EFFECTIVENESS OF HEPATIALE FORTE IN NORMALISING LIVER FUNCTION IN DOGS

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Abstract
The liver is one of the most important organs, participating in metabolic, detoxification and immunological processes. Early diagnosis of liver diseases allows for a relatively quick response and introduction of hepatoprotective preparations, based on, among others, phospholipids and amino acids: arginine and glutamine. In the presented study, 20 dogs with impaired activity of liver enzymes received a preparation containing soy phospholipids, arginine and glutamine for 8 weeks. After the study was completed, a statistically significant decrease in liver enzyme activity and an increase in albumin concentration were found, which indicates normalization of the organ's functioning and its regeneration.

Keywords
liver, dog, dietary therapy, phospholipids, arginine, glutamine

One of the most important 'super-organs' in the living organism is the liver. It plays a central role in many (over 2000) processes in the body: carbohydrate, fat and protein metabolism, detoxification of metabolites and xenobiotics, storage of vitamins, trace metals, fat, glycogen, immune regulation. The liver is located between the gastrointestinal tract and the centre of the circulatory system, is highly vascularised and synthesises, detoxifies, transforms, accumulates, secretes and produces many compounds and chemicals. The liver's weight varies considerably, from 125 to 1,350 grams, representing 1.33 to 5.95 percent of the body weight. The average liver weight for an adult dog is approximately 3.4 percent of the body weight (2, 3, 13). The clinical signs, physical signs, and pathological changes that accompany liver disease reflect damage and disruption of these functions. One particularly noteworthy feature of the liver is its remarkable functional reserve, which can reach up to 65%. Consequently, the occurrence of specific hepatic and hepatobiliary symptoms—such as jaundice, hypoglycaemia, a tendency to bleeding, hepatic encephalopathy or ascites—which signify the exceeding of this reserve, typically occurs late, usually in the final phase of the disease. The initial symptoms of liver disease – a lack of appetite, increased thirst, polyuria, vomiting, weakness – are similar to those observed in diseases affecting other organs. While the majority of liver disease symptoms lack specificity, there are certain indications that suggest the possibility of liver and/or biliary tract disease. One such indicator is information regarding the animal's exposure to potentially hepatotoxic drugs, including anaesthetics, anticonvulsants, and non-steroidal anti-inflammatory drugs (NSAIDs) (4, 5). Extrahepatic biliary duct obstruction is frequently a consequence of biliary tract tumours or acute pancreatitis. The latter, together with inflammatory bowel disease (IBD), can cause reactionary hepatopathy (4, 5). Elevated liver enzymes can also be a result of endocrine disorders. According to the Center, approximately 85% of cases of adrenal hyperadrenocorticism are associated with an increase in ALP and GGTP activity, and 50-80% are associated with an increase in ALP activity (4). Increases in ALP and ALT activity are also seen in hypothyroidism, but are mild and not always detected (4).

Because of its location and function, the liver is directly and indirectly involved in many of the body's metabolic processes and transformations. The variety of symptoms, the lack of characteristic, typical symptoms and the often asymptomatic course mean that these conditions are often detected incidentally, e.g. during screening, routine geriatric examinations or when qualifying a patient for general anaesthesia (5,13). Liver damage does not affect all hepatocytes simultaneously, hence a considerable proportion of these disorders are subclinical and self-healing, without residual effects. Clinical symptoms manifest in cases of severe and/or extensive liver damage. It is crucial to emphasise that the severity of the damage is not necessarily correlated with the severity of the clinical symptoms (4, 5, 13).

