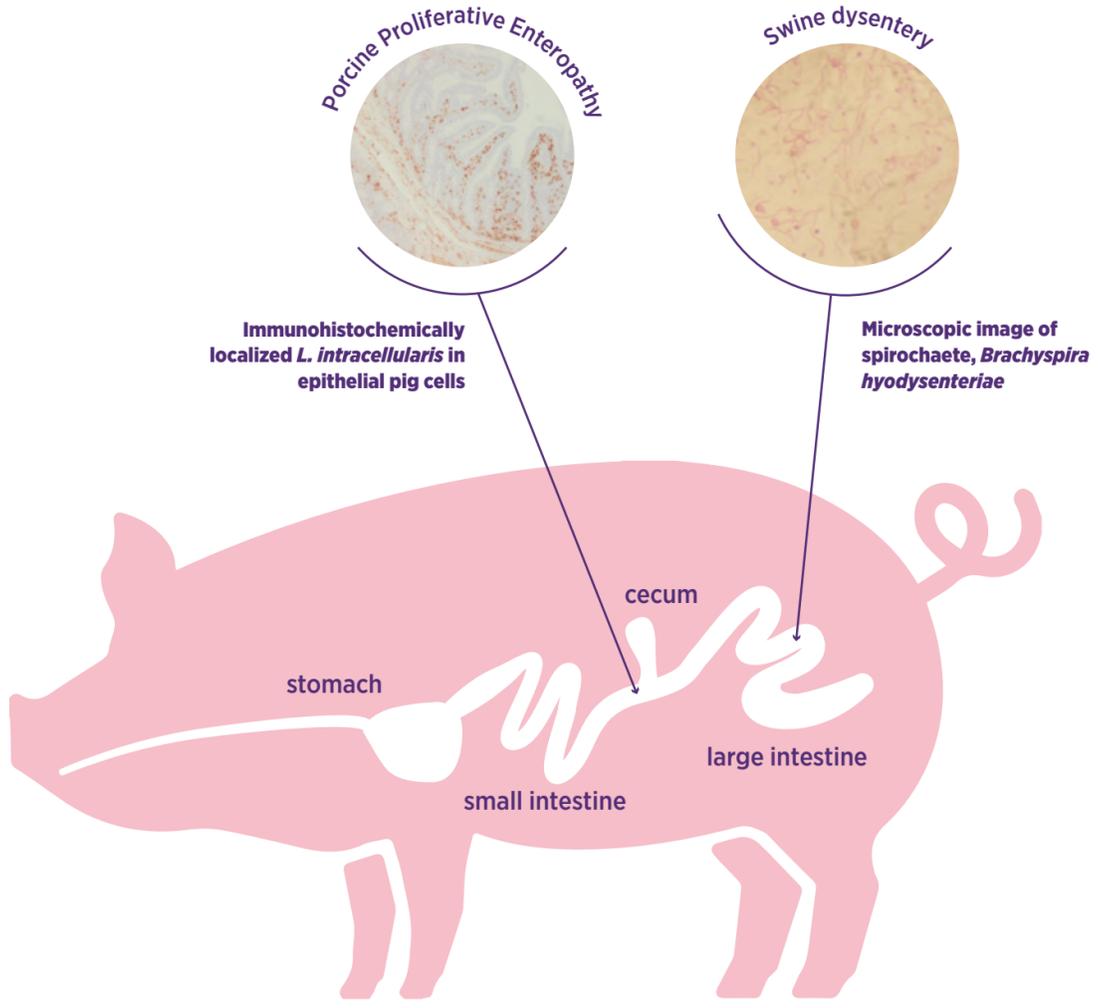
2. ACUTE, less common

a) Proliferative Hemorrhagic Enteropathy (PHE),

- Affecting 4-12 month old pigs
- Clinical signs include severe, dark brown-bloody watery diarrhea, abortions and sudden death.
- Necrotic



When guts look like a brain - It is *L. intracellularis*



—Etiology and Pathogenesis

B. hyodysenteriae is the main causative agents involved in pathogenesis of swine dysentery.

The bacteria is a Gram-negative, motile, anaerobic, loosely coiled spirochaete and demonstrates haemolytic activity on blood agar. The main virulence factors of *B. hyodysenteriae* are haemolysin, endotoxin, lipopolysaccharide (LPS). The pathogen is present in mucous of the lumen and crypts of the porcine cecum and colon. Pathogen penetrates through mucous and damage enterocytes.

