CHAPTER 01

Therapeutic Potential of Garlic *(Allium sativum)* in Ruminants

FURQAN MUNIR[1], AMNA SHAKOOR[2*], ZIA UD DIN SINDHU[1], MUHAMMAD SALMAN[1], MUBASHAR SHAREEF[3], MUHAMMAD ABDULLAH ARIF[4], MUHAMMAD SHAHZAD SHAFIQ[3], ARSLAN MUHAMMAD ALI KHAN[1]

1Department of Parasitology, Faculty of Veterinary Science, University of Agriculture, Faisalabad-38040, Punjab, Pakistan.
2Department of Anatomy, Faculty of Veterinary Science, University of Agriculture, Faisalabad-38040, Punjab, Pakistan.
3Department of Pathology, Faculty of Veterinary Science, University of Agriculture, Faisalabad-38040, Punjab, Pakistan.
4Faculty of Veterinary Science, University of Agriculture, Faisalabad-38040, Punjab, Pakistan.
*Corresponding author: amnashakoor131@gmail.com

SUMMARY

Parasites pose a potential threat to livestock farming by inflicting heavy economic losses, thus, emphasizing their control for successful farming. Conventionally, this control has long been achieved through anti-parasitic drugs. However, due to the emergence of resistance in parasites against these drugs and the presence of their residues in animal products, there is an increased interest in searching for safe and effective alternatives like garlic. Garlic is a natural spice that is enriched with many health-beneficial compounds. Historically, it has long been used as a natural remedy for certain diseases. Recent research on garlic, especially its organosulfur compounds, has shown a wide range of therapeutic effects. It bears antioxidant, antiparasitic, antihypertensive, and antimicrobial properties. It is effective against various protozoa and helminths of ruminants. It modulates the gastrointestinal environment and works as a growth-promoting agent in ruminants. However, there exist some barriers to the practical application of garlic in ruminants which are also discussed in this chapter.

INTRODUCTION

The feeds of animals play a key role in maintaining the health of animals. Across various types of pastures and grazing areas, people provide diets to their animals according to the season and availability of fodder (Ortikova et al., 2020). The diet of animals is very important as it has a direct influence on the health of ruminants (Salobir et al., 2012). Mostly the diet of ruminants includes green fodder along with a certain amount of concentrated feed (Huque and Sarker, 2014). Garlic (*Allium sativum*) is well known in Asia and its leaves, cloves, and flowers have been widely used in traditional medicine for a long time; refer to Fig 1. (Mikaili et al., 2013). It is historically proven that various cultures have used garlic for the control, prevention, and treatment of many diseases (Gebreselema and Mebrahtu, 2013). Garlic is traditionally recognized as a medicinal plant for its prophylactic as well as therapeutic applications (Bayan et al., 2014).

In the history of China and India, garlic was recommended for the treatment of respiratory and digestive problems including the treatment of parasitic infestations and leprosy (Rivlin, 2001). It is also used as a spice and food additive (Shang et al., 2019). In a well-known book, Qanoon Fil Tib written by Avicenna, it is elaborated that the compounds of garlic are useful in the treatment of toothache, arthritis, chronic cough, parasitic infestations, constipation, insect and snake bites, gynecological diseases, and as an antibiotic for infectious diseases (Kamra et al., 2012). Experimental and clinical investigations also suggest many beneficial effects of garlic such as antioxidants, antimicrobial, detoxification of harmful compounds, protection of the liver, and reduction of cancer risk and cardiovascular diseases (Bayan et al., 2014; Oh et al., 2017).

Garlic and its compounds are beneficial for the health of the cardiac system and are used for the prevention and treatment of cardiovascular diseases. Aqueous garlic extract prevents

How to Cite: Munir F, A Shakoor, ZuD Sindhu, M Salman, M Shareef, MA Arif, MS Shafiq & AM Ali. 2023. Therapeutic potential of garlic (*Allium sativum*) in ruminants. In: Complementary and Alternative Medicine: One Health Perspective (Sindhu ZuD, B Aslam, U Uslu & M Mohsin, eds): FahumSci, Lahore, Pakistan, pp: 01-09. ISBN: 978-627-7745-01-1. https://doi.org/10.61748/CAM.2023/001

systolic blood pressure, oxidative stress, vascular remodeling, and aortic NAD(P)H oxidase activity (Mikaili et al., 2013). It has a significant effect on blood pressure lowering, serum cholesterol and triglyceride reduction, atherosclerosis prevention, increasing fibrinolytic activity, and inhibition of platelet aggregation. The oral administration of garlic effectively lowers the high blood pressure of animals. The mechanism behind the antihypertensive effect of garlic is due to its prostaglandin-like activity which results in a decrease in peripheral vascular resistance (Bayan et al., 2014; Shang et al., 2019; Ku-Vera et al., 2020).

Experimental studies also show the hypoglycemic effect of garlic in animals (Saikat et al., 2021). In many studies, it was found that garlic can reduce the level of glucose in the blood of diabetic patients. The volatile compounds present in garlic are responsible for lowering the blood glucose level such as alliin, allicin, diallyl disulfide, and trisulfide (Ribeiro et al., 2021). The extract of garlic is effective in the reduction of insulin resistance (Bayan et al., 2014).

Garlic is also useful for the health of the liver as it acts as an antioxidizing agent and detoxifies the harmful chemicals or compounds produced by the liver during the metabolism of certain medicines (Manal, 2018; Yamaguchi et al., 2019). Acetaminophen is an analgesic and antipyretic drug used worldwide but its overdose may lead to hepatic and nephrotic toxicity. It is proven that the hepatotoxicity induced by acetaminophen can be prevented with garlic (Dorrigiv et al., 2020). The inclusion of garlic in the diet of animals is also beneficial for the cure of hepatotoxicity induced by gentamycin (an antibiotic commonly used in ruminants) (Ademiluyi et al., 2013). The compounds of garlic enhance the antioxidant defense system of animals and can also reduce lipid peroxidation (Kamra et al., 2012).