The underlying mechanism of hepatic cell

degeneration and/or death remains unclear. Cellular ischaemia and hypoxia, free radical action and oxidation of the cell, deficiency or absence of intracellular elements or cofactors, intracellular production of toxins and the possibility of their incorporation into the protein, DNA and RNA structure of the cell, and finally, cholestasis and the action of endotoxins from bacteria, viruses, parasites and immune factors are common pathomechanisms of liver damage. Specific focus is directed towards damage to the hepatocyte cell membrane, which occurs through oxidation and the subsequent loss of phospholipids, which are the primary structural components of the cell membrane. Oxidative stress, a consequence of free radical attack, invariably results in damage to cell membrane lipids, which, being subject to increased peroxidation, exacerbate the oxidative stress on hepatocytes, ultimately leading to their necrosis (4, 7). Oxidised lipids released from damaged hepatocytes induce inflammation and hepatic venous damage. Chronic inflammation causes excessive synthesis of, inter alia, tumour necrosis factor (TNF-α) and pro-inflammatory interleukins. This results in hepatic steatosis and fibrosis (10). The most extensively documented cause of liver necrosis is damage to hepatocyte cell membranes. Therefore, the use of phospholipids, the main building blocks of cell membranes, as a repair substance to replenish its defects or deficiencies in hepatocyte cell membranes. Phospholipids are glycerol esters of choline phosphate and the unsaturated fatty acids linoleic, linolenic and oleic. They are not synthesised in the body because of the presence of polyunsaturated fatty acids in the side chains. They have the ability to be incorporated into the cytoplasmic cell membranes of liver cells and to fill the defects created during disease processes – thus regenerating hepatocytes and restoring their function. The activity of membrane receptors, enzyme systems located in cytoplasmic membranes, active and passive transport is improved. Phospholipids are also essential for the differentiation and proliferation of liver cells. They inhibit fibrotic processes in liver tissue by reducing collagen production and increasing collagenase activity. They also play a crucial role in the digestion of fats and the absorption of vitamins, increasing the solubility of cholesterol in bile. Furthermore, they are involved in the digestion of fats and the absorption of fat-soluble vitamins, increasing the transport of cholesterol from extrahepatic tissues to the liver and activating lipolytic enzymes (4, 10, 11). Another crucial pathway for liver regeneration and protection is the utilisation of substances that enhance liver function. Ornithine, S-adenosine-methionine, zinc, silymarin and silybin are frequently employed. The search for new substances, often substrates for liver metabolism, is ongoing, with the aim of optimising the organ's processes. Such compounds include the amino acids L-arginine and L-glutamine. These are relatively exogenous amino acids, produced partly by the body or supplied from the diet, but external supplementation is required for the cells to function properly. L-arginine plays a role in numerous physiological processes. It affects the functioning of the circulatory system by influencing the secretion of nitric oxide, a factor that strengthens and dilates blood vessels. Additionally, it impacts the immune system, muscular system, digestive system, and sexual system. L-arginine stimulates the production of neurotransmitters and proteins, including creatine, proline, polyamines, and most notably, urea. Furthermore, it contributes to the synthesis and release of growth hormone. This amino acid plays a role in the processes of bone fusion and wound healing. It facilitates the removal of harmful substances, particularly ammonia, from the body. It participates in the urea cycle in the liver. During the catabolic reaction, arginine, formed from citrulline in the small intestine, produces α-ketoglutarate, from which, through the removal of carbon and nitrogen atoms, ornithine is formed (17, 24). L-glutamine is a building block amino acid. It has a beneficial effect on the production of immune cells and leukocytes. Additionally, it has been shown to enhance the proliferation of beneficial intestinal bacteria and to facilitate the regenerative processes of an organism fighting cachexia caused by disease. It serves as a precursor for the synthesis of proteins and amino acids, including glutamic acid, γ-aminobutyric acid, arginine, ornithine, citrulline, and proline. Glutamine is involved in nitrogen metabolism and regulates toxic levels of ammonium ions in the body. It causes ammonia to be attached to organic compounds, and can use ammonia to produce urea, thus detoxifying the body. Additionally, glutamine is an important regulator of nitric oxide synthesis (18). An attempt was therefore made to determine the efficacy of a hepatoprotective preparation containing phospholipids, L-arginine and L-glutamine in canine liver disease. These are common in these animals and the only symptom may be elevated liver enzymes. As the treatment of liver disease is based on the use of several drugs and diet, for the purposes of this paper we have limited ourselves to describing those cases where only Hepatiale Forte was used.

