

# OPPORTUNITIES FOR THE IMPROVEMENT OF THE REPRODUCTIVE PERFORMANCES IN FEMALE ANIMALS

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Invited paper

**Abstract:** The paper analyzes the scientific data included the author's own results about the opportunities to increase the reproductive potential of female animals by application of the natural no hormonal substances and the supposed mechanisms of their action on the reproductive system. Also the new scientific data related to the discovering of the "metabolic" hormones (leptin, ghrelin) and kisspeptin/GPR54 system as well as their relationship with metabolism and reproductive function in animals is discussed.

**Kew words:** reproductive potential, biological active food components, leptin, ghrelin, kisspeptin

## Introduction

The strong requests to the food quality and safety for human health necessitate searching the new approaches to the enhancement of reproductive potential in farm animals. Direct hormonal stimulation of reproduction is gone away, while the hormones are accumulated in milk and meat.

## "Metabolic" hormones and reproduction

Well known that the function of the female reproductive system is under strictly control of sex and gonadotropic hormones, which secretion is regulated on the base of positive and negative feedback through the hypothalamic-pituitary-gonadal axis.

During the last decade researchers (*Budak et al., 2006; Akhter et al., 2007; De Placido et al., 2006; Labrethon et al., 2007; Miller et al., 2005*) added two new members to this hormonal "family", namely leptin and ghrelin, hormones secreted by adipocytes and the gastrointestinal tract. In addition to their effect on the metabolism and appetite, these hormones affecting on the hypothalamic-pituitary-

gonadal axis, influence on reproductive function, implantation, and embryo development (*Budak et al, 2006*).

Leptin is produced by adipose tissue and reflects the feeding state in different animals. It transfers information about the body's energy resources to the brain and thus regulates a number of physiological processes, including reproduction (*Smith et al, 2002; Farooqi and O'Rahilly, 2009*). Neuroendocrine stimulation of reproductive properties is associated with increased circulating levels of leptin (*Adam et al, 2003*).

Ghrelin, beside the main source - gastrointestinal tract, was found in steroidogenically active luteal and interstitial cells of the ovary (*Viani et al., 2008*). Receptors of acylated-ghrelin was also shown in follicular, luteal, surface epithelial and interstitial cells of the ovary (*Viani et al., 2008*). This hormone is involved in the regulation of endocrine and non-endocrine functions, including the control of GnRH pulse activity, food intake, energy balance and control of adiposity (*Tena-Sempere M, 2005*). Some authors (*Fernandez-Fernandez et al., 2007; Vulliamoz et al., 2004*) reported that ghrelin inhibits LH secretion, but FSH is unaffected. *Tena-Sempere (2005)* also showed that ghrelin could reduce circulating steroid hormones in pre-pubertal male rats. Recently results from animal studies showed that both leptin and ghrelin have a role in GnRH production at different reproductive stages (*Budak et.al., 2006; Labrethon et.al., 2007; Smith et al., 2002; Garcia et al., 2007; El-Eshrawy et al., 2010*).

This research data indicate that a balance between leptin and ghrelin is essential for appropriate puberty timing. In accordance with hypothesis of *Moshtaghi-Kashanian and Razavi (2009)* decreased leptin/acylated-ghrelin ratio may constitute one of the mechanisms involved in delayed puberty.

The discovering of a central role of kisspeptins (peptide products of the *KISS1* gene) in the metabolic regulation of reproductive function shown that they regulate the reproductive axis by stimulation of their receptor GPR-54 on GnRH neurons, affecting LH and FSH secretion (*Roa et al, 2008*). Administration of kisspeptin leads to increase plasma LH, FSH and testosterone in a dose-dependent manner in a number of species (*Smith et al., 2006*). As the kisspeptins are an essential component of the HPG axis controlling gonadotrophin secretion, the KISS/ GPR-54 signalling may play a critical role in the transduction of ghrelin and leptin -induced changes in the secretion of gonadotropic hormones. Furthermore, the kisspeptins neurons express leptin receptors (*Gutierrez-Pascual et al, 2007*).

