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METHOD OF PREVENTING HIGH-YIELDING COWS' KETOSIS**Ovsiienko S.***Candidate of Agricultural Sciences, Associate Professor
Vinnytsia National Agrarian University
Ukraine***Abstract**

The feeding by feed additives made from such plant mono components as hay flour from milk thistle and welted thistle reduces the ketone bodies by 34.7-33.3% in the body of high-yielding cows; the addition of saponite flour and molasses decreases the level of ketone bodies by 43.3-44.6%. The content of ketone bodies in the blood of experimental cows at 7 and 21 days after calving was in the range of 0.95-0.78 mmol / l, it is an acceptable physiological value for its level in control cows of 1.31-1.41 mmol / l.

Keywords: high-yielding cows, ketosis, ketone bodies, milk thistle, welted thistle, feed additive.

Statement of the problem. A significant obstacle to increasing animal productivity is metabolic pathology in all countries with intensive dairy farming. Metabolic diseases lead to significant economic losses in livestock due to shortage of offspring, milk, increased production costs and reduced profitability of dairy farming. Metabolic disorders reduce resistance, change the functions of organs, systems and the vital functions of the whole organism. The consequences are reduced milk productivity, body weight, impaired reproductive capacity and increased culling of cows [15].

The common metabolic disorders are often registered in countries with highly developed dairy farming, i.e. Germany, the Netherlands, and Denmark. However, according to V. Horzheiev [1], in Ukraine metabolic diseases were registered in 50–80% of dairy cows with a productivity of 8–10 thousand kg of milk per lactation.

Ketosis is observed in cattle, pigs, and sheep. It is characterized by impaired metabolism of proteins, carbohydrates, lipids, high content of ketone bodies (acetone, acetoacetic, beta-oxybutyric acid) and other underoxidized metabolic products in blood, urine, and milk. It is most common for highly productive fattened cows in the first period of lactation (with a milk yield of 5,000 kg and more), pregnant sows and ewes. However, there are reports that monogastric animals don't suffer from ketosis as a separate disease. It is a symptom of other diseases. Ketosis occurs with an excess of protein, fat and lack of carbohydrates in the cows' diet. Chronic deficiency of such trace elements as copper, zinc, manganese, cobalt and iodine, resulting in impaired biosynthesis of propionic acid, B vitamins, microbial protein in the pancreas reducing protein synthesis, hormones, enzymes and, as a consequence, to disturbance of all types of a metabolism, accumulation in an organism of ketone bodies and other underoxidized products of a metabolism plays a crucial role for ketosis development [12].

The most common diseases are ketosis, postpartum hypocalcemia, abomasum displacement, acidosis, mastitis, endometritis and laminitis. These diseases cause the biggest problems in highly productive herds, because they are caused by metabolic disorders in cows at the beginning of lactation [6].

There are significant changes in cows' metabolism during the transition from pregnancy to lactation in a few days. Three weeks before calving is a short but very

important period of time in a cow's life, it determines the health and productivity of the next lactation and the safety. The consumption of nutrients for fetal growth, enlargement of the placenta and breast is high, and in the first month of lactation due to energy deficiency, there is a decrease in body weight in the last three weeks of pregnancy [16].

According to Bayer, ketosis of dairy cows was registered in 36.5% of the studied cows in Ukraine.

Ketosis is a disease of ruminants characterized by profound metabolic disorders (mainly carbohydrate-lipid and protein), it is accompanied by increased formation and a sharp increase in the content of ketone bodies in blood, urine and milk, resulting in damage to the central nervous and pituitary-adrenal systems, thyroid and thyroid glands, liver, kidneys and other organs [6].

The predisposition of ruminants to ketosis is due to the peculiarities of their cicatricial digestion.