MATERIAL AND METHODS

The preparation used in the study was Hepatiale Forte or Hepatiale Forte Large Breed +25 kg from Vet Expert (Vet Planet, Łomianki Polska) containing Glycine max soya bean seeds as a source of soya bean phospholipids, L-arginine and L-glutamine. The preparation was administered once daily at a dose

of 1 tablet per 15 kg of body weight (Hepatiale Forte) or 1 tablet per 25 kg of body weight (Hepatiale Forte Large Breed + 25 kg). The study group consisted of 20 dogs of different sex, age and breed, patients of the Veterinary Polyclinic of the Faculty of Veterinary Medicine of the University of Warmia and Mazury in Olsztyn. Patients were selected for the study on the basis of elevated liver enzymes found during geriatric screening and tests performed prior to general anaesthesia. None of the patients had clinical symptoms suggestive of disease. However, all patients underwent an ultrasound examination of the liver and biliary system after the laboratory results were obtained, which was repeated after the end of the application of Hepatiale Forte/Hepatiale Forte Large Breed. The preparation was administered to all animals for 8 weeks at the above dose according to the manufacturer's recommendations, directly or crushed, mixed with food, before or during meals. A morphological blood test (white blood cell count Lkcs, red blood cell count Erys, hematocrit HCT, hemoglobin content HGB, platelet count PLT, neutrophil count Neut, lymphocyte count Lymph, monocyte count Mono, Basocytes Baso and Eosinocytes Eos) and serum biochemicals (activity of alanine aminotransferase ALT, aspartate aminotransferase AST, alkaline phosphatase ALP, gamma glutamyl transpeptidase GGTP, glutamate dehydrogenase GLDH, total protein TP, albumin ALB, glucose GLUC, total bilirubin TB and bile acids SBA). The tests were performed on day 0 - before administration of the preparation and after 8 weeks of use of Hepatiale Forte/Hepatiale Forte Large Breed. At the same time, the pet owners were asked to complete a questionnaire with questions about their perception of the effect of the preparation: any side effects of the preparation (vomiting, diarrhoea, constipation, grumbling, increase/decrease in thirst, appetite, polyuria/diphtheria, pruritus, salivation, jaundice), intake of the preparation (size and number of tablets, how the dogs liked them, willingness/unwillingness to take the preparation) and comments on how their dog felt after treatment.

RESULTS

No clinical side effects were observed in any of the patients during the trial when Hepatiale Forte/Hepatiale Forte Large Breed was administered.

In haematological examinations performed prior to the introduction (day '0') of Hepatiale Forte/Hepatiale Forte Large Breed, no erythrocyte changes were observed in any dog. The values of Lkcs, Erys, HBG, HCT, PLT, Neut, Lymph, Mono, Baso and Eos were within the reference values established for dogs. The complete results of the blood tests performed on the dogs before and after the study are shown in Table 1.

On ultrasound examination, the majority (14 patients) showed no macroscopic changes. In three patients there was a slight thickening of the bile in the gallbladder without thickening of the gallbladder walls and bile ducts. The liver parenchyma was generally hypoechogenic. Three patients showed diffuse hyperechoic changes of the liver parenchyma with mild thickening of the gallbladder wall and bile ducts, but without features of cholestasis.

After 8 weeks of treatment with Hepatiale Forte, there were no significant changes in haematological parameters (Table 1). However, on biochemical examination, 19 dogs showed marked changes in liver enzyme activity; 17 dogs showed a decrease in enzyme activity, two dogs showed an increase in activity, and one patient's enzyme activity remained unchanged. It is noteworthy that the decline in ALT, AST, GLDH, GGTP enzymes and AP after eight weeks of Hepatiale Forte/Hepatiale Forte Large Breed was statistically significant (Figure 1). In contrast, total protein concentration remained unchanged, although there was a statistically significant increase in blood albumin concentration. Furthermore, there was a statistically significant decrease in bilirubin and bile acids (Figure 1).

