

Chou HI, Chen KS, Wang HC, Lee WM. [Effects of cranberry extract on prevention of urinary tract infection in dogs and on adhesion of Escherichia coli to Madin-Darby canine kidney cells.](#) Am J Vet Res. 2016 Apr;77(4):421-7.

To determine effects of cranberry extract on development of urinary tract infection (UTI) in dogs and on adherence of Escherichia coli to Madin-Darby canine kidney (MDCK) cells. ANIMALS 12 client-owned dogs (in vivo experiment) and 6 client-owned dogs (in vitro experiment). 12 dogs with a history of recurrent UTI received an antimicrobial (n = 6) or cranberry extract (6) orally for 6 months. Dogs were monitored for a UTI. For the in vitro experiment, cranberry extract was orally administered to 6 dogs for 60 days. Voided urine samples were collected from each dog before and 30 and 60 days after onset of extract administration. Urine was evaluated by use of a bacteriostasis assay. An antiadhesion assay and microscopic examination were used to determine inhibition of bacterial adherence to MDCK cells. None of the 12 dogs developed a UTI. The bacteriostasis assay revealed no zone of inhibition for any urine samples. Bacterial adhesion was significantly reduced after culture with urine samples obtained at 30 and 60 days, compared with results for urine samples obtained before extract administration. Microscopic examination revealed that bacterial adherence to MDCK cells was significantly reduced after culture with urine samples obtained at 30 and 60 days, compared with results after culture with urine samples obtained before extract administration. Oral administration of cranberry extract prevented development of a UTI and prevented E coli adherence to MDCK cells, which may indicate it has benefit for preventing UTIs in dogs.

Nardoni S, Costanzo AG, Mugnaini L, Pisseri F, Rocchigiani G, Papini R, Mancianti F. [An open-field study comparing an essential oil-based shampoo with miconazole/chlorhexidine for hair coat disinfection in cats with spontaneous microsporiasis.](#) J Feline Med Surg. 2016 Jan 18

The goal of the present study was to compare the antifungal efficacy of an essential oil (EO) shampoo proven to be effective against Microsporum canis with miconazole/chlorhexidine for topical hair coat disinfection in cats treated concurrently with oral itraconazole. Cats received treatment with oral itraconazole (Itrafungol) at a dose of 5 mg/kg/day pulse administration for 1 week, every 2 weeks for at least 6 weeks and were washed twice a week with a neutral shampoo with added EOs of Thymus serpyllum (2%), Origanum vulgare and Rosmarinus officinalis (5% each) for the period of systemic treatment. This protocol was compared with a conventional treatment (oral itraconazole + 2% miconazole/2% chlorhexidine shampoo). The treatment was well tolerated and adverse effects were not recorded. All cats were clinically negative at week 11. With respect to animals with extensive

lesions, the speed of resolution was higher in cats with focal lesions. The animals showing diffuse lesions required more than a course of treatment to achieve a mycological cure. There was no significant difference between the number of weeks to obtain mycological cure for cats treated with EOs and animals treated conventionally. The treatment appeared to be effective and well appreciated by the owners. The use of shampoo with the added EOs of *T serpyllum*, *O vulgare* and *R officinalis* would seem an interesting, natural alternative to conventional topical treatment.

Blaskovic M, Rosenkrantz W, Neuber A, Sauter-Louis C, Mueller RS. [The effect of a spot-on formulation containing polyunsaturated fatty acids and essential oils on dogs with atopic dermatitis.](#) Vet J. 2014 Jan;199(1):39-43

Recent studies have shown that immunological aberrations and epidermal barrier defects could be important in the pathogenesis of canine atopic dermatitis (CAD) and that oral polyunsaturated fatty acids (PUFAs) might influence the epidermal barrier. The aim of this study was to evaluate the effects of a spot-on formulation containing PUFAs and essential oils on pruritus and lesions caused by CAD. Forty-eight privately owned dogs of different breeds, ages and genders diagnosed with atopic dermatitis were included in a randomized, double-blinded, placebo-controlled, multicentre clinical trial. Dogs were treated with a spot-on formulation containing PUFAs and essential oils or placebo on the dorsal neck once weekly for 8 weeks. Before and after the study, CAD extent and severity index-03 (CADESI-03) and pruritus scores were determined by veterinarians and owners, respectively. There was significantly more improvement in CADESI-03 and pruritus scores in the treatment group than in the placebo group ( $P=0.011$  and  $P=0.036$ , respectively). Additionally, more dogs improved by at least 50% in CADESI-03 and pruritus scores in the treatment group than in the placebo group ( $P=0.008$  and  $P=0.070$ , respectively). No adverse reactions were observed. The topical preparation containing PUFAs and essential oils was a safe treatment and beneficial in ameliorating the clinical signs of CAD.

Moreau M, Lussier B, Pelletier JP, Martel-Pelletier J, Bédard C, Gauvin D, Troncy E. [A medicinal herb-based natural health product improves the condition of a canine natural osteoarthritis model: a randomized placebo-controlled trial.](#) Res Vet Sci. 2014 Dec;97(3):574-81.

