

USE OF *SILYBUM MARIANUM* PRODUCTS AS NUTRITIONAL SUPPLEMENT IN CATTLE REARING

Nadya Bozakova^{1*}, Veselin Ivanov²

¹Department of General Animal Breeding, Animal Hygiene,
Ethology and Animal Protection Section, Faculty of Veterinary Medicine, Trakia University,
Student`s campus, 6000 Stara Zagora, Bulgaria

²Department of Social Medicine, Health Management and Disaster Medicine,
Faculty of Medicine, Trakia University, Armeyska 11, 6000 Stara Zagora, Bulgaria

*e-mail: nadiab@abv.bg

Abstract

In modern cattle rearing, alternative methods are actively sought to stimulate milk yield and growth and protect high-yielding cattle from metabolic disorders. The different parts of the milk thistle plant (*Silybum marianum*) can be successfully used to prevent both metabolic diseases in cows and aflatoxicosis in calves and to stimulate their productivity. The purpose of this publication is to analyze, systematize, and highlight the possibilities of using *Silybum marianum* products as a feed additive in cattle breeding.

To achieve this goal, we performed an electronic keyword search in PubMed, ResearchGate, and Elsevier of official documents and reports from the Food and Agriculture Organization - FAO, as well as over 85 scientific publications related to the active ingredients extracted from different parts of milk thistle and their positive effect on the body of cattle. This publication summarizes and highlights the hepatoprotective effect of silymarin in cows with postpartum metabolic diseases - fatty liver degeneration, mastitis, endometritis, disorders of phosphorus-calcium metabolism, hypocalcemia, and impaired fertility in high-yielding cows. The publication also summarizes and systematizes the use of *Silybum marianum* products for the prevention of aflatoxicosis in cattle due to the specific detoxifying and antihepatotoxic effect of milk thistle.

Based on the review, it can be concluded that *Silybum marianum* products can be successfully used for the prevention of postpartum metabolic diseases in cows and aflatoxicosis in cattle, and to stimulate milk

yield and productivity due to their hepatoprotective, detoxifying, antioxidant, and anti-stress actions.

Key words: *Silybum marianum*, Silymarin, Prevention of metabolic diseases in cattle.

1. Introduction

In modern cattle breeding, some serious stressors - postpartum metabolic disorders in cows, and aflatoxicosis affect the raising of different categories of large ruminants and significantly impair the health and productivity of the animals due to chronic liver damage and related gastrointestinal disorders.

It is during these periods that cows need detoxifying, hepatoprotective, antioxidant, and anti-stress compounds such as silymarin and the derivatives of milk thistle (*Silybum marianum*). In this way, the protection of the liver and the metabolism of high-yielding cows could be supported, and the milk productivity of cows with metabolic disorders after parturition could be stimulated.

The milk thistle, *Silybum marianum* L. (Gaertn.) belongs to the Asteraceae family. It is an undemanding plant, widespread in different areas of the world (Karkanis *et al.*, [1]). It is easily adaptable and can be cultivated as a medicinal plant in Eastern Europe, as well as in Asia (Martinelli *et al.*, [2]; Martinelli *et al.*, [3]; Tedesco and Guerrini [4]).

The medicinal properties of milk thistle have been explored in an official report of the European Medicines

Agency (EMA) based on published scientific literature (European Medicines Agency [5]). The pharmacological potential of *Silybum marianum* is documented by many scientific data confirming the safety of preparations used in liver disorders (European Medicines Agency [5]; Franz *et al.*, [6]). The essential bioactive compounds in *Silybum marianum* are flavonolignans obtained from the seeds of the plant, possessing proven antioxidant and hepatoprotective properties (Flora *et al.*, [7]; Franz *et al.*, [6]; Saller *et al.*, [8]).

There are international regulations on the use of feed additives for farm and domestic animals (Tedesco *et al.*, [9]) in the European Union. For the safety of herbs and herbal products, EFSA has defined guidelines for their assessment, as these products can be included in the feeding of farm animals and transferred into the food chain (Franz *et al.*, [6]). Milk thistle can be administered as silymarin seed extracts; in such a case, the silymarin is an addition and is communicated in Regulation (EC) No. 1831/2003 of the European Parliament and the Council of the European Union on additives for use in animal nutrition (subclassification natural products, botanically defined) [10]. Milk thistle can be used as a feed ingredient, only when it complies with Regulation (EU) No. 68/2013 of the Commission of the Union (EU) [11].

