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ANTI-FASCIOLIC EFFECT OF RAW SEEDS OF *Nigella sativa*, *Fumaria parviflora* (AERIAL PARTS), IN NATURALLY INFECTED BUFFALOES

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Abstract

In the present study *Nigella sativa* (seeds) and *Fumaria parviflora* (aerial), were used to treat buffaloes naturally infected with fasciolosis and their efficacy (%) was compared. *In vivo,* pre-and post-treatment (50 mg, 100 mg, and 150 mg/ kg body weight of the two medicinal plants) fecal egg counts were determined following standard fecal egg count reduction in buffaloes (*Babulus sp.*) of Nili Ravi breed naturally parasitized with *Fasciola* sp. The infected buffaloes were randomly divided into 3 main groups' i.e. A, B, and C. Animals in groups A and B were further subdivided into three subgroups i.e. A1, A2, A3; B1, B2, B3. Sub-groups A1 and B1 were given dose levels of 50mg/kg body weight, A2, and B2, 100mg while A3 and B3, 150mg/kg body weight of *Nigella sativa* (seeds) and *Fumaria parviflora* (aerial), respectively. Group C with infected animals served as a control. 2 medicinal plants has been found significantly ($P<0.05$) efficient (42-100%) and safe to use against fasciolosis.

Keywords: Buffaloes. Comparative Efficacy. Fasciolosis**.** Medicinal Plants.

1. Introduction

Fascioliasis treatment is not always optimal. Various drugs are used to treat animal and human fasciolosis, among which emetine, dehydroemetine, biothinol, and paraziquantel are commercialized and licensed for use (Oritz et al. 2000; Cosme et al. 2001; Giorgi et al. 2001). The effectiveness of these treatments is controversial, and a few have been described as having negative effects. Paraziquantel, once used for the treatment of foodborne trematode illnesses, is unsuccessful against fasciolosis (Farid et al. 1986; Salvioli et al. 1999). Biothinol, though not adequate, has been the drug of choice for fasciolosis treatment (Oritz et al. 2000). Levamisole, netobimin, clorsulon, oxyclozamide, niclofan, nitroxynil, and ivermectin have also been used to treat fasciolosis in animals (Maqbool et al. 1992; Maqbool et al. 1994; Maqbool et al. 1996; Ibarra-Velarde et al. 2001; Sanchez-Andrade et al. 2001).

A safe medicine with high activity is required for effective chemotherapy and strategic chemoprophylaxis for fasciolosis. Triclabendazole has been used in humans and animals for this purpose. However, the risk of triclabendazole resistance cannot be ignored, as reported by Mitchell et al. (1998), Moll et al. (2000) and Gaasenbeek et al. (2001). Therefore, there is a need to identify new drugs that can be used as substitutes for triclabendazole.

Plants have been used since ancient times to treat diseases in humans and animals. This system of therapy is commonly referred to as 'Unani, folk, Eastern, or indigenous medicine (Akhtar et al. 2000). In the

present study, the anti-fasciolic activities of two herbal medicines, N. sativa (seeds) and F. parviflora (aerial parts), were evaluated. Nigella sativa seeds have been widely used to treat several diseases and ailments, and have proven to be effective anti-diabetic, anti-microbial, anti-inflammatory, gastro-protective, hepato-protective, and bronchodilator (Khaled 2009; Assayed 2010; Boskabady et al. 2010; Abdel-Zaher et al. 2011; Abel-Salam 2012). The remedial properties of black seeds are attributed to the presence of alkaloids, quinines, alpha-hederin, unsaturated fatty acids, and sterols (Yarnell et al. 2011). Phytochemical analysis of F. parviflora leaves revealed the presence of glycosides, sterols, alkaloids, and fatty acids (Modi et al. 2016). The presence of these bioactive compounds imparts anti-inflammatory, anthelmintic, antiprotozoal, and anti-nociceptive properties. Considering the beneficial aspects of *N. sativa* (seeds) and *F. parviflora* (aerial parts), these herbal medicines were evaluated for the treatment of fasciolosis and overall health improvement of buffaloes from a local dairy.

2. Material and Methods

A total of 63 buffaloes (Babulus sp.) of Nili Ravi breed, 6.0±0.1 years of age, and both sexes naturally infected with fasciolosis were used for anthelmintic trials at a private dairy farm on Barki Road Lahore. The farm area was 1 acre. All animals were kept under similar feeding and management conditions throughout the treatment and provided seasonal food and water ad libitum. A veterinary doctor was available for routine checkup.

