Managing Internal Parasites of Small Ruminants using Medicinal Plants a Review on Alternative Remedies, Efficacy Evaluation Techniques and Conservational Strategies

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Abstract: Throughout the world, internal parasites are a major hindrance to small ruminant production. The most common internal parasites in grazing small ruminants are likely to be gastrointestinal nematodes. They cause a reduction in live-weight gain, wool growth, poor reproductive performance, and increased production costs and thus hamper global food security. Pharmaceutical control continues to be the main measure used to manage or control internal parasites, however as the resistance of internal parasite populations spreads, the efficiency of this method in resource-limited environments becomes limited and complex. Efforts to curb production losses caused by internal parasites have led communal farmers to use other treatments such as locally available indigenous medicinal plants to control internal parasites as an alternative to pharmaceuticals. However, many medicinal plants still need to be evaluated for their efficacy and efficiency using both in vitro as well as in vivo methods. Furthermore, in many developing countries, the use of these plants is not well documented nor they are guided by certain rules and regulations to conserve them. Therefore, the objective of this review was to document various remedies prepared from medicinal plants to manage internal parasites in small ruminants. A further objective was to evaluate techniques used to determine the safety and efficacy of these plants and to suggest possible strategies to conserve such useful plants and the knowledge associated with them.

Keywords: Internal Parasites, Ruminants, Medicinal Plants, Anthelmintic

Introduction

Livestock farming is one of the most important agricultural activities for resource-limited farmers. According to Kweghe et al. (2015), livestock in many African developing countries contributes approximately 30% of total agricultural gross domestic product. Despite the economic importance of livestock, the prevalence of disease and internal parasites continues to be a major hindrance to livestock production due to inaccessibility to commercial pharmaceutical remedies. Normally, the prevalence of internal parasites is worsened by prevailing environmental factors such as improper management practices, poor nutrition, and seasonal changes (Fisihia and Kinde, 2021). Ademola (2016) noted that grazing animals are prone to risk due to high degrees of larval contamination in pastures. In large-scale production, the parasitic infestation is largely controlled by pharmaceutical remedies which may not be cost-effective or available for resource-limited livestock farmers. Moreover, there are severe disadvantages of using different anthelmintic drugs, notable fast escalation of resistance to helminths and some anthelmintic residues can remain as contaminants in livestock products such as meat and milk destined for human consumption if withdrawal periods are not followed (Gilleard et al., 2021). In such scenarios, control measures to reduce internal parasite infestations on small ruminants continue to challenge farmers and animal health specialists. For these reasons, communal farmers have resorted to cheaper alternative strategies to manage internal parasites in small ruminants, by using locally available indigenous medicinal plants (Maphosa et al., 2009). The objectives of this review are three-fold and are to (1) review alternative remedies commonly used by communal or resource-limited farmers to manage internal parasites in their small ruminants, (2) review plant extract efficacy evaluation techniques used, and (3) suggest strategies of conserving medicinal plant knowledge and the associated information.
Internal Parasites and their Impact on Livestock Production

Internal parasitism is one of the most important constraints in the economy because they decrease livestock production (Chitura et al., 2019). Globally, helminth parasites are the most common parasites of grazing ruminants, and they have direct negative effects on nutrient intake and absorption, growth performance, wool growth, carcass composition, fertility, and milk production (Fitzpatrick, 2013). Stepek et al. (2004) reported similar findings that gastrointestinal helminth parasites are associated with low outputs of animal products, which then negatively affect the livelihoods of resource-limited farmers. Schoenian (2012) noted that small ruminants are more vulnerable to internal parasites than other livestock because of their tendency to graze close together and poor immunity. In developing countries, gastrointestinal parasites such as coccidia and helminths are major constraints to the productivity of small ruminants and thus can increase food insecurity (Paul et al., 2021). Highly pathogenic internal parasites including nematodes in small ruminants, for example, Haemonchus contortus, can cause serious disease and high mortality (Chiejina, 2001).