The ultrasound findings were comparable to those obtained prior to the commencement of Hepatiale Forte/Hepatiale Forte Large Breed. In three patients, the bile within the gallbladder was clear, and the walls of the gallbladder and bile ducts were not thickened. In three patients, the ultrasound image remained unchanged, with the presence of diffuse hyperechoic lesions in the liver. These patients were referred for further diagnostic evaluation.

DISCUSSION

The increase in life expectancy, coupled with a deeper understanding of the anatomy, cytology and physiology of the liver, has prompted the search for compounds and substances that can prolong the functioning of the organ and potentially prevent its damage. Consequently, research is being conducted into the fundamental building block of liver cells, namely phospholipids. Given that liver damage can be multifactorial, research into phospholipids takes into account the various factors that damage the organ. A significant body of research has been dedicated to investigating the impact of phospholipids in cases of post-alcoholic cirrhosis. In rats that have been subjected to prolonged alcohol intoxication, a notable reduction in histopathological alterations within the liver was observed following phospholipid administration. Additionally, biochemical parameters exhibited a tendency towards normalisation and stability, while the severity of histological inflammatory and degenerative changes in the liver also demonstrated a decline. This resulted in an

improvement in the clinical status and laboratory results of the patients (21, 22). Similar results have been obtained in studies of liver fibrosis and liver failure caused by toxins such as carbon tetrachloride or drugs such as isoniazid (19, 20, 22). Phospholipids were used together with mangiferin for 7 days in rats given a single dose of carbon tetrachloride on day 8. The study showed a decrease in ALT, AST, ALP and bilirubin activity and an increase in total protein levels (19). In an experimental poisoning study with isoniazid (an anti-tuberculosis drug), the effects on liver function, oxidative stress, levels of the tumour necrosis factor TNF-α and interleukin 10 were investigated. The results demonstrated antioxidant effects, decreased levels of bound and free bilirubin, TNF-α, decreased ALT activity, ALP, and increased levels of the anti-inflammatory IL-10. This corroborates the study by Jaisval et al., who found that phospholipids protect hepatic cells and mitochondrial membranes by increasing cell proliferation and incorporation of drug-metabolising enzymes into the cytoplasmic reticulum (9). The hepatoprotective and anti-inflammatory effects of phospholipids have also been documented in the treatment of hepatitis C in humans (6). They impede the transfer of collagen mediated by TNF β1, thus preventing its accumulation (1). Phospholipids have been also shown to have a protective effect on the liver of patients on parenteral nutrition, which can lead to a disruption of hepatocyte structure and function and an increase in liver enzyme activity. In the study group receiving phospholipids, a statistically non-significant increase in ALT activity was observed after two weeks, whereas a statistically significant increase in ALT, AST, and GGTP activity was noted in the control group (12). Additionally, phospholipids have been demonstrated to lower cholesterol, alleviate pain and indigestion symptoms, and normalise biochemical parameters (15). The normalisation of biochemical parameters in the dogs studied provides further evidence to support this. It is also noteworthy that phospholipids exert a range of beneficial effects beyond their impact on the liver. They play a pivotal role in the physiology and pathology of cell membranes and membrane structures of intracellular organelles, serving as the fundamental structural and functional building blocks of these structures. Moreover, they are indispensable in the processes of cell differentiation, proliferation