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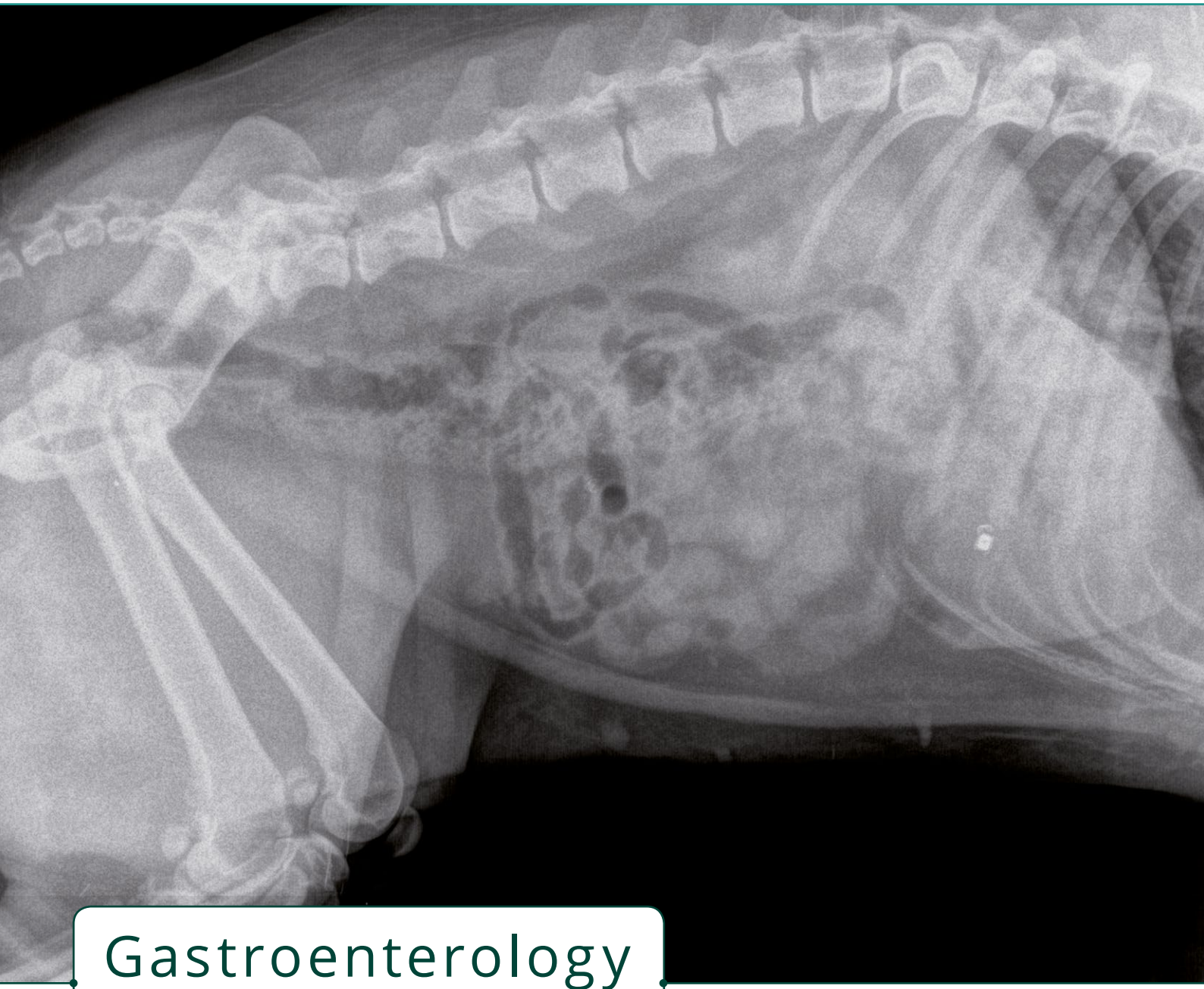

Gastroenterology

How to see the stomach from inside – gastroscopy in small animals.

Biochemical evaluation of hepatocyte damage and metabolic function in dogs and cat

Effectiveness of Hepatiale Forte supplements in the treatment of liver disease in dogs

VET EXPERT
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Dear Readers,

Thousands of years of domestication of dogs and cats have significantly changed the importance of these animals in human life.

Their initial roles, typically supportive for humans, such as pest control (cats) or assistance during hunting (dogs), have been replaced by social and recreational roles and these animals have thus become one of the most faithful friends to humans.But even 10,000 years of domestication will not change the fact that dogs or cats are carnivores, which is evidenced by the size and shape of internal organs, relatively short intestines, jaw formation, lack of amylase in saliva and initial digestion in the mouth, or adaptation of the stomach to digest large, rapidly swallowed bits of food.The gastrointestinal tract diseases are one of the most numerous groups of clinical cases in the daily work of small animal practitioners.

The current edition of Veterinary Life discusses many interesting gastro-enterological issues: from nutrition and diagnostics to "on the shelf" hands-on solutions, namely the studies on applicative use of many medical preparations.

Enjoy reading!

Anna Rutkowska
Editor-in-chief

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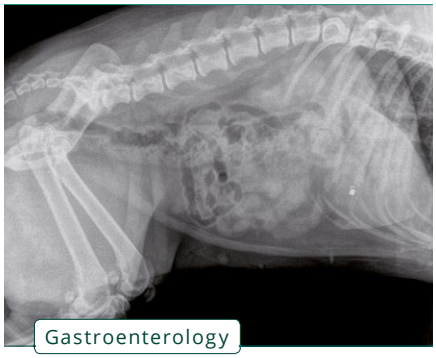

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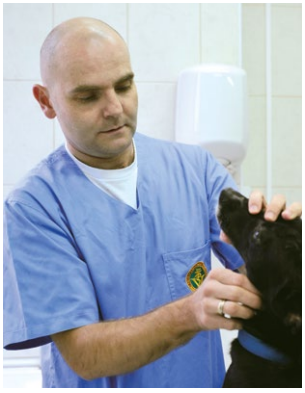
CONTENTS 3/2018

Small Intestinal Bacterial Overgrowth (SIBO) in dogs



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Small intestinal bacterial overgrowth (SIBO), also bacterial overgrowths, small bowel bacterial overgrowth syndrome or dysbiosis of gastrointestinal tract, is a syndrome with overgrowth of the bacterial flora, which is typical for large intestine, in the small intestine, This conditions leads to digestion and absorption disorders, affecting lipids and B12 vitamin in particular. The disease presents with chronic diarrhoeas and loss of body weight (1).

In human medicine, SIBO is diagnosed when the number of bacteria in small intestine increases from 103/mL to 105-106/mL (2,3), whilst in dogs, bacterial overgrowth is defined when the number of anaerobic bacteria is >105 colony forming units (CFUs) in 1 mL of the small intestine content collected from a fasted animal (4). However, it is not only the number of the bacteria, but also the species composition of the intestinal flora that play a role in the development of this syndrome. Intensive proliferation of bacteria that metabolise bile salts to insoluble compounds in the small intestine cause lipid absorption disorders and diarrhoeas with bile present in faeces. The microorganisms that intensively metabolise carbohydrates to short-chain fatty acids may trigger the accumulation of gases in the intestines and resulting flatulence, yet these symptoms may not coincide with diarrhoea. Some Gram-negative bacterial species such as Klebsiella may produce toxins that damage the intestinal mucosa.

The prevalence of SIBO in dogs is not entirely known. The diagnosis of the syndrome largely depends on sensitivity of the tests used in the diagnostic process. It is supposed that some canine breeds, like German shepherd or Shar-pei, are predisposed to bacterial overgrowth in the small intestine. In German shepherd, IgA deficiency in the small intestines may be one of the reasons for higher prevalence of this syndrome in this breed, yet the correlation between these two conditions has not been confirmed. In humans, idiopathic bacterial overgrowth in the small intestine is associated with genetically-determined sensitivity to the disorders in cellular regulation of immunological response. A similar mechanism may lead to chronic enteropathy in dogs (5).

Pathogenesis

Small intestinal bacterial overgrowth develops when the homeostatic mechanisms controlling the number of bacterial population in the intestines are disturbed. The main factors predisposing to SIBO development are believed to be associated with lower production of gastric acid and reduced gut motility. Also, functional disorders and anatomical abnormalities of the intestines may contribute to the development of this condition.

Intensive multiplication of bacteria may cause colitis and damage of the intestinal mucosa, which additionally exacerbates typical SIBO symptoms.

Table 1. Correct values of cobalamin and folic acid in dogs and cats serum

	Concentration of cobalamin	Concentration of folic acid
Dogs	251 – 908 ng/L	7.7 – 24.4 µg/L
Cats	290 – 1,500 ng/L	9.7 – 21.6 µg/L

The cytological assessment of biopsy samples collected from the intestines of dogs and humans with the symptoms of this condition revealed thinning of the mucosa and lymphocytic infiltration on its surface. These lesions ceased with antibiotic therapy (6).

As mentioned above, decreased production of gastric acid predisposes to the development of SIBO. One of the functions of the gastric acid is to destroy the bacteria which enter the intestines with food. Both in humans and animals, hypochlorhydria is associated with intensive colonisation of the stomach with Helicobacter pylori, but it also develops with age (7,8). The use of type 2 histamine receptor blocker (omeprazole and cimetidine) may also contribute to the development of SIBO (9).

The other major causes of small intestinal bacterial overgrowth include the disorders of gastrointestinal tract motility. Gastroparesis is one of such conditions and it consists in delayed emptying of the stomach, which might accompany such pathological conditions as diabetes, connective tissue diseases, viral infections or gastric and intestinal ischaemia. The disorders of the gastrointestinal peristalsis are a predisposing factor for feed stasis in the stomach and intestines, which, in turn, stimulates multiplication of bacteria and induces SIBO. Additionally, bacteria from the small intestines are not mechanically moved to the large intestines, which deteriorates the pathological process.

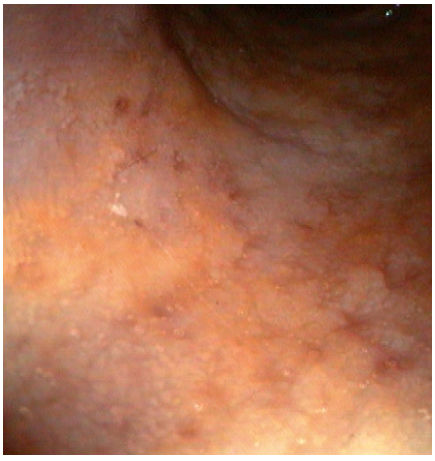

Figure 1.
Visible loss of mucous membrane and irregular positioning and color change intestinal villi in the duodenum of the dog suffering from SIBO.

Figure 1.
Proper fluid therapy is part of the treatment protocol for patients with SIBO.

The disorders of the intestinal motility may also be seen in the patients with chronic renal insufficiency and with myopathies (10).

Other conditions that predispose to the development of SIBO include anatomical abnormalities in the gastrointestinal tract, which provide favourable conditions for multiplication of the bacteria that colonise the intestines (e.g. a surgically made intestinal blind loop in obesity treatment or intestinal diverticula), as well as immunosuppression conditions (in patients with immunology defects when the T cells' role in is distorted or in patients with low IgA levels on the intestinal mucosa the risk of developing this disease is higher)(11).

Predisposing factors for the development of SIBO

In humans and animals, the predisposing factors for the development of SIBO include:

- Diabetes mellitus that may impair the intestinal enervation leading to the impairment of their motility
- Ageing. Generally, SIBO is seen in older patients, both humans and animals, due to the fact that in this group the intestinal motility is lower and, additionally, the immunological activity is also decreased;
- Organ dysfunctions, such as renal insufficiency, biliary atresia, hepatic diseases, and acute pancreatitis, impair the intestinal motility (1,12);
- Uncontrolled antibiotic consumption, of broad-spectrum antibiotics in particular, contributes to changes of the intestinal flora and might predispose to SIBO (1).

Clinical symptoms

The clinical symptoms of small intestinal bacterial overgrowth in dogs are usually non-specific and include flatulence, pain of the abdominal organs, diarrhoea, and severe fatigue. Sometimes vomiting might also occur. The severity of clinical symptoms reflects the degree of bacterial proliferation and intensity of the inflammatory process within intestines. SIBO may lead to absorption disorders and nutritional deficiencies. The lack of clear pathognomonic signs makes it difficult to differentiate the condition from other diseases with a similar clinical course, such as IBD or food intolerances (13,14).

Diarrhoeas may be mild or persistent and the latter form may be complicated with neuropathies caused by the deficiencies of water-soluble vitamins. Impaired lipid absorption results from degradation of bile salts by intestinal bacteria. Free bile acids may damage the intestinal mucosa, which exacerbates absorption disorders (15). As mentioned above, the consequence of the impaired lipid absorption include A, D, E and K hypovitaminosis, resulting in blindness (vitamin A deficiency), hypocalcaemia induced tremors (vitamin D deficiency), prolongation of prothrombin time (vitamin K deficiency)n and neuropathies, retinopathies and impaired T cells function (16).

Carbohydrate absorption disorders result from premature degradation of saccharides by bacteria, whilst protein absorption disorders are triggered by saccharides digestion by bacteria. Additionally, the damage of the intestinal mucosa may lead to the development of protein-losing enteropathies. Cobalamin (B12 vitamin) deficiency is a frequent complication of the bacterial overgrowth, as the vitamin is captured by intestinal bacteria (17).

Diagnosis

The diagnosis of small intestinal bacterial overgrowth is difficult since the sensitivity of diagnostic tests is highly controversial.

A preliminary diagnosis can be made based on the clinical symptoms, serum cobalamin and folic acid levels, and the results of microbiological tests (presence of aerobic and anaerobic bacteria) in the intestinal juice.

Bacteriological assessment of the samples collected from the intestines comes with several inconveniences. The first one is sample collection that requires using the endoscope (Fig.1). When the endoscope is introduced to the small intestine, it first passes through the segments of the gas-

trointestinal tract where it might be contaminated with the colonising microflora and thus the final culture result may not be conclusive.conclusive. Another difficulty is the necessity to make a rapid culture from the collected samples on various types of culture media (both for aerobic and anaerobic bacteria), which increases the costs of diagnostics and makes it more complicated. In addition, every dog has a different intestinal microflora and it is difficult to determine whether it is normal or affected by the disease.

It seems that currently in veterinary medicine, the most useful method for diagnosing SIBO is to determine the concentration of cobalamin and folic acid in blood serum. This test, however, has very low sensitivity (for cobalamin: max. 50%, folic acid: up to 60%) (13); nevertheless, a decrease of cobalamin serum level paired with an increase of folic acid concentration may suggest the disease. Table 1 presents the normal values of cobalamin and folic acid concentrations in canine and feline serum. A decreased cobalamin blood levels in the affected dogs relates to its use by excessively grown bacterial microflora of the gastrointestinal tract and therefore, the absorption of this vitamin from the intestine is minimal in a diseased animal. On the other hand, the bacteria which are in further parts of the small and large intestine produce large amounts of folic acid. The salts of folic acid (these of bacterial origin) are absorbed in the proximal part of small intestine, which consequently increases the serum level (13).

It must be also considered that other conditions (diet rich in folic acid salts or exocrine pancreatic insufficiency) may also trigger a reduction of cobalamin level with an increase of folic acid concentration; therefore, these conditions have to be included in differential diagnostics.

Other diagnostic techniques used for diagnosing SIBO in humans are not widely applied in veterinarian medicine, such as a test for unconjugated bile acids in serum, assessment of C-xylazine absorption, evaluation of bile acid absorption, a test for indoxyl sulphate in urine or hydrogen in exhaled air (1). Individual differences in the results of these tests present even among healthy subjects are so significant that they render these tests useless or almost useless in the diagnostics of small intestinal bacterial overgrowth (5).

Imagining diagnostic modalities can be used to exclude anatomic abnormalities in patients with the symptoms of SIBO. The results of routine blood test, serum biochemistry, and urinalysis are generally not conclusive for the diagnosis, similarly to the results of histopathological examinations (5).

Treatment

The treatment of choice for small intestinal bacterial overgrowth includes broad-spectrum antibiotics that are, active both against aerobic and anaerobic bacteria. The treatment is long – it should last at least six weeks and the response to the therapy is seen no sooner than after a few days or weeks. In the treatment of dogs with SIBO, tylosin (25 mg/kg PO, every 12 hours for 6 weeks), oxytetracycline (20 mg/kg PO every 12 hours for 6 weeks) or metronidazole (10-20 mg/kg PO every 12 hours for 6 weeks) are administered.

Antibiotics therapy should be accompanied with cobalamin supplementation and an appropriate diet.

A cobalamin dose for small dogs (up to 15 kg) equals to 500 µg SC and for large dogs – 500-1200µg SC. The cobalamin administration protocol is as follows: one dose per day for 6 weeks, one dose every two weeks for 6 weeks and one additional dose one month later. After that period the serum cobalamin level should be tested and if it is still low, the therapy should be continued.

The diet includes highly-digestible feed with a limited fat content. Probiotics should be added to the feed. In case of persistent vomiting, appropriate fluid therapy is critically important (Fig.2).

Conclusions

This paper discusses some basic and most recent information on small intestinal bacterial overgrowth (SIBO). The disease is found both in people and in small animals, dogs in particular, yet it is not entirely understood and elucidated. Apart from the possible causes that are discussed above, many authors postulate that SIBO has an idiopathic nature, which translates into therapeutic difficulties faced by the medical team. For patients with small intestinal bacterial overgrowth, the prognosis is generally good (it is essential to establish the cause of the disease). Sometimes the response to antibiotic treatment its good, but the clinical symptoms recur when the therapy is withdrawn. In such cases, it may be necessary to implement a long-term antibiotic therapy with an adjunctive treatment.

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Monitoring diabetes in dogs and cats

Natalia Jackowska DVM,

Diabetes is an endocrinological disease that frequently occurs in dogs and cats. Although the causes are different in these species, the clinical symptoms, diagnosis, and treatment are similar. In most cases, excessive thirst and polyuria are a direct reason for veterinary consultation. Dog and cat owners do not know what is wrong with their pets, but the diagnosis is not a problem for a veterinarian and the basic diagnostic tests are sufficient. Some patients are only brought to a clinic at the stage of diabetic ketoacidosis and they then require intensive treatment and frequent hospitalization.

Although the diagnosis of diabetes is relatively easy, treating diabetic patients is quite a challenge. For both species, the therapy is based on exogenous insulin. Dogs and cats suffer from hyperglycaemic complications, such as retinopathy and kidney or vascular diseases, less frequently than people and therefore, reaching and maintaining normoglycemia (60-130 mg/dl) is not the target at all costs; controlled and mild hyperglycaemia should be the aim. When the diagnosis of diabetes is made, it is crucial to adjust the type and dosage of insulin; this requires frequent check-ups, even every 7-14 days. When the patient has been stabilised, check-ups are carried out every 4-12 weeks. In the past, dogs and cats with diabetes were treated in the same way. The aim was to regulate glycaemia as soon as possible and to eliminate unpleasant symptoms so that animals do not drink excessive amount of water, dogs do not urinate at home and cats do not excessively urinate in litter boxes. Today, treatment of dogs has changed and monitoring, to a larger degree, can be done at home. The changes are more revolutionary in cats as the right diet and correctly adjusted insulin allow a complete remission of the disease. Diabetes can be treated in almost 100% of cats within a few months after the diagnosis. The role of the owner in the right treatment of a diabetic patient is enormous; the awareness of hypoglycaemia symptoms, pet behaviour observation, and home glycaemia monitoring are crucially important. Observation of water intake by the animal seems to be the most essential diabetes monitoring parameter. However, it should be remembered that water intake also depends on other factors, such as temperature and humidity or other diseases, like kidney dysfunction, Cushing syndrome or hyperthyroidism in cats.

Diagnostic methods in monitoring diabetes can generally be divided into direct and indirect. The indirect methods include monitoring water intake or taking urine glucose (and ketones) measurements, and measuring certain serum proteins. The direct methods include repeated measurements of glucose level in blood at predetermined intervals (the so-called glucose curve) or constant measuring with an insulin pump. It is worth remembering that a single measurement of glucose level in blood may be misleading. Obtaining an accurate measurement of glucose level in blood is particularly challenging in cats who can develop the so-called stress hyperglycaemia. The level of glucose in non-diabetic cats may reach even 300 mg/dL, and in diabetic cats – as much as 500 mg/dL. Interpreting such result is quite a challenge. When glucose level in blood exceeds the so-called renal glucose threshold, glycosuria develops (glucose appears in urine). Th renal glucose threshold is 160-220 mg/dL n dogs, while cats have a higher threshold of 230-280 mg/dL. Measuring the level of glucose in urine is a simple method which pet owners can use for monitoring diabetes at home. However, measuring sugar level in urine has one weak point, namely its level in urine covers and reflects a long period of time; this means that the undesired periods of hypoglycaemia can be masked by hyperglycaemia. Therefore, the decisions about increasing insulin dosage should not be based exclusively on testing for glycosuria. In both species (dogs and cats), the so-called Somogyi effect may occur; this is a phenomenon when glycaemia considerably increases in response to extremely low blood sugar. The Somogyi effect is most frequently seen after night-time hypoglycaemia. In response to hypoglycaemia, the body reacts by releasing some hormones (glucagon, adrenaline or growth hormone) increasing thereby the glucose level in blood. Therefore, we should keep in mind that a single recording of high sugar level does not mean that this level has been high all the time. In the case of correctly treated diabetes in dogs, hyperglycaemia and glycosuria occur throughout most of the day. A lack of glucose in urine in a diabetic dog should be alarming and most probably means that the insulin dose is too high. Ketones are another indicator of diabetes in urine. In the first weeks of diabetes the presence of ketones in urine is not surprising, but when they appear in urine in a stabilised patient this means that the insulin dose is too low. Urinalyses in laboratories and clinics frequently show that the urine sediment in diabetic patients includes fat globules, staining red with Sudan III; and, more often than in other patients, Candida can be detected in urine.

