NATURAL COMPOUNDS POTENTIALLY INFLUENCING PIG REPRODUCTION - REVIEW

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Abstract

Breeding pigs has had many problems at present. Due to them number and the range of breeds have been decreasing significantly. Therefore the import of pork to the Czech market seems to be a very probable consequence of this state. This may substantially harm Czech producers. At the same time the solution of the specialist questions in the field of reproduction, solved by the workplaces of the Czech Republic, may be made more complicated. Problems that appear in this field have had a relatively long history. Their accumulation leads to serious thinking about how to reasonably proceed in the field of the research of the reproduction potential of a pig. The complexity of this process is multiplied by the different physiology of both animal sexotypes. The imbalance in these physiological processes has developed in a dissociated way which increases the entropy in a present view of the problem solution. The revision of the state shows that greater chances exist in the case of influencing the reproduction of boars than that of sows. It also shows that the main role is played by the selection of animals for breeding with possible application of additives of natural origin which do not play the role of medicaments. Hormonal interventions in the form of medicaments administered in an exogenic way have not been considered realistic at present. It is being proved that these additives should comprise a wider group of compounds influencing not only the reproduction system but also other physiological functions (stress, colon ecology). This, together with breeding interventions, can significantly contribute to the improvement of reproduction parameters. At the same time it has to be considered that the application of natural substances in pig breeding is new and has not been described yet. Therefore there is no other choice than to use the knowledge from the closest suitable area – human application (Opletal, Šimerda 2008).

Material and Methods

1. Factors influencing fertility

Out of ontogenetic and physiological factors this survey is not going to mention the genetic principle of an organism since breeding animals plays a specific role from the point of view of the subsequent production. The production of sex hormones stems from the formation of releasing factors and reflects not only the somatic potential of the animals and the level of their metabolism, but also the conditions of the outer environment (the standard of breeding, age, nourishment, etc). The level of sex hormones is connected with practical efforts of the intervention into the genotype. Here the important role is played by the contact with the other sex. Based on the knowledge of the process of hormonal metabolism it is possible to choose substances which intervene into target areas of the reproduction activity without influencing other physiological processes unfavourably. It is proved that the level of libido does not have to be in the direct relation with the health state and nutrition. For boars the decisive time is the period of growing up/puberty, testosterone production and also the presence of sows mainly during their whole reproduction cycle. For sows the presence of "odorant" steroid derivatives of the boars is decisive. This topic has been covered by a series of studies. It is difficult though and the results have not been evaluated unambiguously; e.g., in the case of androstenol, which belongs to the group of odour 16-androstene substances (it was isolated from boar testicles and proved in human ones as well), the pheromone activity was proved both at animals and at people. Molecular fundamentals of this activity have still been unknown though. The structure of the substance is similar to that of endogenic neurosteroids (with the reduced A-circle) and the substance itself acts to a certain extent as a positive regulator of $GABA_A$ receptors (Kaminski et al., 2006). Social communication based on odour signals has been proved in the case of pigs not only after the administration of androstenol, but also after the administration of androsteron. They are produced by boars and they are important from the point of view of the positive course of the copulation process (Laska et al., 2005).

Very important factors determining the level of reproduction are: the influence of the outer environment including stress, and the course of some diseases.

Stress is a crucial factor although it has not been perceived as such very often. If there are big differences in temperature in the breeding environment, the quality of sperm is affected significantly. The influence of the air motion, content of ammonia and amine-like substances as well as the humidity cannot be neglected either. The

spermatic liquid (the influence of corticoids), the sperm profile and libido can be significantly affected by the presence of partly oxidized fatty acids in the food (peroxidated lipids), by metabolites of micromycets (*Asperfillus, Fusarium*) and also by the excessive content of phytoestrogens together with saponins (they decrease the surface tension and increase resorption (extracted soya grout + dried trefoil or lucerne)). At the end of the 20th century the significant decrease of male fertility, including the human one, is being claimed. The reasons differ. It seems though that the general reason can be the exposition of the organisms to trace content of lead from earlier used petrol, to constantly occurring residues of DDT and dioxins , but mainly to residues of analogs of steroid hormones from female contraception and to residues of antibiotics which, going to waste water together with urine, influence significantly not only higher organisms, but mainly invasive agents (Kolpin et al., 2002).