The first trimester of lactation in cows is the basis for the current lactation, the whole economy and profitability of milk production. The level of energy supply of dairy cows is one of the leading factors determining productivity and indicators of normal reproduction, i.e. fertility, regularity of sexual cycles during this period. The specified indicators can change easily under the influence of insufficient and excessive feeding. Carbohydrates enter the ruminants' body not as glucose, they enter as short-chain fatty acids (SCFAs), i.e. acetic, propionic, butyric, and others. If the feeding is optimal the ratio of SCFAs is 50–60% of acetic acid, 20–25% of propionic acid and 15–20% of oil acid. The ratio of SCFAs varies depending on the diet structure and other factors. The ruminants need for glucose is satisfied by 10%, the other 90% is covered by gluconeogenesis; it is caused by the influx from the digestive tract. Propionic acid has a pronounced glycogenic effect, and butyric acid has a powerful ketogenic effect. Propionic acid is converted to glucose in the ruminants liver; acetic acid in adipose tissue and mammary glands is used in the synthesis of long-chain fatty acids; it is a source of energy and fat in milk; butyric acid in the wall of the scar is converted into β -hydroxyacetate, it is used in the synthesis of fatty acids in the breast [8]. Thus, insufficient intake of propionic acid and excess butyric acid is a prerequisite for increasing ketogenesis.

If the feed does not fully meet all the nutrient needs of cows, fat is used in large quantities to produce

milk depots and muscle proteins accumulated by the animals in the second half of lactation and especially during the dry period. Abrupt mobilization of internal reserves from fat accumulation leads to increased load on the liver resulting in so-called fatty liver syndrome leading to ketosis, decreased productivity and often to cow death or culling in the first 40-60 days after calving. The cow loses a lot of weight, it affects its productivity and reproduction. These problems in the first 90-100 days of lactation are more common in both palliative and clinical forms for cows with large reserves of fat in the body [5].

Excessive and rapid use of reserve fat in the postpartum period and the emergence of various pathologies has been called lipomobilization syndrome or fat mobilization syndrome. This syndrome is common for high milk productivity cows with. Research of high-yielding dairy cows in different farms of Ukraine showed that obesity is diagnosed in 10-35% of the herd [16].

Lipomobilization syndrome is registered with energy deficiency in the first 20 days after calving, it is typical for obese cows with internal non-infectious, obstetric and gynecological and surgical diseases, hyperfunction of the thyroid gland and adrenal medulla. It is important to note that quite often lipomobilization syndrome precedes ketosis of dairy cows [6].

Cornell University researchers have found that dairy cows use less and less endogenous amino acids with age, and the efficiency of using amino acids that enter the intestinal adsorption increases. M.V. Komaragiri and R.A. Erdman [4] found that a dairy cow mobilizes 21 kg of endogenous protein and 54 kg of endogenous fat two days before calving and on the twelfth day after calving. These studies suggest the importance of the functional state of the liver and kidneys during this physiological period, because the catalytically released substances must be metabolized in the liver, and their breakdown products are excreted through the kidneys. Accordingly, the decrease in the functional state of the liver and kidneys will inevitably lead to complex metabolic disorders in the whole body.

A significant number of publications are devoted to the issue of ketosis of high-yielding cows, further study of this problem and development of new methods of disease prevention is relevant, because Ukraine has shown a positive trend to improve the genetic potential of dairy cows in recent years.

Analysis of recent research and publications.

Increasing milk production is a risk to the health of cows; it means high requirements for feeding, keeping and caring for animals. It is feeding in the first trimester of lactation after calving, which further ensures proper metabolism and preparation for the next lactation. During this critical period, insufficient feeding, in particular energy deficiency, and stress can lead to further metabolic disorders and ketosis leads to reduced milk yield, fattening, reproductive dysfunction and premature culling of cows [8].

It is known that 20% of cows' livers are subject to culling at slaughter at meat processing plants. Liver abscesses are registered in more than 33% of animals at

