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Traditional herbal preparation for gastro-enteritis in ruminants: A pharmacognostic review

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Abstract
Inflammation of the intestinal mucosa causes enteritis which results in severe production loss. The treatment of enteritis with antibiotics, deleteriously alter the intestinal microflora, thereby interfering with competitive antagonism with the pathogenic bacteria. It also results in development of antibiotic resistance in microbes. The ethno-veterinary practices can provide useful alternatives for intensive animal health care. Hence in this review, antidiarrhoeal, anti-spasmodic, anti-inflammatory, anthelmintic, antimicrobial and prebiotic activities of the ethno-veterinary formulation that contains *Cuminum cyminum*, *Papaver somniferum*, *Trigonella foenum-graecum*, *Piper nigrum*, *Curcuma longa*, *Ferula foetida*, *Allium cepa*, *Allium sativum* and *Murraya koenigii* is evidenced by the peer reviewed scientific literature.

Keywords: Enteritis, ethno-veterinary, anti-diarrheal, pre-biotic

Introduction
Enteritis has a huge impact on production performance and well being of the animals particularly, in early stage of rearing ruminants (Luiz *et al.*, 2019) [19]. Use of antimicrobial agents is believed to be able to inhibit rumen fermentation through suppressing rumen microbes (Owens and Basalan, 2016) [27]. Overuse of antibiotics causes many problems such as the disturbance of intestinal microbes and antibiotic resistance (Phillips *et al.*, 2004) [29]. Several reports showed that infections by antimicrobial resistant pathogens in humans may be linked to antimicrobial use and antimicrobial resistance in food-producing animals (Magnusson *et al.*, 2021) [53]. Plants are important source of therapeutic drugs and play a significant role in the survival of the tribal and ethnic communities (Rajesh *et al.*, 2019) [33]. Moreover, medicinal plants can also play an important role against the insurgence of antibiotic resistance both directly for their antimicrobial activities and indirectly by minimizing the resistance against antibiotics (Kumar *et al*. 2017) [18]. Hence, the ethno-veterinary preparation formulated by Dr. N. Punniamurthy, Retired Professor, TANUVAS, which is widely used among the farmers, is Pharmacognostically reviewed.

Enteritis
Inflammation of the intestinal mucosa is enteritis which results in diarrhea and also sometimes causes dysentery, abdominal pain, dehydration and acid-base imbalance depending on the cause, severity and location. There are many causes for enteritis in farm animals and the disease varies considerably in its severity, depending upon the causative agent(s). The enteropathogens include bacteria (*Salmonella* spp., Enterotoxigenic *E. coli*, *Clostridium perfringens* (type B and C), *Proteus*, M*ycobacterium paratuberculosis* and *Pseudomonas* Spp,.) virus (Rota and corona virus, Bovine viral diarrhea, Corona virus, Rinderpest, Bovine malignant catarrh), fungi (Mycotic Candida spp.), protozoa and helminthes. Long term usage of antibacterial agents through oral route may alter the intestinal microflora and permit the development of super infection by organisms (Radostits *et al.*, 2007) [31].

Traditional health practices

Herbal medicines are believed to be effective in curing diarrhea, and for many years, plants and plant extracts have been used to treat various gastrointestinal ailments, including diarrhea (Akram *et al.*, 2020) [2]. Lukmanee *et al.*, (2014) [20] proved that the Thai herbal medicine, Krisanaklan was found to inhibit the Cystic Fibrosis Transmembrane Regulator (CFTR) and Calcium dependant chloride channels in mouse model induced with secretory diarrhoea. Veeresh *et al.*, (2014) [55] stated that the plants with antidiarrhoeal potential contain tannins as one of the major constituents that could reduce the intracellular calcium ions inward current. The ethno-veterinary formulation of Dr. N. Punniamurthy, Retired Professor, TANUVAS for the enteritis contains *Cuminum cymium*, *Papaver somniferum*, *Trigonella foenum-graecum*, *Piper nigrum*, *Curcuma longa*, *Ferula foetida*, *Allium cepa*, *Allium sativum* and *Murraya koenigii* (https://vikaspedia.in/agriculture/livestock/general-management-practices-of-livestock/ ethnoveterinary - formulations -for-important-ailments-in-bovines).

