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POTENTIAL USE OF HERBAL ANTHELMINTICS AS ALTERNATIVE ANTIPARASITIC DRUGS FOR SMALL HOLDER FARMS IN DEVELOPING COUNTRIES

Satrija, F., Retnani, E.B., Ridwan, Y. and Tiuria, R.

Department of Parasitology and Pathology, Faculty of Veterinary medicine, Bogor Agricultural University, Jl. Agatis Kampus IPB Darmaga Bogor-Indonesia. E-mail: fadjar_s@indo.net.id

Abstract

Helminth control programs, base on improvement of farm management and regular anthelmintic treatment, are often impracticable in developing countries due to relatively high price of modern anthelmintics for the smallholder. For centuries farmers have used traditional medicinal plants to treat the parasites. Medicinal plants may become good alternatives for modern synthetic anthelmintics in smallholder farms if their efficacy can be proofed scientifically under controlled studies. Study on the possible use of traditional herbal anthelmintic in our laboratory has been done in three phases. The first screening of plant materials was done by dose titration study in rodent using *Hymenolepis* spp (cestode), *Heligmosomoides polygyrus* (strongyloid) and *Aspiculuris tetraptera* (pinworm) as parasite models. Dose titration trial in second phase study was carried out using target parasite such as *Ascaridia galli* (chicken) and *Haemonchus contortus* (sheep) to get appropriate dose for treatment in the following field trials. A number of plant materials have been screened for anthelmintic properties including *Carica papaya*, *Morinda citrifolia, Ananas comosus, Coleus blumei,* *Codiaceum variegatum* and *Leucana leucocephala*. Results of the studies revealed that papaya seed showed high efficacy against parasite models *Aspiculuris tetraptera* and *Hymenolepis nana* in mice. A high effiucay against *H. nana* was also found in *Coleus blumei, Codiaceum variegatum* Papaya latex has shown high efficacy against ascarid in chicken and pigs, but it caused high toxicity when given to ruminants. Thereby the latex can be considered to be used as a narrow spectrum anthelmintic in monogastric

animals. *Morinda citrifolia* fruit posses potency as broad spectrum anthelmintic as it showed high efficacy against *Haemonchus contortus* and *Hymenolepis nana.* No anthelmintic effect was found when testing *Leucana leucocephala* seed extract.

Introduction

Livestock are an important and integrated component of the agricultural production system in developing countries. They are reared under a wide variety of production systems ranging from large-scale intensive commercial farms to traditional smallholder and village production systems. Like in other developing countries, particularly in Asia, majority of the farmers in Indonesia raise their livestock under traditional production as a sideline to the main agricultural activities. However, the livestock production play a significant role in supporting farmer's income as they contribute from 14 to 25 per cent of the total annual income of smallholders (Knipscheer *et al*., 1983).

As most of the developing countries of the world lie in tropical and subtropical region, warm and humid climatic conditions in the tropic/subtropics provide favourable environment for development of worm eggs to infective larvae almost throughout the year. Thus helminth parasite problem is unquestionably being a major limiting factor in the improvement of livestock production.

Control of gastrointestinal helminth infections in the livestock relies mainly on the use of anthelmintics in combination with farm management. Unfortunately in many developing countries people cannot apply anthelmintic control program using commercial modern anthelmintics for a number of reason include:

- Drugs are unavailable in rural areas or their supply is erratic
- Imported drugs are expensive
- Many stock raisers either under dose to save money, or over dose because they do not understand the instructions for use.
- Commercial anthelmintic available in the market is usually packed for large number of animals (50 – 100 heads), which is more than the average number of animal property in each family.

Development of anthelmintic resistance development, due to long term and continuous drug application, also become a threat to continuing livestock production throughout the tropics/subtropics (Waller, 1998).

For the above mention reasons, one should not neglect the fact that there is a long tradition of ethno-veterinary remedies and practice for the most common animal disease including GIT parasite infection. Unfortunately, many international and national organizations have not yet recognized the role and potential contribution of ethno veterinary medicine in development. This contrasts with the case in human ethno-medicine, which has been widely recognized and used by development organization (IIRR, 1994).