and regeneration. Phosphatidylcholine is a constituent of blood and bile lipoproteins, forming a protective barrier in the gastrointestinal tract and lungs. In conclusion, the antioxidant, anti-inflammatory, anti-fibrotic, regenerative, restorative and protective effects of phospholipids have been demonstrated in vitro and in animal studies. Improvements in clinical, biochemical, imaging and histological parameters have been observed in cases of hepatic steatosis, drug-induced liver injury, viral hepatitis and hepatic coma (7). Amino acids, particularly L-arginine and L-glutamine, also play a significant role in hepatoprotection and hepatocyte regeneration. In a study conducted by Haroun et al. (8), liver damage was induced in 70 mice through the administration of nanoparticulate copper oxide. The accumulation of copper in the liver resulted in the manifestation of liver damage, as evidenced by an increase in ALT activity, a reduction in hepatic arginase activity, a decline in total protein levels, and a transformation in liver architecture. The mice were treated with arginine, quercetin, and a combination of arginine and quercetin for a period of eight weeks. There was a notable reduction in ALT activity and an increase in total protein levels. Additionally, compared to the control group, there was a significant decrease in plasma TNF-α levels, indicating the conclusion of the inflammatory process. In another study, liver damage in rats was induced by intraperitoneal administration of carbon tetrachloride, which initiated the process of lipid peroxidation. The rats were then administered arginine for six days. The liver tissues collected were subsequently analysed for a range of enzymes, including catalase, glutathione reductase and glutathione S-transferase. The livers of the rats that did not receive arginine showed a reduction in antioxidant enzyme activity. The administration of arginine resulted in elevated glutathione levels, which enhanced the activity of all antioxidant enzymes. Administration of arginine has been observed to exert a hepatoprotective and hepatolytic effect on oxidative stress and liver damage. Additionally, the therapeutic effect of arginine has been demonstrated to be more pronounced than its protective effect (23). The impact of L-arginine on post-inflammatory liver damage induced by E. coli has also been investigated. A lipopolysaccharide (LPS) suspension of E. coli was administered intraperitoneally to weaned piglets to induce inflammation, which was hypothesised to occur via the TLR 4 signalling pathway. Serum AST, GGT and ALP activities were examined. Pigs were provided with a 0.5% arginine solution mixed with feed. Administration of LPS was observed to increase liver enzyme activity. However, arginine supplementation decreased this activity and had a beneficial effect on the effects of organ damage in LPS pigs. It is possible that the protective effect of arginine on the liver is related to a reduction in the release of pro-inflammatory cytokines and free radicals through inhibition of TLR 4 signalling (14). In another study, L-glutamine was used to regenerate the liver in rats that had had 60% of the organ removed. The experimental design encompassed the determination of liver weight, the assessment of laboratory parameters

(AST, ALT, GGT, TB, indirect and direct bilirubin, ALB), and the examination of liver histopathology. The test group was administered glutamine in the form of an aqueous solution. Follow-up assessments were conducted at 24, 72 hours, and seven days post-hepatotomy. There was a significant increase in liver weight and albumin levels in the test group. The control group also demonstrated an increase in liver weight, accompanied by an increase in GGT activity. Histopathological examination revealed a higher number of mitoses in the hepatocytes of the glutathione-treated group. These findings suggest that dietary supplementation with glutamine may facilitate liver regeneration (16).