Economic Importance of Internal Parasites on Livestock

Disease caused by internal parasites is a major obstacle to animal health and can result in severe economic losses to all countries where livestock are an important sector of agricultural production (Mravčáková et al., 2020). Heminthiasis is a disease normally caused by internal parasites and it is regarded as one of the most common diseases reducing livestock production (Akhtar et al., 2000; Dawo and Tibbo, 2005; Agaie and Onyeyili, 2007). According to the FAO (2005), helminthiasis causes a reduction in livestock production and profitability because it is associated with high treatment costs. Pharmacotherapy is the most commonly used method to control diseases caused by internal parasites and is generally only affordable to larger-scale commercial farmers (Mapoha et al., 2009). For example, the Eastern Cape is one of the provinces that have more resource-limited farmers with low incomes who cannot afford this expensive treatment of their animals (Masika and Afolayan, 2003).

The losses caused by internal parasites and parasitic diseases have gained the attention of animal health economists. As an example, in New Zealand, it was recorded that farmers spend approximately $27.9 million per year on commercial drugs to control internal parasites and parasitic diseases in cattle (Bisset, 1994). According to Freyre et al. (1999), countries such as Uruguay face economic losses caused by parasitic diseases such as toxoplasmosis in small ruminants. It was noted that the disease cost the country approximately US$ 1.4-4.7 million per year in control measures. Waller (2004) noted that South Africa and Kenya experience annual losses from internal parasites such as nematode infestation of between US$ 26 and US$ 45 million. Recently, global economic losses in livestock due to fasciolosis were evaluated to be approximately US $ 3.2 billion per year because of condemnation of parts such as the liver at the abattoir, mortality, and costs of treatment (Abebe et al., 2010).

Effect of Internal Parasites on Nutrition of Livestock

In livestock, performance and health are mainly dependent on a balanced intake of vitamins as they have diverse functions to play in health. For example, small ruminants like sheep, Vitamin A, and Vitamin E have positive effects on health, resistance to disease as well as performance (Bendich, 2004; Rooke et al., 2004; Debier et al., 2005). According to Sykes and Coop (2001), animals that are infected with intestinal parasites such as nematodes tend to have low voluntary feed intake. This hurts the protein economy because it reduces the nutrient availability that is being used by animals for anabolic processes. Coop and Kyriazakis (1999) noticed that parasitism in ruminants causes indirect negative effects on the metabolism of the host such as the utilization of protein for the immune response and creating exposure to other pathogens. According to Van Houtert and Sykes (1996), the total number of internal parasites or worm species present in the host and the degree of larval development influence the impact of these effects. This leads to gastrointestinal losses of a considerable proportion of endogenous protein in the form of whole blood, sloughed epithelial cells, and mucus. More importantly, the disturbance of protein metabolism also causes retention of minerals like phosphorus that play a crucial role in animal health. In such scenarios, sheep and goats must be supplemented with protein to boost immunity, and this will also result in a reduction in the production of new larvae and a decreased survival of established larvae (Coop and Kyriazakis, 2001).

Measures used to Control Internal Parasites in Goats

There are several methods or strategies used to manage internal parasites in livestock that are well documented in literature. These methods may include good pasture management practices and enhancing host resistance through nutrition and biological control (Rahmann and Seip, 2006). Moreover, the effect of internal parasites can be mitigated through breeding and selection of animals that are more parasite-resistant and through protein supplementation (Sayers and Sweeney, 2005). It must be noted, however, that this review will only emphasize on the use of pharmaceutical remedies as well as herbal remedies as the key methods of controlling goats’ internal parasites by resource-limited farmers. In many developing countries, medicinal plants are the most commonly used method to control internal parasites due to their easy accessibility and affordability.

Use of Pharmaceutical Remedies

The control of internal parasites in small ruminants is mainly by the use of commercial pharmaceutical remedies
in developed countries. They are used through orthodox methods like injection and oral dosing (Shalaby, 2013). The application of these pharmaceutical remedies is regulated by government acts or policies and there are usually penalties given for any form of negligence (Latif and Jongejan, 2002). In most cases, these pharmaceutical remedies are commonly used by commercial farmers because they are expensive to buy (Waller, 2006). As a result of this, most resource-limited farmers cannot afford these pharmaceutical remedies. This has led them to use locally available medicinal plants (Laffont et al., 2001; McGaw et al., 2007). Another major challenge when using these pharmaceutical remedies is that some resource-limited farmers tend to underdose their animals, as a strategy of saving and alleviating costs associated with purchasing these remedies (Van der Merwe et al., 2001). This practice backfires as it results in the ineffectiveness of these pharmaceutical remedies when applied to livestock.