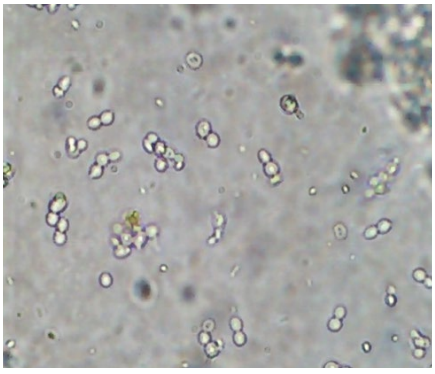

Figure 1.
yeasts in the urine

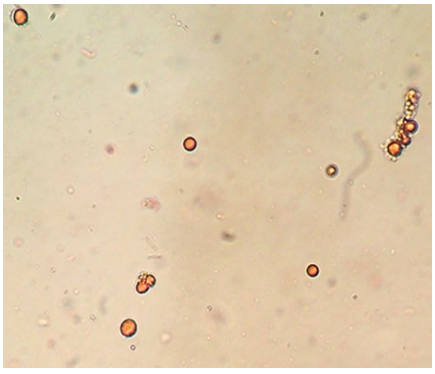

Figure 2.
fat globules in urine, Sudan III staining

Measuring fructosamine level in blood is an essential parameter in monitoring diabetes in dogs and cats. Fructosamine, or isoglucosamine, reflects the blood serum proteins, mainly albumins that have undergone protein glycation. Fructosamine level relates to albumins' half-life and reflects hyperglycaemia in the previous two weeks. In dogs with well-controlled diabetes, fructosamine level oscillates between 350 and 450 µmol/L. The value of >500 µmol/L indicates insufficient control of glycaemia. In cats, fructosamine is a parameter helpful in differentiating between diabetes and stress hyperglycaemia. When interpreting fructosamine level, we should remember that cats with hyperthyroidism have a lower level of fructosamine than expected. On the other hand, dogs with hypothyroidism have a higher level of fructosamine, which results from some changes in protein metabolism: faster in hyperthyroidism and slower in hypothyroidism. Measuring the level of glycosylated haemoglobin could be helpful in monitoring diabetes as it reflects the level of glucose over as many as 6 previous weeks. This parameter is crucial in monitoring diabetes in people, but unfortunately, it is not commercialised in veterinary medicine.

Although direct measuring of glucose level in blood is the quickest method of glycaemic control and superior to the indirect methods, a few nuances should considered. Measuring glucose level in blood provides information that is valuable for selecting the right kind and dose of insulin, it allows estimating how long insulin acts and determining the average daily level of glucose as well as the lowest daily level of glucose (at the peak of glucose action). In contrast to human medicine where the aim is to achieve normoglycemia, in veterinary medicine it is attempted to have controlled hyperglycaemia in a patient, according to the rule that mild hyperglycaemia is safer and better tolerated by the diabetic patient than hypoglycaemia. Most veterinarians try to achieve the lowest level of glucose: 100-150 mg/dL at the peak and the average daily value below 250mg/dL. The traditional glucose curve is measured by testing blood samples at 2-hour intervals; the first blood sampling is done just before insulin administration and blood is taken until the next dose of insulin is administered. The patient should receive food as it does every day: the same type of diet at the same times. If during the glucose curve measurements the level of glucose drops rapidly or becomes lower than 100mg/dL, the next measurement should be done after an hour. The glucose curve procedure can be carried out by the pet owner at home under strict veterinarian supervision. Doing the test at home is certainly less stressful for the patient and allows maintaining the daily routine, which is essential for diabetic patients. It is also easier for the pet owner to complete the test and this prevents delaying glycaemic control for trivial reasons, such as insufficient time or a long distance to the clinic, etc. Monitoring diabetes at home is advisable in feline patients with a tendency for stress hyperglycaemia.

Figure 3.

It is crucial to choose the right glucometer to take direct measurements of glucose level in blood. Handheld devices are based on electrochemical or photometric methods that calculate the total level of glucose based on the glucose concentration in serum/plasma (the displayed value is extrapolated from that number). Human erythrocytes have a large amount of glucose, while canine and feline erythrocytes have a small amount. Consequently, glucometers intended for humans cannot accurately indicate glucose level in blood. In veterinary glucometers that additionally tailored for specific species, the algorithm is written in such a way that the result of glucose level measurement is reliable. Another advantage of the veterinary devices is a possibility to complete the test using a smaller volume of blood – it is especially useful for cats and smaller dogs. The owners of diabetic animals who measure glucose level at home should have the devices dedicated for veterinary use. Haematocrit level influences glucose level in blood, even when a veterinary glucometer is used. In some breeds, haematocrit level is higher, e.g. in greyhounds it may reach 55-65%. In the patients with increased haematocrit, the glucose reading will be low; in anaemic patients, the level of glucose will be high – this should be taken into consideration in determining the lowest daily glucose value.

When a biochemical test for glucose level in serum is carried out, a few aspects should be considered. If blood is collected into the so-called dry tube and then sent to a laboratory, the level of glucose reading will be lower. It is estimated that the blood cells metabolise up to 10% of glucose per hour. If the time between blood taking and testing is too long, the glucose reading may differ from the actual level. There are two methods for preventing this error: after sampling, blood may be centrifuged, and serum put into a new test tube or blood can be additionally drawn into a test tube with sodium fluoride that stabilises the glucose level and eliminates such discrepancies.

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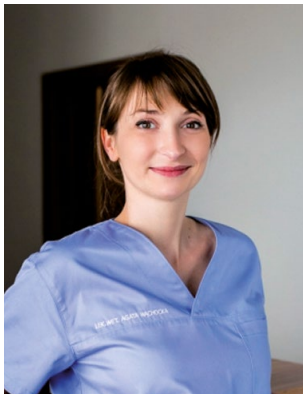
Gastric dilatation/volvulus (GDV) – always a current problem.



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Aetiology

The aetiology of gastric dilatation/volvulus (GDV) is not entirely known. There may be several factors that lead to the disease. This condition is most frequently diagnosed in elderly dogs (>5 years of age), large and giant breeds with deep chest, such as German shepherd, Irish setter, St. Bernard, Rottweiler, Labrador retriever or Alaskan Malamute (7). However, GDV may also develop in small-breed dogs (e.g. Dachshund or Pekingese), as well as in cats or other animal species. Gastric dilatation may occur as a result of intense exercise of a dog (running, jumping) performed shortly after feeding or drinking (especially when the pet is fed once a day with a large meal). Often this condition develops in dogs that eat in a frenzy and ravenous manner. It may also be a consequence of providing a dog with a rich (fat) 6). The causes might also be the anatomical abnormalities or poor functioning of the nervous or muscular system in the stomach or in dog aerophagia (swallowing large quantities of food or air e.g. when eating from a bowl put on the elevated platform) (1).

Pathogenesis

Gastric dilatation is a life-threatening, acute or peracute condition. It is characterised with severe distention of the stomach filled with gas, fluid and feed, making up a foamy content, and accompanied by strong haemodynamic or respiratory disorders. The gas accumulated in the stomach results from bacterial fermentation of food and swallowing the air by the animal. Severe gastric dilatation may lead to volvulus, closing both the cardia and the pyloric canal, which makes the outflow of the contents from the stomach lumen impossible. The pylorus usually rotates to the right side of the abdominal cavity, below the gastric body, and gets located dorsally from the cardia on the left side. The clockwise rotation may translocate the stomach by 360 degrees. The opposite rotation may result in maximum 90-degree rotation. It happens that the disease is accompanied by simultaneous translocation and enlargement of the spleen. The enlarged stomach puts pressure on the diaphragm and lungs, which results in respiratory distress. Moreover, compression of the large veins (caudal vena cava and portal vein) triggers haemodynamic complications resulting from reduced cardiac venous return and decrease of the heart stroke volume and cardiac output. Gastric volvulus leads to gastric wall ischaemia and necrosis (the arterial supply to the gastric mucosa decreases by 75%) (1,9).

The consequences of this condition include severe arrhythmias, shock, and disseminated intravascular coagulation (DIC). The mortality in GDV cases varies from 20 to 45% in treated patients and is higher than 90% in untreated ones (10).

Clinical symptoms

The clinical symptoms reported by the animal owners include abdominal distension, salivation, abdominal pain, empty vomiting, and agitation. In severe cases, due to haemodynamic disorders, loss of consciousness and hypovolemic shock might occur. Without decompression of the gas-filled stomach, collapse is a likely scenario (10).

The results of a clinical examination allow making a preliminary diagnosis of GDV without any significant difficulties. The findings include the enlargement of the anterior part of the abdominal cavity, elbows pulled away, tympanic sound (on abdominal percussion), and vomiting reflexes. Radiological examination in right-lateral and dorsal-ventral view is necessary to diagnose gastric or spleen displacement. Acute gastric dilatation cannot be differentiated from dilatation with volvulus only based on orogastric tube placement (5).

The laboratory findings are not very specific. CBC does not reveal any specific changes. Electrolyte disorders consists primarily of hypokalaemia developing after intensive fluid therapy and stomach decompression. Acid-base balance disorders are the most frequently diagnosed biochemical abnormalities in dogs with GDV. Metabolic acidosis associated with tissue ischaemia and activation of anaerobic respiration pathways is related to the increase of lactic acid concentration in serum (the physiological level in dogs: 1.11-3.89 mmol/L) and is an adverse prognostic factor. An increase of lactic acid concentration to > 6.6 mmol/L is seen in dogs with gastric wall necrosis (in dogs without necrosis the value is <3.3 mmol/L) (7).

Differential diagnosis of gastric dilatation and volvulus should include the following cases: a foreign body in the gastrointestinal tract, splenic volvulus, gastric/splenic cancer, diaphragmatic hernia, and jejunal intussusception. intussusception.

Treatment

There is a number of factors that determine the survival of a patient with GDV. Stabilisation of the patient before the surgery is what matters most. Stomach decompression is the most important procedure in GDV and is performed with direct placement of orogastric tube; it should not be introduced forcefully against the resistance felt as this might cause a rupture of oesophageal wall. To facilitate tube placement, it is advisable to introduce one or two cannulas (18-20G) into the right retro-costal area (on the most convex area with tympanic sound heard on percussion), having shaved and disinfected the area. With left lateral puncture, it must be remembered that the enlarged and displaced spleen may be located in the area of the puncture (4).

Intensive medical treatment for shock is indicated when a cannula with the largest possible diameter is placed in the cephalic vein or the external jugular vein. Venous punctures in the pelvic limns are not indicated when the venous outflow from the abdominal cavity and pelvic limbs is impaired. The correction of the acid-base balance and fluid therapy are necessary to improve the patient's condition and to restore normal organ perfusion. Fluid therapy includes the administration of lactated Ringer's solution and multi-electrolyte fluid. The infusion speed should be 60-90 ml/kg/hour for the first two hours in dogs and 25-30ml/kg/hour in cats and then the patient's condition should be reassessed. The fluid therapy should be continued at 10-20 ml/kg/hour. Hypertonic saline may be also infused (7.5% NaCl: 4-5 mL/kg in dogs and 2 mL/kg in cats) and Dextran 70 or HS may be administered at a dose of 14-20 mL/kg in IV bolus. During the treatment, the patient has to be monitored for normal hydration and the risk of pulmonary oedema. The use of glucocorticoids in medical treatment of

shock therapy in animals with GDV is highly controversial and usually these drugs are avoided in such patients. Dogs with gastric volvulus should also immediately receive analgesics and flunixin should be administered (0.5-1 mg/kg BW) to prevent endotoxic shock. Broad-spectrum antibiotics are also indicated, such as the third generation cephalosporins administered intravenously and quinolones or ampicillin (7,10).

Anti-arrhythmic treatment should be initiated upon diagnosing irregular heart rate (on the electrocardiographic examination with the heart rate > 180 beats/min and the lack of heart rate on the femoral artery during tachycardia). This treatment should include fluid administration, oxygen therapy, and lidocaine (initially in a slow bolus of 2-4 mg/kg, then in continuous intravenous infusion at 25-75 µg/kg/min). When the patient is stabilized, it should be attempted to empty the stomach, flushing out its contents (7,10).

The anaesthesiologic protocol recommended in GDV patients includes benzodiazepines and opioids to calm down the animal. Induction is made with a combination of ketamine and diazepam, according to a required effect. In a patient who has been in shock for a longer period, similar effects are seen when the combination of fentanyl, diazepam and etomidate is administered. For anaesthesia, isoflurane is used. The contraindicated anaesthetics in the gastric dilatation and volvulus cases are primarily acepromazine, alfa-2 agonists, Propofol, and nitric oxide (3).

During stomach probing, the entire content is evacuated and then the stomach is rinsed with warm water. Also activated medical charcoal may be used. When the patient is stable, diagnostic laparotomy is performed. The stomach location and lesions in the gastric wall (ischaemia, necrosis, perforations – they cover mostly the stomach major curvature). The volvulus of the stomach is repositioned, and, if necessary, gastroscopy of the affected wall is performed and next, gastropexy is attempted, according to the surgical procedure of choice. Gastropexy does not prevent excessive dilation of the stomach, but reduces the risk of dislocation and volvulus in the future. Special attention should be paid to the pancreas and the spleen should be evaluated for its location and appearance. The spleen is excised when the gross foci of infarcts are seen or when it is significantly enlarged or grey-blue in colour (7).

In surgically treated dogs, the falls may be a consequence of gastrectomy, splenectomy or both. The adverse prognostic factors include persistent hypotension, sepsis, peritonitis, and DIC. Moreover, a long interval between the occurrence of symptoms and medical intervention (over 6 hours) may contribute to increased risk of animal death affected with the disease (7).

The postoperative protocol consists in fluid therapy, antibiotic treatment, and analgesics. Potassium deficiency is corrected by adding KCl to crystalloids (40-60 mEq/L). The patient should be monitored for arrhythmia during 24-48 hours after the procedure. Proton pump inhibitors administered for 7-10 days are recommended in patients with suspected gastric trauma or ulcers. Such symptoms as nausea, salivation, smacking or unproductive vomiting may be alleviated with prokinetic medications (e.g. cisapride 0.25-0.5 mg/kg every 8-12 hours). Liquid diet may be implemented 24-36 hours after the procedure (2).

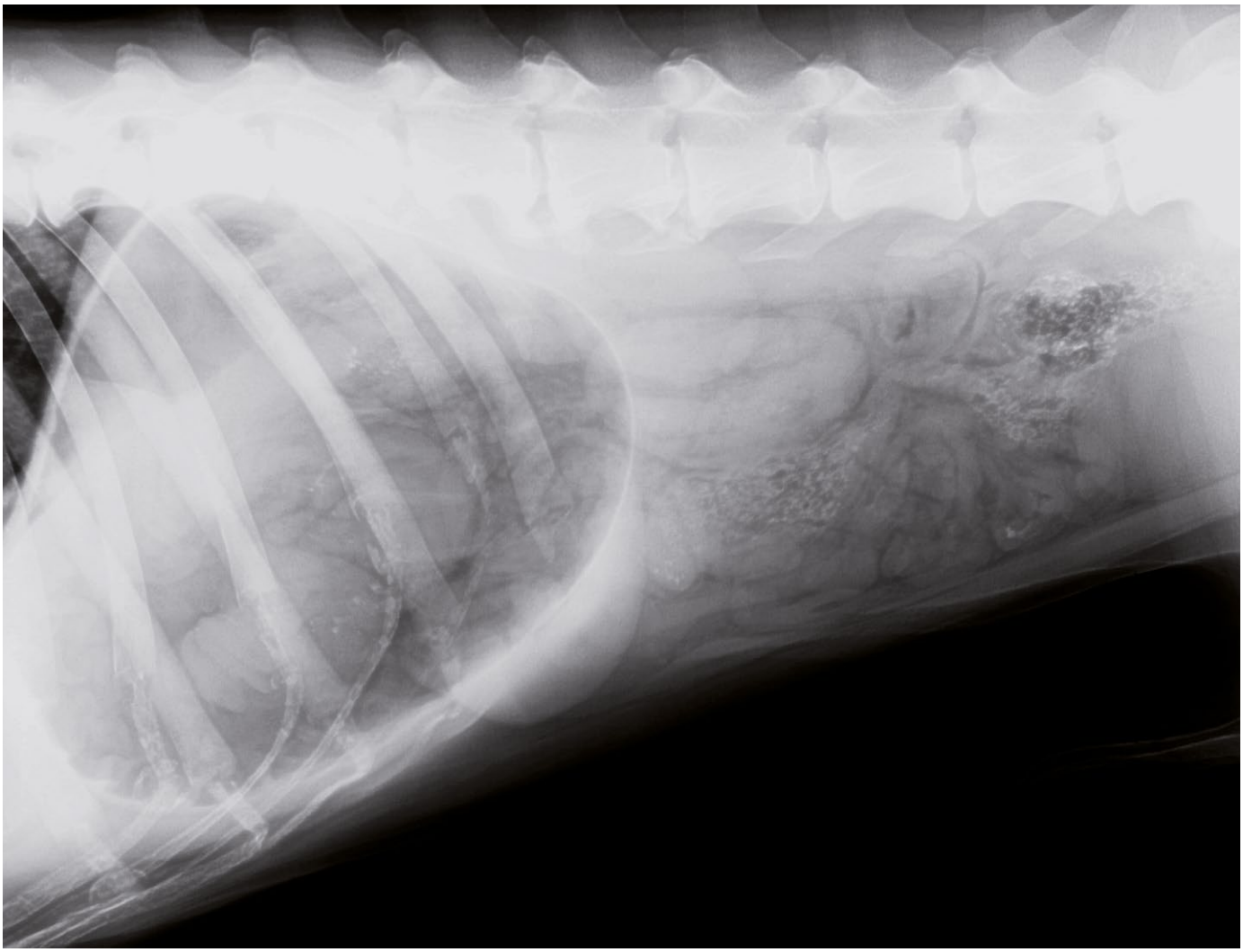

Figure 3.
extended stomach of a Tatra Sheepdog

Conclusions

Gastric dilatation and volvulus syndrome is frequently reported in dogs and it mainly results from incorrect handling of the animal. The prevention of GDV includes primarily appropriate nutritional approach; dogs cannot be fed earlier than 1 hour after physical exercise, and the exercise should be limited for at least 2 hours after feeding. The ration should be divided into 2-3 smaller meals per day. Furthermore, the bowl should not be placed on an elevated platform to reduce the amount of air swallowed by the animal. Once the owners observe these simple rules and once they are made aware of their importance by the veterinarians, the prevalence of this disease will be reduced.

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How to see the stomach from inside: gastroscopy in small animals

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Introduction

Gastroscopy is a method of examination of the upper part of the alimentary tract (oesophagus, stomach, and duodenum: esophagogastroduodenoscopy) with a rigid or flexible endoscope. This is a diagnostic and medical procedure with minor invasiveness, used for investigating of the mucosa and contents of cavernous organs. The possibility to inspect the lumen of the gastrointestinal (GI) tract and to assess the lesions, mainly erosions, fibrin residues or ulcerations, has significantly expanded diagnostic options and treatment methods of the GI tract. This is an essential tool for collecting specimens from the affected areas in the upper part of the gastrointestinal tract, harvesting the lavages, removing of foreign bodies or placing the gastric tube. During the endoscopic examination, it is possible to widen stenosis (e.g. reflux-related, caused by regurgitation of the gastric contents into the oesophagus), to investigate tumour-like lesions, obstructions and other anatomical lesions that cannot be found in X-ray or ultrasound. Undoubtedly, the limitation of this method is that it does not allow to investigate the normal motor activity of the gastrointestinal tract, and peristalsis (the strength of a peristaltic wave) cannot be evaluated in specific segments of the alimentary tract (1,6,9).

Indications for gastroscopy

There are several indications for the gastroscopic investigation of the upper gastrointestinal tract. Gastroscopy is indicated in patients with persistent or recurrent diarrhoeas and/or vomiting, reduction of body mass, haematemesis, melena, posseting, and with suspicion of a foreign body in the alimentary tract. Endoscopy brings invaluable diagnostic and therapeutic benefits. None of the routinely used imaging modalities allow investigating of the examined organ with a precise method of so low invasiveness (2,3,4,5,7).

Preparation of a patient for the procedure

The preparation of a patient consists in 24-hour fasting and withdrawing water/fluids for at least 6 hours before the examination. Moreover, the substances which coat the gastric and intestinal mucosa (e.g. barite or sucralfate) should not be administered for 1-2 days before the planned procedure. The assessment of morphological and biochemical parameters and the evaluation of cardiovascular system and respiratory efficiency should be a golden standard before the general anaesthesia. The recommended anaesthesiologic protocol depends on the condition of a patient and its comorbidities. The adverse reactions of almost all anaesthetic agents are dose-dependent and they should be thus administered according to their effect – (9,10).

A safe patter seems to include opioids in combination with benzodiazepines, with Propofol induction and isoflurane conduction. It should be remembered that due to filling of the stomach with air, the lung capacity is decreased, and during the examination this might result in waking up the patient from the anaesthesia due to inadequate saturation with an anaesthetic agent (because of the change in respiration rate and in the gas exchange surface). The use of alpha 2 – agonists should be avoided because of frequent vomiting seen after their administration (mainly after xylazine), which increases the risk of aspiration when the larynx is relaxed and due to the suppressed coughing reflex. Moreover, these agents are contraindicated in the patients with a suspicion of large sharp-edged foreign bodies in the stomach as there is a risk of damaging (perforation) of the stomach wall (9,10).

How to perform gastroscopy?

The endoscopic inspection of the gastrointestinal tract is connected with filing the lumen of the examined organ with appropriate amount of air. In order to enable it, a probe greased with lubricating agent should be introduced to the stomach trough an oral cavity. Cricopharyngeal sphincter usually is not a large obstacle if it is not surrounded by hyperplastic inflammatory lesions, tumours or polyps. The introduction of some amount of air into the oesophagus will allow for a less traumatic movement of a probe into the stomach and will also allow for the evaluation of the oesophageal mucosa (inflammation, erosions, infiltrations, hyperplasia, stenosis). Not all foreign bodies located in the oesophagus may be safely removed with an endoscopic method. It must be always remembered about an increased risk of tearing an organ wall affected with a disease and causing a tension pneumothorax. The lower sphincter of oesophagus may remain open, e.g. as a result of some drugs effect causing the antacid being released from the stomach into the oesophagus. With the closed sphincter, the probe may be delicately introduced, with the sphincter kept within the range of sight so as not to perforate the oesophageal wall. It sometimes happens that the introduction of the endoscopic tip into the stomach lumen might be more difficult as a result of the presence of the tumour mass or an enlarged spleen which press onto the stomach from outside, and also as a result of the anatomical structure of the stomach. In such cases the patient should be placed on the back to facilitate the examination. The objective of this diagnostic modality should be the assessment of the largest possible part of the gastric mucosa. The assessment should be performed according to the fixed and consistent examination plan in order to avoid missing the lesions or irregularities. The stomach should not be excessively extended as this might lead to circulatory and respiratory disorders. An extended stomach should be evaluated by means of assessing 4 quadrants, beginning from the areas located on 10 o'clock, then 2 o'clock and then 5 and 7, and the gavage should be maximally bent backwards to evaluate the stomach fundus and lower oesophageal sphincter which are the frequent locations of foreign bodies or infiltratory or cancerous lesions (in particular mięśniaka gładkokomorkowego). The next stage is to evaluate the jamy odźwiernika (pylorus) which is visualised with straightened endoscope tip moved along the major gastric curvature. Pumping the air into the pyloric cavity may facilitate the visualisation pyloric otwor odźwiernika and the introduction of endoscope inside it. If difficulties occur, instead of a gavage the biopsy kleszczykow biopsyjnych should be used and the endoscopic tube should be moved along them. Too string manipulation with the instruments should be avoided as this might damage the mucosa leading to string bleeding, in particular in a situation when the organ wall is affected with some pathology. After passing the pylorus, the duodenum is directed towards the right. To pass easily through this initial flexure, it is advisable to fill the duodenal lumen with air in order to increase the field of vision. This will also decrease the abrasions of the mucosa when endoscope is being moved (7,8,9,10).

