

New distribution partnership with Russian key player in poultry feed additives



Moscow - September 18, 2019 - VITOMEK and EW Nutrition are pleased to announce that they have signed a distribution partnership agreement, combining the accumulated knowledge, experience, and effective solutions in the field of animal nutrition at VitOmek with a portfolio of comprehensive programs, innovative products, and services from EW Nutrition.

Dmitry Chudakov, General Director, VitOmek: "The partnership agreement with EW Nutrition has become an important event for us and another milestone on the road to success. We are pleased that our new partner is a company with many years of experience in the animal nutrition industry. We are confident that our scientific and technical potential, in conjunction with the valuable experience of the partner, will bring rich benefits in the form of joint development, creation of unique products and services, and the implementation of even more ambitious projects. Our philosophy: "Focus on high results. Give shape to courageous ideas in the final product. "

VitOmek is one of the largest Russian producers of agricultural feed and feed additives, offering comprehensive, effective solutions for agricultural holdings and small enterprises in the poultry and livestock sector. The company's range of services includes technological, veterinary and engineering support of farms, audit and consulting on microclimate and animal welfare.

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Pavel Vladimirovich Bogatkin, General Director, EW Nutrition Russia: "We are very pleased to cooperate with VitOmek. Years of experience in the market, as well as great resources and coverage, making them an excellent ally in our common efforts. In addition to a similar market development philosophy, we see for ourselves a similar mission: mitigating the effects of antimicrobial resistance by providing comprehensive solutions in the field of animal feeding, toxin risk management, and young animal nutrition. Achieving these goals ultimately helps to [increase the effectiveness of human healthcare.](#) "

EW Nutrition researches, develops, manufactures, markets, and services its products and programs around the world. Headquartered in Germany, EW Nutrition's manufacturing facilities are located on 4 continents. Innovation is carried out by our own research laboratories in Germany, with development centers in 5 major animal nutrition markets. EW Nutrition is active worldwide, with its own staff in 27 countries. Our slogan, "Functional Innovations Backed by Science," is being implemented through technical support at the local, regional, and global level.

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This press release is available in Russian [here](#).

EW Nutrition Opens New Production Plant in China



Press Release

EW Nutrition Opens New Production Plant in China

On 29 October, German-based company EW Nutrition will officially open its new production plant in China. The new plant is the next step in the successful development of EWN Biotechnology Shanghai.

By offering holistic, science-backed solutions, EW Nutrition supports the Chinese industry in its effort to reduce antibiotic use. "With this latest investment," says Craig Allen, General Manager, EWN Biotechnology Shanghai, "we are offering a twofold benefit to our Chinese customers: bringing our high-value products closer to the end-user, while implementing our policy of [supporting antibiotic-free](#)

[production in China.](#)”

The new facility in Haimen will produce the three leading product lines in the company’s portfolio. They represent EW Nutrition’s answer to gut and [respiratory health issues](#), as well as toxin risk management. “We are pleased to bring our programs closer to our customers, further increasing service levels,” says Michael Gerrits, Managing Director, EW Nutrition. “But we are even more pleased and honored to bring here our mission of mitigating the impact of antimicrobial resistance by providing comprehensive animal nutrition solutions.”

The virtual opening will take place at the Melia Hotel in Shanghai, to be followed by a one and a half-day symposium on “Reducing Antibiotic Use and Mitigating the AMR Risk – 2020 Vision”. Speakers include Prof. Chen Junshi, Prof. Jia Yanxiong, Prof. Suwit Chotinun, as well as other prestigious national and international guests.

About EW Nutrition

EWN Biotechnology Ltd. is the Chinese arm of EW Nutrition, an international animal nutrition company that offers integrators, feed producers, and self-mixing farmers comprehensive animal nutrition solutions for antibiotic reduction, young animal nutrition, toxin risk management and more.

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Phytomolecules: A tool against antibiotic-resistant E. coli



Diseases caused by *E. coli* entail use of antibiotics in animal production

E. coli infections are a major problem in pig production. Especially young animals with an incompletely developed immune system are often unable to cope with the cavalcade of pathogens. In poultry, *E. coli* are responsible for oedema, but also for [respiratory diseases](#). In young piglets, *E. coli* cause diarrhoea, oedema, endotoxic shock and death. In order to cure the animals, antibiotics often must be applied. Besides this curative application, antibiotics were and in many countries still are used prophylactically and as growth promoters.