Antidiarrhoeal and antimicrobial properties

***Cuminum cyminum* (Cumin):** *C. cyminum L.* is native of Mediterranean region. Aqueous extract of *C. cyminum* (ACCS) acted against the diarrhoea induced by castor oil, PGE2 and intestinal transit time by charcoal meal in albino rats at the dose rates of 100, 250 and 500 mg/Kg orally. The author revealed that the mechanism of antidiarrhoeal action of ACCS may be due to the presence of flavonoidal and terpenoidal derivatives that inhibit the release of autacoids and prostaglandins in intestinal cells, induced by castor oil. ACCS increased the resorption of water by decreasing the intestinal motility and control the watery secretion by inhibiting the chloride channel in the luminal wall as well as intestinal transit time, as evidenced by charcoal meal test (Sahoo *et al.*, 2014) [39].

Ghanekar and Dixit (2014) [13] proved that the aqueous extract of *C. cyminum* at the dose of 400 mg/Kg significantly ($p \leq 0.001$) reduced the total number of faeces in castor oil induced diarrhoea in mice and the extracts inhibit both acetylcholine and histamine induced contractions in isolated ileum preparation which indicate that the extracts may possess antispasmodic activity. Milan *et al*. (2008) [24] reported that the aqueous extract of cumin increased amylase, lipase, protease and phytase activities.

Table 1: Ethnoveterinary formulation for Enteritis in Ruminants

Formulation I			Formulation II		
S.No	**Items**	**Quantity**	**S.No**	**Items**	**Quantity**
1.	*Cuminum cyminum* (Cumin)	Each 10 grams	7.	*Allium cepa* (Onion)	2 bulbs
2.	*Papaver somniferum* (Poppy seeds)		8.	*Allium sativum* (Garlic)	2 cloves
3.	*Trigonella foenum-graecum* (Fenugreek)		9.	*Murraya koenigii* (Curry leaves)	50 grams
4.	*Piper nigrum* (Black pepper)	Each 5 grams	The items in the formulation 2 were made into a paste.		
5.	*Curcuma longa* (Turmeric)				
6.	*Ferula foetida* (Asafoetida)				
The items in the formulation 1 were dried and roasted on a minimum fire in a metal pan for 5 minutes to convert it charred black in colour. This is allowed to cool and add water then make into a paste, which is ready for application.			The paste from formulation 1 and 2 were mixed thoroughly.		

Sheikh *et al.* (2010) [46] confirmed that the methanolic extract of *C. cyminum* seeds had the best antimicrobial activity against *E.coli*, *S.shinga*, *K.pneumoniae and S.dysentriea* and the MIC and MBC values against the studied bacteria were 20-50mg/ml and 40-60mg/ml respectively. Hawrelak *et al.* (2009) [15] stated that cumin oil displayed high degree of selective inhibition of the growth of the potential pathogens at the concentration that had no effect on the beneficial bacteria examined. This effect is useful in treating dysbiosis, associated with a number of gastrointestinal disorders. Vaishnavi *et al.* (2007) [54] proved that the cumin seeds at the lower concentration were effective against *S. typhi* and *E. coli* 0157.

***Papaver somniferum* (Poppy seeds)**

P. somniferum, opium poppy, is an annual herbaceous plant in the Papaveraceae (poppy family) which originate in southeastern Europe and western Asia and cultivated for the production of opium, heroine and morphine (www.eol.org).

Chaudhry *et al.*, (2008) [8] evaluated the antibacterial activity of aqueous infusions and aqueous decoctions of poppy seed (*P. somniferum* L., Papaveraceae) against 188 bacterial isolates from oral cavity of apparently healthy individuals. 73% of the tested microorganisms were inhibited by aqueous decoction of cumin. Gupta *et al.*, (1993) reported that in rabbit and guinea pig ileal loop models, alcoholic and aqueous extracts of *Papaver somniferum* showed highly significant anti-secretory activity against *Escherichia coli* enterotoxin (Lt, St and Lt/St)-induced secretory responses.

***Trigonella foenum-gracaeum* (Fenugreek)**

The plant is native to North Africa and countries bordering the eastern Mediterranean, widely cultivated in India (Kor and Moradi, 2013) [17]. Mullaicharam *et al.*, (2013) [25] reported that the aqueous extract and a gel fraction isolated from the fenugreek seeds have cytoprotective effect due its anti-secretory action. Virupaksha *et al.*, (2007) [57] reported that in rats at the dose rate of 250mg/Kg fenugreek plant extracts showed significant ($p \leq 0.01$) inhibitory activity against PGE2 induced enteropooling and castor oil induced diarrhoea. The methanolic extract ($p \leq 0.01$) and aqueous extract ($p \leq 0.05$) showed significant reduction in gastrointestinal motility in charcoal meal test in rats. He also explained that this effect may be due to the inhibition of prostaglandin biosynthesis, suppression of propulsion of the intestine thereby increased the absorption of water and electrolytes. Phytochemical compounds like alkaloids, saponins, flavonoids, sterols, terpenes and sugars may be responsible for the antidiarrhoeal activity of the fenugreek extract. Ramya *et al.*, (2011) [36] determined the minimum inhibitory concentration (MIC) of ethanol extract and it showed the MIC value of 1mg/ml for *Staphylococcus aureus* and *Pseudomonas aeruginosa*. From her results she suggested that the ethanolic leaf extract of fenugreek is an important source for antibacterial components and also a potential source of phenolic antioxidants. Vijayalakshmi *et al.*, (2011) [56] concluded *T. foenum graceum*