Is gastroscopy a safe procedure: conclusions

Gastroscopy is a safe procedure, yet the risk of complications which might occur during the procedure or afterwards should always be considered. However, the situations in which the life of a patient is at risk are extremely rare. The position of a patient during the examination has an important effect on the function of cardiovascular and respiratory systems and the patient should be constantly monitored. It should also be remembered that not every patient with the symptoms of gastrointestinal tract diseases requires endoscopic diagnostics (8,9).

Gastroscopy-related complications are extremely rare. In some cases, there are respiratory or cardiovascular symptoms resulting mainly from general anaesthesia. There might be some signs of hypoxia or aspiration pneumonia. Various types of infections, such as angina, related to manipulations with the endoscope, are more frequent. The rarest complication is perforation of the gastrointestinal wall, associated mainly with chronic inflammations or ulcerations. The patients affected with coagulation disorders are also at an increased risk of post-endoscopic complications. It is emphasized, however, that gastroscopy is a safe procedure and the obtained information significantly contributes to the diagnostic process and helps selecting the appropriate therapy protocols (10).

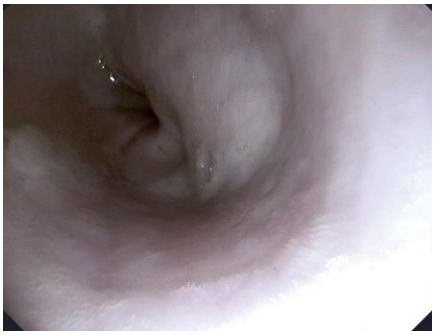
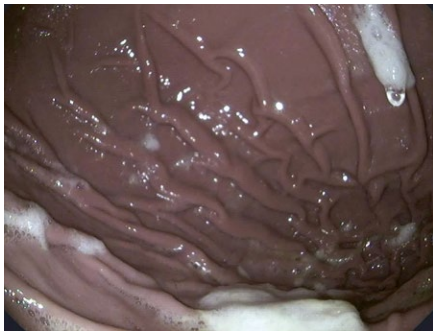


Figure 1.



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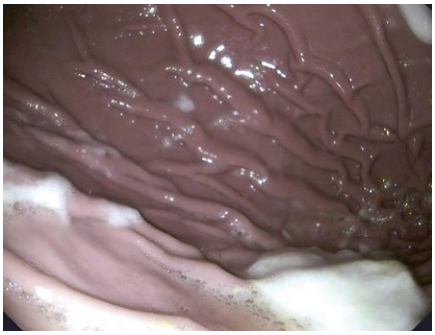
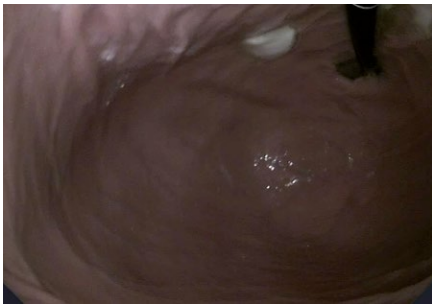


Figure 3.



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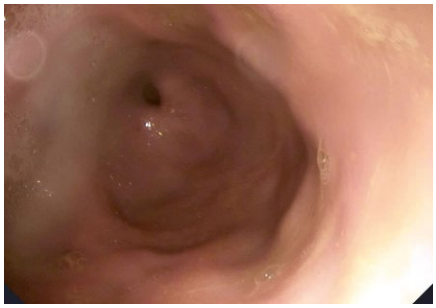

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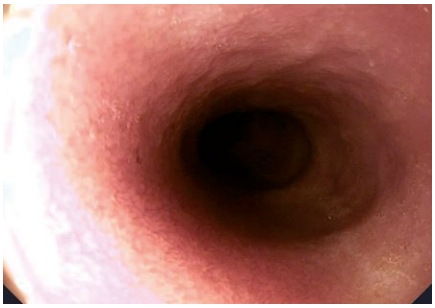

Figure 6.

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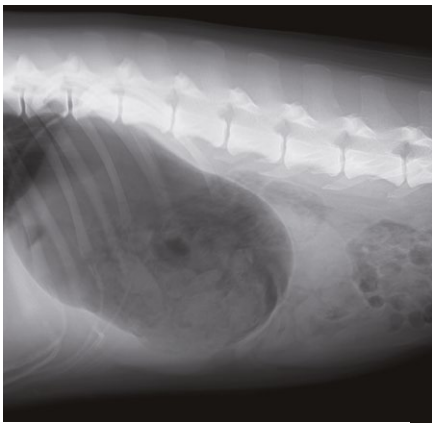

Figure 7.

A dietary approach to food allergy in cats and dogs

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Abstract

Food allergies (FA) are best defined as adverse reactions to food (ARF) that involve the participation of the immune system. An appropriate and balanced elimination diet serves as an important tool in the diagnosis and treatment of cats and dogs with food allergy. Homemade or commercial pet food with alternative or hydrolysed sources of protein can be used in such cases.

Key words: food allergy, diet, dogs, cats

Food allergies (FA) are best defined as adverse reactions to food that involve the immune system (5), while adverse reactions without its involvement are referred to as food intolerances, indiscretions, or poisonings. FA have a systemic or skin presentation that may be often difficult to differentiate from other skin conditions or inflammatory bowel disease (IBD).

A special elimination diet, either homemade or commercial, is required to correctly diagnose and treat food allergy. The diet is designed to eliminate potential allergens from the animal's feed and thus suppresses the allergic response. It is therefore carefully prepared based on an in-depth interview with the owner and a thorough review of the medical records of an animal.

Food allergens

Food allergens usually belong proteins or glycoproteins, but in human subjects, positive reactions have also been observed to certain carbohydrates (2). The animal proteins that are very likely to cause an allergic response in humans include lactic casein, tropomyosin found in fish, and crustaceans and mollusc proteins. (6). Among plants, the most potent allergens belong to such protein superfamilies as Bet v1 (fruits, soy, vegetables), cupins (nuts, vegetables, grains), prolamins (grains, fruits, vegetables), C1 cysteine proteases (soy, kiwi), and profilins (fruits, vegetables, legumes) (6). Their structure may be linear or spatial. Conformational allergens are more likely to undergo denaturation due to thermal processing and digestion, which means, for instance, that children allergic to milk or eggs can easily tolerate the processed types of these products (4, 7).

In dogs, allergic reactions are typically caused by allergens found in beef, dairy, wheat, eggs, and chicken, whereas in cats by beef, dairy, fish, and lamb. Hypersensitivity in animals may also be linked to other substances, e.g. carbohydrates that are a part of hapten-binding proteins, such as inulin, or glycoprotein antigens (8).

Homemade diet in the treatment of food allergy

A homemade elimination diet is recommended in 72% of food allergy cases in dogs and 86% in cats, since it can be more easily adapted to the needs of individual animals, does not contain preservatives, and provides a source of fresh food. This is a highly restrictive regimen based on a source of protein (dog, cat) and carbohydrates (dog) that were not included the original feed of an animal. However, the diet is also low in other nutrients (fats, fatty acids, vitamins, minerals) and thus incomplete in terms of dietary balance. Therefore, it is not recommended for young, growing kittens and puppies, but it is recommended for adult animals that can tolerate short periods (8-12 weeks) of possible nutritional deficits. Preparation and storage of homemade elimination diets challenging (required temperature between 4 and 8°C), and their expiry date is short, as with all fresh foods. Inadequate hygiene during preparation or storage may increase the risk of food poisoning with various bacteria and toxins. Furthermore, the cost is very high because any attempt to find an alternative source of protein excludes the use of the most common, and thus relatively cheap, market products.

The disadvantages of homemade elimination diets for growing animals may in turn prove advantageous in adult animals. This applies to their limited composition, which makes them highly hypoallergenic, provided that the components are carefully selected.

Commercial diets in the treatment of food allergy

Complete and balanced commercial hypoallergenic diets help lower the risk of nutritional deficits. However, when produced on the same manufacturing line as regular feeds, they may be contaminated with potential allergens (6). Most producers thus channel a dedicated line for this purpose. Commercial elimination diets are based

on new/untypical sources of protein or hydrolysed protein. It is essential, however, to ensure that they have the adequate nutritional value for cats and dogs, are easily digestible and tasty. An interesting experiment conducted by Deng et al. compared the chemical composition of 8 selected sources of protein: squid powder, pork peptone, alligator, lamb, venison, chicken and duck meal, as well as their digestibility and calorie content (3). Squid and pork peptone were shown to be highest in protein and total energy and low in ash, compared with alligator, lamb, venison, chicken, and lamb; their fat content was quite low (8.7% DM) relative to other meals (15.5-22.1% DM). Except for histidine, the essential amino acids in squid and pork peptone were also more easily digested. The lowest digestibility values were reported in lamb. For metabolic energy, the highest figures were recorded in squid (4.82 kcal/g DM), and the lowest in lamb meal (3.12 kcal/g DM) (3).

Other untypical sources of protein used in elimination diets include insects. Tests have been conducted on larvae, pupae, and adult specimens of flies (Musca domestica, Hermetia illucens), darkling beetles (Tenebrio melitor, Alphitobius diaperinus), crickets (Acheta domesticus), lesser mealworms (Alphitobius diaperinus), superworms (Zophobas morio), and Blattodea (Eublaberus distanti, Blaberus craniifer, Blaptica dubia) (1). The proteins in dairy, fish, and soy are the golden standard used as the reference in evaluations. For instance, even though the larvae and adult specimens of flies are high in protein and have a good EAA composition, their digestibility is very low. Cricket proteins have a similar amino acid content and profile as fish, but their nitrogen is more easily digested. Blattodea, on the other hand, despite being high in protein, show an incomplete amino acid profile and low digestibility. If insect sources, it is essential to consider their nutritional value and digestibility, but also to investigate whether the feed will be easily mass-produced, safe, and tasty for cats and dogs (1).

Another solution for commercial elimination diets is the use of hydrolysates, which is based on the theory that hydrolysed allergenic proteins cannot stimulate the immune system due to their negligible molecule size. This was shown to be true in studies with dogs allergic to soy protein; the use of hydrolysates was found to inhibit adverse reactions (5). Typical food allergens are usually composed of large molecules, from 10 to 70 kDa; hydrolysis allows reducing their size down to 5 or even 3 kDa. Human nutrition also relies on molecules as small as approx. 1 kDa. Protein hydrolysis, however, may also have an adverse impact on the final taste that is the outcome of all flavours in hydrolysed peptides, while the presence of small-sized peptides with osmotic activity increases the risk of diarrhoea. Commercial diets for cats and dogs are usually based on the hydrolysates of poultry liver or soy. To boost their hypoallergenic properties, protein-free sources of carbohydrates, such as purified starch, are also used.

Conclusions

The elimination diet is just the first step in the nutritional approach to the treatment of food allergy. It helps to reduce or eliminate most clinical symptoms and allows proceeding to the next stage, i.e. a challenge that, involves reintroduction of single ingredients from the previous diet, i.e. potential allergens, for 10 to 14 days to confirm or rule out their allergenic nature. The difficulty of controlling all possible allergens depends on the variety of the original diet.

Once both stages are completed, we can help the owners select an elaborated and balanced homemade or commercial elimination diet for their pet: feed with a new, untypical source of protein or its hydrolysed variant. Most commercial hypoallergenic diets are also gluten-free, which means they can be used both in cases of food allergy and intolerance, as well as in other gastrointestinal disorders (e.g. inflammatory bowel disease, IBD).

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INTRODUCTION

From the anatomical perspective, the liver is a part of the alimentary tract yet from physiological point of view, it constitutes the entire organism. The liver plays a key role in protein, lipid and carbohydrate metabolism, production of bile acids and in storing, detoxicating and excreting of lipid-soluble substances to the bile.

Laboratory diagnostics of a hepatic disease is based on two types of tests. The first ones include the chemical evaluation of hepatic cell status (ALT, AST, and GLDH activity) and enzymatic evaluation of cholestasis (AP and GGTP activity). The latter group are the biomarkers useful for assessing of the liver functions (protein, urea, ammonia, glucose, bile acids, bilirubin, and prothrombin time).

CHEMICAL EVALUATION OF THE HEPATIC CELL STATUS: ALT, AST, AND GLDH

Aminotransferases (alanine aminotransferase, ALT, and aspartate aminotransferase, AST) help to diagnose hepatocyte damage. ALT is liver-specific (tab. 1); AST is an enzyme that, apart from hepatocytes, can be also found in the skeletal muscle cells, cardiac muscle, brain, kidneys, and erythrocytes. The location of these two enzymes within the cell is also different. Alanine aminotransferase is found in the hepatocyte cytoplasm, whilst aspartate aminotransferase – mainly in the cell mitochondria (70%), and also in the cytoplasm in a small part (30%). This translates into how the test results are interpreted. In liver diseases accompanied with inflammation leading to increased permeability of the cell membranes, ALT is the first substance to be released into the bloodstream. A simultaneous increase of AST activity might be indicative of hepatocyte degradation accompanied by the damage of cellular organelle. It must be remembered that an increase of aspartate aminotransferase level without ALT increase does not indicate hepatic damage.

In the case of hepatic damage, ALT activity increases faster than AST. However, when the factor which impairs the AST activity ceases, the level of this enzyme normalises faster (in approx. 3 weeks).

To facilitate a correct interpretation of transaminase activity, the AST/ALT ratio has been introduced to laboratory diagnostics.The physiological value of this ratio

A biochemical evaluation of hepatocyte damage and metabolic functions in dogs and cats

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should be 1.2-1.8. The parameter is calculated only when the activity of these enzymes is elevated. A significant decrease (below 1) might suggest an extra-hepatic cause of transaminase activity increase, whilst the level above 2 is seen in chronic hepatitis cases (1,2,4).

GLDH is a mitochondrial enzyme located mainly in hepatocytes, but also in the brain cells, lungs, skeletal muscles, and kidneys. The highest concentration of this enzyme is found in the hepatocytes situated near the central hepatic vein. An increase of its activity is observed when the hepatocytes located in this region of liver are damaged. The causes for GLDH activity increase include not only parenchymal inflammation, but also the conditions leading to ischaemia of this region, such as cardiogenic shock or septic shock (1,2,4).

ENZYMATIC EVALUATION OF CHOLESTASIS

The assessment of alkaline phosphatase activity is, in fact, an evaluation of the activity of all its isoenzymes. The total result of AP activity consists of the activity of hepatic isoenzyme associated with the cytoplasmic membranes of hepatocytes (located mainly in the hepatocytes near the bile ducts); bone-derived isoenzyme, and cortico-dependent isoenzyme. Therefore, the causes of an increase in total alkaline phosphatase activity are varied (1,2,4).

The elevation of total AP activity resulting from an increased activity of the bone-derived isoenzyme (<3X above the reference range) is found in young dogs (aged to 6-8 months) and this is a normal, physiological situation that should not raise any concern for the clinician. Pathological elevation of the bone-derived isoenzyme is reported in diseases leading to the damage of bone tissue structure (e.g. osteosarcomas) (3).

An increase of total AP activity resulting from an increased activity of the cortico-dependent isoenzyme is seen during corticosteroid treatment (dogs) or in hyperadrenocorticism. To determine the individual isoenzymes, the total phosphatase activity is measured and then, the serum is heated to 56°C and the AP activity measured again.

High temperature completely inactivates the bone-derived isoenzyme and partly the hepatic isoenzyme, whereas the cortico-dependent isoenzyme is not sensitive to high temperature – this is the so-called thermal stability of alkaline phosphatase (1,2).

The elevation of AP activity should be interpreted considering the animal species (Tab. 2). In cats, the most frequent causes of increased alkaline phosphatase activity are liver steatosis, cholangitis, hepatitis with cholangitis, hyperthyroidism, and diabetes. (3) The most frequent causes of AP activity elevation (above 3X) in dogs include hepatitis with intrahepatic cholestasis, endogenous steroids (hyperadrenocorticism, stress), glucocorticoids therapy, anti-epileptic therapy (luminal). (3)

GGTP – Gamma-glutamyl-transpeptidase is an enzyme associated with the endoplasmic reticulum of the hepatic, renal and pancreatic cells. In the liver, the largest amount of GGTP is found in the hepatocytes located near the bile ducts, and it is thus a cholestasis indicator (1,2). The determination of GGTP activity is of special importance in cats as in their case this enzyme seems to be more sensitive and specific for hepatic diseases than alkaline phosphatase (with the exception of liver steatosis) (3).

BIOCHEMICAL EVALUATION OF HEPATIC METABOLIC FUNCTION

The elevation of hepatic enzymes activity is not a symptom of liver dysfunction. A frequent mistake made during a clinical evaluation of the test results is to diagnose hepatic failure on the basis of elevated ALT and AST levels. An increase of their concentration demonstrates only hepatocyte damage and does not give any information on metabolic liver disorders. When hepatic failure is clinically suspected, a number of other tests should be performed to evaluate protein, lipid and carbohydrate metabolism and to determine the blood level of such metabolism products as urea, bilirubin, and ammonia (1, 2, 4).

Tab. 1

Selected causes of elevated alanine transaminase activity (>3X)	
DOGS	**CATS**
Hepatitis	Cholangitis
Hepatitis with cholangitis	Hepatitis and cholangitis
Cholangitis	FIP
Liver cirrhosis	Hepatic lymphoma
Copper storage hepatopathy	Cirrhosis
Toxic hepatic damage	Toxic hepatic damage
Hepatic tumour	Pancreatitis
Pancreatitis	Hyperthyroidism
Medication: acetaminophen, azathioprine, barbiturates, ibuprofen, carprofen, clindamycin, doxycycline, glucocorticoids (only dogs), griseofulvin, itraconazole, ketoconazole, metamizole, nitrofurantoin, phenobarbital, theta sulphonamides	

The decrease of total protein level in hepatic failure results from the decrease of albumins concentration. Albumins are transport and structural proteins synthesized in the liver. Hypalbuminaemia accompanies liver cirrhosis and is due to a reduced number of functional hepatocytes (4). It must be remembered, however, that in hepatic

diseases, there are also some other causes of hypalbuminaemia, such as urine protein loss, decreased supply, impaired absorption, and fluid overload.

In hepatic failure, the synthesis of Vitamin K-dependent coagulation factors might be decreased (factor II, VII, IX, X) as well as a decrease of fibrinogen production might develop. In chronic liver diseases, haemostasis should be evaluated based on the prothrombin time (PT) (4).

Ammonia is a product of protein metabolism synthesized in the intestines and metabolised into urea in the liver. An increased concentration of ammonia reported in portosystemic shunt, severe chronic hepatopathies, and uraemia. This parameter is difficult to determine because blood should be collected into a previously chilled container and immediately centrifuged, and deep-frozen plasma should be sent to a laboratory.

Urea is a metabolic product of protein metabolism, synthesized in the liver and excreted mostly through the kidneys. Its level is decreased in severe hepatopathies and in portosystemic shunt.

Bilirubin is a product of the transformations of haemoglobin haem group (originating from disintegrated erythrocytes and muscle tissue myoglobin). In the liver, bilirubin binds with glucuronic acid and is excreted to bile. Then, in the intestines, it is transformed into urobilinogen that is finally excreted through the kidneys. Bilirubin is excreted as stercobilin with faeces. Laboratories measure the total bilirubin and conjugated bilirubin. In hepatic jaundice, an elevation of the total bilirubin level is mostly seen only with a slight increase in the conjugated bilirubin level and a slight increase of urobilinogen in urine. (1,2)

Bile acids are a product of cholesterol metabolism and they are excreted to bile with which they are transported to the intestines and then, they return to the hepatic portal vein (1) – this phenomenon is known as the hepato-intestinal (enterohepatic) circulation. The total concentration of bile acids is measured twice: as a fasting level, after 12-hour fasting and two hours after a small high fat meal. The interpretation of the results is presented in Table 3. (5)

The way the results refer to the clinical condition of a patient and a collective analysis of the parameters are of key significance for interpreting of the laboratory findings; and only this kind of interpretation leads to correct diagnosis and therapy.

Tab. 2.

Selected causes of elevated alkaline phosphatase levels	
DOGS	**CATS**
Bile duct disorders	
Pancreatitis	
Bile ducts tumours	
Cholecystitis	
Oral mucocele	
Gallbladder perforation	
Hepatic parenchymal diseases	**Hepatic parenchymal diseases**
Hepatitis with cholangitis	Hepatitis with cholangitis
Chronic hepatitis	Liver steatosis
Copper storage hepatopathy	Hepatic lymphoma
Hepatic fibrosis	FIP
Liver cirrhosis	
Hepatic tumours	
Toxic liver damage	
Other causes	**Other causes**
Young animals during the period of growth	Diabetes
Endogenous steroids	Hyperthyroidism
Diaphragmatic hernia	
Diabetes	
Iatrogenic: glucocorticoids (only dogs), azathioprine, barbiturates, cephalosporins, oestrogens, griseofulvin, ibuprofen, metamizole, nitrofurantoin, phenobarbital, primidone, progesterone, salicylates, testosterone, tetracyclines, vitamin A	

Tab. 3

Interpretation of bile acid test results: pre-stimulation level > 45 µmol/L – the result always indicates some pathology		
Physiological	**Dogs:**	fasting <10 µmol/L; post-prandial <20 µmol/L;
	Cats:	fasting <7 µmol/L; post-prandial <15 µmol/L<
Diseases	**fasting:**	>180 µmol/Ll; post-prandial >180 µmol/L – bile duct obstruction
	fasting:	~100 µmol/L; post-prandial ~120 µmol/L – intrahepatic cholestasis
	fasting:	<10 µmol/L; post-prandial >180 µmol/L – portosystemic shunt
	fasting:	25-50 µmol/L; post-prandial <20 µmol/L – slow gastrointestinal peristalsis or spontaneous contractions of the gallbladder
	fasting:	10 µmol/L; post-prandial 10 µmol/L – prolonged digestion, malabsorption

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Diarrhoeas in rodents and lagomorphs

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Rodents and lagomorphs are very popular pets, being an alternative to dogs or cats. Unfortunately, these two groups of animals significantly differ from each other anatomically, physiologically and behaviorally. Rodents and lagomorphs have a specific anatomy of the alimentary tract and thus have very specific nutritional requirements.

