SUMMARY

Liver failure is a complex morbid entity, being the expression of the liver failure to perform one or more of its functions in the body: synthesis, metabolic, immune, storage, digestive, detoxification and excretion.

Many synthetic drugs administered for a long time proved to have traumatic effects on liver function by acting against the intentions to heal.

As a result, various studies based on hepatotoxicity induced on different experimental animal models have been performed nationally and worldwide, demonstrating the extraordinary ability of phytopreparations to restore unbalanced liver function and increase the resistance of the hepatocyte to various harmful factors.

Although the use of herbal remedies is increasing in veterinary medicine, there are few scientific and clinical studies on the role of phytopreparations in the prophylaxis and reduction of liver imbalances in pets.

Since this has not been further investigated, there is a possibility that the importance of using phytotherapy in restoring compromised liver function in pets may be underestimated.

The doctoral thesis entitled **"The hepatoprotective effect of some phytopreparations in pet carnivores"** aimed to evaluate the effectiveness of natural antioxidants obtained from plants in the therapy of various liver diseases in dogs and cats.

The choice of the theme of this thesis was motivated by the desire to rediscover phytotherapy, a discipline as ancestral as it is new that provides unsuspected therapeutic perspectives, the increased interest in using phytotherapy as a complementary method of prevention, amelioration or cure of liver disorders, multifactorial etiology and pathophysiological complexity of liver disease.

The thesis was written and structured in two main parts according to current scientific standards. For documentation were used 153 bibliographic references.

The first part, structured in four chapters, reflects the synthesis of the study of the literature on the current state of knowledge of the etiopathogenesis of liver failure, diagnosis of liver disease, classical drug therapy and plants used in the ancillary treatment of liver disease in dogs and cats.

The first chapter presents current data defining liver failure, highlighting the pathophysiological links of the main specific syndromes: jaundice, ascites, hepatic encephalopathy and coagulopathy, essential elements for understanding the clinical picture, evolution and prognosis of liver disease.

Chapter two summarizes the stages of clinical and paraclinical diagnosis of liver disease with detailed presentation of general paraclinical investigations (hematological examination, serum and urine biochemistry) and special ones (ascitic

fluid examination, radiological and ultrasound examination, liver biopsy, histological evaluation , nuclear magnetic resonance and computed tomography).

Clinical and paraclinical investigations do not have a maximum specificity or sensitivity, the success of the diagnosis and implicitly of the therapy, being the result of the judicious use of the information obtained by all these methods, often being necessary the repeated use of test batteries.

Chapter three extensively develops the desideratum of the classical therapy of liver diseases in dogs and cats. Emphasis is placed on complex therapeutic management that focuses on both the restoration of compromised liver function and all associated organ dysfunction.

Chapter four is structured in two subchapters. The first subchapter addresses the key elements applied in phytotherapy of hepatobiliary diseases.

Hepatoprotective phytopreparations help to relieve symptoms, reduce disease duration and mortality. The second subchapter presents a synthesis from the scientific literature of the hepatoprotective pharmacological properties of the active substances from the studied plants: milk twistle (silymarin), sea buckthorn, curcumin and artichoke.

The second part, **"Personal research"** is structured in five chapters. It begins with a description of the motivation, purpose and objectives pursued for its achievement and ends with the presentation of the final conclusions on the studies addressed. Each chapter describes the objectives of the studies, the materials and methods, the results obtained, their discussion and the underlining of partial conclusions.

Chapter five is a retrospective study of the incidence and etiopathogenesis of liver diseases in canine and feline patients presented between 2014 and January 2018 at the Medical Clinic of the Faculty of Veterinary Medicine in Iasi.

Out of the total of 3842 patients registered during the study period, 198 (5%) expressed different forms of hepatic-biliary suffering, the prevalence of cases in the canine species - 154 (80%) being significantly increased compared to the feline - 44 (20%).

