

Leucaena Leucocephala as Treatment for Ascariasis and Trichuriasis

A Cost Effectiveness Analysis

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Abstract

The purpose of this study was to evaluate the possibility of using *Leucaena leucocephala* seed – an herbal drug, instead of *Pyrantel Pamoate* as an attempt to heal worm-infected children. A total number of 80 worm-infected children were treated either by *Pyrantel Pamoate* 250 milligrams single dose (20 children) or by *Leucaena leucocephala* seed (60 children) with different doses – single dose per day, single dose for two (2) consecutive days and single dose for three (3) consecutive days. The results showed that after three months of treatment either by *Pyrantel Pamoate* or *Leucaena leucocephala* all worm-infected children were cured indicated by the absence of *Ascaris lumbricoides* and *Trichuris trichiura* eggs in their faeces except for those who were treated by a single dose per day of *Leucaena leucocephala* whose recovery rate was only 80%. Further analysis to find out which treatment is the most effective economically, this study by using Cost-Effectiveness Analysis (CEA) found that healing worm-infected children by *Leucaena leucocephala* with single dose for two (2) consecutive days is the most effective one. Based on simple survey, this study also showed that the level of acceptance to using this herbal drug is high. Using *Leucaena leucocephala* as an alternative treatment, therefore is suggested.

Key Words : *Leucaena leucocephala*, Ascariasis and Trichuriasis, Cost Effectiveness Analysis

Introduction

Helminth infection is one of the most common infections among children around the world. Human, affecting a large population of the world. The disease is highly prevalent particularly in third world countries due to health environment problems and poor management practices¹. Chemical control of helminths coupled with improved management has been the important worm control strategy throughout the world¹. It is estimated that 400 million out of 1.2 billion children at primary school age are infected by *Ascaris lumbricoides*, *Trichuris trichiura*, and *Hookworm*. *Ascaris lumbricoides* infection disrupts children growth while *Trichuris trichiura* and *Hookworm* infection causes intestinal bleed and anemia, respectively². In addition to these issues, *Ascaris lumbricoides* and *Trichuris trichiura* may reduce intelligence and cognitive skill as cited Saldivar in Mardiana³. Therefore, the eradication of worm-infected diseases must be carried out Pharmaceutical synthetic