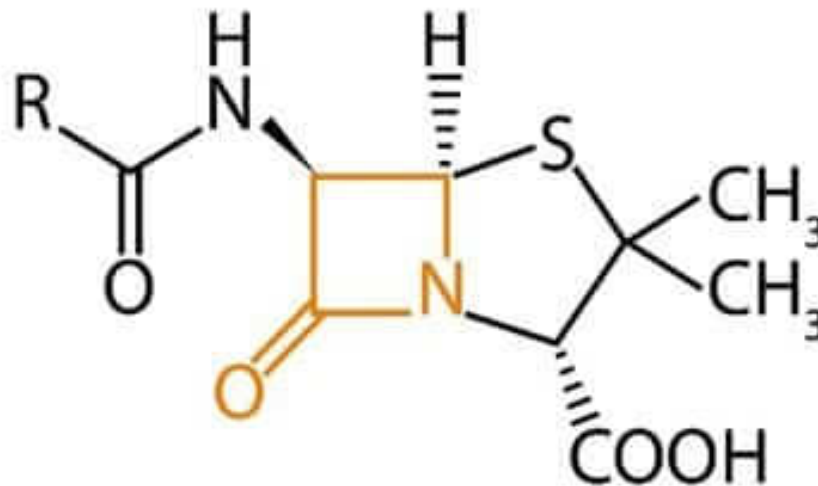
The excessive use of antibiotics, however, leads to the [occurrence of antimicrobial resistance](#) (AMR): due to mutations, resistance genes are created which enable enterobacteria such as *Salmonella*, *Klebsiella* and *E. coli* to produce enzymes (β -lactamases) in order to withstand β -lactam antibiotics. In case of an antibiotic treatment, the resistant bacteria survive whereas the other bacteria die.

The major problem here is that these resistance genes can be transferred to other bacteria. Harmless bacteria can thus transfer resistance genes to dangerous pathogens, which then cannot be combatted with antibiotics anymore. In this article we explore in detail how AMR happens and how phytomolecules, which have antimicrobial properties, could be a key tool to reduce the need for antibiotics in animal production.

How β -lactam antibiotics work

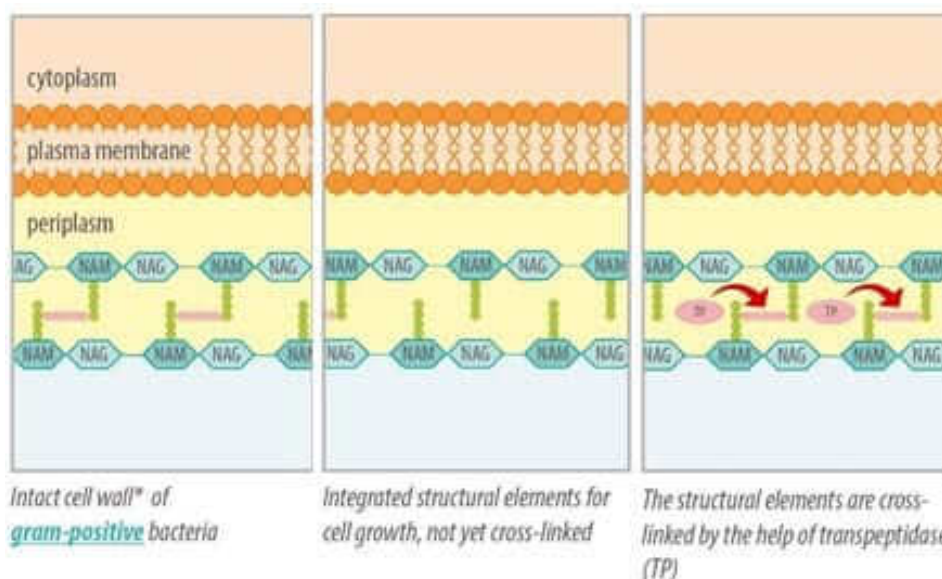
The group of β -lactam antibiotics consists of penicillins, cephalosporins, monobactams, and carbapenems. These antibiotics are characterised by their lactam ring (Figure 1).

