

Clinical Studies

A Randomized Controlled Study Comparing *Da Xiang Lian Wan* to Metronidazole in the Treatment of Stress Colitis in Shelter/Rescued Dogs

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ABSTRACT

Traditional Chinese Veterinary Medicine (TCVM), which can include treatment with Chinese herbal medicine, is being used increasingly in Western medicine to treat a variety of diseases in dogs. With the increased interest in Chinese herbal medicines, evidence-based research to prove efficacy and safety of these traditional medicines is necessary. The objective of this research was to compare the effectiveness of the Chinese herbal medicine, *Da Xiang Lian Wan* (*DXLW*), to the Western pharmaceutical, metronidazole, in the treatment of stress colitis in sheltered/rescued dogs utilizing a randomized controlled study with a hypothesis that successful treatment with *DXLW* would not be less than metronidazole. Fifty-six dogs were randomly assigned to either metronidazole treatment group or *DXLW* treatment group. Each medication was administered orally twice daily at recommended clinical doses for a maximum of 10 doses. The results indicate that dogs in the metronidazole treatment group had an 89% response rate (normal stools) within the 10 dose protocol while the *DXLW* group had a 97% positive response rate ($p < 0.05$, non-inferiority test). This study demonstrates that *DXLW* is as effective as metronidazole in resolving stress colitis in sheltered dogs and can be an effective alternative treatment for patients that do not respond to metronidazole or cannot tolerate it.

Key words: colitis, dog, stress, traditional Chinese veterinary medicine, *Da Xiang Lian Wan*, Coptis, Saussurea, *Huang Lian*, *Mu Xiang*, Great Saussurea Coptis

ABBREVIATIONS

TCVM Traditional Chinese Veterinary Medicine
DXLW *Da Xiang Lian Wan*
BID twice daily
TID three times daily

Stress colitis is a common problem in rescued or sheltered dogs housed in a kennel type environment and in the case of kill shelters, can result in euthanasia of affected dogs.¹ Colitis is defined as a high frequency of defecation with small fecal volume. Affected dogs often display prolonged tenesmus after defecation and the loose stools typically contain mucus and/or blood.² The syndrome may be multi-factorial involving gastrointestinal parasites, bacterial or viral infections, diet changes, anxiety and stress. Abandoned dogs in kennel type facilities are particularly under a high degree of psychological stress

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from fear, anxiety and sometimes over-crowding. Their gastrointestinal tract is also physiologically stressed from diet changes. While no medical literature could be found discussing the role of stress in dogs with colitis, in humans a higher perceived level of stress in patients appeared to be a contributing factor in ulcerative colitis and Crohn's disease and experimental work with mice demonstrated that stress aggravated existing colitis.^{3,4}

Colitis and ulcerative colitis in dogs and other species have been well discussed in veterinary journals. Several conventional medications have been used as a treatment addition or alternative to metronidazole, including tylosin, fluoroquinolones, azathioprine, sulfasalazine, amoxicillin and prednisone. Often no one single agent such as metronidazole is effective and combinations of medications can be required.⁵ The role of bacteria in the development of colitis has been discussed and demonstrated along with the failure of antibiotics such as metronidazole in the treatment of canine colitis due to antibiotic resistance.^{5,6,7}

Metronidazole is listed as the drug of choice for Inflammatory Bowel Disease and Large Bowel Diarrhea

(colitis) at dosages in dogs of 10-15 mg/kg of body weight two (BID) to three (TID) times daily or 20-25 mg/kg BID.⁸ It is typically effective, inexpensive, and is the drug of choice for colitis in shelter facilities at dosages of 10-22 mg/kg of body weight BID. Metronidazole, however, carries a risk of adverse reactions such as neurotoxicity including ataxia and seizures, lethargy, weakness, neutropenia, hepatotoxicity, hematuria, anorexia, nausea, vomiting and diarrhea, and may be teratogenic.^{8,9} These toxic side-effects, in addition to poor clinical response in some dogs, limit the drug's usage in a subset of shelter patients.

With metronidazole's ineffectiveness and intolerable side effects for some patients, alternative treatments are being considered by pet owners, shelters and veterinarians in conventional clinical practice. In traditional Chinese veterinary medicine, disease patterns (TCVM patterns) are identified and associated with imbalances. Colitis, as defined in this study, is consistent with a TCVM Excess Pattern of Large Intestine Damp Heat.¹⁰ Chinese herbal medicines are formulated to correct these imbalances to assist healing and restore health. *Da Xiang Lian Wan* (Great Saussurea Coptis®)^a is an ancient Chinese herbal medicine to clear Damp-Heat, move *Qi*, relieve pain and is appropriate for the Excess Pattern diagnosed in enrolled study dogs (Table 1).¹⁰