Preparation of Herbal Drugs

Nigella sativa (seeds) and Fumaria parviflora (all aerial parts) were purchased from a local market in Lahore. These herbs were washed in tap water to remove dirt, dried in the shade, and powdered in a grinder. These powdered medicines were orally administered in capsules, as described by Jhangir et al. (2003).

Experimental Design

Before starting treatment, the eggs per gram of feces (EPG) of each animal were calculated from fecal samples obtained directly from the rectum.

Buffaloes infected were divided into three main groups: A, B, and C. The animals from groups A and B were further subdivided into three subgroups. A1, A2, and A3; B1, B2, and B3, comprising nine animals.

Animals in subgroups A1, A2, and A3 were given Nigella sativa (seeds) and those in subgroups B1, B2, and B3 were given Fumaria parviflora (aerial parts) at dosage rate of 50,100,150 mg/kg body mass, respectively. Group C, with nine infected animals, served as a control for comparison with each group.

Eggs (EPG) were observed using the McMaster egg counting method (Soulsby 1982). Fecal specimens were examined at zero, third, seventh, and 18 days after treatment. Animals that remained positive after 18 days were administered a 2nd dose of the corresponding drug on the eighteen day and their fecal specimens were observed on the twenty-first and twenty-eight days. Drug efficacy was analyzed using the procedure described by Moskey and Harwood (1941).

Effects of Treatment

The effects on body weight, feed intake, milk yield (in case of lactating buffaloes), and pregnancy (in case of pregnant buffaloes) were also recorded, along with any abnormalities. The side effects of the herbs were also recorded, including shivering, sweating, salivation, and diarrhea.

Statistical Analysis

The results are expressed as eggs per gram (mean ±SEM) of feces. Mean values of pre- and post-treatment were compared using Student's t-test and comparison between all experimental doses using ANOVA.

3. Results

The efficacy (%) of the drugs was calculated based on the reduction in the egg count after treatment (Table 1 and 2). The mean percentage of fluke eggs in each treated group was compared with that of the control group (Table 2).

Table 1. Comparison of different local herbs with Triclabendazole against Fasciolosis in naturally infected buffaloes in terms of Eggs per gram of feces (EPG).

Groups	Sub-Group (n=9)	Treatment	Dose (mg/kg bw)	Eggs per gram of feces (EPG)		
				0 day	After 1st dose	After 2nd dose
A	A1	*Nigella sativa* (seeds)	50	967±88	867±120	567±120*
	A2		100	967±67	567±67*	67±33***
	A3		150	1000±58	267±88*	0±0***
B	B1	*Fumaria parviflora* (aerial parts)	50	967±33	833±33	633±33***
	B2		100	967±33	733±33**	133±67***
	B3		150	900±58	133±33***	0±0***
F (infected)		+ve control	-	867±33	1033±33	1167±67^{NS}

Mean± Standared error ($\overline{X} \pm$ S.E); Student's t-test: *P<0.05, **P<0.01, ***P<0.001, NS=non-significant.

Table 2. Comparative efficacy (%) of local herbs with Triclabendazole against Fasciolosis in naturally infected buffaloes.

Groups	Sub-Groups (n=9)	Treatment	Dose (mg/kg bw)	Efficacy (%)	
				After 1st dose	After 2nd dose
A	A1	*Nigella sativa* (seeds)	50	10.83	42.33
	A2		100	40.43	93.3 aaa
	A3		150	73.87	100
B	B1	*Fumaria parviflora* (aerial parts)	50	27.31	66.20
	B2		100	61.31	95.83 aaa
	B3		150	80.56	100

ANOVA: Comparison within group by Tukey's test: a=P<0.05, aa=P<0.01, aaa=P<0.001.

Efficiency of Nigella sativa Seeds (Group A)

The effectiveness of N. sativa (seeds) in group A1 was 10.83% and 42.33% at 1st and 2nd dose levels, respectively (Table 2). Advanced doses (100 mg and 150 mg/kg of body weight) increased the efficiency by up to 40.43% and 73.87% at the 1st, and 93.3% and 100% at the 2nd dose levels in groups A2 and A3, respectively (Table 2). These efficacies were statistically significant ($P < 0.05$). It was also detected following the execution of a second dose of 150 mg/kg BW of N. sativa, and the egg output became zero.

Efficiency of Fumaria parviflora Aerial Parts (Group B)

F. parviflora (aerial parts) (group B) at 50mg/kg body weight dose produce about 27.3% and 66.20% decline in EPG amounts on 18th and 28th day, respectively. Upon increasing the dose up to 100 mg and 150 mg/kg body weight, the efficacy was 61.3% and 85.1%, respectively, at one dose level, whereas at two dose levels, the drug was effective at 85.1% and 100%, respectively (Table 2). Student's t-test showed a significant ($P<0.05$) decrease in egg output (EPG) after treatment at all three dose levels, and in sub-group B3, the number of eggs became zero on the 28th day (Figure 1A).

