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Tristania Sumatrana Effect On Female Mus Musculus Fertility

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Abstract. The use of traditional medicinal plants are generally based on empirical experience, therefore it is necessary scientific approach in order to bring traditional medicine into medical practice and the formal health services. *Tristania sumatrana* Miq. is one of the traditional medicinal plants are often used as a contraceptive for women in West Sumatra *Tristania sumatrana* Miq. extract can prolong the estrous cycle in mice to eleven days. This study aimed to influence *Tristania sumatrana* Miq. extract treatment on fertility of female mice. Experiments conducted a randomized block design 5x2. Five dose groups: control with no treatment, placebo, treatment with doses of 600, 900 and 1200 mg/kgbw and the old two treatment groups: 10 and 20 days. Fertility parameters studied were ovarian weight follicle Graaf number, the corpus luteum and fetal life. The research proves of *Tristania sumatrana* Miq. extract treatment causes a decrease very significantly the ovarian weight (treatment of 900 mg/kgbw for 10 days), follicles Graaf number (900 mg/kgbw for 20 days), the corpus luteum (600 mg/kgbw for 10 days) and live fetuses (900 mg/kgbw for 10 days). *Tristania sumatrana* Miq. extract treatment can lead to decreased fertility of female mice.

1. Introduction

The use of herbs as medicine have been done a long time as a remedy for family planning (1). This situation is supported by geographic and demographic factors. The Indonesia archipelago in tropical regions rich in various species of flora. Of the forty thousand species of flora in the world, thirty thousand of them grow in Indonesia. Indonesia population mostly live in rural areas, so that equitable health services difficult. This situation causes not all residents can enjoy modern health services, including family planning services. The Government supports the traditional medical treatment can be responsible for equitable distribution of health services. WHO also recommends ways to use traditional medicine as complementary to equitable health services to the public (2).

The use of traditional medicine is generally based on empirical experience alone. It required a scientific approach in order to bring traditional medicine into the medical practice and the formal health services. These conditions make traditional medicines have priority to be developed to support autonomy in drug procurement indispensable for equitable distribution of health services. Step-by-step development of traditional medicine include: testing drug efficacy; research and development of traditional medicine as well as the cultivation of sources of natural medicinal substances.

Already the collected 87 species of Indonesian plants have anti-fertility effect with an active ingredient of steroids such as diosgenin, hekogenin and stigmasterol (3). About 50 species have been

scrutinized anti fertility effects in experimental animals and human females. Results of the study showed that the plant's proficiency level can act as anti-gonadotropic, anti-implantation or anti ovulation (4).

The survey in the Valley Bawan village, West Sumatra obtained information that *Tristania sumatrana* Miq. is often used as a contraceptive for women. How to use it is to make lotion bark steeping dried, then drank the water once in two days after the menstrual period for 10-14 days. After drinking water steeping the bark lotion usually they do not menstruate, or if menstruation is not much and not for long.

Tristania sumatrana Miq. extract can prolong the estrous cycle of white mice *(Mus musculus)* to eleven days (5). While the mice were normal estrous cycle is 4-5 days. The phenomenon is an early indication of the presence of a disorder of the reproductive system in animals after administration of wood extract lotion. A plant substance that can show its activity as an anti-fertility in female animals, generally associated with the ability to intervene in the reproductive system that includes the organs of the hypothalamus, anterior pituitary and ovaries (6) chemical analysis bark *Tristania Sumatrana* Miq. steroids obtained from the type of β-sitosterol and stigmasterol (7) which are anti-fertility (8). More detailed biological activity has not been fully studied, such as its effect on ovarian weight, number of follicles, primary, secondary, tertiary, Graaf, atresia, corpus luteum, the child (fetus), and resorption.