Among small pet mammals, there are typical herbivores, such as rabbits and domestic cavies (once guinea pigs); there are also omnivore rats and hedgehogs that, contrary to common belief, have a diet based mostly on animal-origin food. In these specific groups, there is also some "specialisation" e.g. high fibre diet in rabbits or low-sugar diet in common degus that are sensitive to monosaccharides. A balanced diet relates to the changes in the anatomy and functioning of the alimentary tract between individual discussed species. A common feature of all small mammals is their fast metabolism, which translates to the fact that they need a more frequent access to food – and in many cases even continuous access. A bad diet (inappropriate food for a given species or incorrect amount of food) directly leads to digestion and absorption disorders and consequently to diarrhoeas. A very specific, worth discussing anatomy of the alimentary tract, worth discussing here is characteristic of such animals as rabbits, cavies or chinchillas. An important element of the digestion system of the above animals is the caecum. Large quantities of bacteria, present there, facilitate the digestion of the digestible fibre. The products of this fermentation are excreted, in a form of so-called cecotropes (softened faeces forming aggregated packets and non-hard droppings), which the animal consumes to regain bacteria and processed fibre. Non-digestible fibre helps the food to pass through the alimentary tract, thereby activating peristalsis. Another feature of these animals is the rootless teeth that grow continually during their entire life. These teeth are involved in preliminary food digestion. Such specific tooth anatomy makes some diseases very likely to develop, and, once present, they cause incorrect food consumption (avoidance of hard bites, inappropriate chewing and a general reduction of the volume of ingested food); as a result, digestion disorders further down the gastrointestinal tract are triggered. In the case of diarrhoeas in the discussed species, apart from the standard examination, it is necessary to perform a thorough survey of the dentition, obviously under general anaesthesia. When the animal is anesthetised, the oral cavity and the most distant molars can be inspected (this is impossible in a non-anesthetised animal since the procedure is associated with profound stress and the risk of an injury, such as injuries to the oral mucosa, fractures of the molars, and even the temporomandibular joint sprains).

Diarrhoeas

To understand the essence of the problem in such small patients, one must refer to the definition of diarrhoea that is frequently mistaken with other health problems in these animals or even the behaviour type which is completely physiological. **Diarrhoea** (Latin: *diarrhoea*) is a clinical symptom presenting as the increased frequency of defecation or the increased volume of faeces with a change of the consistency into liquid or semi-liquid. In small mammals, especially in typical herbivores, diarrhoeas are one of the most frequent causes of veterinarian consultations.

In many species, diarrhoea presenting with liquid faeces may lead to serious dehydration or even death of the animal. Due a very diverse anatomy of the alimentary tract in the individual species, the causes of diarrhoeas may have various aetiologies. Pet owners should never ignore these symptoms, and an immediate veterinary consultation is necessary for a correct diagnosis and treatment. In the animals weighing less than 1 kg, diarrhoea is always a life-threatening condition and 1-2-day fasting, which is a common practice among dog owners, may only precipitate death of the animal.

The causes of diarrhoeas

Rodents and lagomorphs are very sensitive to stress, and diarrhoea may be one of its symptoms. Strong stressors include transport, diet change, change of the place of living, changes in a herd, and excessively high temperature (mainly in rabbits, chinchillas and domestic cavies). The improvement of living conditions, elimination of the stressor, providing the access to good quality hay, and administration of probiotics are usually a solution to the problem. However, even such diarrhoeas cannot be underestimated, because in animals with weaker immune system even a minor problem may progress into a serious disease.

Disorders of the intestinal flora may be another cause of diarrhoeas in these patients. This problem usually occurs in the animals that are weaned from their mothers too early, which is a frequent procedure in rabbits and cavies. The alimentary tract in young animals is incompletely adapted to digesting of solid food and the caecum is not colonised with appropriate bacterial flora. The gastrointestinal tract in infant rabbits is almost completely sterile: the stomach pH is 5-6.5. Before bacterial colonisation, the stomach is protected by maternal antibodies and so-called "stomach oil" or "milk oil". In new-borns fed by mothers, there is virtually no risk of diarrhoea before 4 weeks of age. The situation is different in animals fed with artificial formulas. The alimentary tract is not properly protected, and therefore, acute bacterial diarrhoeas frequently occur. Around 15 days of age, the phenomenon of cecotrophia develops: the young ones initially develops: the young animals initially consume the cecotropes of their mother, thanks to which their caecum is colonised with appropriate bacterial

flora, and then they eat their own faeces. Around 30 days of age, the consumption of maternal milk is minimal, and the main feed is solid food whilst cecotrophia is already fully developed. At the same time, the amount of the "stomach oil" production decreases and stomach pH changes to 1-2. Low pH is supposed to protect the stomach and the small intestine against bacteria. The capacity of a young rabbit to protect itself against pathogenic microorganisms depends on a balanced and undisturbed process of the change of protective "systems". Therefore, most diarrhoea-related problems such as colibacillosis, mucinous colitis or an acute form of coccidiosis occur in rabbits around weaning, when all the stress factors disturb the correct development of protective mechanisms in the gastrointestinal tract. During this process in the alimentary tract of rabbits, mucinous colitis or mucinous enteropathy are quite frequent. These conditions cause high mortality in young rabbits. When these conditions develop, the animals do not suffer from typical diarrhoea: instead of faeces, a kind of thick sticky jelly-like discharge is defecated. The cause of the disease is believed to be the dysbiosis of the caecum combined with a decrease of gastric pH level.

It must be remembered that the intestinal flora in rabbits is specific, and the typical content include rabbit yeasts, *Saccharomyces (Cyniclomyces) guttulatulus* at 106/g. Yeasts are found in faecal smears, but inexperienced persons mistake them for coccidia. Under normal conditions, the lactic acid bacteria are absent.

Both veterinarians and uneducated owners may trigger the intestinal flora disorders with their unpremeditated actions. The incorrect selection of antibiotics or prolonged oral administration of antibiotics without probiotics are the main iatrogenic causes of diarrhoeas in rodents and lagomorphs. The use of beta-lactams (PO in particular) is associated with the risk of destroying of the Gram-positive bacterial flora. This would lead to uncontrolled proliferation of Gram-negative bacteria, such as *E. coli* and *Clostridium sp.*, that cause bacteraemia, intestinal inflammations, and diarrhoea.

A sudden diet change, introduction of fresh food in a large quantity and the lack of hay do not serve these animals. Many nutritional errors are made by new pet owners who provide the animals with "what is best" and excessive amounts of "out of real care". For the young animal, the travel to its new home is stressful and full of situations in which it is exposed to different pathogens. The scenario is usually like this: the breeder (too early weaning) – animal fair (no food for about 24 hours) – animal wholesalers – pet shop – new home. It is quite easy to contract diarrhoea during this period. Therefore, the new owner should first put the pet in a peaceful and quiet place, should provide it with good quality hay and good basic feed, but they should not experiment with new food. Green fodder should be introduced gradually in a small amount, and then the behaviour of the animal should be observed. After the fresh food has been introduced, the faeces structure may temporarily change into moistener stool, yet it should still be well-formed. All abnormalities should be consulted with the veterinarian. A common dietary error is to feed the animal with large quantities of fresh fruit. Rabbits, chinchillas, and domestic cavies have some specific nutritional features: they would consume mostly leaves. Fruit and some root vegetables, such as carrot, contain a lot of sugar that then ferments in the gastrointestinal tract causing bloats, and additionally, this might lead to the changes of the caecum pH and thus to the disorders of bacterial flora and, as a result, to diarrhoeas. The veterinarian investigating a rodent or a lagomorph with diarrhoea should not only perform a thorough clinical examination and teeth survey but should also focus on a detailed history of the patient concerning nutrition and the environment. It must be remembered that in these animals, the statement that they are fed with fruit and vegetables is not very specific and thus not relevant for the history.

Bacteria diarrhoeas

Intestinal infections caused by bacteria may be primary but they can also be iatrogenic, due to treatment (e.g. resulting from incorrect administration of beta-lactams).

Wet tail

Wet tail (proliferative ileitis) is one of the most frequent bacterial conditions; this disease occurs most frequently in hamsters and other rodents. This is an acute condition associated with high mortality, bringing heavy losses to animal wholesalers and pet shops. Diarrhoea connected with malabsorption leads to rapid emaciation and dehydration of the animal and, as a result, to electrolyte disorders. also remembered that the animals like hamsters are physiologically able to consume only very small amounts of fluids. The bacteria responsible for this disease include *E. coli, Clostridium perfringens*, and *Campylobacter jejuni*. The main pathogen is an intracellular bacterium – *Lawsonnia intracellularis*. These infections are usually secondary to generalised weakness or stress. The increased morbidity is reported in spring and autumn. Weaning and transport on cold and wet days facilitate the development of this disease. The course of the disease depends on the individual level of immunity. Not all animals in a herd will contract the disease.

The affected individuals are depressed, apathetic, inactive, with hunched posture, dull and matted hair coat, and with sunken body walls; severe dehydration is also found. In sick animals, body temperature drops very fast, and the perianal area is wet and smudged with yellow-brownish faeces.

Tyzzer's disease

Like larger animals, small mammals are susceptible to infections with *Clostridium piliforme* – the anaerobic bacterium causing Tyzzer's disease. The disease spreads via oral route with faeces, dirty bedding, contaminated water and direct contact with the host. The cysts are resistant to most disinfectants; it is best to eradicate them with high temperature. These features facilitate spreading the infection in a herd. A high-protein diet, stress, excessive density, and poor hygienic conditions favour the development of the disease. In peracute form of the disease, sudden deaths might occur, whilst in milder cases, the typical symptoms include diarrhoea, dehydration, apathy, hunched postures, reluctance to exercise, and inappetence. The post-mortem examination reveal necrotic foci in the liver and necrotising colitis with dark, almost black colour of the intestines. Band-like necrotic foci can also be found in the myocardium. Unfortunately, despite the treatment based on fluid therapy, liver protection, antibiotics and probiotics, the mortality exceeds 50%. The authors of this paper have most often diagnosed the Tyzzer's disease in gerbils.

Parasitic diarrhoeas

In small mammals, parasitic infestations may spread between species relatively easily (*Giardia intestinalis*), but there are also infestations specific only to the individual species (some subspecies of coccidia *Eimeria* in rabbits or domestic cavies). In many cases, the symptoms of a parasitic infestation are frequently invisible or quite unspecific. Prophylactic parasitological tests of the entire herd are very important. It happens for example that *Hymenolepis diminuta* tapeworms are detected in all animals in a herd, whereas the owner is concerned about the condition of only one animal. In the case of pathogenesis of diarrhoeas, parasites most frequently play an intermediary role. They cause emaciation

and weakness of the body, and also, they damage the intestinal epithelium – as a result, secondary bacterial infections develop, leading to diarrhoeas. Many parasites (such as protozoan dinoflagellates) may be present in the intestinal flora, but only in some specific situations they multiply excessively. In our practice, we most frequently encounter coccidia infestations: *Eimeria sp.* (rabbits, Guinea pigs), *Giardia intestinalis* (all species), tapeworms' infestations: *Hymenolepis nana* and *Hymenolepis diminuta*. Parasitic infestations are a significant problem in large commercial herds and on breeding farms. In many cases, the parasitic spores are resistant to most disinfectants, and despite treatment and reduction of disease symptoms, one must bear in mind that the disease may recur after some time. it should also be considered that many parasitic diseases (including *Eimeria coccidia*) are frequently incompletely cured, which means that the number of parasites was reduced to the level that does not give any clinical symptoms. Therefore, a thorough parasitological assessment is necessary both during and after treatment. The residual parasites, even in a small number, may multiply in favourable circumstances (stress, poor diet) in the future, causing the recurrence of diarrhoea and other symptoms of the disease.

Treatment

Irrespectively of the pathogenic factor, diarrhoeas are frequently the outcome of nutritional errors, poor breeding conditions or stressful situations. Together with the medical treatment, it is necessary to improve the hygienic conditions (thorough disinfection of the environment, complete change of the bedding), to provide the appropriate diet and peaceful living conditions for the animals, as well as maintaining these standards when the therapy has been completed.

Irrespectively of the cause of diarrhoea, the degree of dehydration must be first assessed, and the fluid deficiency must be compensated, as dehydration is the most common cause of death in such cases. When the fluids are to be chosen, the glucose level should be measured, and urine should be tested (pH level and the presence of ketone bodies, because acidosis is a frequent condition). In the case of stress-induced diarrhoeas, the fluid therapy and fibre-rich diet (it is necessary to withdraw fresh feed, especially fruit that is rich in sugars) might turn out to be sufficient to resolve the problem but a detailed diagnostic process should never be overlooked.

Faecal examination is a basic test necessary for further treatment planning. The macroscopic image of faeces is often typical in many diseases (e.g. jelly-like mucous in many bacteraemia cases); however, the microscopic evaluation is far more important. A faecal smear will allow to evaluate the microflora in a sample (the number of bacteria, protozoa, yeasts, undigested food, the presence of fat), and it may also reveal the presence of parasites: in such case, the diagnostics must include additional techniques (floatation, staining, immunochromatographic assays). In recurrent and chronic diarrhoeas, it might be necessary to perform microbiological tests together with sensitivity survey to evaluate the drug resistance of the pathogens.

The choice of medication depends very much on the animal species and the type of pathogen. The differences may be substantial, with the drug doses being fivefold different between the individual species; it is always worthwhile to verify a given substance and the administration route in one of the popular issues of "Formulary, as the general doses defined as "for rodents" are no longer applicable.

The most frequently used anti-parasitic substances include fenbendazole (and related substances such as albendazole, flubendazole, oxibendazole), administered to treat the infestations of nematodes and *Giardia*; praziquantel is used in tapeworm infestations, whereas metronidazole stabilizes the protozoic part of the intestinal flora; and toltrazuril or trimethoprim-potentiated sulphonamides are administered in the treatment of coccidiosis.

In bacterial infections, broad-spectrum antibiotics (fluoroquinolones with enrofloxacin as the first choice, a combination of sulphonamides with trimethoprim) as well as doxycycline are used; the same protocol is applied for supportive antiparasitic treatment.

A problem occurs with the choice of supportive treatment. Many agents, available on the market, are indicated only for dogs and cats. A lot of probiotics is based on *Lactobacillus* bacteria that are rarely or even never found in rodents or lagomorphs, so the formulas containing these bacteria are useless. The products that work well include complex, multi-ingredient preparations containing not only varied bacterial species, but also prebiotics and electrolytes. However, the market offers more and more specialised products for small mammals, e.g. the products for rabbits containing such yeast species as *Saccharomyces* that are a part of their natural flora. Like in all animals, the owners should be educated that human medications from "the first aid kit" should never be administered. The agents that might slow down or inhibit the peristalsis should be avoided as they might lead to serious complications (in rabbits, cavies or chinchillas).

Pseudo-diarrhoeas

Apart from true diarrhoeas, the animals may be referred with the symptoms wrongly interpreted as diarrhoeas. The owners frequently mistake cecotropes for diarrhoea because their structure differs from the droppings. The animal usually eats cecotropes directly from the anal area (at night), so the owners may be unaware of them for a very long time, while cecotropes are considered pathological. Rabbits, cavies and chinchillas may also have very specific urine, which results from the diet. Sometimes the urine is very concentrated, even dark-brown in colour. When such urine is found in the cage and the animal has smudges on the perianal area, the situation may be linked to diarrhoea. The owners of rodents often try to make the diet more varied, adding semi-liquid mousses and fruit with vegetable purees. Such a diet may produce the faeces with softened consistency yet defecated in the normal volume and with regular frequency. It is important to educate the owners and work with them on how to improve the living conditions of the pets and to maintain the correct diet.

In conclusion, diarrhoea, irrespectively of its cause, should not be overlooked in small animals. Although diarrhoeas are only symptoms, they should be appropriately addressed with correct and detailed examination to prevent any harmful issues in the animal.

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The Effectiveness of Hepatiale Forte Advanced as hepatoprotective agent in dogs

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Abstract

Liver plays a vital role in various body processes, including the metabolism of carbohydrates, fats, and proteins, the detoxification of metabolites and xenobiotics, the storage of vitamins, trace metals, fat, glycogen, as well as immune regulation. Dietary supplementation of phospholipids could help support the management of selected hepatic diseases in dogs. Using a mix of s-adenosyl methionine, silymarin, zinc, soy phospholipids, and ornithine for dietary supplementation in dogs with liver and/or biliary disease for 8 weeks led to a statistically significant decrease in the activity of ALT, AST, and GGTP enzymes in the serum.

Key words: dog, cat, liver disease, dietary supplement, s-adenosyl methionine, silymarin.

Introduction

Liver plays a vital role in various body processes, including the metabolism of carbohydrates, fats, and proteins, the detoxification of metabolites and xenobiotics, the storage of vitamins, trace metals, fat, glycogen, as well as immune regulation. Liver disease is accompanied by a variety of clinical, physical symptoms and pathological lesions that reflect the damage to the organ. The liver, however, stands out for its incredibly large functional reserve. This means that organ-specific symptoms, including jaundice, hypoglycaemia, bleeding, hepatic encephalopathy and ascites, only set in after the reserve has been exceeded, i.e. usually in the later stages of the disease. Early symptoms, such as a recurrent loss of appetite, increased thirst, polyuria, vomiting, and fatigue tend to mimic those observed in other pathological conditions. Even though the initial presentation is usually non-specific, certain indications exist that allow us to suspect that the animal might be suffering from liver and/or biliary disease. One of these is breed; some dogs are predisposed to be born with or develop liver and biliary syndromes with a range of symptoms, such as gastrointestinal ulcers, hepatic encephalopathy, jaundice, coagulopathy, and ascites (20). For instance, the congenital portosystemic shunt that damages hepatocytes and bile ducts, for instance, tends to affect Irish wolfhounds, Yorkshire terriers, dachshunds, and Persian and Himalayan cats, and may often come accompanied by small vessel dysplasia. Depending on the stage of the disease and the volume of blood that bypasses the liver, more or less subtle clinical symptom tend to appear, leading all the way up to the liver failure (7). Congenital hepatic copper accumulation, which may result in cholangiohepatitis, is often diagnosed in Bedlington terriers, Dalmatians, and Siamese cats, while Dobermans, cocker spaniels, and poodles often suffer from idiopathic chronic hepatitis. Hepatic amyloidosis, on the other hand, typically affects Shar-Peis, Oriental and Abyssinian cats. A good reason to suspect liver and bile duct disease is the use of potentially hepatotoxic drugs, such as anaesthetics, anticonvulsants, or NSAIDs (4,7). Patients are also screened for suspected biliary disease, if they manifest symptoms of jaundice and an elevated liver enzyme activity that suggests cholestatic abnormalities. Extrahepatic bile duct obstruction, for instance, is often caused by bile duct cancers or acute pancreatitis. The latter, alongside inflammatory bowel disease (IBD), often leads to reactive hepatopathy (3,7). Increased liver enzyme activity may also be caused by certain endocrine disorders. According to Center, c. 85% of all cases of Cushing's syndrome are accompanied by an elevated activity of ALP and GGTP, and 50-80% with an increased activity of ALP (5). A similar increase in ALP an ALT is also observed in hypothyroidism, but it is mild and not always detected (3).

Elevated liver enzyme activity requires the intervention of a veterinary doctor; its cause must be determined by means of appropriate diagnostic procedures. If disorders of the liver and/or the bile ducts are detected, pharmacological and dietary treatment needs to be supplemented with hepatoprotective medication, designed as an adjunctive therapy, to prevent further damage to hepatocytes and stimulate their regeneration, both in terms of histological and anatomical structure and function. Adjunctive treatment may rely, for instance, on phospholipids, i.e. glycerol esters of choline phosphoric acid and unsaturated fatty acids (linoleic, linolenic, oleic), which show protective and regenerative effects on liver cells, where they are incorporated into cellular and cytoplasmic membranes and supplement disease-related deficiencies. This speeds up their regeneration and restores normal cell function. Phospholipids have also been found to inhibit liver fibrosis, lower the ratio of cholesterol/phospholipids, improve the solubility of cholesterol in bile, play an important role in the digestion of fats and the absorption of their vitamin content, enhance the transport of cholesterol from extrahepatic cells to the liver, activate lipolytic enzymes, and improve blood flow by reducing platelet adhesion and increasing erythrocyte elasticity. Importantly, they also show beneficial anti-sclerotic effects in human subjects by normalizing the level of molecules that contain cholesterol, proteins, and triglycerides (11). S-adenosyl methionine (SAM, SAMe) is a natural metabolite of all living cells and the precursor of cysteine, an amino acid that helps make glutathione, which plays an important role in preventing intoxication and reducing oxidative stress. SAMe protects cells against free radicals, showing combined hepatoprotective and antioxidant properties, and initiates all three metabolic pathways: membrane function, glutathione production, and cell regeneration and growth (18). Studies have shown that, alongside milk thistle extract, SAMe effectively protects against liver damage (14). Hepatoprotective supplements may also contain ornithine and zinc. The former has been shown to regulate the urea cycle in cats and dogs and take part in the conversion of ammonia into urea, thus reducing its toxicity, while in cats, it is implicated in energy generation. Zinc, on the other hand, forms part of many enzymes involved in the regulation of nucleic acid and carbohydrate transformations. It promotes wound healing, cell growth and reproduction. Zinc therapy inhibits fibrosis and protects the liver against copper accumulation in patients previously treated with chelating agents. Its oral administration induces the intestinal binding of copper with metallothionein. Dietary copper shows an affinity with the metallothionein found in erythrocytes, which prevents its transfer from the intestine to the blood system. After an intestinal cell dies and is peeled off into the digestive tract, metallothionein helps excrete leftover copper from the body (18). In human medicine, silymarin, the main component of milk this-

Table 1. Blood parameters in 8 dogs with suspected liver and/or biliary disease treated with Hepatiale Forte Advanced (VetExpert).

