Jurnal Kedokteran Hewan December 2023, 17(4):116-120
P-ISSN : 1978-225X; E-ISSN : 2502-5600 DOI: https://doi.org/10.21157/j.ked.hewan.v17i2.33189

COMBINATION OF BASIL, TURMERIC AND BEAN SPROUTS TO HEMATOLOGY AND BIOCHEMISTRY OF FEMALE RAT BLOOD BEFORE PREGNANCY

Andriyanto[1], Aulia Andi Mustika[1], Wasmen Manalu[2], Mawar Subangkit[3], Sharon Aurelia[4], Leliana Nugrahaning Widi[4], Hamdika Yendri Putra[5], Elpita Tarigan[5], Yusa Irarang[5]

[1]Division of Pharmacology and Toxicology, Department Anatomy, Physiology and Pharmacology, Faculty of Veterinary Medicine, IPB University, Bogor 16680, West Java, Indonesia

[2]Division of Physiology, Department Anatomy, Physiology and Pharmacology, School of Veterinary Medicine and Biomedical Science, IPB University, Bogor, 16680, West Java, Indonesia

[3]Division of Pathology, Department Clinical, Reproduction and Pathology, School of Veterinary Medicine and Biomedical Science, IPB University, Bogor, 16680, West Java, Indonesia

[4]Laboratory Animal Management, School of Veterinary Medicine and Biomedical Science, IPB University, Bogor 16680, West Java, Indonesia

[5]eLRosa Laboratory, Bogor 16680, West Java, Indonesia

*Corresponding author: andriyanto@apps.ipb.ac.id

ABSTRACT

The purpose of the study was to examine the safety of combination of basil, turmeric and bean sprouts extract solution on the hematological parameters and blood biochemistry profile of rats. The combined ingredients used in the study were obtained from different places. A total of 15 rats were divided into 3 groups based on the treatment dose. Each group consisted of 5 rats. The rats in control group (K) did not given extract combination, while the rats in group KKT 1 % and KKT 5% received combination of basil, turmeric and bean sprouts extract at dose of 1% and 5%, respectively. Effectiveness and safety tests were carried out by evaluating the hematological and blood biochemical profiles of female rats. The data were analyzed using *one-way analysis of variance* (ANOVA). The results showed that the rats given combination of basil, turmeric and bean sprouts extract at a dose of 1% and, dose of 5% did not had significant different compared to control ($P<0.05$), but tend to have positive effects in increasing several blood components that play an important role in maintaining immunity during pregnancy. It can be concluded that the combination of basil, turmeric and bean sprouts at dose of 1% and 5% do not adversely affect hematology profile and blood biochemistry of rats. This indicates that the extract combination does not cause any toxicity effects on the rats.

Key words: fertility, herbs, rat, safety, traditional medicine

ABSTRAK

Tujuan penelitian adalah mengkaji efektivitas dan keamanan dari maserasi yang berbahan dasar kombinasi dari kemangi, kunyit dan tauge. Bahan-bahan kombinasi dalam penelitian ini diperoleh dari berbagai tempat. Penelitian menggunakan mencit yang dibagi menjadi tiga kelompok berdasarkan dosis perlakuan dan setiap kelompok terdiri atas lima ekor mencit. Uji efektivitas dan keamanan dilakukan dengan menguji profil hematologi dan biokimia darah tikus betina. Data yang diperoleh dianalisis dengan menggunakan Microsoft Excel 2019 dan Minitab 19. Perbedaan yang tidak nyata dari rata-rata setiap kelompok ditunjukan secara statistik dengan analysis of variance (ANOVA) one way. Hasil penelitian menunjukkan bahwa mencit yang diberikan maserasi kombinasi kemangi, kunyit, dan tauge dengan dosis 1%, dosis 5%, dan kontrol tidak memiliki perbedaan nyata, akan tetapi memiliki efek positif seperti menaikkan beberapa komponen sel darah yang berperan penting dalam menjaga imunitas selama kehamilan. Hal ini dapat disimpulkan bahwa kombinasi maserasi tersebut dapat digunakan sebagai stimulator fertilitas dengan keamanan yang terjamin.