Based on the background formulated research problem: Is *Tristania sumatranaMiq.* extract effect on the fertility of female mice which include ovarian weight, number Graaf follicle, corpus luteum, and live fetuses. Hypothesis: The *Tristania sumatrana* Miq. extract can decrease the fertility of female Swiss Webster mice. This study aimed to extract the effect of *Tristania sumatrana Miq.* on fertility of female mice. This research is expected to be useful in providing information about the effects of extract of *Tristania sumatrana Miq*.on fertility of female mice which include ovarian weight, number Graaf follicle, corpus luteum, and live fetuses as well as provide information to explore the possibility of the use of *Tristania sumatrana* Miq. as a raw material for contraceptives.

2. Method

The study design is a randomized block design 5 x 2 factorial pattern with two independent variables. The first independent variable is the dose to 5 treatments. The second independent variable is the duration of the 2 treatments. For more details, kind of treatment given to the female experimental animals can be seen in Table 1.

Table 1 Kind of treatment given to the female experimental animals

Factor		B				
	Stage	b 1	b 2	b 3	b 4	b 5
A	a 1	a 1 b 1	a 1 b 2	a 1 b 3	a 1 b 4	a 1 b 5
	a 2	a 2 b 1	a 2 b 2	a 2 b 3	a 2 b 4	a 2 b 5

Legend:			a1b1	:	Treatment of 10 days, 600 mg/kg bw
A	:	Long treatment	a1b2	:	Treatment of 10 days, 900 mg/kg bw
a1	:	Treatment of 10 days	a1b3	:	Treatment of 10 days, 1200 mg/kg bw
a2	:	Treatment of 20 days	a1b4	:	Positive control of 10 days, CMC 1%
B	:	Dose	a1b5	:	Negative control of 10 days
b1	:	Treatment of dose 600 mg/kg bw	a2b1	:	Treatment of 20 days, 600 mg/kg bw
b2	:	Treatment of dose 900 mg/kg bw	a2b2	:	Treatment of 20 days, 900 mg/kg bw
b3	:	Treatment of dose 1200 mg/kg bw	a2b3	:	Treatment of 20 days, 1200 mg/kg bw
b4	:	Positive control of CMC 1%	a2b4	:	Positive control of 20 days, CMC 1%
b5	:	Negative control	a2b5	:	Negative control of 20 days

Number of replications of each treatment four times, are determined using a formula Federer. Animal experiments used female mice were healthy, had never been pregnant, have regular estrous cycles 4-5

days. 20-30 gr body weight and 2-3 months old. Animals females were selected based on vaginal smears every day at the same time for 3 estrous cycle. Mice with regular estrous cycles 4-5 days designated as experimental animals. Having obtained 40 head of experimental animals with normal estrous cycles, then grouped randomly into 10 cages. Each cage contained 4 mice.

Wood extract dose *Tristania Sumatrana Miq.* given in experimental animals refers to Musdja who has researched the effect of lotion timber on the estrous cycle in mice taking doses of 300 and 600 mg/kgbw. Based on that, to see its effect on oogenesis, the initial dose of the initial dose used in this study is there a 600 mg/kgbw (b1), for a dose of 300 mg / kb bb yet to show tangible results. The next treatment groups, the dose was increased to 900 mg/kgbw (b2) and 1200 mg/kgbw (b3). The volume of extract for once-feeding is 0,20 ml.

Tristania sumatrana Miq. extract in experimental animals conducted over 10 days in the first five groups, five other groups is extended to 20 days. Increasing the dose and administration time extension aims to further assure the effect of treatment of experimental animals and to determine the dose and duration of administration effective to suppress fertility.

Tristania Sumatrana Miq. obtained in Agam, West Sumatra manufacture bark Tristania sumatrana Miq. extract by taking 100 grams of powdered bark of *Tristania sumatrana Miq.* then dissolved in 1 L of 95% ethanol for 24 hours (maceration). Extracts were formed was concentrated by *rotary vacuum evaporator* (rovapor). Concentrated extract obtained is evaporated with a water bath, stirring until dry extract (39), then extract from the bark of *Tristania sumatrana* Miq. ready to be made according to the dosage solution.