In the following sections, the authors review studies in the development of traditional herbal anthelmintics done at the Laboratory of Helminthology, Department of Parasitology and Pathology, Faculty of Veterinary Medicine, Bogor Agricultural University.

Compilation of ethno veterinary information

The development of traditional herbal anthelmintics can be initiated with collection of information concerning species of plants, which have been used to treat parasites. An ethno veterinary medicine survey, involving questionnaire and/or interview with farmer who hold the information on traditional animal health care, probably one of the most effective manner revealing farmer's beliefs, experiences and insight on parasite control. Survey has listed some 25 species of medicinal plants, including papaya (*Carica papaya*) and Indian mulberry, locally known as mengkudu, or pace (*Morinda citrifolia* L.) trees, which are used by farmers in Java to treat gastrointestinal helmith parasites in livestock (Mathias-Mundy and Murdiati, 1991; Wahyuni *et al*., 1992). More comprehensive compilation has been done in an IIRR's workshop on ethno veterinary medicine to compile plant species that have been used by farmers in Asia to treat internal parasites of ruminants, swine and poultry (IIRR, 1994). Base on the compiled information, species of plants will be selected for anthelmintic study.

Screening for anthelmintic activity

Utilization of herbal anthelmintics should be based on a more-or-less standard procedure of testing anthelmintic compound. Thus study on the possible use of traditional herbal anthelmintic in our laboratory has been done in three phases. Anthelmintic activity of plant material is screened using parasite models in rodents such as *Hymenolepis* spp (cestode), *Heligmosomoides polygyrus* (strongyloid) and *Aspiculuris tetraptera* (pinworm). Plant with anthelmintic acitivity will the be tested in a dose titration trial using target parasites such as *Ascaridia galli* (chicken) and *Haemonchus contortus* (sheep) to get appropriate dose for treatment in the following field trials.

A number of plants have been screened for anthelmintic activity including seed and sap from Papaya (*Carica papaya*), young pineapple (*Ananas comosus*) fruit juice, extracts of coleus (*Coleus blumei)* leaves, croton (C*odiaceum variegatum)* twigs, and cholorom extract of Indian mulberry (*Morinda citrifolia*) fruit (Table 1). Screening for anthelmintic activity was carried out using crude form, i.e. dried herbal material, or extracts of plan materials. Extractions range from a simple infusion, to purification with a chemical solvent in sohlext extractor such as chloroform or ethanol.

A high efficacy of papaya latex against *Heligmosomoides polygyrus* has also been demonstrated in mice (Satrija *et al*., 1995). In this experiment oral administration of 8 g latex per kg body weight reduced the worm burden by 84.5%. Using probit analysis, the calculated that ED100 of papaya latex against adult *Heligmosomoides polygyrus* was 12 g per kg body weight.

Infusion of papaya seed also showed high efficacy against parasite models *Aspiculuris tetraptera* and *Hymenolepis nana* in mice. A worm count reduction as high as 100 per cent was reached in *H. nana* infected mice receiving papaya seed infusion at dose level of 1.2 g kg^{-1} BW for three consecutive days (Lamtiur, 2000). The efficacy was slightly lower (96.4 per cent) in *A. tetraptera* infected mice (Elisa, 2000). These results clearly demonstrated the potency of papaya seed as broad-spectrum herbal anthelmintic in the future.

Young pine apple fruit juice showed anthelmintic activity against *H. nana* and *A. tetraptera* in vitro but not in vivo. Whole extract of coleus leaves and croton twigs did not show anthelmintic activity against *A. tetraptera* in vitro and in vivo, however, they showed anthelmintic activity against *H. nana* in vitro and in vivo. The ED100 of extract of coleus leaves against *H. nana* was 0.5 ml of 42% solution (v/v) in distilled water, whereas the ED100 of extract of croton twigs against the parasite was 0.5 ml of 72.46% solution (v/v) in distilled water. The extracts were given once a day for three consecutive days (He *et al*., 1992).