Decreased ability of the mucosa to reabsorb endogenous secretions from the unaffected small intestine results in diarrhea.

—Clinical symptoms

B. hyodysenteriae causes a severe mucohemorrhagic diarrheal disease of weaning to finishing pigs. Infection is characterized by mucosal swelling, increased mucus production, lesion formation and hemorrhages, necrosis of tissue and reabsorption failure.

- **The incubation period usually lasts 1-2 weeks;**
- The first evidence of the disease is soft yellow to gray feces that last for one day.
- After a few hours or days, feces has large amounts of mucus, mucofibrinous or bloody pieces appear in the feces.
- High fever (40°C) in some animals;
- Apathy, anorexia, weak legs;
- Occur in a cyclic manner at 3 to 4 weeks intervals, with these recurring symptoms often appearing only after removal of therapeutic antibiotics
- Prolonged diarrhea leads to dehydration and increased thirst.



Typical for swine dysentery: mucofibrinous grains in the bloody stool

—stress

the major risk factors for both diseases:



Changes in nutrition



Transport



Inadequate praxis



Overcrowding of pigs in pens



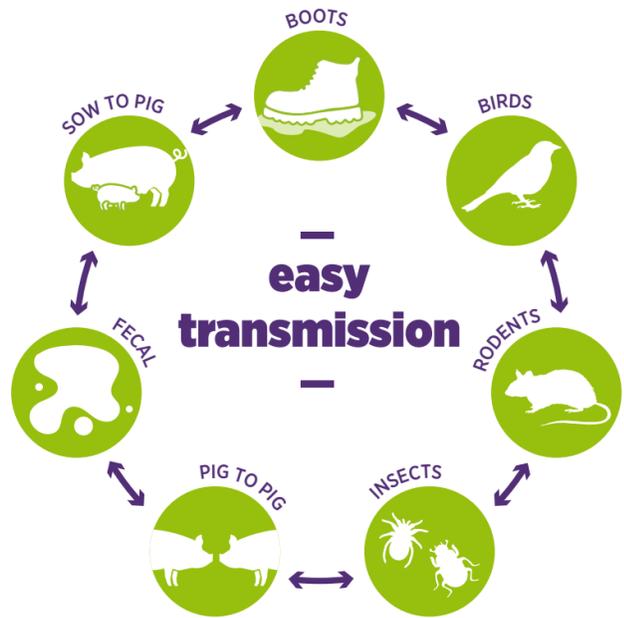
Castration



Mycotoxicosis



Exposure to large temperature changes



PATENTE HERBA PLUS

advanced natural pig gut health enhancer

PATENTE HERBA PLUS is an innovative nature-based solution to improve pig performance by promoting stable gut health. The product is composed of a carefully balanced mix of essential oils (dominantly *Thymus vulgaris*, *Origanum vulgare*, *Coriandrum sp.*), extract of *Castanea sativa*, encapsulated lysozyme and nicotine amide. PATENTE HERBA PLUS as a naturally-derived feed additive belongs to the group of NGP feed additives.

—nature's patent

• mixture of essential oils blend



• suppl. encapsulated lysozyme • suppl. nicotinamide

—PATENT CO's quality control

Efficacy and Safety of all PATENT CO's natural products are ensured by monitoring processes from procurement of raw materials through production to final control and distribution. All QC procedures in PATENT CO are in accordance with implemented practice of FAMI QS, HACCP, and ISO 2200.



—mode of action

DIRECT

- Antimicrobial effects of thymol, carvacrol and tannins
- Synergetic antimicrobial effect of lysozyme and essential oils
- Antioxidant effect of essential oils and tannins

INDIRECT

- Essential oils and tannins increase feed palatability and digestive juices secretion → fewer nutrients for pathogenic agents such as *B. hyodysenteriae* in the large intestine;
- Prebiotic effects of tannins from *Castanea sativa*
- Nicotinamide has an indirect antimicrobial effect due to specific immunomodulatory actions and it has no significant side effects.

