CSCanada
Advances in Natural Science
Vol. 5, No. 2, 2012, pp. 51-55
DOI:10.3968/j.ans.1715787020120502.1339

ISSN 1715-7862 [PRINT]
ISSN 1715-7870 [ONLINE]
www.cscanada.net
www.cscanada.org

The Comparative Double Blind Clinical Trial of Antihelmintic Efficacy Among Mebendazole, Thai Traditional Herbal Formulae and *Areca Catechu* L.

Buavaroon Srichaikul[a],*; Supachai Samappito[b]; Choosak Nitiketkoon[c]; Surapote Wongyai[d]; Gordon Bakker[e]

[a] Faculty of Public Health, Mahasarakham University, Mahasarakham 44000, Thailand.
[b] Department of Biotechnology, Faculty of Technology, Mahasarakham University, Mahasarakham 44000, Thailand.
[c] Faculty of Medicine, Mahasarakham University, Mahasarakham 44000, Thailand.
[d] Faculty of Oriental Medicine, Rungsit University, Thailand.
[e] Editor, Mahasarakham University, Mahasarakham 44000, Thailand.
*Corresponding author.

Received 20 February 2012; accepted 15 May 2012

Abstract

This study was carried out in Mahasarakham Primary Healthcare Centre, Mahasarakham province in the area of Northeastern of Thailand. The experiment was randomized control trial clinical comparative study in order to examine the antihelmintic activity efficacy among **Mebendazole, Thai Traditional Formulae, *Areca catechu* Linn.** in the treatment of 200 mixed worms infection in human. The experimental group consisted of 150 patients and 50 patients for control group with inclusion and exclusion criteria which were screened by the selected mix worm infected patients samples. The investigation and extraction of worm eggs per gram of patient feces method (EPG) were performed with Ether Formalin Sedimentation test. The percentage of reduction of eggs per gram (EPG) of patient feces were collected, counted and confirmed by parasitologist and the clinical efficacy were investigated by the physician and the pharmacist. The % EPG data were collected before and after the treatment with **Mebendazole, Thai Traditional Formulae, *Areca catechu* Linn.** and with **placebo**. The result showed that **Thai Traditional Formulae** had the highest efficacy in antihelmintic activity followed by the efficacy of Mebendazole and ***Areca catechu*** Linn. respectively. The antihelmintic efficacy which were measured by the % reduction of egg worm per gram of patient feces were 93.69, 87.50, 68.12 respectively. The statistical analysis confirmation in this study were carried out by Wilcoxson Signed Ranks test and Kruskal Wallis method.

The suggestion of this study should increase the number of samples of worm infected patients which the samples can be identified with more specific helminthes genus and species in order to obtain various types of efficacy by the treatment of different medicine as mentioned above.

Key words: Efficacy; Thai traditional formula medicine; Mebendazole; *Areca catechu* Lin.; Egg per gram

Buavaroon Srichaikul, Supachai Samappito, Choosak Nitiketkoon, Surapote Wongyai, Gordon Bakker (2012). The Comparative Double Blind Clinical Trial of Antihelmintic Efficacy Among Mebendazole, Thai Traditional Herbal Formulae and Areca Catechu L.. *Advances in Natural Science*, *5*(2), 51-55. Available from URL: http://www.cscanada.net/index.php/ans/article/view/j.ans.1715787020120502.1339
DOI: http://dx.doi.org/10.3968/j.ans.1715787020120502.1339

INTRODUCTION

In the tropical countries such as Thailand we have a high incidence rate of human parasitic infection which can be very harmful to humans. The initial stage of parasitic infection such as Nematode, tapeworm, hook worm do not have sudden severe harmful effects to the human body. The symptoms will develop gradually and slowly which can destroy the internal organs. Some parasites can withdraw blood from human intestines or other internal cell wall organs and also nutrients from human bodies. The patients will slowly lose their weight and turn pale. The patients will also possess a lack of cognitive thinking and less intellect.

Over 32 countries faced the problems of clean food consumption and clean drinking tap water management supplied to the main population. There are over 12 million people who suffer from helminthes infection.