Patient number	Lkcs 10^9/l			Erys 10^{12}/l			HGB mmol/l			HCT 1/1			PLT 10^9/l			GRA 10^9/l		
	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks
1	8,9	8,2		6,9	7,2		8,2	8,7		0,45	0,46		317	363		6,3	6,8	
2	8,8	8,9		5,6	6,3		7,2	7,5		0,47	0,45		387	404		8,6	7,9	
3	13,1	9,3		6,1	6,4		8,9	8,4		0,49	0,44		335	348		9,4	8,5	
4	9,8	9,2		5,9	6,3		5,7	6,3		0,42	0,48		338	376		8,9	8,7	
5	7,7	8,2		5,9	6,5		7,7	8,4		0,49	0,48		353	335		11,2	9,6	
6	10,5	9,1		5,3	5,7		6,7	7,1		0,42	0,44		402	418		7,1	7,6	
7	8,6	8,6	8,4	8,1	7,8	8,6	7,0	7,2	7,1	0,50	0,49	0,49	287	302	328	8,4	7,8	8,0
8	9,1	8,8	9,0	6,6	7,2	7,5	7,9	7,8	7,7	0,48	0,51	0,46	312	354	376	6,4	6,5	6,3
Average	**9,6**	**8,8**		**6,3**	**6,7**		**7,4**	**7,7**		**0,47**	**0,47**		**341**	**362**		**8,3**	**7,9**	

tle (Silybum marianum), has been used in the treatment of liver disease for centuries. It is a strong antioxidant that stimulates the production of superoxide dismutase (SOD). Many studies point to its nearly life-saving properties in death cap and acetaminophen poisoning (20). In an experiment with dogs, patients poisoned with death cap and treated with silymarin showed reduced liver enzyme activity, shorter prothrombin time, and greater survival rates, while those in the placebo group all died (16). Silymarin reduces inflammation by inhibiting the activity of lipid oxidase and leukotriene synthesis. In cases of poisoning, it also shows strong cholagogic and gastroprotective effects.

With the above observations in mind, the present study aimed to determine the efficacy of a multi-ingredient hepatoprotective supplement in the treatment of dogs with liver disease. The study was conducted on patients whose condition had led to impaired bile flow or accumulation. Because liver disease therapy relies on many different drugs and a special diet, the present article only focused on cases treated with a dietary supplementation with S-adenosyl methionine.

Material and methods

The study examined the efficacy of Hepatiale Forte Advanced, a dietary supplement produced by VetExpert (Poland), based on soy lecithin as the source of soy phospholipids (rich in phosphatidylcholine), as well as on L-ornithine L-aspartate, S-adenosyl methionine, milk thistle extract, and zinc oxide. Dosage was calibrated to deliver 200 mg of S-adenosyl methionine per 10 kg of body mass and the supplement was administered once daily at a dose of one tablet per 10 kg of body mass. The experimental group included 8 dogs of different sex, age, and breed, all treated at the Veterinary Polyclinic of the University of Warmia and Mazury in Olsztyn. Patients were qualified for the trial based on their liver enzyme activity, confirmed by geriatric profiles and medical examination conducted under general anaesthesia; they were included in the study if their elevated GGTP activity suggested abnormal bile metabolism. In order to rule out other possible causes, such as acute or chronic pancreatitis, Cushing's syndrome, or the portosystemic shunt, all dogs were tested for their levels of pancreatic lipase (spec cPL (ldexx)), cortisol/creatinine in urine, and underwent the bile acid stimulation test. The supplement was administered to all dogs in the experimental group for 8 weeks at a dose specified above, either directly or mixed in with food, before or during meals. Because test results proved promising, in two patients, the treatment was prolonged to a total duration of 12 weeks. All animals were tested for blood cell parameters (white blood cells Lkcs, red blood cells, Erys, haematocrit number Ht, haemoglobin HB, platelets PLT, granulocytes GRA), and biochemical serum indicators (the activity of alanine aminotransferase ALT, aspartate transaminase AST, alkaline phosphatase ALP, gamma-glutamyl transferase GGTP, total protein TP, albumins ALB, and glucose GLU). Tests were performed on day 0, before the supplement was first administered, and then repeated after 8 and 12 (2 patients) weeks of therapy with Hepatiale Forte Advanced. At the same time, owners were requested to fill in a questionnaire concerning their perceptions of treatment results: possible side effects (vomiting, diarrhoea, constipation, sadness, increased/decreased thirst, appetite, oliguria/polyuria, itching, hypersalivation, jaundice), administration (tablet size and number, their tastiness, and how willingly they were swallowed), as well as remarks about their dogs' health.

Table 2. Biochemical parameters in 8 dogs with suspected liver and/or biliary disease treated with Hepatiale Forte Advanced (VetExpert)

Patient number	ALT IU/l			AST IU/l			ALP IU/l			GGTP IU/l			TP g/l			ALB g/l			GLU mmol/l		
	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks
1	170	42		114	19		213	52		27	6		65	61		38	39		5,7	5,4	
2	575	303		42	27		624	554		120	38		64	57		30	31		6,3	7,1	
3	334	115		213	98		431	156		77	21		58	62		29	31		6,2	6,4	
4	164	62		176	87		215	43		46	11		71	69		34	35		5,6	6,0	
5	225	164		87	35		24	35		15	9		70	71		38	36		5,2	5,8	
6	952	431		121	98		4859	1756		70	35		49	52		24	28		4,7	5,1	
7	98	49	42	85	47	48	229	76	56	17	9	5	71	69	70	35	37	35	4,9	5,0	4,9
8	1254	1047	868	136	111	98	1607	924	547	106	65	18	75	75	80	39	36	26	6,3	5,8	5,7
Average	**472**	**277**		**122**	**65**		**1025**	**450**		**60**	**24**		**65**	**65**		**33**	**34**		**5,6**	**5,8**	

During the trial, patients received full portions of their standard, regular feed, both wet and dry, and were provided with unlimited access to water. No other drugs were used at the same time and no prevention measures against infectious diseases and internal parasites, except ticks, were taken.

Keeping in mind the size of the experimental group, a statistical analysis of biochemical test results obtained on qualification day (Day 0) and in week 8 of the trial was performed. The size of the group (n=8) ensured a normal distribution of analysed variables and results were compared with the use of the Paired Samples T test (Prism 7; GraphPah Software).

Table 3. 201/5000
Results of statistical analysis of biochemical parameters in 8 dogs with suspected liver and bile duct diseases receiving as an adjunct preparation of Hepatiale Forte Advanced (VetExpert) by 8 weeks.

Parameter	Day 0	Day 8	Statistical significance	p value
ALT (IU/l)	471,5	276,6	YES	0,0089
AST (IU/l)	121,8	65,3	YES	0,0041
ALP (IU/l)	1025,0	449,5	NO	0,1621
GGTP (IU/l)	59,8	24,3	YES	0,0053
TP (g/l)	65,4	64,5	NO	0,5187
Alb (g/l)	33,4	34,1	NO	0,3776
GLU (mmol/l)	5,6	5,8	NO	0,2132

Results

No clinical side effects of the supplement were observed in any of the patients throughout the trial.

Likewise, no changes were found in terms of blood parameters obtained before ("0") and after treatment ("8" and "12"). The values of Lkcs, Erys, HBG, HCT, PLI, GRA all fell within the range of reference values. Before the trial, the mean level of leukocytes in the study group equalled 9.6 x 10^9/l (8.6 – 13.1 x 10^9/l), erythrocytes Erys stood at 6.3 x 10^{12}/l (5.3 – 8.1 x 10^{12}/l), haemoglobin HGB at 7.4 mmol/l (5.7 – 8.9 mmol/l), and haematocrit HCT at 0.47 1/1 (0.42 – 0.50 1/1). The mean level of platelets PLT and granulocytes GRA was 341 x 10^9/l (312 – 402 x 10^9/l) and 8.3 x 10^9/l (6.3 – 11.2 x 10^9/l), respectively (Table 1). As far as biochemical serum parameters are concerned, the mean activity of alanine aminotransferase ALT, aspartate transaminase AST, and alkaline phosphatase ALP equalled, respectively, 472 IU/l (98 – 1254 IU/l), 122 IU/l (42 – 176 IU/L), and 1025 IU/l (24 – 4859 IU/l). At a mean level of 60 IU/l (17 – 120 IU/l, the activity of gamma-glutamyl transferase GGTP was considerably elevated. To determine the generative function of the liver, we also tested the mean levels of total protein TP (65 g/l (58 – 75 g/l), albumins ALB (33 g/l (24 – 39 g/l)), and glucose GLU (5.6 mmol/l (4.7 – 6.3 mmol/l)) (Table 2). After 8 weeks of treatment with Hepatiale Forte Advanced, no major haematological changes were observed; the relevant figures were as follows: Lkcs 8.8 x 10^9/l (8.2 – 9.3 x 10^9/l), Erys 6.7 x 10^9/l (5.7 – 7.8 x 10^{12}/l), HGB 7,7 mmol/l (6.3 – 8.7 mmol/l), HCT 0.7 1/1 (0.44 – 0.51 1/1), and PLT 362 x 10^9/l (335 – 418 x 10^9/l) (Table 1). A significant drop, however, occurred in the activity of liver enzymes. ALT activity decreased by nearly 60% to a mean value of approximately 277 IU/l (42 – 1047 IU/l); AST dropped to 65 IU/l (19 – 111 IU/l) and ALP to 450 IU/l (35 – 1756 IU/l). GGTP activity likewise went down by 60% and equalled 24 IU/l (6 – 65 IU/l). Statistical analysis of biochemical parameters showed that the difference between day 0 and week 8 of the trial was statistically significant for ALT, AST, and GGTP (Table 3). The level of total protein, albumins, and glucose did not change significantly in comparison with test results obtained before the trial. The mean level of total protein TP equalled 65 g/l (52 – 75 g/l), albumins ALB 34 g/l (28 – 39 g/l), and glucose GLU 5.8 mmol/l (5.0 – 6.4 mmol/l) (Table 2). As mentioned before, because of the decreasing trend in liver enzyme activity, the treatment with Hepatiale Forte Advanced was extended for 4 more weeks, up to a total of 12 weeks, in two patients from the study group. A further decrease in the activity of liver enzymes was recorded after that period, while the level of total protein, albumins, and glucose remained unchanged. After 12 weeks of treatment with the hepatoprotective agent, the figures equaled: ALT 42 IU/l (down from 98 and 49 IU/l) and 868 U/l (down from 1254 and 1047 IU/l), AST – 48 IU/l (down from 85 and 47 IU/l) and 547 IU/l (down from 1607 and 924 IU/l), ALP – 56 IU/l (down from 229 and 76 IU/l) and 547 IU/l (down from 1607 and 924 IU/l). An important drop was also observed in the activity of GGTP: 5 IU/l (down from 17 and 9 IU/l) and 18 IU/l (down from 106 and 65 IU/l). The level of total protein equalled 70 and 80 g/l, albumins – 35 and 26 g/l, and glucose – 4.9 i 5.7 mmol/l (Table 2).

Owners who filled in the questionnaires reported that dogs willingly swallowed the supplement. No side effects or negative behavioural changes were observed. On the contrary, the animals became more cheerful, more active, and seemingly "rejuvenated".

Discussion

As previously mentioned, alongside medication and an appropriate dietary approach, a vital role in the treatment of liver disease is also played by hepatoprotection, i.e. a series of measures taken to protect healthy liver cells and restore the function of damaged hepatocytes. Hepatoprotective agents are usually composed of several components in different configurations, including substances that boost the function of liver cells (ornithine) or repair them (phospholipids) and multi-functional compounds that prevent liver inflammation or fibrosis (silymarin). Attempts to protect and boost liver function have been under taken for centuries. Before the advent of modern pharmacies, liver disease was usually treated with a variety of herbs and plant extracts. The curative properties of *Silybum marianum* were already known in Ancient Egypt. The Bible mentions the "Lebanese thistle", while Pliny the Elder reports that its juice and seeds were used to cure snake bites and melancholia, once believed to result from liver malfunction (9). Hepatoprotective drugs show a wide range of properties, which is why several substances with different mechanisms of action are often combined for therapeutic purposes. Falasca et al. studied the efficacy of a complex of silybin, vitamin E, and phospholipids in the treatment of hepatitis C in human subjects. The trial included 40 patients with hepatitis C; thirty were treated with a hepatoprotective complex and 10 served as the control group. The former received two doses of 94 mg of silybin and 30 mg of vitamin E every day for 3 months. Compared to the control group, a lasting and statistically significant decrease in the activity of ALT and AST was observed, accompanied by lower levels of CRP and pro-inflammatory interleukin IL-6; the level of anti-inflammatory interleukin IL-2, on the other hand, was found to be increased. In the same trial, a complex of silybin, vitamin E and phospholipids was used to treat 10 patients with fatty liver but without HCV and the treatment was shown to cause a statistically significant reduction in the activity of ALT, AST,GGTP, and ALP, as well as the levels of triglycerides, CRP, and IL-6 (8). Yang et al. reported a decrease in the RNA levels of the HCV virus in patients with hepatitis C treated with silymarin; at the same time, the treatment was well tolerated by all subjects (21). The beneficial effect of silymarin on the liver functions of patients with hepatitis C

has been confirmed in many other studies. Some authors even suggest that the dose of silymarin should be increased threefold to have a major impact on HCV replication (13). The efficacy of milk thistle extract in the treatment of drug-induced liver injury has also been tested. By restoring the activity of superoxide dismutase, silybin reduces liver damage in anti-tuberculosis drug-induced hepatotoxicity (12). Phospholipids also have an ability to protect the liver against the toxic impact of anti-tuberculosis medication, such as isoniazid. An experiment with isoniazid-induced liver damage showed that treatment with phospholipids helped reduce the level of bilirubin and TNF-α, lowered the activity of aminotransferases and ALP, and increased the levels of interleukin IL-10. Phospholipids were shown to boost ATP synthesis and, in conjunction with succinic acid, improved the kinetic profile of liver mitochondria (19). Silymarin may also prove effective in the treatment of liver damage caused by anti-epileptic drugs. In a study by Asgarshirazi et al., epileptic children received silymarin at a dose of 5 mg/kg/day for one month. Tests of liver enzyme activity were conducted immediately after the end of treatment and three months later. The activity of ALT, AST, and GGTP were significantly decreased. In some children, their normative levels persisted for as long as 3 months after the end of the trial (1). In another study, patients with chronic alcohol disease were treated with silymarin for 6 months; their ALT, AST and bilirubin parameters normalized, GGTP activity decreased, and the histological structure of their hepatocytes improved considerably (10). Similar minimizing effects on inflammation and degenerative lesions in alcohol-damaged liver were also observed after treatment with phospholipids, which translated directly into the clinical and laboratory status of studied patients (2). Silybin has also been shown to have possible anti-cancer effects. In vitro and in vivo studies are currently underway to examine its efficacy in skin, breast, lung, bladder, prostate, and kidney cancer (6). The anti-inflammatory, anti-fibrosis, and antioxidant effects of milk thistle extract are also tapped, as previously mentioned, in the treatment of non-alcoholic fatty liver disease. Liver plays a prominent role in the metabolism of fats and bile acid homeostasis. If the flow of fats from the liver to bile acids and the intestine is impaired, the accumulation of bile components in hepatocytes may induce profound changes in liver structure and function. Toxic fat in the liver will spark the inflammatory response and reactive fibrosis, which often leads to liver cirrhosis and other complications due to oxidative stress. Thanks to its anti-inflammatory and antioxidant properties, silymarin is a potential solution for preventing and counteracting these processes (15). The substance also reduces the production of inflammatory lipids during cholestasis, protects the mitochondria, prevents energy loss, reduces the production of hydrogen peroxide, and prevents the decrease in cardiolipin levels. Scientists currently recommend the use of silybin as a nutraceutical in the prevention of serious liver disease (17). According to Twedt, 31% of patients treated in liver clinics throughout the US receive hepatoprotective supplements, and milk thistle extract is the most frequently chosen substance. Silybin inhibits the peroxidation of fats in hepatocytes and microsomal membranes, and prevents gene damage by normalizing the formation of hydrogen peroxide, peroxide anions, and lipoxygenase. It also increases the levels of glutathione and slows down the accumulation of collagen. It has been suggested that its hepatoprotective effect relies on the inhibition of Kupffer cells, reducing the production of leukotriene B4 and binding hepatotoxins to the hepatocyte membrane receptor, which stabilizes the liver and prevents its damage by xenobiotics (18).

In the present trial with dogs with liver and/or biliary dysfunction, treatment with Hepatiale Forte Advanced gave results similar to those described above. Patient qualification criteria, which ruled out gastrointestinal diseases and endocrine disorders as the cause of elevated liver enzyme activity, allowed identifying a group of dogs with potential liver and/or biliary disease. The significant decrease in liver enzyme activity observed after hepatoprotective treatment may suggest that: 1) the elevated liver enzyme activity was originally caused by liver malfunction; 2) the use of Hepatiale Forte Advanced was well-targeted and effective; 3) no side effects were observed during treatment, and 4) it is worth considering possible benefits of long-term treatment with hepatoprotective supplements. The results of the trial indicate that using a mix of s-adenosyl methionine, silymarin, zinc, soy phospholipids, and ornithine for dietary supplementation in dogs with liver and/or biliary disease for 8 weeks led to a statistically significant decrease in the activity of ALT, AST, and GGTP enzymes in the serum.

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VetExpert preparations in supporting digestive tract disorders in dogs and cats

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Digestive tract disorders are one of the most common reasons for which dogs and cats are brought to veterinary clinics. However, the clinical symptoms, most frequently diarrhoea and/or vomiting, are non-specific and thus, it is impossible to determine whether the disorders are caused by feeding errors, illnesses of the organs responsible for producing digestive enzymes, absorption disorders or infectious agents (bacteria, viruses or other microorganisms). Appropriate therapy supporting patients with digestive tract symptoms is crucial to maintain the general level of health, because the bacteria and microorganisms living in the digestive tract play an important role in regulating the immunological processes in the body, which means that digestive tract disorders may very quickly affect the systemic immunity. The following short description of VetExpert preparations for supporting digestive tracts in dogs and cats may help select the right supplements for the individual patients.

DiarVet in supporting patients with acute diarrhoea

Dogs suffer from diarrhoea relatively often, which is caused by their natural eating behaviours and a possibility of eating food which can be spoiled. Obviously, gastrointestinal disorders are not the only reason of diarrhoea in pets, as clinical gastrointestinal symptoms might be brought about by viral or bacterial infections. However, in such cases, the therapy consists in antibacterial or antiviral treatment. Irrespectively of whether the diarrhoea is caused by a feeding error, eating inappropriate food, or an infectious agent, supporting the patient health is mostly based on inhibition fluid and electrolyte loss

from the organism and, potentially, providing the substances the animal has lost. Consequently, absorbent substances whose role is to bind water in the lumen of the digestive tract are relatively often used in supporting patients with diarrhoea.

DiarVet as a preparation with absorbent and supplementary properties

DiarVet preparation in the form of paste is designed for supporting dogs and cats with acute diarrhoea. It includes nutrients, absorbents and ingredients stabilising the digestive tract function.

The most important substances capable of binding water in the lumen of the digestive tract are montmorillonite and pectin. Montmorillonite is a mineral from the silicates group, classified as clay minerals (the smectites group). It is the basic component of bentonite which, similarly to other clays, has a capacity to absorb water and its volume increases considerably because water penetrates into the space between the layers of its molecules. Montmorillonite hydrous can increase its volume even several times. Apart from water-absorbing properties, it can also absorb some toxins present in the digestive tract, which is of high importance in the case of diarrhoea of a toxin origin. Pectin has similar water-complexing properties, although its mechanism of action is completely different from montmorillonite. Pectin, above all, has the gelling capacity so its action is mostly limited to eliminating excessive liquids from the lumen of the digestive tract.

Excreting excessive amounts of liquids through the gastrointestinal wall is one of the mechanisms behind diarrhoea, therefore tannins exert positive effects. Tannins are natural substances, phenol derivatives, which have astringent action on the intestinal mucosa. They cause coagulation (curdling) of proteins on mucosal surfaces, which results in the creation of a protective layer and is the basis of their anti-inflammatory properties in the case of skin inflammation and mucositis. The same mechanism is responsible for stopping minor bleeding and eliminating swelling. In diarrhoeal patients, tannins impede water penetrating the gastrointestinal wall, which significantly decreases fluidity (wateriness) of faecal mass in the large intestine.

Another ingredient of the paste – chicory, a source of inulin – is also active in the digestive tract. Inulin is a fructo-oligosaccharide and belongs to the prebiotic group, i.e. it is a substance capable of modifying the digestive tract microflora composition. Fructo-oligosaccharides are preferentially used by beneficial probiotic bacteria as a source of energy, but they are not used by harmful bacteria. Therefore, by increasing the supply of prebiotics in the lumen of the digestive tract, we support the growth of probiotic bacteria which, in turn, inhibit the growth of the bacteria potentially causing diarrhoea.

Additionally, DiarVet includes dextrose – a simple sugar which provides easily-released energy, necessary for the proper functioning of the organism; and zinc, which has the quality of reducing diarrhoea caused by microorganisms, although the anti-diarrhoea mechanism of zinc salts in animals is not known very well.

DiarVet is a product whose role is to support acute diarrhoea therapy, designed to be applied for a period of a few days. The substances included in it are intended to reduce the excretion of fluids into the lumen of the digestive tract and bond fluids which have already penetrated into the digestive tract. Consequently, faecal masses are less hydrated and they decrease in volume. DiarVet also stabilises the digestive tract microflora, which is to facilitate the digestion of nutrients introduced into the digestive tract after diarrhoea has been successfully treated.

BioProtect as a product supporting the functioning of microflora in canine and feline digestive tracts.

Every disfunction of the proper functioning of the digestive tract, irrespectively of whether it is caused by maldigestion or inadequate absorption, poisoning, feeding errors, or an illness brought about by pathogenic micro-organisms, always leads to disorders in intestinal microflora composition. For several years, the digestive tract microflora has been a subject of extraordinarily intensive scientific research, which have led among others, to introduction of the term *microbiota* (from the Greek 'bios' meaning 'life'). Among all the micro-organisms living in the digestive tract, bacteria constitute the largest group, although fungi, protozoa, and other micro-organisms are also present. Between the microbiome inhabiting the digestive tract and the host's organism – human's or animal's – exist mutual dependencies determining the host's health condition and immunity.

Micro-organisms are present throughout the entire length of animal digestive tract, from the mouth to the colon. Their amount and dominating species differ in every section of the digestive tract. In dog's small intestine, their estimated number is 10^2 to 10^5 colony-forming units (CFU)/g. The rule is that the number of micro-organisms increases gradually in consecutive sections and in dog's colon it amounts to 10^8 to 10^{11} CFU/g. However, in clinical practice not the number of micro-organisms in individual digestive tract section is of basic importance, but rather their mutual relationships and stability. In the small intestine there are aerobic and facultative anaerobic bacteria; on the other hand, in the large intestine there are almost exclusively anaerobic bacteria.