Acerbation of inflammation processes affecting mainly skeletal system, but in recent years also other tissues, as a result of autoimmune reactions, is made possible by stress (and in certain consequences also by the invasive activity of microorganisms). We are sure that in spite of all breeding efforts similar state will occur at pigs as well although it does not have to be demonstrated apparently. The reasons can be quiet microbial infections and of them developing stress with increased metabolic turnover of corticosteroids. Due to comprehensible reasons unambiguous studies that would confirm this supposition are not known from the literature. Primarily paradoxical idea of supporting the sexuality of boars and the development of the foetus in sows by preventive addition of anti-inflammatory (resp. antioxidative) substances and prebiotics acting in normalizing the intestinal (and abdominal) microflora, is from this point of view logical and even desirable.

2. Processes leading to the increase of fertility

At present two facts are apparent: administration of natural substances stimulating sexual activity brings more significant effect mainly at boars determined for sperm donation, not at boars in natural breeding. The other fact is the opinion which is being put through in the agricultural practice – this matter deals with a relatively low number of animals. Therefore it is possible to release financial means into it and the money will come back in the form of quality sperm. Breeding boars do not have such a profile of their spermiograms as would be desirable and their libido decreases. Some of these reasons cannot be practically removed (special purification of drinking water without the residues of hormones and undesirablesubstances, ecologically pure foodstuff, problematic application of pheromones, non-stress environment).

Additive substances can quite unambiguously improve the state of animals. The selection of suitable animals and breeding procedure remain primary factors (Opletal, Šimerda 2008).

Contemporary practice proves that using additives is suitable practically only for boars. Fertilization of sows and their becoming pregnant is the moment into which it is very difficult to intervene. Supposing the sperm was of good quality and the sows are healthy the number of fertilized ova and implanted embryos will be corresponding. When administering natural substances (and there is a very low number of them in this field) it is not known whether they would not affect the development of a foetus unfavourably. Hormonal system of sows is consequently regulated in a complex, sensitive and rigid way and it is practically impossible to affect any of its parts by the administration of natural substances according to the ideas of the breeders. In reality affecting rut including the "tuning in" of the sow organism to this process together with the improvement of the intermediary metabolism remains the possible solution.

2.1. Application of substances to boars

2.1.1 LH and testosterone elicitors

***Tribulus*-saponins (saponins of the puncturevine plant)** *(Tribulus terrestris L.)* (Opletal, in press)

Herb with fruit contain spirostanol and furostanol saponins. The mixture of these substances has aphrodisiac effects, it improves spermatogenesis, decreases manifestation of erectile impotence. At males it increases the level of DHEA, LH and testosterone, it does not affect FSH. At females it increases the level of FSH and estradiol, it does not affect testosterone. It increases conversion of testosterone into DH-testosterone, contributes to the increase of blood circulation and to the improvement of the effectiveness of oxygen transport systems. Saponins also act against inflammations (inhibition of COX-2).

2.1.2 Substances improving erectivity (influence on PDE5)

All selective inhibitors of cGMP phosphodiesterase of the 5 (PDE5) type in corpus cavernosum, where PDE5 is responsible for cGMP degradation, are effective. Sexual stimulation, i.e. corresponding libido level, is necessary.

***Epimedium*-flavonoids (flavonoids of Korean epimedium)** (*E. koreanum* NAKAI) (Opletal, in press)

Herb contains: prenylated flavonolic glycosides (icariine), phenolic glycosides (salidroside). Flavonoid glycosides increase the sperm secretion, stimulate the growth of the prostate gland, testicles and of muscles of anus rector. They can increase the testosterone secretion. They decrease trombocyte aggregation, act against microbes and increase immunity. Salidroside decreases the negative influence of stress factors (Opletal, Opletalová 1990). The Clavertin® preparation was tested on boars with very good results (Volný et al. 2008).

Fruit of Monnier´s snowparsley (osthol) (*Cnidium monnieri*(L.) CUSS.) (Opletal, in press)

Fruit contains cumarins, sterols. Extracts from achenes increase sexual efficiency; coumarins (osthol) have a relaxing effect on corpus cavernosum and therefore facilitation of erection can be reached. In the mixture with

some other components (*Borago officinalis L., Coleus forskohlii* BENTH., ferrulic acid, etc.) they support male sexual activity. The anti-inflammatory effect is accompanied by the analgesic one as well.