In contrast to metronidazole, *DXLW* lists no contraindications for its use.¹⁰ A review of scientific and medical literature was conducted on the use of *DXLW* and its ingredients in dogs prior to this study, and it was determined that very little research information on this subject was available. In relation to the herbal formula *Da Xiang Lian Wan* and the individual ingredient herbs, *Huang Lian* (Coptis) and *Mu Xiang* (Saussurea), some references could be found on scientific research conducted in-vitro or in-vivo in humans or non-canine species.^{11,12,13,14,15} There was, however, no statistically valid controlled randomized research studies using dogs as subjects. There were several claims of the effectiveness of this Chinese herbal medicine for the treatment of colitis, diarrhea or inflammatory bowel disease in dogs, but none had been extensively studied in dogs.^{10,12,16,17,18}

With the potential clinical benefit of less side effects than metronidazole, successful efficacy validation of *DXLW* would support its use in rescue dogs with stress related colitis, the general pet dog population with colitis, as well as stress prone Military Working Dogs

and Police Dogs. A well designed experimental study could also provide further scientific evidence to validate the use of Chinese herbal medicine in Western clinical practice. The aim of the study was to provide evidence based experimental support of an effective alternative treatment for stress diarrhea in dogs. The objective of this randomized, controlled study focused specifically on stress colitis in shelter dogs and compared treatment efficacy of *Da Xiang Lian Wan* to metronidazole. The hypothesis was that *Da Xiang Lian Wan* was at least as effective (speed of diarrhea resolution, % response rate of treated dogs) as the conventional medication metronidazole in the treatment of stress colitis in dogs held in a rescue dog sanctuary or shelter.

MATERIALS AND METHODS

Over a period of 8 months, there were a total of 56 dogs enrolled in the study located at one of the 3 participating animal shelters in the United States: Alaqua Animal Refuge located at 914 Whitfield Road, Freeport FL, 32439, Low Country Lab Rescue located at 1612 Harbor View Rd, Charleston, SC 29412, and Cape May County Animal Shelter located at 110 Shelter Road, Cape May Court House, NJ 08210. Shelters were screened to be certain a staff veterinarian supportive of the research was available and that shelter staff members were adequately trained on the importance of adhering to study protocols, testing procedures and medication administration.

When a shelter dog presented with acute onset diarrhea, a standardized flowsheet was utilized to determine eligibility for the study (Figure 1). Inclusion criteria for the study from this flowsheet required that the dog must be older than 5 months of age and have an odiferous, bloody or mucus diarrhea typical of a colitis or frequent small volumes of loose stool with straining. If a dog qualified through the first 3 steps of the flow sheet (Figure 1), a fecal sample was then obtained and a fecal floatation and an IDEXX Giardia Snap Test^b were run to rule out contributing parasites. Flowsheets on dogs that did not qualify based on parasite test results were retained for further review (19 dogs). Exclusion criteria included subjects with a positive fecal floatation parasite test or IDEXX Giardia Snap Test, watery diarrhea typical of a TCVM Deficiency pattern diarrhea (i.e. Spleen *Qi* Deficiency) or evidence of severe debilitation, emaciation, or other serious known health issues (i.e. kidney insufficiency, heart failure, liver disease, life-

Table 1: Ingredients and actions of *Da Xiang Lian Wan* (Great Saussurea Coptis®)

English Name	Chinese Pin-Yin	Ingredient %	Action
Saussurea	<i>Mu Xiang</i>	50	Move <i>Qi</i> and relieve pain
Coptis	<i>Huang Lian</i>	25	Clear Damp-Heat in the intestines
Evodia	<i>Wu Zhu Yu</i>	25	Warm the Middle <i>Jiao</i> and stop vomiting

