

*The Influence of Bitter (*Andrographis Paniculata* Ness.) Extract to Reproductive Performance of Mice (*Mus Musculus* L. Swiss Webster)*

Wendikal Abadi¹, Ramadhan Sumarmin²

¹ Student of Biology Program Study Biology

FMIPA Universitas Negeri Padang

² Lecturer of Biology Education Program Study Biology

FMIPA Universitas Negeri Padang



Abstract - Sambiloto (*Andrographispaniculata* Ness) is one of the folk remedies that are expected to be a herbal anti fertility. Chemically this plant contain diterpenoid lactones do. On the components of diterpenoid lactones do contains andrografolid which is the main active substances from the plant that acts as an anti fertility. Andrografolid function to prevent cell division (cytokinesis). this research aims to know the influence of the giving of the extract (*Andrographispaniculata* Ness.) against the appearance of the reproduction of Mice (*Musmusculus* l. Switzerland Webster). This research is a research experiment with a random Design method complete (RAL) that use animal testing mice are females (*Musmusculus* l.) by as much as 4 treatments and 4 replicates. The treatment given is the extract of Sambiloto with various doses, IE: A is the control treatment, without given extract, sambiloto treatments 1, 2 and 3 is the treatment given the extract of sambiloto orally (gavage) for 24 days with each dose is 1. 0.2 g/head/day, 2. 0.4 g/head/day, 3. 0.6 g/head/day. The parameters observed were stem weight, number of corpus luteum, implantation, resorpsi, dead fetus, fetus alive and the average weight of the fetus. The data are tested with the parametric ANOVA (analysis of Variance) and then in the advanced test BNT on drajat α 5%. The results showed that the extract of sambiloto ((*Andrographispaniculata* Ness.) effect on the amount of the foetus is born where every real different treatment when compared to controls. as well as the number of implantation and the number of corpus luteum that has decreased when compared with controls. Stem weight added on P1, P2 and P3 are experiencing the decline in when compared with controls. Foetus alive decline on P1, P2 and P3 if compared to the control. Then it can be inferred that the extract of sambiloto given orally during the 24 days led to a decrease in the number of corpus luteum, decline number of fetus born and decreased the number of implantation.

Keywords - Sambiloto; Andrografolid; Reproductive Performance.

I. INTRODUCTION

Indonesia is a developing country with a population growth rate of about 1.38 percent per year. The population was one of considerable problems facing developing countries including Indonesia. One of the efforts to suppress the rate of population growth which was proposed by the Government through the Ministry of health, i.e. family planning programs (KB). Indonesia is a developing country with a population growth rate of about 1.38 percent per year.

The population was one of considerable problems facing developing countries including Indonesia (BPS, 2013). One of the efforts to suppress the rate of population growth which was proposed by the Government through the Ministry of health, i.e. family planning programs (KB).

Control of the population through the provision of means of contraception is still a problem caused due to inadequate health services and poor socioeconomic conditions, to buy interest societies towards contraception the more low.

Efforts to find new compounds from the natural riches of Indonesia so that cheaper, and can be used as an effective contraceptives became one alternative problem solving population in Indonesia (Palupi, 2008).

Traditional herbal remedies one is Sambiloto (*a. paniculata* Ness) has the primary component that is andrografolid which has a bitter taste, almost colorless crystals form and structured like a ring (Mohan dkk, 2013). Andrografolid is a chemical compound found in sambiloto (*a. paniculata* Nees.) which acts as a antifertilitas. Andrografolid is the active substances contained in sambiloto that serves to prevent cell division (sitokenesis) (Margaretta, 2013).

The appearance of the reproductive capacity of the reproduction is at one birth. The observed data includes the amount of added weight, fetus alive from the uterus right and left, the number of dead fetus, the number of corpus luteum, abnormality or defect, the number of implantation and the number of resorpsi as well as the average weight of the body of the fetus. The living fetus is inserted into the NaCl 0.9%. A decrease in the weight of the fetus in animal experiments compared growth barriers occur reflect control in General (Siburian, 2009)

Based on the description of this research was conducted to find out the influence of the giving of the extract of sambiloto herbs (*A paniculata* Ness.) against the appearance of the reproduction of mice (*Mus musculus* L.).