The EPG count increased in the untreated control group C (34.6%), but the difference was not significant.

Intragroup comparison ~~by~~ using Tukey's test showed a significant difference ($P<0.05$) between dose levels of 50 mg/kg and 100 mg/kg body weight (BW), but non-significant differences between 100 and 150 mg/kg BW of both herbal drugs. Intergroup comparison between the efficacy of the same doses showed a non-significant difference between them, except for sub-groups B1 and C1, which showed a significant ($P<0.05$) difference (Table 2).

Effect on Milk Production (in lactating buffaloes)

Of the 16 infected lactating buffaloes, two were present in each of the following group/sub-groups: A1, A2, B1, and C, whereas three buffaloes were present in A3, B2, B3, and C.

Before treatment milk production was noted at 2.55±0.05, 2.90±0.10 and 2.4±0.2 liters in sub-groups A1, A2 and A3, while after treatment 2.90±0.10, 3.65±0.15 and 4.37±0.19 liters respectively, after treatment. A significant ($P<0.001$) increase (82.1%) was noted only in subgroup A3 (Figure 1).

In subgroups B1, B2, and B3, a 32.0%, 40.8%, and 79.0% increase was noted, respectively. A significant ($P<0.001$) increase (79.0%) was noted only in subgroup B3. Infected buffaloes without any treatment (group C) showed a decrease of 1.24 liters in milk production after treatment (Figure 1). The decrease in milk production was statistically significant ($P<0.001$).

Effect on Body Weight and Feed Intake

In all groups, body weight increased, except in group C (infected control), which showed a decrease in body weight. No significant differences were observed in any of the cases. In all treated groups, a 50-150% increase in feed intake was noted, which was highly significant ($P<0.001$). A decrease of 19.44% was observed in group C (Infected control) as shown (Figure 1).

Effect on Pregnancy

Only five infected pregnant buffaloes were randomly placed in each sub-group A2 (100 mg/kg bw Nigella sativa) and B3 (150 mg/kg bw Fumaria parviflora). No abortions were noted during therapy, and no abnormalities were found in newborn animals after delivery.

Side Effects

With the onset of herbal treatment, a buffalo in sub-group A2 showed sweating on the 3rd day after drug administration, which became normal on the 7th day, while all other animals did not show any side effects.

4. Discussion

The results revealed the anti-fasciolic efficacy of N. sativa and F. parviflora. The plants used in this study have been reported to have individual anthelmintic activities. For example, Kailani et al. (1995) and Maqbool et al. (2004) reported 88.2% and 81.25% efficacy, respectively, of N. sativa against fasciolosis. Akhtar and Javed (1991) and Akhtar et al. (1997), Akhtar et al. (2000), and Jhangir et al. (2003) reported the anthelmintic activity of this herb against nematodes and cestodes in animals. Nath (1983) and Akhtar and Farah (1986) reported that N. sativa contains negelline, metarbin, melanthin, melanthiginin, and saponin. In addition, it contains fixed oils (37.5%) and volatile oils (1.5%), which delay its passage and, ultimately, the onset of action (Ghazanvi 1988). Therefore, the maximum efficacy of the drug was recorded 28 days post-treatment (Maqbool et al. 2004). Daba and Abdel-Rehman (1998) reported that thymoquinone is an active constituent of N. sativa that acts as a hepatoprotective agent by decreasing liver enzyme leakage from hepatocytes.