Manufactured by Jing Tang Herbal, Reddick, FL, USA

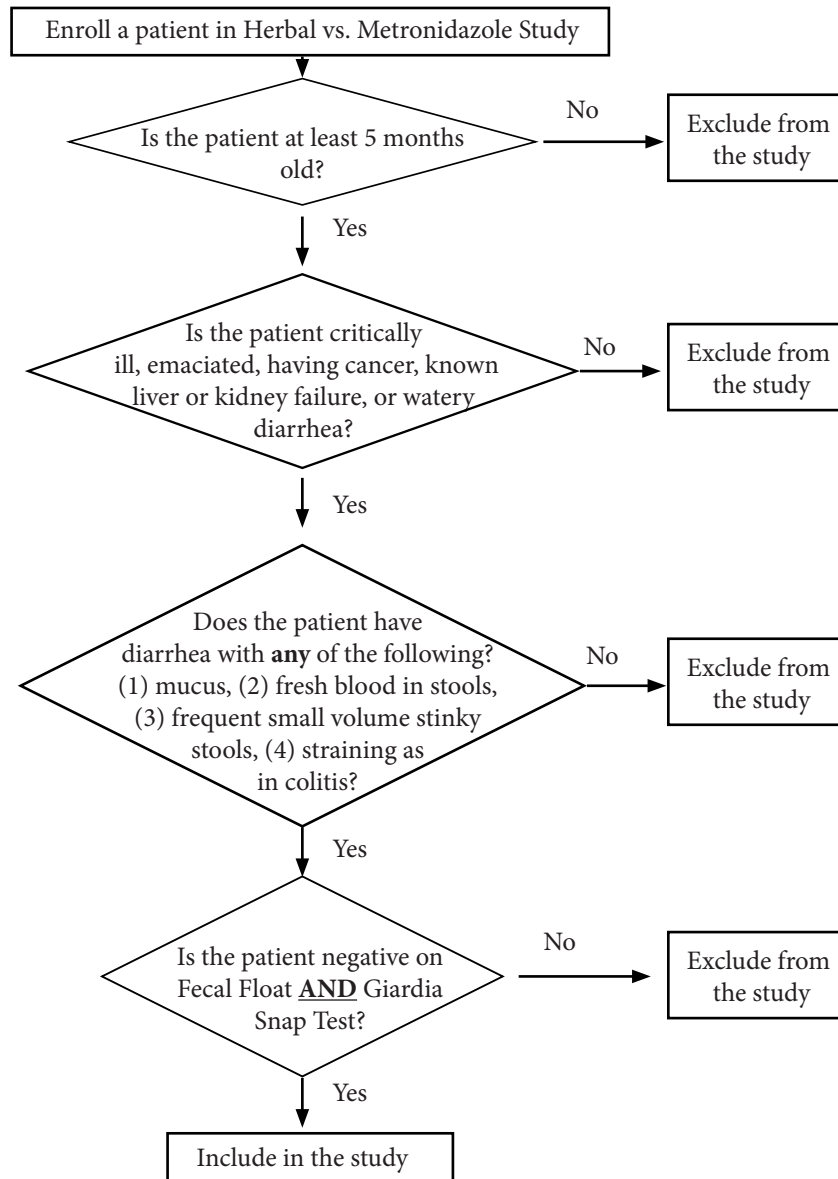


Figure 1: Subject recruitment form used at all participating shelters for study dog enrollment.

threatening cancer). Dogs that qualified for the study were randomly assigned to either the metronidazole treatment group or the *DXLW* treatment group using a commercial software program⁹. For each participating facility, a separate list of computer generated random assignment numbers based on the anticipated number of eligible dogs was utilized to prevent assignment bias. The study identification number, the facility identification, age, sex, dose, weight, and breed were recorded for each dog. Each facility had its own data sheet to record information on each dog in the study (Figure 2). The study was conducted unblinded in order to efficiently use the small pool of trained personnel available to conduct this study in a shelter environment. Each medication was administered in the morning and late afternoon, for a maximum of

10 doses and administration of each dose was recorded. All medications were administered directly by trained personnel preferably with or immediately after feeding.

A chart was supplied to each shelter by the investigator (Fowler) with preset *DXLW* doses which were calculated based on weight ranges that fell within the recommended dose (Table 2). The same approach was predominately used for dosing metronidazole. This was done to provide consistency and simplify study dosing calculations for shelter staff irrespective of who was attending the study dog on a particular day. Based on the weight ranges, metronidazole was orally dosed at 10-22 mg per kilogram of body weight twice daily and *DXLW* was orally dosed at 0.5 grams per 10-20 pounds of body weight twice daily.

Trained technicians/caregivers documented the

Table 2: Da Xiang Lian Wan Dosing Protocol*

	< 5# BW	5.1- 10# BW	10.1- 15# BW	15.1- 19# BW	19.1- 25# BW	25.1- 30# BW	30.1- 45# BW	45.1- 60# BW	60.1- 80# BW	>80# BW
0.2g capsule	1	2								
0.5g capsule			1	1.5	2	2.5	3	4	5	6

BW= Study Dog's Body Weight *Each study dog was dosed twice daily based on a weight range

<u>ALAQUA DATA SHEET FOR HERBAL/METRONIDAZOLE STUDY</u>					
DATE:					
1. Has Dog Qualified from Flowsheet? If Yes , attach flowsheet and continue. Keep Excluded flowsheets and note reason for Exclusion.					
2. Randomly assign to Herbal or Metronidazole group based on admission sequence (below).					
HERB			METRONIDAZOLE		
HERB GROUP: Consists of Dogs 1 3 6 9 10 11 12 15 20 22 23 25 27 28 30					
METRONIDAZOLE GROUP: Consists of Dogs 2 4 5 7 8 13 14 16 17 18 19 21 24 26 29					
3. Dose prescribed:					
4. Dog ID: Study Number () Alaqua ID () AGE: SEX: WEIGHT: BREED:					
DAY	DIARRHEA		MEDS GIVEN		COMMENTS (i.e. vomiting, not eating, did not take meds, died, etc.)
	AM	PM	AM	PM	
1	Y N	Y N	Y N	Y N	
2	Y N	Y N	Y N	Y N	
3	Y N	Y N	Y N	Y N	
4	Y N	Y N	Y N	Y N	
5	Y N	Y N	Y N	Y N	
HERBAL: Give for 2 doses AFTER diarrhea has resolved up to a MAXIMUM of 10 doses. Give preferably with food in stomach.					
Metronidazole: Give for 10 doses.					