II. REVIEW OF LITERATURE

A. Sambiloto



Figure 1. *Andrographis paniculata* Ness.

Sambiloto, also known as the "King of Bitter" is not native to Indonesia, but it is thought to originate from India. According to the data of the existing specimens in the Herbarium Bogoriense at Bogor, Indonesia already sambiloto since 1893. In India, the wild plant is sambiloto used to treat the disease, diarrhea, dysentery or malaria. In Traditional Chinese Medicine (TCM), known as sambiloto plant "cold property" and is used as a heat loss as well as

cleaning up toxins in the body. This plant then spread to tropical Asia until Indonesia (Rahayu, 2007).

Sambiloto known by various names. Communities of Central Java and East Java to call it by the name of *Ziziphus mauritiana*, *sadilata*., *paitan*, and *takilo sambiloto*. In West Java, called *Orey ki*, *takila*, or *ki peurat*. In Bali, better known as *samiroto*. Some Malay mayarakat call it with *pepaitan* or *ampadu ground*. Meanwhile, foreign names are *chuan xin lian sambiloto*, or *lan he* (china), *kirayat*, or *kalmegh*, *kirata* (India), *nilavenhu* (tamil). *Xuyen tam lien*, or *cong-cong* (Vietnamese). *Quasabhuva* (Arabic), *nainehavandi* (Persian), *gren chireta* and *king of bitter* (United Kingdom). The scientific name for *Andrographis paniculata* Ness is *sambiloto*. (Rosidah, 2010).

Chemically, sambiloto contains flavonoids and lactones do. On its main components, respectively is Andrografolid which is also the main active substances of plants. Andrografolid have already been isolated in pure form and showed a variety of pharmacological activities (Widyawati, 2007).

B. Mouse



Figure 2. *Mus musculus* L. Swiss Webster

House mouse (*Mus musculus* l. Switzerland Webster) is an animal that is often used in research because it is easy to be fed and nourished. In addition, it has a short gestation period (18-21 days) and the easy proliferation (Rugh, 1968:2). House mouse (*Mus musculus* l. Switzerland Webster) is a popular experiment animals used in laboratory studies that observed intensively. This is supported by the prominence of mice as the animal with a relatively short life cycle, the number of children *pekelahiran* much higher nature, variety, easy to handle and the nature of the production or reproduction of the same with the other mammals (animal Tolistiawaty dkk, 2014).

The appearance of the reproductive capacity of the reproduction is at one birth. The observed data covering

stem weight increase, the number of living fetus from the uterus right and left, the number of dead fetus, the number of corpus luteum, abnormality or defect, the number of implantation, the reabsorption and average weight body fetus. The living fetus is inserted into the NaCl 0.9%. A decrease in the weight of the fetus in animal experiments compared growth barriers occur reflect control in General (Siburian, 2009).

Fertilisation occurs in mammals oviduk. Egg and a Zygote mammals do not exhibit the polarity or pengutuban are clear, and the cleavage of the Zygote that has no yolk so that holobastik are regular Division i.e. Division at the different areas of the Zygote (disc) (Sumarmin, 2016). Effect of teratologi early uterine weights decrease, an increase in the number of dead fetus, morphological disorders (hemologi), and the barriers to the development of the skeleton which is characterized by a decrease in the number of sections metakarpus and menulang, as well as the metatarsus abnormalities costae form (Setiawaty, 2011). Malformation of the external morphology shows the presence of abnormalities in the form mikrophthalmia, anophthalmia, acorea while the internal malformations in the form hidroshepalus (Sabri dkk, 2006).

III. METHODOLOGY

Research carried out in February-April 2018 in the laboratory of zoology and Animal biology majors of engineering Division of UNP. Tools used in this research is the animal enclosure, stereo microscopes, cotton bud, glass objects, glass cover, glass bottles, analytic scales, spoons, porcelain kamera digital, knives, brushes, mortar and pestle, dissecting set, gavage, needle feed containers, water bath, incubators, Desiccator, petri dish, Erlenmeyer flask, funnel, Ohaus balance, dropper drops, the cuvac (spuit syringe), condenser, measuring cup, measuring flasks, refrigerator, filter paper, vial bottle, aluminum foil, stationery, plastic bottles and drinking place animal test.

