THE HEPATOPROTECTIVE EFFECT OF SOME HERBAL AND MINERAL PREPARATIONS IN THE TREATMENT OF VARIOUS HEPATOPATHIES IN DOGS AND CATS

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Abstract

A series of herbal medicines and minerals such as milk thistle, curcumin, sea buckthorn, artichoke and zeolite can be used as alternative solutions in scavenging oxygen free radicals incriminated in triggering of liver disease. The aim of this study was the therapeutic application of different herbal and mineral preparations with antioxidant properties and evaluation of their hepatoprotective potential in the complex therapy management of various types of liver disorders diagnosed in dogs and cats. The study was performed between October 2016 – September 2017 on 16 dogs and 4 cats of different breeds, sexes and ages which were presented and diagnosed with different degrees of liver failure in Medical Clinic of the Faculty of Veterinary Medicine from Iasi. Anamnesis and physical examination have highlighted that the clinical onset of liver disease was nonspecific, in most cases, the diagnosis of a liver disorder could be deduced from the results of the biochemical tests corroborated with the ultrasound findings. The therapeutic management of liver disease has depended on the etiopathology, the degree of biochemical resonance of the cytolytic, cholestatic process and the synthesis imbalance in the liver as well as the presence or absence of complications of the liver pathology. Thus, according to the established protocol, patients were divided in three groups and they received the basic drug treatment in combination with hepatoprotective preparations of vegetal and mineral origin, respectively, milk thistle (silymarin), curcumin, sea buckthorn and zeolite. The inclusion of phytotherapy in the complex treatment of liver disease has contributed to the normalization of hepatic transaminases and cholestasis parameters. A positive therapeutic result was obtained after therapy with antioxidants from vegetable origin in mild and average forms of liver disease. In the final stage of the liver disease, treatment with natural hepatoprotective agents had a palliative character with transient reduction of clinical signs and temporary improvement of quality of life.

Keywords*:antioxidant, cytoprotection, hepatoprotective activity, herbal medicines, liver disease*

Introduction

In the last decade, a multitude of pharmacotoxicological studies have been carried out in animal models and human clinical trials in order to find natural solutions for decontracing adverse reactions of synthetic drugs, restoring unbalanced hepatic functions and increasing hepatocyte resistance to the action of various harmful factors. The association of allopathic therapies with plant supplements is gaining ground to potentiate the therapeutic strategies and prevent adverse effects. A series of plant compounds with proven antioxidant principles, such as flavonoids, polyphenols, carotenoids complexes, tocopherols, terpene, phytosterols, ascorbic acid, can be used in scavenging oxygen free radicals incriminated in triggering liver pathology (Stănescu and al., 2002). Thus, numerous studies have concluded that biologically active substances found in certain plants such as milk thistle, sea buckthorn, artichoke, curcumin have the role of rebuilding the hepatic cell and increasing the ability of the liver to defend against oxidative stress.

Material and methods

The study was conducted between October 2016 and September 2017 at the Medical Clinic of the Faculty of Veterinary Medicine in Iaşi and included 16 patients with clinical signs and biochemical results associated with a hepatobiliary disorder, of which 12 were dogs and 4 cats of

different ages, sexes and breeds. Patients underwent a clinical, biochemical and ultrasound examination. The evaluation of each patient's condition involved the development of an individual clinical diagnosis card that included data from the history of the disease (early signs of the disease, preexisting or coexisting conditions, potential hepatotoxic treatments, vaccine status, diet) and data on the current state of the animal at the time of consultation obtained by general semiological methods. Functional liver status was assessed according to basic biochemical syndromes: cytolytic (ALT / TGP, AST / TGO), cholestasis (GGT, alkaline phosphatase / ALP) and insufficient synthesis function (total protein, urea and serum glucose).

The ultrasound examination of abdominal organs was performed using Aquila Pro Vet with a convex probe of 5 and 7.5 MHz to highlight the changes in size, shape and echogenity of the liver, canals and gall bladder, spleen and stomach before and after treatment.