Figure 2: Sample Data Collection Form used by all participating shelter/rescue facilities to record study information for each dog each day.

presence or absence of diarrhea twice daily (in the morning and late afternoon), recorded the administration of *DXLW* or metronidazole, and recorded the number of doses of *DXLW* or metronidazole required to resolve the diarrhea. *DXLW* treatment was continued for 2 doses after resolution of diarrhea or 10 doses, whichever came first. Metronidazole treatment was administered for a total of 10 doses. Minor adverse reactions including vomiting and any major adverse reactions including mortality were documented. Diarrhea was considered resolved when the clinical signs of colitis including blood or mucus in the stools or tenesmus were absent. Study dogs had to then remain free of clinical signs of colitis for a 24-hour period before qualifying as a treatment success. Subjects were considered a treatment failure if clinical resolution failed to occur during the treatment protocol period or within 24 hours of completing the treatment protocol.

Two outcome measures were recorded for statistical analysis; either the diarrhea resolved or persisted within 10 doses, and the number of doses that were required for resolution of clinical signs was tracked as continuous measures data. The two statistical hypotheses were: (1) Within 10 doses of the treatment, the proportion of subjects successfully treated by the proposed *DXLW* treatment is not smaller than (i.e., not inferior to) that by the standard metronidazole treatment and (2) For subjects successfully treated by either the *DXLW* or metronidazole treatment, the mean number of dosages required for the *DXLW* treatment is not more than that required for the metronidazole treatment.

A 95% confidence interval of the success rate difference (*DXLW* Group – Metronidazole Group) was calculated based on the two-sample test for equality of

proportions (first non-inferiority hypothesis). The null hypothesis would be rejected if the lower bound of the 95% confidence interval was greater than the preset non-inferiority limit (-0.15). A 95% confidence interval of the mean dose difference (*DXLW* Group – Metronidazole Group) was calculated based on the two-sample t-test for equality of means (second non-inferiority hypothesis). The null hypothesis would be rejected if the upper bound of the 95% confidence interval was less than the preset non-inferiority limit (2 doses). It was anticipated that the standard metronidazole treatment would have a success rate of 75% and the *DXLW* treatment a success rate of 90%. With the non-inferiority limit set to be 15%, 54 subjects (27 per group) were required to reach a test power of 90% to reject the null hypothesis (inferiority) with 95% confidence. With this sample size, the study could guarantee a 90% power to reject the null hypothesis (inferiority) with 95% confidence, with the non-inferiority limit set to be 2 doses. For each of the statistical tests, a p -value < 0.05 was considered statistically significant.

RESULTS

All 56 dogs which were enrolled completed this study with 29 in the *DXLW* Group and the remaining 27 in the Metronidazole Group. Study dogs were randomly assigned to study groups, therefore, a comparison of the distribution of gender, age, and body weight of study animals between the 2 groups was evaluated for effects on study results. Of the 56 dogs in the study, 35 (62.5%) were male or neutered males and 21 (37.5%) were female or spayed females. In the Metronidazole Group, 18 were male and 9 were female, a 2:1 ratio. In the *DXLW* Group, 17 were male and 12 were female, an approximately 3:2 ratio (Figure 3). The

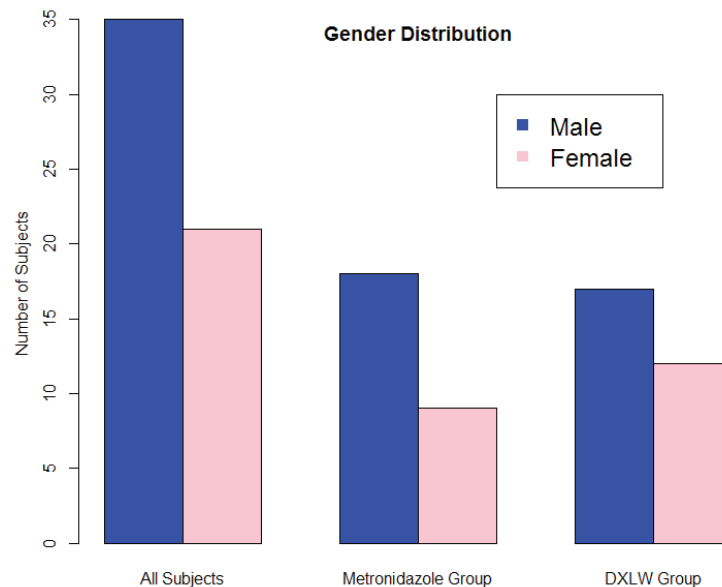


Figure 3: Gender distribution of study dogs with an overall population of 35 males and 21 females. The Metronidazole Group contained 18 males and 9 females (2:1 ratio) while the *DXLW* Group contained 17 males and 12 females (3:2 ratio). The difference in gender between the 2 groups was not statistically significant ($p = 0.73$).

