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Review articles

Alimentary infertility in female cattle: Part III – the modulation of reproductive function with vitamins and plant derivatives (Overview)

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Abstract. Vitamins are involved in the synthesis of several organic compounds serve as coenzymes. Therefore, they are necessary for different processes such as metabolic regulation, the course of many biochemical reactions, the processes of cellular respiration, the maintenance of acid-base and electrolyte balance, and the protection of cells from oxidative stress. Thus, they support various body functions, including reproductive ones. Consequently, using diets that are not balanced in the composition of micronutrients and, in particular, vitamins can lead to several pathological conditions that affect their reproductive function and the state of the offspring. A deficiency in vitamins often results in reduced enzyme activity. Thus, specific metabolic processes are inhibited, including those in the endocrine glands associated with animal reproduction (such as the pituitary gland, adrenal glands, and ovaries), leading to disruption in the synthesis of gonadotropic and sex hormones. Delayed puberty, disruption of sexual cycles and ovulation, low fertility, and perinatal losses (impaired development and survival of embryos, early death and abortions, osteodystrophy in pregnant women, impaired development and skeletal defects in the fetus, and weak or dead offspring) are registered. Premature births occur, the contractility of the uterus and expulsion of the fetal membranes decreases, and postpartum activity is disturbed. Additionally, the period of manifestation of the first estrus after calving is prolonged, and inflammatory processes such as placentitis, cervicitis, metritis may develop. Moreover, milk fever may occur along with an increase in the frequency of cystic and atrophic ovaries. With excessive or long-term consumption of phytoestrogens, violations of the sexual cycle (from anestrus to nymphomania) can occur. Changes in the structure (cysts or their compaction) and function of the ovaries (synthesis of hormones in the follicles and corpus luteum), hyperemia of the mucous membranes, edema of the reproductive organs and post libido metrorrhagia are observed. Other effects may include prolapse of the vagina, cystic hyperplasia of the endometrium and purulent inflammation of the uterus, the onset of heat during pregnancy, a decrease in the frequency of fertilization, an increase in the loss of embryos, and the death of the fetus, difficult births, a high percentage of stillbirths. Thus, vitamins and biologically active substances of plants significantly impact the reproductive function of animals, so regulating their supply to the body of cows and heifers is an essential factor in ensuring the proper level of herd reproduction.

Keywords: cows; heifers; disorders of reproductive capacity; vitamins; plant biologically active compounds.

Аліментарна неплідність самок великої рогатої худоби: III – вплив вітамінів та біологічно активних речовини рослин на функції відтворення (літературний огляд)

Анотація. Вітаміни беруть участь у синтезі ряду органічних сполук, утворенні коферментів чи самі ними є і тому виключно необхідні для регулювання обмінних процесів, перебігу багатьох біохімічних реакцій, процесів клітинного дихання, підтримки кислотно-лужного та електролітного балансу, захисту клітин від окисного стресу. Тим самим вони підтримують різні функції організму, в тому числі й репродуктивну. Тож використання раціонів, не збалансованих за складом мікронутрієнтів і, зокрема вітамінів, може призвести до ряду патологічних станів, що впливають на їх репродуктивну функцію і стан потомства. Так, за дефіциту вітамінів знижується активність ферментів і тим самим гальмуються специфічні процеси обміну речовин, в тому числі в інкреторних залозах, пов'язаних з репродукцією тварин (гіпофіз, наднирники, яєчники), порушується синтез гонадотропних та статевих гормонів. Реєструють затримку статевого дозрівання, порушення статевих циклів та овуляції, низьку заплідненість, перинатальні втрати (порушення розвитку та виживання ембріонів, їх рання загибель та аборти, остеодистрофія у вагітних, порушення розвитку та дефектів скелета у плода, слабкий або мертвий приплід). Відбуваються передчасні роди, знижується скоротливість матки та вигнання плодових оболонок, порушується післяродова діяльність, подовжується термін прояву першої тічки після отелення, розвиваються запальні процеси

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(плацентити, цервіцити, метрити), молочна лихоманка, підвищується частота кістозних та атрофічних яєчників. За надмірної кількості чи тривалого споживання фітоестрогенів спостерігаються порушення статевого циклу (від анеструсу до німфоманії), зміни структури (кісти або їх ущільнення) та функції яєчників (синтез гормонів у фолікулах і жовтому тілі), гіперемія слизових оболонок, набряк органів відтворення та постлібідні метрорагії, випадання піхви, кістозна гіперплазія ендометрія і гнійне запалення матки, настання охоти під час вагітності, зниження частоти запліднення, збільшення втрат ембріонів та загибель плоду, тяжкі роди, високий відсоток народження мертвого приплоду. Таким чином, вітаміни і біологічно активні речовини рослин чинять значний вплив на репродуктивну функцію тварин, тож регулювання надходження їх до організму корів та телиць є важливими фактором забезпечення належного рівня відтворення стада.

Ключові слова: корови; телиці; порушення репродуктивної здатності; вітаміни; біологічно активні речовини рослин.

Introduction

Providing the body and, accordingly, the proper functioning of the reproductive system with feed micronutrients is much more complex than balancing the diet in the right proportions so that it covers the need for proteins, fats, and carbohydrates (macronutrients) (McDowell, 2002; Khan et al., 2014; Sabitov et al., 2021).