The materials used in this research is the animal testing mice (*Mus musculus* l. Switzerland Webster), absolute methanol extract, sambiloto (*Andrograpis paniculata* Nees.), the pellets fed mice, plain water, rice husk, Giemsa Staining, Eosin, CMC (Carboxy Methyl Cellulose) 1% NaCl 0.9% solution of bouin and aquabides, aluminum foil, paper, filter paper, paper label.

This research is a research experiment in which the test animals are given the treatment extracts sambiloto (*A paniculata* Ness) with different doses. Research design used was Complete Randsom Design (RAL), which consists of 4

treatments with different dose and repeat as many as 6 times. The fourth group of the treatment is: control: without the pemberia extract of sambiloto Treatment 1: given an extract of sambiloto doses of 0.2 g/head/day Treatment 2: given an extract of sambiloto dose of 0.4 g/hesad/day Treatment 3: given an extract of sambiloto 0.6 g/dose head/day.

A dose of extract of sambiloto given in accordance with the dosage conversion. The doses administered in three doses range i.e. 0.2 0.4 0.6 g/head/day and plus a control group. Long the granting of extracts is based on cycle estrus. In one stretch of estrus cycle in give one a test on animals per treatment oral gavage with a needle once a day, every morning at 09.00 BST. Each of the mice given 0.5 cc/tail mice for 24 days (Rugh, 1968).

Data Analysis

Data taken in the research is primary data. Data obtained directly from the results of observation of the appearance of such reproduction observed number of foetus lives, the number of dead fetus, the fetus abnormalities, the number of Corpus luteum (CL), the number of resorpsi, the number of implantation, the start and end of the heavy weight mice after after the giving of the extract of sambiloto (*a. paniculata* Ness) and the average weight of the fetus after the giving of the extract of sambiloto (*Andrographis paniculata* Ness.) in mice (*Mus musculus* l. Switzerland Webster) females.

The data captured is primary data, i.e. data obtained directly from the observation post treatment already mating which is characterized by the presence of either a vagina as day 0 kebuntingan. In mice (*Mus musculus* l. Switzerland Webster) who successfully mate and bunting are maintained until the 18th day kebuntingan, on day 18 kebuntingan done weighing a stem agency Western and then the murine didislokasi neck to count the number of fetus alive, the number of the dead fetus, the number of implantation, the number resorpsi, the number of fetus abnormalities, the number of Corpus luteum (CL) and the average weight of the body of the foetus then compared with controls.

The data in this study tested with (ANOVA) (analysis of Variance) and if there is a difference do advanced test BNT (Hanafiah,,2004)

IV. RESULTS AND DISCUSSION

A. Research Results

The results of the research on the influence of extract of sambiloto (*Andrograpispaniculata.*) given orally in mice

(*Musmusculus* l. Switzerland Webster) for 24 days. After test ANOVA is known that differences seen from the murine body weight increase, the number of corpus luteum, number of implantation, the foetus born foetus and weight and resorpsi. Such data can be seen in table .

Treatment	Average amount					
	stem weight increase	Corpus Luteum	Implantation	the average body weight of fetus	Resorption	fetus born
Control	39,5	10,8	10,3 ^a	1,03	0,6	10,3 ^a
P1	32,1	6,5	4,8 ^b	0,95	0,5	4,8 ^b
P2	33,9	6,1	3,1 ^b	0,82	0,5	3,1 ^b
P3	31,7	5,8	1,5 ^b	0,46	0,16	1,5 ^b

Description: the figures on the same column followed by the same superscript letters do not differ markedly according to test BNT

Looks average number of stem weight increase no effect between controls with all treatment on P1 32.1 grams, P2 33.9 g, P3 31.7 grams and controls 39.5 grams. However, existing data tend to occur Where a decrease in the average amount of weight added parent it is influenced by the bitter taste of sambiloto causes depletion servings packed from House mouse.

Furthermore the average body weight of fetus do not affect real look at table 1 P1 0.95 gram, P2 0.82 grams, P3 0.46 grams, and control 1.03 grams. But it is likely to lose if each treatment compared to control where the most significant on P3 0.46 grams. While the number of resorpsi seen from the average number of results in table 1 do not affect real Control 0.6 P1 0.5 P2 0.5 P1 and P3 0.16. At P3 significant decline occurred 0.16.