An oral herb-based natural health product (NHP) was evaluated in the canine natural osteoarthritis model. At baseline, the peak vertical force (PVF, primary endpoint) and

case-specific outcome measure of disability (CSOM) were recorded in privately-owned dogs. Dogs (16/group) were randomized to receive NHP formulations or a negative control. The PVF was measured at week (W) 4 and W8. Daily locomotor activity was recorded using accelerometer. The CSOMs were assessed bi-weekly by the owner. The NHP-treated dogs (n = 13) had higher PVF at W4 (p = 0.020) and W8 (p <0.001) when compared to baseline. The changes at W8 were higher than control dogs (n = 14, p <0.027) and consistent with Cohen's d effect size of 0.7 (95% confidence interval: 0.0-1.5). The NHP-treated dogs had higher locomotor activity at W8 (p = 0.025) when compared to baseline. No significant change was observed for the CSOM. The NHP improved the clinical signs of osteoarthritis in this model.

Szweda M, Szarek J, Dublan K, Męcik-Kronenberg T, Kiełbowicz Z, Bigoszewski M. [Effect of mucoprotective plant-derived therapies on damage to colonic mucosa caused by carprofen and robenacoxib administered to healthy dogs for 21 days.](#) Vet Q. 2014;34(4):185-93.

The hypothesis was that Non-steroidal anti-inflammatory drugs (NSAIDs) may cause gastrointestinal damage in dogs. To determine the extent to which lansoprazole, liquorice extract, and a herbal solution exhibit protective effects on colonic mucosa when administered to dogs concurrently with the NSAIDs carprofen or robenacoxib, thirty-five healthy beagle dogs (15 male and 20 female) aged 13-14 weeks and weighing 4.3-5.5 kg at the beginning of the experiment were included. Endoscopy and biopsy of the caudal gastrointestinal tract were performed pretreatment and on the last day of a 21-day treatment period with (1) oral carprofen; (2) carprofen and the proton-pump inhibitor lansoprazole; (3) carprofen, liquorice extract, and a herbal solution that contained extracts of thyme, icelandic lichen, hyssop, and saponariae root; (4) robenacoxib; (5) robenacoxib and lansoprazole; (6) robenacoxib, liquorice extract, and herbal solution; or (7) an empty gelatin capsule. Statistical analyses were performed with the Kruskal-Wallis, Cochran's Q, and chi-squared test with p < 0.05 considered significant. Both carprofen and robenacoxib tested damaged the colonic mucosa with most severe microscopic lesions following administration of robenacoxib with lansoprazole. The risk of histopathological lesions in the colon increased most rapidly in robenacoxib with lansoprazole (absolute risk increase -0.85) similar to robenacoxib only (-0.75), whereas the best result was recorded following the plant remedies together with carprofen (-0.15) and the plant remedies together with robenacoxib (-0.2). Concurrent administration of liquorice extract and an herbal solution with robenacoxib was associated with decreased severity of the NSAID-induced mucosal lesions.

Torkan S, Khamesipour F, Katsande S. [Evaluating the effect of oral administration of Echinacea hydroethanolic extract on the immune system in dog.](#) Auton Autacoid Pharmacol. 2015 Jul;35(1-2):9-13.

This study was designed to evaluate the effects of oral administration of Echinacea hydroethanolic extract on the dog's immune system. The study was performed on 14 dogs that were referred to the veterinary clinic. These dogs were randomly allocated to two equal treatment groups. The first group received 1 ml of 5% Echinacea hydroethanolic extract two times a day for 2 months, and the second group received a placebo (water). To do haematology and immunology tests, the dogs were bled on days 0, 30 and 60. Blood tests, including packed cell volume (PCV), haemoglobin (Hb), red blood cell count (RBC), white blood cell count (WBC), counting neutrophils (Nut), lymphocytes (Lym), monocytes (Mon), eosinophils (Eos), basophils (Baso) and B cell, were performed. Furthermore, safety factor IgM and per cent of phagocytosis and phagocyte were measured from the blood sample. The results showed that in the group which received Echinacea PCV, Hb, RBC count, WBC count, Lym, Nut, the per cent of phagocytosis and IgM significantly increased ( $P < 0.05$ ). Moreover, positive effects of Echinacea plant on the immune system were observed. There was a significant change in HTC, RBC, Hb over time in the group that received Echinacea and the per cent of phagocytosis and IgM ( $P < 0.05$ ). The study establishes that these extracts might have appreciable immunostimulatory activity. However, further studies are required to confirm these findings.

Szweda M, Szarek J, Lew M, Szarek-Bęska A, Gulda D. [Can liquorice extract and herbal solution prevent colonic mucosa damage caused by robenacoxib in dogs?](#) Pol J Vet Sci. 2015;18(4):793-8.