Micronutrients are essential compounds that are required in minimal doses. Some micronutrients are synthesized in the organism. However, other micronutrient types enter with food, but in both cases, we are talking about mini-doses (milligrams or micrograms). Unlike macronutrients, which are direct participants in the most important biochemical processes, micronutrients and their derivatives take part in the body's vital activity mostly indirectly, which does not make them less critical (Gombart et al., 2020; Berger et al., 2022; Kumar et al., 2024).

Micronutrients include vitamins and minerals. They contribute to assimilating macronutrients, regulate metabolism and activity, and support various body functions. In chemistry, there is a concept of catalysts, substances that do not themselves enter into a reaction but create the conditions necessary for it, thereby increasing the speed of the process. Micronutrients play a similar role in biochemical reactions. In particular, mini-doses of these substances are necessary for regulating metabolic processes, the course of many biochemical reactions, processes of cellular respiration, maintenance of acid-base and electrolyte balance, protection of cells from oxidative stress, and synthesis of several organic compounds. Almost all vitamins participate in the formation of coenzymes or are themselves coenzymes (Broadley et al., 2012; Alagawany et al., 2020; Fazliddinovna, 2022).

In this regard, a deficiency in micronutrients causes enzymatic dysfunction, impairing animal body metabolism and reproductive capacity. Therefore, the use of unbalanced diets, lacking in vitamins, macro-, and microelements can lead to some pathological conditions that affect their reproductive function and the state of the offspring (Omur et al., 2016; Taov et al., 2019; Skliarov et al., 2021).

Impaired reproductive function due to deficiency or excess of vitamins and plant biologically active compounds

Providing the cows with vitamins is an essential factor in ensuring a high level of herd reproduction. A deficiency or an excess of vitamins leads to a violation of reproductive function. Plant substances that affect the reproductive function significantly impact the reproductive function of animals (Table).

Vitamins

Over the past three decades, significant progress has been made in understanding the importance of adequate vitamin status in dairy cows based on improved nutrition. These advances have significantly redefined the importance of vitamins as critical signaling molecules or cofactors that enable animals to maintain health and optimize performance. For this reason, the concept of optimal vitamin needs of animals in intensive animal husbandry was developed (Baldi, 2005; Spears & Weiss, 2014; Weiss, 2017).

Vitamins are essential nutrients that influence economically important performance indicators of dairy cows, including milk production and reproduction. The effects of vitamins on livestock health and performance are often chronic and associated with suboptimal vitamin intake during critical periods of the production cycle. The specific effect of many vitamins on reproductive function remains unknown (Pradhan & Nakagoshi, 2008).

All vitamins are necessary for animal reproduction (McDowell, 2000; Koshovyj, 2004; Rasikh, 2019). Vitamins are substances of high biological activity that participate in all vital processes occurring in the body (Halver, 2003; Kraemer et al., 2012.; Combs et al., 2016). The supply of the necessary dose of vitamins supports the timely recovery of substances involved in metabolic processes (Yasothai, 2014a). Even though animals need vitamins in minimal quantities, their persistent lack in the diet leads to metabolic disorders, specific diseases, a decrease in the level of productivity and quality of products, as well as a decrease in reproductive capacity (Weiss, 2005, Weiss & Gonzalo, 2006; Marks, 2012).

Vitamins affect the reproduction process both directly and indirectly. Their action is primarily aimed at the endocrine and genital systems. It was established that the content of some vitamins is increased in many endocrine organs (Koshovyj, 2004; Jennings, 2014; Vašková, et al., 2023). Considering the information mentioned above, it can be concluded that the mentioned organs related to the reproductive system need more vitamins.

The number of vitamins entering the body and their ratio are essential for reproduction. An excessive amount of any one vitamin can harm reproductive function. The absorption of vitamins by the body depends on several factors, including the overall balance of the diet (Borel, 2003; Reboul & Borel, 2011; Said, 2011).

During spontaneous hypovitaminosis, many chains of the reproduction process are disrupted. With an insufficient supply of vitamins in the body, the speed of assimilation processes decreases, and dystrophic tissue changes develop, affecting the tissues of the reproductive organs. The accompanying sharp decrease in the body's resistance, inhibition of sexual desire, formation of cysts in the ovaries, decrease in endocrine function, and effectiveness of insemination occurs in cows. The number of cases of intrauterine fetal death, miscarriages, and deaths of weakened newborn calves is increasing (Koshovyj, 2004; Lysenko et al., 2010; Skliarov et al., 2023).

The need for vitamins and the nature of their exchange in the body of ruminants is determined by certain specifics of this species of animals – due to their biological and physiological characteristics; they need the intake of vitamins A, D, and E with feed and at an early age or under specific feeding conditions – vitamins of group B (Nayyar & Jindal, 2010; Schmidt & Zsédely, 2011; Suttle, 2016). Pradhan and Nakagoshi (2008) state that the most common vitamin deficiency is vitamins A and E. According to Antonov (2022), the most negative impact on reproductive health is the lack of these vitamins and carotenoids. As researchers learned about the new functions of fat-soluble vitamins, the need for them increased over time (Weiss, 2017).