Figure 1: An antibiotic with a β -lactam ring (in orange)



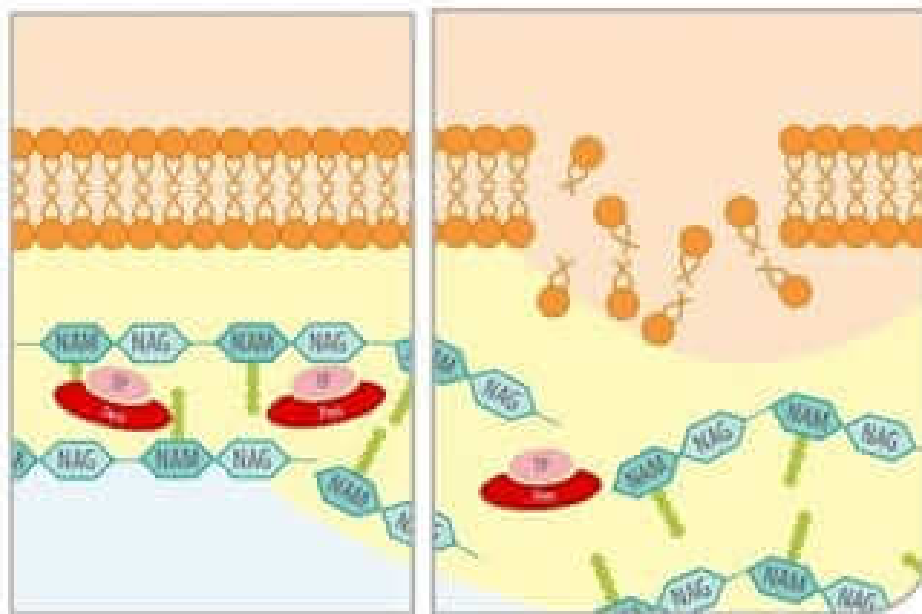
If bacteria are growing, the cell wall also has to grow. For this purpose existing conjunctions are cracked and new components are inserted. In order for the cell wall to remain a solid barrier, the new components must be interconnected by crosslinks. For the creation of these crosslinks an enzyme is essential, the transpeptidase (figure 2).

Figure 2: building up a stable cell wall with the help of transpeptidase



Due to their structure, β -lactam-antibiotics also fit as binding partner for transpeptidase. They bind to the enzyme and block it (Kohanski et al., 2010). The crosslinks cannot be created and the stabilization of the cell wall is prevented. Disturbance of cell wall stability leads to the death of the bacterial cell, hence β -lactam antibiotics act bactericidal.

Figure 3: blocked by β -lactam antibiotics, transpeptidase cannot serve as enzyme for building the cell wall



If the transpeptidase is blocked e.g. by Penicillin (Pen), cross-linking is not possible

The unstable cell wall does not withstand the pressure any more, the bacteria cell gets destroyed

The challenge: *E. coli* producing β -lactamases

Resistant bacteria, which are able to produce β -lactamases – enzymes that destroy the β -lactam ring – prevent their own destruction. Divers point mutations within the β -lactamase genes lead to the occurrence of “extended-spectrum-beta-lactamases” (ESBL). ESBL are able to inactivate most of the β -Lactam-antibiotics.

Another mutation leads to so-called AmpC (aminopenicillin and cephalosporin) β -lactamases. They enable the *E. coli* to express a resistance against penicillins, cephalosporins of the second and third generation as well as against cephamycins.

Phytomolecules - an alternative?

One approach to reduce the use of antibiotics is the utilization of phytomolecules. These secondary metabolites are produced by plants to protect themselves from moulds, yeasts, bacteria and other harmful organisms.

The use of plants and their extracts in human and veterinary medicine is well-established for centuries. Besides digestive and antioxidant characteristics they are well known for their bacteriostatic and bactericidal effects.

Consisting of a high number of chemical compounds, they attack at diverse points and their antimicrobial effect is not caused by only one single specific mechanism. This is crucial because it is therefore very unlikely that bacteria can develop resistances to phytomolecules like they do to antibiotics.