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in animals, especially in dogs, to manage pain due to inflammatory disease. This study investigated whether plant drugs can prevent mucosal injury induced by robenacoxib. We used fifteen healthy beagle dogs (7 male and 8 female) aged 4 months, weighing 4.2-5.1 kg at the beginning of the study. Endoscopy and biopsy of the colon were performed before and on the 21 day treatment with robenacoxib (1), robenacoxib, herbal solution with liquorice extract (2), placebo - an empty capsule (3). There were 5 animals in each group. The greatest microscopic damage in the colon was observed in animals which received robenacoxib. Plant drug administration reduced the severity of lesions in the colon when administered with robenacoxib (ARI = - 0.15). Conclusion: concurrent administration of liquorice extract and plant solution with robenacoxib was associated with significant decreased severity of the robenacoxib-induced colonic mucosal lesions.

Al-Mohizea AM, Ahad A, El-Maghraby GM, Al-Jenoobi FI, AlKharfy KM, Al-Suwayeh SA. [Effects of Nigella sativa, Lepidium sativum and Trigonella foenum-graecum on sildenafil disposition in beagle dogs.](#) Eur J Drug Metab Pharmacokinet. 2015 Jun;40(2):219-24.

The present study was conducted to investigate the effects of some commonly used herbs namely Nigella sativa, Lepidium sativum and Trigonella foenum-graecum on the pharmacokinetics of sildenafil in beagle dogs. The study design involved four treatments in a non-balanced crossover design. Sildenafil was given one tablet 100 mg orally to each dog and blood samples were obtained. After a suitable washout period, animals were commenced on a specific herb treatment for 1 week. Blood samples were withdrawn at different time intervals and sildenafil was analyzed by HPLC method. Oral administration of Nigella sativa resulted in reduction of AUC<sub>0-∞</sub>, C<sub>max</sub> and t<sub>1/2</sub> as compared to the control. Treatment of Lepidium sativum resulted in a significant reduction in the C<sub>max</sub> and AUC. There were no significant differences between the rests of the pharmacokinetic parameters relative to those of the control. For Trigonella foenum-graecum, the effects were similar to those obtained in case of Lepidium sativum. It was concluded that concurrent use of investigated herbs alters the pharmacokinetics of sildenafil. Co-administration of investigated herbs should be cautious since their concomitant use might result in decrease in sildenafil bioavailability.

van Dooren I, Faouzi Mel A, Foubert K, Theunis M, Pieters L, Cherrah Y, Apers S. [Cholesterol lowering effect in the gall bladder of dogs by a standardized infusion of Herniaria hirsuta L.](#) J Ethnopharmacol. 2015 Jul 1;169:69-75.

To investigate the efficacy of a standardized infusion of Herniaria hirsuta against cholelithiasis, and evaluation of its genotoxicity. An in vivo experiment to evaluate the cholesterol lowering effect of a infusion of H. hirsuta in the gall bladder of dogs was carried out. Dogs were divided into 3 groups i.e. control dogs (CG), dogs treated with ursodeoxycholic acid (UDCA) (2×7.35mg/kg body weight/day) and dogs treated with the standardized infusion (HG) (2×48.5mg/kg body weight/day). Dogs were fed a fatty diet during 120 days after which a diet without additional fat was introduced till day 180. Treatment started 30 days after introduction of the fatty diet and lasted till the end of the experiment. A bile and blood sample of each dog was collected every 30 days, after which the concentration of cholesterol was determined. An Ames test was performed according to the OECD-guidelines. Conclusion: Prolonged use of this standardized H. hirsuta extract resulted in a cholesterol-lowering effect in the bile of

dogs. Since this pharmacological effect prevents the formation of gallstones and can contribute to solving existing gallstones, a standardized infusion of *H. hirsuta* may have a positive effect in the treatment of gallstones in human patients.

Hanzlicek AS, Roof CJ, Sanderson MW, Grauer GF. [The Effect of Chinese rhubarb, \*Rheum officinale\*, with and without benazepril on the progression of naturally occurring chronic kidney disease in cats.](#) J Vet Intern Med. 2014 Jul-Aug;28(4):1221-8.

Renal fibrosis is common in progressive kidney disease. Transforming growth factors  $\beta$  (TGF- $\beta$ ) are important mediators of all types of fibrosis, including renal fibrosis. Chinese rhubarb has been shown to have antifibrotic properties in part because of inhibition of TGF- $\beta$  and has slowed the progression of kidney disease in rodent models. The hypothesis is that administration of a Chinese rhubarb supplement will slow the progression of chronic kidney disease (CKD) in cats and the concurrent administration of Chinese rhubarb and benazepril will be more effective than either alone. Cats with naturally occurring IRIS Stage 2 or early Stage 3 CKD and without comorbidity such as cancer, urinary tract obstruction, urinary tract infection, poorly controlled hyperthyroidism, or systemic hypertension were enrolled in the study. A randomized, positive-controlled, prospective study was performed. Cats received Chinese rhubarb, benazepril, or both in addition to standard treatment for CKD. Repeated measures ANOVA was used to assess changes in serum creatinine concentration, body weight, hematocrit, urine protein: urine creatinine ratio (UPC), and systemic arterial blood pressure over time between and within treatment groups over an average of 22 months. No significant differences were detected in serum creatinine concentration, body weight, hematocrit, UPC, and systemic arterial pressure over time between or within treatment groups. This study failed to detect a significant difference in the progression of CKD in cats treated with Chinese rhubarb, benazepril, or both. Further study in specific subsets of cats with CKD is warranted.