medications for worm-infected diseases are: *Albendazole*, *Mebendazole*, and *Pyrantel Pamoate*⁴. Meanwhile, herbal medications such as brewed *Leucaena leucocephala* powder are not commonly used by society although *Leucaena leucocephala* seed has been famous as vegetable dish⁵. *Leucaena leucocephala* seed contains mimosine, leucanine, and leucanol that inhibit animal reproductive function⁶. A study conducted by Susilowati found that *Leucaena leucocephala* seeds may inhibit spermatogenesis process of mice⁷. Meanwhile, Susanti, Sethi and Kulharni as cited in Susilowati stated that in addition to mimosine, *Leucaena leucocephala* seed also contains sterol compounds, which basic structure is composed of cyclopentana perhydro phenanthrene⁷. It is also stated that about 35% of *Leucaena leucocephala* seeds components are sterol, consisting of methyl sterol 8%, triterpenoid alcohol 20%, and tocopherol 7%⁷. According to Martin et al. as cited in Susilowati tocopherols which is also called alpha tocopherols is a vitamin E that is important for animal fertility⁷. However, since the concentration of tocopherol is smaller than triterpenoid which inhibits spermatogenesis process on animal, the consumption of *Leucaena leucocephala* seeds may cause infertility⁷. It is assumed that their function also works on parasitic worms by inhibiting spermatogenesis process and therefore cutting the cycle of transmission. A study conducted by Diah has also proven the effectiveness of in vivo *Leucaena leucocephala* seeds to heal the worm-infected diseases⁸. Worm infected patients that were treated by *Leucaena leucocephala* indicated that three days after the treatment, the number of *Ascaris lumbricoides* infected patients, based on faeces examination, decreased from 634 to 260 patients, and the number of patients infected by *Trichuris trichiura* decreased from 518 to 233⁸. This result indicates that a single dose of *Leucaena leucocephala* treatment has reduced the morbidity rate of *Ascariasis* from 88% to 41% and the morbidity rate of *Trichuriasis* from 72% to 45%⁸. Based on the aforementioned arguments on the effectiveness of using *Leucaena leucocephala* seeds to heal the worm-infected diseases, this present study aims to evaluate, from health economics perspective, the uses of *Leucaena leucocephala* as an alternative treatment for *Ascariasis* and *Trichuriasis*, given the same study, as far as we know, has never been done before. To accomplish this, firstly, 80 worm-infected children aged between 3-12 years old living at Bidara Cina flats, Cawang, East Jakarta were treated either by *Pyrantel Pamoate* or by *Leucaena leucocephala* seed. This sample was grouped into four – 20 children each. The first group was then treated by *Pyrantel Pamoate* 250 milligrams single dose. The second group was treated by *Leucaena leucocephala* seeds – single dose for one day. The third group was treated by *Leucaena leucocephala* seeds – single dose for 2 consecutive days, and the fourth group was treated by *Leucaena leucocephala* seeds – single dose for three (3) consecutive days. To know the effectiveness of these treatments, we have to wait for three months until after the feces examination has been done. The second step of this study was comparing these treatments based on Cost Effectiveness Analysis (CEA) to find out which treatment is the most effective one. Finally we conducted simple survey to find out the level of acceptance on which treatment is the most feasible. Note that, before conducting this present study, we conducted faeces examination on 134 children aged 3-12 years old living at Bidara Cina flats, Cawang, East Jakarta. Of these, we found that 87 children were positive containing *Ascaris lumbricoides* eggs and 72 children contained *Trichuris trichiura*. This result indicated the incidence rate of *Ascariasis* and *Trichuriasis* were 64.92% and 53.73%. Based on this result, we determined 80 children as our sample study.

Materials and Methods

Plant Material

Powdered *Leucaena leucocephala* seeds was brewed and diluted in warm water. A single dose of *Leucaena leucocephala* seeds brew was made by powdering dried seeds and diluting 5 grams grams of powdered *Leucaena leucocephala* seeds in 100 cc warm water⁵.

Drugs

1. Pyrantel Pamoate 250 milligrams
2. *Leucaena leucocephala* seeds powder

Chemical Material

There were two chemical materials used in this reseach, it was Eosin 2% and Luqol 2%. Those chemicals were used as reagents in feces examination⁹.

Methods Faeces that were indicated positive containing *Ascaris lumbricoides* and *Trichuris trichiura* based on preliminary feces examination were used as sample in this study. The samples were divided into four treatment groups. Each group consisted of 20 children while other children (feces contained *Ascaris lumbricoides* and *Trichuris trichiura*) were prepared as substitute in case of there was a member of the treatment groups quitting from this study. The first group (as the control group) was administered by *Pyrantel Pamoate* 250 milligrams single dose. The second group was administered by a single dose of *Leucaena leucocephala* seeds treatment (5 grams of *Leucaena leucocephala* seeds powder diluted in 100 cc warm water). The third group was administered by a single dose of *Leucaena leucocephala* seeds for 2 consecutive days (a single dose/day). The fourth group was administered by a single dose of *Leucaena leucocephala* seeds for three (3) consecutive days (a single dose/day). The samples were let for 3 months to allow the worms undergo its life-cycle. It takes about three months for parasitic worms to undergo its life-cycle (starting from entering its host as eggs until fully grown and ready to lay its eggs).