Doses of 600 mg/kgbw was prepared by dissolving bark *Tristania sumatrana* Miq. extract as much as 15.024 mg in 0.2 ml of CMC 1%. The calculations are as follows: the average weight of female mice strain Swiss Webster 2,5- age 3 months after the weighing is 25.04 g. Many extracts are used for a dose of 600 mg/kgbw determined by calculation 25.04 / 1000 x 60 = 15.024 mg. The same was done way in determining many extracts used in doses of 900 and 1200 mg / kg bw. Doses of 900 mg/kgbw was prepared by dissolving bark *Tristania sumatrana* Miq. extract A total of 22, 536 mg in 0.2 mL of 1% CMC. A dose of 1200 mg/kgbw was prepared by dissolving bark *Tristania sumatrana* Miq. extract. A total of 30.048 mg in 0.2 ml 1% CMC.

Chemicals used include: fixative Bouin's fixation organ ovary, ether to kill animals, paraffin for infiltration and printing (blocking) stocks histology of the ovary, staining for staining smears of the vagina, benzyl benzoate to remove any residual alcohol in the ovaries, serial alcohol 50%, 70%, 80%, 95%, and 100% for the elimination of water (dehydration) from the ovary, a solution of hematoxylin-eosin to stain preparations histology of the ovary, distilled water, aquades, albumin to attach the specimen to the glass slide and xylol to clear stocks histology.

Tools experiments. Enclosures and accessories; one set of extraction: *rotary vacuum evaporator*, water bath, the type Sartorius 4202 balance to the nearest 0.1 mg, goblets, aluminum foil, a pipette, a tool grinder *Milley Mill.* A set of surgical tools; one set of tooling and observations preparations: microtome, the bottles are 30 ml for spot fixing, the dye bath*(staining jar),*a light microscope, the scales of mice that *Triple Bean OHAUSS Balance Scale Corp. Union NJ USA* no. 2610 to the nearest 0,1g.

Treatment of experimental animals. Treatment done every morning at 08.00 am. Giving begins at the stage of diestrus to the experimental animals were treated 10 days and at the estrous stage to the experimental animals were treated 20 days. Animal experiments are grouped as in Table I. Completed treatment (female mice), the experimental animals mated with female mice by placing first on stage with a 1 male-fertile pro estrus in one cage a maximum of 10 days. During this period the observed presence or absence of the vagina as a sign stopper has occurred copulation. When copulation has occurred then the female mice were separated from the male and maintained for 18 days from the occurrence of copulation. After that, the mice were sacrificed pregnant or not pregnant.

Anti-fertility drug action in living beings females can be divided into a number of purposes, including preventing the maturation of the egg, preventing ovulation, preventing fertilization. The parameters studied from the *Tristania sumatrana* Miq. extract fertility test animals are 1) Weight ovary; both ovaries are left and right ovaries weighed. 2) The number of follicles Graaf; follicle Graaf studied

through histological preparations of ovaries. 3) The number of corpus luteum; the amount of the corpus luteum can be obtained in two ways. First, the corpus luteum of the ovary directly observed macroscopically. The corpus luteum will appear as bright red bumps. Second, the observation of a microscopic amount of the corpus luteum of the ovary and through histological preparations necessary to ensure the observations made by microscopic. 4) The number of live fetuses; female mice that were pregnant or not pregnant anesthetized with ether on the 18th day after the marriage. After the death of experimental animals dissected through the ventral abdominal area to open the uterus and took the fetus, then calculated the number of live fetuses.

Data obtained from observations of normality was tested using the method of Shapiro and Wilk. Homogeneity Barlett test data. If both tests are met, then the data were normally distributed population and its variations homogeneous, followed by a two-way ANOVA test. If the normality and homogeneity is not met then the transformation $\sqrt{(x + ½)}$ in the non-parametric statistics were analyzed with Friedman. If based on the Friedman test there is significant then forwarded the data analysis with the Advanced Friedman test.