Wirth KA, Kow K, Salute ME, Bacon NJ, Milner RJ. [In vitro effects of Yunnan Baiyao on canine hemangiosarcoma cell lines.](#) Vet Comp Oncol. 2014 Jun 29.

Yunnan Baiyao is a Chinese herbal medicine that has been utilized for its anti-inflammatory, haemostatic, wound healing and pain relieving properties in people. It has been utilized in the veterinary profession to control bleeding in dogs with hemangiosarcoma (HSA) and has been anecdotally reported to prolong survival times in dogs with this neoplasm. This study evaluated the in vitro activity of Yunnan Baiyao

against three canine HSA cell lines after treatment with increasing concentrations of Yunnan Baiyao (50, 100, 200, 400, 600 and 800  $\mu\text{g mL}^{-1}$ ) at 24, 48 and 72 h. Mean half maximum inhibitory concentration (IC<sub>50</sub>) at 72 h for DEN, Fitz, SB was 369.9, 275.9 and 325.3  $\mu\text{g mL}^{-1}$ , respectively. Caspase-3/7 activity increased in correlation with the IC<sub>50</sub> in each cell line which was confirmed by the terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL, APO-BRDU Kit; BD Biosciences, San Jose, CA, USA) assay. VEGF in cell supernatant was also quantified. Overall, the study found that Yunnan Baiyao causes dose and time dependent HSA cell death through initiation of caspase-mediated apoptosis, which supports future studies involving Yunnan Baiyao.

Low SB, Peak RM, Smithson CW, Perrone J, Gaddis B, Kontogiorgos E. [Evaluation of a topical gel containing a novel combination of essential oils and antioxidants for reducing oral malodor in dogs.](#) Am J Vet Res. 2014 Jul;75(7):653-7

The objective of this study was to evaluate the effectiveness of a topically applied gel containing essential oils (menthol and thymol) and polyphenolic antioxidants (phloretin and ferulic acid) for reducing halitosis in dogs. A blinded crossover clinical trial was conducted. 20 Dogs received a dental cleaning and examination (periodontal examination including periodontal probing and assessments of plaque, calculus, and gingivitis). Owners then applied a gel (active or placebo) to oral soft tissues twice daily for a 4-week period. Teeth of the dogs were cleaned again, and owners applied the other gel for a 4-week period. Clinicians scored halitosis immediately after the initial cleaning and at 4 and 8 weeks, and owners scored halitosis weekly. Halitosis assessment by clinicians revealed that both groups had improvement in halitosis scores. Two dogs were removed because of owner noncompliance. In the active-to-placebo group (n = 9), halitosis was significantly reduced during application of the active gel but increased during application of the placebo. Seven of 9 owners reported increased halitosis when treatment was changed from the active gel to the placebo. In the placebo-to-active group (n = 9), halitosis decreased during application of the placebo and continued to decrease during application of the active gel. Seven of 9 owners reported a decrease in halitosis with the active gel. An oral topically applied gel with essential oils and polyphenolic antioxidants applied daily after an initial professional dental cleaning decreased oral malodor in dogs.

Breuer E, Efferth T. [Treatment of Iron-Loaded Veterinary Sarcoma by Artemisia annua.](#) Nat Prod Bioprospect. 2014 Apr;4(2):113-8.

Artemisinin, a constituent of *Artemisia annua* L., is a well-known antimalarial drug. Artemisinin-type drugs also inhibit cancer growth in vitro and in vivo. Herbal extracts of *A. annua* inhibit the growth of cancer cell lines. Here, we report on the use of capsules containing powder of *Herba Artemisiae annuae* to treat pet sarcoma. The surgical tumor removal as standard treatment was supplemented by adjuvant therapy with *A. annua*. One cat and one dog with fibrosarcoma survived 40 and 37 months, respectively, without tumor relapse. Two other dogs suffering from fibrosarcoma and hemangioendothelial sarcoma also showed complete remission and are still alive after 39 and 26 months, respectively. *A. annua* was well tolerated without noticeable side effects. These four cases indicate that *A. annua* may be a promising herbal drug for cancer therapy.

Helmerick EC, Loftus JP, Wakshlag JJ. [The effects of baicalein on canine osteosarcoma cell proliferation and death.](#) *Vet Comp Oncol.* 2014 Dec;12(4):299-309.

