Research Advances in Nutrient Regulation of Oocyte Quality and Reproductive Performance in Sows: Postprint

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Abstract

Dietary energy, fat, crude protein, and fiber affect follicular development, estrous cycle, hormone levels, embryo implantation, and litter size. Oocyte quality is a critical factor determining reproductive performance in mammals, influencing the number of high-quality embryos and pregnancy rates. Oocyte quality is regulated by nutrients such as carbohydrates, amino acids, and fats, and abnormal nutrient metabolism can reduce oocyte quality. This article reviews recent research on the effects of nutrients on oocyte maturation, early embryonic development, and reproductive performance in sows, providing a reference for research and practical applications aimed at improving oocyte developmental potential and reproductive performance through nutritional regulation.

Full Text

Research Progress in Nutrient Regulation of Sow Oocyte Quality and Reproductive Performance

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Abstract

Dietary energy, fat, crude protein, and fiber all influence follicular development, estrous cycles, hormone levels, embryo implantation, and litter size in sows. Oocyte quality is a critical determinant of reproductive performance in mammals, directly affecting the number of high-quality embryos and pregnancy rates. Oocyte quality is regulated by nutrients such as carbohydrates, amino acids, and fats, and abnormal nutrient metabolism can compromise oocyte quality. This

review synthesizes recent research on how nutrients affect oocyte maturation, early embryonic development, and reproductive performance in sows, providing a reference for future studies and practical applications aimed at improving oocyte developmental potential and reproductive performance through nutritional modulation.

Keywords: sows; oocyte quality; reproductive performance; energy; amino acids; fat

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Early embryonic development profoundly impacts reproductive performance in mammals, with early embryonic mortality rates ranging from 30% to 50% across species [1]. Enhancing early embryonic development and improving oocyte quality have therefore become key strategies for boosting reproductive performance. Oocyte maturation and development are accompanied by active metabolic and energetic processes, with nutrients including carbohydrates, amino acids, and fats playing regulatory roles in oocyte quality, fertilization capacity, and embryonic development [2]. These nutrients are intimately linked to reproductive performance, as energy, protein, fat, and fiber all affect estrus, pregnancy, and litter size in sows. Consequently, nutritional approaches to enhance oocyte and embryonic developmental potential hold significant importance for improving sow reproductive performance.

1.1 Dietary Energy Sources

Carbohydrates serve as an energy source that promotes ovarian follicular development. In gilts from the rearing period through estrus, starch-based diets are more effective than fat-based diets at promoting oocyte maturation [3], possibly due to elevated insulin-like growth factor (IGF) levels in serum and follicular fluid of the starch group. IGF can stimulate the hypothalamus to secrete follicle-stimulating hormone (FSH) and luteinizing hormone (LH), while also increasing LH receptor mRNA expression in cumulus-oocyte complexes, with elevated LH benefiting subsequent follicular development. In primiparous sows, insufficient feed intake during lactation increases catabolism, which is detrimental to follicular development and hormone secretion [4]. To increase energy intake, adding sucrose to lactation diets shortens the weaning-to-estrus interval, significantly improves pregnancy rates and plasma progesterone levels, and increases litter size in the subsequent parity without affecting body weight loss or feed intake during lactation [5]. Research indicates that when primiparous sows experience minimal body weight loss during lactation, diets supplemented with extruded wheat, glucose, and sucrose promote post-weaning estrus and reduce negative energy balance more effectively than added fat, without compromising litter size [6]. Glucose can significantly increase serum estrogen, LH, and FSH levels in gilts at estrus, advancing puberty onset [7]. Thus, dietary starch, sucrose, and glucose can be utilized by the body to reduce maternal fat mobilization and weight loss, promoting elevated hormone levels during the estrous cycle and

thereby stimulating follicular development.

As an important energy source, both the content and type of dietary fat affect sow reproductive performance. Feeding high-fat diets during gestation increases sow body weight, significantly improving total born, born alive, and piglet weaning weights while shortening the weaning-to-estrus interval [8]. Maternal diets also influence offspring fat metabolism; feeding high levels of corn oil during late gestation and lactation results in piglet subcutaneous fat composition matching that of sow milk, while significantly decreasing stearoyl-CoA desaturase involved in fatty acid metabolism [9]. Different fat types exert varying effects on sows and piglets; some fats induce oxidative stress [8]. For example, fish oil increases malondialdehyde content in sow serum, colostrum, and piglet serum, indicating oxidative stress in both sows and piglets. In contrast, olive oil decreases interleukin-6 and tumor necrosis factor levels in milk, reducing pre-weaning piglet mortality [10]. High-fat sow diets can adversely affect offspring reproductive performance, reducing antioxidant capacity and decreasing follicle numbers in replacement gilts at puberty [11].

