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# Correction of dyslipidemia with combined use of beta-sitosterol and polyprenyl phosphates in dogs with type 1 diabetes mellitus

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*This study considers the efficiency of use of a combined drug based on beta-sitosterol and polyprenyl phosphates in dogs with type I diabetes mellitus complicated by hyperlipidemia. It was shown that after 1 month of the therapy, there was a significant decrease of the level of cholesterol, triglycerides and glucose vs. control animals. After 2 months of the therapy, in the control group the level of cholesterol and triglycerides was at the upper limit of the norm, which can lead to an exacerbation of the disease in future.*
***Keywords:*** *dogs, hyperlipidemia, caninsulin, diabetes mellitus, polyprenyl phosphate, beta-sitosterol.*

# Коррекция дислипидемии у собак, больных сахарным диабетом первого типа, с помощью комплекса бета-ситостерина и полипренилфосфатов

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*В работе изучена эффективность применения комплексного лекарственного средства на основе бета-ситостерина и полипренилфосфатов при терапии собак, больных сахарным диабетом первого типа, осложненным гиперлипидемией. Через 1 месяц терапии в сыворотке крови отмечено достоверное снижение уровня холестерола, триглицеридов и глюкозы по сравнению с животными контрольной группы. Через 2 месяца терапии в контрольной группе уровень холестерола и триглицеридов находился на верхней границе нормы, что может привести в будущем к обострению заболевания.*
***Ключевые слова:*** *собаки, гиперлипидемия, канинсулин, сахарный диабет, полипренилфосфат, бета-ситостерин.*

**Abbreviation (Сокращения): ESR** — erythrocyte sedimentation rate (скорость оседания эритроцитов)

## Introduction

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia due to impaired insulin secretion, insulin action, or both of these factors [2]. One of the most common manifestations of impaired lipid metabolism in diabetes is hyperlipidemia characterized by an increased level of lipids (blood triglycerides and/or cholesterol) due to impaired lipid metabolism [6].

In humanistic medicine, the correction of hyperlipidemia in diabetes mellitus increases the life expectancy of patients [4].

In previous studies, hyperlipidemia (in particular, hypertriglyceridemia) in dogs occurs in approximately 15 % of cases [1, 12].

It shall be noted that all the drugs currently recommended in Russia for managing hyperlipidemia in veterinary practice are not veterinary drugs.

The scientists of the N.F. Gamaleya Federal Research Center for Epidemiology and Microbiology of the Ministry of Health of the Russian Federation has developed a combined drug based on beta-sitosterol and polyprenyl phosphate (BSPP). It is effective for the correction of hyperlipidemia in vivo experiments, however, to date, there is no data on the efficiency of this drug in dogs that suffer from diabetes with concomitant dyslipidemia.

## Purpose of the study

The purpose of our study was to assess the therapeutic efficiency of BSPP in the treatment of dogs suffering from type I diabetes mellitus with concomitant dyslipidemia based on clinical and hemo-biochemical changes.

## Materials and methods

The studies were conducted on the basis of doctor V.V. Annikov's veterinary clinic (Saratov) and the Department of Animal Diseases and Veterinary Sanitary Examination of the Saratov State Agrarian University named after N.I. Vavilov.

The subject of the study was clinical and hemo-biological changes that occur after inclusion of a BSPP-based combined drug in the therapy regimen of animals.

The material for the study was 10 sick dogs with a diagnosis of diabetes mellitus and hyperlipidemia.

During the study, we examined 629 dogs brought for initial consultation; 10 animals from them had type 1 diabetes mellitus and concomitant hyperlipidemia. The dogs were divided into two equivalent groups with 5 animals each on the analogue principle.

The therapy of animals from Group 1 involved subcutaneous injection of caninsulin in an initial dose of 1 U/kg of body weight plus a correction dose that depended on the animal's body weight (<10 kg — 1 U, 10…12 kg — 2 U, 12…20 kg — 3 U, >20 kg — 4 U per animal). A symptomatic therapy was also conducted, when necessary.

Animals from Group 2 were additionally treated with BSPP in a dose of 3…6 mg/kg of body weight orally, twice a day, for 2 months. The animals were examined before the treatment, after 1 and 2 months of the treatment, with daily measurements of the glucose level by the dogs' owners at home in blood once a day using an Accu Chek glucose meter and in urine three times a day using Ketogluc-1 test strips.

Animals of both groups had Hill's w /d super premium dietary feed according to the norms recommended by the manufacturer throughout the study. This feed contains the optimal amount of fat to normalize the weight, a high amount of fiber to give a sense of fullness, hereby suppressing hunger, minimizes fluctuations in glucose that occur in diabetes.

Hematological studies (the number of leukocytes, erythrocyte, the level of hemoglobin and hematocrit) were conducted using a Mindray BC-2300 hematology analyzer (China) with original reagents. The ESR was measured using Panchenkov's device and the leukogram was counted by examining a blood smear stained with a Leukodif-200 kit.