This study consists of three phases, namely:

- Phase I : Data collection to gather information on the effectiveness of the administration
- Phase II : Cost Effectiveness Analysis (CEA) measurement
- Phase III : Data collection to gather information on the feasibility of the administration

The instruments used in CEA examination were: 1) the effectiveness of the drugs; and 2) total cost spent consisting of the price of the drugs and transportation cost. The price of *Leucaena leucocephala* seeds medication was assumed from its preparation cost until ready to drink. CEA measurement of the two types of drugs was conducted by comparing the total cost and effectiveness of the program to gain Cost Effectiveness Ratio (CER) value. The lowest CER value was considered as cost effective¹⁰. The feasibility of administration was measured through questionnaire asked to the respondents (i.e. the family of the children receiving treatments). The feasibility of the administration was measured through scoring technique by giving score on several variables, namely: affordability, technology, cost, and community participation.

¹ Ethical Approval LB.02.01/KE/33/303a/2016 from Ethical Council, Health Research, Health Polytechnic Institute II, Jakarta

Results

Table 1 below describes the results of faeces examination before and after the treatment.

Table 1 Results of Faeces Examination (Before and After the Treatment) on Primary School Aged Children Living at Bidara Cina Flats, Cawang, East Jakarta, September 2016

No	Treatment Groups	Number of Patients Before Administration	Number of Patients After Administration	Number of Patients Cured from Worm-Infection Diseases	Effectiveness
1	Group I	20	0	20	100%
2	Group II	20	4	16	80%
3	Group III	20	0	20	100%
4	Group IV	20	0	20	100%

In Group I, after medication of Pirantel Pamoat, faeces of twenty (20) children who were previously infected by *Ascaris lumbrocoides* and *Trichuris trichiura* show that they are free of worm infection. The effectivity of Pirantel Pamoat in this group is then deemed to be a hundred percent, i.e. $(20/20) \times 100\% = 100\%$. Furthermore, in Group II, faeces of four (4) out of twenty (20) children who were previously worm-infested show that, after one-time of medication of *Leucaena leucocephala*, these four (4) children are still not free of worm infection. Thus, the effectivity of the medication in this group is 80%, i.e. $(16/20) \times 100\% = 80\%$. Meanwhile, when the *Leucaena leucocephala* was administered twice (2x) each day for two (2) days in a row, none of these twenty (20) children is found to still be worm-infected. This means that the effectivity of the medication in this group is 100%. The same result is also shown for Group IV where the *Leucaena leucocephala* was administered for three times (3x) each day for three (3) days in a row.

Results of CEA Measurement

Table 2 Comparison of Total Cost Spent for *Pyrantel Pamoate* and *Leucaena leucocephala* Seeds Powder by Primary School Aged Children at Bidara Cina Flats, Cawang, East Jakarta, September 2016

Cost Assumption	Pyrantel Pamoate	Leucaena leucocephala Seeds Power (single dose)	Leucaena leucocephala Seeds Powder (2 doses)	Leucaena leucocephala Seeds Powder (3 doses)
Price of Drugs	IDR 28,000,-	IDR 5,100,-	IDR 10,200,-	IDR 15,300,-
Transportation Cost	IDR 10,000,-	IDR 10,000,-	IDR 20,000,-	IDR 30,000,-
Total Cost	IDR 38,000,-	IDR 15,100,-	IDR 30,200,-	IDR 45,300,-

From the total cost of the drugs (which serves as input (IP)) and the effectiveness of the drugs as the output (OP)) used in worm-infection disease eradication program presented on Table 1 and Table 2 above we can measure the Cost Effectiveness Ratio (CER). Since the number of the samples in each treatment groups are same, CEA = output/input or drug effectiveness ratio/total cost spent. The achievement of drug effectiveness was standardized in the value of 100%. The ratio of total cost spent and drug effectiveness is presented on Table 3 below:

Table 3 Ratio of Total Cost and the Effectiveness of Worm-Infection Disease Eradication Program at Bidara Cina, Cawang, East Jakarta September 2016

Treatment Groups	Total Cost	Number of Patients Cured after Treatment	CER	Ranking
Group I	IDR 38.000,-	20	1.900	III
Group II	IDR 15.100,-	16	943,75	I
Group III	IDR 30.200,-	20	1.510	II
Group IV	IDR 45.300,-	20	2.265	IV

Table 3 clearly shows that Group II has the lowest CER.