Flavonoids are a group of modified triphenolic compounds from plants with medicinal properties. Baicalein, a specific flavone primarily isolated from plant roots (*Scutellaria baicalensis*), is commonly used in Eastern medicine for its anti-inflammatory and antineoplastic properties. Previous research shows greater efficacy for baicalein than most flavonoids; however, there has been little work examining their effects on sarcoma cells, let alone canine cells. Three canine osteosarcoma cell lines (HMPOS, D17 and OS 2.4) were treated with baicalein to examine cell viability, cell cycle kinetics, anchorage-independent growth and apoptosis. Results showed that osteosarcoma cells were sensitive to baicalein at concentrations from approximately 1 to 25  $\mu$ M. Modest cell cycle changes were observed in one cell line. Baicalein was effective in inducing apoptosis and did not prevent doxorubicin cell proliferation inhibition in all the cell lines. The mechanism for induction of apoptosis has not been fully elucidated; however, changes in mitochondrial permeability supersede the apoptotic response.

Furukawa N, Manabe N, Kase Y, Hattori T, Imamura H, Kusunoki H, Haruma K. [Intragastric infusion of rikkunshito \(kampo\) induces proximal stomach relaxation in conscious dogs.](#) *Auton Neurosci.* 2013 Dec;179(1-2):14-22. (Note: This is Liu Jun Zi Tang used by veterinary herbalists for many gastrointestinal conditions.)

Abnormal proximal gastric relaxation is one of the causes of functional dyspepsia. The purpose of this study is to use a barostat in conscious dogs to determine the effects of rikkunshito, which is considered to have beneficial effects on functional dyspepsia, on the proximal stomach. Eight beagles were used. A gastrocutaneous fistula and force transducers were surgically implanted in the middle corpus and gastric antrum



and duodenum, respectively. After a recovery period, a plastic bag was inserted through the gastrocutaneous fistula and the proximal stomach was distended using a barostat. First, four dogs were used to investigate the pressure-volume relation in the fasted and postprandial phases. Second, the stomachs of four different dogs were continuously distended at minimal distending pressure +2 mmHg, and 5 min later were infused with warmed liquid rikkunshito (2 g/20 mL) or water through the gastrocutaneous fistula. Finally, changes in the proximal gastric volume and gastrointestinal motility were observed. The proximal stomach was significantly more pliable in the postprandial phase than in the fasted phase. The proximal gastric volume increased immediately after liquid infusion under constant pressure in both phases and duodenal motility was accelerated. The effect of rikkunshito was significantly greater and lasted longer than that of water. No significant difference between the effects during the fasted or postprandial phase and no change in the gastric antrum motility were observed when rikkunshito was infused. These results indicate that rikkunshito accelerates duodenal motility and relaxes the proximal stomach.

Ogbu SO, Agwu KK, Asuzu IU. [Effect of Gongronema latifolium on gastric emptying in healthy dogs.](#) World J Gastroenterol. 2013 Feb 14;19(6):897-902.

The aim of this study was to investigate sonographically the effect of *Gongronema latifolium* (*G. latifolium*) on gastric emptying of semi-solid meals in healthy dogs. In a randomized, placebo-controlled experiment, twenty-five clinically healthy dogs were randomly allotted into five groups of five dogs in each group. The placebo group served as the control, and the low, moderate and high dose groups ingested the methanolic leaf extract of *G. latifolium* in capsules at 100 mg/kg, 250 mg/kg and 500 mg/kg, respectively, while the prokinetic group ingested 0.5 mg/kg capsules of metoclopramide. After a 12-h fast, each group ingested its treatment capsules 30 min before the administration of a test meal. Measurements of gastric emptying and blood glucose levels were obtained 30 min before and immediately after the ingestion of the test meal and thereafter every 15 min for 4 h. This was followed by further measurements every 30 min for another 2 h. The gastric emptying times of the placebo, low dose, moderate dose, high dose and prokinetic dose groups were  $127.0 \pm 8.2$  min,  $135.5 \pm 3.7$  min,  $155.5 \pm 3.9$  min,  $198.0 \pm 5.3$  min and  $59.0 \pm 2.5$  min, respectively. Gastric emptying times of the moderate and high dose groups were significantly slower than in the placebo control group ( $155.5 \pm 3.9$  min,  $198.0 \pm 5.3$  min vs  $127.0 \pm 8.2$  min,  $P = 0.000$ ). No significant difference in gastric emptying between the low dose and placebo control groups was noted ( $135.5 \pm 3.7$  min vs  $127.0 \pm 8.2$  min,  $P = 0.072$ ). Gastric emptying of the prokinetic group was significantly faster than that of the control group ( $59.0 \pm 2.5$  min vs  $127.0 \pm 8.2$  min,  $P = 0.000$ ). The hypoglycaemic effect of *G. latifolium* and gastric emptying were inversely related ( $r = -0.95$ ,  $P = 0.000$ ).