**Setbacks of using Pharmaceutical Remedies**

Fissiha and Kinde (2021) noted that the continuous use of commercial pharmaceutical remedies to control internal parasites has resulted in numerous challenges and problems like the resistance of internal parasites such as helminths to various groups of anthelmintic drugs. The resistance of helminths has been noted in studies carried out to validate the efficacy of benzimidazole, ivermectin, and levamisole against internal parasites (Terrill et al., 2004; Kaplan, 2004). As a consequence of this problem, researchers are interested in conducting studies that seek to evaluate the efficacy of pharmaceutical remedies used to manage internal parasites in small ruminants. For example, in a study conducted in southeast regions of the United States using the fecal egg count reduction test to validate the efficacy of pharmaceutical remedies, all the evaluated classes of commercial anthelmintics showed a high degree of resistance in goats (Zajac and Gipson, 2000; Terrill et al., 2001; Mortensen et al., 2003; Howell et al., 2008). Nielsen et al. (2010) argued that this anthelmintic resistance was a result of misuse, poor formulation, and continuous use of these products.

It has also been noted that the use of pharmaceutical remedies leads to some side effects in the animal and causes environmental toxicity problems as well as chemical residues in products (Jabbar et al., 2006; Saeed et al., 2007; Ji et al., 2012). According to Anumol et al. (2017), improper administration of pharmaceutical remedies in livestock can result in extreme residues being present in animal products such as meat, milk, or other regulatory marker tissues, which shows the illegal use of veterinary drugs with potential human health risks. The presence of residues in food is putting consumers' health at high risk of allergic reactions in individuals with hypersensitivity and can also be responsible for toxic effects (Dasenaki and Thomaidis, 2015). With this in mind, modern-day consumers prefer products from small ruminants that are managed with the least chemical involvement in systems known as organic farming (Sujon et al., 2008).

**Using Indigenous Medicinal Plants as a Cheap Alternative Tool to Manage Internal Parasites of Small Ruminants**

Ethnoveterinary medicine is the traditional animal health care system normally used by members of rural communities (Mwale and Masika, 2009). The IIRR (1994) explains this practice as a traditional practice where a variety of plant extracts that are suitable to control and treat livestock disease and internal parasites are used. Across the world, many people have been using medicinal plants for centuries to combat parasitic infection and they are still being used for this purpose (Danso and Bohg, 1999). Interestingly, this practice gains more popularity as pharmaceutical remedies exacerbate environmental pollution and result in residues in livestock products (Mravčáková et al., 2020). This results in further research on alternative medications such as the use of medicinal plants which are not only used in ruminants but also donkeys, and camels and they are sustainable and environmentally friendly.

Many plant species have been identified by traditional practitioners for treating ailments in both humans and livestock, but only relatively few plants have been researched for their efficacy. The identification of these plants by these traditional practitioners is solely dependent on their indigenous knowledge and cultural belief systems. Plants like the neem tree Azadirachta indica have been recommended to have wormicidal activity and can be used to treat internal parasites like gastro-intestinal nematodes and other related problems throughout the world (Biswas et al., 2002; Subapriya and Nagini, 2005). Guerrera, (1999) reported that most foliage plants like garlic, onion, dill, and walnuts are used to treat livestock that suffers from internal parasites such as gastro-intestinal parasitism. According to Guerrera (1999), cucumber and pumpkin are used to remove tapeworms that are found in the gastrointestinal tract. In countries like the United Kingdom, nematode parasite infections such as Ascaris spp., Strongylus, and Parascaris in monogastric animals and humans were treated by chenopodium derived from Chenopodium ambrosioides (Saini et al., 2019). Such claims have increased interest in the use of indigenous medicinal plants, especially in developing countries. However, most of these medicinal plants are lacking in scientific validation and their conservation status is not known. The value of these medicinal plants can be realized if their local use can be scientifically validated, and their conservation status determined. Otherwise, many medicinal plant species with potential uses may become extinct before their scientific efficacy can be investigated.
Available Bioactive Compounds in some Medicinal Plants