Probiotics – key bacteria for maintaining the proper function of the digestive tract

Normalisation of changes in the composition of the digestive tract microflora, which take place after any disturbances in the digestive tract functioning, is the basis for an animal's prompt recovery. Restoring the balance between harmful (pathogenic) and beneficial bacteria is crucial in proper digestion and absorption of nutrients for the small and large intestine. Due to the fact that in most digestive tract disorders harmful bacteria gain an advantage, the basis for treating digestive tract diseases should be the application of bacteria manifesting beneficial effects, classified as probiotic bacteria (probiotics). There are a few definitions of probiotics, the most popular one says that probiotics are live (and killed) micro-organisms (and products of their metabolism) added to human or animal food and intended to change the composition of the recipient's microflora so that it

would be beneficial for their health and/or productivity. Another definition says that probiotics are food supplements including live micro-organisms which positively influence the host's organism through improving intestinal microflora balance. Such bacteria bring a number of benefits:

- they stimulate the production of short-chain fatty acids (acetic and lactic) which:
  - ▹ are an additional source of energy for the colon epithelial cells,
  - ▹ facilitate ion absorption, which decreases the risk of diarrhoea,
  - ▹ stimulate ileum emptying of various substrates and inhibit colon contractions;
- they regulate lipid and cholesterol metabolism;
- lower pH in the intestines;
- produce final metabolites which directly inhibit pathogenic bacteria;
- at least *in vitro*, they block the adherence of pathogenic bacteria to intestinal cells;
- they decrease the amount of ammonia and urea in blood.
- produce group B vitamins

Through those mechanisms of action, probiotics reduce animal's susceptibility to the effects of stressors, they speed up animals' growth, increase feed conversion, raise appetite, improve the animal's general condition, and strengthen the immune system.

Bioprotect – universal and effective probiotic

The results of research confirming beneficial influence of probiotic bacteria in functioning of the digestive tract have brought about new strategies for using them in treating digestive tract diseases in humans and animals. One of such strategies is administration of preparations including probiotics in the form of products with such an amount of live and well-defined micro-organisms that they change the composition of microflora in the digestive tracts through colonization and, thanks to that, they positively influence the host's health. Additionally, those bacteria are highly antagonistic towards pathogenic micro-organisms, such as *Salmonella, Shigella sp., Escherichia coli* or *Clostridium sp.*. The minimum number of live bacteria necessary to obtain a probiotic effect is, according to various sources, from 10^6 to 10^9 live cells a day, to 10^9 to 10^{11} bacteria. Only several bacterial strains of *Lactobacillus, Enterococcus* and Bifidobacterium species have documented probiotic properties. Particularly beneficial impact of *Actinobacillus acidophilus, Enterococcus feacium, Bifidobacterium longum* and *Lactobacillus rhamnosus* in dogs has been described in scientific literature, but only *Enterococcus faecium* and *Lactobacillus rhamnosus* have been authorized by the European Committee of the EU for the use in dogs. Therefore, BioProtect (VetExpert) preparation includes the latter two strains in the amount of 2,5 x 10^9 of colony-forming units (CFU)/g of the product. Moreover, the preparation has been supplemented with mannan oligosaccharides (MOS) and fructooligosaccharides (FOS), which are carbohydrates forming dietary fibre fraction.

Sometimes they are also called prebiotics. They are fermented by the beneficial microflora (i.e. probiotic bacteria) of the digestive tract, mostly in the large intestine, to short-chain fatty acids which are the main source of energy for the cells in the large intestine – colonocytes. FOS and MOS may increase the number of *Lactobacillus* and *Bifidobacterium bacteria* and decrease the amount of putrefactive compounds (phenols and indoles) in the large intestine. Prebiotics lower faeces pH, which in turn leads to the stimulation of beneficial bacteria growth in the digestive tract and, simultaneously, to the limitation of potentially harmful bacteria growth, such as *Clostridium perfringens*. They also modify the amount of microflora in the digestive tract and facilitate nutrient absorption. Importantly, MOS can stimulate local resistance of large intestine mucosa through increasing specific IgA antibodies

BioProtect – possibilities of use

BioProtect preparation includes both probiotics and prebiotics, therefore it can be called a synbiotic, i.e., a preparation which, includes probiotic bacteria as well as fermentable carbohydrates that are a 'source of food' for these bacteria. Therefore, it is a complex preparation supporting the digestive tract functioning, and especially, the large intestine in dogs. Both probiotics and prebiotics are widely used in feed and diets for dogs, mostly in chronic or recurrent diarrhoea. Yet, it is not their only indication. One of the most harmful side-effects of oral antibiotic therapy is impairment of the beneficial intestinal microflora – e.g., clindamycin may lead to excessive growth of *Clostridum sp.* bacteria consequently resulting in development of pseudomembranous colitis. Therefore, in human medicine, a standard procedure is to administer a preparation including probiotic bacteria (*Lactobacillus, Bifidibacterium*) when oral antibiotic therapy is used. These bacteria act protectively and prevent excessive growth of harmful bacteria in the digestive tract. There is still no such standard in veterinary medicine, and yet, the canine digestive tract is very similar to the human digestive tract. Therefore, it should be emphasised that each oral antibiotic therapy in dogs ought to be accompanied by simultaneous administering of probiotic dedicated for dogs and ensuring regulation of intestinal microflora functioning.

Increasing the population of probiotic bacteria in the intestine improves the absorption of nutrients by the animal's organism, so the effects of probiotics include not only prevention and recovery from diarrhoea, but also improvement of digestion and food absorption, which supports faster recovery from an illness.

Another possibility for using BioProtect preparation is administering it to growing animals in order to stimulate the production of the correct digestive tract microflora. This concerns especially orphaned puppies which, due to the lack of contact with mother and being fed with milk replacer, have limited possibilities to develop beneficial bacteria strains in their digestive tracts.

All in all, BioProtect includes probiotic bacteria strains and prebiotics with proven positive effects in dogs and it is an especially effective solution to any disorders causing unfavourable changes in the composition of the digestive tract microflora in dogs.

Possibilities for applying TriDigest (VetExpert) preparation in clinical practice of digestion disorders treatment in dogs

Nutrients digestion disorders are a serious problem not only for an animal but also for its owner. In most cases, they are manifested by chronic profuse diarrhoea from the small intestine and they lead to a gradual weight loss of the ill animals. In most cases, the set of clinical symptoms called maldigestion is caused by the impairment of organs responsible for the production of digestive enzymes, thus mainly the pancreas, but also the stomach and the liver. In the case of the so-called digestive juices production impairment and an insufficient supply of digestive enzymes, full digestion of nutrients does not take place in the stomach or the intestines, which leads to the development of osmotic diarrhoea characterised by a considerable volume of excreted soft faeces.

Contemporary medicine does not have any pharmacological substances capable of stimulating natural secretion of gastric acid, bile, or pancreatic juice. This results from the fact that in healthy organisms the very presence of food and individual nutrients in the digestive tract is the factor which most effectively stimulates the secretion of digestive enzymes. Food components have, the ability to stimulate the stomach to produce gastric acid, the liver – to produce bile, and the pancreas – to produce pancreatic juice. In clinical practice, preparations that are most often used are those that stimulate bile secretion and preparations containing pancreatic enzymes which can support digestion in the digestive tract. The latter, however, have a limited capability for digesting protein products, therefore their effectiveness may be limited. From the physiological point of view, it is of key importance to stimulate natural processes leading to the secretion of gastric acid, bile, and pancreatic juice. Thus, it is worth administering TriDigest – the first supplement including substances stimulating the secretion of gastric acid, bile, and pancreatic juice – to patients with digestive disorders.

TriDigest – bases of action

The aim of using TriDigest preparation in patients with nutrients digestion disorders is to stimulate the secretion of natural digestive juices, to prevent diarrhoea, and to improve the quality of life, concerning also their owners. The mechanism of action of this preparation is based on the described effects of its each component:

1. Betaine is a trimethyl derivative of glycerol amino acid. It is accessible to buy as a food supplement after isolating it from sugar beets. It is a substance with strong osmotic qualities, therefore it stimulates the growth and the activity of digestive tract cells, which potentially improves digestibility of nutrients (Eklund et al., 2005). Applied in the form of betaine hydrochloride, it is capable of stimulating the secretion of gastric acid in the stomach, which can improve digestion, especially of protein substances. This is due to the fact that betaine hydrochloride can lower the pH of stomach contents, which facilitates protein food denaturation and increases the efficiency of protein digestion by pancreatic enzymes (Yago et al., 2013).
2. Liquorice (Glycyrrhiza glabra) has been known for many years for its healing qualities. Liquorice extract has antiseptic, antibacterial and antiviral, as well as secretory and hepatoprotective properties (Yu et al., 2015). Active substances in the extract include glycyrrhizin, liquiritin, galbradin and liquiritigenin. It is recommended among other in gastric ulcers and dyspeptic disorders treatment. Conducted research shows that application of liquorice root extract stimulates the secretion of endogenous secretin which, in turn, stimulates the secretion of bicarbonates and, consequently, increases the amount of pancreatic juice, which facilitates digestion in the intestines (Shiratori et al., 1986). This effect may arise from the fact that active substances in liquorice stimulate the production of mucus through increasing the amount of prostaglandins in the digestive tract wall (Bone and Millis, 2013).
3. Artichoke (*Cynara scolymus L*) has been used for many years in treating liver diseases and stomach secretion disorders. At least some of its qualities arise from antioxidant activities of artichoke extracts or their components, mainly flavones, flavanones, flavonols, coumarins and phenolic acids. Additionally, artichoke extract increases bile secretion, increases the content of bile acid in bile and stimulates its flow through the bile ducts. This therapeutic activity is connected with the presence of mono- and dicaffeoylquinic acids in the extract. The extract includes luteolin and cynarine, which have strong hepatoprotective properties, they also stabilise cholesterol and fatty acids metabolism in the liver (Speroni et al., 2003).

In addition, the preparation includes phospholipids and ornithine which have beneficial effects on the liver. Phospholipids protect and regenerate liver cells, they increase the regeneration of damaged hepatocytes and are indispensable in the process of liver cell differentiation and proliferation. Ornithine, on the other hand, is recommended in order to support the proper liver function through the regulation of the urea cycle. It is particularly important for cats, as it decreases ammonia toxicity, and is therefore especially recommended for cats suffering from or suspected of hepatic encephalopathy.

TriDigest – basic recommendations

- Disorders in gastric acid, bile, and pancreatic juice secretion
- Disorders in protein, fat, and carbohydrates digestion
- As an auxiliary, together with digestive enzymes preparations, in exocrine pancreatic insufficiency.

TriDigest – Summary

TriDigest preparation is the first complementary feed on the market, which supports the secretion of digestive juices produced by the canine digestive tract. It's components naturally stimulate the secretion of gastric acid (betaine), bile (artichoke) and pancreatic juice (liquorice). They also act protectively on liver cells (phospholipids and ornithine).

Digestibility trial report no. 3/2015 for Intestinal NEW Dog, a dry veterinary feed for adult dogs with gastrointestinal disorders

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The digestibility trial was performed in accordance with the guidelines published by FEDIAF (Nutritional Guidelines 2013) and included 6 adult dogs aged 2-6 years (3 males, 3 females), of different breeds (4 beagles, 1 fox terrier, 1 Labrador), and body mass between 10 and 30 kg.

The report is divided into 3 sections dealing, respectively, with product intake, faeces quality, and the nutritional value and digestibility level of individual feed components.

I. Assessment of product intake and changes in body mass

Intake:

Intestinal NEW Dog was administered at doses calculated in accordance with the accepted daily energy requirement for dogs (appendix no. 1). The mean intake of the feed equalled 286.67 g/day/dog, i.e. 100% of the total food intake in the study group, which should be considered a very good result. The dogs eagerly consumed their entire daily portions, which made it possible to establish the individual intake rate at 100% as well.

Body mass during the trial:

The mean difference in the body mass of tested dogs on the first and the last day of the trial equalled: -0.2% ±5.0 (-30.6g/day±174.9).

An increase of 4.2 to 6.8% was observed for two dogs, a beagle and a fox terrier; the Labrador retriever and two beagles each lost -6.7 to -1.7% of their body mass over the duration of the trial. This was probably due to the underestimation of their actual energy requirements rather than the low calorie content of the feed. The body mass of one beagle remained unchanged over time.

II. Faeces quality during the digestibility trial

During the trial (7 days), faeces were assessed and scored on a point scale (appendix no. 2) on a daily basis. The samples were judged to be 100% acceptable and of proper quality (hard, well-formed); 7.81% were ideal (1.5-2.5 pts) (table 3). Throughout the trial, not a single case of unacceptable faeces (> 3.5 points) was recorded (table 4).

Table 1. Amount of feed administered and consumed and the % of intake during the test

Dog no.	1	2	3	4	5	6	Average
administered dose (g/day)	400.00	320.00	300.00	300.00	200.00	200.00	286.67
consumed dose (g/day)	400.00	320.00	300.00	300.00	200.00	200.00	286.67
% of intake	100.00	100.00	100.00	100.00	100.00	100.00	100.00

Table 2. Changes in body mass during the trial.

Dog no.	Body mass (kg) on day 1	Body mass (kg) on day 7	Change in body mass %	Change in body mass g/day
1	30	28	-6.7	-333.3
2	14	14.95	6.8	158.3
3	15.5	15.5	0.0	0.0
4	16.5	17.2	4.2	116.7
5	13	12.5	-3.8	-83.3
6	15	14.75	-1.7	-41.7
mean	17.3	17.2	-0.2	-30.6
SD	6.3	5.5	5.0	174.9
SE	2.6	2.3	2.0	71.4

Table 3. Faeces quality in tested dogs

No.	Tested parameter	Value
1	Total number of defecations	64
2	% of normal defecations, including the % of ideal defecations (1.5-2.5 points)	100% including: 7.81% of ideal quality
3	% of abnormal defecations, i.e. > 3.5 pts	0
4	Mean faeces quality	2.90

The defecation rate decreased (64) in comparison with that observed on the Premium diet, which also suggests that the feed is highly digestible.

The mean score for all samples collected in the study group equalled 2.90 points, i.e. fell within the range of acceptable faeces of normal quality.

Table 4. Individual assessment of faeces quality and number of defecations in the study group

	Number of defecations	Point score for faeces quality																Average
No.		1	1.25	1.5	2	2.25	2.5	2.75	3	3.25	3.5	3.75	4	4.25	4.5	4.75	5	
1.-LR	11							1	8		2							3.07
2.-F	11							4	5		2							3.00
3.-B	10							5	5									2.88
4.-B	11						1	5	5									2.84
5.-B	14						3	7	4									2.77
6-B	7						1	3	3									2.82
Suma	64	0	0	0	0	0	5	25	30	0	4	0	0	0	0	0	0	
													Mean point score					2.90

(LR- Labrador retriever; F-fox terrier, B-beagle)

Table 5. Nutritional content per 100 g of the feed, % of dry matter (% DM), and the % of metabolic energy (% ME), compared to values recommended for "intestinal" diets by Hand et al. (2010) and Saker (2010)

Nutrient/ component	Unit	Content in g/100g of final product	% of dry mass	% metabolic energy	Values recommended for intestinal diets, listed as % DM (Hand et al. 2010)	Values recommended for intestinal diets, listed as % DM (Saker, 2010)
Protein	g	29.91	31.7	calculated	≤ 30	16-30; min. 18
Fat	g	8.24	8.72	32	Digestibility ≥ 87%	Digestibility ≥ 87%
Ash	g	8.66	9.17	21	12-15	10-15; min. 5
Fibre	g	3.09	3.27	47	Digestibility ≥ 90%	
Nitrogen-free extracts	g	44.53	47.16			1-2.5
Water	g	5.57			≤ 5	
Metabolic energy (ME)	kcal	341.1			Digestibility ≥ 90%	
Digestible energy (DE)	kcal	352.3				

Table 6. Digestibility of individual nutrients

Digestibility (%):	Mean	SE
Dry matter	82.7	2.39
Organic matter	86.2	1.99
Raw protein	86.4	1.90
Raw fat	94.2	1.17
Carbohydrates	87.6	1.90
Energy	95.3	0.79
Mean digestibility	89.4	1.66

III. Assessment of nutritional value and digestibility

A chemical analysis was performed to assess the level of essential nutrients in the feed and evaluate their digestibility, as well as to compare these figures to data found in relevant literature (Hand et al. 2010; Saker 2010) (table 5 and 6).

The protein content of the feed equalled 29.91%; when converted into the percentage of dry matter, i.e. 31.7% DM, the value proved slightly higher than the recommendations of the above two sources. However, the Producer specifies that the feed may also be used in the period of convalescence, as well as in the treatment of the malabsorption and maldigestion syndrome, when the body needs a greater supply of digestible protein of high biological quality. The fat content of the product was 8.24%, i.e. 8.72% DM, which is equal to the intake mentioned by Saker (2010). The Producer further specifies that the feed is recommended for dogs with exocrine pancreatic insufficiency. In such cases, the recommended fat content in the diet should not exceed 10% DM. The corresponding figure for fibre, on the other hand, equalled 3.09, i.e. 3.27% DM and stayed within the range recommended by Hand et al. (2010). Animals with pancreatic disorders should reduce their intake of raw fibre, which considerably improves the general digestibility of the diet. In summary, considering the indications for use specified by the Producer, i.e. gastrointestinal conditions (inflammation, malabsorption, maldigestion), convalescence, and pancreatic disorders (exocrine pancreatic insufficiency, chronic and acute pancreatitis), the nutritional value of the feed was deemed adequate.

Digestibility

The trial also involved an assessment of the digestibility of individual nutrients. The following results were obtained: very high for fats (94.2%±1.17) and energy (95.3%±0.79), and high for carbohydrates (87.6%±1,90) and proteins (86.4%±1.90) (table 6). The high digestibility of individual components also accounts for the high total digestibility of the feed, which equals 89.4±1.66. These results are better than the corresponding figures for the previously tested diet: Intestinal for Dog (Report no. 1/2015 of 31 March 2015).

An analysis of the digestibility of specific nutrients for individual dogs showed that 83% of animals easily digested fats (> 90%), 67% – carbohydrates (> 87%), and 50% – proteins (> 87%) (table 7).

Conclusions and recommendations:

1. When the Intestinal New Dog feed was used as the only source of food for adult dogs, the total intake equalled 100% of the daily dose.
2. The mean difference in body mass on the first and the last day of the experiment equalled: -0.2%±5.0
3. Faeces quality was assessed as acceptable in 100%, and ideal in 7.81%, of cases. The mean score equalled 2.9 pts.
4. The nutritional content was judged as adequate with respect to the typical values recommended for "intestinal diets".
5. The general digestibility of the feed (89.4), seems optimal for this type of diet.

Table 7. Digestibility of fats, proteins, and carbohydrates in individual dogs.

No.	Breed	Fat digestibility	Protein digestibility	Carbohydrate digestibility
1	Labrador retriever	97.1	91.5	91.5
2	Fox terrier	94.9	85.1	89.0
3	Beagle	93.8	87.1	90.0
4	Beagle	95.4	89.6	90.0
5	Beagle	88.8	78.0	78.8
6	Beagle	95.4	86.3	86.2

Effectiveness of Hepatiale Forte supplements in the treatment of liver disease in dogs

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Abstract

Liver is the largest and one of the most important organs in the body. Oxidative damage to the cellular membranes of hepatocytes causes the loss of phospholipids that serve as their main building blocks. Dietary supplementation of phospholipids could help support the management of selected hepatic conditions in dogs. An eight-week treatment with a mixture of phospholipids and ornithine in dogs with liver disease without any co-morbidities resulted in a statistically significant decrease in the levels of AST, ALT and ALP enzymes.

Key words: dog, cat, liver disease, dietary supplement, phospholipids

Introduction

Liver is the largest gland and the most important metabolic organ, responsible for more than 2000 different functions in the body. Highly vascularized, couched between the gastrointestinal tract and the middle of the circulatory system, it synthesizes, detoxifies, transforms, accumulates, secretes, and produces many different chemical substances and compounds. With a weight of 125 to 1350 g, the liver represents 1.33-5.95% of total body mass. On average, it is said to account for c. 3.4 % of the body mass of an adult dog; in young animals, the proportion may be even greater (4, 5, 15).

Because of its strategic role and location, the liver is directly or indirectly involved in many metabolic processes and transformations taking place in the body and easily adapts to its changes. Its incredible functional reserve (c. 65%) and regenerative ability mean that clinical symptoms often appear when a massive damage to the organ has already occurred. The clinical presentation of liver disease is manifold and the symptoms do not always show up in the organ itself. The most frequent among them, including anorexia, vomiting, diarrhoea, constipation, and weight loss, manifest in the gastrointestinal tract. Mucous membranes may also be affected, leading to jaundice, paleness, and haemorrhage. Other possible signals of liver malfunction include increased thirst, polyuria, hypersalivation, fasciculations and neurological symptoms, ranging from mild sadness to loss of consciousness. As demonstrated by the list, the symptomatology of liver disease may be very diverse; from non-typical to, liver-specific symptoms, but very often the disease is completely asymptomatic. This is why it is frequently diagnosed by accident, e.g. during screening tests, planned geriatric profiles, or qualification for general anaesthesia (8, 15). At the same time, the damage does not affect all hepatocytes, which is why many disorders have a subclinical presentation and recede without leaving any sequelae. Clinical symptoms occur only in very serious and/or extensive liver damage. It is important to bear in mind, however, that the degree of damage does not need to be proportional to the intensity of clinical presentation (6, 7, 15).

The patomechanism of liver cell degeneration and/or death has not been entirely explained. Possible causes of hepatocyte damage include ischemia and hypoxia, free radicals and oxidative stress, shortage or lack of intracellular elements or co-factors, intracellular toxins and their incorporation

Table 1. Blood parameters in 8 dogs with liver disease without any co-morbidities treated with Hepatiale Forte (VetExpert) as adjunctive therapy.

	Lkcs 10^9/l			Erys 10^{12}/l			HGB mmol/l			HCT 1/1			PLT 10^9/l			GRA 10^9/l		
	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks
1	10.9	10.2		8.1	8.2		10.2	9.7		0.47	0.45		303	353		7.8	6.9	
2	9.8	8.9		5.9	6.3		8.5	8.4		0.42	0.45		416	420		6.6	7.1	
3	11.1	10.3		6.4	6.8		9.9	9.9		0.45	0.43		398	385		8.5	8.1	
4	19.8	14.2		7.1	7.3		6.7	7.1		0.51	0.50		382	338		9.1	8.9	
5	9.7	9.2	9.0	6.9	6.3	6.1	9.8	8.9	9.9	0.49	0.48	0.45	215	305	330	8.4	7.7	7.1
6	6.5	7.1	6.9	5.3	5.8	5.8	7.1	7.5	7.4	0.38	0.41	0.42	431	464	410	8.0	7.9	8.6
7	9.8	8.8	9.5	9.1	8.8	6.6	7.0	6.9	8.1	0.54	0.53	0.49	345	398	380	7.4	6.9	9.1
8	10.2	9.8	13.9	8.4	8.1	7.1	6.9	7.1	7.1	0.49	0.50	0.43	412	398	405	6.2	7.5	8.0
x	**10.9**	**9.8**	**9.8**	**7.2**	**7.2**	**6.4**	**8.3**	**8.2**	**8.1**	**0.47**	**0.47**	**0.45**	**366**	**383**	**307**	**7.7**	**7.6**	**8.2**

Table 2. Biochemical parameters in 8 dogs with liver disease without any co-morbidities treated with Hepatiale Forte (VetExpert) as adjunctive therapy.