contains many important phytochemicals like aziridine, 1, 2, 3-trimethyl-, trans-, which was proved to be a potent antimicrobial agent.

Table 2: Phytochemical Constituents of the herbal ingredients

S. No	Herbal ingredient	Phytochemicals	Reference
1.	*Cuminum cyminum*	Alkaloids, Cardiac Glycosides, Terpenes, Sterols, Isoflavonoids, Flavonoid Glucosides, Lignins, Monoterpenoid Glucosides, Phenolic, Alkaloids, Compounds, Limonene, Cuminaldehyde, A- and B- Pinene, 1, 8-Cineole, O-and P-Cymene, A- and T- Terpinene, Linalool and Safranal.	Takayanagi *et al.* (2003) [50], Aamir *et al.* (2014) [1]
2.	*Papaver somniferum*	Isoquiline Alkaloids, Morphine, Noscapine, Codeine, Thebaine, Narceine, Papaverine, Codamine, Narcotoline, Narcotine, Groscopine, Oxynarcotine, Narceine, Laudamine, Laudanosine.	Masihuddin *et al.* 2018 [22]
3.	*Trigonella foenum-graecum*	Gentianine, Carpaine, Flavonoids Luteolin, Apigenin, Orientin, Vitexin, Quercetin, Isovitexin, Saponins, Fenugreekine, Coumarin, Nicotinic Acid, Phytic Acid, Scopoletin, Sapogenins and Trigonelline Sesquiterpenes.	Mehrafarin *et al*., (2010) [23] Mullaicharam *et al.*, (2013) [25]
4.	*Piper nigrum*	Phenolics, Flavonoids, Alkaloids, Amides, Lignans, Neolignans, Steroids, Terpenes, Piperamide, Piperamine, Chalcones, Piperettine, Pipericide, Sarmentine, Piperine, Piperolein B, Pipene, Retrofractamide A and Sarmentosine.	Damanhouri and Ahmad (2014) [9]
5.	*Curcuma longa*	Tannins, Alkaloids, Saponins, Flavonoids, Terpenoids, Cardiac Glycosides, Curcuminoids that contains Bisdemethoxy Curcumin, Flavonoid Curcumin, Demethoxy Curcumin and Various Volatile Oils, including Atlantone, Tumerone and Zingiberone.	Akram *et al*., (2010) [3] Rajesh *et al.*, (2013) [34-35]
6.	*Ferula foetida*	Resin fraction contains ferulic acid and its esters, coumarins, sesquiterpene coumarins and other terpenoids. The gum includes glucose, l-arabinose, rhamnose, galactose, glucuronic acid, polysaccharides and glycoproteins, and the volatile fraction includes sulfur-containing compounds, monoterpenes and other volatile Galbanic acid and terpenoids.	Irnashahy and Iranshahy *et al.*, (2011) [16] Shahverdi *et al*., (2007) [41]
7.	*Allium cepa*	Onionin A, Cysteine Sulfoxides, Quercetin, Flavanoids, Glycosides, Saponin and Tannins.	Bidakar *et al*., (2012) [59] Zhao *et al*., 2021 [58]
8.	*Allium sativum*	Allicin, Steroidal Saponins, Flavones, Alkaloids, Cardiac Glycosides, Flavonoids, Terpenes and Resins.	Singh *et al.*, (2001) [49] Gazuwa *et al.*, (2013)
9.	*Murraya koenigii*	Alkaloid, Phytosterol, Flavonoid, Glycosides, Saponin, Phenolic Compounds, Terpenoid, Koenimbine, Murrayafoline, Mahanimbine, Mahanine, Isomahanine, Koenoline, Murrayazoline, Mahanimboline, and Mahanimbinine, Mukoline, Murrayacinine.	Bansode *et al*., (2014) [5] Tan *et al*., (2022) [51]