Fat-soluble vitamins A, D, E, and K are a group of biologically active compounds essential for life, as they affect various links of

Table – Impaired reproductive function of alimentary origin due to deficiency or excess of vitamins and plant biologically active compounds

A type of alimentary infertility	Nature of violations
Deficiency of carotene/vitamin A	- delayed maturity; - violation of sexual cycles and ovulation; - low fertility; - perinatal losses (early death of embryos and abortions, weak or dead offspring); - premature births and litter retention; - subinvolution of the uterus; - delay of the first estrus after calving; - inflammatory processes (placentitis, cervicitis, metritis); - increased frequency of ovarian cysts and atrophy.
Vitamin D deficiency	- violation of the sexual cycle (anestrus); - osteodystrophy in pregnant women, developmental disorders, and skeletal defects in the fetus; - the birth of weak and rickety calves; - inhibiting the development of genital organs during the period of active growth; - milk fever, metritis, and retained placenta in dairy cows.
Vitamin E deficiency	- violation of the processes of synthesis of steroids, prostaglandins, and development of embryos; - deterioration of the level of ovulation, fertilization, and survival of embryos; - reduction of uterine contractility, the expulsion of fetal membranes, postpartum activity, and postnatal growth.
Deficiency of group B vitamins	- violation of the reproductive function due to a decrease in the activity of certain enzymes and thereby inhibition of specific metabolic processes.
Deficiency of vitamin C	- dysfunction of incretory glands associated with animal reproduction (pituitary gland, adrenal glands, ovaries).
Vitamin K deficiency	- a mediated effect on reproductive function due to disruption of cellular metabolism, in particular, a decrease in the production of hormones of the anterior lobe of the pituitary gland.
Excessive or long-term consumption of phytoestrogens	- violation of the sexual cycle (from anestrus to nymphomania); - violation of ovarian function, hormone synthesis in follicles and corpus luteum; - hyperemia of the mucous membranes of reproductive organs; - enlargement of the vulva to swelling; - cystic hyperplasia of the endometrium and purulent inflammation of the uterus; - cysts in the ovaries or their lump-like compaction; - hemorrhages after estrus; - coming into the hunt during pregnancy; - decrease in the frequency of fertilization; - increase in embryo loss and fetal death; - vaginal prolapse; - difficult births; - a high percentage of offspring death; - udder enlargement with swelling.

metabolism and the functional activity of organs and systems, and their lack leads to animal diseases. Control of the level and entry into the body with feed, synthesis, and amount in tissues and organs of fat-soluble vitamins is an essential aspect of ensuring high productivity and health of animals (Kurtjak & Janovych, 2004; Vlizlo et al., 2007).

Deficiency of specific fat-soluble vitamins in the body of cows is rare (Golovey et al., 2022; Borel et al., 2023; Skliarov et al., 2023). Fat-soluble vitamin and phytochemical metabolites: Production, gastrointestinal absorption, and health effects. Progress in Lipid Research, 90, 101220.). In Ukrainian farms, there is often a simultaneous deficiency of all these vitamins (Kurtjak & Janovych, 2004), negatively affecting various physiological functions, especially the reproductive, immune, and antioxidant systems.

Vitamins A, D, E, and K play an essential role in the nutrition of dairy cattle due to a wide range of their biological effects and influence on metabolism and physiological functions (Vlizlo et al., 2007). The most sensitive to the lack of vitamin A or complex A, D, and E are highly productive cows; they are diagnosed with metaplastic hyperkeratosis of the mucous membranes, ovarian atrophy, sexual cycle disorders, reduced fertility, abortions, premature births, litter retention, mastitis (Medvedev et al., 2019).

The functions of vitamin A are diverse. According to the established opinion, hardly any other vitamin performs as essential functions for preserving the life of animals and the whole species as vitamin A (retinol) (Koshovyj, 2004; Skljarov, 2015; Carazo, et al., 2021). This is confirmed by the definitions adopted for it, including synonyms such as 'growth vitamin', 'a vitamin involved in the vision process', 'vitamin that protects the skin', and 'anti-infective'. Vitamin A is involved in the metabolism of proteins, lipids, and carbohydrates, as well as amino acids and phosphorous compounds. A lack of vitamin A can lead to the accumulation of under-oxidized products of lipid metabolism in the blood. Vitamin A is essential because it prevents bacterial infections in many body tissues (Vlizlo et al., 2007; Chen & Chen, 2014; Skliarov, 2020, 2021).

Perhaps the most important is its positive effect on the reproductive function of animals. Vitamin A is a peculiar regulator of reproductive function. Therefore, retinol is often referred to as the vitamin of reproduction (Koshovyj, 2004; Skliarov, 2020; Shastak & Pelletier, 2024).

An essential source of dietary vitamin A is plant pigments – carotenoids, which can be transformed into retinol in the body (Bindari et al., 2013; Blaner, 2020;). Until recently, it was

believed that the physiological effect of carotene was due to its transformation into vitamin A. However, the works of recent years indicate that carotene for cattle is not only a source of vitamin A but also a substance with a completely independent biological activity (Yasothai, 2014a). ß-carotene plays a unique role in reproduction (Gaikwad et al., 2001; Schweigert, 2003; Chawla & Kaur, 2004; Noakes et al., 2018). Konnerman (1967) was the first to report a correlation between cow insemination frequency and β-carotene intake (cited in Tekpetey et al., 1987). Subsequent controlled studies have suggested that β-carotene plays a unique role, independent of vitamin A, in reproduction in cattle (Lotthammer, 1979). Studies conducted in Europe (Friesecke, 1978; Jackson, 1981; Bonsembiante et al., 1980) and North America (Olentine, 1982) have provided evidence that generally supports this hypothesis.