1.2 Dietary Energy Levels

Feeding multiparous sows diets with varying energy levels for 7 days during early, mid, and late gestation increases sow body weight and backfat thickness with higher energy levels, which helps reduce body weight loss during lactation despite decreasing feed intake. This approach also improves piglet birth weight without affecting weaning weight and does not compromise reproductive performance in the subsequent parity [12]. Short-term high-energy diets benefit gilts, significantly increasing large follicle numbers and oocyte maturation rates when fed from the rearing period through estrus [3]. Conversely, low energy levels impair reproduction; restricting feed intake during the early follicular phase in gilts significantly reduces blood progesterone, kisspeptin, and IGF levels, decreases large follicle and corpus luteum numbers, and causes abnormal estrus expression [13]. Therefore, maternal energy requirements increase during the early follicular phase, with low-energy diets suppressing reproductive performance while short-term high-energy diets exert promotional effects.

1.3 Dietary Crude Protein Levels

Research shows that low-nitrogen diets affect nitrogen utilization efficiency in lactating sows. Reducing dietary crude protein from 16.0% to 14.3% while supplementing limiting amino acids does not affect average daily feed intake or body weight changes. Net protein utilization efficiency, casein, and true milk protein levels show no significant differences during early lactation, but net protein utilization efficiency and casein levels increase significantly during peak lactation, with piglet growth rate showing an upward trend [14]. However, excessive crude protein reduction without limiting amino acid supplementation inhibits piglet growth. Decreasing dietary crude protein by 50% during gestation and lactation significantly upregulates mRNA expression of myostatin and its activating pro-

tein forkhead box protein O3 (FoxO3), resulting in significantly reduced daily gain and growth retardation in piglets [15]. Insufficient dietary crude protein also impairs offspring reproductive performance; a 50% reduction in crude protein during gestation and lactation increases cytochrome aromatase content in piglet ovaries while decreasing RNase Drosha and cytochrome aromatase microRNA content, hindering follicular maturation and reducing mature follicle numbers. This also increases caspase activity and granulosa cell apoptosis [16].

The ratio of crude protein to carbohydrates in sow diets also affects sow and piglet metabolism. Low-protein, high-carbohydrate diets increase the blood glucose-to-insulin ratio while decreasing insulin content. High-protein, low-carbohydrate diets increase glucagon and postprandial glucose concentrations. Both dietary approaches increase hepatic mRNA levels of phosphoenolpyruvate carboxykinase and glucose-6-phosphatase in piglets, thereby promoting glucose utilization [17].

1.4 Dietary Fiber Sources

Dietary fiber promotes reproductive performance, with lupin fiber proving superior to wheat bran fiber because it increases the number of oocytes developing to metaphase II (MII) and improves embryo survival when fed short-term before mating [18]. Previous research indicates that compared to insoluble fiber, soluble fiber improves embryo survival rate and increases viable embryo numbers without affecting ovulation [19]. Konjac flour, rich in soluble fiber, enhances neutral detergent fiber digestibility, increases sow feed intake during lactation, and shows a trend toward increasing piglet weaning weight [20]. Certain levels of crude fiber do not affect reproductive performance; adding 13.4% Tifton hay does not influence litter size or piglet weaning weight [21]. Partially replacing dietary barley and wheat with fiber-rich vegetables does not affect blood glucose and insulin levels in gestating sows but increases serum short-chain fatty acids and non-esterified fatty acids, with betaine, dimethyl sulfone, and scyllo-inositol serving as biomarkers for vegetable intake [22].

2 Oocyte Quality and Its Nutritional Regulation

Oocyte quality partially determines early embryonic development and implantation. Poor-quality oocytes, even when successfully fertilized, exhibit significantly reduced cleavage rates, numbers of high-quality embryos [23], and embryo implantation rates [24]. Oocyte maturation and early embryonic development are regulated by carbohydrates, amino acids, and fats, as summarized in Figure 1 [Figure 1: see original paper].