Historically, garlic has long been used by different cultures for combating infectious diseases owing to its antimicrobial activity. This antimicrobial activity is attributed to the sulfur compounds present in garlic such as allicin (Mikaili et al., 2013). This compound has sulfhydryl-modifying activity and causes inhibition of sulfhydryl enzymes (Bhatwalkar et al., 2021). Moreover, garlic has shown differential inhibition of harmful enteric microbes and beneficial intestinal microflora (Chidinma et al., 2019). It has proven to be very effective against many gram-negative, gram-positive, and acid-fast bacteria such as *Escherichia coli*, *Pseudomonas*, *Salmonella*, *Staphylococcus aureus*, *Proteus*, *Klebsiella*, *Bacillus subtilis*, *Micrococcus*, *Mycobacterium*, and *Helicobacter* (EL-Mahmood, 2009; Hannan et al., 2011; Zardast et al., 2016; El-Azzouny et al., 2018; Elmowalid et al., 2019; Fufa, 2019; Lionel et al., 2020; Al-Shoaibi and Benedicts, 2021; Oyawoye et al., 2022). Garlic when used in combination with ciprofloxacin exhibited a synergistic response (Arguello-Garcia et al., 2018).

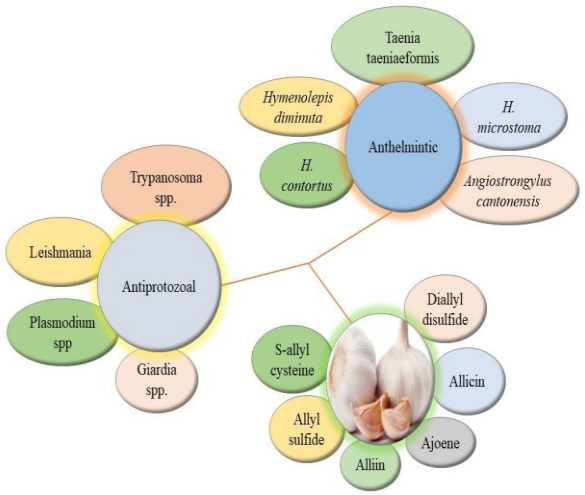

Fig 1. Therapeutic effects of garlic compounds

The extract of *A. sativum* also has anti-inflammatory effects (Batiha et al., 2020). The mechanism behind the anti-inflammatory activity of garlic is through inhibition of the cytoskeleton assembly-disassembly process (Shih et al., 2010). The organosulfur compounds of garlic have shown preventive effects against intestinal damage and endotoxin-induced systemic inflammation (Lee et al., 2012). Thiacremonone is a sulfur compound present in garlic that works through the inhibition of NF-κB activity and prevents amyloidogenesis and neuroinflammation (Arreola et al., 2015). Thus, garlic extract can also be used in neurodegenerative diseases such as Alzheimer's disease (Mikaili et al., 2013).

Immunomodulation is also one of the properties of garlic extract. It is observed that aged garlic extract is more potent than raw garlic extract due to the transformation of organosulfur compounds (Bazaraliyeva et al., 2022). The immunomodulatory effect of garlic is due to its property of proliferating interferon-γ and interleukin-2 gene expression of stimulated lymphocytes. It is also involved in the induction of nitric oxide that reduces the infection of macrophages (Arreola et al., 2015).

CHEMICAL COMPOSITION OF GARLIC

Recent research has shown many pharmacological effects of *A. sativum* and its compounds such as allicin. The studies conducted on the chemical composition of garlic; refer to Tab 1. have shown that it has many therapeutically important

Tab 1. Diversified effects of garlic compounds against various species of parasites

Compound	From Extract/Solvent	Antiparasitic effect	Mode of action	Antiparasite effect	References
Allicin (Diallyl trisulfide)	Aqueous extract or raw garlic	*Schistosoma mansoni, Plasmodium falciparum, Trypanosoma brucei, Entamoeba histolytica, Giardia lamblia*	Sulfhydryl modifying activity, decrease oxygen uptake, inhibit synthesis of lipids, proteins, and nucleic acids and damage membranes, o inhibition of succinate dehydrogenase	*Sehistosoma mansoni, Plasmodium, Falciparum, Trypanosoma brucei, Entamoeba Histolytiea, Giardia Lamblia*	Arreola et al., 2015
S-allyl cysteine	Aqueous extract	*Hymenolepis* and *Giardia* spp.	Prevent reactive oxygen species formation through modulation of NADPH oxidase subunit expression	*Hymenolepis* and *Giardia* spp	Arreola et al., 2015
Diallyl disulfide	Garlic oil	*Plasmodium* spp, *Trypanosoma* spp, *Leishmania* spp, *Giardia* spp, and *Cochlospermum planchoni*	Activation of metabolizing enzymes that detoxify carcinogens, antioxidant, histone modification	*Plasmodium* spp, *Trypanosoma* spp, *Leishmania* spp, *Giardia* spp and *Cochlospermum planchoni*	Kamra et al., 2012
Allyl sulfide	Garlic oil	*Plasmodium* spp, *Trypanosoma* spp, *Leishmania* spp, *Giardia* spp, and *Cochlospermum planchoni*	Suppress cellular proliferation by blocking cells in the G2/M phase and by the induction of apoptosis	*Plasmodium* spp, *Trypanosoma* spp, *Leishmania* spp, *Giardia* spp and	Hayes, 2020
Ajoene	Garlic oil	*Trypanosoma cruzi*	Inhibit glutathione reductase, trypanothione reductase, and has multiple cytostatic effect on the key enzymes of the antioxidant thiol metabolism		Mikaili et al., 2013
Diallyl trisulfide	Extract	*Plasmodium* spp, *Trypanosoma* spp, *Leishmania* spp, *Giardia* spp, and *Cochlospermum planchoni*	Decrease oxygen uptake, inhibit synthesis of lipids, proteins, and nucleic acids and damage membranes		Mikaili et al., 2013; Arguello-Garcia et al., 2018
Garlic compounds mixture					
Alchinal	Extract		γ-aminobutyric acid (GABA)	*Trichinella spiralis* (adult form and muscular larvae)	
Ethanol, dichloromethane, and water extracts of *A. sativum*	Extract		GABA	*Haemonchus contortus*	Iqbal et al., 2001
Ethanol	Extract		GABA	Decrease larval count	Arreola et al., 2015
Aqueous and chloroform extract	Extract		GABA	*Trichuris muris* and *Angiostrongylus cantonensis*	Mikaili et al., 2013
Garlic recipe (Prepared from the extracts of coconut, onion, garlic, fig, date tree, chicory, ananas, and cistrose	Mixture	Cestodes *Hymenolepis diminuta*, *H. microstoma*, *Taenia taeniaeformis* trematodes *Fasciola hepatica* *Echinostoma caproni* *Echino caproni*	Not known		Mikaili et al., 2013
Essential oil of *A. sativum*	Oil	*Fasciola gigantica*	paralytic effect		Mikaili et al., 2013