3. Results

3.1. Ovary weight

Weighing ovaries results of mice left and right on surgery day 18 of pregnancy are presented in Table 2. The results of normality and homogeneity test proved that ovary weight data were normally distributed with a homogeneous variation. Based on ANOVA test is known there are differences in ovarian weight were highly significant ($P < 0.01$) for all doses of treatment. BNT obtained through further test weight differences ovarian highly significant ($P < 0.01$) between the group treated extract *Tristania sumatrana* Mig. at doses of 600, 900 and 1200 mg/kg/bw for 10 and 20 days. In addition, there are differences in ovarian weight were not significant ($P > 0.05$) for the duration of the treatment, which is between the treatment groups for 10 days compared with 20 days treatment at all doses. Similarly, the dose level with the old administration (T1T2) using extracts *Tristania sumatrana* Miq. do not interact significantly ($P > 0.05$) in ovarian weight. Test multiple ovarian weight BNT can be seen in Table 3.

Table 2. Mice ovarian weight (mg) after treatment with *Tristania sumatrana* Mig. Extract at doses of 600, 900, and 1200 mg/kg bw for 10 and 20 days.

Group		600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
Repeat	1	23.05	18.35	23.70	33.70	36.80	25.04	26.15	25.47	30.75	31.68
	2	33.84	26.10	28.43	30.42	42.30	21.91	26.79	24.92	32.70	32.30
	3	20.00	17.50	27.30	33.25	45.90	16.20	18.80	16.20	33.50	33.30
	4	26.73	20.60	18.00	31.97	31.90	19.70	19.00	24.60	33.50	31.44
Avg		25.91	20.64	24.36	32.34	39.23	20.71	22.69	22.80	32.61	32.18
SD		5.16	3.35	4.06	1.27	5.33	3.22	3.79	3.82	1.12	0.72

Description: 600/100, treatment group treated with *Tristania sumatrana Mig*. ekstact with dose 600 mg/kg bw for 10 days. Likewise 900/10, 1200/10, PC/10 (positive control), and NC (negative control). 600/20, treatment group treated with *Tristania sumatrana Mig*. ekstact with dose 600 mg/kg bw for 20 days. So did 900/20, 1200/20, PC/20 and NC/20.

Table 3. Test multiple ovarian weight BNT

Doses	N T	600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
600/10	25.91	-									
900/10	20.64	5.27	-								
1200/10	24.63	1.55	3.72	-							
PC/10	27.89	1.99	7.52*	3.53	-						
NC/10	32.94	7.04*	12.30**	8.58*	5.05	-					
600/20	20.71	5.19	0.07	3.65	7.18*	12.23**	-				
900/20	22.69	3.22	2.05	1.67	5.21	10.26**	1.97	-			
1200/20	22.80	3.11	2.16	1.56	5.10	10.15**	2.08	0.11	-		
PC/20	29.48	3.57	8.84*	5.12	1.58	3.47	8.76*	6.79*	6.68*	-	
NC/20	29.56	3.65	8.92**	5.20	1.66	3.39	8.84*	6.87*	6.76*	0.08	-

* = P < 0.05; ** = p < 0,01 P_{table} 5% = 6.57; 1% = 8.88

3.2. The number of Graaf follicles

A number of Graaf follicles in the ovaries of mice left and right are presented in Table 4. Results of normality test data on the number of Graaf follicles turns distribution is not normal, then the data is transformed. The test results of normality and homogeneity tests showed that the amount of data that has been transformed Graaf follicles normally distributed, with variance homogeneity. Two-way ANOVA test results showed that: There are differences in the number of Graaf follicles highly significant (P <0.01) in the combination of Tristania sumatrana Miq. extractnamely between doses of 600, 900 and 1200 mg/kgbw with a duration of 10 and 20 days. Based on BNT multiple test proved no difference Graff follicles were highly significant (P <0.01) between the group treated with the extract of *Tristania sumatrana* Miq. at doses of 600, 900 and 1200 mg/kgbw for 10 and 20 days compared to controls. Similarly, the dose level with the old treatment (T1T2) using extracts *Tristania sumatrana Mig.* do not interact significantly (P>0.05) in reducing the number of follicles Graaf. Test multiple BNT number of follicles Graaf for the combination treatment can be seen in Table 5.