industrial complexes for intensive young cattle fattening. The cows' liver decreasing is associated with changes in the structure of feed consumption, intensive use of silage, molasses and the presence in their composition of fungal toxins and other harmful substances. It has become clear that the prevention of disorders is based on the ability to relieve the burden of gluconeogenesis and release, thus, oxaloacetate for energy. This bypass involves the use of propionate blood glucose. The most suitable substrate is propylene glycol propane. All over the world, this drug is used to prevent ketosis. It is used for healthy animals to prevent ketosis in the amount of 150 g per head per day for 2 weeks before calving and for 4 weeks after calving. However, there are a number of drugs, such as acetone-energy, catozal and others that contain propylene glycol [14]. The use of propylene glycol has been shown to have a number of negative effects on cow scarring. It is partially oxidized to lactate, and its excess can affect brain function, it is clinically manifested by inhibition or disruption of the motor centers of the brain. The excess of propylene glycol (overdose) is quite real due to its introduction with the diet and insufficient mixing. Cows do not eat feed containing propylene glycol. There is also information about its inefficiency. Intravenous administration of large doses of drugs containing propylene glycol can lead to hypotension, bradycardia, abnormalities of the T wave and QRS complex on the ECG, arrhythmia, cardiac arrest, hyperosmolarity syndrome, lactic acidosis and hemolysis. According to a 2010 study by the Swiss University of Karlstad, the concentration of platinoids, propylene glycol and glycol esters in indoor air leads to an increased risk of respiratory and immune disorders. Frequent inhalation of propylene glycol esters has been shown to lead to asthma, hay fever, eczema and high-risk allergies in the range of 50% to 180% [9].

The main method of treatment of cows with ketosis is intravenous glucose and subcutaneous insulin. This allows the blood glucose level to equalize. However, after intravenous glucose, it is excreted in the urine. The concentration of glucose in the blood increases sharply by 8 times, it returns to baseline in two hours [16]. The insulin concentration increases more than 5 times, then it gradually decreases to baseline in 2 hours after. There is a decrease in the concentration of ketone bodies in the blood in this short period of time. There have been examples where blood glucose and insulin levels fall to baseline the next day (even after 5 days of 50% glucose solution), but there are examples of animals recovering for 7-10 days, and in more severe cases this process continues 20-25 days. It should also be added that patients with ketosis of cows reduce the effectiveness of exogenous hormones and antibodies, as they very quickly lose their properties in an acidic environment. It is typical to other substances that are part the endocrine organs tissues and enzymes. It reduces the activity of the immune system of cows and their calves. Newborn calves from cows with ketosis often become exhausted from toxic dyspepsia and die due to opportunistic pathogens. The activity of digestive enzymes is 3-5 times lower than in calves born from healthy cows. There are enough scientific world

data proving the negative impact of elevated levels of ketone bodies on immunogenesis and immune response [3]. According to V. Pedan [10], the subclinical form of ketosis is more expensive because it is more common. For example, if the average dairy herd has a 5% incidence of clinical ketosis and the disease per animal costs UAH 1,300 (at 2012 prices), then the treatment of 100 dairy cows is UAH 6,500 net loss ($5 \times 1,300$). The average subclinical form of ketosis (the percentage of animals with a concentration of d-isomeric beta-oxybutyric acid in the blood above 1 mmol per l) will be close to 40% of animals. It happens during the first 20 – 30 days of the lactation period.

It is known that the main negative consequences of subclinical ketosis are a 3 liter decrease in daily milk production per cows, increase the service period by 16 days, reduce fertility by 50%, increase the risk of clinical ketosis 6 times, endometritis 4.4 times, rennet displacement three times, mastitis and laminate twice. This is approximately UAH 650 per one head. Total losses on the herd of 100 cows will amount to 26 thousand UAH (40×650). Thus, selecting an antiketosis program for a particular herd special attention should be paid to the percentage of subclinical ketosis in the herd. It is necessary to establish proper feeding of cows in all phases of lactation and in the dry season to prevent ketosis. Therefore, the best prevention of ketosis is one that prevents its occurrence and that does not involve the use of any special drugs.

All the above-mentioned facts forced us to carefully analyze the situation. Considering the prophylactic and therapeutic properties of milk thistle and welted thistle, we saw the need to create a feed additive for high-yielding cows with the properties of maintaining metabolic processes at a sufficient level to prevent the development of ketosis.

Unresolved parts of the problem. Milk thistle is one of the most popular plant hepatoprotectors. Silymarin (the active ingredient) is isolated from its mature fruits, it is a part of many medicines. The action mechanism is the destruction of toxic compounds coming from outside or those that are formed in the body before they penetrate into hepatocytes. Silymarin can stimulate the synthesis of its own phospholipids, which repair cell membranes.