2.1.3 Substances influencing libido by the direct brain effect

Bremelanotide (PL-6983, Palatin Technologies, U.S.A.) (Anonymous author 2008a)

It is a heptacyclic lactame-analogue of the alpha-melanocyte stimulating hormone (alpha-MSH), which activates melanocortine receptors MC3-R and MC4-R in CNS, induces sexual arousal and spontaneous, completely unexpected erection both at males and at females.

Eurycome root (*Eurycoma longifolia* JACK.) (Opletal, in press)

Root contains: quassionoids (eurycomalactons), biphenylneolignans, alkaloids of the canthine-6-on type. Quasinoids have a strong proandrogennic effect. They cause increase of the sexual activity at middle-aged sewer rat males by the extension of coitus time and by decreasing the refractor period between copulation series. They cause increase of testosterone in Leydig cells together with sexual motivation. They exert anxiolytic activity, elicitation effect on production of odour 16-androstene derivatives in testicles.

The root of maca (*Lepidum meyenii* WALP.) (Anonymous author 2008b)

Root (hypocotyl) contains: alkaloids, glucosinolates, sterols. The substances show antioxidative activity, glucosinolates increase testosterone level, sperm production and movability of sperm cells apparently without the frame of the influence on LH, FSH; at Yellow maca male fertility increase was observed.

2.1.4 Substances with adaptogenic effect

Out of the whole group of adaptogenic plants it is suitable to administer only some. The main reason is above all the final price of the preparation and then also the complementary biological effects that do not have to be very suitable (centrally stimulating effect). Extracts of two plants are being considered.

Dry extract of Ginkgo biloba leaves (*Ginkgo biloba* L.EGb 761®, LI 1370). (Blaschek et al. 2005)

This is not an adaptogenic preparation in the real sense, although with its complex effect it contributes to the normalization of physiological activities and it increases the effect of adaptogenic plants.

Extract contains: diterpens (ginkgolides, bilobalid), flavonoids. Content substances increase the blood flow in the brain, the eye ground, limbs and in other tissues. They improve metabolism of neurotransmitters of cholinergic system, decrease biosynthesis of glucocorticoids and play the main role in a certain antistress and neuroprotective effect. They increase synergic effects of administered aphrodisiac substances.

Dry extract of Siberian ginseng (*Eleutherococcus senticosus* (RUPR. et MAXIM.) MAXIM (syn. *Acanthopanax senticosus* (RUPR. et MAXIM). HARMS., *Araliaceae*). (Opletal, L., Opletalová, V. 1990)

Extract contains: triterpenic aglycones and saponins, lignans, sterols and coumarins. The complex mixture of substances acts against negative effects of stress factors and increases libido.

2.1.5 Substances against invasive agents (Opletal, in press)

Ursolic acid gained from herb of heather (*Calluna vulgaris* (L.) HULL., *Ericaceae*), fruit of cornel (*Cornus officianlis* SIEB. et ZUCC., *Cornaceae*) or from herb of ground ivy acts in protection of liver, against inflammation, oxidation and invasions (it slows down the growth of *Staphylococcus aureus,* G-positive as well as G-negative microorganisms, *Micropsporum lenosum*), it inhibits activity of elastase; this effect is favourably demonstrated mainly in the urinary tract.

Dry extract of fen-berry fruit (*Oxycoccus macrocarpus* (AITON) PERS. (syn. *Vaccinium macrocarpon* AITON – Ericaceae)

Extract contains: esters of ursolic acid, flavonoids, antocyanidines. It does not acidify urine, the substances interfere with the bacteria adherence tendency on the epithelium of urinary tract (*E. coli, Staphylococcus aureus*, etc); they act against inflammation, they deodorise urine, protect against inflammation around the urinary opening. It is a non-toxic substance which is highly suitable for the protection of the urogenital system.

2.1.6 Antioxidative and anti-inflammatory substances (Blaschek et al. 2005; Opletal, in press)

Pycnogenol (mixture of flavan-3-ols and oligomeric proanthocyanidins) decreases capillary permeability which contributes to oedema formation and to microbleeding, it increases resistance of elastin against elastase degradation, it affects matrix-metalloproteinases (MMPs), iNOS, COX-1, COX-2, it favourably affects sperm parameters, acts as free radical sweeper and it stimulates immune system.

Leucoselect® (extract of wine grape seeds with flavonols; *Vitis vinifera* L., *Vitaceae*).