Studies to explore possible anthelmintic activity of Indian mulberry were initially conducted *in vitro* using *Ascaris* and *Haemonchus* adult worm (Soemardji *et al*., 1994; Beriajaya and Tetriana, 1999). Anthelmintic activity of Indian mulberry fruit juice has also been demonstrated *in vitro* against *A. galli* (Priyanto, 1995). Subsequent in vitro study using the fruit, which have been extracted using various solvents, revealed that highest in-vitro anthelmintic activity against *H. contortus* was found in chloroform extract of Indian mulberry (Hildasari, 1999). Efficacy of chloroform and hexan extracts of Indian mulberry fruit was tested in mice experimentally infected with tapeworm *H. nana*. The study revealed a significant reduction in faecal egg count and worm counts in mice receiving chloroform extract of Indian Mulberry. ED50 of chloroform extract of Indian mulberry against *H. nana* was 0.669 g kg^{-1} BW (Widdhiasmoro, 2000). No significant reduction of faecal egg counts or worm burden was seen in mice treated with the hexane extract of Indian mulberry.

Table 1: Anthelmintic activity of various medicinal plants tested at Laboratory of Helminthology, Bogor Agricultural University

Plant Species	Plant material	Host-parasite model	Dose* (g kg^{-1} BW)	Worm reduction (%)	Reference
Papaya (*Carica papaya*)	Latex	*Heligmosomoides Polygirus* (mice)	2 – 8	55.5 – 84.5	Satrija *et al.* (1995)
		Ascaridia galli (chicken)	0002 – 1,0	16 - 100	Mursof and He (1993)
		Ascaris suum (pigs)	2 – 8	39.5 – 100	Satrija *et al.* (1994)
		Haemonchus contortus (sheep)	0.4 - 1	No reduction	Satrija *et al.* (1999)
	Seed infusion	*Hymenolepis nana* (mice)	0.2 – 1.2	48.2 – 100	Lamtiur (2000)
		Aspiculuris tetraptera (mice)	0.2 – 1.2	69.3 – 96.4	Elisa (2000)

Pine apple (*Ananas comosus*)	Young fruit juice	*Hymenolepis nana* (mice)	0.4 – 50%	No reduction	He *et al*. (1992)
		Aspiculuris tetraptera(mice)	0.4 – 50%	No reduction	
Coleus (*Coleus blumei)*	Leave extract	*Hymenolepis nana* (mice)	0.4 – 50%	3.8 – 100	He *et al*. (1992)
		Aspiculuris tetraptera(mice)	0.4 – 50%	No reduction	
Croton (C*odiaceum variegatum)*	Twig extract	*Hymenolepis nana* (mice)	0.4 – 50%	0 – 100	He *et al*. (1992)
		Aspiculuris tetraptera(mice)	0.4 – 50%	No reduction	
Leucana leucocephala	Seed infusion	*Hymenolepis nana* (mice)	0.1 – 0.8	- 46.2 (-) - 692.3	Kustiawan (2001)
Indian mulberry (*Morinda citrifolia*)	Dried fruit	*Haemonchus contortus*	0.4 – 1	73.6 – 88.8	Satrija (1999)
	Chloro form Extract	*Hymenolepis nana* (mice)	0.42 – 3.33	27.6 – 85.3	Widdhiasmoro (2000)
	Hexane extract	*Hymenolepis nana* (mice)	0.42 – 3.33	3.33 – 24.6	Widdhiasmoro (2000)

*) All dose expressed as g kg^{-1} BW unless noticed

Not all tested plants showed anthelmintic activity in the bioassay using model parasite. Infusion of *Leucana leucocephala* seed may be an example of such case. Instead of finding worm counts reduction, Kustiawan (2001) observed a significant increase number of *H. nana.* It was suggested that mimosine as one of compound found in the seed may depress mice immune response thereby delaying natural worm expulsion from gut.