Plants with medicinal value have various bioactive compounds that produce a positive physiological action in both humans and animals. These bioactive compounds are called phytochemicals and they are useful in treating or curing disease in the form of herbal medicines (Chitravadivu et al., 2009). *Elephantorrhiza elephantina* is a practical example of a medicinal plant with diverse medicinal properties which is used to cure different human and animal ailments (Maroyi, 2017). This plant species contains multiple classes of bioactive compounds in its rhizome extract, such as anthraquinones, anthocyanidins, tannins, esters, fatty acids, phenolic compounds, flavonoids, glycosides, polyesters, saponins, sugars, and triterpenoids (Mthembu, 2007; Mpofu et al., 2014). *Verbascum thapsus* (mullein) is another medicinal plant that contains tannins, flavonoids, terpenoids, saponins, carbohydrates, glycosides, proteins, fats, and fixed oils in the plant's extracts (Ali et al., 2012). Some medicinal fruits like papaya and pineapple also contain bioactive compounds such as saponins (Stepek et al., 2004).

Functions of Common Compounds Found in Various Medicinal Plants

Tannins

Tannins are defined as polymeric phenolic substances that possess astringent properties. Basri and Fan (2005) described these compounds as those that can dissolve in water, acetone, and alcohol and can precipitate or react with proteins. This enables tannins to have anthelmintic effects by binding to free proteins in the gastrointestinal tract of infected animals, or glycoprotein on the cuticle of the parasite and cause death (Patel et al., 2010). According to Athanasiadou et al. (2001), parasitized ruminants such as sheep and red deer that graze on forages with high condensed tannins normally have lower fecal egg counts and worm loads compared with ruminant animals that graze on forages with low condensed tannins. In addition, the study conducted by Ali et al. (2012) proved that *V. thapsus* extracts had wormicidal activity better than that of albendazole against tapeworms owing to its tannin content.

Saponins

According to Oda et al. (2000), saponins have based adjuvants that enable them to have the distinctive ability to boost the cell-mediated immune system and antibody production. Saponins can influence membrane permeability and pore formation which allows them to have similar properties as commercial drugs such as toltrazuril and praziquantel (Oda et al., 2000). Hence, they can affect the permeability of the cell membrane in internal parasites and can cause vacuolization and disintegration of monogenean teguments (Melzig et al., 2001).

Alkaloids

Alkaloids comprise a class of nitrogenous organic compounds that normally characterize a very diverse group of bioactive compounds that are only associated with the presence of a nitrogen atom in the heterocyclic ring. The nitrogen in the alkaloid molecule is derived from amino acid metabolism (Hrckova and Velebny, 2013). These compounds can act on the central nervous system to cause paralysis. Roy et al. (2010) noted that steroidal alkaloids and oligoglycosides are also present in alkaloids and they can prevent the transmission of sucrose from the stomach to the small intestine. Alkaloids act as antioxidants and can alleviate nitrate production, which can interfere with local homeostasis which is essential for the development of helminths (Roy et al., 2010). Furthermore, isoquinoline alkaloids have shown strong wormicidal activity on *Strongyloides venezuelensis* in a rat model (Satou et al., 2002).

Cysteine Proteinases

Cysteine proteinases are phytochemicals contained in some early medicinal fruits such as papaya and pineapple and are known for their anthelmintic properties (Stepek et al., 2008). They can affect parasite invasion and growth (Moyo et al., 2014). Furthermore, proteases are the group of enzymes that enable the splitting of proteins into smaller fragments and can be grouped into different classes. These classes can be cysteine, serine, aspartate, threonine, and metalloproteases (Grzonka et al., 2001).

Human Activities that Result in Indigenous Medicinal Plant Exploitation

Throughout the world, the use of herbal remedies, organic health products, and secondary metabolites of indigenous plants is increasing (Nalawade et al., 2003; Cole et al., 2007). This has resulted in the exploitation of some plant populations, especially those plants that have commercial value. For instance, Pelargonium species are used to extract essential oils from leaves. This has resulted in the commercial exploitation of these species as their use has increased, especially in cosmetic and pharmaceutical companies (Lalli et al., 2008).