—healthy gut!

- ▲ Improved balance of gut microbiota
- ▲ Improved animal welfare
- ▲ Improved immune defense
- ▲ Improved digestion and absorption of feed
- ▼ Reduced enteric diseases
- ▲ Increased feed intake
- ▼ Reduced incidence of diarrhea
- ▼ Reduced mortality
- ▼ Reduced cost of treatment
- ▲ Higher profitability

—product characteristics

EFFECTIVE

In preventing and controlling all non-specific diarrhea especially associated with *B. hyodysenteriae* and *L. intracellularis*, through out the hole post-weaned and fattening period

PROFITABLE

- Improves weight gain and FCR
- Decreases mortality
- Reduces use of antibiotics

FAST

In eliminating the symptoms of diarrhea caused by *B. hyodysenteriae* and *L. intracellularis* only a few days after application

SAFE

- No withdrawal period
- No development of bacterial resistance
- No contraindication



—dosage



In vitro trial

PATENTE HERBA PLUS influence on *B. hyodysenteriae* growth *in vitro*



CLSI, Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition. CLSI document M11-A8. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.

▶ PATENTE HERBA PLUS inhibits growth of *B. hyodysenteriae*

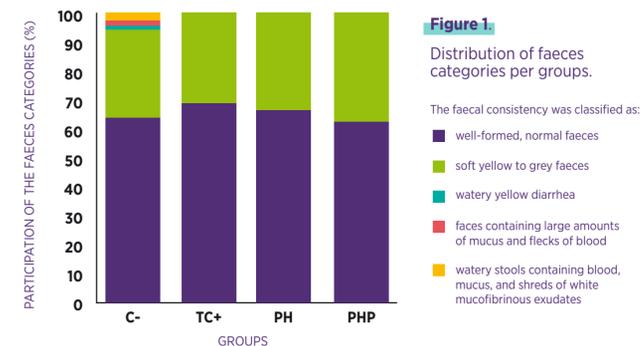
*National Chaiyi University, College of Veterinary Medicine, Taiwan

In vivo trial I

The efficacy of PATENTE HERBA PLUS in the control of swine dysentery

4 groups
 PHP- trial group
 PATENTE HERBA PLUS dose 1 kg/ton
 PH - trial group
 PATENTE HERBA dose 2 kg/ton
 C- - negative control
 TC+ - positive control group
 2 kg/ton Tiamulin

21 days
64 pigs
 seven weeks old post-weaning piglets in every group



The presence of *B. hyodysenteriae* in the feces was investigated weekly using microbiological assays and the PCR test.

CONCLUSION:

PATENTE HERBA PLUS prevents an outbreak of SD and improves ADG and FCR parameters in post weaned piglets, highly affected with SD.

PATENTE HERBA PLUS is reliable in controlling SD.

References:
 1. Delic et al., 2018. The Efficacy of Two Phytogetic Feed Additives in the Control of Swine Dysentery. Acta veterinaria, 68(2), 178-189.
 2. Draskovic et al., 2019 Effects of phytogetic feed additive on post-weaned piglets naturally infected with Brachyspira hyodysenteriae. Asian Pig Veterinary Society Congress (APVS 2019)- August 25-28, 2019, Seoul, Korea (Poster).

In vivo trial II

PATENTE HERBA PLUS efficacy in young fattening pigs with *L. intracellularis* associated diarrhea

2 groups
 T - trial group
 C1 - negative control

35 days
10 pigs
 aged 12 weeks at the start of the trial in every group

Analyses:
 Determination of *L. Intracellularis* DNA copies number in a gram of feces by real-time qPCR

Parameters	Trial Group	Control group
N° animal at the beginning of the trial	10	10
Mortality (N° animals)	0	0
N° of DNA copy of <i>Lawsonia intracellularis</i> 1 st day in pooled fecal sample	0	0
N° of DNA copy of <i>Lawsonia intracellularis</i> 14 th day in pooled fecal sample	55	1930
N° of DNA copy of <i>Lawsonia intracellularis</i> 35 th day in pooled fecal sample	13	195

*trial in Denmark

CONCLUSION:

The presence of *L. intracellularis* DNA copies was 35 times less in the group that consumed PATENTE HERBA PLUS during the 2nd week of the experiment!