Table 4. A number of Graaf follicles in the ovaries of mice left and right

Group	600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
Repeat										
1	12	16	7	16	33	17	8	7	35	8
2	15	14	14	28	23	11	12	10	22	30
3	16	15	23	22	23	17	3	8	23	23
4	14	14	4	17	10	7	11	9	20	20
Avg	14.25	14.75	12.00	20.75	22.25	13.00	9.00	8.50	25.00	20.25
SD	1.48	0.93	7.31	4.76	8.17	4.24	2.74	1.12	5.87	7.95

Table 5. BNT multiple test of Graaf follicles for combination of *Tristania sumatrana* Mig. Extract with doses of 600, 900 and 1200 mg/kg/bw of 10 and 20 days.

Doses	NT	600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
600/10	3.77	-									
900/10	3.84	0.07	-								
1200/10	3.30	0.47	0.54	-							
PC/10	4.53	0.76	0.69	1.23*	-						
NC/10	4.62	0.85	0.79	1.33	0.10	-					
600/20	3.55	0.22	0.29	0.26	0.97	1.07*	-				
900/20	2.96	0.81	0.88	0.33	1.56**	1.66**	0.59	-			
1200/20	2.91	0.86	0.93	0.39	1.62**	1.72**	0.64	0.05	-		
PC/20	4.97	1.20*	1.13	1.67**	0.44	0.34	1.42**	2.01**	2.06**	-	
NC/20	4.39	0.62	0.55	1.10*	0.13	0.23	0.84	1.43**	1.48**	0.58	-

* = P < 0,05 ** = P < 0,01 P table 5% = 1,04 ; 1% = 1,41

3.3. Total corpus Luteum

Calculation result of ovarian corpus luteum in the number of left and right mouse are presented in Table 6. The results of normality and homogeneity test data on the number of corpus luteum normal distribution with variance homogeneity. The results of a two-way ANOVA test showed: There are differences in the number of corpus luteum were highly significant (P <0.01) in the combination of *Tristania sumatrana* Miq. extract namely between doses of 600, 900 and 1200 mg/kg/bw with a duration of 10 and 20 days. Based on BNT multiple test proved no difference in the number of corpus luteum were highly significant (P <0.01) between the group treated with the extract of *Tristania sumatrana Mig.* at doses of 600, 900 and 1200 mg/kgbw for 10 and 20 days compared to controls. Test multiple BNT number of corpus luteum can be seen in Table 7.

Table 6. Number of corpus luteum after treatment with *Tristania sumatrana* Mig. Extract at doses of 600, 900 and 1200 mg/kg/bw of 10 and 20 days.

Group		600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
Repeat	1	10	12	6	11	24	7	11	4	11	17
	2	10	9	11	18	14	8	10	8	12	11
	3	8	10	8	12	11	11	9	7	13	12
	4	9	2	8	14	13	11	10	4	9	12
Avg		9.25	8.25	8.25	13.75	15.50	9.25	10.00	5.75	11.25	13.00
SD		0.83	3.77	1.79	2.68	5.03	1.79	0.71	1.79	1.48	2.35

Table 7. BNT multiple test corpus luteum number for combination of Tristania sumatrana mig. Extract with doses of 600, 900 and 1200 mg/kg/bw of 10 and 20 days