WHO (World Health Organization) has considered

the parasitic problem as one of the major health communicable disease issues in the world. In Thailand the Ministry of Health has launched the project in order to decrease the incidence of food borne diseases especially parasitic diseases which occurred in people who have less exposed to sanitation of food and water intake. Normally these patients will contact the parasites through food intake, water intake and skin transmission. One cause is the style of Thai Northeastern food preparation which is involved undercooked foods. The villagers like to consume raw food from fish, pork, beef which promote worm diseases. Another reason is the polluted local drinking water that the people consume on a daily basis from the river which was not clean and was contaminated with bacteria, worms and viruses. WHO is responsible for the record of 133 million of infected worm diseases patients throughout the world. The indication showed that the numbers of infected patients were under the age below 5 years mostly. Since 2006-2011 the incident rate of parasitic human diseases was decreased gradually from 1,051,447 to 800,000 patients.

The worms which were discovered in Thailand were multi cellular and one structure. Helminthes live in human body and also in animal body. They work as possible parasitic condition consuming the nutrients and blood from the body. There are many species of parasites which live in soil, weed, water in the fresh of terrestrial, in aquatic and in amphibians etc.. Helminthes can transmit through oral skin absorption and even through placenta movement from mother to baby. Helminthes are tapeworm, Strongyloides, liver flukes, lung flukes and some may be travel through skin such as Trichunoris.

The patients who was infected may show the symptoms as more food intakes, weight loss, diarrhea, irritable colon, Bloating, body pain, blurred vision. The patients should go to see the physician in order to have stool examination test for Worm Eggs per Gram of fecae by any method such as Kato Katz method or Ether-Formalin sedimentation test method. Some patients have shown the severe symptoms which cause paralysis or death. Types, size, volumes and location of helminthes and also the duration of infection are important for indicating the severity of infection. Some patients exhibit signs of Jaundice, Liver Cirrhosis and result in liver carcinoma.

The side effect of antihelminthic medicines may cause stomachache, diarrhea, and irritable colon. Some also cause nausea, vomitting. The research team had introduced Thai Traditional Formula medicine (TTFM) in the treatment of helminthes and compared the efficacy and side effects among Mebendazole (500 mg) and ***Areca catechu*** Lin.

Thai Traditional Formula medicine consists of 8 herbals which are

1. Terminalia chebula **(Retz) (SamaoThai)**

2. ***Terminalia citrina*** **(Roxb.) (Samao Ted) (Arjun)**

3. Curcuma zedoaria **(Berg) Rosco. (Kamin Aoi)**

4. Terminalia citriva **(Gaertn). Roxb. Flem (Samao Ngu**

5. Cuttle Bone **(Tricosan) (Lintalay)**

6. purified water

7. Croton tiglium Lin. **(Purging croton)**

8. Diospyros mollis **(Griff.) (Ebony tree)**

Dosage of TTFM is orally, 3-6 capsules daily before breakfast (500 mg), continue for 3 days. Each of 7 medicinal herbs and purified water is mixed as dry powder in equal portions and was filled into capsules.

Mebendazole 500 mg is the drug of choice in treatment of helminthes infection in this research and considered as modern medicine. Dosage form is chewable tablet, 500 mg, and taken as once daily for 3 days continuously.

Areca catechu Lin. was prepared for herbal medicine in the treatment of mixed antihelminthes infection. Dosage was 60 mg in dried powder capsules and taken by mixing with syrup water as once daily for 3 days continuously. All medicine were tested to meet the standardization quality with free from bacterial or foreign contamination, free from steroidal substance and free from pesticide from the Department of Oriental Medicine, Rungsit University, Thailand.

MATERIAL AND METHOD

This research was proceeded during September, 2011 at Primary Health Care Center Mahasarakham Hospital, Mahasarakham, Thailand. The 200 samples of patients were screened and selected purposively for mixed worm infection relevance to the inclusion and exclusion criteria of 16-65 years old with both genders males and females. The inclusion criteria were not pregnant patients, non-medicated with any of antihelminthic drugs, non-medicated with any of antibiotic, phenytoin, carbamazepine, no complication of gastrointestinal symptoms, no hepatitis or liver diseases. Then 200 collected samples were divided by randomized double blind control trial for 50 patients in 4 groups as follows: 50 patients treated with placebo as a control group, 50 patients treated with Mebendazole 500mg as an experimental 1 st group, 50 patients treated with Thai Traditional Herbal Formula (TTHF) as an experimental 2nd group and 50 patients treated with ***Areca catechu*** Lin. as an experimental 3rd group. The study was performed during 15th December, 2011 to 18th December, 2011. The data was collected before and after 3 days after administering the placebo, Mebendazole, TTHF and ***Areca catechu*** in each groups respectively.