The Administration Feasibility

The result of questionnaire asked to the parents of the patients indicated the average score of *Pyrantel Pamoate* affordability (i.e. the availability of efforts to obtain the drug) and the availability of personnel/technology to process *Leucaena leucocephala* seeds to be used in worm-infection disease eradication program are presented on Table 4 and Table 5:

Table 4 The Affordability and Availability of Effort to Obtain *Pyrantel Pamoate* to be used in Worm-Infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta, September, 2016

Affordability	Rate	N	Percentage	Score
Very Affordable	4	0	0%	0
Affordable	3	1	5%	3
Less Affordable	2	5	25%	10
Unaffordable	1	14	70%	14
Total		20	100%	27

From Table 4 above, it is apparent that respondents are quite reluctant to go to pharmacies to buy *Pyrantel pamoate*.

Table 5 The Availability of Personnel and Technology to Process *Leucaena leucocephala* Seed Powder used in Worm Infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta, September, 2016

Availability	Rate	N	Percentage	Score
Many	4	17	85%	68
Sufficient	3	3	15%	9
Insufficient	2	0	0%	0
Unavailable	1	0	0%	0
Total		20	100%	77

From Table 5 above, it is shown that respondents are not as reluctant to grow the plant of *Leucaena leucocephala* or look for one as an alternative medicine for worm infection condition, compared to if they have to buy pyrantel pamoate in the pharmacies.

The perception of the respondents (i.e. parents and families of the patients) about the availability of *Pyrantel Pamoate* and *Leucaena leucocephala* seeds used in worm-infection disease eradication program are presented on Table 6 and Table 7.

Table 6 Respondents' Perception about the Availability of *Pyrantel Pamoate* used in Worm-infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta, September 2016

Availability	Rate	N	Percentage	Score
Available Everywhere	4	2	10%	8
Only available at Community Health Center	3	3	15%	9
Only available at Pharmacies	2	4	20%	8
Only available at Drugstores	1	11	55%	11
Total		20	100%	36

From Table 6 we can see that respondents' perception about the availability of *Pyrantel pamoate* is that it is only available at the pharmacies, whereas pharmacies usually either are quite far to reach or require additional cost to travel to.

Table 7 Respondents' Perception about the Availability of *Leucaena leucocephala* seeds used in Worm-infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta, September, 2016

Availabelity	Rate	N	Percentage	Score
Available Everywhere	4	14	70%	54
Only available at Community Health Center	3	6	30%	18
Only available at Pharmacies	2	0	0%	0
Only available at Drugstores	1	0	0%	0
Total		20	100%	72

From Table 7 above, it is apparent that respondents perceive *Leucaena leucocephala* to be easy to get everywhere (e.g. homegrown, in traditional market, etc.).

Respondents' acceptance to *Pyrantel Pamoate* and every dose of *Leucaena leucocephala* seeds used in worm-infection disease eradication program at Bidara Cina flats Cawang, East Jakarta are described in Table 8, Table 9, Table 10, and Table 11.

Table 8 The Distribution of Respondents' Acceptance towards *Pyrantel Pamoate* Used in Worm-infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta September 2016

Acceptance	Rate	N	Percentage	Score
Accepting	4	10	50%	40
Willing to try	3	6	30%	18
Interested	2	3	15%	6
Refusing	1	1	5%	1
Total		20	100%	65

Table 8 shows that most respondents have accepting attitude towards Pyrantel pamoate usage in worm infection.