Doses	NT	600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
600/10	9.25	-									
900/10	8.25	1.00	-								
1200/10	8.25	1.00	0.00	-							
PC/10	13.75	4.50*	5.50*	5.50*	-						
NC/10	15.50	6.25**	7.25**	7.25**	1.75	-					
600/20	9.25	0.00	1.00	1.00	4.50*	6.25**	-				
900/20	10.00	0.75	1.75	1.75	3.75	5.50*	0.75	-			
1200/20	5.75	3.50	2.50	2.50	8.00**	9.75**	3.50	4.25*	-		
PC/20	11.25	2.00	3.00	3.00	2.50	4.24	2.00	1.25	5.50*	-	
NC/20	13.00	3.75	4.75*	4.75*	0.75	2.50	3.75	3.00	7.25**	1.75	-

* = P < 0,05 ; P = < 0,01 P table 5% = 4,25 ; 1% = 5,74

3.4. Life Fetus amount

Calculation result of the number of live fetuses in the uterus of mice left and right are presented in Table 8. The results indicate that the homogeneity test data on the number of live fetuses that have been transformed not homogeneous. Furthermore, the data is processed using Friedman's non-parametric statistical test. Friedman test results showed differences in the number of live fetuses were highly significant (P <0.01) in the combination of *Tristania sumatrana* Miq. extract between doses of 600, 900 and 1200 mg/kgbw with a duration of 10 and 20 days. Friedman test results the number of live fetuses can be seen in Table 9.

Table 8. The number of live fetuses after treatment with Tristania sumatrana Mig. Extract at doses of 600, 900 and 1200 mg/kgbw of 10 and 20 days

Group		600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
Repeat	1	8	12	6	11	13	4	10	0	10	12
	2	10	9	11	11	12	9	10	10	12	11
	3	7	8	8	11	12	10	9	1	12	11
	4	10	2	4	13	12	8	9	0	8	12
Avg		8.75	7.75	7.25	11.50	12.25	7.75	9.50	2.75	10.50	11.55
SD		1.30	3.63	2.59	0.87	0.43	2.28	0.50	4.21	1.66	0.50

Table 9. Friedman test number of live fetus for combination of Tristania sumatrana Mig. Extract with doses 600, 900, and 129

Dosis	NT	600/10	900/10	1200/10	PC/10	NC/10	600/20	900/20	1200/20	PC/20	NC/20
600/10	17.0	-									
900/10	14.5	1.5	-								
1200/10	16.5	0.5	2.0	-							
PC/10	31.5	14.5	17.0*	15.0	-						
NC/10	37.5	20.5*	23.0**	21.0*	6.0	-					
600/20	14.0	3.0	0.5	2.5	17.5*	23.5**	-				
900/20	20.5	3.5	6.0	4.0	11.0	17.0*	6.5	-			
1200/20	7.0	10.0	7.5	9.5	24.5**	30.5**	7.0	13.5	-		
PC/20	29.0	12.0	14.5	12.5	2.5	8.5	15.0	8.5	22.0**	-	
NC/20	31.5	14.5	17.0*	15.0	0.0	6.0	17.5*	11.0	24.5**	2.5	-

* = P < 0,05 ; ** = P < 0,01 R table 5% = 16,78 ; 1% = 22,01

4. Discussion

The results of the two-way ANOVA test showed differences in ovarian weight, number of follicles, corpus luteum and Graff very significant in the combination of extract *Tristania sumatrana* Miq. at doses of 600, 900 and 1200 mg/kgbw with a duration of 10 and 20 days. The LSD shows these extracts award at doses of 600, 900 and 1200 mg/kgbw for 10 and 20 days led to a significant reduction of ovarian weight, number Graaf follicle and corpus luteum. Weight loss can be due to the reduced number of ovarian follicles, primary, secondary, tertiary and Graaf. Weight will decrease if there is ovarian follicle development barriers (9, 10) .

The Tristania sumatrana Miq. extract turned out to cause a decrease in primary follicles, secondary and tertiary (11). *Tristania sumatrana Miq*. known to contain steroids from the class of β-sitosterol and stigmasterol (1, 8, 12). Steroids are one of the factors that may hinder the development of the follicle through suppressing FSH levels (13). Plants that contain estrogenic steroid generally so that it can affect the menstrual cycle and follicular development (11, 14, 15).

