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Anthelmintic Activity of *Foeniculum vulgare* Seeds and Meta-Analysis of Some Other Medicinal Plants from Pakistan

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Abstract: Helminthiasis diseases caused by parasitic worms in animals have been a significant challenge worldwide, resulting in substantial economic losses and decreased productivity in the agricultural sector. The use of synthetic drugs to treat these infections has several drawbacks, including the development of drug resistance, high costs, and potential toxicities to both animals and humans. Therefore, researchers looked for other ways to solve the problem and found that medicinal plants might have anthelmintic activities because they have many secondary metabolites. These metabolites have demonstrated the potential to act as natural anthelmintics, making them attractive options for developing novel drugs. Firstly, an experiment was done to test the effectiveness of *Foeniculum vulgare* seed extract against *Gastrothylax crumenifer*. Subsequently, we employed a meta-analysis approach to identify plant species and compounds with the most promising anthelmintic activities. The methodology will involve a comprehensive search of various databases to identify relevant research articles on the anthelmintic activity of medicinal plants. The study found that *Foeniculum vulgare* seed extract was effective against *Gastrothylax crumenifer*. The study also identified the most active and promising medicinal plants that warrant further investigation for their potential to eradicate parasites. Furthermore, a meta-analysis revealed anthelmintic activity in 34 plants, with the *Musaceae*, *Solanaceae*, and *Asteraceae* families receiving the most extensive research. The findings have implications for developing cost-effective and safe anthelmintic treatments for animals.

Keywords: *Foeniculum vulgare*; Meta-analysis; Anthelmintic activity; Parasite

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1. Introduction

Parasitic infections are a major concern for animals, including livestock, pets, and wildlife [1]. These infections can cause a range of health problems, including reduced growth rates, decreased milk production, anemia, and even death [2]. Helminthiasis poses a significant challenge in limited-scale dairy farming systems in developing nations such as Pakistan [3,4]. In these regions, farmers and veterinarians commonly employ chemical regulation