Table 9 The Distribution of Respondents' Acceptance towards 5 grams *Leucaena leucocephala* Seeds Powder (Single Dose) Used in Worm-infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta September 2016

Acceptance	Rate	N	Percentage	Score
Accepting	4	5	25%	20
Willing to try	3	9	45%	27
Interested	2	6	30%	12
Refusing	1	0	0%	0
Total		20	100%	59

Table 9 above shows that most respondents are willing to try 5 grams of *Leucaena leucocephala* seeds powder as a single dosage medication to treat worm infection

Table 10 The Distribution of Respondents' Acceptance towards 10 grams *Leucaena leucocephala* Seeds Powder (Two Doses administered Once a day in two consecutive days) Used in Worm-infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta, September 2016

Acceptance	Rate	N	Percentage	Score
Accepting	4	7	35%	28
Willing to try	3	10	50%	30
Interested	2	1	5%	2
Refusing	1	2	10%	2
Total		20	100%	62

Table 10 shows that most respondents are willing to try 10 grams of *Leucaena leucocephala* seeds powder as a two-times dosage medication to treat worm infection

Table 11 The Distribution of Respondents' Acceptance towards 15 grams *Leucaena leucocephala* Seeds Powder (Three Doses administered Once a day in three consecutive days) Used in Worm-infection Disease Eradication Program at Bidara Cina Flats, Cawang, East Jakarta September, 2016

Acceptance	Rate	N	Percentage	Score
Accepting	4	0	0%	0
Willing to try	3	1	5%	3
Interested	2	5	25%	10
Refusing	1	14	70%	14
Total		20	100%	27

Table 11 shows that most respondents are reluctant to try 15 grams of *Leucaena leucocephala* seeds powder as a three-times dosage medication to treat worm infection

Table 12 The Feasibility of Drug Administration Based on Efforts, Technology, Financial, and Participation Variables in Bidara Cina Flats, Cawang, East Jakarta, September 2016

Drug Criteria	Effort (a)	Technology (b)	Financial (c)	Participation (d)	Composite Index (a x b x c x d)	Ranking
Pyrantel Pamoate	1	$2+1+4=7:3=2,33$	2	3	13.98	IV
<i>Leucaena leucocephala</i> Seeds Powder (single dose)	4	$4+4+4=12:3=4$	4	3	192	I
<i>Leucaena leucocephala</i> Seeds Powder (two doses)	4	$4+4+3=11:3=3,667$	4	3	176	II
<i>Leucaena leucocephala</i> Seeds Powder (three doses)	4	$4+3+2=9:3=3$	4	3	144	III

Table 12 shows that the composite index of the option where *Leucaena leucocephala* seeds powder being administered as a single dose is the highest and, thus is the most feasible. With

only 10 grams of *Leucaena leucocephala* which could be easily homegrown or bought in traditional markets, worm infection can be treated successfully.

Discussions:

Respondents consider that *Leucaena leucocephala* seeds have been effective as a medication for worm infections disease based on technological aspects, material availability, easy preparation and administration. In addition, the plants also do not require a complicated processes in pharmaceutical industry. Ten (10) grams of *Leucaena leucocephala* seeds has already been used as medication to kill worms infecting human intestine. From the financial aspect, some respondents (parents and families of patients) assume that the price of Pyrantel Pamoate is not affordable compared to the price of *Leucaena leucocephala* seeds. Most parents do not use Pyrantel Pamoate because the price is expensive or can only be obtained from health centers or pharmacies that are located very far from where they lived. According to Gandahasada⁹ one of the criteria in choosing a treatment used in mass treatment is affordability. Malvankar said that in general herbal formulations do not have undesirable, safe, natural effects and have mild side effects. Other than that the raw materials needed for the formulation are easily obtained at low cost¹¹. Another important factor is participation of the society. If people have intention to try and use *Leucaena leucocephala* seeds as medication for worm-infection diseases, they do not need to go to community health centers to obtain medication for worm-infection disease. Indirectly, they have been able to treat their own health problems. Treatment Group II (5 grams of *Leucaena leucocephala* seeds powder once in a day) has the most feasible administration and dosage although the effectiveness of administration is only 80%. From the aspect of availability of personnel or the efforts carried out to obtain the drug, this study found that most of the respondents admitted that the effort to obtain *Pyrantel Pamoate* in pharmacies or drugstores was unaffordable because they were busy and the location of drugstores/pharmacies were far from their residence. On the other hand, the respondents admitted that they had many personnel or willing to spend much efforts to use *Leucaena leucocephala* seeds as medication for worm-infection diseases because they considered *Leucaena leucocephala* seeds was easier to obtain (they admitted that they could buy the bean in the market or picking the seeds directly from its stalk which grew everywhere). This finding supports the finding of a study on properness conducted by Umar¹² stating that the success (or failure) of a program depends on the quality and quantity of the personnel (human resources) who realize the program. Therefore, in a study on properness, analysis on human resources utilization (in addition to procurement system and the development of human resources) is very significant¹³. From the aspect of availability of worm-infection disease drug material, *Pyrantel Pamoate* are only available at pharmacies and drugstores while *Leucaena leucocephala* seeds as material for worm-infection disease medication is very affordable. *Leucaena leucocephala* seeds can be found everywhere, in backyards, in markets, and even on roadside. *Leucaena leucocephala* seeds can be procured easily so that the success of worm disease eradication program can be assured. This condition is supported by a statement proposed by Umar¹² indicating that the success of program (especially physical program) depends on the availability of natural resources (i.e. all potentialities contained in the earth and grown on earth) that need to be involved in production process to improve the availability of goods and service in economics. Natural resources that can be used directly without any sophisticated factory processes, such as *Leucaena leucocephala* seeds as medication for worm infection diseases will give greater contribution compared to synthetic medication produced by pharmaceutical companies. This potential needs to be accompanied by comprehensive information that there are many natural

resources that can be used to cure worm-infection diseases, such as *Leucaena leucocephala* seeds. The result of 250 milligrams *Pyrantel Pamoate* administration shows the cure rate 100%. This finding strengthens the findings of a research conducted by Hemamalini¹⁴ stating that this dose may result 100% cure rate. On the other hand, the administration of *Leucaena leucocephala* seeds a dose/day results 80% cure rate and two doses and three doses of *Leucaena leucocephala* seeds (administered 1 dose/day) result 100% cure rate. According to Berndt, Kosasih and Soediro as cited in Susilowati⁷ *Leucaena leucocephala* seeds contains 35% sterol, comprises of 8% methyl sterol, 20% triterpenoid alcohol, and 7% tocopherol. Alongside diosgenine, Methyl sterol (also known as stigma sterol) is the main ingredient in contraceptives production. Bremmer and Matsumoto as cited in Susilowati⁷ stated that *Leucaena leucocephala* seeds should not be consumed continuously in long period (more than one week) because it contains 5%-10% mimosine, which is toxic and may cause health and reproductive problems in animals¹³. Based on acceptance aspect, *Pyrantel Pamoate*, 1 x 1 *Leucaena leucocephala* seeds, and 1 x 2 *Leucaena leucocephala* seeds are easily accepted by the children. Yet the children hesitate to take three doses of *Leucaena leucocephala* seeds because they get bored.

Conclusion

After comparing the cost effectivity, medication effectivity, and administering feasibility between *Pyrantel pamoate* and *Leucaena leucocephala*, we can safely conclude that *Leucaena leucocephala* seeds can be used as alternative medication for worm-infection diseases caused by *Ascaris lumbricoides* and *Trichuris trichiura*

Conflict of Interest

When this research was conducted, none of the respondents refused to consume *Leucaena leucocephala* seeds. In daily life, Indonesians actually already occasionally consume *Leucaena leucocephala* seeds as raw vegetables, etc. but unfortunately, to date there are many of them who are still unaware of the seeds' benefit as a treatment for Ascariasis and Trichuriasis.