Dose titration study in target animal

The use of latex from papaya trees for anthelmintic against gastrointestinal nematodes of monogastric animals has been studied extensively. Mursof and He (1991) tested the efficacy of various dose of papaya latex, given per orally as a 20% watery solution, in 9 groups of laying hens, which harboured a patent experimental *Ascaridia galli* infection. Results of the study showed that the effective dose (ED100) of single treatment with papaya latex 20% is 1120 mg/bird (777.8 mg/kg bodyweight). Following the treatment body weight and egg production in the treated groups increased significantly. Further study have shown that treatment with papaya latex at dose levels of 2, 4 or 8 grams/kg body weight reduced worm burdens of pigs naturally infected with *Ascaris suum* by 39.5, 80.1 and 100 per cent, respectively, compared with those of the non treated controls (Satrija *et al*., 1994). Papaya latex seem to have a lower anthelmintic activity against *Haemochus contortus* in sheep. Murdiati *et al*. (1997) and Satrija *et al* (1999) demonstrated that papaya latex treatment reduced faecal egg counts significantly. However, no significant difference in the post-mortem worm counts was found despite the worm burden was lower compared with those of the non-treated controls. Mursof and He (1991) suggested that the strong anthelmintic activity of papaya latex might be due to protease in papaya latex, such as papain, chymopapain and lysozyme (Winarno, 1983). Papain alone comprises as much as approximately 10 per cent of the papaya latex (Winarno, 1983).

Results of previous trials suggest that the latex has a high safety margin when given to poultry. In an in-vitro study Purwati and He (1991b) showed the papaya exerted little decomposing effect on small intestines of chicken whereas at the same time the latex completely dissolved adult *A. galli* incubated at ambient temperature (Purwati and He, 1991b). Papaya latex has also been shown to be able to reduce the infectivity of *A. galli* eggs following incubation of the eggs in latex for 21 days prior to infection (Purwati and He, 1991a). Further histopathological observation showed reduction in the chicken intestinal mucuos thickness due to papaya treatments was recovered 7 days after the last treatment of the chicken (Ridwan *et al*., 1995) without causing any significant changes in production parameters (Mursof and He, 1991). Studies in other monogastric models showed that high dose level of papaya latex may also produce a mild diarrhoea or constipation in pigs (Satrija *et al*., 1994) and mice (Satrija *et al*., 1995).

A dose titration study showed that administration of Indian mulberry dried fruit powder at dose level of 0.8 g kg^{-1} BW have reduced worm burden of *Haemonchus contortus* in the experimentally infected sheep up 85 per cent (Satrija, 1999). Mechanism behind anthelmintic activity of Indian mulberry seem due to direct effect of the active compound(s) on the parasites in combination with indirect effect on gastrointestinal tract and immune response of the host. Soedarmadji *et al*. (1994) demonstrated that a 20% solution of Indian mulberry leaf infusion in physiological saline paralysed adult *A. suum* worms. Furthermore they observed purgative effect when the extract was given to mice at a dose level of 25 ml/kg BW that may possibly facilitate expulsion of worm from small intestine. Effect of Indian mulberry on cellular immune response was shown in sheep drenched daily to sheep at the dose level of 0.4 g kg body weight^{-1}, or given single dose of 6 g kg body weight^{-1} of Indian mulberry powder (Satrija *et al*., 2001). The treatment increased significantly total leukocyte and blood eosinophil counts and stimulating proliferation of mast cell in gut.

Field trial and future development

The plant material with reasonably high efficacy against target parasites in dose titration trial may become potential candidate for herbal anthelmintic. However, it must be tested under field condition before used in larger scale control program. The field trials involve animal having natural helminth infection and allocated into herbal treated group and non-treated controls. The dose used in the field trial should be the calculated effective dose (ED100) that derived from previous dose titration trial. Possible side effects of drug on host should also be evaluated in the field trial by clinical observations of the experimental animals.

In attempt to produce herbal anthelmintic that meets with the need of smallholder farmers, herbal medicine should be available in the simplest formulation. Our experience showed that dry plant materials are easy to prepare and can be stored for a long period. It can be directly drenched to animals after mixing with tap water, or given in the form of decoct or infusion. Simple brochure should be produced and distributed among farmer for guidance of herbal anthelmintic preparation.

Other strategy of herbal anthelmintic may be through development of herbal anthelmintic industry. Learning from marketing strategy of large-scale phytopharmaceutical industry in Indonesia, that locally called the ‘Jamu’ industry, commercial herbal anthelmintics in the future should be prepared in single dose packages. Such single dose packing strategy makes the price of Jamu affordable to poor people thereby it become widespread in villages.

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