The metabolism of vitamin A and carotene significantly depends on the quantitative and qualitative composition of the diet, the state of the gastrointestinal system and digestion of nutrients, the physiological and hormonal status of the body, the consumption of various physiologically active substances, age, sex, season, environmental temperature and other factors (Koshovyj, 2004; Yasothai, 2014a). This influence occurs at different levels of metabolic transformations: transport, deposition, tissue, cellular and subcellular distribution, utilization, and removal from the body. Alimentary factors, compared to others, most actively influence the exchange of vitamin A and carotene (Koshovyj, 2004; Ljubec'kyj & Masalovych, 2016).

In recent years, the question of the causes of insufficient supply of the body of cattle with carotene (vitamin A) and the ways it adversely affects herd reproduction has become a significant concern (Vlizlo et al., 2007; Bindari et al., 2013). This issue becomes particularly acute during the winter stall keeping of cows and heifers (Koshovyj, 2004; Shevchenko, 2008; et al., 2015). During winter, it is challenging to provide cows with carotene through feed rations because roughage becomes much poorer in carotene over time in storage, and reserves in the animal's body are depleted in winter (Valjushkin and Luferov, 2003). Interest in β-carotene deficiency as a cause of reproductive problems stems from research conducted in Germany. Their results showed that dairy cows and heifers fed diets deficient in β-carotene suffered from the following reproductive problems: increased incidence of cystic ovaries, delayed uterine involution, first estrus after calving and ovulation, early embryonic death and abortion (Bindari et al., 2013; Yasothai, 2014a).

The need for it in animals depends on many conditions. For example, animals need a lot of vitamin A at high ambient air temperatures. It has been established that at additional high temperatures (over 30°C) and solar radiation, especially in July-August, fertility decreases, anovulatory sexual cycles, and high embryonic mortality are recorded, which leads to multiple ineffective inseminations. In summer, A-hypovitaminosis can develop during prolonged droughts when the grass dries up, turns yellow, and almost does not contain carotene. It should be considered that the digestibility of feed carotene is affected by the diet's vitamin D content and soluble carbohydrates (Glaz et al., 2011).

The animal's body can accumulate vitamin A in the summer and use it in the winter. Thus, the carotene content in the blood of cows during summer pasture maintenance reaches 1-2 mg%, but by the end of the winter-stall period, due to its lack in the rations, it decreases to 0.06 mg%. This affected the viability of newborn calves, the state of reproductive function, and the incidence of gynecological diseases (Glaz et al., 2011). According to Kuz'mich (2018) blood-carotene deficiency is registered in more than 60% of cows on some farms throughout the year. In Canada, some dairy herds that do not receive quality hay are likely to have deficient blood-carotene levels (<100 pg dl-l). A survey of eight herds in Ontario and Quebec showed that serum β-carotene levels were low (<300 pg Ot-t) in five herds primarily fed corn silage and grain diets (Harvey & Smith, 1979). This study had the following objectives: 1) to determine the extent of seasonal fluctuations in the concentration of β-carotene and vitamin A in the serum of cows that were kept in winter and received a sufficient amount of quality forage in winter and pasture in summer and 2) to determine whether the postpartum reproductive performance of these cows was correlated with carotene concentration in serum and vitamin A during the prenatal and early postpartum period (Tekpetey et al., 1987).

Vitamin A regulates development, cell growth and differentiation, and tissue function. Its metabolites affect ovarian follicle growth, the uterine environment, and oocyte maturation (Schweigert & Zucker, 1988). Reproductive disorders observed with vitamin A deficiency in farm animals include delayed puberty, low fertilization rates, and high embryonic and perinatal mortality (Pradhan & Nakagoshi, 2008). Placental accretion, retention, and metritis have been reported (Vlizlo et al., 2007; Bindari et al., 2013; Tsai, 2021).

Vitamin A deficiency directly affects the structure and function of the pituitary gland, gonads, and uterus (Pradhan & Nakagoshi, 2008; Bindari et al., 2013). Vitamin A deficiency can directly affect reproductive function by suppressing the synthesis of sex hormones (Glaz et al., 2011). It is known that carotene and vitamin A contributes to the maintenance of the specificity of the epithelium of the mucous membranes and the preservation of the protective factors of the endometrium (Kuz'mich, 2018). Therefore, due to a violation of the metabolism of carotene and vitamin A in the body of beef cows, there is a tendency for the occurrence of an inflammatory process in the placenta and the mucous membrane of the uterus at the end of pregnancy and the postpartum period (Bendich, 1994). Metaplasmic hyperkeratosis of the mucous membrane of the cervix, increased sensitivity to infection of the mucous membranes of this organ, atrophy of the ovaries, reduced fertilization, disruption of sexual cycles, death of embryos, premature births, delayed litter, etc., are observed (Vlizlo et al., 2007; Bindari et al., 2013; Skliarov, 2020).