mean age of the entire study subject population was 4.30 years (range 0.4 - 13.0), with the Metronidazole Group mean at 3.64 years (range 0.4 - 10.0) and the *DXLW* Group mean at 4.91 years (range 0.9 - 13.0) (Figure 4). The mean body weight over all study subjects was 38.2 pounds (range 4.4 - 84.0) with the Metronidazole Group averaging 42.0 pounds (range 4.4 - 75.0) and the *DXLW* Group 34.6 pounds (range 6.8 - 84.0) (Figure 5). The

DXLW Group had a higher proportion of females relative to the entire population and the Metronidazole Group, but the difference was not statistically significant ($p = 0.73$). Since there is no evidence that a certain gender would respond better to either treatment, this difference was considered not to have impacted the results of the study. Age and body weight distribution between the groups were evaluated with a two-sample t-test. Again, the mean age

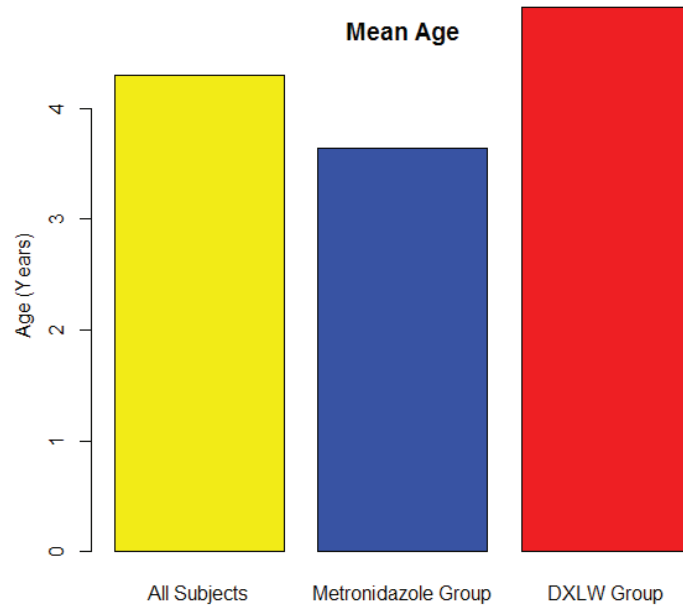


Figure 4: Mean age of the overall population of study dogs is 4.30 (range 0.4- 13.0) years. The Metronidazole Group's mean age is 3.64 (range 0.4- 10.0) years and the *DXLW* Group has a mean of 4.91 (range 0.9- 13.0) years. There was no statistically significant difference in mean age between treatment groups ($p = 0.169$).

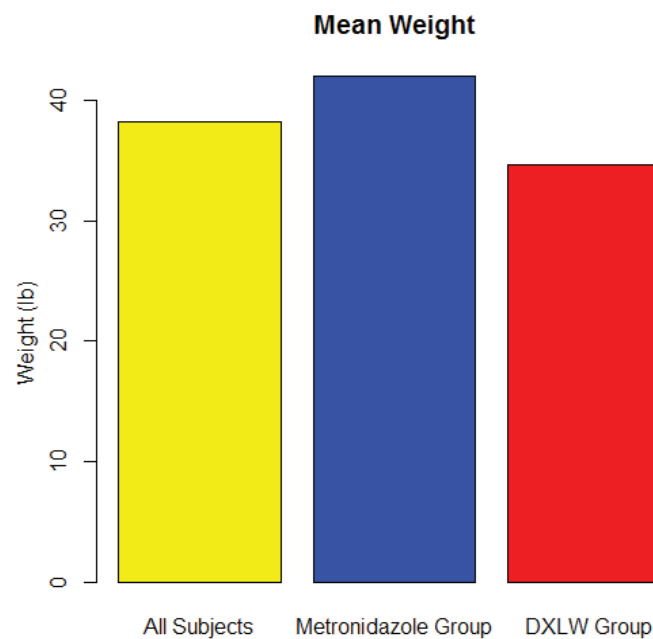


Figure 5: The body weight distribution of study dogs with the overall population mean weight equal to 38.2 pounds (range 4.4-84.0). The Metronidazole Group had a mean of 42.0 (range 4.4-75.0) and *DXLW* Group a mean of 34.6 pounds (range 6.8-84.0). There was no statistically significant difference in mean weight between treatment groups ($p = 0.284$).

and body weight comparison between the two treatment groups was not significantly different ($p = 0.169$ and $p = 0.248$, respectively) which reduced the possibility that age or body weight would affect the outcomes of the study.