Piper nigrum (Black Pepper)

P. nigrum is the most commonly used spices and known as 'The King of spices' and it is native to south India (Damanhouri and Ahmad, 2014) [9]. The effect of *P. nigrum* on nitric oxide (NO) pathway was studied by Shamkuwar (2013) [43] to detect antidiarrhoeal mechanism in mice. 2.5 ml /Kg of *P. nigrum* caused significant dose dependant delay in the onset of copious diarrhoea, decrease in the frequency of purging, weight of wet stools and total weight of stools in castor oil induced diarrhoea in mice. Castor oil induced diarrhoea and intestinal secretion involves NO as one of the mediator. Hence it was revealed that Isosorbide dinitrate (NO donar) has reduced the antidiarrhoeal effect of *P.nigrum.* Shamkuwar *et al.* (2012) [42] concluded that aqueous black pepper extract (ABPE) possesses antidiarrhoeal effect in magnesium sulphate and castor oil induced diarrhoea in mice, through the inhibition of prostaglandin biosynthesis and increasing the absorption of water and electrolytes from the gastrointestinal tract. Singh and Duggal (2009) [48] documented that GM-CSF, IL-6, TNF- α and IL-1β, the proinflammatory cytokines was dramatically reduced by administration of piperine. Platel and Srinivasan (2000) [30] evaluated the influence of piperine (20 mg %) on pancreatic enzymes in rats. Dietary piperine significantly increased the activities of pancreatic lipase, trypsin, chymotrypsin and amylase enzyme. Ganesh *et al.*, 2014 [12] proved the antibacterial activity of ethanolic extract of *P. nigrum* against *Escherichia coli*, *Proteus sp.*, *Salmonella typhi* and *Staphylococcus aureus.*

Curcuma longa (Turmeric)

C. longa is native to India and also referred to as 'Indian saffron'. It had reached china, West Africa, East Africa and also had begun to popular all through the world (Akram *et al.*, 2010) [3]. Akram *et al.*, (2010) [3] stated that sodium curcuminate inhibited intestinal spasm and p-tolymethylcarbinol increased secretin, gastrin and pancreatic enzyme secretion. Thong-Ngam *et al.*, (2013) [52] reported that in rats the curcumin inhibit nuclear factor (NF)-κB and it lowers the production of adhesion molecules and inflammatory cytokines, resulting in the amelioration of gastropathy induced by NSAIDs. Aldin *et al.*, (2012) [4] stated that on mouse ileum and colon *C. longa* extract has indirect and direct myorelaxant effect independent of the anti-inflammatory effect and suggested the use of *C. longa* as a spasmolytic agent. Deshmuk (2014) [10] showed that *E.coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterobacter aerogenes*, *Salmonella typhimurium* and *Staphylococcus epidermidis* were highly sensitive to turmeric extract and concluded that the curcumin is responsible for the antibacterial activity of turmeric.

Ferula foetida (Asa-foetida)

F. foetida, a perennial plant, was native to Afganistan and Iran and widespread from Mediterranean region to central Asia (Rahman *et al.*, 2008) [32]. Sadraei *et al.*, (2003) [37] proved that *F. foetida* essential oil has potent inhibitory effect on contraction of ileum induced KCl, acetylycholine and 5-hydroxytryptamine. The study supports the potential spasmolytic activity of *F. foetida*. Sadraei *et al.*, (2001) [38]

reported that from the identified components of *F. foetida* essential oil, α-pinene (12.2%) and β- pinene are the two components with known antispasmodic effect on ileum contraction induced by KCl and acetylcholine. Gundamaraju (2013) [14] proved that resin extracts of *F. foetida* has a significant dose dependant anthelmintic activity, that might be due to flavonoids and polyphenolic compounds especially tannins present in the resin extract. Rahman *et al.*, (2008) [32] proved the antibacterial activity of *F. foetida* oil against gram positive (*Bacillus megaterium*, *Lactobacillus acidophilus*, *B. subtilis*, *Micrococcus luteus*, *S. aureus*, *Staphylococcus epidermidis*,) and negative bacteria (*Salmonella typhi*, *Escherichia coli*, *Shigella flexneri*).