The screening method used in this experiment was Ether Formalin Stool Sedimentation Examination which could be used to identify and quantify the EPG (numbers

of eggs worm per gram of feces of infected patients). The study was randomized control double blind trial in the comparative study of the efficacy and side effects. The primary outcome of the study was to compare the efficacy by the % reduction of EPG in each group with treated with Mebendazole, ***Areca catechu*** and TTHF medicine.

Preparation of Thai Traditional Herbal Formula (TTHF)

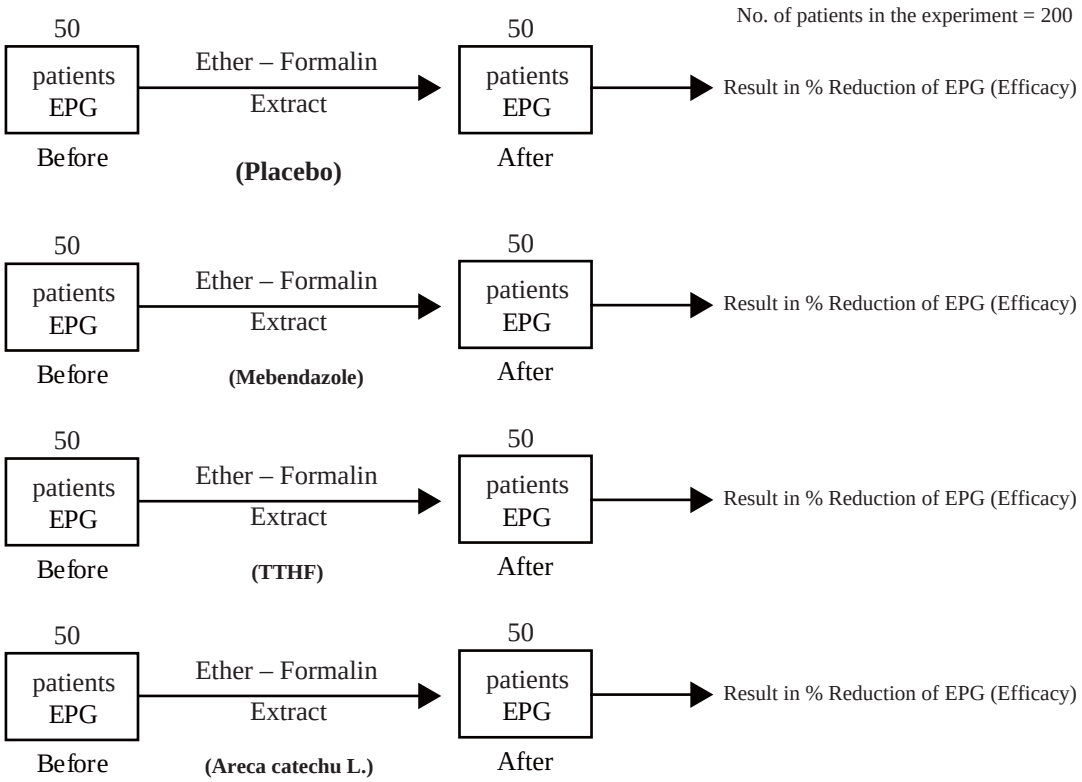
TTHF was prepared from 7 herbs as listed from the above. Firstly we extracted ***Terminalia chebula*** (Retz). By boiling the immature fruits of ***Terminalia chebula*** (Retz) with portable water and dried it with the Spraying Technique in order to obtain dry powder. Then we repeated the same process of extraction with ***Terminalia citrina*** and ***Terminalia citriva*** to obtain the purified dry powder of them. Then we took the underground stem of ***Curcuma zedroaria*** and grated it. The grated ***Curcuma zedroaria*** was blended in very fine powder. The cuttle bone was triturated as fine powder. We also took the seed of ***Croton triglium*** and was triturated as fine powder. We took the fresh fruits of ***Diospyros mollis*** and sliced them to very thin pieces and triturated as the fine powder, then mixed it with coconut milk and dried with Spray Drying Technique. Each of them was weighed equally and mixed together with the amount of 72 mg in each prepared dried herbal powder and were filled in 500 mg aseptic capsules by using encapsulation method. All herbs were collected with uncontaminated of bacteria, heavy metals, viruses, and free of pesticides with adequate cleansing methods. They were passed through Gamma – rays for aseptic purposes. The process for preparation and purified of all sample capsules were also tested for quality control at the Faculty of Oriental Medicine, Rungsit University, Thailand to assure quality, safety in production. Therefore the products were free from any toxicity. TTHF (500 mg) contained 7 plant species as mentioned above used for antihelmintic formulae in this experiment.