Of the 27 dogs entered into the Metronidazole Group, 24 (88.9%) had resolution of their colitis type diarrhea within the 10 dose protocol while out of the 29 dogs entered in the *DXLW* Group, 28 (96.6%) resolved

within 10 doses or less (Figure 6). The mean dose for successful resolution of the stress induced colitis was 3.46 doses for metronidazole and 3.26 doses for *DXLW*. There was no mortality associated with the administration of either study therapeutic compound (Figure 7). Adverse reactions were minimal and limited to vomiting in 1 dog in the Metronidazole Group which resolved with antiemetics and 1 dog in the *DXLW* Group which resolved

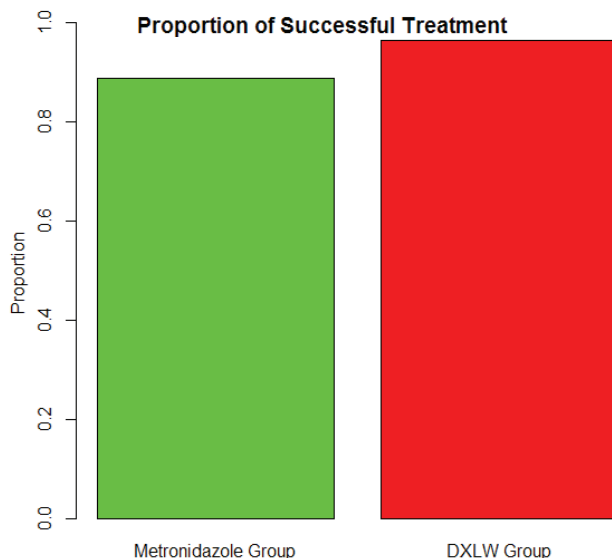


Figure 6: Proportion of successful treatment for resolving the colitis type diarrhea in study dogs with either metronidazole (88.9%) or *DXLW* (96.6%) within 10 doses, $p < 0.05$ in testing the non-inferiority of *DXLW* group against Metronidazole Group.

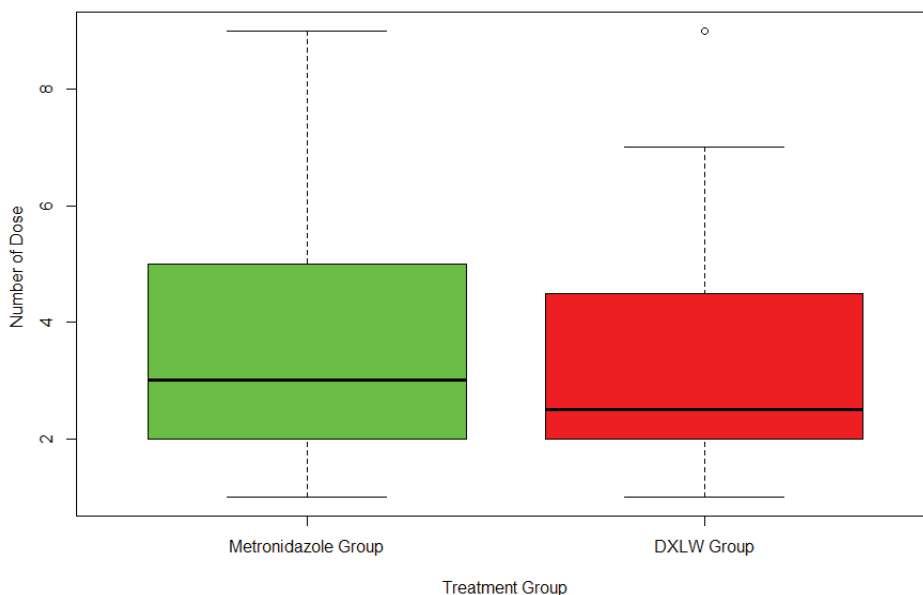


Figure 7: Box plot: Comparison of the observed mean dose required to resolve the colitis type diarrhea in the metronidazole (3.46 doses) and *DXLW* (3.26 doses) treatment groups ($p < 0.05$, non-inferiority testing). The two treatments had very similar distribution of the “effective” doses, as both the median (the bold horizontal black line inside the box) and the range (the height of the box and between the two whiskers) are very close between the two distributions. The only obvious difference is an outlier in the *DXLW* group (the data point above the upper whisker). This particular subject required 9 doses to resolve the colitis type diarrhea.

without treatment. The 4 dogs that failed to resolve with treatment were equally represented by male and female, with an age range of 2 to 10 years, and a weight range of 33 to 62 pounds. There was no commonality in their representation.