Tedesco [12], shared the importance of using natural bioactive compounds as supplements in farm animals instead of synthetic chemical drugs. In highly productive cows, before and especially after calving, there is a lack of energy sources, and oxaloacetate, which is actively involved in the tricarboxylic acid cycle and is used in the system of gluconeogenesis as an energy source. This is the so-called negative energy balance in the body of cows. Therefore, the active use of fat in the liver is observed, with the formation of large amounts of ketone bodies (acetoacetate, hydroxybutyrate, and acetone) and the occurrence of fatty degeneration of the liver. As a result, serious metabolic disorders occur - fatty degeneration of the liver, mastitis, endometritis, disorders of phosphorus-calcium metabolism, hypocalcemia, and impaired fertility in high-yielding cows (Vojtisek *et al.*, [13]; Tedesco *et al.*, [14], Tedesco *et al.*, [15], Tedesco *et al.*, [16]; Ovsienko, [17]; Tedesco and Guerrini [4]).

The plant milk thistle (*Silybum marianum*) is rich in compounds with antioxidant and radical scavenging activity, and seeds and fruits contain large amounts of carbohydrates, proteins, and lipids. According to Dabbour *et al.*, [18] the seeds contain about 17.64 percent protein, 26.90 percent fat, 5.10 percent ash, 25.32% fiber, and 4.61% moisture. Cold pressing produces an oil rich in antioxidants and radical scavengers - phenols and vitamin E.

An extract called silymarin is obtained from the fruits of the plant. It is used as a powerful hepatoprotective agent. The extract consists of about 65 - 80% silymarin (flavonolignan complex) and 20 - 35% fatty acids, including linoleic acid (Kroll *et al.*, [19]). Silymarin is a complex mixture of polyphenolic molecules, comprising seven closely related flavonolignans (silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, silidianin) and one flavonoid (taxifoline).

On the other hand, there is widespread contamination of feed with aflatoxins (mycotoxins), secondary metabolites produced by *Aspergillus* spp., which is toxic to humans and animals, and significantly reduces animal productivity, especially in calves for fattening. In this regard, one of the innovative methods to overcome the toxic and carcinogenic effects of aflatoxins and to stimulate the metabolism of animals through natural products are derivatives of milk thistle (*Silybum marianum*), due to their strong detoxifying and anti-hepatotoxic effects (Tedesco *et al.*, [20]; Naseer *et al.*, [21]; Pickova *et al.*, [22]; Tedesco and Guerrini [4]).

Due to the relevance of the hepatoprotective, detoxifying, antioxidant, and anti-stress effects of silymarin and milk thistle derivatives in cattle rearing, we were motivated to study the literature and summarize the use of silymarin and its products.

The purpose of this publication is to summarize and highlight the possibilities of using *Silybum marianum* products as a dietary supplement to prevent postpartum metabolic disorders in cows, stimulate milk productivity, as well as to prevent aflatoxicosis, and improve productivity in cattle.

2. *Silybum marianum* products as a nutritional supplement in cattle rearing

To achieve the objectives of this publication, a theoretical analysis of official documents and reports from international organizations such as the Food and Agriculture Organization (FAO) and the official website of the European Commission is made concerning the use of silymarin in cattle breeding.

A detailed analysis of many scientific articles related to the active ingredients, properties, and applications of milk thistle (*Silybum marianum*) products is performed. These scientific articles are obtained from scientific databases such as PubMed (1966-June 2021), EMBASE (1973-May 2021), Research Gate, and Elsevier by keyword filtering.

The data on the hepatoprotective, detoxifying, and antioxidant action of *Silybum marianum* and silymarin in cows with metabolic disorders - fatty

liver degeneration, mastitis, endometritis, disorders of phosphorus-calcium metabolism, hypocalcemia, and hypocalcium are summarized. Emphasis is placed on the lactogenic and lactative-stimulating effects of silymarin and *Silybum marianum* products.