On table 1. Influence of the extract of sambiloto granting look (*Andrographispaniculata* Ness.) against the number of fetus born ascendant real if each treatment compared with the control. Which when compared with the control treatment among all treatment then the result is real different but P1, P2 and P3 in comparison data are no different then it is not real. Obtained an average of P1 4.8 tail, P2 3.1 tail, P3 1.5 tail and controls 10.3 tail.

Where the results are visible on the Tabel1 the average number of implantation berdeba real control compared to all the treatments. On the treatment of control i.e. 10.3, P1 4.6, P2 6.1 and P3 (0.6) 5.8. While the P1, P2 and P3 if compared the results obtained then is no different. Then the granting of sambiloto extract (*Andrographispaniculata* Ness.)

lowers the number of implantation of neonatal mice. The influence of the giving of the extract of sambiloto (*Androphispaniculata* Ness) influential real against the amount of the foetus is born, number of implantation, the number of corpus luteum and influential not real against the murine stem weight increase, the average weight of the body of the fetus and the number of resorpsi.

V. DISCUSSION

A. Stem Weight Increase

Based on observation data which has been made regarding the influence of the giving of the extract of sambiloto (*Andrographispaniculata* Ness.) do not affect the real value against the murine stem weight, but from the table we can see that the granting of extracts sambiloto tend it matter if P1, P2, P3 as compared with controls. Weight loss occurs where the parent murine which are quite clearly visible on table 1.

Where weight is a very influential parameters to know how the influence of the compound against the fetus, which can be seen from a decrease in the weight of the fetus. The rate of growth and development was strongly influenced by consumption and foreign compounds are ingested by the next iduk to determine the variation of the size of the puppies. Possibly because there are individual developments in disorders of the uterus causes abnormalities of one is a disorder with abnormal body weight. The occurrence of a reduction in the weight of the fetus indicates a disturbance of fetus growth barriers. Where according to Wilson (1973) States that the resistance of growth occurs when agencies affect cell proliferation, cell interactions and a reduction in the rate of biosynthesis of barriers related to the synthesis of nucleic acids.

Change the parent murine body weight of each group's treatment is the result of weighing weight weight and early end of the murine parent prior to surgery. Stem weight increase of mice can be used as an indication of mice (*Musmusculus* l. Switzerland Webster) experience dapregnancy (pregnancy).

B. The number of Corpus luteum

Granting of sambiloto extract (*Andrographispaniculata* Ness) influential real against the number of corpus luteum, found higher concentrations of visible number of corpus luteum declined. This is because *Andrografolid* LH secretion decreases, causing impaired oogenesis the ovum to mature, come down, come down, ovulation and corpus luteum that is formed into a little. The corpus luteum (yellow body) is the governing body of the ovary (bubble

place eggs). The corpus luteum is called yellow bodies, also because the granulosa cells build it contains yellow pigments, also called lipokrom (Yatim, 1984)

According to Syahrums (1994) the process of ovulation were derived from the development and maturation of the follicle cells which is ripe will secrete estrogen which would suppress the secretion of FSH and Lh secretion triggers ovulation, so next will form the corpus luteum the growth is stimulated by LH so will produce progesterone. If fertilization happens then it will be kebuntingan and the corpus luteum will be maintained.

C. Number of Implantation

In table 2 it can be seen that the awarding of the extract of sambiloto (*Andrographis paniculata* Ness.) real effect against Implantation. So the higher the concentration of the extract given the declining number of implantation. This could be due to the growth of the uterine wall is not good, because the corpus luteum which formed a little and it is estimated the hormone progesterone secreted the less thus causing the growth of uterine didinding not good, allowing the failed implantation be great. According to Campbell et al., (2004) contraception i.e. the form of the prevention of conception (fertilization) or pregnancy intentionally, can be achieved in different ways. Some contraceptive method prevents fertilization by means of keeping the sperm cells and egg cells remain separate and have never met, and other methods that prevent implantation of the embryo or cause an abortion of the embryo. Rugh (1968) stated that the average number of implantation of an already mature mice reproductive age 3-5 months i.e., 11.42.