compounds, especially the organosulfur compounds such as alliin, diallyl disulfide, allicin, ajoene diallyl trisulfide, and S-allyl cysteine (Martins et al., 2016). In the last decades, the popularity of organosulfur compounds present in the extract of garlic has increased tremendously (Hart et al., 2010). It is documented in many studies that *A. sativum* and its organosulfur constituents have the characteristics of antioxidants, antibacterial, anti-inflammatory, immuno-modulatory, antifungal, as well as protective properties for the cardiovascular and digestive systems including hepatoprotection, anticancer, antidiabetic, anti-obesity, renal and neuroprotective properties (Gudalwar et al., 2021). Garlic as a good source of sulfur-containing bioactive compounds can be used in the formulation of food and nutraceutical products for the control and prevention of various diseases (Mikaili et al., 2013). However, among these compounds, allicin is the most studied naturally occurring compound (Choo et al., 2020).

Besides organic sulfides, garlic is also enriched with phenolic compounds, saponins, and polysaccharides. The saponin compounds that are present in the garlic include desgalactotigonin, proto-desgalactotigonin-rhamnose, proto-desgalactotigonin, sativoside B1-rhamnose, voghieroside D1, and sativoside R1 (De Greef et al., 2021). There are more than 20 phenolic compounds in garlic and the most important phenolic constituents are β-resorcylic acid, gallic acid, pyrogallol, rutin, quercetin, and protocatechuic (Sasi et al., 2021). The polysaccharides present in garlic include galactose (1%), glucose (14%), and fructose (85%) (Mikaili et al., 2013).

It is observed that temperature has a direct effect on the active ingredient of garlic during processing and about 38 constituents of garlic will be changed after thermal treatment. High temperature degrades polysaccharides and the amount of reducing sugar as well as polyphenols are increased during processing (Hasan et al., 2015). In one study it was found that the organosulfur compounds are more digestible in raw garlic than in cooked garlic while saponin compounds are more digestible in cooked garlic than in raw garlic (Lanzotti et al., 2014; Torres-Palazzolo et al., 2018).

ANTI-PROTOZOAL ACTIVITY OF GARLIC IN RUMINANTS

The digestive system of ruminants mainly comprises the rumen, reticulum, omasum, and abomasum (Sari et al., 2022). Rumen is the most important and largest chamber that harbors a large number of microorganisms (Paswan et al., 2022). Among these micro-organisms, protozoa are a major group accounting for 10^4-10^6 cells per milliliter of ruminal contents and almost 50% of the microbial mass of the rumen (Sirohi et al., 2012; Choudhury et al., 2015). These protozoa live a symbiotic life in the rumen of animals helping in the fermentation, metabolism, and digestion of feed. They are involved in the synthesis of volatile fatty acids (Vasta et al., 2019). They do so by engulfing exogenous fatty acids and converting them into volatile fatty acids (Harun and Sali, 2019). Moreover, they are also responsible for the enhancement of methanogenesis (Levy and Jami, 2018). Holotrich ciliate protozoans produce H_2 in their hydrogenosome (mitochondria-like organelle of protozoa) which is used by methanogens for the production of CH_4 (Newbold et al., 2015). They are involved in episymbiotic and endosymbiotic relationships with methanogens protecting the host from the toxicity of oxygen and their elimination from the rumen leads to reduced CH_4 emission (Tapio et al., 2017; Zhong et al., 2019; Williams et al., 2020). However, apart from these beneficial effects, there are some parasitic protozoa which can cause harm to the animals. For example, *Cryptosporidium* species cause gastrointestinal disease in ruminants ultimately affecting their production (Delling and Daugschies, 2022). Hence, the control of these harmful protozoa becomes necessary.

This control has long been achieved through the use of synthetic drugs. However, owing to the emergence of resistance against these traditional drugs, botanicals have gained importance in parasitic control practices (Bajwa et al., 2022). Among these botanicals, garlic has also shown antiparasitic properties in various studies. It is effective against many protozoa such as *Scedosporium prolificans*, *Candida albicans*, *Tinea pedis*, *Leptomonas*, *Opalina ranarum*, *Blantidium entozoon*, *Leishmania*, *Entamoeba histolytica*, *Crithidia*, and *Trypanosomes* (Mikaili et al., 2013). Allicin also has an antiparasitic effect against *Plasmodium falciparum*, and *Trypanosoma brucei*. Due to the emergence of resistance in synthetic drugs, garlic can be used for the treatment of protozoal such as *Giardia* (Bayan et al., 2014).