Researches conducted with this substance have shown that silymarin can be used in combination therapy for poisoning by the pale toadstool with steroids. Clinical pharmacology of hepatoprotectors has collected data that milk thistle has an antioxidant effect, prevents the development of connective tissue in the liver, has anti-inflammatory properties. The positive effect of the plant affects both the liver and the gastrointestinal tract. Milk thistle should be used as a powder because it works at the micro level cleaning liver cells [11].

Milk thistle (*Carduus marianus* L., genus *Silybum* Adans L., family Asteraceae) is a plant that contains essential oils and flavonoids (silibin, silicocristine, silidiamine), which have a powerful detoxifying, hepatoprotective, antioxidant and anti-oxidant effect on humans. The plant contains alkaloids, saponins, oils (up to 32%), proteins, vitamin K, resins, mucus, tyramine,

histamine, as well as macro- and micronutrients. The leaves, roots and seeds of milk thistle have medicinal properties. Thistle goes well with various herbal fees and tinctures for the treatment of certain diseases.

In many countries pharmaceutical companies produce a number of effective drugs on the basis of extracts from milk thistle. These medicines are Silibor, Lehalon, Carsyl, Hepabene, Sylibinin, Sylimaryn-Heksal, Sylehon, Heparsyl, Hepatofalk-planta, Levasyl, Syrepar etc. The plant is successfully cultivated, and it is found in small quantities in the wild in some regions of Ukraine. It should be noted that plant raw materials phylogenetically close to *Carduus marianus* L. species of the genus *Carduus* L., the genus *Thistle* (*Carduus* L.) is used in the medicine of some countries as a hepatoprotective agent. It has up to 120 species of plants that are common in Europe, Asia and North Africa. More than 30 main species are growing in Ukraine. The most common are welted thistle (*Carduus acanthoides* L.) and nodding thistle (*Carduus nutans* L.) throughout the country. Plants grow in different regions on roadsides, in fields, on dry hills, wastelands, pastures, and in littered places. The practically unlimited biological raw material stock of *Carduus acanthoides* L., *Carduus nutans* L. is promising for procurement, production of modern medicines and medical application in the form of galenic preparations [7].

The aim of the research was to study the theoretical basis of the causes of metabolic disorders in the body of high-yielding cows in the transit period, to develop a plan to eliminate them by using in feeding, feed additives from milk thistle and welted thistle taking into account their prophylactic and therapeutic properties in ketosis preventing.

We aimed to develop a feed additive recipe and the method of its manufacture, to conduct comparative studies aimed at reducing the content of ketone bodies in the blood of high-yielding cows in the transit period.

Material and method of research. The theoretical basis for the effective use of feed additives in the prevention of ketosis of high-yielding cows is confirmed by the research studies; two variants of recipes for the manufacture of feed additives were developed.

Two types of hay flour were made from milk thistle and welted thistle as a basis for feed additives in granular form in the first sample.

Hay flour of milk thistle and welted thistle was mixed with saponite flour and molasses in the appropriate ratios: 94% of hay flour, 3% of saponite flour, and 3% of molasses before granulation in the second sample.

The object of the research was cows in the transit period of black-spotted breed with the second - fourth lactations and the average milk yield of 7.0-8.7 thousand kg for the last lactation. Five groups were formed; each group has 7 heads; analogues groups were formed considering such characteristics as age, lactation, productivity for the last lactation, the concentration of ketone bodies in the blood.

The first control group received feed from the main diet.

The second experimental group was additionally fed 0.8 kg of feed additive in granular form, made from hay flour, milk thistle twice a day.

The third experimental group was additionally fed 0.8 kg of feed additive in granular form, made from hay flour, welted thistle twice a day.

The fourth experimental group was additionally fed 0.8 kg of feed additive in granular form, made from milk thistle, saponite flour and molasses twice a day.

The fifth experimental group was additionally fed 0.8 kg of feed additive in granular form, made from welted thistle, saponite flour and molasses twice a day.

The blood was taken from cows from the tail vein to measure the level of ketone bodies, namely beta-hydroxybutyrate. The Freestyle Optium device was used to determine the beta-hydroxybutyrate concentration. Iwersen et al. (2009) reports that the reliability of the results obtained on such devices and during laboratory tests is 95% [cited. for 2].