The therapeutic management of liver disease depended on the etiopatology, the degree of biochemical resonance of the cytolytic, cholestatic process and the synthesis imbalance in the liver as well as the presence or absence of complications of the liver pathology. Thus, according to the established protocol, patients received basic drug therapy in combination with hepatoprotective preparations from herbal and mineral origin, respectively, silymarin (milk thistle), curcumin, sea buckthorn, artichoke and zeolite (Table 1).

Table 1

Herbal and mineral medication used in outpatient / hospital treatment of hepatopathies in dogs and cats

Herbal / mineral product Active ingredient	**Indications**	**Dose, duration and frequency of treatment**
Milk thistle Silymarin / silybin	Different types of liver disorders, Cholangitis Cholecystitis	20-50 mg/kg/day/p.o., 1-2 months, 2-3 times/year
Curcumin		350 mg/day/p.o., 1-3 months
Artichoke		3.25 mg/p.o., 30 days
Sea buckthorn		300 mg/animal/p.o., 1-2 months, 2 times/year
Zeolite		600 mg/animal/day/p.o, 3 months

The duration of treatment was between 1 - 3 months, 2-3 times/year. Regarding the classic hepatic therapy strategies, it has been used IV fluid therapy with isotonic solutions (0.9% Saline, Ringer, glucose 5%), antioxidants (ascorbic acid - vitamin C, tocopherol - vitamin E, N - acetylcysteine), vitamins (thiamine, pyridoxine), anti-hemorragic agents (phytomenadione, ethamsylate), diuretics (spironolactone and furosemide), antisecretory drugs (H2 antagonists: ranitidine, famotidine and proton pump inhibitors: pantoprazole), choleretic agents (dry artichoke extract, ursodeoxycholic acid), antibiotics (amoxicillin and clavulanic acid, metronidazole, enrofloxacin, third generation cephalosporin: ceftriaxone,), glucocorticoids (prednisone, methylprednisolone, dexamethasone), antipyretic (metamizol).

Depending on the treatment applied, the patients were divided into 3 groups:

● Patients with jaundice secundary to an acute toxic hepatitis or parasitic hepatitis (babesiosis, dirofilariosis) who received silymarin + sea buckthorn (4 dogs) and silymarin + curcumin (2 dogs) for 30 days;

● Patients with ascitic syndrome as a result of a straight heart failure or a neoplastic process (2 dogs), which has been prescribed the combination of silymarin + sea buckthorn + curcumin + zeolite for 3 months, 2-3 times/year;

● Patients with cholestasis syndrome in angiocolites, colangitis, triadites (2 dogs and 4 cats) who received silymarin + sea buckthorn + artichokes for 30 days.

Results and discussions

Of the 16 patients diagnosed with different hepatopathies, 14, respectively 10 dogs and 4 cats of different breeds, sexes and ages responded positively clinically and biochemically to therapy with hepatoprotective plant products (Table 2).

Anamnesis and clinical examination have highlighted that the clinical onset of liver disease was nonspecific and included the appearance of a dyspeptic syndrome such as loss of appetite, nausea and vomiting, intestinal metheorism, diarrhea or constipation, abdominal colic, various degrees of dehydration, discrete to severe weight loss within a few weeks, polyuria / polydipsia, hyperkeroma urine, apathy to coma, multiple organ failure, and symptoms of advanced hepatic disease such as ascites, jaundice and coagulopathy (bruising, petechiae). In most cases, the diagnosis of a liver disorder could be deduced from the paraclinical results corroborated with the ultrasound findings. In terms of hepatobiliary pathology in patients following adjuvant therapy with herbal active principles have prevailed toxic hepatitis (7/10 dogs), ascites secondary to neoplasia or heart failure (2/10 dogs); and in cats have predominated cholangiohepatitis (2/4 cats) and triadites (2/4) (Table 2).