The age of animals diagnosed with various liver diseases ranged from 4 months to 17 years in dogs and 2 months to 23 years in cats. There was a slightly increased frequency of liver disease in animals up to 5 years.

Regarding the sex criteria, there was an increased predominance of liver disease in male canine (56%) compared to female (21%). The same was reported for cats, but to a lesser extent: 12% male cats / tomcat and 11% female cats.

The evolution of hepato-biliary diseases was evident in 45 dogs of the common breed (29%), followed by 29 half-breeds (19%), 21 German Shepherds (14%), 13 Bichon (8%) and 10 of the Rotweiller breed (6%). The least cases were registered with the representatives of the Cocker (9 cases, respectively, 6%), Schnauzer (7 cases, respectively, 5%) and Mioritic Shepherd (5 cases, respectively,

3%). Other breeds (5%) were 1 Bourdeaux Dog, 1 Amstaff, 1 Pit Bull Terrier, 1 Shih Tzu, 1 Westie and 2 Yorkshire Terriers. Most hepato-biliary lesions were diagnosed in 7 European cats (61%) and 8 Burmese cats (18%). Persian (2) and Siamese (2) cats were the least affected (5%). Other breeds were represented by 1 British Shorthair, 1 Russian Blue, 1 American Shorthair, 1 Scottish Fold and 1 Siberian half-breed.

Depending on the etiopathogenesis, the most diagnosed hepato-biliary diseases in dogs and cats consulted in the Medical Clinic of F.M.V. Iaşi in the doctoral period, were those caused by infectious factors of parasitic and viral nature, toxic liverworts and pathological echoes. secondary to functional, metabolic or neoplastic multisystemic disorders.

Chapter six, **"Research on the clinical diagnosis of liver diseases in dogs and cats"** aimed to highlight, depending on the observed etiopathogenetic factors, the clinical signs characteristic of the installation of a disease with hepato-biliary impact, their evolution from the most insignificant signs of disease to complications resulting from decompensation of liver function.

The study was performed in 146 patients with manifestations associated with a hepato-biliary disorder of various etiologies and in different stages of the disease, of which 104 were dogs and 42 cats. The age of the animals varied between 4 months and 17 years in dogs and between 2 months and 23 years in cats, the average age for the entire population being 11.5 years. Patients were selected based on clinical, laboratory and imaging criteria to certify the evolution of a liver pathology.

The analysis of the accumulation of symptoms specific to liver disease revealed a high percentage of jaundice syndrome in 78.08% (114 patients), followed by ascites syndrome in 21.23% of cases (31 patients), the signs of coagulopathy being reported in only 6 patients. - 4.10% of the total cases analyzed.

Secondary, non-specific clinical manifestations evolved in parallel with the characteristic signs of liver disease, with relativly high incidence, in the studied group of 96.57% (141 patients). Clinical signs of biliary involvement had a share of 17.80% (26 patients).

Chapter seven, "Research on the paraclinical diagnosis of hepatopathies in dogs and cats, highlighted and corroborated the clinical signs with biochemical, hematological and ultrasound aspects in canine and feline patients who expressed symptoms of liver damage and was monitored and evaluated cerebral bioelectrical activity in 6 dogs diagnosed with babesiosis. The analysis of the results of the main biochemical parameters used to assess the intensity, complexity and predominance of hepatic morpho-functional impairment revealed significant increases in mean values above physiological limits. The activity of hepatic transaminases ALT and AST was significantly increased, more than 10 times compared to normal values in hepatitis of viral origin or liver cirrhosis.