References

1. C. Alekhya N. Yasodamma and D. Chaithra. Anthelmintic Activity Studies On *Pheretima Posthuma* with *Cycas beddomei* Dyer. Leaf, Bark, and Male Cone Extracts. *International Journal of Pharma and Bio Sciences* [Internet]. 2013 April [cited 2017 Feb 19]; 4(2): 34 – 38. Available from: www.ijpbs.net DOI://doi.org/10.22376/ijpbs
2. Departemen Kesehatan Republik Indonesia. Pedoman Program Pemberantasan Penyakit Kecacingan; 2008 Feb. p. 45-57
3. Mardiana; Djarismawati, 2008. Prevalensi Cacing Usus Pada Murid Sekolah Dasar Wajib Belajar Pelayanan Gerakan Terpadu Pengentasan Kemiskinan Daerah Kumuh Di Wilayah DKI Jakarta. *Jurnal Ekologi Kesehatan* 7(2): 69 – 74
4. Olsen A. The Proportion of Helminth Infections in a Community in Western Kenya Which Would be Treated by Mass Chemotherapy of School Children. *Trans R Soc Trop Med Hyg Sciences* [Internet]. 1998 April [cited 2015 Feb 19]; 92(2): 144 – 48. [https://doi.org/10.1016/S0035-9203\(98\)90721-0](https://doi.org/10.1016/S0035-9203(98)90721-0)

5. Hembing. *Tanaman Obat Tradisional dan Manfaatnya*. 3rd ed. Indonesia: Balai Pustaka Press; 2010. p. 56 – 57
6. Ruskin. *Manfaat Tanaman Lamtoro* 2nd ed. Indonesia: Balai Pustaka Press; 2011. p. 22 – 27
7. Susilowati RP. Pengaruh Biji Lamtoro Gung Terhadap Spermatogenesis Pada Tikus Putih (*Rattus rattus*): Universitas Airlangga Surabaya Indonesia; 2014. p. 10-19
8. Diah TM. (Riset dan Bimbingan Tenaga Kesehatan, Surabaya, Indonesia). Dosis Pemberian Biji Lamtoro (*Leucaena leucocephala*) Untuk Memperpanjang Masa Bebas Cacing; 2014 Dec. 72-87
9. Gandahusada. *Parasitologi Kedokteran*. 2nd ed. Indonesia: Fakultas Kedokteran Universitas Indonesia Press; 2009. p. 63 – 66
10. Widyawati. *Analisis Biaya Rumah Sakit*. 2nd ed. Indonesia: Fakultas Kedokteran Universitas Indonesia Press; 2013. p. 20 – 27
11. P.R.Malvankar. Anthelmintic Activity Of Water Extracts Of Trikatu Churna And Its Individual Ingredients On Indian Earthworms. *International Journal of Pharma and Bio Sciences* [Internet]. 2012 April – June [cited 2017 Feb 19]; 3(2): 374 – 78. Available from: www.ijpbs.net DOI://doi.org/10.22376/ijpbs
12. Umar H. *Studi Kelayakan Bisnis: Manajemen, Metode dan Kasus*. 4th ed. Indonesia: PT. Gramedia Pustaka Utama Press; 2014. p. 64 – 69
13. Reinke WA. *Perencanaan Kesehatan Untuk Meningkatkan Efektivitas Manajemen*. 3rd ed. Indonesia: Universitas Gajah Mada Press; 2010. p. 95 – 99
14. K.Hemamalini, A.Rajani, DR. Uma Vasireddy and E.G. Ratna Sundari. Anthelmintic Activity of Methanolic Leaf Extract Of *Tabebuia Rosea* (Bertol) DC. *International Journal of Pharma and Bio Sciences* [Internet]. 2013 Oct [cited 2017 Feb 19]; 4(4): 765 – 68. Available from: www.ijpbs.net DOI://doi.org/10.22376/ijpbs