ANTHELMINTIC ACTIVITY OF GARLIC IN RUMINANTS

Helminths are one of the most important causes of diseases in ruminants which decrease their production and also economically influence farming. They are responsible for the loss of the average daily gain of the host. This loss of production significantly affects the economic outcome of the farm. The primary method for the control of parasitic worm infestations in ruminants is the use of anthelmintics (Charlier et al., 2015). Currently, the increased demand of consumers using numerous pharmaceutical preparations in animals, the development of drug resistance, and the appearance of drug residues in the products of animals such as meat and milk have posed serious public health concerns (Iqbal et al., 2001; Atta et al., 2022; Chylinski et al., 2022). Therefore, it is required to investigate alternative methods and techniques that can be used for the prevention and control of worm infestations in animals. Garlic

is a naturally occurring plant that is enriched with many therapeutically active ingredients and can serve as the best alternative to synthetic anthelmintic drugs for the treatment of parasitic infestations in ruminants (Hayes, 2020). It can be used to decrease the parasitic load of ruminants and thus enhance the average daily gain of animals. In this way, the increase in average daily gain will be beneficial to the profitability of livestock production (Mikaili et al., 2013).

Tab 2. Factors influencing the microbiota in ruminants

Factor	Species	Function	Remarks	References
Genetics	*Bacteroidetes* (Prevotella)	Genes encoding a broad spectrum of carbohydrates active enzymes such as glycoside hydrolases, glycosyl transferase	Diet is the major factor determining their abundance, have low heritability	Li et al., 2019
	Firmicutes (Ruminococcaceae, Clostridiales)	Ruminococcaceae are involved in starch hydrolysis and produce acetate, formate, and succinate while Clostridiales are involved in biohydrogenation	Host and diet are the major factors determining their abundance except for Lachnospiraceae which are not influenced by the host genetics, have moderate heritability	Li et al., 2019
Age	*Firmicutes*	Involved in fermentation	Become abundant with increase in age	Yin et al., 2021
	Bacteroidetes	Involved in the digestion of milk	Become abundant with increase in age	Yin et al., 2021
	Proteobacteria	Involved in fermentation	Decrease with increase in age	Liu et al., 2021
	Prevotella	Involved in fermentation	Become abundant with increase in age	Yin et al., 2021
	Ruminococcus	Involved in fermentation	Become abundant with increase in age	Liu et al., 2021
Diet	*Bacteroidetes, Firmicutes, Ruminococcus flavefaciens, Fibrobacter succinogenes,* and *Butyrivibrio fibrisolvens*	Involved in fermentation	Increase with increase in solid diet	Loor et al., 2016
	Bifidobacterium	Enhance immune system, improve gut barrier, and reduce enteric pathogens	Increase with colostrum feeding	Loor et al., 2016
	Lactobacillus, Streptococcus bovis, Ruminobacter amylophilus, Megasphaera elsdenii, Prevotella ruminicola, and *Selenomonas ruminantium*	Involved in fermentation	Increase with colostrum feeding	Loor et al., 2016
	Litostomatea (Protozoal taxa)	Not given	Become abundant with high energy diet	Loor et al., 2016

The antiparasitic activity of garlic is due to its special structure that interacts with the sulfhydryl group of proteins of parasites to block the physiological mechanism (Mikaili et al., 2013). Allicin is a compound present in garlic that can make morphological changes in *Schistosoma mansoni*. Alchinal prepared from garlic extract, cocoa, and *Echinacea purpurea* is proven to be very effective in significantly decreasing the number of muscular larvae and adult forms of *Trichinella spiralis* (Zhong et al., 2019). The anthelmintic activity of *A. stivum* against *Haemonchus contortus* in sheep is also documented. The aqueous extract of garlic is proven to be very effective against gastrointestinal nematodes such as *Trichuris muris* and *Angiostrongylus cantonensis*. A recipe of garlic mixture (extracts of coconut, garlic, onion, fig, chicory, date tree, ananas, and cistrose) showed anthelmintic activity against trematodes such as *Fasciola hepatica* and *Echinostoma caproni,* and cestodes such as *Hymenolepis diminuta, Taenia taeniaeformis,* and *H. microstoma* (Mikaili et al., 2013).

The allicin compound of garlic has a wide safety margin and can be used as an anthelminthic in ruminants. The mechanism of action of allicin resides within its high permeability through cell membranes and its rapid interaction with thiols. Therefore, it is equally effective against both types of parasites viz intercellular and intracellular parasites (Fawzi and Elsohaby, 2017).

EFFECT OF GARLIC ON GASTRO-INTESTINAL MICROBIOTA AND GROWTH PERFORMANCE OF RUMINANTS

The anatomy and physiology of the digestive system of ruminants are different from that of monogastric animals such as horses. These animals have three additional parts of the gastrointestinal tract namely the rumen, reticulum, and omasum along with the abomasum (which is involved in gastric digestion) which allow the normal microflora of the animals to perform enzymatic action on the fibrous fodder that animals eat and allow them to absorb energy extracted by the microbiota of the rumen which will otherwise not be available to the host enzymes (Clauss and Hummel, 2017). The digestion of food in ruminants occurs by the combination of the physical breakdown of food during rumination in the mouth and microbial digestion through fermentation in the rumen. The rumen is a fermentation chamber where feed is digested by a mixed population of bacteria, ciliated protozoa, and a small population of metabolically important anaerobic fungi before gastric and intestinal digestion (Hart et al., 2010).

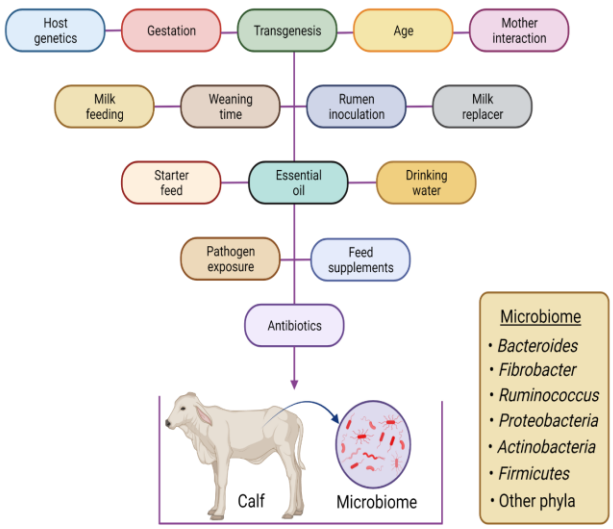

Fig 2. Factors affecting the growth of microbiota in the GIT of ruminants.