To test the hypothesis that, within 10 doses of the treatment, the proportion of subjects successfully treated by the proposed *DXLW* treatment is not smaller than (i.e., not inferior to) the standard metronidazole treatment, the study applied both the two-sample proportion test and the bootstrap method to generate the 95% confidence interval of the proportion difference between the two groups, as described in the previous section. With the observed successful treatment rate at 0.89 (24/27) and 0.966 (28/29) for the Metronidazole Group and *DXLW* Group, respectively, since the 95% confidence interval of the proportion difference calculated based on the two-sample test for equality of proportions has a lower bound greater than the preset non-inferiority limit -0.15 and even more significant result obtained through the bootstrap method, the null hypothesis could be rejected ($p < 0.05$).

Similar statistical evaluation of the hypothesis that, for subjects successfully treated by either the *DXLW* or metronidazole treatment, the mean number of doses required for the *DXLW* treatment is not more than that required for the metronidazole treatment, the study applied both the two-sample t-test and again the bootstrap method to generate the 95% confidence interval of the difference of means between the two treatment groups. With the mean dose required for success at 3.46 and 3.25 doses for the Metronidazole Group and *DXLW* Group, respectively, since the 95% confidence interval of the mean dose difference calculated based on the two-sample t test for equality of means had an upper bound smaller than the non-inferiority limit of 2 doses and similar results obtained through the bootstrap method, the null hypothesis could be rejected ($p < 0.05$).

DISCUSSION

Pet owners are increasingly seeking out herbal therapies to replace conventional pharmaceuticals which often have adverse side-effects. Animal shelters are also frequently looking at TCVM as a better way to manage their populations, prevent and treat medical issues. The test formula selected to evaluate in this experimental study, *DXLW* (Table 1) was identified as a good Chinese herbal formula to use because of the safety and efficacy observed when treating canine colitis in one of the investigators' TCVM practice (Fowler), even in cases in which other conventional treatments such as metronidazole had failed. Additionally, a need to identify a safe, cost-effective alternative medication to the limited choices available to treat stress related colitis in sheltered dogs was needed. The formula's effectiveness in other species, including humans, is well demonstrated in medical literature which also made it attractive to assess as a treatment strategy for

dogs.

Although no clinical research studies on colitis or stress induced colitis in dogs were found, several TCVM textbooks describe the effectiveness of *DXLW* herbal formula or the individual herbs contained within it for the treatment of gastrointestinal disorders including those conventionally labeled as colitis.^{10,16,17} In both TCVM clinical and herbal textbooks, *DXLW* is recommended for treatment of the TCVM pattern Damp Heat or Heat Toxin at a dosage of 0.5 grams per 10-20 pounds body weight. Its excellent effects when used as a treatment for the Western diagnosis of Inflammatory Bowel disease is described.^{10,16} The single herbs, *Huang Lian* (Coptis) and *Mu Xiang* (Saussurea) are cited in Xie's Chinese Veterinary Herbology text for Damp Heat in the intestines with clinical signs of "Bloody mucous diarrhea, dysentery, and tenesmus".¹⁷ Similarly, *Mu Xiang* combined with *Huang Lian* is listed as an excellent Chinese herbal medicine for Damp Heat dysentery.¹⁷ Other journal articles recommended further research on plants which have been recommended for gastrointestinal disorders including Inflammatory Bowel Disease.^{19,20}

In this research project, through the design of a randomized controlled clinical study, the investigators sought to demonstrate statistical evidence to support the hypothesis that treating stress colitis in sheltered dogs with the Chinese herbal *DXLW* is just as effective as treating them with the conventional treatment of metronidazole. Dogs from 3 shelters were enrolled in the study. An enrollment flow sheet which applied inclusion and exclusion criteria to each potential study dog was performed. Overall distribution differences in gender, body weight and age were evaluated and found to be statistically insignificant between the 2 treatment groups, which suggests that these subject characteristics were deemed unlikely to impact the outcomes of the study.

The most common reason for exclusion from the study for dogs that had qualified in all other enrollment aspects (19 potential subjects) was disqualification due to positive parasite tests. This represented 25% of otherwise eligible presenting subjects, a higher than anticipated ratio. IDEXX Giardia Snap Tests were positive in 84% of the parasitized dogs demonstrating that Giardia was the primary disqualifying parasite, but additionally 21% of the potential subjects were positive for *Ancylostoma* (hookworms), 11% for *Isospora* (coccidia), and 5% for *Trichuris* (whipworms). This higher than anticipated ratio by both the investigator (Fowler) and attending shelter veterinarians unfortunately encumbered the study through subject disqualification. It also resulted in one shelter changing their protocol to include an IDEXX Giardia Snap Test.