methods [5]. There is a renewed interest in checking out traditional veterinary methods, though, because of problems like anthelmintic resistance [6] and worries about the side effects and residues of fabricated medicines, along with the fact that farmers lack money to spend on animal care. The government does not pay enough for it. Resistance development is one of anthelmintic drugs' major drawbacks. Over time, the repeated use of unchanged medicines may lead to the development of unaffected strains of parasites, making the drugs less effective [7]. Given these limitations, there is an emergent awareness of the use of alternative approaches to treat parasitic infections in animals. Researchers have identified medicinal plants as a potential alternative due to their extensive history in outdated medicine and their general safety and environmental friendliness. *Foeniculum vulgare* (*F. vulgare*), a medicinal and aromatic plant belonging to the *Apiaceous* family and commonly known as fennel, holds significant importance [8]. Fennel, widely recognized for its therapeutic properties, serves as a digestive, carminative, lactogogue, and diuretic, especially in the management of respiratory and gastrointestinal disorders. Beyond their medicinal applications, fennel seeds serve as flavor enhancers in various culinary preparations, including baked items, meat and fish entrees, ice cream, alcoholic drinks, and blends of herbs. Phenolic compounds in *F. vulgare* contribute to its antioxidant activity, while volatile aromatic compounds enhance its excellence as a flavoring agent [9]. In developing nations like Pakistan, veterinary personnel often face challenges in reaching herdsmen easily. In such situations, ethnoveterinary systems emerge as the primary substitute for Western veterinary therapy. Ethnoveterinary medicine (EVM) constitutes a system for conserving animal fitness and treating illnesses based on general beliefs, outmoded information like traditional knowledge (TK), and a repertoire of expertise, methods, and practices [10]. The transmission of EVM knowledge, like other TK systems, occurs orally from one generation to the next. Unfortunately, like other TK systems, EVM is facing a decline due to speedy socioeconomic, eco-friendly, and technological changes. *Foeniculum vulgare*, frequently known as fennel and belonging to the family *Apiaceous/Umbelliferae*, holds significance as a well-known medicinal and scented herb. People widely use it for various health benefits, including aiding digestion, acting as a diuretic, addressing asthma, supporting breastfeeding women, helping lower cholesterol levels in diabetes, alleviating edema, managing anxiety, and depression, and treating gastrointestinal disorders. People use the seeds of fennel to regulate blood pressure, reduce asthma symptoms, alleviate water retention, purify the blood, and improve eyesight. Many drug studies [11], both *in vitro* and *in vivo*, have shown that *Foeniculum vulgare* has a lot of potential to help with antifungal, antibacterial, antioxidant, antidepressant, and anxiety disorders. Phenolic compounds isolated from fennel are credited with their antioxidant activity, while their volatile aromatic compounds contribute to their excellence as a flavoring agent. This comprehensive review provides an up-to-date analysis of the chemistry, pharmacology, traditional uses, and safety considerations of *Foeniculum vulgare*. In a time when drug resistance is a problem, the study also looked at how well a herbal complex (HC) made up of *Origanum vulgare*, *Rosmarinus officinalis*, *Cinnamomum verum*, and *Capsicum annuum* kills eggs and adults of the *Haemonchus contortus* parasite. The findings indicate the herbal complex's anthelmintic power [12]. Additionally, the study delved into the essential oils of three organically grown varieties of Egyptian fennel, assessing their chemical components, antimicrobial, and antioxidant activities. Different amounts of major monoterpenoids were found in the essential oils. Trans-anethole, estragole, fenchone, and limonene were found in high amounts. We evaluated the antioxidant activities of the oils and found that those from specific cultivars showed superior effectiveness. We found all three cultivars to have similar antimicrobial activities. The primary objective of this study was to identify ethnoveterinary practices (EVPs) employed in the treatment of parasitic diseases in livestock from Jhung, an area located in Punjab, Pakistan. To accomplish this, we conducted a preliminary assessment to classify 200 outmoded veterinary healers from the local farming community. We gathered evidence over six months through verbal talks, group consultations, and field surveys.

We recognized 96 EVPs, comprising 66 medicinal plants and 30 organic and inorganic substances [13]. We identified 35 plants from 23 families for the treatment of various parasitic diseases. The ten most habitually used herbs included *Eruca vesicaria*, *Azadirachta indica*, *Citrullus colocynthis*, *Brassica rapa*, *Ocimum basilicum*, *Ferula asafetida*, *Nicotiana tabacum*, *Allium cepa*, *Withania coagulans*, and *Aloe vera*. Notably, there was diversity in the dosage, preparation method, parts used, and indications for the plants. Researchers reported 63 plants with helminthiasis and 57 with tick infestations. The study's discoveries underscored the richness of indigenous knowledge and its effective application by local farming communities in treating prevalent parasitic diseases. The potential for value addition lies in standardizing plant doses and validating them through scientific procedures, which would be beneficial to farmers, scientists, and the therapeutic industry.

2. Materials and methods

2.1. Collection of parasites

Live *Haemonchus contortus* parasites were collected from the rumen of newly slaughtered domestic goats in Rawalpindi and Islamabad. The parasites were kept in a phosphate-buffered saline solution (PBS).

2.2. Preparation of plant extract

Foeniculum vulgare seeds were bought from the local market in Islamabad and used to prepare a plant extract. The seeds were ground and dissolved in water. Once the solution was fully prepared and ready, the water was evaporated to isolate the extract [14]. The *Foeniculum vulgare* seed extract was tested for its ability to kill worms using the well plate method and compared to the manufactured drug albendazole. The ovicidal and larvicidal activity of the seed extract was assessed by counting the number of unhatched eggs and dead larvae using a modified method.

2.3. Mortality rate calculation

Using the following formula, we calculated the number of dead parasites in each experimental set as well as the average mortality percentage: average mortality rate = total number of dead parasites x 100 / total number of experimental parasites.