	ALT IU/l			AST IU/l			ALP IU/l			GGTP IU/l			TP g/l			ALB g/l			GLU mmol/l		
	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks	0 wks	8 wks	12 wks
1	184	119		73	46		355	262		4	4		70	66		32	37		7.6	6.3	
2	185	439		82	64		3498	2657		14	7		69	71		36	35		6.4	6.1	
3	486	187		112	73		654	252		8	6		70	68		38	36		5.9	5.1	
4	569	249		95	53		1537	879		39	28		61	70		40	33		6.8	5.5	
5	136	82	61	87	25	22	786	561	379	3	3	3	64	57	60	30	33	33	5.2	5.6	5.1
6	284	164	130	62	32	30	538	401	315	7	6	6	77	67	70	36	36	37	6.4	6.2	5.0
7	192	171	128	82	26	24	1014	877	370	3	3	3	67	68	62	34	38	40	5.6	5.2	5.2
8	165	109	85	75	25	24	768	568	475	5	3	4	72	66	67	32	34	34	4.9	5.2	5.0
x	**361**	**190**	**101**	**84**	**43**	**25**	**1144**	**807**	**384**	**11**	**8**	**4**	**69**	**67**	**65**	**35**	**35**	**36**	**6.1**	**5.7**	**5.1**

into protein structures, DNA and RNA, cholestasis and, last but not least, the activity of endotoxins produced by bacteria, viruses, parasites, and other immune factors (5, 6, 7). In discussions of metabolic liver disorders, particular attention has been drawn to the oxidative damage sustained by cellular membranes and the associated loss of phospholipids, their chief building blocks. Under an assault free radicals, oxidative stress damages lipids in cellular membranes (5, 10); these undergo intensified peroxidation and further increase oxidative stress in hepatocytes, finally leading to their necrosis. Damaged liver cells then release the oxidized lipids, which induce inflammation and damage hepatic veins. In turn, chronic inflammation causes an excessive synthesis of the tumour necrosis factor (TNF – α) and certain interleukins, particularly IL-1 and IL-6, and often leads to fatty liver disease and liver fibrosis (12). Thus far, the best documented cause of liver necrosis has been linked to extensive damage of the cellular membranes of hepatocytes. This is why phospholipids, their main building blocks, are often used to repair liver damage and supplement associated deficiencies to regenerate and/or strengthen liver cells. The first such substance to be studied was phosphatidylcholine, tested in patients with active chronic hepatitis and alcohol-induced necrosis (6). Phospholipids are esters of choline-phosphoric acid and unsaturated fatty acids; they cannot be synthesized by the body because of the poly-unsaturated fatty acids in their side chains. They become part of cellular and cytoplasmic membranes, which allows them to supplement disease-related deficiencies in the liver. This promotes faster regeneration and restores the function of damaged hepatocytes, causing considerable improvement in the activity of membrane receptors, enzymatic systems active in cytoplasmic membranes, as well as the processes of active and passive transport. Phospholipids are also essential during the differentiation and proliferation of liver cells. They inhibit the fibrosis of liver tissue by reducing the production of collagen and boosting the activity of collagenase. They also play an important role in fat digestion and vitamin absorption (6, 12, 13).

Bearing in mind the vital importance of phospholipids for liver cell function, the present study proposed to examine whether their supplementation may support the treatment of selected liver conditions in dogs. Liver disease is frequent in the species, and, as mentioned above, may be signalled by little more than elevated liver enzyme activity. Because its treatment relies on many different drugs, the present study focused on cases treated exclusively with Hepatiale Forte, a dietary supplement based on phospholipids.

Material and methods

The trial assessed the efficacy of Hepatiale Forte, Hepatiale Forte Large Breed (+25 kg), and Hepatiale Forte Small breed & cats produced by VetExpert, which contained, respectively, 150, 275, and 85 mg of soy phospholipids (phosphatidylcholine) and 150, 275, and 85 mg of ornithine in the form of L-ornithine L-aspartate. The supplement was administered once per day at a dose recommended by the producer, i.e. 1 tablet/15 kg of body mass (Hepatiale Forte), 1 tablet/25 kg of body mass (Hepatiale Forte Large Breed), and 1 capsule/5 kg of body mass (small dogs) and 1 capsule/cat (Hepa-

tiale Forte Small breed & cats). Tablets were crushed and mixed in with food; Twist Off capsules were opened and emptied into wet feed. The study group included 12 dogs of different age, sex, and breed, all treated at the Veterinary Polyclinic of the Faculty of Veterinary Medicine at the University of Warmia and Mazury in Olsztyn. The common trait of eight patients qualified for the trial was older age, ranging from 10 to 13 years. The four younger dogs in the group (4-6 years old) were Yorkshire terriers. Patients were qualified for the trial based on their elevated liver enzyme activity, confirmed by geriatric profiles and medical exams conducted under general anaesthesia. In order to rule out other possible causes, such as acute or chronic pancreatitis, Cushing's syndrome, or the portosystemic shunt, all dogs were tested for their levels of pancreatic lipase (spec cPL (ldexx)), cortisol/creatinine in urine, and underwent the bile acid stimulation test. In the end, eight patients with normal pancreatic test results and normal cortisol/creatinine ratio in urine were selected for the trial. The study group also included four patients with suspected portosystemic shunt, with a view to testing the effects of phospholipids on secondary liver conditions induced by vascular disease. In all patients, elevated liver enzymes activity was confirmed through screening tests, geriatric profiles, and exams conducted under general anesthesia. None showed any clinical symptoms. One dog from the group with vascular liver disorders was reported to become sad and apathetic after meals, which was the original reason for seeking medical attention. Hepatiale Forte supplements were administered for 8 weeks at a previously specified dose, in accordance with producer guidelines. Because of promising test results, treatment was extended until 12 weeks in four patients.

Blood parameters (white blood cells Lkcs, red blood cells Erys, hematocrit Ht, hemoglobin HB, platelets PLT, granulocytes GRA) and biochemical serum indicators (the activity of alanine aminotransferase ALT, aspartate transaminase AST, alkaline phosphatase ALP, gamma-glutamyltransferase GGTP, total protein TP, albumins ALB, and glucose GLU) were determined in all animals included in the study. Tests were performed on day 0, before the supplement was first administered, and then repeated after 8 (8 patients) and 12 (4 patients) weeks of treatment with Hepatiale Forte. At the same time, owners were requested to fill in a questionnaire concerning their perceptions of treatment results: possible side effects (vomiting, diarrhoea, constipation, sadness, increased/decreased thirst, appetite, oliguria/polyuria, itching, hypersalivation, jaundice), administration (tablet size and number, their tastiness, and how willingly they were swallowed), as well as remarks about their dogs' health.

Table 3. Blood parameters in 4 dogs with portosystemic shunt treated with Hepatiale Forte (VetExpert) as adjunctive therapy.

	Lkcs 10^9/l		Erys 10^{12}/l		HGB mmol/l		HCT 1/1		PLT 10^9/l		GRA 10^9/l	
	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks
1	5.7	6.2	7.3	6.9	9.3	8.9	0.48	0.46	287	305	9.4	8.6
2	11.0	10.5	6.7	6.5	9.5	9.5	0.50	0.48	238	298	7.1	6.9
3	8.6	9.0	6.8	6.5	9.3	9.2	0.48	0.46	324	385	6.8	7.6
4	17.3	12.6	5.0	5.2	9.87	10	0.48	0.47	380	361	7.8	7.2
x	**10.7**	**9.6**	**6.5**	**6.3**	**9.5**	**9.4**	**0.49**	**0.47**	**307**	**337**	**7.8**	**7.6**

Table 4. Biochemical parameters in 4 dogs with portosystemic shunt treated with Hepatiale Forte (VetExpert) as adjunctive therapy.

	ALT IU/l		AST IU/l		ALP IU/l		GGTP IU/l		TP g/l		ALB g/l		GLU mmol/l	
	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks
1	119	19	98	27	190	62	5	4	58	67	40	32	5.9	6.1
2	411	214	143	92	213	126	6	5	59	62	22	27	4.7	5.2
3	613	302	115	87	246	121	7	7	62	61	23	22	5.2	5.3
4	367	126	98	43	321	113	7	6	69	70	28	27	5.9	5.6
x	**378**	**166**	**114**	**62**	**243**	**106**	**6**	**6**	**62**	**65**	**28**	**27**	**5.4**	**5.6**

The principal subjects were dogs, but two cats with elevated liver enzyme activity were also qualified for the study. One showed gastrointestinal symptoms, such as appetite loss, vomiting, diarrhoea; the other tested positive for elevated enzyme activity during a routine geriatric profile.

During the trial, patients received full portions of their standard, regular feed, both wet and dry, and were provided with unlimited access to water. No other drugs were used at the same time and no prevention measures against infectious diseases and internal parasites, except ticks, were taken.

Bearing in mind the size of individual patient groups, a statistical analysis of biochemical test results obtained on qualification day (Day 0) and in week 8 of the trial was only performed for dogs without any co-morbidities. The size of the group (n=8) ensured a normal distribution of analysed variables and results were compared with the use of the Paired Samples T test (Prism 7; GraphPah Software).

Results

No clinical side effects of the supplement were observed in any of the patients throughout the trial.

Likewise, no changes were found in terms of blood parameters measured before ("0") and after treatment ("8" and "12"). The values of Lkcs, Erys, HBG, HCT, PLI, GRA all fell within the range of reference values. Before the trial, the mean number of leukocytes Lkcs in the group of 8 dogs (without vascular liver conditions) equalled 10.9 x 10^9/l (6.5 - 19.8 x 10^9/l), erythrocytes Erys – 7.2 x 10^{12}/l (5.3 - 9.1 x 10^{12}/l), haemoglobin HGB – 8.3 mmol/l (6.7 - 10.2 mmol/l), and haematocrit HCT – 0.47 1/1 (0.38 - 0.55 1/1). The mean level of platelets PLT and granulocytes GRA was 366 x 10^9/l (303 - 431 x 10^9/l) and 7.7 x 10^9/l (6.2 - 9.1 x 10^9/l), respectively (Table 1). In the four dogs with portosystemic shunt, white and red blood cell parameters also fell within the normal range. The mean level of leukocytes Lkcs stood at 10.7 x 10^9/l (5.7 - 17.3 x 10^9/l), erythrocytes – 6.5 x 10^{12}/l (5.0 - 7.3 x 10^{12}/l), haemoglobin HGB – 9.5 mmol/l (9.3 - 9.9 mmol/l), and haematocrit HCT – 0.49 1/1 (0.48 - 0.50 1/1). Platelets PLT hovered between 238 - 380 x 10^9/l (x – 307 x 10^9/l) and granulocytes GRA between 6.8 - 9.4 x 10^9/l (x – 7.8 x 10^9/l) (Table 3). In cats, the number of leukocytes and red blood cell parameters also fell within the range of reference values and equalled, respectively: Lkcs – 11.1 and 13.2 x 10^9/l, Erys – 7.2 and 8.3 x 1012/l, HGB – 10.2 and 10.3 mmol/l, HCT – 0.55 and 0.55 1/1. Platelets PLT – 455 and 493 x - 10^9/l, granulocytes GRA – 9.8 i 8.3 x 10^9/l (Table 5). To determine the generative function of the liver, we also tested the mean levels of total protein (69 g/l (61 - 77 g/l)), albumins ALB (35 g/l (32 - 40 g/l)), and glucose GLU (6.1 mmol/l (5.2 - 7.6 mmol/l)) (Table 2). In 4 Yorkshire terrier with suspected vascular liver disease, the corresponding parameters were as follows: ALT – 378 IU/l (119 - 613 IU/l), AST – 114 IU/l (98 - 143 IU/l), ALP - 243 IU/l (190 - 321 IU/l), and GGTP - 6 IU/l (5 - 7 IU/l).

The levels of total protein, albumins, and glucose stood at, respectively: TP – 62g/l (58 - 69 g/l), ALB – 28,3 g/l (22 - 40 g/l), GLU – 5.4 mmol/l (4.7 - 5.2 mmol/l) (Table 4). In the 2 cats qualified for the trial, the mean activity of liver enzymes equalled: ALT – 403 and 512 IU/l, AST – 168 and 276 IU/l, ALP – 34 and 135 IU/l, GGTP – 3 and 6 IU/l. The mean levels of total protein, albumins, and glucose were as follows: TP – 72 and 70 g/l, ALB – 30 and 31 g/l, GLU – 6.8 and 7.9 mmol/l (Table 6). After 8 weeks of treatment with Hepatiale Forte, Hepatiale Forte Large Breed (+25 kg), and Hepatiale Forte Small breed & cats, no major haematological changes were observed in any of the studied subgroups. Among the eight dogs, the parameters were as follows: Lkcs – 9.8 x 10^9/l (7.1 - 14.2 x 10^9/l), Erys – 7.2 x 10^9/l (5.8 - 8.8 x 10^{12}/l), HGB – 8.2 mmol/l (6.9 - 9.7 mmol/l), HCT – 0.47 1/1 (0.41 - 0.53 1/1), PLT – 383 x 10^9/l (305 - 464 x 10^9/l) (Table 1). In the four dogs with portosystemic shunt the mean values were: Lkcs 9.6 x 10^9/l (6.2 - 12.6 x 10^9/l), Erys – 6.3 x 10^{12}/l (5.2 - 6.9 x 10^9/l), HGB – 9.4 mmol/l (8.9 - 10 mmol/l), and HCT – 0.47 1/1 (0.46 - 0.48 1/1). The mean levels of platelets and granulocytes, respectively, equalled 337 x 109/l (298 - 385 x 10^9/l) and 7.6 x 10^9/l (6.9 - 8.6 x 10^9/l) (Table 3). Likewise, no significant changes in white and red blood cell count parameters were observed in the cats qualified for the trial. The mean number of leukocytes Lkcs equalled 12.1 and 12.5 x 10^9/l, erythrocytes Erys – 8.0 and 7.9 x 10^{12}/l, haemoglobin HGB – 9.9 and 10.1 mmol/l, haematocrit HCT – 0.55 and 0.54 1/1, platelets PLT – 493 and 472 x 10^9/l, and granulocytes GRA – 8.8 and 8.4 x 10^9/l (Table 5). On the other hand, all animals in all studied subgroups, showed a considerable decrease in liver enzyme activity. In the eight dogs without any co-morbidities, the mean activity of ALT equalled 190 IU/l (82 - 439 IU/l), AST – 43 IU/l (25 - 73 IU/l), ALP – 807 IU/l (252 - 2657 IU/l), and GGTP – 8 IU/l (3 - 28 IU/l). No major changes were observed in the levels of total protein, albumins, and glucose between the tests conducted before and after treatment. Their mean values, equalled: TP – 67 g/l (57 - 71 g/l), ALB – 36 g/l (33 - 38 g/l), and GLU – 5.7 mmol/l (5.1 - 6.3 mmol/l), respectively (Table 2). A similar decrease in the activity of liver enzymes was recorded in the group of 4 Yorkshire terriers with portosystemic shunt, with the mean values of ALT at 165 IU/l (19 - 302 IU/l), AST – 62 IU/l (27 - 92 Iu/l), ALP – 106 IU/l (62 - 126 IU/l), and GGTP – 6 IU/l (4 - 7 IU/l). Again, the levels of total protein, albumins, and glucose remained unchanged and equalled, respectively: TP – 65 g/l (61 - 70 g/l), ALB – 27 g/l (22 - 32 g/l), GLU – 5.6 mmol/l (5.2 - 6.1 mmol/l) (Table 4). A similar drop in liver enzyme activity without any changes in total protein, albumins, and glucose was also recorded in cats. The mean enzyme activity equalled: ALT – 52 and 172 IU/l, AST – 30 and 87 IU/l, ALP – 52 and 96 IU/l, GGTP – 3 and 5 IU/l, with the mean levels of total protein at 79 and 71 g/l, albumins – 34 and 33 g/l, and glucose – 7.1 and 8.3 mmol/l (Table 6). Statistical analysis of biochemical parameters showed a significant difference between day 0 and week 8 for ALT, AST and ALP (Table 7).

As mentioned before, because of the promising decreasing trend in the activity of liver enzymes, in four dogs from the group without any co-morbidities, the treatment with Hepatiale Forte was extended for 4 more weeks up to a total of 12 weeks. A further decrease in the activity of liver enzymes was recorded after that period, while the level of total protein, albumins, and glucose remained unchanged. Mean liver enzyme activity after 12 weeks of treatment with hepatoprotective agents equalled: ALT – 101 IU/l (61 - 130 IU/l), AST – 25 IU/l (22 - 30 IU/l), ALP – 384 IU/l (315 - 475 IU/l), and GGTP – 4 IU/l (3 - 6 IU/l). The levels of total protein stood at a mean value of 65 g/l (62 - 70 g/l), albumins - 36 g/l (33 - 40 g/l), and glucose – 5.1 mmol/l (5.0 - 5.2 mmol/l) (Table 2).

Owners who filled in questionnaires reported that their pets, dogs and cats, willingly swallowed the supplement. Some did not notice any major behavioural changes, but others reported that the dog seemed more cheerful, more active, seemingly "rejuvenated", and mentioned "improvements in mood and wellbeing". Three owners also reported a reduction in waistline and greater defecation rate; some animals passed more wind (2 owners).

The values of individual parameters are shown in tables 1 - 6. In order to better illustrate the normalizing tendencies and changes in tested parameters after treatment with Hepatiale Forte, we decided to present the cases of specific patients.

Table 5. Blood parameters in two cats with liver disease treated with Hepatiale Forte (VetExpert) as adjunctive therapy.

	Lkcs 10^9/l		Erys 10^{12}/l		HGB mmol/l		HCT 1/1		PLT 10^9/l		GRA 10^9/l	
	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks
1	11.1	12.1	7.2	8.0	10.2	9.9	0.55	0.51	455	451	9.8	8.8
2	13.2	12.5	8.3	7.9	10.3	10.1	0.55	0.54	493	472	8.3	8.4

Table 6. Biochemical parameters in two cats with liver disease treated with Hepatiale Forte (VetExpert) as adjunctive therapy.

	ALT IU/l		AST IU/l		ALP IU/l		GGTP IU/l		TP g/l		ALB g/l		GLU mmol/l	
	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks	0 wks	8 wks
1	403	52	168	30	34	52	3	3	72	79	30	34	6.8	7.1
2	512	172	276	87	135	96	6	5	70	71	31	33	7.9	8.3

Discussion

Research on the hepatoprotective applications of phospholipids has been conducted since the 1980s. In human subjects, they are chiefly recommended in the treatment of liver damage of various origin. Many studies, for instance, have investigated the hepatoprotective properties of phospholipids in alcohol-induced liver cirrhosis (2, 19, 21, 22). In rats intoxicated with alcohol over a long period of time, phospholipids

Table 7. Statistical analysis of the biochemical parameters in 8 dogs with liver disease without any co-morbidities treated with Hepatiale Forte (VetExpert) over a period of eight weeks.

Parameter	Day 0	Week 8	Statistical significance	p value
ALT (IU/l)	360.8	190.0	TAK	0.0172
AST (IU/l)	83.5	43.0	TAK	0.0001
ALP (IU/l)	1144.0	807.1	TAK	0.0106
GGTP (IU/l)	10.4	7.5	NIE	0.0825
TP (g/l)	68.7	66.6	NIE	0.3524
Alb (g/l)	34.7	35.2	NIE	0.7270
GLU (mmol/l)	6.1	5.6	NIE	0.0903

were shown to reduce histopathological lesions, normalize and stabilize biochemical parameters, and lower the intensity of inflammatory and degenerative processes in the liver, which translated into an overall improvement in clinical condition and better test results (2, 21). Similar findings were obtained in experiments with patients suffering from liver fibrosis and failure caused by toxins such as carbon tetrachloride or drugs like isoniazid (18, 20, 22). For seven days, phospholipids were used alongside mangiferin, a mango tree extract with antioxidant properties, to treat a group of rats; on day 8, all patients received a single dose of carbon tetrachloride. Compared to the control group, which had received distilled water, the rats showed a major drop in the activity of ALT, AST, ASP and bilirubin, along with an increase in the level of total protein (18). In an experimental poisoning with isoniazid (an anti-tuberculosis drug), researchers examined liver function, oxidative stress, and the level of the tumour necrosis factor TNF - α and interleukin 10. The study demonstrated that phospholipids had an antioxidant effect, lowered the levels of free and bound bilirubin, TNFα, and the activity of ALT, ALP, and, at the same time, boosted the level of anti-inflammatory IL-10. Phospholipids are known to increase the coupling of oxidation with ATP synthesis, and thus enhance the kinetic profile of mitochondria in the liver cells (20). This was confirmed by Jaisval et al., who found that phospholipids protect liver cells and mitochondrial membranes by increasing cell proliferation and incorporating metabolic enzymes into the cytoplasmic reticulum (11). Phospholipids also show hepatoprotective and anti-inflammatory effects in the treatment of hepatitis C in human subjects (9). In 1996, Ma et al. showed that they play an essential role in inhibiting the development of liver fibrosis in rats and chimpanzees (16). Phospholipids prevent the transfer of TNFβ1-dependent collagen, thus preventing its accumulation (3). Lata et al. also studied the impact on phospholipids on liver damage caused by total parenteral nutrition, which leads to disorders in hepatocyte structure and function and increases the activity of liver enzymes. The experimental group received an intravenous dose of phospholipids (50 mg/kg) every 6 hours, while; the control group received no medication at all. After 2 weeks of treatment, the former showed a statistically insignificant increase in the activity of ALT, in the latter an increase was observed in ALT, AST, and GGTP on day 7 and day 14 of the trial (14). In another study with 58 patients, phospholipids were also shown to have a positive effect on the treatment of post-cholecystectomy syndrome. They were reported to lower cholesterol levels, eliminate pain and indigestion, and normalize biochemical parameters (16). This may also explain the improved mood, greater defecation rate, and winds reported by dog owners in our trial. Perhaps the phospholipids in Hepatiale Forte eliminated indigestion and increased the rate of metabolism. Phospholipids also have many other positive effects, not limited to the liver alone. They are of key importance to the physiology and pathology of cellular and organelle membranes as their basic structural and functional building blocks. They improve elasticity, fluidity, and permeability of cellular membranes, and maintain and restore the appropriate activity of their proteins and receptors. They are essential for the processes of cell differentiation, proliferation, and regeneration, and serve as a substrate for the production of a range of important chemical compounds, such as the ATP. They help emulgate and digest fats in the gastrointestinal tract and improve the absorption of fat-soluble vitamins. They are also the chief emulgators in bile. They have an important impact on immune response at the cellular level (13). Lecithin, i.e. the phosphatidylcholine found in phospholipids, crosses the blood-brain barrier and takes part in neurotransmission. This property is currently used in the treatment of seniors with memory loss, neurological disorders, and Alzheimer's disease (1). Phosphatidylcholine also forms part of lipoproteins in blood and bile, and creates a protective layer in the gastrointestinal tract and the lungs. To sum up, in vitro and in vivo trials confirm the antioxidant, anti-inflammatory, anti-fibrosis, regenerative, reparatory, and protective properties of phospholipids, which lead to important improvements in clinical, biochemical, histological, and imaging parameters in the treatment of fatty liver, drug intoxication, viral liver diseases, and hepatic encephalopathy (10).