The effect of vitamin A on the morphological and functional state of the regulatory systems of reproductive function in cows and heifers, as well as on the morphological and functional state of the fetoplacental complex in cows and heifers, was studied. Thus, with a lack of vitamin A, the function of the epithelial tissue is disturbed, which leads to its drying, keratinization, and desquamation, their protective function decreases, and inflammatory processes appear. Corning of the mucous membrane of the cervix and other areas of the genital tract is noted in cows and heifers; it increases its sensitivity to infection, which contributes to the occurrence of endometritis and cervicitis, prevents the attachment of the zygote or causes congenital anomalies, the death of the fetus and its expulsion in the first weeks or months of intrauterine development (Koshovyj, 2004; Medvedev et al., 2019; Skliarov et al., 2020).

Hypervitaminosis A does not occur in cows (Vlizlo et al., 2007). Thus, it can be concluded that carotene and vitamin A, one of many balanced biological systems, perform a protective function in the body. Beta-carotene plays an essential role in regulating the functional state and the occurrence of the pathology of the reproductive organs in cows.

Vitamin D (calciferol) encompasses a group of related compounds, but the most important are D2 and D3, ergocalciferol, and cholecalciferol, respectively (Vlizlo et al., 2007). Cattle have almost the same biological effect and are formed from precursors (sterols – provitamin D) under natural sunlight or artificial exposure to ultraviolet rays (Koshovyj, 2004). Calciferol affects nitrogen, carbohydrate, and energy metabolism and participates in the absorption and retention of Calcium and Phosphorus (Koshovyj, 2004; Bindari et al., 2013;). However, its role is not limited to this and is related to immunity (Hodnik et al., 2020; Eder & Grundmann, 2022; Ismailova & White, 2022).

Cows' need for vitamin D increases with productivity, the absolute level of which simultaneously depends on the availability of Calcium and Phosphorus (Vlizlo et al., 2007; Yasothai, 2014b). During the second half of pregnancy in cows and at the beginning of lactation, as well as due to the predominance of silage, beets, potatoes, and sugar industry waste in the diet, the need for vitamin D increases significantly (Koshovyj, 2004). The reproduction level depends on the body's supply of vitamin D (Peixoto de Souza et al., 2022).

Plant foods contain a small amount of vitamin D, so their level in the diet is only 35% of the needed. Lack of vitamin D negatively affects the assimilation of Calcium and Phosphorus; therefore, even with a sufficient amount of Calcium in the diet, animals cannot use it to the full extent (Cheremnjakova & Nekrasov, 2008).

The negative effect of vitamin D deficiency on reproduction is often found in cows during the stall period due to insufficient intake of ergosterols with feed, as well as due to keeping them in dark rooms and lack of regular walks under sunlight. At the same time, the exchange of Calcium is disturbed, the general condition of the animal worsens, the sexual cycle (anestrus) is disturbed; skeletal development in the fetus is disturbed, and calves are born weak (Koshovyj, 2004; Medvedev et al., 2019).

Pronounced D-hypovitaminosis in animals during the period of active growth inhibits the development of genital organs (Vizner, 1976) and the birth of calves with rickets (Linn et al., 1990) and also leads to milk fever, metritis, and retained placenta in dairy cows (Yasothai, 2014a). Vitamin D can be toxic if cows receive excessive supplementation or consume large amounts of plants such as Trisetum flavescens, which contain the active form of vitamin D—calcitriol or its glycosides—activated during digestion in the rumen (Hodnik et al., 2020).

Vitamin E (tocopherol) is involved in the metabolism of muscle and nervous tissue, ensuring the function of reproductive organs, affects the activity of the pituitary gland and thyroid gland, as well as in exchange reactions with amino acids, vitamins A and C, neutral fats, hormones and Selenium. Vitamin E has the most significant activity. It is contained in almost all body tissues. Still, in the uterus, adrenal glands, and pituitary gland, it is much more than in other organs, which indicates the specificity of the functions of this vitamin in the listed organs (Koshovyj, 2004; Haga et al., 2021; Shastak et al., 2023).

The physiological role of vitamin E in the body of animals is diverse. It functions as an intracellular antioxidant by scavenging free reactive oxygen and lipid hydroperoxides and converting them to non-reactive forms, thus preserving the integrity of membrane phospholipids from oxidative damage and peroxidation (Surai, 1999). That is, vitamin E prevents the oxidation of substances; helps to improve the use of oxygen by tissues in the process of breathing; takes part in the process of oxidative phosphorylation in the metabolism of nucleic acids, and regulates protein, carbohydrate and lipid metabolism; prevents the formation of toxic metabolic products in the body; promotes the synthesis of ascorbic acid; normalizes the action of several enzyme systems; is an anticoagulant and antithrombin; has an antispasmodic effect; encourages the expansion of capillaries; eliminates fatty degeneration and prevents a decrease in the elasticity of the wall of blood vessels; plays a significant role as an antioxidant in stabilizing fat in the body; stimulates the conversion of carotenoids into vitamin A and the production of gonadotropins, adrenocorticotropic and thyroidotropic hormones by the anterior lobe of the pituitary gland (Koshovyj, 2004). In addition, vitamin E plays a critical role in the functioning of the immune system, so adding supra-nutritive levels of the vitamin in some cases results in an improved immune response (Baldi, 2005). One of the most significant functions of vitamin E is antioxidant, which minimizes the harmful effects of excessive production of reactive oxygen species (Xiao et al., 2021).