Table 2

Hepatic biochemical changes (values before and after treatment) in dogs and cats diagnosed with different hepatopathies

ALT alanine aminotransferase, AST aspartate aminotransferase, ALP alkaline phosphatase, GGT –glutamyl transferase, BUN - Blood urea nitrogen

No.	Patient	Diagnosis	Previous treatment	Phytohepato-protective products	Biochemical changes
1.	**2.**	**3.**	**4.**	**5.**	**6.**
1.	Dog Shit-Tzu, ♀, 2 y, 3.6 kg	Gastroenteritis Pyloric spasm Toxic hepatitis	Imizol	Silymarin 150 mg/day, 1 month Sea buckthorn, 2X300mg /day, 1 month	AST 317→30 ALT 215→105 ALP 255→181 BUN 57→25
2.	Dog, Mixed breed, ♀, 12 y,3 kg	Hepatic failure Jaundice Polyradiculo-neuritis	Antibiotics Imizol Physiotherapy	Silymarin 150 mg/day, Curcumin 350mg/day, 1 month	ALT 77→39 AST 333→119 GGT 23→12 ALP 184→110

3.	Dog, Bichon, ♂, 5 y, 8 kg	Hemorrhagic gastroenteritis Toxic hepatitis Acute kidney injury (AKI) Urinary lithiasis Prostatitis	Dental scaling Uretrostoma	Silymarin 2X150 mg /day, Curcumin, 350mg/ day, 3 months	AST 219→29 ALT 284→48 BUN 34→33.5
4.	Dog, Mixed breed, ♂, 10 y	Babesiosis Heartworm	Imizol Doxycycline	Silymarin, 250 mg/day Sea buckthorn, 2X300 mg /day	ALT 123→87 AST 56→25
5.	Dog, Bichon, ♀, 8 y, 8kg	Congestive heart failure Hepatomegaly Ascites	Paracentesis	Silymarin, 2X150 mg/day; Sea buckthorn, 300 mg/day, Curcumin, 500 mg/day, 3 months; Zeolit clinoptilolit, 600 mg/day, 6 months	No changes
6.	Dog, Boxer, ♀, 14 y, 10 kg	Hepatobiliary carcinoma Ascites	Paracentesis	Silymarin, 2X150 mg/day; Sea buckthorn, 300 mg/day, Curcumin, 350 mg/day, 3 months; Zeolit clinoptilolit, 600 mg/day, 3 months	ALT 192→100 AST 76→55 ALP 1345→1200 GGT 31→24
7.	Dog, Akita Inu, ♂, 9 y, 25 kg	Babesiosis Acute liver failure Jaundice Acute kidney injury (AKI)	Imizol	Silymarin, 2X150 mg/day; Sea buckthorn, 2X300 mg/day 1 month	ALT 87→44 AST 329→117 ALP 157→103 BT 4,57→0,2
8.	Dog, Caniche, ♂, 7 y, 20 kg	Cholangiohepatitis Jaundice Babesiosis	Imizol	Silymarin, 2X150 mg/day; Sea buckthorn, 2X300 mg/day 1 month	ALT 92 →45 AST 58 →11 ALP 98→97 GGT 4→no changes
9.	Dog, Westie, ♀, 15 y, 6 kg	Cholangiohepatitis Polyradiculo-neuritis	Ursofalk 250 mg/day	Curcumin 350 mg/day, Silymarin, 100mg/day, Artichoke 3.25 mg/day, 6 months	ALT 167→30.3 AST 47.7→23.5 ALP 353→69.1 GGT 8.93→2.80