The enzymes of the cholestatic syndrome, ALP and GGT, registered normal or slightly modified values in all parenchymal hepatopathies (hepatitis and cirrhosis) as well as in bladder and bile duct diseases - angiocolecystitis. Significant increases in total bilirubin have been reported in liver diseases associated with jaundice syndrome - hepatitis, cirrhosis, as well as in jaundice caused by parasitic hemolytic anemias - babesiosis. Low serum glucose levels were detected in the final stage of cirrhosis or in liver tumors. The results of the hematological examination showed in all hepatopathies the presence of normochromic normocytic anemia, neutrophilia with left deviation of the neutrophilic index, leukocytosis, monocytosis, eosinopenia, lymphopenia, thrombocytopenia and the presence of an intraerythrocytic parasitosis. An inflammatory leukogram has been reported for neoplastic or infectious processes (babesiosis, PIF). Analysis of ascitic fluid revealed color changes that varied depending on the type of hepatopathy from pink to straw yellow in inflammatory to bloody processes in neoplastic processes with associated inflammation.

In dogs diagnosed with neoplastic processes, the necropsy examination showed metastasis to the liver of head tumors of the pancreas, stomach, intestine or kidney.

Cytological examination of ascitic fluid in viral diseases (feline infectious peritonitis - PIF) showed in most cases the presence of inflammatory cells: numerous degenerated neutrophils, foamy-looking macrophages or cytophagocytosis, rare lymphocytes and plasmacells, rare red blood cells and erythrophagocytosis and an eosinophilic background due to the abundance of proteins. Ultrasonography of the liver of the patients studied allowed the identification of both diffuse morphological changes that corroborated with data obtained from other categories of tests allowed the diagnosis to focus on the evolution of hepatopathy and obvious organ damage in advanced stages, by identifying a wide range of physical and functional changes. In all dogs with babesiosis that showed neurological signs, EEG examination of brain activity showed epileptiform discharges.

Chapter eight describes a study on classical drug therapy of liver disease in 23 dogs and 4 cats that were divided into 3 groups according to the etiopathogenesis of the reflected symptoms: ascites, jaundice and cholestasis.

Drug treatment was initiated in order to improve the affected liver function. A positive therapeutic result was obtained after therapy with antioxidants of plant origin in mild and moderate forms of liver disease.

In the case of pathologies in the terminal stage (liver cirrhosis, neoplasia), the classic drug therapy associated with hepatoprotective phytopreparations had a palliative character, with the temporary improvement of the quality of life.

Chapter nine, **"Research on auxiliary phytotherapy of hepatopathies in dogs and cats"** is structured in two subchapters.

The first subchapter estimates the hepatoprotective role of some phytopreparations and products of mineral origin, respectively: silymarin, curcumin,

sea buckthorn and zeolite in different hepatopathies in 33 patients (25 dogs and 8 cats) divided into 3 groups depending on the clinical condition expressed. In all patients in the studied groups, there was a significant improvement in clinical status, liver transaminases and biochemical indices of cholestasis (alkaline phosphatase).

Second subchapter describes the retrospective evaluation of the effects of complementary treatment in 18 patients (13 dogs and 5 cats) at one month and six months after initiating outpatient treatment with associations of antioxidant drugs, such as: silymarin, sea buckthorn oil, vitamin E, pentoxifylline with acetylcysteine, coenzyme Q10 and choleretics: ursodeoxycholic acid, artichoke extract (Anghirol). The positive therapeutic effect was observed in mild and moderate forms of liver disease, in case of severe liver disease, phytotherapeutics had a palliative character expressed by transient decrease in clinical signs and temporary improvement in quality of life or no therapeutic response, with evolution to exitus (4 deaths).

As concluding remarks, we mention that phytotherapy had a favorable result in mild and moderate forms of liver disease. In the case of severe liver disease, phytotherapy was palliative, with a transient decrease in clinical signs and a temporary improvement in quality of life or was without a therapeutic response.

The improvement in the clinical condition of the patients was confirmed by the significant improvement of the hepatic functional parameters (decrease of ALT, AST, ALP and GGT). In patients with good therapeutic responses, it is necessary to establish a maintenance therapy with periodic ultrasound and biochemical monitoring of liver indices.