2.4. Data collection for meta-analysis

To conduct a meta-analysis, the current research employed a methodical review and meta-analysis of existing scientific writings to evaluate the anthelmintic activity of selected medicinal plants. We thoroughly examined research articles and limited the search to studies conducted in Pakistan and included articles published from 2000 to the present. The search terms include relevant keywords such as "medicinal plants," "anthelmintic activity," and "parasite infections." The random-effects model conducted the meta-analysis to estimate the overall effect size of the anthelmintic activity of selected medicinal plants [15]. We calculated the effect size as the standardized mean variance between the experimental and control groups. Heterogeneity was measured using the I^2 statistic, and potential sources of heterogeneity were explored through subgroup examination and meta-regression. Sensitivity analysis was conducted to assess the robustness of the results [16].

3. Results

The present study was designed to analyze the anthelmintic activity of *Foeniculum vulgare* seeds and meta-analysis of some other medicinal plants from Pakistan. Several groups of plants express anthelmintic activity. A total number of 34 families were studied and data revealed that plants from families *Moraceae*, *Solanaceae*,

and *Asteraceae* possess more anthelmintic activity. Meta-analysis of several plants along with their family detail having abilities of anthelmintic activity in Pakistan are listed in **Table 1**. Furthermore, some of the plants expressed more anthelmintic activity as compared to the others. We collected data from previously published data to give shreds of evidence for the association of plants with such activity. The *Moracea* plant showed maximum anthelmintic activity from our selected data in Pakistan followed by the activity of *Solanaceae* and *Asteraceae* plants. **Figure 1** shows the number and distribution of plants with anthelmintic activity

Table 1. Meta-analysis of several plants with family depicting anthelmintic activity from Pakistan

No.	Family	Plants	References
1	*Moraceae*	*Morus alba*	Nawaz et al. (2014) [17]
		Ficus bengalensis	Mughal et al. (2013) [18]
		Ficus religiosa	Mughal et al. (2013) [18]
		Ficus glomerata	Mughal et al. (2013) [18]
		Morus indica	Mughal et al. (2013) [18]
		Morus laevigata	Mughal et al. (2013) [18]
2	*Asteraceae*	*Artemisia parviflora*	Irum et al. (2017) [19]
		Artemisia sieversiana	Irum et al. (2017) [19]
		Vernonia anthelmintica	Irum et al. (2017) [19]
		Artemisia brevifolia	Irum et al. (2017) [19]
		Artemisia maritima	Irum et al. (2017) [19]
3	*Solanaceae*	*Nicotiana tabacum*	Farooq et al. (2008) [20]
		Withania somnifera	Jabbar et al. (2006) [21]
		Capsicum annuum	Farooq et al. (2008) [20]
		Nicotiana tabacum	Iqbal et al. (2006) [22]
		Solanum surratens	Farooq et al. (2008) [20]
4	*Meliaceae*	*Azadirachta indica*	Iqbal et al. (2010) [23]
		A. Juss	Jabbar et al. (2006) [21]
		Azadirachta indica	Farooq et al. (2008) [20]
5	*Chenopodiaceae*	*Salsola imbricata*	Ajaib et al. (2019) [24]
		Haloxylon salicornicum	Farooq et al. (2008) [20]
		Salsola baryosma	Farooq et al. (2008) [20]
6	*Amaranthaceae*	*Chenopodium album*	Jabbar et al. (2007) [6]
		Aerva javanica	Farooq et al. (2008) [20]
7	*Cucurbitaceae*	*Citrullus colocynthis*	Farooq et al. (2008) [20]
		Cucurbita mexicana	Iqbal et al. (2014) [25]
8	*Fabaceae*	*Acacia nilotica*	Bachaya et al. (2009) [26]
		Dalbergia sisso	Nawaz et al. (2014) [17]
9	*Umbelliferae*	*Ferula costata*	Kakar et al. (2013) [27]
		Ferula assafoetida	Farooq et al. (2008) [20]

Table 1 (Continued)