In addition, numerous data on the use of milk thistle (*Silybum marianum*) products for the treatment and prevention of aflatoxicosis in cattle due to their strong detoxifying and anti-hepatotoxic effects are summarized.

As a result of these mechanisms, the effect of *Silybum marianum* products on improving live weight and milk yield in large ruminants is explained.

Milk thistle extract (*Silybum marianum*) has proven hepatoprotective and detoxifying properties, which determine its wide usage in cattle breeding - in the prevention and treatment of postpartum metabolic disorders in high-yielding cows, as a stimulant for their milk production, prophylaxis in calves, and as an enhancing agent for productivity in large ruminants.

2.1 Derivatives of *Silybum marianum* and prevention of postpartum metabolic disorders in high-yielding cows

After calving, high-yielding cows experience a shortage of energy carbohydrate sources. Therefore, the liver is involved in an active use of fats, with the formation of large amounts of ketone bodies - ketonuria. Enhanced lipid mobilization leads to increased uptake of non-esterified fatty acids by the liver and excessive accumulation of triglycerides (Drackley [23]; Tedesco and Guerrini [4]). Hepatic lipidosis is a common problem in the perinatal period due to the influx of large amounts of non-esterified fatty acids (Gerloff [24]; Bertics [25]). As a result, serious metabolic disorders occur. Therefore, several authors recommend the use of *Silybum marianum* extract for the effective prevention and treatment of ketosis and mastitis in cows.

Vojtisek *et al.*, [26], conducted two comparative studies on 16 cows with ketosis and the presence of acetone in milk - 7.9 mg/L, two and six weeks after birth. The cows in the test group were fed for two weeks with food containing seeds of *Silybum marianum*, 0.3 kg per head/day, containing 2.34% silibinin and silidianin. In the blood and milk of experimental animals, there was a decrease in the amount of acetone + acetoacetic acid, as well as beta-hydroxybutyric acid in the blood ($P < 0.05$). The degree of ketonuria decreased remarkably. The milk yield of the test cows was 7.7% (test 1) and 3.4% (test 2) higher than the milk yield at the beginning of the study. The milk yield of experimental

cows (with the addition of milk thistle in the diet) was significantly higher than the control, even two weeks after discontinuing the diet.

In addition, Ovsienko [17], established the preventive effect of a food supplement from milk thistle (*Silybum marianum*) in the form of pellets against ketonuria and mastitis in cows before and after calving. Milk thistle extract has proven hepatoprotective properties. When introducing a food supplement in the form of pellets, at a dose of 1 kg/day, from 21 days before and 21 days after calving, protection against ketosis and mastitis in cows was established. The level of ketone bodies did not exceed the reference value on the 21st day after calving and was lower than in the control group.

Furthermore, Tian *et al.*, [27], used silymarin *in vitro/ex vivo* to determine whether it has a protective effect on primary dermal cells of the hoof of dairy cows. At a dose of 1 $\mu\text{g/mL}$, silymarin can reduce inflammatory responses in dermal hoof cells, ie. supplemental administration of silymarin in and for laminitis.

Therefore, the use of feed additives from milk thistle (*Silybum marianum*) in the feed of first-born cows prevents the development of ketosis and mastitis. The stimulating effect of this additive on milk synthesis, milk productivity, and physical and chemical composition of milk for 42 days in first-born cows has been established.

In addition, Hackett *et al.*, [28], found that the addition of silymarin in the diet of cows did not detect residual amounts of silymarin in milk.

2.2 Derivatives of *Silybum marianum* and increase of the milk yield of cows

Simultaneously with the prevention of metabolic disorders - ketosis and mastitis in cows, *Silybum marianum* products stimulate milk productivity.

Tedesco *et al.*, [14, 15, and 16] found that the addition of silymarin as an aqueous suspension, orally, in cows after calving, helps to increase milk yield. Tedesco *et al.*, [16], used silymarin supplementation in cows at a dose of 10 g/day (silybin 49.1%, isosilybin 14.3%, silydianin 14.6%, silycristin 8.3%, and taxifolin 4.3%), which were administered from 10 days before calving to 15 days after calving. Treated animals showed a significant increase in milk yield at one week with a mean milk yield of 41.6 ± 1.05 kg in the treatment compared to 39.1 ± 1.44 kg for the control. Supplementation of silymarin resulted in optimal milk production throughout lactation (at 305 days, 9922.1 ± 215.7 kg for treated cows and 9597.8 ± 225.4 kg for control cows), although silymarin was administered over a short period.