In countries like South Africa, the exploitation of these plants has been a subject of debate for numerous decades. In 1946, a Zululand missionary called Jacob Gerstner wrote about the extinctions of indigenous medicinal plants used by traditional herbalists and suggested their cultivation be taken up by the state nurseries to conserve them (Williams et al., 2013). Factors like urbanization, agriculture expansion, habitat transformation, illegal harvesting of medicinal plants, and overgrazing can also contribute to the depletion of these plants (Chigor, 2014). According to Cunningham (1997), trading with
indigenous medicinal plants has increased compared to previous years, which makes it difficult for conservation agencies to manage the exploitation of resources in South Africa. When there are challenges like this, many species are seriously threatened with extinction and there is no assurance that future generations will benefit from these plants (Kambizi and Afolayan, 2006). In South Africa, *Gunnera perpensa* is a practical example of a plant species that has been exploited and faces the threat of extinction (Raimondo et al., 2009).

**Conservation Strategies and Efficient use of Indigenous Medicinal Plants**

In countries like South Africa and China, numerous medicinal plant species are at high risk of extinction due to high demand from the large population (Chigor, 2014). As a result, various recommendations for conservation strategies have been compiled. According to Chen et al. (2016), there must be systems in place such as status monitoring and co-ordinate conservation practices based on both in situ and ex situ strategies in order to conserve these plants. Indigenous medicinal plants with restricted abundance and those with slow growth should be considered and sustainable harvesting regulations and practices must be formulated (Chen et al., 2016). Schippmann et al. (2006) observed that there is a serious need to cultivate those plants that become scarce to maintain their sustainability. In addition, increased cultivation of medicinal plants contributes to the alleviation of harvesting large quantities of indigenous medicinal plants and benefits their recovery in the wild (Hamilton, 2004; Chen et al., 2016).

On the other hand, Bodeker (2004) proposed that it must be a prerequisite for the national government to invest more in research on indigenous medicinal plants and develop respectable policies, regulations, and trade standards to avoid overexploitation. Hence, the South African government encourages research institutions like the National Research Foundation to focus more on studies that seek to enhance the sustainable use of the country’s natural resources (Light et al., 2005). Furthermore, other methods that could be used are to encourage traditional healers to harvest plant leaves, and flowers instead of collecting bulbs or roots (Zschocke et al., 2000). To conserve plants with high medicinal value in African countries, there must be binding laws that seek to develop safeguards for the sustainable use of medicinal plants (African Union, 2007). As part of efforts in African countries, community village heads, chiefs, councilors, and traditional healers in Zimbabwe have played an important role in ensuring plants with medicinal properties are not exploited. Furthermore, they also motivate communities to practice sustainable harvesting and to grow trees with medicinal value in their gardens, to alleviate over-use of these medicinal plants (Matongo, 2012). The South African government has set up projects that seek to ensure the conservation of indigenous medicinal plants. For example, in 2009 the Gauteng government established an incubator project that protects indigenous medicinal plants that grow these plants in a nursery environment so that they can be sold to traditional herbalists (Ndawonde, 2015). Moreover, indigenous knowledge of using medicinal plants is also facing extinction since the information is normally held by old people and they are dying with this knowledge without documentation (Cosminsky, 1983; Rukangira, 2001). Hence the late Health Minister Manto Tshabalala-Msimang encouraged more research as part of conserving indigenous use of medicinal plants to control disease in both humans and livestock (Matongo, 2012)

**Efficacy Evaluation of Indigenous Medicinal Plants**

The increasing use of indigenous medicinal plants to manage internal parasites in both livestock and humans has led researchers to employ various methods to validate their efficacy and safety. These methods include in vitro and in vivo validation. In this review, different scientific methods of validating the efficacy and safety of medicinal plants will be discussed. These can be broadly categorized into in-vitro and in-vivo methods.

**In Vitro Methods**

*In vitro* techniques comprise various methods that can be employed to explore the efficacy of anthelmintic substances which have the potential to act against internal parasites such as nematodes. For example, the egg hatch assay, larval feeding inhibition, larval migration inhibition, and larval development are some of the in vitro methods (Amarante et al., 1997). According to Athanasiadou et al. (2001), larval migration inhibition and larval feeding inhibition are one of the best essays that are normally used to evaluate the anthelmintic effect of bioactive substances in vitro. *In vitro* methods such as larval development and egg hatch assay involve placing plant extracts directly in contact with eggs or larvae of the internal parasites to determine the effect on egg hatching and larval development (Hammond et al., 1997; Akhtar et al., 2000). These anthelmintic studies require measuring the survival and reproductive potential of the worms after exposing them to plant extracts for a specific period. Normally the efficacy of tested plant extracts is determined based on the behavioral response of worms after being exposed to extracts for a period (McGaw et al., 2007).