Levels of the ghrelin increase before meals, decrease after meals, and serve as the counterpart of leptin. The high level of leptin induces satiation. Despite the proven link between energy homeostasis and fertility, the potential role of ghrelin in the control of gonadal function depends on intake of different food components has not been clearly assessed.

## Diet and reproduction

The recent discovering the ability of "metabolic state" to influence a reproductive function gives an opportunity to study stimulating effect of different diets on the reproduction in farm animals.

One direction of diet improving is the enhancement of the diet's energetic value. In accordance of the data (Downing *et al.*, 1995), the high energetic diets in sheep lead to the raise of glucose content in the follicular fluid reflected in the number of follicles and ovulations.

Additional input of fat in the diet of sows and cows affected directly the structure of ovary and enhanced the level of progesterone (Hawkins *et al.*, 1995; Rhodes *et al.*, 1978). The same effect was observed by Mansour *et al.* (2000) in goats. According to their results, the high fat diet increases the ovulation response to the PMGH and the output of quality of embryos. From other hand, the addition of fat to the diet should be done carefully and in the agreement with follicle developmental state. Robinson *et al.* (2002) noticed that the input of unsaturated fatty acids in the diet of cows at the beginning of luteal phase decrease the progesterone concentration and delay the ovulation.

The other direction of diet improving is the use of the biological active substances such vitamins, micro and macro elements, plants components as flavonoids, saponins and pigments. The role of vitamins in the reproduction is indisputable. In Table 1 is presented the recent data about main acting of vitamins in different reproductive organs.

**Table 1. Vitamins and reproductive functions**

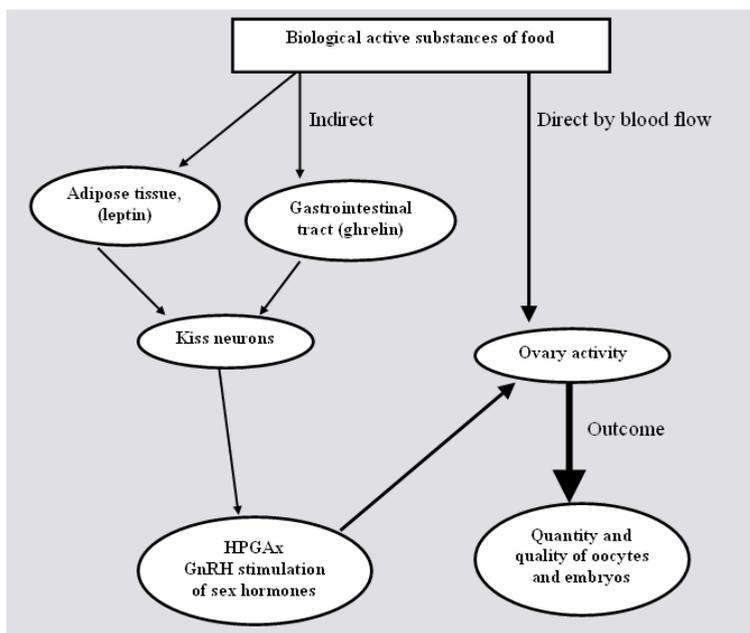
Vitamins	Subject of investigations	Results	Target part of the reproductive system	Reference
E	cows	deficiency decreases the progesterone level	ovary	<i>Liurba u dp., 2004</i>
A	cows sheep	stimulate the oocytes maturation by the expression of the gonadotropic receptors	oocytes	<i>Livingston u dp., 2009;</i> <i>Ikeda u dp., 2005</i>
B <sub>6</sub> , B <sub>12</sub>	human sheep	participate in the steroid synthesis; keep the membrane potential of mitochondria and decrease the lipid peroxidation	oocytes embryos	<i>Eberhardt u dp., 1999;</i> <i>Kannan K. and S.K.Jain, 2004;</i> <i>Randomized, 2008</i>
D	human rat	participate in the oestrogen synthesis	ovary	<i>Uhland u dp., 1992;</i> <i>Kinuta u dp., 2000</i>