10.	Dog, Terrier, ♂, 7 y	Arthritis Cholestasis	AINS	Silymarin, 150mg/day, Sea buckthorn, 2X300 mg/day Artichoke 3.25 mg/day, 21 days	ALP 1056→165 AST 365→102
11.	Cat, Mixed breed, ♀, 6 y, 3,6 kg	Dyspepsia Triadites	Antibiotics	Silymarin, 150mg/day, Sea buckthorn, 300 mg/day 3 months	ALT 105→64 AST 174→19
12.	Cat, European Shorthair, ♂ 10 y, 3 kg	Chronic kidney injury Hepatic failure Triadites	IV fluid therapy	Silymarin, 150mg/day, Sea buckthorn, 300 mg/day 1 month	ALT 136→46 ALP 97→44
13.	Cat, British Shorthair, ♀, 4 y	Cholangitis/ Cholangiohepatitis syndrome (CCHS)	Antibiotics	Silymarin, 150 mg/daily, 3 weeks, Artichoke, 3.25 mg/daily, 2 weeks	ALP 86→61 ALT 57→45 GGT 7 →no changes
14.	Cat, European Shorthair, ♀, 6 y	Cholangitis/ Cholangiohepatitis syndrome (CCHS)	Antibiotics	mg/daily, 3 weeks, Artichoke, 3.25 mg/daily, 2 weeks Sea buckthorn, 2 X 300 mg/day 1 month	No biochemical changes

All patients had a positive clinic evolution after administration of different combinations of herbal active substances. Thus, asthenic, dyspepsic or algic syndrome have improved in 7-14 days after administration of hepatoprotective plant products, and the jaundice has relieved after approximately one month beyond treatment initiation. Also, in patients who developed a weight loss syndrome, the association of sea buckthorn oil with silymarin contributed to the improvement in body weight decline as a result of loss of appetite.

In a patient (Bichon female, 8 years old) with ascites syndrome as a result of a neoplastic process associated with congestive heart failure, 2 months after following hepatoprotective herbal and mineral products therapy (silymarin + sea buckthorn + curcumin + zeolite) associated with weekly therapeutic paracentesis, it seen a marked improvement in the state of health and quality of life, with decreasing intensity to disappearance of ascites (Figure 1). In another patient diagnosed with hepatobiliary carcinoma and secondary ascites, being at the final stage of the disease, therapy with silymarin + sea buckthorn+ curcumin + zeolite was palliative, with transient decrease of

clinical signs, temporary improvement of quality of life and biochemical results, corresponded by a slight decrease in liver transaminases and cholestatic parameters.

Figure 1

Dog, Bichon, ♀, 8 years old, diagnosed with mixed ascitic syndrome, clinical and ultrasound aspects before (left pictures) and after treatment (right pictures)

In the majority of patients from the three groups diagnosed with different hepatopathies, administration of various herbal drugs combinations has been beneficial in the evolution of biochemical indices. Thus, in patients diagnosed with cholangiohepatitis or cholestasis who received artichoke extract in addition to silymarin and sea buckthorn oil, an improvement of liver enzymes was observed and the alkaline phosphatase activity decreased to normal values.

The reports from medical literature shows that silymarin, sea buckthorn, curcumin and artichoke exhibit antioxidant, anti-inflammatory, antifibrotic, cytoprotective, membrane-stabilizing, detoxifying and improving liver function synthesis properties (Webster & Cooper, 2009; Loguercio et al. 2011; He et al., 2015, Colak et al., 2016). Interesting data on the antitumor action of these hepatoprotective agents have been reported due to the ability to regulates hepatocyte apoptosis and down-regulate gene products involved in profilation of tumor cells, angiogenesis and metastasis (Agarwal et al., 2006; López-Lázaro, 2008; Ramos et al., 2014). These effects confirm that the active principles of these plants can be used in the complex treatment of different kinds of hepatic diseases.

Conclusions

1. The association of various medical plants with allopathic therapy in the complex management of liver disease has helped to normalize the activities of hepatic transaminases and cholestasis indices, with a high degree of cytoprotection.

2. A positive therapeutic result was obtained after therapy with antioxidants from herbal origin in the mild and average forms of liver disease.

3. The administration of silymarin + sea buckthorn, silymarin + curcumin or artichoke for a period of 14 -30 days in patients with toxic, infectious or gall bladder disease lead to improvement of liver function and cytolytic indices, as well as reducing the activity of cholestasis markers.

4. For end-stage diseases, natural hepatoprotective therapy was palliative, with transient diminution of clinical signs and temporary improvement in quality of life.

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