The decline in the number of follicles can also be caused by steroid β-sitosterol and stigmasterol of *Tristania sumatrana Miq*. These steroids can disrupt the balance shaft hypothalamus, pituitary and ovaries. Steroid β-sitosterol and stigmasterol thought to cause increased levels of estrogen in the blood, thus inhibiting the secretion of FSH and LH. FSH regulates the development and the number of follicles. Decreased levels of FSH may lead to follicular development is inhibited from primary follicles, secondary, tertiary and Graaf (6). β-sitosterol and stigmasterol in Lichenes can also suppress fertility albino mice (13).

Another possibility is the active substance contained in *Tristania sumatrana Miq*. directly inhibit follicle development in the ovary. This was shown by the declining number of primary and secondary follicles (9, 16).

Decrease in the number of follicles in the treatment of 600 mg/kgbw for 10 days, has reached an optimal effect against ovarian weight, number Graaf follicle and corpus luteum. Increasing the dose to 900 and 1200 mg/kgbw and the addition of the treatment time to 20 days did not significantly decrease the research parameters. Drug response in organisms such as sinusoidal curve, dose escalation will lead to increased response of the organism. Optimal doses above the curve going up exponentially but tends to be linear (17) (10).

The optimal dose may also occur due to the active compound contained in *Tristania sumatrana Miq*. Exceed the number of specific receptors (17). Although the concentration of β-sitosterol and stigmasterol in the body is very high but it can not form a complex with the receptor to be brought to

the target cells. Thus increased levels of steroid β-sitosterol and stigmasterol in blood plasma through increasing the dose or duration of administration not necessarily add to its effectiveness.

The interaction between the old dose administration (T1T2) is not meaningful for all parameters. This means that between increasing doses (600 to 900 and 1200 mg / kg bw) and duration of administration (10 and 20 days) Tristania sumatrana Miq. extract not interdependent in affecting ovarian weight, number Graaf follicle and corpus luteum (18). Based on advanced Friedman test showed that the majority of the extract *Tristania sumatrana*Miq.at doses of 600, 900 and 1200 mg/kgbw for 10 and 20 days can reduce significantly the number of live fetuses. Tristania sumatrana Miq. extract can extend into the eleventh day of the estrous cycle (5, 19). Extension of the estrous cycle is an indication of their reproductive system disorders as a result of disruption of the balance gonadotropin (17, 20).

Based on the analysis that has been done against suspected follicle β-sitosterol and stigmasterol derived from extracts of *Tristania sumatrana Miq*. reduce the number of follicles Graaf. The decline in the number of follicles causes a decrease in ovulatory proven to be a highly significant decrease in the number of corpus luteum. Decreased ovulation will minimize the amount of fertilization, thus reducing the number of fetuses.

Increasing doses of the Tristania sumatrana Miq. extract from 600 to 900 and 1200 mg/kgbw and duration of administration of the addition of 10 to 20 days to show the difference in the number of fetuses that are not significant compared to the treatment at a dose of 600 mg/kgbw for 10 days. As has been earlier that the treatment at a dose of 600 mg/kgbw for 10 days is optimum, as a result of an increase in the dose and duration of administration is no longer statistically significant effect on the reduction in the number of fetuses.

The interaction between the old dose administration (T1T2) is not meaningful for the parameter number of fetuses. This means that between increasing doses (from 600 to 900 and 1200 mg/kg bw) and duration of administration (10 and 20 days) *Tristania sumatrana* Miq. extract not inter dependent in influencing the number of fetuses.

5. Conclusion

Based on the results of this study concluded that the Tristania sumatrana Miq. extract can decrease the fertility of female mice *Mus musculus*L. Swiss Webster strain, which include: a decrease in ovarian weight; a decrease in the number of follicles Graaf; a decrease in the number of corpus luteum and decreased number of live fetuses.

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