Areca catechu Linn.

Preparations

In this experiment we used ***Areca catechu*** Linn. (Betel Nut) seeds in order to prepare antihelminthic medicines. We have chosen the brownish white color derived from thin sliced pieces of the nuts which have a high qualitative content of Arecoline as one of the active ingredients in antihelmintic action of ***Areca catechu*** Linn. The betel nut seeds were weighed 60 mg, then triturated as a very fine powder. The powder was mixed with the syrup water for

Conceptual Research Framework



oral administration. The dosage suggested was taken in syrup once daily for 3 days before breakfast.

RESULTS

The study was quantitative analysis research. The statistical used were analyzed by

Willcoxon Signed Ranks Test. It showed that there were differences among % reduction of EPG among all 200 patients of sample group treated with **Mebendazole (500 mg)**, **TTHF (500 mg) and *Areca catechu L.* (60 mg)** for 3 days and the result had showed the statistical significant differences at *p-value* = .05. or 95 % confidence interval. It could stated that there were statistical significant difference in reduction of egg worms per gram of feces after the experiment by treating with Mebendazole 500 mg, TTHF 500 mg and Areca catechu 60 mg better than before the experiment by treating with placebo.

The efficacy of **Mebendazole (500 mg), TTHF (500 mg)** and ***Areca catechu*** L. (60 mg) were comparative studied by % reduction of eggs worm per gram of feces in mixed worm infection patients were **87.50 %, 93.69 %, 68.12 %** respectively. We used the Ether Formalin Sedimentation Method for the extraction of egg worm and then the result was also confirmed with **Kruskal – Wallis statistical test** to show the mean ranks. The findings of the statistical calculation showed that the highest ranking of **13th**, **8th** and **3rd** in efficacy **were TTHF, Mebendazole** and ***Areca catechu*** L. respectively. In conclusion, the result showed that the efficacy of TTHF was the highest in the antihelminthes activity and higher than Mebendazole and *Areca catechu* L.

Table 1
% Eggs Worm Per Gram of Feces Before and After Treated with Mebendazole (Analyse with Wilcoxon Signed Ranks Test)

Name of	Numbers of patients	Mean	Z	p-value
Before	50	463.40		
After	50	65.80	-2.023	.031

Table 2
Numbers of Eggs Per Grams of Feces Before and After Treated with Thai Traditional Formulae (Analyse with Wilcoxon Signed Ranks Test)

TTHF	Number of patients	Mean	Z	p-value
Before	50	383.00		
After	50	25.00	-2.023	.031

Table 3
Numbers of Eggs Worm Before and After Treated with *Areca catechu* (Analyse with Wilcoxon Signed Ranks Test)

Areca catechu	Numbers of Patients)	Mean	Z	p-value
Before	50	427.20		
After	50	136.80	-2.023	.031

Table 4
Anti Helmintic Efficacy Among Mebendazole, TTHF and *Areca catechu* (Analyse with Wilcoxon Signed Ranks Test)

Drug Name	% Efficacy
Mebendazole	87.50
TTHF	93.69
Areca catechu	68.12

Table 5
Comparison in Efficacy Among Mebendazole, TTHF, *Areca catechu* (Analyse with Kruskal-Wallis Test)