How phytomolecules work

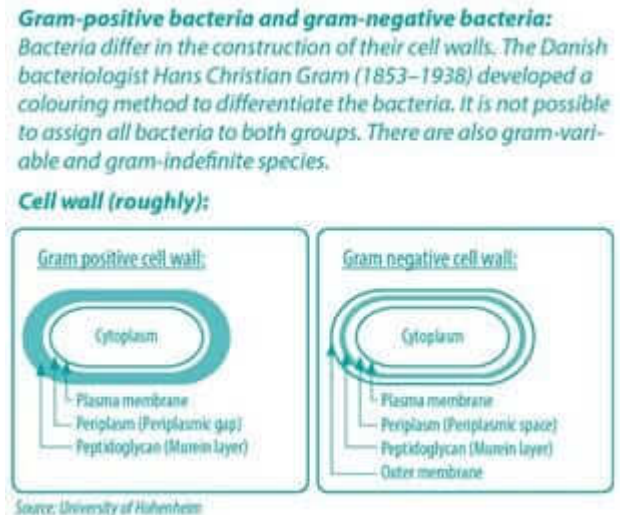
Mostly, phytomolecules act at the cell wall and the cytoplasm membrane level. Sometimes they change the whole morphology of the cell. This mode of action has been studied extensively for thymol and carvacrol, the major components of the oils of thyme and oregano.

They are able to incorporate into the bacterial membrane and to disrupt its integrity. This increases the permeability of the cell membrane for ions and other small molecules such as the energy carrier ATP

(Adenosin-tri-phosphate). It leads to the decrease of the electrochemical gradient above the cell membrane and to the loss of energy equivalents of the cell.

A special challenge: gram-negative bacteria

Gram-negative bacteria such as *E. coli* and *Salmonella* pose a special challenge. The presence of lipopolysaccharides in the outer membrane (OM) provides the gram-negative bacteria with a hydrophilic surface (Nikaido, 2003; Nazarro et al., 2013) (see also blue infobox).



The cell wall therefore only allows the passage of small hydrophilic solutes and is a barrier against macromolecules and hydrophobic compounds such as hydrophobic antibiotics and toxic drugs. The bypassing of the OM therefore is a prerequisite for any solute to exert bactericidal activity toward gram-negative bacteria (Helander et al., 1998).

Based on their trial results Helander et al. (1998) (1998) concluded that trans-cinnamaldehyde and partly also thymol and carvacrol gain access to the periplasm and to the deeper parts of the cell. Nikaido (1996) also concluded that OM-traversing porin proteins allow the penetration of lipophilic probes at significant rates.

Evaluating phytomolecules I - in vitro trial, Scotland

A trial conducted in Scotland evaluated the effects of Activo Liquid, a mixture of selected phytomolecules and citric acid, on ESBL-producing *E. coli* as well as on *E. coli* that generate AmpC.

Material and methods

For the trial two strains for each group were isolated from the field, a non-resistant strain of *E. coli* served as control. Suspensions of the strains with 1×10^4 CFU/ml were incubated for 6-7 h at 37°C (98.6°F) together with diverse concentrations of Activo Liquid or with cefotaxime, a cephalosporin. The cefotaxime group saved as a control for differentiating resistant and non-resistant *E. coli*.

The suspensions were put on LB agar plates and bacteria colonies were counted after further 18-22h incubation at 37°C.

Results

The antimicrobial efficacy of the blend of phytomolecules depended on the concentration at which they were used (see table 1). A bacteriostatic effect could be shown at dilutions up to 0.1 %, a bactericidal effect at higher concentrations.

Table 1: Effect of phytomolecules against resistant *E. coli* producing ESBL and AmpC in poultry

Poultry Microbiology Laboratory, Edinburgh, Scotland	Cefotaxime	Phytomolecules (Activo® Liquid)			
	30 µg / ml	0.1 %	0.2 %	0.4 %	0.5 %
<i>E. coli</i> ESBL 1 (Poultry)	-	+	++	++	++
<i>E. coli</i> ESBL 2 (Poultry)	-	+	++	++	++
<i>E. coli</i> AmpC 1 (Poultry)	-	+	++	++	++
<i>E. coli</i> AmpC 2 (Poultry)	-	++	++	++	++
<i>E. coli</i> non-resistant	+	+	++	++	++
- no effect + growth inhibiting (bacteriostatic) ++ bactericidal					

Evaluating phytomolecules II - in vitro trial, Germany

A further trial was conducted in Germany (Vaxxinova, Münster), confirming the preceding results.

Material and methods

Four ESBL producing *E. coli* all isolated from farms and a non-resistant reference strain as control were tested concerning their sensitivity against Activo Liquid. Every bacteria strain (Conc.: 1×10^4 CFU/ml) was subjected to a bacterial inhibition assay in an appropriate medium at 37°C for 6-7 hours.