Biochemical studies of blood serum were performed on a BioSystems BTS-350 analyzer (Spain) using reagents of Diacon DDS.

The clinical analysis of urine was performed using UrineRS H10 test strips and sediment microscopy.

Statistic processing of data was carried out using the Statistica 6 software.

## Results and discussion

Clinically, before the start of the therapy, animals from both groups had pale mucous membranes, a dull, tousled coat with alopecia spots (in 2 dogs from Group 2), polyuria, polydipsia, polyphagy, cachexia (in 3 animals from Group 1 and 2 animals of Group 2), increased body weight (2 dogs from Group 1 and 2 dogs from Group 2), 1 dog from Group 2 had a normal body weight, halitosis, 2 animals from Group 1 and 1 dog from Group 2 had the smell of acetone from the mouth.

1 month after the start of the therapy, mucous membranes were pale pink, the coat remained dull, the appetite was poor. Hydroadipsia resulted in oligouria. There was a slight increase in the body weight of dogs with cachexia and a decrease in animals with overweight. Halitosis remained in 3 dogs from Group 1 and 2 dogs from Group 2.

After 2 months of the beginning of treatment, animals from both groups had pale pink mucous membranes, new hair began to grow in alopecia spots, the appetite, thirst and urination were normal. The dynamics of normalization of the body weight was observed.

The data in Table 1 show that before the start of the therapy dogs had decreased levels of hemoglobin and hematocrit and slightly decreased number of red blood cells, the level of white blood cells was at the lower limit of the norm. In our view, all the changes are due to increased water intake by animals.

After 1 month of the therapy, all hematological parameters were within reference values.

Biochemical studies (Table 2) showed blood serum chylosis, although blood aspiration was carried out in the morning under fasting conditions. Before the beginning of the therapy, there was an increased level of cholesterol (13.2 mmol/l in Group 1 and 14.8 mmol/l in Group 2), triglycerides (3.1 mmol/l in Group 1 and 2.9 mmol/l in Group 2), which shows a lipid metabolism disorder. The glucose level was also above the norm (20.8 mmol/l and 25.1 mmol/l in animals from Group 1 and 2, respectively), which is the most pathognomonic sign of diabetes mellitus.

After 1 month of the therapy, the level of cholesterol and triglycerides in animals from Group 1 remained increased (8.3 mmol/l and 1.2 mmol/l, respectively), but in animals from Group 2 both parameters were at the upper limit of the norm (6.2 mmol/l and 0.8 mmol/l, respectively). The faster normalization of the parameters was obviously associated with the use of BSPP. The glucose level was still increased in both groups, but in Group 2 its concentration was lower (13.7 mmol/l in Group 1 and 11.9 mmol/l in Group 2). Blood serum chylosis was not observed.

After 2 months of the therapy, the cholesterol level in Group 1 was at the upper limit of the norm (5.5 mmol/l), in Group 2, it was within reference values (3.7 mmol/l). The concentration of triglycerides in animals from Group

**1. Dynamics of hematological parameters during the treatment of dogs with diabetes mellitus and hyperlipidemia (M ± m)**

| Parameters | Norm | Group of animals | | | | | |
|---|---|---|---|---|---|---|---|
| | | Before treatment | | 1 month of treatment | | 2 months of treatment | |
| | | 1 | 2 | 1 | 2 | 1 | 2 |
| Hemoglobin, g/l | 115…180 | 108.2±3.6 | 101.7±2.9 | 135.8±4.3 | 147.6±5.2 | 146.7±3.2 | 139.5±5.9 |
| Hematocrit, % | 37…54 | 33.8±2.1 | 32.2±2.5 | 41.6±2.9 | 48.2±1.8 | 43.5±3.4 | 45.9±2.4 |
| ESR, mm/h | 0…22 | 8.3±2.4 | 13.1±3.2 | 9.3±1.9 | 11.5±2.1 | 12.8±2.6 | 9.6±2.3 |
| Red blood cell count, $10^{12}$/l | 5.5…8.5 | 4.9±0.2 | 5.2±0.4 | 6.2±1.1 | 7.1±1.3 | 7.2±1.6 | 7.9±1.4 |
| White blood cell count, $10^{9}$/l | 6.0…17.0 | 6.5±1.8 | 7.1±0.7 | 13.2±2.8 | 10.8±2.4 | 15.7±3.2 | 11.9±2.2 |
| Eosinophils, % | 2…10 | 4.3±1.3 | 6.9±2.8 | 5.6±1.4 | 4.8±0.9 | 3.6±1.1 | 5.9±1.2 |
| Immature, % | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Basophils, % | 0…1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Stab neutrophils, % | 0…3 | 0.8 ± 0.3 | 0.2…0.3 | 0 | 1.2±0.4 | 2.2±0.4 | 1.6±0.2 |
| Segmented neutrophils, % | 60…70 | 65.8±3.6 | 67.2±2.9 | 63.5±2.1 | 66.2±1.9 | 66.8±2.4 | 68.2±2.2 |
| Monocytes, % | 3…10 | 5.7±2.1 | 4.1±2.4 | 3.9±1.0 | 6.3±1.9 | 5.8±2.3 | 8.4±2.6 |
| Lymphocytes, % | 12…30 | 16.6±4.0 | 21.2±3.8 | 25.4±3.7 | 23.9±3.4 | 19.6±2.7 | 21.8±3.1 |