	Number of patients	Mean Rank	X^2	p-value	95%CI
Mebendazole	50	8			
TTHF	50	13	12.50	.000	.000 -0.181
Areca catechu	50	3			

CONCLUSION AND SUGGESTIONS

This study was carried out 3 days dosages in 200 patients of both Thai females and males. The samples were randomized controlled trial with inclusion criteria and exclusion and the % reduction of worm eggs per gram of feces in mixed wormed human infection were collected after the 4th day of the experiments in each group of samples. This study revealed that % reduction of eggs per gram by treating with **Thai Traditional Herbal Formulae**, Mebendazole and ***Areca catechu*** Linn. were **93.69% , 87.50%, 68.12%** respectively. The result was also confirmed by **Kruskal Wallis** method for statistical which showed the mean rank positions of **TTHF, Mebendazole** and ***Thai Areca catechu*** Linn. were 13th, 8th, 3id respectively. Therefore, the efficacy of TTHF had the highest efficacy among the three medicines. We suggest to increase more sample sizes and in different demographical locations to study further research in the future study. There may be some variations of the result of efficacy of each vermicidal medicine which can occur by the facts of the migration of parasites in different locations of the human bodies such as blood stream, lung, liver, etc. However, the efficacy was also different in different species of helminthes. Therefore the extensive study may recommend to conduct the experimental study in various dosages and with repeated dosages of 7 days, 14 days and 20 days. The evaluation of efficacy should be measured at the end period of times with the % reduction of Eggs per Gram of Feces (EPG). The benefit of this study can lead some physician and pharmacists to consider the herbal medicine or combination of herbal medicinal formula as the alternative choices since the herbal medicine has lower cost and fewer side effects as in synthetic drugs. In this study, the authors have studied the efficacy of ***Areca catechu*** and a combination of **7 herbals of Thai Traditional Herbal formula (TTHF)** in the treatment of mixed worm infection patients in the area of Northeastern of Thailand which normally the people are not so conscious in consuming well cooked food and prefer to have raw fish or meat in their daily diet.

ACKNOWLEDGEMENT

This research study was supported for funding by Division of Research Dissemination and Facilitation, Mahasarakham University, Thailand. The research team would like to express our special thank to Assist. Prof. Dr. Supachai Samappito, Prof. Dr. Preecha Prathepa , Sunthorn Dejchai , Mahasarakjham University, Thailand and also to Assoc. Prof. Dr. Surapote Wongyai in preparation of Thai Traditional Herbal Formula, Faculty of Oriental Medicine, Rungsit University, Thailand.

REFERENCES

[1] Ajima Karphrom, *et al.* (2009, August). *The anti-microbial activities of betel nut (Areca catechu Linn) Seed Extracts* (pp. 23–29). Thailand: Rajamangala University of Technology Lanna.

[2] Chanchai Sardsaengjun, *et al.* (2010, Jaunary-March). The Effect of Temperature and Duration Time on Polyphenols Extract of *Areca catechu* Linn. Seeds. Department of Pharmacognosy, Faculty of Pharmacy, Huachiew chalermprakiet University, Samutprakarn province, Thailand, 10540, *5*(1).

[3] Freda, M. Paul, *et al*. (1975, March). The Trial of Mebendazole in Trichuriasis (Whipworm) Infestation in Singapore Children. *Singapore Medical Journal, 16*(1).

[4] Albonico, M., *et al.* (2003). The Efficacy of Mebendazole and Levamisole Alone or in Combination Against Intestinal Nematode Infections After Repeated Targeted Mebendazole Treatment in Zanzibar. *Bulletin of the World Health Organization, 81*.

[5] Dawson, M., *et al.* (1985). The Effect of Dose Form on the Bioavailability of Mebendazole in Man. Department of Pharmacy, The University of Sydney, Sydney, N.S.W.2006, Australia, 87–90, 19.

[6] Preetee Jaiswal, *et al.* (2011). Studied the *Areca catechu* L.: A valuable Herbal Medicine Against Different Health Problem. *Research Journal of Medicinal Plant*, 145–152.

[7] Sajala Kafle, *et al.* (2011,September-October). Antifertility effect of *areca Catechu* in male albino rats. *International Journal of Pharmaceutical Sciences Review and Research, 10*(1).