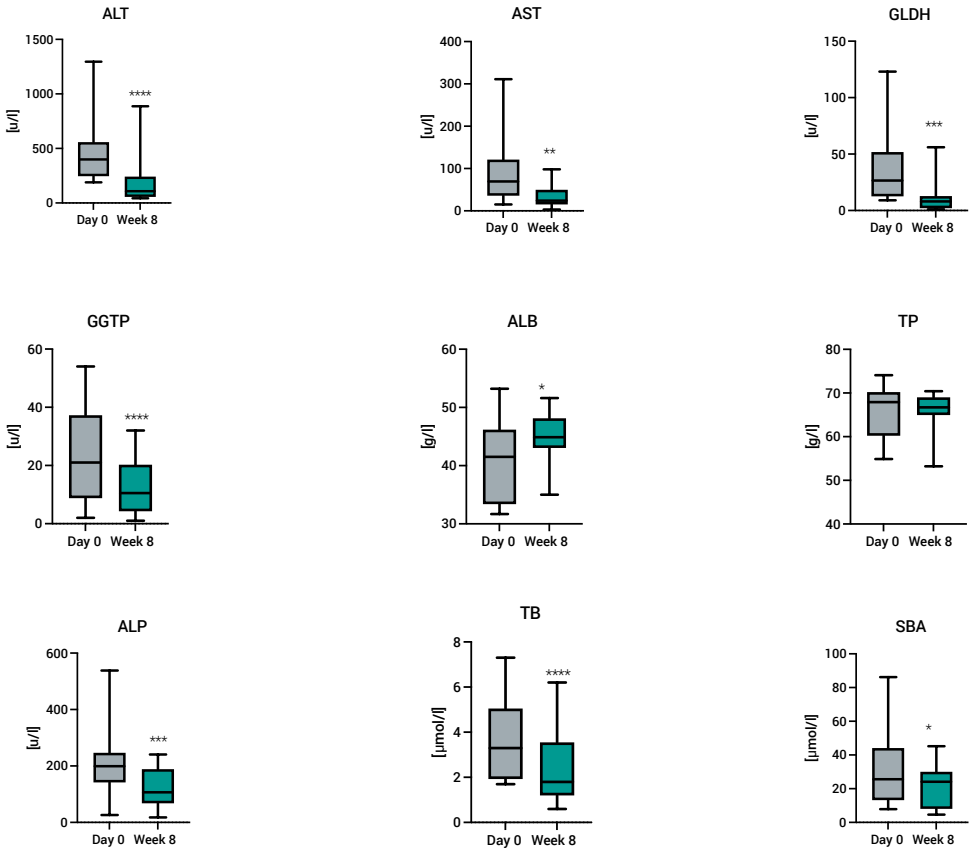
The results of in-house studies have confirmed the beneficial effects of phospholipids and amino acids on liver condition and function. The elevated liver enzymes observed in the patients studied on day '0' without any accompanying clinical symptoms are indicative of liver cell damage. After 8 weeks of administration, a statistically significant decrease and/or normalisation of liver enzymes ALT, AST, ALP, GGTP, GLDH was observed in the vast majority of patients. Furthermore, levels of total protein, albumin, glucose, total bilirubin and bile acids may indicate adequate liver function. Whether the cause of the changes is due to drugs, toxins, diet, post-inflammatory, infectious or senile changes, in all these cases a reduction in liver enzymes was achieved after taking only a dietary supplement containing phospholipids and L-arginine and L-glutamine. This may be evidence of the effective and beneficial effect of Hepatiale Forte on liver function. In the context of the data obtained by other researchers, it is worth considering whether the therapeutic and protective effects of phospholipids and amino acids should be exploited and used on a long-term basis.