***Allium cepa* (Onion)**

A.cepa is a perennial that are cultivated worldwide. The fresh bulb of *A. cepa* that grows below the ground is used medicinally (Sampathkumar *et al.*, 2010) [40]. Naseri *et al.*, (2008) [26] stated the spasmolytic effect of quercetin via calcium channels in onion peel extract. Rajeshkumar *et al.*, (2013) [34-35] evaluated the antidiarrhoeal activity of aqueous bulb extract of *A. cepa* against castor oil induced model in rats. The extract tested at 150 and 300 mg/Kg significantly inhibited the frequency of defecation compared to untreated control and the effect was similar to the standard drug, loperamide. The mechanism appears to be anti-enteropooling and spasmolytic properties of the plant extract. Shinkafi and Dauda, (2013) [47] proved the antibacterial activity of fresh onion extract against *Escherichia coli*, *Streptococcus pyogenes*, *Streptococcus pneumonia* and *Staphylococcus aureus.*

***Allium sativum* (Garlic)**

Garlic is one of the oldest cultivated plants which is native to the mountainous regions of central Asia, which later spread to China, the Near East, and the Mediterranean regions (Cardelle-cobas *et al.*, 2010) [7]. Allicin, a disulphide compound in garlic have antibacterial activity by inhibiting the RNA synthesis in bacteria (Singh *et al.*, 2001) [49]. Dkhil *et al.*, (2011) [11] proved the effect of garlic against the coccidiosis caused by *Eimeria papillata* in mice. Cardelle-cobas *et al.*, (2010) [7] stated that the garlic exerts 10 times greater inhibition against potentially harmful enterobacteria (*E. coli*) than beneficial intestinal microflora (*Lactobacillus casei*). The above effect may be due difference in the composition of the bacterial cell membrane. Sharma *et al.*, (2006) [44] reported that the garlic acts as a prebiotic due to the presence of fructo-oligosaccharides that found to selectively stimulate the growth and activity of beneficial bacteria (bifidobacteria and lactobacilli) in the colon.

***Murraya koenigii* (Curry leaves)**

The plant *M. koenigi* was native of India and now is distributed to most parts of the southern Asian countries (Mandal *et al.*, 2010) [21]. Sharma *et al.*, (2012) [45] proved the anti-diarrhoeal activity of aqueous (200 mg/Kg) and alcoholic (400 mg/Kg) extract of the leaves of *M. koenigii* in rats and the result suggested that the extract possess anti-muscarinic activity and inhibit the PGE2 to exhibit its antidiarrhoeal activity. Pagariya and Maithili (2009) [28] reported that the ethanol and aqueous root extracts of *M. koenigii* showed significant reduction in the number of wet faecal droppings and inhibition in the frequency of defecation in castor oil-induced diarrhoea and charcoal meal test which may be due to non specific spasmolytic activity of *M. koenigii.*

Bansode *et al.*, (2014) [5] stated that the Ethanol, methanol, diethyl ether and acetone extracts of curry leaves showed significant antimicrobial activity against *E. coli*, *Shigella sonnei*, *Salmonella paratyphi A* and *Salmonella typhi* respectively. Baskaran *et al.*, (2011) [6] proved that ethanol, ethyl acetate, methanol, chloroform, acetone, petroleum ether, hexane and hot water leaf extracts of *M. Koenigii* have antibacterial activity against six tested bacterias *viz.*, *E. Coli*, *Micrococcus luteus*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Staphylococcus aureus.*

Conclusion

The ethno-veterinary practices can provide useful alternatives for animal health care and production. *C. cyminum*, *T. foenum-graecum*, *M. koenigii*, *P. nigrum* and *C. longa* inhibit release of autacoids, synthesis of prostagalndins and release of proinflammatory cytokines. *C. cyminum*, *F. foetida*, *A. cepa* and *M. koenigii* possess spasmolytic property. *P. somniferum* and *T. foenum* exhibit antisecretory action. *T. foenum* forms the protective coating as a lubricant, over the inflamed areas and results in healing and soothing action. *P. nigrum* and *T. foenum* enhances the digestive enzymes and its activity. All the ingredients possess antibacterial activity. *A. cepa* and *A. sativum* has anthelmintic and anticoccidial property respectively. *C. cyminum* and *A. sativum* selectively inhibits the pathogenic bacteria without affecting the beneficial bacteria in the gut. The fructo-oligosaccharides present in garlic act as prebiotic. Thus the formulation with antibacterial, anthelmintic, anti-coccidial, anti-inflammatory, spasmolytic, anti-secretory, pre-biotic and mucosal protective properties, act synergistically and clinically effective in all forms of enteritis than the currently used synthetic antibiotics without the problem of antimicrobial resistance and super-infection. The review substantiates its use in clinical enteritis, based on its pharmacological actions as evidenced by the peer reviewed scientific literature.

Conflict of interest

The Author(s) declare(s) that there is no conflict of interest.

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