2.1.1 Glucose

As the most important monosaccharide, glucose metabolism plays a crucial role in oocyte maturation and development. In vitro studies with porcine oocytes show that adding glucose or pyruvate increases the number of oocytes reaching

MII and improves blastocyst rates. Oocytes require cumulus cells to convert glucose into pyruvate for utilization; consequently, oocytes without cumulus cells can only use pyruvate, not glucose [25]. Aged porcine oocytes exhibit decreased glucose transport [26], indicating that abnormal glucose transport reduces oocyte quality. Cryopreservation damages porcine embryos, decreasing survival rates and increasing apoptosis. Compared to pyruvate supplementation, adding glucose to maturation medium significantly improves blastocyst rates after embryo freezing [27]. Oocyte glucose uptake and utilization are regulated by multiple factors: bone morphogenetic proteins promote glucose utilization by cumulus-oocyte complexes [28], insulin enhances glucose utilization by stimulating granulosa cell proliferation [29], and carnitine promotes fatty acid -oxidation while inhibiting glucose uptake [30].

Glucose is converted to lactate through glycolysis, producing ATP, and generates nicotinamide adenine dinucleotide phosphate (NADP) and ribose-5-phosphate via the pentose phosphate pathway. Both pathways are essential for oocyte maturation and development. Adding inhibitors of the pentose phosphate pathway and glycolysis to porcine oocyte maturation medium significantly reduces intracellular ATP and glutathione, inhibiting oocyte maturation and increasing expression of apoptosis-related genes (caspases and Bax), which elevates blastocyst apoptosis rates [25]. Physiological inhibitors such as ADP and NADP do not affect oocyte maturation, whereas pharmacological inhibitors like sodium fluoride and nicotinamide inhibit oocyte maturation by altering oocyte oxidative status and mitochondrial activity [31].

2.2 Amino Acids

Glutamine, alanine, glycine, glutamate, and proline are the most abundant amino acids in sow follicular fluid [32]. Porcine embryos exhibit continuous amino acid uptake and production during culture; some amino acids like glutamine, threonine, and arginine consistently decrease, while others like glutamate and glycine increase [33], indicating differential amino acid utilization across developmental stages.

2.2.1 Arginine and Its Metabolites

Arginine is a conditionally essential amino acid, with increased maternal requirements during gestation. As the sole precursor for endogenous nitric oxide (NO) synthesis, arginine regulates multiple intracellular signaling pathways and promotes angiogenesis. Dietary supplementation with arginine or N-carbamylglutamate (which promotes endogenous arginine synthesis) activates the mTOR signaling pathway, promoting trophoblast growth and embryo implantation, thereby improving reproductive performance in mice and pigs [34-35]. In porcine oocyte in vitro maturation, adding NO synthase inhibitors significantly suppresses meiotic resumption and cumulus cell expansion [36].

Arginine is metabolized to ornithine via the urea cycle, and ornithine is con-

verted to putrescine by decarboxylase. Ornithine and putrescine levels in mouse ovaries fluctuate cyclically with oocyte maturation. Ornithine decarboxylase and putrescine tend to be deficient in aged mice; putrescine supplementation via drinking water increases ovarian putrescine levels, reduces embryo resorption, and increases live litter size [37]. In in vitro maturation of aged mouse oocytes, putrescine significantly increases blastocyst cell numbers and the proportion of high-quality embryos [38].

2.2.2 Branched-Chain Amino Acids

Branched-chain amino acids regulate not only muscle protein synthesis but also oocyte development. In Mongolian gerbil embryo culture, eight-cell embryos show significantly increased valine uptake, which is used for oxidative energy production. Isotope labeling demonstrates that its carbon skeleton is incorporated into lipid synthesis [39], establishing valine as an energy source. However, recent research indicates that dietary valine supplementation does not improve sow metabolism, milk production, or piglet growth in lactating sows with litter sizes exceeding 12 [40].