References

1. Cao O., Mak K.M., Lieber C.S.: Dilinoleoylphosphatidylocholine prevents transforming growth factor - beta1 - mediated collagen accumulation in cultured rat hepatic stellate cells. J Lab Clin Med, 2139, 202 - 210, 2002
2. Center S.A., Strombeck D.R.: Liver: Normal Structure and Function. W: Grant Guliford W., Center S.A., Strombeck D.R., Williams D.A., Meyer D.J. eds. Strombeck´s Small Animal Gastroenterology. 3. Ed Philadelphia, W.B. Saunders Company, 540 – 552, 1996
3. Center S.A.: Chronic Hepatitis, Cirrhosis, Breed-Specific Hapatopathy, Suppurative Hepatitis, Granulomatous Hepatitis, and Idiopathic Hepatic Fibrosis. W: Grant Guliford W., Center S.A., Strombeck D.R., Williams D.A., Meyer D.J. eds. Center S.A.: Diseases of the Gallbladder and Biliary Tree. W: Grant Guliford W., Center S.A., Strombeck D.R.,
4. Center S.A.: Hepatic lipidosis, glucocorticoid hepatopathy, vascuolar hepatopathy, storage disorders, amyloidosis and iron toxicity. W: Grant Guliford W., Center S.A., Strombeck D.R., Williams D.A., Meyer D.J. eds. Strombeck´s Small Animal Gastroenterology. 3. Ed Philadelphia, W.B. Saunders Company, 782, 788
5. Cooper J., Webster C.R.L.: Postępowanie diagnostyczne u psów bez objawów klinicznych I z podwyższoną aktywnością enzymów wątrobowych. Weterynaria po Dyplomie, 9,1, 6 - 14, 2008
6. Falasca K., Ucciferri C., Mancino P., Vitacolonna E., De Tullio D., Pizzigallo E., Conti P., Vecchiet J.: Treatment With Sylibin-Vitamin E-Phospholipid Complex in Patients With Hepatitis C Infection. J Med Virol, 80, 1900 - 1906, 2008
7. Gundermann K.J., Kuenker A., Kuntz E., Droździk M.: Activity of essentials phospholipids (EPL) from soybean in liver diseases. Pharmacol Rep., 63, 3, 643 - 59, 2011
8. Haroun A.H., El-Sayed W.M., Hessan R.E.: Quercetin and L-Arginine Ameliorated the Deleterious Effects of Copper Oxide Nanoparticles on the Liver of Mice Through Anti-inflammatory and Anti-apoptotic Pathways. Biol Trace Elem Ros, 202(7), 3128 - 3140, 2024
9. Jaiswal R.K., Rama Sastry B.V., Landon E.J.: Changes in microsomal membrane microviscosity and phospholipid methyltransferases during rat liver regeneration. Pharmacology, 24,6, 355 - 65, 1982
10. Konstantynowicz K., Mikłosz A., Stepek T., Chabowski A.: Akumulacja lipidów (triacylo-diacylogliceroli i ceramidów) wewnątrz hepatocytów, a rozwój insulinooporności wątrobowej. Postępy Hig Med. Dosw, 65, 236 - 243, 2011
11. Kozłowska – Wojcechowska M.: Niezbędne fosfolipidy.Terapia, 6,2, 13-15, 2014
12. Lata J., Dastych M. Jr., Senkyrik M., Husova M., Stary K.: Protective effect of Essentials phospholipids on liver injury due to Total parenteral nutrition. Vnitr Lek, 47, 9, 599 - 603, 2001
13. Lechowski R. red: Choroby wątroby psów i kotów, Wydawnictwo SIMA,41 - 43, Warszawa 2003
14. Li Q., Liu Y., Che Z., Zhu H., Meng G., Hou Y., Ding B., Yin Y., Chen F.: Dietary L-arginine supplementation alleviates liver injury caused by Escherichia coli LPS in weaned pigs. Innate Immun, 18(6):804 - 14, 2012
15. Ma X., Zhao J., Lieber C.S.: Polyenylphosphatidylcholine attenuates non-alkoholic hepatic fibrosis and accelerates its regression. J Hepatol, 24, 604 - 613, 1996
16. Magalhães C.R., Malafaia O., Martins Torres O.J., Bugmann Moreira L., da Silva Gonçalves Tefil S.C., da Rocha Pinherio M., Harada B.A.: Liver regeneration with l -glutamine supplemented diet: experimental study in rats. Rev Col Bras Cir, 41(2):117 - 21, 2014
17. Matuszak M., Suliborski J.: Rola argininy w prewencji i leczeniu chorób metabolicznych. Forum Zaburzeń Metabolicznych, 3, 3, 50 - 53, 2012
18. Min-Hyun K., Hyeyong K.: The Roles of Glutamine in the Intestine and Its Implications in Intestinal Diseases. Int J Mol SCi, 18 (5), 1051, 2017
19. Sauvik B., Sk Milan A., Bishnu P.S., Pulok K.M.: Soya phospholipid complex of mangiferin enhances its hepatoprotectivity by improving its bioavailability and pharmacokinetics. J Sci Food Agric, 94, 1380 - 1388, 2014
20. Udut V.V., Vengerovskii A.I., Burkova V.N., Vaizova O.E., Korshunov D.A.: The effect of phospholipid hepatoprotectors on lipid peroxidation in liver and content of cytokines in the blood in experimental pathology caused by isoniazid. Eksp Klin Gastroenterol, 6, 47 - 52, 2012
21. Vasilevskaia A.S., Butov M.A., Uzbekova D.G., Mnikhovich M.V., Nikiforov A.A.: Hepatoprotectors in treatment of alcoholic liver disease. Eksp Klin Gastroenterol, 12, 79 - 82, 2013
22. Venkatesh M., Kakali M., Kuntal M., Pulok K.M.: Enhanced Oral Bioavailability and Antioxidant Profile of Ellagic Acid by Phospholipids. J Agric Food Chem, 57, 11, 4559 -4565, 2009
23. Voloshin I., Hahn - Obercyger M., Anavi S., Tirosh O.: L-arginine conjugates of bile acids-a possible treatment for non - alcoholic fatty liver disease. Lipids Health Dis, 4, 22:13:69, 2014
24. Zdrojewicz Z., Winiarski J., Popowicz E., Szyra M., Śmieszniak B.: Rola argininy w organizmie człowieka. Zeszyty Naukowe państwowej Wyższej Szkoły Zawodowej im. Witelona , 1,30, 163 - 171, 2019