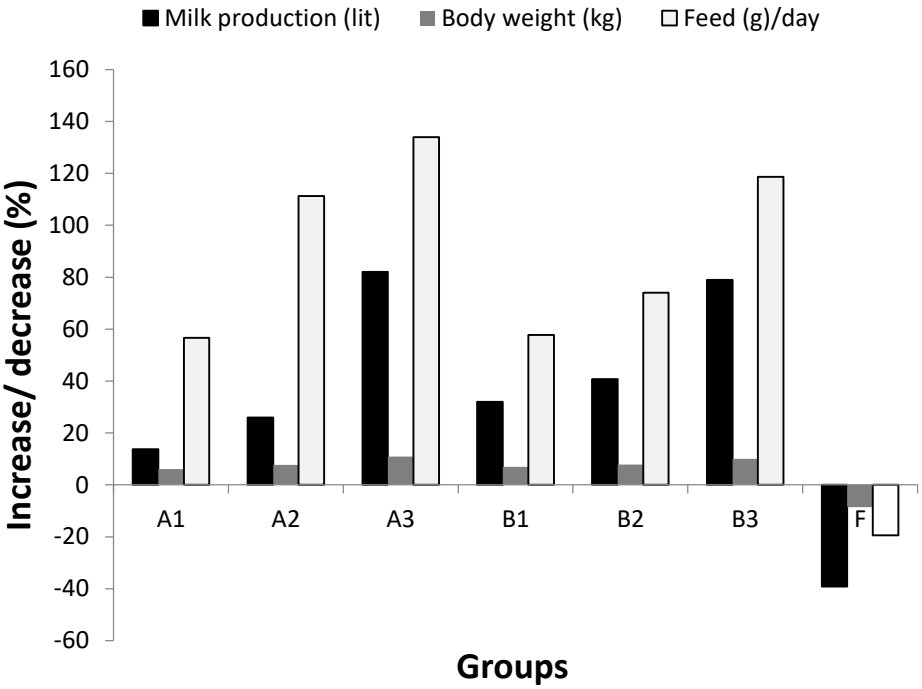

Figure 1. Effect of treatment (%) on: (a) milk production (liters), (b) body weight (kg) and (c) feed (kg) intake of buffaloes.

A diverse array of phytochemicals present in N. sativa helps to regulate the overall health and treat certain diseases in livestock. For instance, dietary supplementation with N. sativa has been reported to inhibit oxidative stress and alleviate hepato-carcinogens, including dibutyl amine and Sodium Nitrate, because of the presence of antioxidants in the seeds (Gendy et al. 2007). Similarly, regular intake of black seeds has been shown to increase the activity of certain enzymes, such as adenosine deaminase, myeloperoxidase, and glutathione-S-transferase, which maintain overall health, protect against erythrocyte damage, and augment the overall efficiency of existing antioxidant enzymes. Moreover, its anti-inflammatory and analgesic effects lead to reduced osteoporosis in animals and humans. Inflammation leads to certain tumor malignancies and the anti-inflammatory properties of N. sativa suppress the production of inflammatory cytokines and transcription factors. The results of this study are also reported in the literature, where immunomodulatory, antioxidant, and gastro-protective properties of N. sativa seeds have been shown to significantly restore buffalo health, increase milk production, and reduce the incidence of fasciolosis in buffaloes.

Kailani et al. (1995) also evaluated the anti-fasciolic efficacy of F. parviflora in buffaloes and reported maximum anti-fasciolic efficacy up to 93.2%. Maqbool et al. (2004) also reported a 95.74% antifascolic efficacy for F. parviflora. Whole plant powder of F. parviflora was compared for its efficacy against Trichostrongylus, Haemonchus, and Trichuris nematodes in sheep (Akhtar and Javed 1985). Maqbool et al. (2004) also reported that these herbs are safe for use in pregnancy without any side effects. The anthelmintic properties of F. parviflora have demonstrated considerable nematocidal activity against several infectious nematodes. Two nematocidal phytochemicals named nonacosane-10-ol, and 23ahomostigmast-5-en-3β-ol from the extracts of F. parviflora were reported for bioactivity against hepatic nematodes of buffaloes and sheep (Naz et al. 2013). Likewise, several phenolic compounds, organic acids, esters, and fatty acids, which are reported phytochemicals of F. parviflora, have demonstrated antiparasitic activity, determining their potential role in cattle health and enhancing milk production. Moreover, sterols present in F. parviflora, including β-sitosterol, stigmasterol, and campesterol, have been shown to regulate gastrointestinal functions in sheep and buffaloes (Modi et al. 2016). In addition to sterols, alkaloids such as protopine, adlumidiceine, parfumine, oxyberberine, berberine, palmatine, dihydrosanguinarine, fumaricine, 8-oxocoptisine, protocatechuic acid, and caffeic acid have also been shown to enhance milk production by regulating bowel movements, controlling parasites, nematodes, and immunomodulation (Akbary et al. 2011). It was concluded from the study that

the plant herbs tested, that is, N. sativa and F. parviflora, are not only effective against fasciolosis, but also strengthen the immune system and regulate metabolism, ultimately improving the health of livestock. However, further work is needed on pregnant and lactating buffaloes to declare them safe under these conditions.

5. Conclusions

It was concluded from the study that the plant herbs tested, that is, N. sativa and F. parviflora, are not only effective against fasciolosis, but also strengthen the immune system and regulate metabolism, ultimately improving the health of livestock. However, further studies are needed on pregnant and lactating buffaloes ensure their safety under these conditions.

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Ethics Approval: Research project is approved from Advanced Studies and Research Board (ASBR) of University of the Punjab, Pakistan.

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