The goal of scientists is to manipulate the ecosystem of rumen for the growth of beneficial microbes; refer to Tab 2. to improve the efficacy of conversion of feed to use products that are available to the animal so that they grow enough to be consumable by humans (Soltan and Patra, 2021). Antibiotics are used as feed additives that stop the growth of gas-forming microorganisms to lower the wastage of energy in the form of methane gas produced by these microbes. The use of extracts from plants such as garlic extract appears to be one of the safest alternatives to antibiotics that are recognized for their antimicrobial properties. It can be used to mitigate harmful microbes from the GIT, thereby, preventing the loss of energy, promoting the effective absorption of nutrients, and good health of the animals (Busquet et al., 2005).

Garlic oil obtained from heating crushed garlic cloves at 100°C and then collecting the vapors as a distillate exhibits good antibacterial activity against both the gram-negative and gram-positive bacteria; refer to Fig 2. The use of this oil is proven to be very effective in the reduction of branched-chain volatile fatty acids and acetic acid. It also increases propionic acid, butyric acid, and small peptides. These changes are consistent with those of methane inhibitors used in ruminants (Kamra et al., 2012).

The restriction on the use of growth-promoting antibiotics in animals has opened the gate for researchers to find alternate methods (Hart et al., 2010). Garlic is recognized as a therapeutic agent for the treatment of gastric tissue injury (El-Shewehy et al., 2022). In a study, it was evaluated that garlic has the property of stimulating gastrointestinal peristalsis, thereby, promoting the emptying of the gastrointestinal tract (GIT) and facilitating the process of defecation (Chen et al., 2018). It can be utilized to improve the functions of GIT as well as prevent gastric ulcers, colitis, and certain other GIT diseases by inhibiting inflammation, reducing oxidative stress, and *helicobacter pylori* (Hart et al., 2010).

CONCLUSION

Garlic is a worldwide consumed spice which has a characteristic odor. It is enriched with many active ingredients such as organosulfur compounds, phenolic compounds, saponins, and polysaccharides. The major bioactive compounds of garlic have shown many health-beneficial effects. Its consumption lowers the parasitic load of ruminants and maintains the proper environment of the GIT of the animals, thus, promoting the health and vigor of animals. Generally, garlic has low or no toxicity at all. Therefore, garlic as a whole or its different constituent preparations can have promising use as a nutraceutical and functional food for the control, prevention, and treatment of various diseases (Kamra et al., 2012).

A recent increase in people's interest in the use of organic products in food animals is due to the emergence of resistance and the appearance of drug residues in the products of animals. Garlic as a natural product can serve as the best alternative medicine for the treatment and prevention of various diseases (Zhong et al., 2019). Although garlic is proven to be a good therapeutic agent for certain diseases, some issues are barriers to the practical application of garlic in the field. These include

inadequacy of methods being used in the experiments for knowing more about the therapeutic properties of garlic, small sample sizes, availability of limited or no information regarding the dose of garlic, lack of knowledge about the efficacy and effectiveness of garlic compounds, and the absence of control groups. Researchers are required to discover more about the beneficial effects of garlic against various diseases (Mikaili et al., 2013).

REFERENCES

Ademiluyi AO, G Oboh, TR Owoloye & OJ Agbebi, 2013. Modulatory effects of dietary inclusion of garlic (*Allium sativum*) on gentamycin-induced hepatotoxicity and oxidative stress in rats. Asian Pacific Journal of Tropical Biomedicine 3:470-5. doi: 10.1016/S2221-1691(13)60098-2.

Al-Shoaibi F & S Benedicts, 2021. Inhibitory effect of garlic oil, clove oil and thyme oil on *Micrococcus luteus* and *Staphylococcus epidermidis*. Journal of Student Research 10(3).

Argüello-García R, M de-la-Vega-Arnaud, IJ Loredo-Rodríguez, AM Mejía-Corona, E Melgarejo-Trejo, EA Espinoza-Contreras, R Fonseca-Liñán, A González-Robles, N Pérez-Hernández, & MG Ortega-Pierres, 2018. Activity of thioallyl compounds from garlic against *Giardia duodenalis* trophozoites and in experimental giardiasis. Frontiers in Cellular and Infection Microbiology 15:8:353. doi: 10.3389/fcimb.2018.00353.

Arreola R, S Quintero-Fabián, RI López-Roa, EO Flores-Gutiérrez, JP Reyes-Grajeda, L Carrera-Quintanar & D Ortuño-Sahagún, 2015. Immunomodulation and anti-inflammatory effects of garlic compounds. Journal of Immunology Research. 2015:401630. doi: 10.1155/2015/401630.

Atta AH, SA Atta, SM Nasr & SM Mouneir, 2022. Current perspective on veterinary drug and chemical residues in food of animal origin. Environmental Science and Pollution Research 29(11):15282-15302. doi: 10.1007/s11356-021-18239-y.

Bajwa HUR, MK Khan, Z Abbas, R Riaz, TU Rehman, RZ Abbas, MT Aleem, A Abbas, MM Almutairi, FA Alshammari, Y Alraey & A Alouffi, 2022. Nanoparticles: synthesis and their role as potential drug candidates for the treatment of parasitic diseases. Life (Basel) 12(5):750. doi: 10.3390/life12050750.

Bayan L, PH Koulivand, & A Gorji, 2014. Garlic: a review of potential therapeutic effects. Avicenna Journal of Phytomedicine 4(1):1-14.

Bazaraliyeva A, D Moldashov, A Turgumbayeva, E Kartbayeva, A Kalykova, L Sarsenova, & R Issayeva, 2022. Chemical and biological properties of bio-active compounds from garlic (*Allium sativum*). Pharmacia. 69(4), 955-964.