**2. Dynamics of biochemical parameters during the treatment of dogs with diabetes mellitus and hyperlipidemia (M ± m)**

| Parameters | Norm | Group of animals | | | | | |
|---|---|---|---|---|---|---|---|
| | | Before treatment | | 1 month of treatment | | 2 months of treatment | |
| | | 1 | 2 | 1 | 2 | 1 | 2 |
| Cholesterol, mmol/l | 2.9…6.0 | 13.2±2.8 | 14.8±3.1** | 8.3±1.4 | 6.2±1.8*** | 5.5±1.2 | 3.7± 1.1*** |
| Triglycerides, mmol/l | 0.2…1.0 | 3.1± 0.3 | 2.9±0.4* | 1.2±0.4 | 0.8±0.3** | 0.8 ± 0.2 | 0.4± 0.2** |
| Glucose, mmol/L | 3.4…6.5 | 20.8±4.3 | 25.1±3.4*** | 13.7±2.4 | 11.9±2.8*** | 8.4±1.9 | 7.1± 1.2** |

*Designations: *P≥0.05, **P≥0.01, ***P≥0.001).*

2 returned to the norm (0.4 mmol/l), but in animals from Group 1 it remained at the upper level of the norm (0.8 mmol/l). The glucose level was slightly increased (8.4 mmol/l in Group 1 and 7.1 mmol/l in Group 2).

The clinical analysis of urine and study of physical and chemical characteristics before the therapy start showed that animals of both groups had less intensive color of urine and ketone bodies, which indicates decompensation of diabetes mellitus and glucosuria, which is a rather specific sign of diabetes mellitus. The microscopy of urine sediment did not show any significant deviations.

According to published data, the incidence of diabetes mellitus in dogs is approximately 1:100 [5]. The disease is often observed on the background of disorders of the adrenal and chronic inflammation of the pancreas [11].

The combined drug based on beta-sitosterol and polyprenyl phosphates (BSPP) suppresses the activity of cholesterol synthesis and presents is reabsorption in

the intestines [8] and contributes to the correction of hyperlipidemia in cats and dogs [7]. It is also known that phosphorylated polyprenols have anti-inflammatory [3] and antioxidant properties [10], which greatly contribute to their therapeutic efficacy in dogs with pancreatitis [9]. However, to date, there has been no evidence of the efficiency of BSPP in dogs with diabetes and concomitant dyslipidemia. As shown in this study, BSPP contributes to the correction of dyslipidemia in sick animals, resulting in a significant decrease in serum cholesterol and triglycerides, which prevents the recurrence of the disease and allows the reduction of the dose of caninsulin in future.

## Conclusions

1. The use of caninsulin in type 1 diabetes mellitus does not result in stable improvement of biochemical parameters, as evidenced by an increased concentration of cholesterol and triglycerides 1 month after the start of the therapy (8.3 mmol/l and 1.2 mmol/l, respectively) and retention of the parameters at the upper limit of the norm after 2 months of the therapy (5.5 mmol/l and 0.8 mmol/l, respectively).

2. The inclusion of a drug based on beta-sitosterol and polyprenyl phosphates in the treatment regime for diabetes mellitus contributes to the correction of dyslipidaemia in sick animals.

## Conflict of interest

The authors state that no conflict of interest exists.