In the adult mortality assay, live worms are exposed directly to various concentrations of plant extracts and observed for their mortality at various intervals (Iqbal et al., 2004). Then the efficacy is reported based on the number of non-motile or dead worms inhibited by the extracts compared to the untreated control.

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Moreover, Gnoula et al. (2007) reported that most times it is challenging to differentiate between paralyzed and dead worms. While Rahmann and Seip (2007) highlighted that once the plants have been tested using in-vitro techniques, which saves time and costs, those with potential must be tested again using in-vivo methods to confirm results and also to evaluate associated risks and side effects. It is generally understood that results obtained using in vitro efficacy evaluation techniques sometimes differ from results obtained with in vivo efficacy evaluation techniques. This is because the efficacy of plants in vivo may be affected by physiological and bioavailability factors in the animal body and the stage of the parasitic life cycle tested (Githiori, 2004).

Table 1 highlights several studies that have been carried out to validate the effectiveness of medicinal plants against internal parasites using in vitro techniques.

**Table 1: Plants evaluated against H. contortus using in vitro techniques**

<table>
<thead>
<tr>
<th>Plant Names</th>
<th>Plant part used</th>
<th>Method</th>
<th>Results</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leonotis leonurus</td>
<td>Leaves</td>
<td>Egg Hatch Assay and Larval development</td>
<td>Active against H. contortus</td>
<td>Maphosa et al. (2010)</td>
</tr>
<tr>
<td>Aloe ferox</td>
<td>Leaves</td>
<td>Egg Hatch Assay and Larval development</td>
<td>Active against H. contortus</td>
<td>Maphosa et al. (2010)</td>
</tr>
<tr>
<td>Acacia nilotica</td>
<td>Seeds</td>
<td>Egg Hatch</td>
<td>Active against H. contortus</td>
<td>Habtemariam (2005)</td>
</tr>
<tr>
<td>Annona senegalensis</td>
<td>Stem bark</td>
<td>Egg Hatch Assay</td>
<td>Active against H. contortus</td>
<td>Alawa et al. (2003)</td>
</tr>
<tr>
<td>Vernonia amygdalina</td>
<td>Leaves</td>
<td>Egg Hatch Assay</td>
<td>Active against H. contortus</td>
<td>Alawa et al. (2003)</td>
</tr>
<tr>
<td>Acacia nilotica</td>
<td>Seeds</td>
<td>Egg Hatch Assay</td>
<td>Active against H. contortus</td>
<td>Habtemariam (2005)</td>
</tr>
<tr>
<td>Annona squamosa</td>
<td>Seeds</td>
<td>Egg Hatch Assay and larval development</td>
<td>Active against H. contortus</td>
<td>Kamaraj and Rahuman (2011)</td>
</tr>
<tr>
<td>Euphorbia prostrata</td>
<td>Leaves</td>
<td>Egg Hatch Assay and larval development</td>
<td>Active against H. contortus</td>
<td>Kamaraj and Rahuman (2011)</td>
</tr>
<tr>
<td>Terminalia chebula</td>
<td>Seeds</td>
<td>Egg Hatch Assay and larval development</td>
<td>Active against H. contortus</td>
<td>Kamaraj and Rahuman (2011)</td>
</tr>
</tbody>
</table>

Due to the escalating development of internal parasite resistance to currently used pharmaceuticals and increasing societal demand for organic products, there is an urgent need for scientific intervention to validate the efficacy and safety of medicinal plants. Despite existing recommendations for conservation strategies, many medicinal plants still face extinction. There is therefore a need for research that will investigate innovative methods of conserving indigenous information and local medicinal plants in countries like South Africa.

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**Author’s Contributions**

Wandile Nikelo: Contributed to design the study, writing, and edited the manuscript.

Maliviwe Mpayipheli and Lyndy McGaw: Contributed to the design of the study and edited the manuscript.

The final version of this manuscript has been read by all authors and confirmed for publication.

**Ethics**

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and no ethical issues involved.
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