D. The average Body weight of Fetus

Research results are obtained, the granting of the extract of sambiloto (*Andrographis paniculata* Ness.) effect is not real against the weight of the fetus. This is caused by the extract of sambiloto is not embriotoksik so there happen fetus weight loss significant enough when compared with the control treatment, andrografolid including substance safe enough (Practically Non Toxic) According to Gleason in Nuratmi et al., (1996).

Growth and development of fetus in animals especially mice begins with increasing the number of cells is followed by differensiasi and the development of various organ systems. The development of the fetus is also influenced by a variety of factors, namely the potential genetic and nutritional status of both parents. Source of nutrition comes from the parent who moved through the placenta (Muna dkk, 2011).

Low berdosis teratogen compounds capable of causing the death of some cells and can also lead to turn some cells. If one or a group of cells damaged by toxic compounds are impaired. Then the surrounding normal cells will divide and replace the role of damaged cells. Substitution of damaged cells will be in pertehankan during the period of organogenesis will be formed morphologically normal fetus. But when damaged cells are not able to fix it will cause malformation/disability so formed fetus with normal morphology, but small sized (Ritter, 1977).

E. Number Of Resorpsi

Granting of sambiloto extract (*Andrographis paniculata* Ness.) effect is not real, it is thought that the extract of sambiloto non toxic against the murine embryo in consumption with concentrations are not too high. According to the Harbinson (1980) in Setyawati (2006) stating any toxic substances that enter the body with high doses may interfere with the body's physiological balance. When the parent is consumed in large quantities exceeds reasonable consumption will be able to bring up the effect embriotoksik. Where the nature of the embriotoksik of a substance may occur if accumulated in embryos. Resorpsi fetus is one indication of an agent that is Teratology. Where on any treatment there is no dead foetus found that extract of sambiloto well enough to antifertilitas substances.

F. Number of Fetus Born

based on the treatment given to the P1, P2, and P3. Resulted in a decrease in the number of birth fetus occurred when compared with control a. based on statistical tests, each treatment gives the real influence against the number of fetus born on 5% significant level. The higher the dosage given the least amount of foetus born.

This can be caused because of the andrografolid contained in the extract of sambiloto can interfere with pre-industrial stage of implantation. An inability to impregnate could also be influenced by the work of hormones that regulate the reproductive cycle. An inability to bunting could be influenced by the work of hormones that regulate the reproductive cycle. Toxic substances can also disrupt reproductive systems directly on the (contraceptive) or indirectly through specific endocrine organs (Lu, 1995). According to Rugh (1968) the number of children sekelahiran ranges between 8-12 tail.

Of any such research that extracts parameters sambiloto (*Andrographis paniculata* Ness) serve as a worthy tool KB. where things can support can be seen among the number of parameters of the foetus is born a little, a little number of

implantation, the number of corpus luteum declines and the fetus weight loss does not occur, whereas parameter does not support including the following occurs parent weight loss and the amount of the little resorpsi.

VI. CONCLUSION

Based on the results of the research, it can be concluded that the extract of sambiloto (*Andrographis paniculata* Ness.) given orally for 24 days on murine murine appearance can affect reproduction (*Mus musculus* L. Switzerland Webster), which lowers the number of fetus born, number of implantation, the corpus luteum and do not cause a decrease in the weight of the fetus.