Cattle were tested for silymarin residues in milk. After 10 g/d administration for more than a week, no residual silybin was detected (detection limit = 10 ppb). Additionally, after calving, the silymarin-treated cows had a lower loss of body condition score, an estimate of body fat, than the control cows. Treated animals maintained higher milk yields, compared to control cows throughout lactation. Biochemical parameters and histological findings showed better health in the treated animals compared to controls. In conclusion, silymarin was found to have a beneficial effect on lactation and the health status of treated animals (Tedesco *et al.*, [16]). Similar results were reported by Grabowicz *et al.*, [29] with 16 cows.

Tedesco *et al.*, [30], found that administration of silymarin for 15 days significantly increased milk production without changing normal quality.

Grigoriev *et al.*, [31], investigated the effects of "preparation C", developed based on a meal from milk thistle (*Silybum marianum*). The cows in the experimental group received 250 grams of the preparation 21 days before and 21 days after calving. The rest of the food was the same as the control group. In experimental cows, the average milk yield per day during the experiment was 39.73 ± 0.98 kg, which was significantly higher than in control animals, $P < 0.01$. The content of milk fats and proteins was higher in experimental animals, compared to control animals, respectively $3.71 \pm 0.15\%$, against $3.14 \pm 0.13\%$ and $3.14 \pm 0.13\%$, against $3.08 \pm 0.09\%$. Blood bilirubin levels in experimental animals were significantly lower ($1.51 \pm 0.31 \mu\text{mol/L}$), compared to controls, and albumin levels in experimental cows (37.39 ± 0.89 g/L) were higher than in the control. The content of calcium in the blood plasma of the treated animals (2.37 ± 0.02 mmol/L) also exceeded the control, $P < 0.05$. The addition of the preparation, based on flour from *Silybum marianum* contributes to increasing milk yield, has a positive effect on the biochemical parameters of the blood, and has a significant economic effect - an additional income of 270 euros per animal (Grigoriev *et al.*, [31]).

2.3 Derivatives of *Silybum marianum* and prevention of aflatoxicosis in cattle

One of the innovative methods for overcoming the toxic and carcinogenic effects of aflatoxins is to enhance their metabolism through natural products with hepatoprotective properties. Milk thistle (*Silybum marianum*) has strong detoxifying and anti-hepatotoxic properties, therefore, it is widely used in the prevention of aflatoxicosis in large ruminants and to stimulate their productivity (Tedesco *et al.*, [20]; Naseer *et al.*, [21]; Gao *et al.*, [32]; Stoev *et al.*, [33]; Khazaei *et al.*, [34]; Tedesco and Guerrini, [4]).

Tedesco *et al.*, [20], reported the effect of silymarin, a potent antihepatotoxic agent used as a hepatoprotection in humans, on reducing the excretion of aflatoxin M1 (AFM1) in cow's milk and reducing the toxic effects of AFB1 in broiler chickens.

Naseer *et al.*, [21], tested the efficacy of two liver tonics - silymarin, 600 mg/kg, and choline chloride 500 mg/kg, to reduce the effects of aflatoxin B1 (AFB1) on average daily food intake (ADFI), daily gain (ADWG), hematological and serum biochemical parameters in calves fed with 1.0 mg/kg AFB1 for 10 days. The results revealed that the ADFI and ADWG of calves treated with AFB1 were significantly reduced. Serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), and creatinine increased significantly due to AFB1. Hematological studies showed that total erythrocyte count (TEC), total leukocyte count (TLC), hemoglobin concentration (HGB), hematocrit (HCT) levels, mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV) and the mean concentration of corpuscular hemoglobin (MCHC), % lymphocytes, % neutrophils, and monocytes decreased significantly in calves treated with AFB1 after 10 days of feeding. After treatment with liver tonics for 7 days, all reported parameters in cows were improved ($p < 0.05$), including ADFI, ADWG, and hematological, and serum biochemical tests. The tonic silymarin improved significantly more effectively the effects caused by aflatoxin B1 AFB1 than choline chloride (Naseer *et al.*, [21]).