Cattle are usually not deficient in vitamin E because it is found in green plants. Its deficiency in the diet of cows is observed only when they are fed low-quality fodder or when it is stored for a long time when its losses are as significant as carotene, and this can lead to its deficiency in the body (Vlizlo et al., 2007).

Vitamin E deficiency is associated with selenium deficiency (Villar et al., 2002; Pradhan & Nakagoshi, 2008). Under conditions of deficiency of vitamin E and Selenium, free radicals accumulate and not only damage cell membranes but also disrupt some processes related to the synthesis of steroids, prostaglandins, and embryo development (Hemler & Lands, 1980; Staats et al., 1988; Goto et al. al., 1992). Therefore, it is not surprising that there is a negative effect of vitamin E and selenium deficiency on various components of the reproductive process, including ovulation rate (Harrison & Conrad, 1984), uterine contractility (Segerson & Libby, 1982), fertilization rate and postpartum activity (Arechiga et al., 1994), the expulsion of fruit membranes (Wichtell et al., 1996), embryo survival, postnatal growth (Anke et al., 1989; Bindari et al., 2013; Yasothai, 2014a).

However, Vizner (1976) concludes that vitamin E does not play a decisive role in cattle reproduction. These conflicting data limit its role but only partially disprove it, just that it is less prominent than previously claimed. However, research into the role of vitamin E in reproduction continues. There is no documented evidence that vitamin E deficiency is a significant cause of reproductive failure in dairy herds. Furthermore, the vitamin E requirement of cows has yet to be discovered with certainty. In one experiment, cows were fed diets low in vitamin E for four generations. There was no measurable effect on reproduction (Bindari et al., 2013).

Research on water-soluble vitamins has yet to catch up. It is now known that adding specific water-soluble vitamins can improve cow health and increase milk production in certain situations. However, more research is needed to determine the specific requirements for many water-soluble vitamins (Weiss, 2017).

Vitamins of group B differ little in terms of their chemical properties and biological mechanism of action; they are soluble in water and can be synthesized in significant quantities in ruminant foreskins. They take an active part as coenzymes in many enzymatic processes. Most group B of vitamins (as well as vitamin K) are thought to be synthesized by bacteria in the rumen in amounts sufficient to meet the animal's needs (Spears & Weiss, 2014). Thus, diets typically contain significant B vitamins, and rumen bacteria can synthesize many group B vitamins (Weiss, 2017; Girard & Graulet, 2021; Brisson et al., 2022).

Supplementation of vitamin B complex molecules has previously shown benefits in improving dairy cows' milk production, health, and reproductive performance (Kaur et al., 2019). With their deficiency, there is a decrease in the activity of certain enzymes and, thus, inhibition of specific metabolic processes. Experimental animals with B-avitaminosis show significant violations of reproductive function, which is consistent with the well-known theory about the participation of enzymes in the reproduction process. However, the lack of vitamins in group B is not as often the cause of reduced reproductive capacity in animals as the lack of other vitamins (Koshovyj, 2004).

In the studies of Kaur et al. (2019), vitamin B supplementation did not affect embryo and ovulatory follicle size or corpus luteum diameter. In summary, the benefits of the strategic addition of vitamin B to diets during the transition and early lactation may be directly related to endometrial functions necessary for embryo survival in the preimplantation period.

Vitamin B12 is an enzyme cofactor (Rizzo & Laganà, 2020; Deniz & Aksoy, 2022; Halczuk et al., 2023). Cobalt is a crucial component of this vitamin, so the latter plays an indirect role in the functions performed by vitamin B12 (Van Emon et al., 2020).

Sufficient amounts of vitamin B12 pass through the placenta and are contained in colostrum. Milk also contains high vitamin B12, necessary for converting propionate to glucose and folic acid

metabolism. Depletion of vitamin B12 during parturition causes a decrease in milk production and colostrum productivity and quality (Bindari et al., 2013).

A deficiency of vitamin B12 reduces appetite and feed intake, leading to delayed puberty and ovarian and uterine atrophy in cows (Yasothai, 2014a).

Vitamin C (ascorbic acid) is found in all body tissues, but there is much more vitamin C in the pituitary gland, adrenal glands, and ovaries than in the blood. Its presence in the above organs makes us admit that ascorbic acid is necessary to function in these incretory glands associated with animal reproduction. It is an active stimulator of metabolism and is associated with steroid hormones in the cortex of the adrenal glands, takes part in blood clotting, stimulates the phagocytic activity of leukocytes, the reticulohistiocytic system, and the formation of antibodies, increases the body's defenses against infection. It significantly transfers iron ions from plasma protein, transferrin, to organ protein and ferritin, ensuring iron deposition in the bone marrow, spleen, and liver (Doseděl et al., 2021; Abdullah et al., 2022).

Some functional disorders in the reproductive organs of cows, especially the ovaries, arise due to the low ascorbic acid content in the blood. The author believes that the issue of satisfying the body's needs for vitamin C is a problem of the microbiology of the rumen. Since it became known that rumen bacteria can destroy and synthesize vitamin C, this can partially explain the development of hypovitaminosis C in ruminants (Koshovyj, 2004; Kirdeci et al., 2021).

In the vast majority of studies, the effects of vitamin C are considered in combination with other vitamins (Ataman et al., 2010).