REFERENCES

- [1] Badan Pusat Statistik (BPS). 2013. *Proyeksi Penduduk Indonesia 2010-2035*. Jakarta
- [2] Campbell, N. A, J. B. Reece dan L. G. Mitchell. 2014. *Biologi Edisi Kelima Jilid II*. Jakarta: Erlangga
- [3] Lu, Frank. C. 1995. *Toksikologi Dasar, Asas Organ Sasaran dan Penilaian Resiko*. Penerjemah, Edi Nugroho. Jakarta: UI Press.
- [4] Margaretta. 2013. Pengaruh Ekstrak Sambiloto (*Andrographis paniculata* Ness.) Terhadap Kualitas Spermatozoa Epididimis Mencit (*Mus musculus* L.) Swiss Webster (*Skripsi*). Prodi pendidikan Biologi (STKIP) PGRI Sumbar. Padang.
- [5] Muna, L., O.P. Astirin., dan Sugiyarto. 2011. Uji Teratogenik Pandanus conoideus Varietas Buah Kuning Terhadap Perkembangan Embrio Tikus Putih (*Rattus norvegicus*). Nusantara Bioscience. 2. pp 126-134.
- [6] Mohan, M., S. Khanam., and B.G. Shivananda. 2013. "Optimization of Microwave Assisted Extraction of *Andrographolide* from *Andrographis paniculata* and its Comparison with Refluxation Extraction Method". *Journal of Pharmacognosy and Phytochemistry*. Vol 2(1): 342-348.
- [7] Nuratmi, B., Adjirni, D.L. Paramita. 1996. Beberapa Penelitian Farmakologi Sambiloto (*Andrographis paniculata* Ness). *Warta Tumbuhan Obat Indonesia* 3: 1-24.
- [8] Palupi, J. 2008. "Pengaruh Pemberian Ekstrak Kulit Buah Manggis (*Garcinia mangostana* L.) Per Oral Terhadap Folikulogenesis Ovarium Mencit (*Mus musculus* L.)". *Jurnal Kesehatan*, Vol 6 (2).
- [9] Rahayu, M dan F. M. Setiowati. 2007. "Etnobotani Sambiloto, Pemanfaatannya Sebagai Bahan Obat Tradisional." *Pusat Penelitian dan Pengembangan Biologi-LIPI Bogor*. Vol 3 (1): 29.
- [10] Ritter, E.J. 1977. *Altered biosynthesis in: Wilson, J.G and F.C. Fraser (eds) Hand Book of Teratology*. Vol.2. New York: Plenum Press.
- [11] Rosidah, I. 2010. *Mikroenkapsula Fraksi Aktif Dari Herba Sambiloto (Andrographis paniculata Ness.) yang Berkhasiat Sitotoksik Dengan Metode Semprot Kering*. (tesis). Depok. FMIPAUI.
- [12] Rugh, R. 1968. *The Mouse its Reproduction and Development*. Burgess Publishing Company: United State of America.
- [13] Sabri, E., D. Supriharti, dan G. E. Utama., 2006. "Efek Pemberian Monosodium Glutamat (MSG) Terhadap Perkembangan Embrio Mencit (*Mus musculus* L.) Strain DDW Selama periode Praimplantasi Sampai Organogenesis." *Jurnal Biologi Sumatera*. Vol 1 (1):8-14.
- [14] Setyawati, I. dan D.A. Yulihastuti. 2011. "Penampilan Reproduksi dan Perkembangan Skeleton Fetus Mencit Setelah Pemberian Ekstrak Buah Nanas Muda". *Jurnal Veteriner*. Vol 12 (3): 192-199.
- [15] Setyawati, I. 2009. "Morfologi Fetus Mencit (*Mus musculus* L.) Setelah Pemberian Ekstrak Daun Sambiloto (*Andrographis paniculata* Ness.)". *Jurnal Biologi*. Vol 13 (2): 41-44.
- [16] Siburian, J., dan R. Marlinza. 2009. "Efek Pemberian Ekstrak Akar Pasak Bumi (*Eurycoma longifolia* Jack) Pada Tahap Prakopulasi Terhadap Fertilitas Mencit (*Mus Musculus* L.) Betina". *Biospecies*. Vol 2 (2): 24-30.
- [17] Sumarmin, R. 2016. *Perkembangan Hewan*. Jakarta: Kencana.
- [18] Syahrur, H. M. 1994. *Reproduksi dan Embriologi : Dari Satu Sel Menjadi Organisme*. Jakarta : Fakultas Kedokteran Universitas Indonesia.
- [19] Tolistiawaty, I., J. Widjaja., P. P. F. Sumolang., dkk. 2014. "Gambaran Kesehatan pada Mencit (*Mus musculus*) di Instalasi Hewan Coba". *Jurnal Vektor Penyakit*. Vol 8(1): 27-32.
- [20] Widiyawati, Tri. 2007. "Aspek Farmakologi Sambiloto". *Majalah Kedokteran Nusantara*. Vol 40 (3): 216-222.
- [21] Wilson, J.G. 1973. *Buku Teks Kimia Farmasi dan Medisinal Organik*. Penerjemah, Achmad Mustafa Fatah (1982). Semarang: IKIP Semarang Press.
- [22] Yatim, Wildan. 1984. *Embriologi Untuk Mahasiswa Biologi dan Kedokteran Bandung*: Tarsito.