Bhatwalkar SB, R Mondal, SBN Krishna, JK Adam, P Govender, & R Anupam, 2021. Antibacterial Properties of Organosulfur Compounds of Garlic (*Allium sativum*). Frontiers in Microbiology. 12:613077. doi: 10.3389/fmicb.2021.613077. PMID: 34394014; PMCID: PMC8362743.

Busquet M, S Calsamiglia, A Ferret, MD Carro, & C Kamel, 2005. Effect of garlic oil and four of its compounds on rumen microbial fermentation. Journal of Dairy Science 88(12):4393-404. doi: 10.3168/jds.S0022-0302(05)73126-X.

Charlier J, FV Velde, M van-der-Voort, J Van Meensel, L Lauwers, V Cauberghe, J Vercruysse, & E Claerebout, 2015. Placing helminth infections of livestock in an economic and social context. Veterinary Parasitology. 212(1-2):62-7 (2015). doi: 10.1016/j.vetpar.2015.06.018.

Chen YA, JC Tsai, KC Cheng, KF Liu, CK Chang, & CW Hsieh, 2018. Extracts of black garlic exhibits gastrointestinal motility effect. Food Research International. 107:102-109. doi: 10.1016/j.foodres.2018.02.003.

Chidinma O, OC Timothy, S Samuel, E Isaac, & S Hauwa, 2019. Therapeutic Effects of Garlic: A Review. Scientific Journal of Biology and Life Science 1(1):1-5.

Choo S, VK Chin, EH Wong, P Madhavan, ST Tay, PVC Yong, & PP Chong, 2020. Antimicrobial properties of allicin used alone or in combination with other medications. Folia Microbiologica 65(3):451-465. doi: 10.1007/s12223-020-00786-5.

Choudhury PK, AZM Salem, R Jena, S Kumar, R Singh & AK Puniya, 2015. Rumen microbiology: An overview. Rumen microbiology: from evolution to revolution 3-16. doi:10.1007/978-81-322-2401-3_1

Chylinski C, S Athanasiadou, S Thüer, C Grovermann, S Moakes, H Hoste, S Petkevicius, C Verwer, J Verkaik & S Werne, 2023. Reducing anthelmintic inputs in organic farming: Are small ruminant farmers integrating alternative strategies to control gastrointestinal nematodes? Veterinary Parasitology 315:109864. doi: 10.1016/j.vetpar.2022.109864.

Clauss M & J Hummel, 2017. Physiological adaptations of ruminants and their potential relevance for production systems. Revista Brasileira de Zootecnia 46: 606-613. https://doi.org/10.1590/S1806-92902017000700008

De Greef D, EM Barton, EN Sandberg, CR Croley, J Pumarol, TL Wong, N Das & A Bishayee, 2020. Anticancer potential of garlic and its bioactive constituents: a systematic and comprehensive review. Seminars in Cancer Biology 73:219-264 2021. doi: 10.1016/j.semcancer.2020.11.020.

Delling C & A Daugschies, 2022. Coinfection in young ruminant livestock-*Cryptosporidium* spp. and its companions. Pathogens 15:11(1):103. doi: 10.3390/pathogens11010103.

Dorrigiv M, A Zareiyan, & H Hosseinzadeh, 2020. Garlic (*Allium sativum*) as an antidote or a protective agent against natural or chemical toxicities: A comprehensive update review. Phytotherapy Research 34(8):1770-1797. doi: 10.1002/ptr.6645.

El-Azzouny MM, AS El-Demerdash, HG Seadawy & SH Abou-Khadra, 2018. Antimicrobial effect of garlic (*Allium sativum*) and thyme (*Zataria multiflora Boiss*) extracts on some food borne pathogens and their effect on virulence gene expression. Cellular and Molecular Biology 64(10):79-86.

EL-mahmood MA, 2009. Efficacy of crude extracts of garlic (*Allium sativum* Linn.) against nosocomial *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniea* and *Pseudomonas aeruginosa*. Journal of Medicinal Plants Research 3(4):179-185.

Elmowalid GA, MI Abd El-Hamid, AM Abd El-Wahab, M Atta, G Abd El-Naser & AM Attia, 2019. Garlic and ginger extracts modulated broiler chicks innate immune responses and enhanced multidrug resistant *Escherichia coli* O78 clearance. Comparative Immunology, Microbiology, and Infectious Diseases. 66:101334. doi: 10.1016/j.cimid.2019.101334.

El-Saber Batiha G, AM Beshbishy, GL Wasef, YHA Elewa, Al-Sagan, ME Abd El-Hack, AE Taha, MY Abd-Elhakim & HP Devkota, 2020. Chemical constituents and pharmacological activities of garlic (*Allium sativum* L.). Nutrients. 12(3):872. doi: 10.3390/nu12030872.

El-Shewehy DMM, GE Elshopakey, A Ismail, SS Hassan, & AM Ramez, 2023. Therapeutic potency of ginger, garlic, and pomegranate extracts against *Cryptosporidium parvum*-mediated gastro-splenic damage in mice. Acta Parasitologica 68(1):32-41. doi: 10.1007/s11686-022-00635-0.

Fawzi EMV & I Elsohabym, 2017. Prevalence of gastrointestinal nematodes and the role of allicin in treatment of cattle in sharkia governorate. Zagazig Veterinary Journal 45(Supplementary 1): 109-117. doi: 10.21608/zvjz.2019.28655.

Fufa BK, 2019. Anti-bacterial and anti-fungal properties of garlic extract (*Allium sativum*): A review. Microbiology Research 28:1-5.

Gebreselema G & G Mebrahtu, 2013. Medicinal values of garlic: A review. International Journal of Medicine and Medical Sciences 5(9):401-408.

Gudalwar BR, MG Nimbalwar, WA Panchale, AB Wadekar, JV Manwar, & RL Bakal, 2021. *Allium sativum*, a potential phytopharmacological source of natural medicine for better health. GSC Advanced Research and Reviews 6(3):220-232.