Previous studies show that different developmental stages of oocytes and blastocysts utilize different leucine transporters: oocytes primarily use sodium-dependent carriers, while blastocysts mainly use sodium-independent transporters [41]. Recent findings reveal differential leucine uptake rates across follicular developmental stages, with mouse follicles showing gradually increasing leucine absorption during progression from preantral to antral and tertiary follicles. This suggests that enhanced cell division and metabolism during follicular development require more leucine, with granulosa cell proliferation increasing membrane transporters and tight junctions to improve leucine transport efficiency. However, leucine uptake decreases in preovulatory follicles, possibly due to increased collagenase and gelatinase reducing amino acid transport between oocytes and granulosa cells [42].

2.2.3 Methionine

Epigenetic modifications include DNA and histone modifications. Oocyte maturation and early embryonic development involve epigenetic changes, with methionine and betaine as important methyl donors affecting piglet epigenetics. Research shows that dietary betaine supplementation during gestation significantly reduces hepatic triglyceride content in piglets and downregulates expression of lipogenic genes such as acetyl-CoA carboxylase, stearoyl-CoA desaturase, and fatty acid synthase. This may be related to betaine' s ability to increase the hepatic S-adenosylmethionine to S-adenosylhomocysteine ratio, promoting DNA hypermethylation of promoters for fatty acid synthase and stearoyl-CoA desaturase genes [43]. Similarly, gestational betaine supplementation promotes betaine/methionine metabolism and DNA methyltransferase expression in piglets, causing hypermethylation of IGF2 gene segments and increasing IGF2 expression and cell proliferation/anti-apoptosis in the hippocampus of newborn piglets

[44].

2.3.1 Fatty Acid -Oxidation

Fatty acid metabolism provides ATP for oocytes. Fatty acids must enter mitochondria for -oxidation, a rate-limiting step requiring carnitine palmitoyltransferase catalysis. Co-localization studies of lipid droplets and mitochondria in oocytes show that lipid droplets gradually approach mitochondria during porcine oocyte maturation, facilitating fatty acid -oxidation. Adding -oxidation inhibitors significantly suppresses meiotic resumption and early embryonic development [45-46]. Studies demonstrate that carnitine improves cleavage rates of porcine oocytes even without carbohydrate energy sources, and carnitine supplementation in culture medium improves survival rates of frozen-thawed porcine embryos [47].

2.3.2 Unsaturated Fatty Acids

Unsaturated fatty acids are more beneficial for oocyte quality than saturated fatty acids. High-resolution nuclear magnetic resonance analysis of follicular fluid reveals that follicular fluid from non-cleaving oocytes contains significantly higher saturated fatty acids and lower polyunsaturated fatty acids, with these differential fatty acids serving as potential biomarkers for predicting post-fertilization cleavage capacity [48]. Polyunsaturated fatty acid content is significantly higher in granulosa cells of mature porcine oocytes than in immature ones, while saturated fatty acid composition shows no significant changes during oocyte maturation [49], suggesting minimal metabolic involvement of saturated fatty acids.

Research shows that supplementing lactating sow diets with the essential fatty acid -linolenic acid promotes post-weaning estrus in sows with more than three parities and shows a trend toward increasing litter size in the subsequent parity [50]. In porcine oocyte in vitro maturation, -linolenic acid supplementation significantly increases intracellular glutathione content, reduces oxidative stress, accelerates nuclear maturation, improves blastocyst rates, and increases somatic cell nuclear transfer numbers. While MAPK inhibitors impair oocyte maturation and early embryonic development, -linolenic acid completely alleviates these detrimental effects [51]. Conjugated linoleic acid exerts similar promotional effects on oocytes, significantly increasing MAPK expression levels [52] and reducing cytoplasmic lipid droplet density [53], indicating that conjugated linoleic acid promotes lipid droplet breakdown in the cytoplasm to accelerate fatty acid metabolism for energy production.

Dietary energy sources and levels, crude protein, fat, and fiber directly affect reproductive performance, including estrous cycles, hormone levels, and litter size. Nutrients such as carbohydrates, amino acids, and fats influence oocyte maturation and early embryonic development by regulating energy supply, epigenetic modifications, mitochondrial function, and oxidative balance. Abnormal nutri-

ent metabolism reduces oocyte quality and reproductive performance. Several questions remain to be addressed: first, how to identify biomarkers of oocyte quality; second, how to optimize nutrient supplementation to maximize reproductive potential. In summary, further research is needed to explore the relationship between reproductive performance and nutrients, ultimately providing theoretical support for improving reproductive performance through nutritional approaches.

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Note: Figure translations are in progress. See original paper for figures.