Research results and their discussion.

The chemical composition of feed additives is given in table 1.

Table 1.

Chemical composition of ADM* and nutritional value of feed additive according to manufacturing options

Indicator	Sample			
	First hay flour		Second hay flour with additional components	
	milk thistle	welting thistle	milk thistle	welting thistle
Crude protein, %	7.81	8.56	7.87	8.60
Crude fat, %	3.79	2.37	4.08	2.30
Crude fiber, %	31.25	33.49	30.31	32.48
Crude ash, %	13.04	13.17	15.94	16.07
Nitrogen-free extractives, %	44.11	42.41	41.80	40.55
Exchange energy, MJ	8.03	8.39	8.00	8.47

* Absolutely dry matter

According to Table 1 data, the chemical composition of feed additives had relative values of metabolic energy between the first and second samples with some differences in crude ash content, the value of which in the second sample was greater by 22% due to the additional components, i.e. mineral additive saponite flour and sugar beet molasses.

Blood was taken from cows to determine the concentration of ketone bodies by the express method at the beginning of the research and production experiment (three weeks before calving). According to the obtained data (Table 2), their content in the blood of all group cows did not exceed the permissible levels; it was in the range of 1.11–1.17 mmol / l.

Table 2.

Dynamics of ketone bodies concentration in the cows' blood

Group of animals	Concentration of ketone bodies, mmol-l				on the 21 st day after calving, % to the 1 st group
	three weeks before calving	a week before calving	on the 7 th day after calving	on the 21 st day after calving	
I – control	1.11±0.058	1.30±0.048	1.31±0.037	1.41±0.032	+27.0
II – experimental	1.14±0.054	0.97±0.036	0.95±0.041	0.92±0.026	-34.7
III – experimental	1.14±0.053	0.94±0.033	0.93±0.026	0.94±0.034	-33.3
IV – experimental	1.12±0.064	0.89±0.033	0.86±0.029	0.80±0.031	-43.3
V – experimental	1.17±0.068	0.84±0.032	0.81±0.028	0.78±0.026	-44.6

However, the cows of the control group showed positive dynamics of increasing the concentration of ketone bodies in the blood in the transit period, which lasted 42 days. On the 21st day after calving, it was 1.41 mmol / l; it was higher by 27%. Cows in the control group were treated with propylene glycol and other veterinary drugs.

Feeding cows of the experimental groups by feed additives significantly affected the content of ketone bodies in their blood.

The cows of the second and third experimental groups were fed by feed additives made from hay flour, milk thistle and welting thistle, the level of ketone bodies was lower by 34.7 and 33.3% than the control group. The decrease was 43.3% and 44.6%, respectively. The cows of the fourth and fifth groups in this comparison.

Comparing the results obtained in the 4th and 5th groups and 2nd and 3rd groups, we conclude that feed

additives including saponite flour and molasses provided a reduction in the concentration of ketone bodies by 13 % and 17%, respectively. The higher positive effect on the reduction of ketone bodies in the cows' blood is explained by the fact that saponite flour has a sorption capacity against free radicals; it is a source of mineral elements including metals with variable valence; it leads to an increase in the activity of antioxidant enzymes [13]. The additional number of mineral elements partially reduces nutritional stress by normalizing mineral metabolism. The molasses is a partial source of additional energy and mineral nutrition enhancing the positive effect on metabolic processes in the body of highly productive cows.

Thus, a feed additive with hay flour from milk thistle or welting thistle, additionally including saponite flour and molasses, is a more effective way to prevent ketosis in high-yielding cows during the transit period,

compared to a feed additive made only from hay flour from milk thistle or welted thistle.

Conclusions. 1. Granular feed additive from hay flour of milk thistle or welted thistle used for feeding high-yielding cows in the transit period reduces the level of ketone bodies by 34.7-33.3% compared with animals of the control group.

2. Feed additive with hay flour from milk thistle or welted thistle, additionally including saponite flour and molasses provides a lower concentration of ketone bodies by 13 and 17%, respectively, compared with feed additive from hay flour of milk thistle or welted thistle.

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