It has antioxidative, vasodilating, antilipoperoxidative and trombocyte antiaggregative properties and can be used basically in the same way as pycnogenol.

Tocopherols (a group of E vitamins) generally have antioxidative properties in most tissues, they act against inflammation, can increase immune response of the organism, significantly intervene into the metabolism of tissues of embryonic epithelium, they improve maturing of spermatic cells and erection. The mixture of natural isomers is more effective than the synthetic vitamin.

Frankincense – Olibanum (Oliban gummiserina) (*Boswellia carteri* BIRDW., *Burseraceae*).

Resin contains: pentacyclic triterpenes (boswellic acid), which have anti-inflammatory, antiarthritic and in some cases also antipyretic effects. They inhibit 5-LOX as well as leucotrien synthesis, and activity of leucocyte elastase; they can decrease degradation of glycosylaminoglycanes, affection of cartilage and they can inhibit autoimmune disease mediators. They support cell-mediated immunity.

2.2. Application of substances to sows

6 Substances acting as estrogens (Blaschek et al. 2005)

***Cimicifuga* - triterpenes – substances from the root of black cohosh** (*Cimicifuga racemosa* (L.) NUTT. – Ranunculaceae).

Root contains: triterpenic glycosides of cycloartane-type, esters of hydroxycinnamic acid, alkaloids. Some substances strongly inhibit neutrophile elastase which acts in the process of inflammation, they have an estrogenic activity performed by a so far unknown mechanism. Neither the tissue of endometrium nor hormonal levels of estradiol, LH, FSH and prolactine are affected. They are not bound to estrogenic receptors and do not activate estrogen-dependent genes. They can increase activity of osteoblasts. Safety of biological effect of these substances (and with it connected safety of food chain) has still to be examined.

Discussion

Application of substances of natural character which would favourably influence mainly spermatogeneseis is at present at the beginning of its practical use. In the literature very few studies can be found which solve this problem. If so, they are not on the level that would enable their instant use (double-blind study). It is apparent that with respect to physiology of both sexotypes the statement can be made that positive intervention can be carried out at boars, where libido can be increased and the spermiogram profile improved. In the case of sows this possibility is limited – it can be carried out practically only by increasing the estrogen level (and it is still not certain). When a sow becomes pregnant, it is practically impossible to reach the decrease of embryonic mortality in the period of the so called progesterone shock. Hormonal process of pregnancy is regulated in a very sensitive way, it is strictly consequent and it is very difficult, almost impossible, to intervene into it, for us in a desirable way. That is why in case of sows other methods are under study. They aim at using biotechnological and alternative methods in increasing the level of reproduction of little sows and sows. Mainly methods of stimulation of embryo donors, synchronisation of cycles of receivers, laparoscopic resp. laparotomic methods of extracting and transmition of embryos, cultivation of embryos between extraction and transmition, are being solved. Solving problem reproduction include mainly the study of progressive methods of stimulation of embryo donors (superovulation), cryoconservation of embryos, study of procedures of inducing puberty of little sows, stimulation of rut of anesteric pubertal little sows and anesteric sows after ablactation of piglets, level of fertility and elimination (decrease) of high level of embryonic mortality in the early stage of pregnancy. When improving procedures of embryo transmission, a simplified, biologically effective procedure of superovulation treatment of embryo donors was developed. It decreases labour demandingness and stress of animals, it ensures a corresponding amount and quality of embryos. In the sector of cryoconservation a simple and effective procedure of freezing for direct transmission to receivers has been worked out. It increases usability of embryos and of receivers. In the field of modern embryotechnologies a repeated transvagianl aspiration of oocytes from donor ovaries and production of embryos from a known parental pair has been managed. In all the mentioned fields the efforts were successful. It is a matter of a question of how these scientific contributions will be applied to everyday practice and what financial demands will have to be developed for their application. We are not able to answer these questions so far. We have to state though that when solving these problems at present, procedures of hormonal therapy (considered problematic for future), means harmonizing activity of an organism as well as various alternative methods, resp. their combinations, are being used. It is this field where reasonable application of natural substances brings great prospects. Mentioned substances are not of hormonal origin. Their negative effects on organoleptic properties of final products are not known, rather vice versa (e.g., in the case of E vitamins and majority of antioxidative agents). Therefore from the point of view of the safety of the food chain they are, except for some minor cases, wholly acceptable.

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