Hannan A, MI Ullah, M Usman, S Hussain, M Absar, K Javed, 2011. Anti-mycobacterial activity of garlic (*Allium sativum*) against multi-drug resistant and non-multi-drug resistant mycobacterium tuberculosis. Pakistan Journal of Pharmaceutical Science 24(1):81-5.

Hart KJ, DR Yanez-Ruiz, SM Duval, NR McEwan & CJ Newbold, 2008. Plant extracts to manipulate rumen fermentation. Animal feed science and technology 147(1-3): 8-35. https://doi.org/10.1016/j.anifeedsci.2007.09.007

Harun AY & K Sali, 2019. Factors affecting rumen microbial protein synthesis. Open Journal of Veterinary Medicine 4(1):27-35.

Hasan MMI, S Begum, S Islam, MM Rahman, SA Belal, MA Hossain, & MMR Howlader. Effects of garlic supplementation on parasitic infestation, live weight, and hematological parameters in Black Bengal goat. Journal of Advanced Veterinary and Animal Research 2(3):326-331. http://dx.doi.org/10.5455/javar.2015.b102

Hayes C, 2020. Determining the ovicidal capabilities of allicin, s-allyl cysteine, and pumpkin seed oil for mitigation of *Haemonchus contortus* infections in goats (Unpublished thesis). Texas State University, San Marcos, Texas. https://digital.library.txstate.edu/handle/10877/13061

Huque KS & NR Sarker, 2014. Feeds and feeding of livestock in Bangladesh: performance, constraints and options forward. Bangladesh Journal of Animal Science 43(1):1-10.

Iqbal Z, QK Nadeem, MN Khan, MS Akhtar, & FN Waraich, 2001. *In vitro* anthelmintic activity of *Allium sativum*, *Zingiber officinale*, *Curcurbita Mexicana*, and *Ficus religiosa*. International Journal of Agriculture and Biology 3(4):454-457.

Kamra DN, N Agarwal, PC Sakthivel, & LC Chaudhary, 2012. Garlic as a rumen modifier for eco-friendly and economic livestock production. Journal of Applied Animal Research 40(2):90-96. https://doi.org/10.1080/09712119.2011.607764

Ku-Vera JC, R Jiménez-Ocampo, SS Valencia-Salazar, MD Montoya-Flores, I Molina-Botero, J Arango & FJ Solorio-Sánchez, 2020. Role of secondary plant metabolites on enteric methane mitigation in ruminants. Frontiers in Veterinary Science 584. https://doi.org/10.3389/fvets.2020.00584

Lanzotti V, F Scala & G Bonanomi, 2014. Compounds from *Allium* species with cytotoxic and antimicrobial activity. Phytochemistry Reviews. 13(4):769-791.

Lee SH, YT Liu, KM Chen, CK Lii & CT Liu, 2012. Effect of garlic sulfur compounds on neutrophil infiltration and damage to the intestinal mucosa by endotoxin in rats. Food and Chemical Toxicology 50(3-4):567-74. doi: 10.1016/j.fct.2011.11.027.

Levy B & E Jami, 2018. Exploring the Prokaryotic Community Associated With the Rumen Ciliate Protozoa Population. Frontiers in Microbiology 9:2526. doi: 10.3389/fmicb.2018.02526.

Li F, C Li, Y Chen, J Liu, C Zhang, B Irving, C Fitzsimmons, G Plastow & LL Guan, 2019. Host genetics influence the rumen microbiota and heritable rumen microbial features associate with feed efficiency in cattle. Microbiome 7(1):92. doi: 10.1186/s40168-019-0699-1.

Lionel OO, IP Adegboyega, AO Ezekiel & BC Olufunke, 2020. Antimicrobial activity of garlic (*Allium sativum*) on selected uropathogens from cases of urinary tract infection. Annals of Tropical Pathology 11(2):133.

Liu K, Y Zhang, Z Yu, Q Xu, N Zheng, S Zhao, G Huang & J Wang. Ruminal microbiota-host interaction and its effect on nutrient metabolism. Animal Nutrition 7(1):49-55. doi: 10.1016/j.aninu.2020.12.001.

Loor JJ, AA Elolimy & JC McCann, 2016. Dietary impacts on rumen microbiota in beef and dairy production. Animal Frontiers 6(3):22-29. https://doi.org/10.2527/af.2016-0030.

Manal I, 2018. Impact of garlic and curcumin on the hepatic histology and cytochrome P450 gene expression of aflatoxicosis *Oreochromis niloticus* using RT-PCR. Turkish Journal of Fisheries and Aquatic Sciences 18(3):405-415.

Martins N, S Petropoulos & IC Ferreira, 2016. Chemical composition and bioactive compounds of garlic (*Allium sativum* L.) as affected by pre- and post-harvest conditions: A review. Food Chemistry 211:41-50. doi: 10.1016/j.foodchem.2016.05.029.

Mikaili P, S Maadirad, M Moloudizargari, S Aghajanshakeri & S Sarahroodi 2013. Therapeutic uses and pharmacological properties of garlic, shallot, and their biologically active compounds. Iranian Journal of Basic Medical Science. 16(10):1031-48.

Newbold CJ, G de la Fuente, A Belanche, E Ramos-Morales & NR McEwan, 2015. The role of ciliate protozoa in the rumen. Frontiers in Microbiology. 6:1313. doi: 10.3389/fmicb.2015.01313.

Oh J, EH Wall, DM Bravo, & AN Hristov, 2017. Host-mediated effects of phytonutrients in ruminants. Journal of Dairy Science 100(7):5974-5983. doi: 10.3168/jds.2016-12341.

Ortikova LS, NT Khamraeva, SA Siddikova, O Sayfiev, & ZSO Karshiboev, 2020. Ecological characteristics of pasture and fodder conditions of natural vegetation of Kyzylkum. The American Journal of Horticulture and Floriculture Research. 2(09):7-11. https://doi.org/10.37547/tajhfr/Volume02Issue09-03

Oyawoye OM, TM Olotu, SC Nzekwe, JA Idowu, TA Abdullahi, SO Babatunde & H Faidah, 2022. Antioxidant potential and antibacterial activities of *Allium cepa* (onion) and *Allium sativum* (garlic) against the multidrug resistance bacteria. Bulletin of the National Research Centre 46(1):1-7.