TABLES AND FIGURES

Fig. 1. Changes in plasma levels of selected liver parameters in dogs given Hepatiale Forte or Hepatiale Forte Large Breed Liver Support (VetExpert) for 8 weeks. ALT – alanine aminotransferase activity; AST – aspartate aminotransferase activity; GLDH – glutamic dehydrogenase activity; GLTP – gamma glutamyl transpeptidase activity; ALB – albumin concentration; TP – total protein concentration; ALP – alkaline phosphatase activity; TB – total bilirubin concentration; SBA – bile acid concentration. The presence of * indicates statistically significant differences at p<0.05; ** at p<0.01; *** at p<0.001 and **** at p<0.0001.



Tab. 1. Values of haematological parameters in dogs treated with Hepatiale Forte or Hepatiale Forte Large Breed for 8 weeks.

Index (unit)	Day 0 (mean ± standard deviation)	Week 8 (mean ± standard deviation)	Statistical significance (p-value)
White blood cell count (Lkcs 10^9/l)	8.990 ± 2.287	8.790 ± 1.817	No (p=0.5384)
Red blood cell count (Erys 10^{12}/l)	6.665 ± 0.764	6.775 ± 0.665	No (p=0.4270)
Haemoglobin concentration (mmol/l)	14.63 ± 1.628	14.69 ± 1.730	No (p=0.8413)
Haematocrit (%)	49.7 ± 4.7	49.3 ± 2.8	No (p=0.5895)
Platelet count (PLT 10^9/l)	276.5 ± 65.3	276.7 ± 41.7	No (p=0.9847)
Neutrophil count (Neut 10^3/l)	7.795 ± 2.469	7.145 ± 1.431	Yes (p=0.0321)
Lymphocyte count (Lymph 10^3/l)	3.553 ± 1.778	3.085 ± 0.938	No (p=0.0788)
Monocyte count (Mono 10^3/l)	0.860 ± 0.535	0.770 ± 0.326	No (p=0.1625)
Basophil count (Baso 10^3/l)	0.085 ± 0.104	0.055 ± 0.051	No (p=0.2088)
Eosinophil count (Eos 10^3/l)	0.220 ± 0.219	0.170 ± 0.126	No (p=0.3665)