**References**


1. Annikov V.V., Belyaeva M.V., Lapina E.O., Etiological factors of hyperlipidemia in dogs, *Issues of legal regulation in veterinary medicine*, 2014, No. 2, pp. 30–33.
2. World Health Organization. *Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia. Report of a WHO/IDF Consultation*, Geneva, 2007, 46 p.
3. Ganshina I.V., Sudyina G.F., Sanina V.Yu., Kozhevnikova T.N., Pronin A.V., Narovlyansky A.N., Sukhanova S.A., Proskurina O.V., Mitrokhin N.M., Sanin A.V., Phosphorylated polyprenols are a new class of compounds with anti-inflammatory and bronchodilator activity, *Infection and Immunity*, 2011, Vol. 1, No. 4, pp. 355-360.
4. Elagin R.I., Cost-effectiveness of treating hyperlipidemia in patients with diabetes mellitus, *Consilium Medicum*, 2001, Vol. 3, No. 2, pp. 102-103 (In russ.).
5. Ignatenko N., Diabetes mellitus in dogs, *VetPharma*, 2012, No.3, pp. 46-51 (In russ).
6. Jörg M., Use of low-lipid diets in dogs with gastrointestinal diseases, *VetPharma*, 2013, No. 1, pp. 58-59 (In russ.).
7. Pereslegina I.O., Sanin A.V., Pronin A.V., Narovlyansky A.N., Pharmacologic correction of hyperlipidemia in dogs and cats, *Russian Veterinary Journal. SDA*, 2015, No. 4, pp. 36-38 (In russ.).
8. Pronin A.V., Danilov L.L., Narovlyansky A.N., Sanin A.V., Plant Polyisoprenoids and Control of Cholesterol Level, *Archivum Immunologiae et Therapiae Experimentalis,* 2014, Vol. 62, Is. 1, pp. 31-39.
9. Sanin A.V., Narovlyansky A.N., Pronin A.V., Kozhevnikova T.N., Sanina V.Yu., Izmestieva Anastasia V., Annikova L.V., Annikov V.V., Efficiency of Phosprenyl in the treatment of pancreatitis in dogs, *Veterinary medicine of Kuban*, 2017, No. 2, pp. 24-27 (In russ.).
10. Sanin A.V., Narovlyansky A.N., Pronin A.V., Kozhevnikova T.N., Sanina V.Yu., Agafonova A.D., Study of the antioxidant properties of Phosprenyl in various biological test systems, *Russian Veterinary Journal. SDA,* 2017, No. 10, pp. 28-31.
11. Sanin A.V, Lipin A.V., Zinchenko E.V., *Veterinary handbook of traditional and nontraditional methods of treatment of dogs,* Moscow, Tsentrpoligraf, 2006, 608 p. (In russ.).
12. Xenoulis P.G., Steiner J.M., Lipid metabolism and hyperlipidemia in dogs, *Vet J.,* 2010 Jan, No. 183(1), pp. 12-21.


# Идентификация животных

### Министерством сельского хозяйства Российской Федерации издан «приказ от 22.04.2016 № 161 «Об утверждении Перечня видов животных, подлежащих идентификации и учету»

***Идентификация животных*** — система учета животных, включающая в себя присвоение идентификационного номера животному путем мечения, регистрацию сведений о животном в базе данных и выдачу паспорта на животное.

***Мечение животных*** — это присвоение и нанесение на теле животного различными способами индивидуального номера.

***Носитель идентификационного номера*** — бирка (в том числе навесная с радиочастотной меткой), болюс, чип, ошейник и другие средства, соответствующие стандартам ISO 11784 и 11785 и содержащие уникальный цифровой 15-тизначный код.

На территориях многих стран единственным методом мечения домашних животных является чипирование, где применяются микрочипы, соответствующие стандарту ISO 11784 и ISO 11785.

***Чипирование,*** или электронная идентификация животных (кошек, собак, сельскохозяйственных и экзотических животных, птиц, рыб и др.) представляет собой имплантацию под кожу животного микрочипа, содержащего в себе уникальный индивидуальный 15-ти-значный номер, который остается с ним в течение всей его жизни. Микрочип — маленькая стерильная капсула из биосовместимого стекла длиной 12 мм, диаметром 2,1 мм и весом всего 0,6 гр. Внутри капсулы расположен сам микрочип, состоящий из катушки индуктивности и микросхемы. Пятнадцать цифровых ячеек гарантируют безопасную и надежную идентификацию животного на протяжении всей его жизни, отсутствие повтора номера в течение ближайших ста лет, а биосовместимое стекло исключает возможность миграции микрочипа.

Чипирование должно обеспечить невозможность подменить одно животное другим; исключить перевозку животных, которые не вакцинированы против бешенства и других заразных болезней; помочь найти животное владельцу в случае его потери, а при находке чужого животного определить координаты его владельца, связавшись со специализированной локальной базой или с базой в информационно-телекоммуникационной сети «Интернет». Чипирование является весомым аргументом при возникновении споров по владению тем или иным животным.

Природоохранные организации с помощью системы идентификации проводят контроль над миграцией диких животных и животных, занесенных в Красную Книгу Российской Федерации, и содержащихся в неволе.

***Ветеринарный врач может только тогда оформить ветеринарный сопроводительный документ для перевозки животного, когда сможет вписать в этот документ сведения, позволяющие идентифицировать предназначенное для перевозки животное. Такими идентифицирующими сведениями являются – номер микрочипа, клейма, дермографической метки.***

*По материалам https://www.gov.spb.ru/helper/zdrav/informaciya-dlya-vladelcev-zhivotnyh/identifikaciya-zhivotnyh/*