The most important function of vitamin K in the body is participating in blood clotting (Vlizlo et al., 2007; Mladěnka et al., 2022). In addition, it also participates in cellular metabolism and therefore plays an essential role in the vital activity of cells (Koshovyj, 2004). There are very few reports on the effects of vitamin K on reproductive function in animals (Wang et al., 2023). Effects of vitamin K supplementation on reproductive performance and bone metabolism-related biochemical markers in lactation sows. Animal Bioscience, 36(10), 1578.). Vizner (1976), referring to the data of Italian authors, indicates the positive effect of vitamin K on the reproductive capacity, which, it is assumed, is connected with its stimulation of the production of hormones in the anterior lobe of the pituitary gland.

Plant biologically active compounds affecting the reproductive function

Recently, the issue of the effect of hormonally active substances contained in plants on the reproductive capacity of animals has been studied quite actively. As it is now known, more than 300 species of plants, including widespread fodder plants, contain various substances that exhibit hormonal effects (Koshovyj, 2004).

Phytoestrogens are the most well-known plant substances affecting reproductive function. These are nonsteroidal natural plant compounds structurally or functionally similar to mammalian estrogens, particularly 17β-estradiol (Mostrom & Evans, 2011; Wocławek-Potocka et al., 2013; Adnan et al., 2022). As a rule, phytoestrogens or their active metabolites exert their estrogenic effect on the central nervous and reproductive systems, causing estrus and stimulating the growth of the genital tract and mammary glands in females; in fact, at many levels – from the hypothalamic-pituitary to the local ovary-uterus – through numerous mechanisms. Their effects may vary depending on the individual phytoestrogen, species exposed, sex, route, dose, and duration of exposure, especially timing during reproductive development and the cycle (Mostrom & Evans, 2011; Morales Ramírez et al., 2022). Phytoestrogens can either be harmful to reproduction and estrogen-dependent diseases or beneficial to those who are steroid-deficient (Bennetau-Pelissero, 2016).

Phytoestrogens have recently attracted considerable interest due to increasing information about their harmful effects on human and animal reproduction (Adnan et al., 2022). When livestock consumes high concentrations of phytoestrogens, the latter can cause long-term reproductive impairment due to their structural similarity to mammalian estrogens and propensity to bind estrogen receptors (Wyse et al., 2021). Acting as destroyers of the endocrine system, they can cause various pathologies of the female reproductive system (Wolawek-Potocka et al., 2005). Phytoestrogens and their metabolites can impair corpus luteum function by inhibiting prostaglandin- and luteinizing hormone-stimulated progesterone secretion (Piotrowska et al., 2006).

Phytoestrogens can have the same effect as sex hormones of animal origin – they regulate egg development, ovulation, fertilization, childbirth, and lactation. They are found in various crops: clover, alfalfa, peas, corn, ryegrass, barley, oats, licorice, fodder cabbage.

The content of active estrogenic substances in diets ensures the normalization of many metabolic processes in the body. The level of estrogens and antiestrogens determines resistance and detoxification processes in the body of animals, their reproduction, growth, and development. In this regard, it is essential to know the level of phytoestrogen content in fodder crops depending on the different conditions of their cultivation, harvesting, and preparation of fodder for feeding.

The positive effect of estrogenically active substances on the physiological processes of the animal body can change to a negative one if plants with high phytoestrogens are unilaterally fed to animals – however, excess plant estrogens and their limited content cause sexual dysfunction.

A large number of estrogens, which animals receive due to excessive consumption of legumes and particular cereal feeds, can cause a violation of the sexual cycle (from anestrus to nymphomania), hyperemia of the mucous membranes of the reproductive organs, swelling of the vulva, cystic hyperplasia of the endometrium, and purulent inflammation of the uterus, cysts in the ovaries or shot-like their compaction, coming into heat during pregnancy, death of the fetus, prolapse of the vagina and complicated births, a high percentage of death of the fetus, enlargement of the udder with edema, changes in productivity (Palfij, 1982).

Cows fed estrogenic feed may experience ovarian dysfunction, often accompanied by reduced fertilization rates and increased embryo loss. Clinical signs resemble those associated with cystic ovaries. Infertility is temporary and usually resolves within one month after cessation of estrogen feeding. At the same time, the cervix defeminizes and loses the ability to store sperm, so the frequency of fertilization decreases, although the function of the ovaries remains normal. Both temporary and permanent infertility often occur without visible signs and can only be detected by determining the content of phytoestrogens in the diet or their effect on the animal. Low background concentrations of forage phytoestrogens are believed to play an essential role in disease prevention, but their subclinical effects in cattle have yet to be described. The effects of low concentrations of phytoestrogens on ruminant reproductive function are likely to receive increasing attention (Adams, 1995).

The effect of phytoestrogens on the reproductive function of cattle was observed in several European countries. In particular, in Finland, the reproductive function of cows was disturbed after long-term feeding of red clover silage, which contained phytoestrogens in 100 kg of dry matter in an amount equivalent to 16 μg of diethylstilbestrol (Preobrazhenskij & Preobrazhenskij, 1974). In Germany, the saturation of rations with silage from a mixture of alfalfa and cereal grass with a high content of antiestrogens caused short-term changes in the cyclicity and reduction of fertilization in cows and heifers – severe and long-lasting (more than eight days) hemorrhages after oestrus (Gnojevyj, 2006).