PATENTE HERBA PLUS decreases the presence of *L. intracellularis* in feces

Reference:
 Bosnjak-Neumüller et al., (2019) Phytogetic Feed Additive In Controlling the Presence Of Lawsonia Intracellularis In Young Fattening Pigs. Asian Pig Veterinary Society Congress (APVS 2019)- August 25-28, 2019, Seoul, Korea (Oral).

In vivo trial III

Effect of phytogetic feed additive on the level of *Lawsonia intracellularis* antigen expression on the intestinal mucosa of pigs

2 groups
28 days
12 post-weaned piglets

Analyses:
 Determination of *L. Intracellularis* expression in pig ileum by immunohistochemical (IHC) examination

Criteria for grading presence of *L. intracellularis* in samples of ileum by IHC assay

Grade 0 *L. intracellularis* antigens are not detected
Grade 1 *L. intracellularis* expression of the antigen is detected in smaller focuses
Grade 2 *L. intracellularis* antigen expression is observed in multifocal areas
Grade 3 *L. intracellularis* antigen expression is visible in huge numbers of macrophages

Experimental groups	Number of animals n=12	Grade of <i>L. intracellularis</i> antigen			
		0	1	2	3
Treatment group (T)	(n=6)	2	4		
Control group (C)	(n=6)		3	2	1

*trial in Serbia

CONCLUSION:

Results obtained by IHC method indicate that the piglets fed with a diet where PATENTE HERBA PLUS was added had significantly lower expression of the antigen *L. intracellularis* on the intestinal mucosa as compared to the control group.

PATENTE HERBA PLUS lowers expression of *L. intracellularis* in ileum

References:
 1. Draskovic et al., 8th Asian Pig Veterinary Academic Conference, 12-15 May 2017 pp. 300-301.
 2. Draskovic et al., 2018. Influence of phytogetic feed additive on Lawsonia intracellularis infection in pigs. Preventive veterinary medicine. 151 (2018): 46-51.
 3. Draskovic et al., 2018. A technique to monitor plant-based feed additive's efficacy in controlling Lawsonia intracellularis infections in pigs. International Pig Veterinary Society Congress (IPVS 2018)- June 11-14, 2018, Chongqing, China (Oral).

In vivo trial IV

A large scale experiment with PATENTE HERBA PLUS

3 groups
 T - trial group
 C1 - control 1
 C2 - control 2

6897 animals
60 from 60 kg until slaughtering

Parameters	T	C1	C2
N° animal at the beginning of the trial	2285	2297	2315
N° animal at the end of the trial	2204	2205	2195
Mortality (N° animals)	83	94	120
Mortality (%)	3.6	4.0	5.2
Incidence of swine dysentery (N° animals)	72	158	133
The cost of medical treatment, EUR/animal	1.28	1.77	2.11

*trial in Romania

CONCLUSION:

PATENTE HERBA PLUS reduces the incidence of swine dysentery, mortality, and medical treatment in finishing pigs.

PATENTE HERBA PLUS improves profitability





ABOUT US

PATENT CO. is a multinational company established in 1990 in the heart of Europe, in Serbia. Today we operate on 5 continents.

PATENT CO. strives to be an innovative and internationally-oriented company that is always one step ahead in introducing new technologies in animal nutrition.

RESEARCH AND DEVELOPMENT

Every year, **PATENT CO.** invests significant resources in research and development programmes in laboratories, research centres and farms. This programme facilitates the development of new products, with a view to finding optimal animal feed production solutions.

QUALITY AND SAFETY

PATENT CO. invests in state-of-the-art equipment for the production of animal feed additives and premixtures, allowing us to achieve final products of a consistently high quality. This process ensures full traceability, from the reception of raw materials to delivery of the product to the customer.



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