Results

In this trial Activo Liquid also showed a dose-dependent efficacy, with no or just a bacteriostatic effect up to a concentration of 0.1 %, but bactericidal effects at a concentration of ≥ 0.2 % (table 2).

Table 2: Effect of phytomolecules against resistant ESBL producing *E. coli* in pig and in poultry

Vaxxinova GmbH, Münster	Phytomolecules (Activo® Liquid)			
	0.1 %	0.2 %	0.4 %	1 %
<i>E. coli</i> ATCC25922	+	++	++	++
<i>E. coli</i> ESBL 1 (Pig)	-	++	++	++
<i>E. coli</i> ESBL 2 (Pig)	+	++	++	++
<i>E. coli</i> ESBL 3 (Poultry)	+	++	++	++
<i>E. coli</i> ESBL 4 (Poultry)	-	++	++	++
- no effect + growth inhibiting (bacteriostatic) ++ bactericidal				

Phytomolecules: a promising outlook

E. coli infections have devastating effects on animals, from diarrhea to edema, enterotoxic shock and even death. Antibiotic treatments have long been the only practicable answer. However, their excessive use– for instance, the metaphylactic application to thousands of animals in a flock– has led to the development of resistant strains. There is evidence that a reduction of antibiotic use reduces the occurrence of resistances ([Dutil et al., 2010](#)).

The results of the two in vitro trials in Scotland and Germany demonstrate the bactericidal effects of [phytomolecules](#) on *E. coli* that produce ESBL and AmpC. Using phytomolecules could thus reduce the use of antibiotics and therefore also the occurrence of AMR.

While it is theoretically possible for bacteria to also become resistant against phytomolecules, the probability of this happening is very low: unlike antibiotics, phytomolecules contain hundreds of chemical components with different modes of action. This makes it exceedingly difficult for bacteria to adapt and develop resistance. To tackle the problem of antibiotic-resistant *E. coli*, antimicrobial phytomolecules therefore offer a promising, sustainable and long-term solution.

By Dr. Inge Heinzl, Editor, EW Nutrition

Literature

Dutil, Lucie, Rebecca Irwin, Rita Finley, Lai King Ng, Brent Avery, Patrick Boerlin, Anne-Marie Bourgault, Linda Cole, Danielle Daignault, Andrea Desruisseau, Walter Demczuk, Linda Hoang, Greg B. Horsman, Johanne Ismail, Frances Jamieson, Anne Maki, Ana Pacagnella, and Dylan R. Pillai. 2010. "Ceftiofur Resistance in *Salmonella enterica* Serovar Heidelberg from Chicken Meat and Humans, Canada." *Emerg Infect Dis* 16 (1): 48-54.

Helander, Ilkka M., Hanna-Leena Alakomi, Kyösti Latva-Kala, Tiina Mattila-Sandholm, Irene Pol, Eddy J. Smid, Leon G. M. Gorris, and Atte von Wright. 1998. "Characterization of the Action of Selected Essential Oil Components on Gram-Negative Bacteria." *J. Agric. Food Chem* 46: 3590-595.

Kohanski, Michael A., Daniel J. Dwyer, and James J. Collins. 2010. "How Antibiotics Kill Bacteria: From Targets to Networks." *Nature Reviews* 8: 423-435.

Nazarro, Filomena, Florinda Fratianni, Laura De Martino, Raffaele Coppola, and Vincenzo De Feo. 2013. "Effect of Essential Oils on Pathogenic Bacteria." *Pharmaceuticals* 6 (12): 1451-1474.

Nikaido, Hiroshi "Molecular Basis of Bacterial Outer Membrane Permeability Revisited. 2003. " *Microbiology and Molecular Biology Reviews*, 67 (4): 593-656.

Rodriguez, Tori. 2015 "Essential Oils Might Be the New Antibiotics." *The Atlantic*.

<http://www.theatlantic.com/health/archive/2015/01/the-new-antibiotics-might-be-essential-oils/384247/>

Rüben, Christiane. 2009. "Antimikrobielle Wirksamkeit von chemischen Einzelkomponenten ätherischer Öle gegenüber ausgewählten Lebensmittelverderbniserregern". PhD diss, TeHo Hannover.