Gardon, Pache, Magnenat, Pin, Parvis. [Viscum album L. \(Iscador\) in the cat: tolerance, adverse reactions and indications.](#) Schweiz Arch Tierheilkd. 2014 Aug;156(8):381-8.

In this retrospective study, the tolerance to subcutaneous mistletoe injections (*Viscum album L.*), adverse reactions and possible indications have been evaluated in feline patients of a small animal clinic. Among the 22 cats treated between 2008 and 2013, 4 did not accept the injections done by the owner, 7 showed slight short time adverse reactions, that disappeared spontaneously. No long term (more than 70 days) adverse reaction directly related to the *Viscum album* treatment could be identified. This study shows that Iscador(®) can be injected subcutaneously without a risk of worsening of the clinical signs or exacerbation of tumors. The antitumoral, but also immune-modulating and anti-inflammatory properties offer interesting treatment opportunities for dermatologic, odonto-stomatologic or allergic patients.

Hanzlicek AS, Roof CJ, Sanderson MW, Grauer GF. [The Effect of Chinese rhubarb, \*Rheum officinale\*, with and without benazepril on the progression of naturally occurring chronic kidney disease in cats.](#) J Vet Intern Med. 2014 Jul-Aug;28(4):1221-8.

Renal fibrosis is common in progressive kidney disease. Transforming growth factors  $\beta$  (TGF- $\beta$ ) are important mediators of all types of fibrosis, including renal fibrosis. Chinese rhubarb has been shown to have antifibrotic properties in part because of inhibition of TGF- $\beta$  and has slowed the progression of kidney disease in rodent models. The hypothesis was that the administration of a Chinese rhubarb supplement will slow the progression of chronic kidney disease (CKD) in cats and the concurrent administration of Chinese rhubarb and benazepril will be more effective than either alone. Twenty-nine client-owned cats with naturally occurring IRIS Stage 2 or early Stage 3 CKD and without comorbidity such as cancer, urinary tract obstruction, urinary tract infection, poorly controlled hyperthyroidism, or systemic hypertension were enrolled in the study. A randomized, positive-controlled, prospective study was performed. Cats received Chinese rhubarb, benazepril, or both in addition to standard treatment for CKD. Repeated measures ANOVA was used to assess changes in serum creatinine concentration, body weight, hematocrit, urine protein: urine creatinine ratio (UPC), and systemic arterial blood pressure over time between and within treatment groups over an average of 22 months. No significant differences were detected in serum creatinine concentration, body weight, hematocrit, UPC, and systemic arterial pressure over time between or within treatment groups. This study failed to detect a significant difference in the progression of CKD in cats treated with Chinese rhubarb, benazepril, or both. Further study in specific subsets of cats with CKD is warranted.

Yanai M, Mochiki E, Ogawa A, Morita H et al [Intragastric administration of rikkunshito stimulates upper gastrointestinal motility and gastric emptying in conscious dogs.](#) Gastroenterol. 2013 May;48(5):611-9.

Traditional Japanese medicine, known as Kampo medicine, consists of mixtures of several medicinal herbs widely used to treat upper gastrointestinal disorders in Japan. Rikkunshito, one of these medicines, has not been evaluated with respect to its influence on gastrointestinal motor activity. We investigated the effect of rikkunshito on upper gastrointestinal motility and plasma ghrelin concentrations in conscious dogs. Contractile response to intragastric administration of rikkunshito was studied via surgically implanted force transducers. A powdered extract of rikkunshito (1.3, 2.7, and 4.0 g) dissolved in water was administered into the stomachs of normal and vagotomized dogs before feeding and gastric emptying was evaluated. Several inhibitors of gastrointestinal motility (atropine, hexamethonium, and ondansetron) were injected intravenously before intragastric administration of rikkunshito. Plasma acylated ghrelin levels after intragastric administration of rikkunshito were measured. In a fasting state, intragastric administration of rikkunshito induced phasic contractions in the duodenum and jejunum in normal dogs. Rikkunshito-induced contractions were inhibited by atropine, hexamethonium and ondansetron. In vagotomized dogs, rikkunshito induced phasic contractions, similar to normal dogs. Gastric emptying was accelerated by intragastric administration of rikkunshito in a dose-dependent manner. The plasma acylated ghrelin level 150 min after intragastric administration of 4.0 g of rikkunshito was significantly higher than the control value. Intragastric administration of rikkunshito stimulates gastrointestinal contractions in the interdigestive state through cholinergic neurons and 5-HT type 3 receptors. Moreover, rikkunshito increases plasma acylated ghrelin levels. Rikkunshito may alleviate gastrointestinal disorders through its prokinetic effects.