The essential role of micro and macro elements (Se, Zn, Mn, Mg, Ca, Fe) for reproduction is confirmed by array of investigations (Corah and Ives, 1991; Jukola *et al.*, 1996; Basini. and Tamanini, 2000; Smith and Akinbamijo, 2000). As

an enzymes compound, they participate in the synthetic processes and in defense of sex cells against oxidative stress.

The best effect on reproduction should be achieved by complex use of biological active compounds in the diet. Such mix of active substances possessed the ability to improve the reproductive performances are natural products as the algae (*Spirulina platensis* and *Spirulina maxima*, *Chlorella*) and plants extracts. *Janezykl et al. (2006)* reported about the effect of *Chlorella vulgaris* on the oestral cycle in the experimental mouse. The investigations with different varieties of *Sprulina* have shown the positive influence on the female reproduction. It protects the ovary against the intoxications (*Karacat and Simsek, 2007*) increase the number of live and healthy offspring and enhance the quantity and quality of eggs in poultry (*Fevrier and Seve, 1975; Kapoor and Mehta, 1993*).

Analyzing the literature data we constructed our hypothesis about acting of food biological active substances in the female reproduction presented on the Figure 1.



**Figure 1.** Effect of food active compounds on the female reproductive system. HPGAx- hypothalamic-pituitary-gonadal axis, GnRH- gonadoliberin hormone.

They should be acting in two ways : transfer by blood flow to the ovary (direct) and mediated by system metabolic hormones leptin/ghrelin - kisspeptins/ GPR54 - hypothalamic-pituitary-gonadal axis( indirect).

## Own results

We investigated the effect of selenium organic compound selenopyran on the reproductive system of growing gilts. The selenopyran treatment leads to an increase of selenium levels in blood ( $P < 0.05$ ). The ovaries of the gilts in the experimental group showed a higher number of preovulatory follicles. High positive correlations were found between the selenium concentration in ovaries and ovarian weights ( $r=0.76$ ;  $P < 0.05$ ) as well as between the selenium concentration in ovaries and the serum levels of estradiol-17 $\beta$  ( $r=0.78$ ;  $P < 0.01$ ) (Kacheva *et al.*, 2008).

In the next experiments with mouse feed additives of *Spirulina platensis* and selenium organic compound was observed that the ovary of experimental animal groups have better response to the hormonal stimulation aimed superovulation thus reflect to the higher embryo outcome. The biochemical analysis of ovary homogenate showed increasing the activity of mitochondrial enzyme cytochrom C oxidase (Kistanova *et al.*, 2009).

In both cases we confirmed that the input of biological active compounds in the diet reflected to the ovary activity. But the problem about detailed mechanisms of this acting is not clear and will be solved.

## Conclusion

Now is clear that the fertility is determined by a multi-hormonal effect, included not only sex and gonadotropic hormones, but also "metabolic" hormones. A functional defect in any of the components of this hormonal complex directly affects reproduction. The new scientific data confirms the strictly dependence of reproduction on energy sources and metabolic state and shows their signaling ways. The both have a big importance for good fertility.

## Mogućnosti poboljšanja reproduktivnih performansi ženskih grla

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## Rezime

U radu su analizirani naučni podaci kao i podaci autora o mogućnostima povećanja reproduktivnog potencijala ženskih životinja aplikacijom prirodnih ne hormonskih supstanci kao i očekivani mehanizmi reakcije njihovog reproduktivnog sistema. Takođe u radu su diskutovani naučni podaci koji su u vezi sa otkrićem

metaboličkih hormona (leptin, grelin) i kisleptin/GPR54 sistema kao i veza između metabolizma i reproduktivnih funkcija kod životinja.

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