Based on the 56 dogs that qualified and completed the study, 89% of the animals assigned to the Metronidazole Group responded to the treatment, while 97% of the *DXLW* Group had successful resolution of their stress

colitis. These observations provided statistical evidence ($p < 0.05$) that the success rate of *DXLW* Chinese herbal medicine is not inferior to that of the standard treatment Metronidazole when treating stress colitis in sheltered dogs. In addition, study dogs that responded to the assigned treatment (52 out of 56), had a mean dose of 3.46 doses in the Metronidazole Group and 3.26 doses in the *DXLW* Group (3.26 versus 3.46; $p < 0.05$). These observations statistically support that *DXLW* works as quickly as the current conventional treatment metronidazole.

Based on the population in the investigator's TCVM practice (Fowler), where most colitis affected dogs were failed or untreatable with metronidazole, the anticipated success rate of metronidazole was postulated to be 75%. The measured success rate for study dogs, however, was 89%. The higher than anticipated success rate of metronidazole in this study is most likely due to the fact that the study subjects represented acute cases or acute exacerbations of stress induced colitis. This is in contrast to the often more chronic cases of colitis and ulcerative colitis seen in the general dog population and veterinary practices. With multiple treatments of metronidazole and other antimicrobials, presumably antibiotic resistance becomes a factor in metronidazole failure in dogs seen in conventional practices.^{18,20}

While the anticipated success rate of *DXLW* was 90%, the final study results demonstrated a 97% success rate which again was better than the anticipated success rate. This may be associated with *DXLW* not being encumbered by microbial antibiotic resistance as a cause of treatment failure in canine colitis. Treatment failures associated with *DXLW* administration are typically the result of inappropriate use due to incorrectly identified TCVM patterns. After study completion, some dogs in both treatment groups, that had met treatment success criteria during the study, had stress colitis relapses as long as they continued to be held in the facility. In these cases, following recovery, administration of a Chinese herbal medicine such as *Xiang Lian San* could be considered for effective long term maintenance.¹⁰

Useful information provided by the shelter reports indicated that encapsulated *DXLW* was as easily administered in food as metronidazole. Purchased in bulk powder, the formula *DXLW* was cost effective even for animal shelters at less than 10 cents per gram. The investigator (Fowler) observed that the higher end *DXLW* dose of 0.5 grams per 10 pounds body weight worked more effectively and quickly at resolving the stress colitis than the lower end of 0.5 grams per 20 pounds body weight. In future studies, administering *DXLW* for the full 10 doses rather than discontinuing treatment 2 doses after the cessation of diarrhea may be even more effective, and help prevent relapses.

This research is in agreement with previously conducted studies on the efficacy of *DXLW* and its ingredients in treating colitis in humans and non-canine

species. The 97% success rate of *DXLW* in treating sheltered dogs with stress colitis demonstrated in this study is close to the 90% success rate in humans cited in the literature review.¹² This research helps to bridge the gap that exists between human and non-canine species versus dogs on the subject of *DXLW* and provides the scientific community with validation of the efficacy of *DXLW* in stress colitis in sheltered dogs. This validation also supports the use of *DXLW* in stress colitis prone Military Working, Search and Rescue, and Police Dogs. The pet dog population prone to colitis benefits as well by providing an effective alternative treatment to metronidazole and other conventional colitis medications, with fewer potential side effects. Additionally, this research helps to validate the effectiveness of Chinese herbal medicine in general.

In conclusion, *DXLW*, is an effective alternative to the standard metronidazole treatment in treating stress colitis in sheltered dogs. It is easily administered, is free of any significant adverse side-effects and is not encumbered by antibiotic resistance seen in some cases. Lastly, this research project lays the groundwork for a more detailed study to further validate *DXLW* and other Chinese herbal medicines. A well-funded study at a major university could recruit a larger number of eligible subjects and test additional measurable indices such as routine clinical pathology, inflammatory factors, hormones, etc. Potential subjects could also be evaluated by an experienced TCVM veterinarian using tongue and pulse observations and other TCVM diagnostic criteria. These potential subjects could then be diagnosed with a specific TCVM Pattern to determine that an Excess Pattern of Intestinal Damp Heat appropriate for *DXLW* qualified them for the study. Possible Deficiency patterns for which *DXLW* would not be appropriate would then more effectively be excluded from the study. A more detailed medical and background history, which is not available in rescued and abandoned dogs, could be taken and yield additional useful information. Additionally, *DXLW* could be compared to other conventional medications used to treat colitis in dogs and evaluated for bacterial resistance, the postulated factor in failure of conventional antimicrobial colitis medications. This could offer insight into *DXLW* efficacy in resolving cases that have failed with metronidazole treatment.

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FOOTNOTES

- a. Great Saussurea Coptis, Jing Tang Herbal, Reddick, Florida, USA
- b. IDEXX Laboratories, Inc., Westbrook, Maine
- c. “R” version 3.2.2; The R Foundation for Statistical Computing, Vienna, Austria

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