The influence of licorice phytoestrogens on the etiology of infertility in cattle has already been reported in the literature (Shimanov, 1972). With an increase in the content of hay from this crop in the diet, the frequency of abortions and female infertility increased, and the yield of calves per 100 cows decreased. Feeding 25% sweet hay in the diet positively affected the reproductive function of cows. Feeding 100% licorice in the diet lengthened the period from childbirth to fertilization, reduced the fertility of cows against the background of disruption of the course of sexual cycles, and increased the insemination index. Licorice root accelerated puberty in immature heifers, but sexual function was impaired.

The body of animals that constantly receive active estrogenic substances with feed is adapted to intake a certain dose of phytoestrogens. However, with long-term consumption of such meals by animals, phytoestrogens can accumulate in the body in large quantities. Consequently, there may be violations of the hormonal balance and several pathological changes, particularly infertility (Gnojevyj, 2006).

The results of studies by Mlynarczuk et al. (2011) demonstrate that phytoestrogens (genistein, daidzein, coumestrol) can disrupt bovine ovarian function, negatively affecting hormone synthesis in follicles and corpus luteum. However, their effect on ovarian steroid secretion was less pronounced.

Morales Ramírez et al. (2022) found that consuming high polyphenolic compounds from different forages by cattle was associated with reduced fertility, abortions, and ovarian cysts.

A decrease in fertility can also be explained by the local – direct effect of phytoestrogens on the reproductive tract. Phytoestrogens can suppress endogenous estrogen production in the ovary, leading to immune dysregulation, follicular development, and the absence of estrus (Rosselli et al., 2000).

Other plant substances affecting reproductive function are antiestrogens (Schramm et al., 1991; Adams, 1995; Doualla-Bell et al., 1995), antigonadotropins (Shupnik, 1996; Fike et al., 1997; Schneider et al., 2006), antithyroid (Scolari et al., 1962; Villar et al., 2002b; Krassas et al., 2010), androgens (Hoffmann & Schuler, 2000; Earl Gray Jr et al., 2006; Akbarinejad et al., 2019).

In connection with the above, balancing rations according to explicit norms and considering the primary nutrients, macro-, microelements, and vitamins still need to guarantee a high animal reproductive capacity. It is still necessary to ensure a sufficient supply of hormonally active feed substances that influence the functional state of the reproductive organs of animals (Koshovyj, 2004).

Conclusion

As micronutrients, vitamins are catalysts in biochemical reactions, thereby regulating metabolism and supporting various body functions, including reproductive ones. Even though these substances are needed in mini-doses, they are indispensable for regulating metabolic processes, the course of many biochemical reactions, the processes of cellular respiration, the maintenance of acid-alkaline and electrolyte balance, and the protection of cells from oxidative stress. Almost all vitamins participate in synthesizing many organic compounds, forming coenzymes, or are themselves.

Therefore, using diets that are not balanced in the composition of micronutrients and, in particular, vitamins can lead to several pathological conditions that affect their reproductive function and the state of the offspring. Thus, delayed puberty, violations of sexual cycles and ovulation, low fertility, perinatal losses (early death of embryos and abortions, weak or dead offspring), premature births, and retention of litter, subinvolution of the uterus, prolongation of the first manifestation of oestrus after calving, inflammatory processes (placentitis, cervicitis, metritis), increased frequency of cystic and atrophic ovaries can result from a deficiency of carotene/vitamin A.

Vitamin D deficiency leads to changes in the sexual cycle (anestrus), osteodystrophy in pregnant females, impaired development and skeletal defects in the fetus, the birth of weak and rickety calves, retardation of the development of the genitals during the period of active growth, milk fever, metritis, and retained placenta.

Deficiency of vitamin E leads to violation of the processes of synthesis of steroids, prostaglandins, and development of embryos, deterioration of the level of ovulation, fertilization, and survival of embryos, reduction of contractility of the uterus, the expulsion of fetal membranes, postpartum activity, and postnatal growth.

With a deficiency of vitamins of group B, reproductive function is impaired due to a decrease in the activity of certain enzymes and, thereby, inhibiting of specific metabolic processes.

A deficiency of vitamin C creates conditions for disrupting the functioning of secretory glands associated with animal reproduction (pituitary gland, adrenal glands, ovaries).

A deficiency of vitamin K indirectly influences the function of reproduction due to a violation of cellular metabolism, particularly a decrease in the production of hormones in the anterior lobe of the pituitary gland.

With excessive or long-term consumption of phytoestrogens, violations of the sexual cycle (from anestrus to nymphomania), changes in the structure (cysts or their compaction) and function of the ovaries (synthesis of hormones in the follicles and corpus luteum), hyperemia of the mucous membranes, edema of the reproductive organs and post libido metrorrhagia are observed. Other reproductive issues include prolapse of the vagina, cystic hyperplasia of the endometrium and purulent inflammation of the uterus, the onset of heat during pregnancy, a decrease in the frequency of fertilization, an increase in the loss of embryos, and the death of the fetus, difficult births, a high percentage of stillbirths.

Thus, vitamins and biologically active substances of plants significantly impact the reproductive function of animals, so regulating their supply to the body of cows and heifers is a crucial factor in ensuring the proper level of herd reproduction.

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