The present study lends additional weight to previous findings about the impact of phospholipids on liver health and function. Both the group of patients without any co-morbidities and patients with portosystemic shunt, as well as cats, showed a statistically significant drop in the activity of liver enzymes ALT, AST, and ALP after 8 weeks of treatment with Hepatiale Forte. The levels of GGTP, total protein, albumins, and glucose may also indicate correct liver function. In the absence of clinical symptoms, the elevated liver enzyme activity in tested patients must have resulted from the damage to hepatocytes. Regardless of its original cause (drugs, toxins, diet, inflammation, infection, or geriatric processes), a significant decrease in the liver enzyme activity was observed in all cases after treatment with a single dietary supplement based on phospholipids and ornithine. The fact that the enzymes behaved in a similar manner in patients with congenital vascular liver disease likewise attests to their positive impact on the organ. The improved mood of the animals, their return to their "puppy years", may have resulted from the supplement's direct positive effects on the gastrointestinal tract, as well as, as has been demonstrated in human subjects, the central nervous system; this aspect, however, requires further research in animals. The decreasing trend in liver enzyme activity observed in the present study may indicate a positive impact of Hepatiale Forte supplements on liver function. Since enzymes never returned to normal in some patients during the trial, it is worth considering a longer period of treatment. In the context of data obtained by other researchers, the hepatoprotective influence of phospholipids could be tapped and introduced as a staple dietary supplement in the nutrition of patients with chronic and/or incurable liver conditions, such as the intrahepatic portosystemic shunt..

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HEPATIALE® FORTE

Composition: 2.21.1 Lecithin powder, L-aspartate L-ornithine, 11.2.10 magnesium stearate

Technological Additives

1E460 microcrystalline cellulose	230 mg
E551b colloidal silica	5 mg

Indications: is recommended for dogs and cats to support liver functions in case of liver failure or disorders.

Properties and usage: Phospholipids, which are glycerol esters of choline-phosphoric acid and unsaturated fatty acids (linoleic, linolenic and oleic) have protective and regenerating effects on liver cells. Due to their content of poly-unsaturated fatty acids in side chains, phospholipids cannot be synthetized in the body. Once delivered to the body, they build themselves into the cell and cytoplasmic membranes of the liver and fill in defects resulting from pathological processes. This allows faster regeneration of the damaged liver cells and restoration of their functions. As a result, the functions of cell receptors, enzymatic cell systems and active and passive transport processes improve. Phospholipids are crucial for the process of liver cell division and proliferation. They inhibit the process of liver tissue fibrosis by reducing the production of collagen and activating collagenase (enzyme which breaks down the collagen). Phospholipids and biliary acids play a vital role in the digestion of fats and absorption of fat-soluble vitamins.

Ornithine regulates the urea cycle of cats and dogs. It plays a role in transforming the ammonia formed from the process of breaking down amino-acids into urea. It also reduces the ammonia's toxicity level. Ornithine is particularly important for cats which use amino-acids also during the process of energy production. As the processes of deamination are very energy consuming, ornithine is necessary for cats. Ornithine is recommended in the treatment of cats with diagnosed or suspected hepatic encephalopathy or for cats which have had long breaks from eating The combination of phospholipids and ornithine in cats and dogs has protective and regenerating properties in the treatment of liver diseases.

Dosage: 1 tablet for every 15 kg of body weight
Tablets should be administered whole or crushed, before or with food. If the daily dosage is more than one tablet, they may be administered twice or three times a day. The animal should be provided with fresh water at all times.
For optimal results it is recommended to use the product for 1-3 months and in chronic cases for up to 6 months.
The correct dosage and time of treatment depends on the animal's needs and is decided upon by a veterinary surgeon.

Storage conditions: Store in a dry place at temperature of up to 25 degrees Celsius. Protect from humidity.

Additional information: Analytical constituents: General protein – 34,6 %, crude fat – 14,1%, crude ash (including mineral components) – 1,9%, crude fibre – 24,7%, moisture – 5%.

Packaging:
4 blisters of 10 tablets each

Vet Planet Sp. z o.o. Brukowa 36/2 street, 05-092 Lomianki, Poland, www.vetexpert.pl

Please consult your veterinary surgeon before using or prolonging the use of this product as it may be necessary to change the dosage or mode of use. Hepatiale Forte may be supplied exclusively by veterinary surgeons.

HEPATIALE® FORTE
Small breed & cat

Contents: 2.20.1 soybean oil, 2.21.1 crude lecithin, L-aspartate L--ornithine, 2.20.1 palm oil.

Indications: is recommended for dogs small breeds and cats to support liver functions in case of liver failure or disorders.

Properties and usage: Phospholipids which are glycerol esters of choline-phosphoric acid and unsaturated fatty acids (linoleic, linolenic and oleic) have protective and regenerating effects on liver cells. Due to their content of poly-unsaturated fatty acids in side chains, phospholipids cannot be synthetized in the body. Once delivered to the body, they build themselves into the cell and cytoplasmic membranes of the liver and fill in defects resulting from pathological processes. This allows faster regeneration of the damaged liver cells and restoration of their functions. As a result, the functions of cell receptors, enzymatic cell systems and active and passive transport processes improve. Phospholipids are crucial for the process of liver cell division and proliferation. They inhibit the process of liver tissue fibrosis by reducing the production of collagen and activating collagenase (enzyme which breaks down the collagen). Phospholipids and biliary acids play a vital role in the digestion of fats and absorption of fat-soluble vitamins.

Ornithine is an amino acid which is formed from arginine in the liver. It plays a very important role in the processes of the metabolism of protein as it is crucial to transforming ammonium residues that are formed in the process of desamination of amino acids into urea. Cats are particularly sensitive to ornithine deficiency because of their increased need for arginine and thus for the ornithine formed from it. The processes of the desamination and transamination of amino acids happen constantly in cats because cats use amino acids to produce energy. As a result ammonium residues are constantly produced in cats' livers and thus create the need for a sufficient amount of ornithine. Deficiency in ornithine may lead to the inhibition of the process of transforming ammonium residues into urea, their accumulation in the body and an increase in the risk of developing hepatic encephalopathy and toxic damage of many organs. Ornithine is recommended for the treatment of cats suffering from or suspected of hepatic encephalopathy and those with a break in food intake. The combination of phospholipids and ornithine in cats and dogs has protective and regenerating properties in the treatment of liver diseases.

Dosage:
Cats: 1 capsule Twist off a day
Dogs: 1 capsule Twist off for every 5 kg of body weight a day
he correct dosage and time of treatment depends on the animal's needs and is decided upon by a veterinary surgeon.

Storage conditions:
Store in a dry place at temperature of up to 25°C. Protect from humidity.

Additional information: Analytical constituents: Crude protein – 23,26 %, crude fat – 57,92%, crude ash (including mineral components) – 10,68%, moisture – 1,71%.

Packaging: 40 capsules Twist off

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Please consult your veterinary surgeon before using or prolonging the use of this product as it may be necessary to change the dosage or mode of use. Hepatiale® Forte may be supplied exclusively by veterinary surgeons.

HEPATIALE® FORTE Large breed

Composition: 2.21.1 Lecithin powder, L-aspartate L-ornithine, 11.2.10 magnesium stearate.

Technological Additives:

1E460 microcrystalline cellulose 530 mg.

Indications: is recommended for dogs to support liver functions in case of liver failure or disorders.

Properties and usage:

Phospholipids, which are glycerol esters of choline-phosphoric acid and unsaturated fatty acids (linoleic, linolenic and oleic) have protective and regenerating effects on liver cells. Due to their content of poly-unsaturated fatty acids in side chains, phospholipids cannot be synthetized in the body. Once delivered to the body, they build themselves into the cell and cytoplasmic membranes of the liver and fill in defects resulting from pathological processes. This allows faster regeneration of the damaged liver cells and restoration of their functions. As a result, the functions of cell receptors, enzymatic cell systems and active and passive transport processes improve. Phospholipids are crucial for the process of liver cell division and proliferation. They inhibit the process of liver tissue fibrosis by reducing the production of collagen and activating collagenase (enzyme which breaks down the collagen). Phospholipids and biliary acids play a vital role in the digestion of fats and absorption of fat-soluble vitamins.

Ornithine regulates the urea cycle of cats and dogs. It plays a role in transforming the ammonia formed from the process of breaking down amino-acids into urea. It also reduces the ammonia's toxicity level. Ornithine is particularly important for cats which use amino-acids also during the process of energy production. As the processes of deamination are very energy consuming, ornithine is necessary for cats. Ornithine is recommended in the treatment of cats with diagnosed or suspected hepatic encephalopathy or for cats which have had long breaks from eating The combination of phospholipids and ornithine in cats and dogs has protective and regenerating properties in the treatment of liver diseases.

Dosage: 1 tablet for every 25 kg of body weight. Tablets should be administered whole or crushed, before or with food. If the daily dosage is more than one tablet, they may be administered twice or three times a day. The animal should be provided with fresh water at all times. The correct dosage and time of treatment depends on the animal's needs and is decided upon by a veterinary surgeon.

Storage conditions: store in a dry place at temperature of up to 25 degrees Celsius. Protect from humidity.

Analytical constituents: crude protein – 23,97%, crude fat – 20,23%, crude ash (including mineral components) – 3,71%, crude fibre – 36,44%, moisture – 4%.

Packaging: 40 tablets

Please consult your veterinary surgeon before using or prolonging the use of this product as it may be necessary to change the dosage or mode of use. Hepatiale Forte may be supplied exclusively by veterinary surgeons.

HEPATIALE® FORTE Advanced

1. Composition:
Aspartate L-ornithine, 2.21.1. Soya Lecithin (as a source ofphospholipids), 11.2.10 magnesium stearate
Additives (g/kg):
3c Methionine in the form of S-adenosylmethionine 362,3 g, 2b Extract of Silybum marianum (L.) 90,6 g, 3b zinc oxide 22,6 g.
Technological additives:
1E460 microcrystalline cellulose 126,8 g
2. Indications:
Products for dogs and cats is recommended to support liverfunctions in case of failure, functional disorders and poisoning.
3. Properties and usage:
Phospholipids which are glycerolesters of choline-phosphoric acid andunsaturated fatty acids (linoleic, linolenic and oleic) have protective and regenerating effects on liver cells. Due to their content of poly-unsaturated fattyacids in side chains, phospholipids cannot be synthetized inthe body. Once delivered to the body, theybuild themselves into the celland cytoplasmic membranes of the liver and llin defects resulting frompathological processes. This allows faster regeneration of the damagedliver cells and restoration of their functions. As a result, the functions ofcellreceptors, enzymatic cellsystems and active and passive transportprocesses improve. Phospholipids are crucial for the process of livercelldivision and proliferation. Theyinhibit the process of liver tissuebrosis by reducing the production of collagen and activating collagenase (enzyme which breaks down the collagen). Phospholipids andbiliary acids playa vital role in the digestion of fats and absorption offat-soluble vitamins.
S-adenosylmethionine (SAM) is an endogenous substance formedafter joining the group adenosine adenosine-5-triphosphate (ATP) to the sulfur of methionine. Its concentration decreases in the courseof many liver diseases. SAM participates in a number of metabolicprocesses, but the most important role in transmethylation reactionor group transfer - CH3 necessaryfor the synthesis of membranephospholipids. In addition SAM is activelyinvolved in the reactionstranssulfuracji necessaryfor synthesis in the liver of the natural antioxidant glutathione and aminopropylacji which polyamine synthesisstep in stimulating the synthesis of DNA, proteins and proteoglycans, necessaryfor growth and regeneration of liver cells. It is particularlyrecommended as an adjunct to the toxic poisoning of the liver and bilestasis. It can be used protectively long-term use of steroids and afterparacetamol poisoning in cats.
The extract of milk thistle (*Silybum marianum*) contains the activesubstance silymarin or a 4 avonolignans – Silybin, silidianin, silichristinand iso-silibinin. The greatest biological activity has silybin. The mainmechanism of action of silymarin in the liver is the antioxidant and anti-in ammatorye ect, achieved byinhibition of lipid oxidase activity and leukotriene synthesis. It can also act protectively cholagogic and in cases of poisoning. Silymarin is a compound safe and low toxic, the preferred poisoning, and chronic in ammation of the liver. A particularly potent protective action on liver originates a call silibinin phospholipids.
Ornithine regulates the urea cycle in dogs and cats. It is involved in the conversion of amino acids resulting from the decomposition of ammonia into urea, lowering the level of toxicity. Ornithine plays a special role in cats, which use amino acids also in the processes of energygeneration. The processes are the deamination of these very intensive which makes ornithine is necessary for them. Ornithine is recommended for the treatment of cats su ering from or suspected of hepatic encephalopathy and those who for a long time do not take food.
Zinc is a component of many enzymes that regulate metabolism of nucleic acids, carbohydrates, supporting wound healing, growth and reproduction. In the case of liver disorders to use zinc reduces the absorption of copper from the gastrointestinal tract, which is an element with a strong toxicityto liver. In other words, the tip protects the liver against excess copper and mayalso act as an antioxidant. In patients with liver disease it is recommended to increase the amounts in the diet.
The combination of phospholipids and ornithine in cats and dogs hasprotective and regenerating properties in the treat- ment of liver diseases.
4. Dosage:
Dogs – 1 tablet per 10kg body weight
Cats – half a tablet per cat
Administered before or during meals. Tablets administered in whole orcrushed. If your daily dose provides for administration of several tabletscan be divided into 2-3 portions. The animal must have permanentaccess to fresh water.
5. Storage conditions:
Store in a dry place at temperature of up to 25 degrees Celsius. Protectfrom humidity.
6. Additional information :
Analytical constituents: crude protein – 27,60%, crude fat – 31,30%,crude ash – 28,20%, crude fibre – 7,60%, moisture – 2,40%, magnesium – 1,320 g/kg
Packaging: 30 tablets
Please consult your veterinary surgeon before using or prolonging the use of this product as it may be necessary to change

BIOPROTECT

Composition: 12.1.5 yeast (MOS), 4.1.14 Fructo-oligosaccharides (FOS, 13.3.1. Potato starch, 11.2.10 Magnesium stearate

Additives: 4b Enterococcus faecium, 1 k Lactobacillus rhamnosus, 1E55b1 colloidal silica 4 mg.

Technological additives: 1E460 Microcrystalline cellulose 100 mg.

Indications: The product is recommended for dogs and cats with gastrointestinal microflora disorders.

Dosage: Dose 1-2 capsules per day. Capsules may be administered directly to the animal's mouth or they can be mixed with food. The animal should be provided with fresh water at all times.

Storage conditions: Store in a dry place in room temperature.

Additional information: Analytical constituents: crude protein – 0,92%, crude ash – 0,40%, crude fat – 0,55%, crude fibre – 35,44%, moisture – 3,94%.

Please consult your veterinary surgeon before using or prolonging the use of this product as it may be necessary to change the dosage or mode of use.

PASTE BioProtect

Nutritional purpose: Reduction of acute intestinal absorptive disorders.

Composition: Dextrose, glycerine, carob our, fructo-oligosaccharides, wood charcoal, sodium chloride, potassium chloride, magnesium chloride.

Analytical contents: Crude protein 0.1%, crude fat 0.1%, crude ber 0.3%, crude ash 25%, Sodium 1.4%.

Additives: Microorganisms: 4b1705 Enterococcus faecium NCIMB 10415: 550000000 CFU/ml –

Flavouring: Sensory additives - Binders - anticaking agents: E558 – Bentonite-montmorillonite: 345 000 mg/L.

Dosage:

DIRECTION FOR USE:	WEIGHT DOSE TWICE DAILY
< 5 kg	1 ml (2 ml)
5 – 10 kg	2 ml (4 ml)
11 – 25 kg	4 ml (8 ml)
26 – 40 kg	6 ml (12 ml)
> 40 kg	8 ml (16 ml)

Administer orally for 3 days or as instructed by your veterinarian.

Further informations: In case of acute diarrhea and during the period which follows. Before use or extension of use, it is recommended to ask for the opinion of a specialist.

Storage: Store at ambient temperature and out of direct sunlight.

Shelf life: 24 months in original packing – after opening use within 3 months and keep in a cool place.

PASTE DiarVet

Nutritional purpose: supportive care in patients with acute or severe diarrhea.

Composition: 1.1.18 malt extract, 13.2.2 dextrose, 4.4.6 chicory powder, 9.6.1 liver hydrolysate, 5.4.1. apple fiber.

Additives per kg: Vitamins, pro-vitamins and chemically well-defined substances having similar effect: 400.000,00 I.U. (3a672a) vitamin A as retinyl acetate.

Compounds of trace elements: 4.000.00 mg (3b603) zinc as zinc oxide, binders: 50.000.00 mg (1m558i) Bentonite. Flavouring compounds: 5.000.00 mg mixture of flavoring compounds (contains tannin). The simultaneous oral use with macrolides shall be avoided.

Analytical constituents and levels: 5.20% crude protein, 1.50% crude fat, 7.10% crude fibre, 8.10% crude ash, 8.80% moisture.

Recommended dosage:
Administer orally for 3 days 3 times daily 1 g paste per 10 kg dog/cat weight. Storage condition:
Product stability maintained only under appropriate storage conditions. Store in a cool and dry place.
Keep out of the reach of children and animals. Keep packaging closed after use.

TriDigest

Indication: Product is indicated for dogs and cats with digestive alimentary tract disorders. Ingredients contained in the product support digestive juices in stomach, pancreas and liver.

Dosage:
Dog – 1 tablet per 15 kg b.w. once a day
Cat – ½ tablet once a day

Ingredients: L-ornithine aspartate, 2.21.1 lecithin, 11.3.2 calcium phosphate, 7.9.1 Licorice root extract (*Glycyrrhiza L.*), 11.2.10 magnesium stearate, 13.6.6 stearic acid.

Additives per 1 kg of product: 2b artichoke extract (Cynara scolymus L), 89 g, betaine hydrochloride 133 g, colloidal silica 6,5 g

Technological additives: 1E460 microcrystalline cellulose 222 g.

Analytical constituents: crude protein 20.90%, crude fat 3.45%, crude Íber 15.45%, crude ash (including minerals) 14.85%, moisture 4.9%, calcium 156.60 g/kg, phosphorus 69.50 g/kg.

Storage: store in a dry place at room temperature. Keep away from children and pets.

VETEXPERT diet intestinal dog

`` 'Expert Diet Intestinal Dog is a complete and balanced dietetic feed dogs for the reduction of intestinal digestion and absorption disor-'s and in case of exocrine pancreatic insuÙciency. This feed is easily estible and contains increased amount of electrolytes and reduced ount of fat.

eding instructions: The feed given in amounts showed in ding guide meets nutritional requirements of dog. The initial ounts are shown in the table on the packaging. The doses may be divided into two or more meals. It is advised to consult a veterinarian before first use of the product or extending the period of feeding. The recommended period of administration in case of acute diarrhoeas and during convalescence is 1 to 2 weeks. The balancing of deficiencies caused by malabsorption: 3 to 12 weeks. In the case of chronic pancreatic insuÙciency the product should be used until the death of the animal. Keep the fresh water available at all times.

Ingredients: rice, poultry meal, corn, fresh poultry, sugar beet pulps, yeast, vegetable oil, poultry liver hydrolysate, L-glutamine (1%), inulin (FOS source 7500 mg/kg), mineral contents, ginger (1000 mg/kg), glucosamine, chondroitin.

Additives: Vitamin A – 18000 IU/kg, Vitamin D3 – 1750 IU/kg, Vitamin E (alpha-tocopherol) – 500 mg/kg, Iron (iron sulphate monohydrate) – 75 mg/kg, Iodine (potassium iodide) – 1.5 mg/kg, Copper (copper sulphate pentahydrate) – 10 mg/kg, Manganese (sulphate) – 7.5 mg/kg, Zinc (zinc oxide) – 150 mg/kg, Selenium (sodium selenite) – 0.15 mg/kg.

Contains EU permitted antioxidant.

Analytical constituents: Crude protein – 30.00%, Oils and crude fats – 10.00%, Crude fibre – 2.80%, Crude ash – 7.00%, Calcium – 1.30%, Phosphorous – 0.80%, Potassium – 1.20%, Sodium – 0.25%.

Comprehensive liver protection and support

Which product is the best for your patient?

Product	Ornitil Plus	Hepatiale Forte small breed	Hepatiale Forte	Hepatiale Forte large breed	Hepatiale Forte Liquid	Hepatiale Forte Advanced
Relative strenght	★★	★★★★½	★★★★½	★★★★½	★★★★	★★★★★
Form						
Dosage	1 tabl./15 kg b.w.	1 kaps./5 kg b.w.	1 tabl./15 kg b.w.	1 tabl./25 kg b.w.	5 ml/10 kg b.w.	1 tabl./10 kg b.w.
Composition	Ornithine, artichoke	Ornithine, phospholipids	Ornithine, phospholipids	Ornithine, phospholipids	S-adenosylmethionine, *Silybum marianum*, ornithine, phospholipids, magnesium, zinc	S-adenosylmethionine, *Silybum marianum*, ornithine, phospholipids, magnesium, zinc
Indications	Dogs and cats suspected of protein metabolism disorders in the liver	Cats and small breed dogs suspected of liver disorders	Medium breed dogs suspected of liver disorders	Large breed dogs suspected of liver disorders	Dogs and cats suspected of liver disorder with bile secretion dysfunctions (especially in case of increased serum AST, ALP and GGTP levels)	Dogs and cats suspected of liver disorder with bile secretion dysfunctions (especially in case of increased serum AST, ALP and GGTP levels). Especially recommended in case of hepatitis, hepatotoxicity and bile stasis

Hepatic Dog ★★★★★

+

Maximum effect with the VetExpert Hepatic Dog diet

- The only diet containing liver supporting additives – artichoke and phospholipids. Helps to stimulate bile release and to support regenerative processes
- The highest level of – which limits copper absorption and exerts antioxidant properties
- Low copper level – reduces the risk of copper storage disease
- Complex nutrition for patients with liver dysfunction and bile secretion impairement. Especially recommended for patients with protein metabolism disorders in the liver.

SCIENCE AND EMPATHY ARE OUR BYWORDS.

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