No.	Family	Plants	References
10	*Aizoaceae*	*Trianthema portulacastrum*	Hussain et al. (2011) [28]
		Aizoon carariense	Farooq et al. (2008) [20]
11	*Cruciferae*	*Brassica campestris*	Farooq et al. (2008) [20]
		Eruca sativa	Farooq et al. (2008) [20]
12	*Moringaceae*	*Moringa oleifera*	Farooq et al. (2008) [20]
13	*Caesalpiniaceae*	*Caesalpinia crista*	Iqbal et al. (2014) [25]
14	*Gentianaceae*	*Swertia chirata*	Iqbal et al. (2014) [29]
15	*Acanthaceae*	*Adhatoda vesica*	Lateef et al. (2003) [30]
16	*Apocynaceae*	*Calotropis procera*	Iqbal et al. (2005) [31]
17	*Lamiaceae*	*Lamium amplexicaule*	Jabbar et al. (2006) [21]
18	*Euphorbiaceae*	*Mallotus philippinensis*	Hussain et al. (2011) [28]
19	*Rhamnaceae*	*Ziziphus nummularia*	Bachaya et al. (2009) [32]
20	*Zingiberaceae*	*Zingiber officinale*	Iqbal et al. (2006) [4]
21	*Papaveraceae*	*Fumaria parviflora*	Al-Shaibani. (2009) [33]
22	*Rutaceae*	*Skimmia laureola*	Mehmood et al. (2011) [34]
23	*Urticaceae*	*Ficus religiosa*	Iqbal et al. (2006) [35]
24	*Liliaceae*	*Allium sativum*	Iqbal et al. (2006) [35]
25	*Leguminosae*	*Butea monosperma*	Iqbal et al. (2006) [35]
26	*Combretaceae*	*Terminalia arjuna*	Bachaya et al. (2009) [32]
27	*Musaceae*	*Musa paradisiaca*	Hussain et al. (2010) [36]
28	*Lythraceae*	*Punica granatum*	Jabeen et al. (2015) [37]
29	*Berberidaceae*	*Berberis lycium*	Jabeen et al. (2015) [37]
30	*Capparaceae*	*Capparis decidua*	Farooq et al. (2008) [20]
31	*Cyperaceae*	*Cyperus rotundus*	Farooq et al. (2008) [20]
32	*Polygonaceae*	*Calligonum polygonoides*	Farooq et al. (2008) [20]
33	*Scrophulariaceae*	*Verbascum thapsus*	Riaz et al. (2013) [38]
34	*Poaceae*	*Cymbopogon citratus*	Sherwani et al. (2013) [39]