Mugnaini L, Nardoni S, Pinto L, Pistelli L, Leonardi M, Pisseri F, Mancianti F. [In vitro and in vivo antifungal activity of some essential oils against feline isolates of Microsporium canis.](#) J Mycol Med. 2012 Jun;22(2):179-84

The treatment of dermatophytoses due to *Microsporium canis* is cumbersome and relapses can occur. Volatile essential oils (EOs) obtained from plants would seem to represent suitable tools to contrast mycoses both in human and animals. The anti-*M. canis* activity of some EOs chemically characterized was evaluated both in vitro and in vivo. Eleven feline isolates of *M. canis* were tested by microdilution against EOs extracted from *Thymus serpyllum*, *Origanum vulgare*, *Rosmarinus officinalis*, *Illicium verum* and *Citrus limon*. A mixture composed by 5% *O. vulgare*, 5% *R. officinalis* and 2% *T. serpyllum*, in sweet almond oil was administered to seven infected, symptomatic

cats. *T. serpillum* and *O. vulgare* showed the lowest MICs, followed by *I. verum*, *R. officinalis* and *C. limon*. The assay performed on mixture showed that antimycotic activity of each component was enhanced. Four out of seven treated cats recovered both clinically and culturally. *T. serpillum* and *O. vulgare* EOs showed a strong antifungal activity. Preliminary data suggest a possible application in managing feline microsporiasis. Considering the potential zoonotic impact of this infection, the use of alternative antimycotic compounds would be of aid to limit the risk of environmental spreading of arthrospores.

Fukunaga K, Orito K. [Time-course effects of St John's wort on the pharmacokinetics of cyclosporine in dogs: interactions between herbal extracts and drugs.](#) *J Vet Pharmacol Ther.* 2012 Oct;35(5):446-51.

To clarify the interaction between St John's wort (SJW) and cyclosporine (CsA) in dogs, the pharmacokinetics of CsA before and during the repeated administration of SJW were analyzed. In the SJW group, SJW (300 mg) was given orally to four dogs every 24 h for 14 days. A single dose of CsA (5 mg/kg) was given orally 7 days before and 7 and 14 days after the initiation of the repeated administration of SJW. In the Control group, a single dose of CsA (5 mg/kg) was given orally to four other dogs in accordance with that in the SJW group. Blood samples from both groups were collected, and whole-blood concentrations of CsA were determined using high-performance liquid chromatography with UV detection. The maximum whole-blood concentration and AUC(0-∞) of the SJW group were significantly lower and the CL(tot) /F and V(d) /F were significantly higher than those in the Control group 7 and 14 days after the initiation of repeated SJW. Thus, repeated administrations of SJW affect the pharmacokinetic profiles of CsA in dogs. Further studies are necessary to elucidate the mechanisms of interaction between SJW and CsA in dogs.

Head E, Murphey HL, Dowling AL et al. [A combination cocktail improves spatial attention in a canine model of human aging and Alzheimer's disease.](#) *J Alzheimers Dis.* 2012;32(4):1029-42.

Alzheimer's disease (AD) involves multiple pathological processes in the brain, including increased inflammation and oxidative damage, as well as the accumulation of amyloid- $\beta$  (A $\beta$ ) plaques. We hypothesized that a combinatorial therapeutic approach to target these multiple pathways may provide cognitive and neuropathological benefits for AD patients. To test this hypothesis, we used a canine model of human aging and AD. Aged dogs naturally develop learning and memory impairments, human-type A $\beta$  deposits, and oxidative damage in the brain. Thus, 9 aged beagles (98-115 months) were treated with a medical food cocktail containing

(1) an extract of turmeric containing 95% curcuminoids; (2) an extract of green tea containing 50% epigallocatechingallate; (3) N-acetyl cysteine; (4) R-alpha lipoic acid; and (5) an extract of black pepper containing 95% piperine. Nine similarly aged dogs served as placebo-treated controls. After 3 months of treatment, 13 dogs completed a variable distance landmark task used as a measure of spatial attention. As compared to placebo-treated animals, dogs receiving the medical food cocktail had significantly lower error scores ( $t_{11} = 4.3$ ,  $p = 0.001$ ) and were more accurate across all distances ( $F(1,9) = 20.7$ ,  $p = 0.001$ ), suggesting an overall improvement in spatial attention. Measures of visual discrimination learning, executive function and spatial memory, and levels of brain and cerebrospinal fluid A $\beta$  were unaffected by the cocktail. Our results indicate that this medical food cocktail may be beneficial for improving spatial attention and motivation deficits associated with impaired cognition in aging and AD.

Skorupski KA, Hammond GM, Irish AM, Kent MS, Guerrero TA, Rodriguez CO, Griffin DW. [Prospective randomized clinical trial assessing the efficacy of Denamarin for prevention of CCNU-induced hepatopathy in tumor-bearing dogs.](#) J Vet Intern Med. 2011 Jul-Aug;25(4):838-45.