Silymarin can be used as an antidote against various biological venomous agents - snake and scorpion venoms, bacterial toxins, and xenobiotic mycotoxins (Fanoudi *et al.*, [35]; Pickova *et al.*, [22]).

Fanoudi *et al.*, [35], found that the main protective effects of silymarin are due to several main mechanisms - radical removal, antioxidant, chelating, anti-apoptotic properties, and regulation of inflammatory reactions.

The protective effect of silymarin against the toxic effects of several mycotoxins is particularly relevant. Alhidari *et al.*, [36], found a beneficial effect of silymarin on reducing feed consumption and growth in broilers intoxicated with aflatoxin B1- (AFB1). Silymarin prevents immune suppression and has a hepatoprotective and nephroprotective effect in broiler chickens exposed to ochratoxin A- (OTA) (Stoev *et al.*, [33]). In addition, the protective effect of silymarin on zearalenone-induced (ZEA) liver damage and reproductive toxicity in rats has been established (Gao *et al.*, [32]; Khazaei *et al.*, [34]).

In recent years, heavy metal pollution has become very popular in pasture cattle rearing. Silymarin could

reduce the toxic effects of heavy metals (Ivanov *et al.*, [37]) in forage. The mechanism of the toxic action of heavy metals is free radicals. As mentioned above, the plant *Silybum marianum* is rich in radical scavengers and chelators, which can bind heavy metal ions and thus prevent poisoning in large ruminants.

Despite the beneficial effects of milk thistle (*Silybum marianum*) against mycotoxin intoxication, this plant can also be affected by toxic micro-fungi and contaminated with mycotoxins with adverse effects. Pickova *et al.*, [22], found that the beneficial effect of silymarin can be reduced or destroyed by the mycotoxins of micro-fungi of the genera *Fusarium* and *Alternaria*.

2.4 Derivatives of *Silybum marianum* and stimulation of growth in cattle

Due to its strong detoxifying and anti-hepatotoxic properties, milk thistle (*Silybum marianum*) is widely used to stimulate the productivity of large ruminants.

Potkanski *et al.*, [38], investigated the effect of endosperm from milk thistle (*Silybum marianum*), a by-product of the processing of medicinal herbs as feed components for young black-and-white calves. The additive contains 93.53 percent DM; 6.04 percent crude fiber; 15.25 percent crude fat; and 34.29 percent N-free extract. The results of the experiment show a significant increase in calf weight. Biochemical blood indices (hematocrit, hemoglobin, glucose, urea, and cholesterol) vary within physiological norms for all groups of calves.

Kim *et al.*, [39], and Spagnuolo *et al.*, [40], studied the effect of dietary supplements of local herbs - silymarin, on the growth, blood metabolites, and carcass characteristics in the late fattening period of castrated male Hanu cattle (647 ± 32 kg). Cattle received concentrate *ad libitum*, together with 1 kg of rice straw per animal per day throughout the experiment. After a 6-month late fattening period in cattle, silymarin-treated animals were found to have significantly higher urea nitrogen and creatinine concentrations ($p < 0.01$ and $p = 0.071$) than controls. Alanine activity aminotransferase was also lower ($p < 0.06$) in silymarin-treated animals. Final body weight, weight gain, and average weight gain from milk and dry matter did not differ significantly between the groups treated with different supplements. The average daily gain, the degree of fat content, and the degree of meat quality were higher in the silymarin group compared to the control group ($p < 0.05$). Therefore, silymarin can be successfully used as an effective dietary supplement, as an alternative to nutritional antibiotics, and as a means to stimulate productivity in the late fattening period of male castrated cattle of the genus Hanu (Kim *et al.*, [39]).

3. Conclusions

- Based on the literature review, it can be concluded that *Silybum marianum* derivatives can be successfully used to prevent postpartum metabolic disorders in cows and aflatoxicosis in large ruminants.
- They can also stimulate milk production and productivity in cattle due to their hepatoprotective, detoxifying, antioxidant, and anti-stress effects.

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