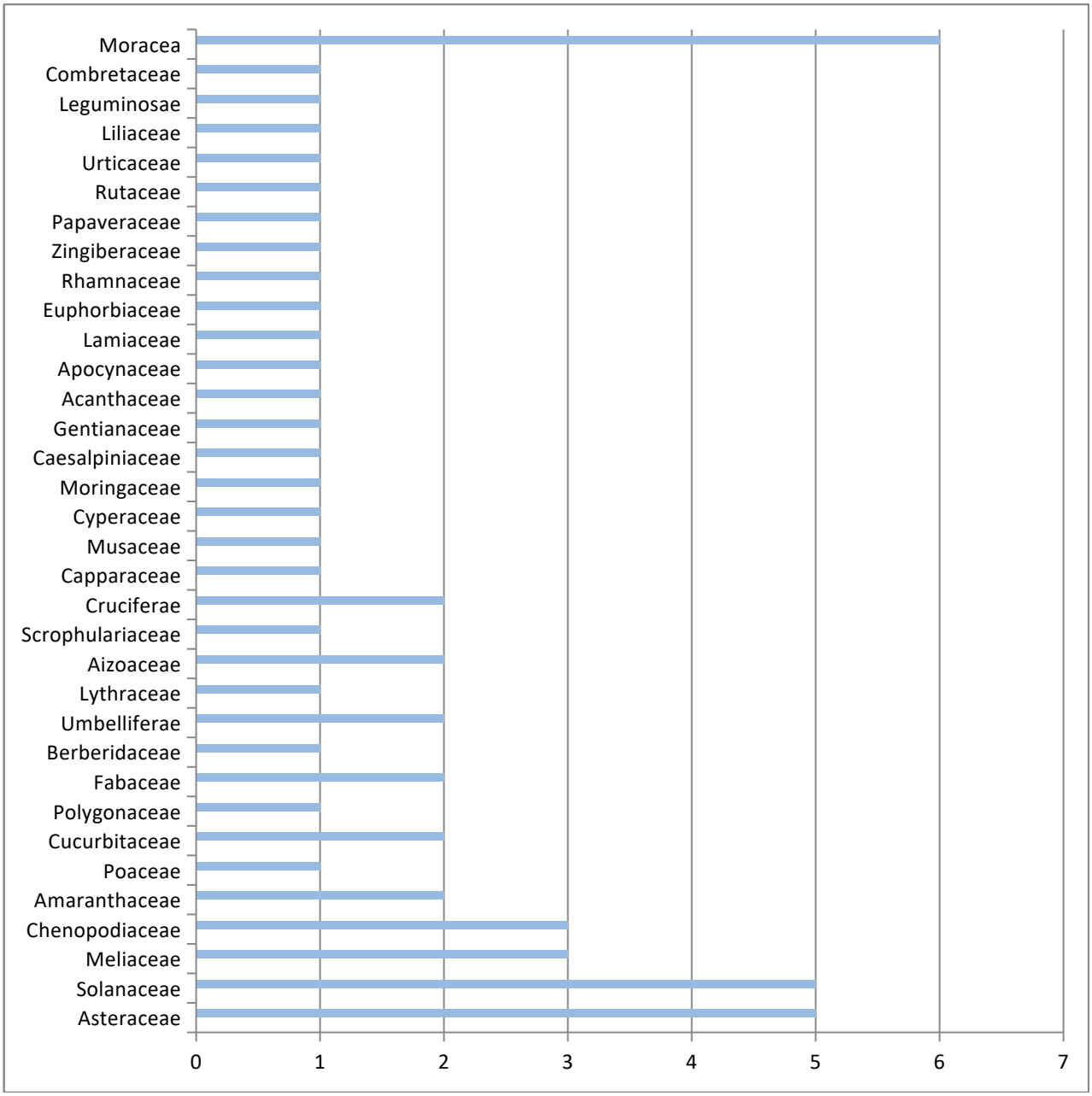

Figure 1. The number and distribution of plants with anthelmintic activity

4. Discussion and conclusion

A variety of organisms, including nematodes, cestodes, and trematodes, collectively referred to as helminths, cause parasitic infections [40]. The risk of toxicity is another drawback of anthelmintic drugs. Many of these drugs have a narrow range of beneficial windows, Son *et al.* [41] explained that the variance between the effective dose and the toxic dose is insignificant. In addition to these drawbacks, there is also growing concern about the environmental impact of anthelmintic drugs. These drugs can accumulate in the soil and water, leading to potential ecological effects [42]. Some of the most important phytochemicals in *Foeniculum vulgare* are phenols, phenolic glycosides, volatile aroma compounds, estragole, trans-anethole, and fenchone [10]. Numerous pharmacological experiments conducted in both *in vitro* and *in vivo* models have substantiated its antifungal, antibacterial, antioxidant, antithrombotic, and hepatoprotective activities. These findings align with the plant's

traditional uses in therapeutic contexts [43]. The current study examined the *Foeniculum vulgare* and some other plants and whether they exhibit potential for use as anthelmintics in Pakistan. Furthermore, a meta-analysis revealed anthelmintic activity in 34 plants, with the *Musaceae*, *Solanaceae*, and *Asteraceae* families receiving the most extensive research and maximum anthelmintic activity and potential in Pakistan. The findings have implications for developing cost-effective and safe anthelmintic treatments for animals and to control parasites.

Disclosure statement

The authors declare no conflict of interest.

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