Increases in liver enzymes occur in up to 86% of dogs receiving CCNU and can result in treatment delay or early discontinuation of treatment. Denamarin contains S-adenosylmethionine and silybin, both of which have been investigated as treatments for various liver diseases. Dogs on CCNU receiving Denamarin have lower alanine aminotransferase (ALT) activity than dogs not receiving Denamarin. Dogs on Denamarin are less likely to require treatment delay because of hepatopathy and are more likely to complete their prescribed course of CCNU. Dogs with lymphoma, mast cell tumor, or histiocytic sarcoma that were prescribed CCNU with or without corticosteroids and with normal ALT activity were eligible for enrolment. Dogs were prospectively randomized to receive either concurrent Denamarin during CCNU chemotherapy or to receive CCNU alone. Liver-specific laboratory tests were run before each dose of CCNU. Increased liver enzyme activity occurred in 84% of dogs receiving CCNU alone and in 68% of dogs on concurrent Denamarin. Dogs receiving CCNU alone had significantly greater increases in ALT, aspartate aminotransferase, alkaline phosphatase, and bilirubin and a significantly greater decrease in serum cholesterol concentrations than dogs receiving concurrent Denamarin. Dogs receiving CCNU alone were significantly more likely to have treatment delayed or discontinued because of increased ALT activity. Increased liver enzyme activity occurs commonly in dogs receiving CCNU chemotherapy. These results support the use of concurrent Denamarin to minimize increased liver enzyme activity in dogs receiving CCNU chemotherapy. Denamarin treatment also increases the likelihood of dogs completing a prescribed CCNU course.

Schmidt V, McEwan N, Volk A, Helps J, Morrell K, Nuttall T. [The glucocorticoid sparing efficacy of Phytopica in the management of canine atopic dermatitis.](#) *Vet Dermatol.* 2010 Feb;21(1):96-105

This double-blind randomized placebo-controlled trial indicates that Phytopica can be an effective glucocorticoid sparing agent in canine atopic dermatitis (AD). Twenty-two dogs with perennial AD [Canine Atopic Dermatitis with Severity Index (CADESI-03)  $\geq 60$ ] were given 200 mg/kg Phytopica or an identical placebo in food once daily for 56 days. All dogs were initially given 0.4 mg/kg methyl-prednisolone once daily, which was then adjusted according to the daily pruritus score (0-100 mm visual analogue scale). The cumulative dose and pruritus score were lower in the Phytopica than the placebo group. There were statistically significant time and treatment effects for the methyl-prednisolone dose and pruritus score, but there were no significant differences between the Phytopica and placebo groups in the proportion of dogs that achieved a  $> 50\%$  reduction in dose or pruritus scores at day 56; the mean CADESI-03 scores at days 0, 28 and 56; the numbers achieving  $>50\%$  reduction in CADESI-03 at days 28 and 56; or in the owners' global efficacy score at days 28 and 56. Adverse events included diarrhoea (three Phytopica and one placebo treated dog), polyuria/polydipsia (three dogs in each group), and polyphagia, intermittent anorexia and panting (one dog each in the placebo group). None of these by themselves required withdrawal of treatment.

Marsella R, Messinger L, Zabel S, Rosychuck R, Griffin C, Cronin PO, Belofsky G, Lindemann J, Stull D. [A randomized, double-blind, placebo-controlled study to evaluate the effect of EFF1001, an Actinidia arguta \(hardy kiwi\) preparation, on CADESI score and pruritus in dogs with mild to moderate atopic dermatitis.](#) *Vet Dermatol.* 2010 Feb;21(1):50-7.

Canine atopic dermatitis (AD) is common and new therapies are beneficial. This multicentric, randomized, double-blind, placebo-controlled study tested the efficacy of Actinidia arguta (hardy kiwi) (EFF1001) in dogs with mild/moderate AD. The study was divided into two stages. Stage 1 lasted 6 weeks. In the first 2 weeks prednisolone [days 1-3: 0.2 mg/kg twice daily (BID), days 4-14: 0.2 mg/kg every other day (EOD)] was administered. Responsive dogs were placed on prednisolone 0.2 mg/kg EOD + assigned test article [either placebo or EFF1001 (30 mg/kg)] once daily for 4 weeks. Stage 1 responders were advanced to stage 2, which involved 4 weeks of just EFF1001. Clinicians scored lesions using Canine Atopic Dermatitis Extent and Severity Index (CADESI) and owners scored pruritus using a Pruritus Visual Analogue Scale. Seventy-seven dogs were enrolled, 76 were randomized on day 14, and 57 (57/76 = 75%) completed stage 1 (27 in EFF1001 and 30 in placebo). At the end of stage 1, 35

of 57 dogs (35/57 = 61%) responded (18 in EFF1001 and 17 in placebo) and advanced to stage 2. At completion of stage 1, CADESI scores did not significantly differ between groups while pruritus decreased in EFF1001 group and approached significance. At completion of stage 2, 19 dogs (19/35 = 54%) responded (15/19 = 79% had received EFF1001 and 4/19 = 21% placebo in stage 1). After completing stage 2, dogs placed on EFF1001 throughout the study were 3.5 times more likely to either maintain or improve scores than those that started it in stage 2. It is concluded that EFF1001 is beneficial adjunctive therapy after prolonged use.

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