Paswan VK, K Kumar & AM Shehata., 2022 Rumen microbiology and microbial degradation of feedstuffs. Animal Manure 45-60.

Ribeiro M, L Alvarenga, LFMF Cardozo, TR Chermut, J Sequeira, L de-Souza Gouveia Moreira, KTR Teixeira, PG Shiels, P Stenvinkel & D Mafra, 2021. From the distinctive smell to therapeutic effects: Garlic for cardiovascular, hepatic, gut, diabetes and chronic kidney disease. Clinical Nutrition 40(7):4807-4819. doi: 10.1016/j.clnu.2021.03.005.

Rivlin RS, 2001. Historical perspective on the use of garlic. The Journal of nutrition 131(3s):951S-4S. doi: 10.1093/jn/131.3.951S.

Saikat ASM, R Hossain, FB Mina, S Das, IN Khan, MS Mubarak & MT Islam, 2021. Antidiabetic effect of garlic. Revista Brasileira de Farmacognosia 1-11.

Salobir J, T Frankič & V Rezar, 2012. Animal nutrition for the health of animals, human and environment. Acta Agriculturae Slovenica 100:41-49.

Oliveira Santos F, APM Cerqueira, A Branco, JMM Batatinha & MB Botura, 2019. Anthelmintic activity of plants against gastrointestinal nematodes of goats: a review. Parasitology 146(10):1233-1246. doi: 10.1017/S0031182019000672.

Sari NF, P Ray, C Rymer, KE Kliem & S Stergiadis, 2022. Garlic and its bioactive compounds: Implications for methane emissions and ruminant nutrition. Animals 12(21):2998. doi: 10.3390/ani12212998.

Sasi M, S Kumar, M Kumar, S Thapa, U Prajapati, Y Tak, S Changan, V Saurabh, S Kumari, A Kumar, M Hasan, D Chandran, Radha, SP Bangar, S Dhumal, M Senapathy, A Thiyagarajan, A Alhariri, A Dey, S Singh, S Prakash, R Pandiselvam & M Mekhemar, 2021. Garlic (*Allium sativum* L.) bioactives and its role in alleviating oral pathologies. Antioxidants 10(11):1847. doi: 10.3390/antiox10111847.

Shang A, SY Cao, XY Xu, RY Gan, GY Tang, H Corke, V Mavumengwana & HB Li, 2019. Bioactive compounds and biological functions of garlic (*Allium sativum* L.). Foods 8(7):246. doi: 10.3390/foods8070246.

Shih PC, CH Kuo, JY Juang, CH Liu, L Hsu & CT Liu, 2010. Effects of garlic oil on the migration of neutrophil-like cell studied by using a chemotactic gradient Labchip. Journal of Biomedicine and Biotechnology. 2010:319059. doi: 10.1155/2010/319059.

Sirohi SK, N Singh, SS Dagar & AK Puniya, 2012. Molecular tools for deciphering the microbial community structure and diversity in rumen ecosystem. Applied Microbiology and Biotechnology 95(5):1135-54. doi: 10.1007/s00253-012-4262-2.

Soltan YA & AK Patra, 2021. Ruminal microbiome manipulation to improve fermentation efficiency in ruminants. In Animal Feed Science and Nutrition Production, Health and Environment. IntechOpen London.

Tapio I, TJ Snelling, F Strozzi, & RJ Wallace, 2017. The ruminal microbiome associated with methane emissions from ruminant livestock. Journal of Animal Science and Biotechnology 8:7. doi: 10.1186/s40104-017-0141-0.

Torres-Palazzolo C, D Ramirez, D Locatelli, W Manucha, C Castro & A Camargo, 2018. Bioaccessibility and permeability of bioactive compounds in raw and cooked garlic. Journal of Food Composition and Analysis 70:49-53.

Vasta V, M Daghio, A Cappucci, A Buccioni, A Serra, C Viti & M Mele, 2019. Plant polyphenols and rumen microbiota responsible for fatty acid biohydrogenation, fiber digestion, and methane emission: Experimental evidence and methodological approaches. Journal of Dairy Science 102(5):3781-3804. doi: 10.3168/jds.2018-14985.

Williams CL, BJ Thomas, NR McEwan, PR Stevens, CJ Creevey & SA Huws, 2020. Rumen Protozoa Play a Significant Role in Fungal Predation and Plant

Carbohydrate Breakdown. Frontiers in Microbiology. 11:720. doi: 10.3389/fmicb.2020.00720.

Yamaguchi Y, R Honma, T Yazaki, T Shibuya, T Sakaguchi, H Uto-Kondo & H Kumagai, 2019. Sulfuric odor precursor *S*-allyl-l-cysteine sulfoxide in garlic induces detoxifying enzymes and prevents hepatic injury. antioxidants. 8(9):385. doi: 10.3390/antiox8090385.

Yin X, S Ji, C Duan, P Tian, S Ju, H Yan, Y Zhang & Y Liu, 2021. Age-related changes in the ruminal microbiota and their relationship with rumen fermentation in lambs. Frontiers in Microbiology 12:679135. doi: 10.3389/fmicb.2021.679135.

Zardast M, K Namakin, J Esmaelian Kaho & SS Hashemi. Assessment of antibacterial effect of garlic in patients infected with *Helicobacter pylori* using urease breath test. Avicenna Journal of Phytomedicine 6(5):495-501.

Zhong R, H Xiang, L Cheng, C Zhao, F Wang, X Zhao & Y Fang, 2019. Effects of feeding garlic powder on growth performance, rumen fermentation, and the health status of lambs infected by gastrointestinal nematodes. Animals 9(3):102. doi: 10.3390/ani9030102.