Kata kunci: fertilitas, herbal, mencit, obat tradisional, keamanan

INTRODUCTION

Fertility is defined as an individual's ability to produce offspring as one of the life survivals goals (Sinaga *et al.* 2017). The capability of having children is something that most of married couples desire (Ahinkorah *et al.* 2020). However, there are still some problems that prevent a person from having children. Some of the problems are miscarriage, neonatal death, and infertility. Infertility is a reproductive system disorder characterized by failure to conceive a child after more than twelve months of regular sexual intercourse without using any contraception (Borght and Wyns 2018). The reproductive age for women is 20-49 years (Hartini *et al.* 2021), while in men is 20-34 years (Sunanda *et al.* 2014). The number of cases of infertility in couples of reproductive ages worldwide reaches 50-80 million cases, while in Indonesia, there are 10-15% of the total population experiencing infertility. The prevalence of reproductive women who experience infertility in Indonesia reaches 6.08% (Panjaitan and Manurung 2020).

Miscarriage is defined as death of the fetus at the age of less than 20 weeks of pregnancy. The frequency of unwanted miscarriages in Indonesia reaches 10-15% for every 5 million pregnancy, or 500.000-750.000 cases each year (Yanti 2018). An analysis conducted by Akbar (2019), stated that eight highest factors that cause miscarriage the most in Indonesia from year 2010 to 2019 are maternal age during pregnancy, parity, history of abortion, interpregnancy interval, education and occupational levels, and anemia. Neonatal death is one of the factors that often occurs in the failure of having children. Causes behind neonatal death, according to Lengkong *et al.* (2020), are the weight of the baby, antenatal check-ups, whether or not the

mother works, and an adequate access to health service during the period of birth. Based on the result of the Indonesian Demographic and Health Survey (IDHS), neonatal death in 2017 was 24/1.000 live births while neonatal mortality reaches 15/1.000 live births.

Infertility, miscarriage and neonatal death can be caused by several factors in women, namely reproductive organ abnormalities, ovulation disorders, uterine disorders, and hormonal imbalances (Indarwati *et al.* 2017). One of the options to overcome failure of conception is to use chemical-based drugs and modern therapy. One of the chemical-based drugs that is often used to treat infertility in women is clomiphene citrate. Clomiphene citrate is consumed as a single drug or in combination with other drugs. This drug is believed to be able to increase the level of estradiol and progesterone (Tomao *et al.* 2014). In addition to clomiphene citrate, drugs such as GnRH analogues, human menopausal gonadotropin (hMG), progesterone, luteinizing hormone and hCG are often used to stimulate fertility either in combination with clomiphene citrate or as a single drug. However, gonadotropin, hCG, progesterone, FSH and LH are recognized as growth factors of ovarian cancer, and their use as fertility-induced drugs is also suspected to have a role in inducing ovarian cancer. According to research conducted by Hillard *et al.* (2013), FSH and LH induced to activate ovarian development, can also stimulate the proliferation of ovarian cancer cells by the same mechanism. Other than the usage of chemical-based drugs, some people choose to do therapies to treat infertility. One of the most common fertility therapies is IVF therapy or in-vitro fertilization (IVF). This therapy is increasingly popular nowadays, but the success rate in Indonesia is still quite low (Dhyani *et al.* 2020). In addition, the price of fertility treatment procedure and the usage of chemical-based drugs have negative effect on the body for long term consumption. Other than that, the success of fertility therapy also has an uncertain rate. Therefore, the tendency of using herbal medicines is increasing among women. Herbal medicine is considered as a suitable alternative to replace the use of chemical-based drugs. The advantages of using herbal medicines are safety for long-term use, low prices, and there are various components with phytoestrogen, antioxidant and nutritional effects (Akbaribazm *et al.* 2021).

Some herbal plants have been proven to be able to enhance fertility, both on women and men. One of the examples is date pollen. According to Rahmadiani (2021), date pollen extract has been proven to have positive effects on spermatogenesis because it contains flavonoid and antioxidant to prevent cell damage due to oxidative effects, and contains estrogen as well. According to research conducted by Askari (2017), extract from the leaves of chastee tree has been proven to stimulate corpus luteum secretion after ovulation to produce progesterone, which can regulate sexual cycle on women. Some other herbs that can be used to enhance fertility and maintain the condition of the fetus and the mother are basil, turmeric and bean sprouts. Basil (*Ocimum basilicum)* can increase estrogen production because of its anethol and boron compounds. According to a research conducted by Wicaksono *et al.* (2013), these compounds can prolong estrus cycle on women and increase fertility.

In addition, basil also has antioxidant, anti-inflammation and antimicrobe effects (Shahrajabian *et al.* 2020). Other than basil, turmeric also has a potential in increasing fertility and maintaining healthy pregnancy. According to Sirotkin *et al.* (2018), turmeric has been shown to increase follicular development in female rabbits by increasing the proliferation of ovarian cells by elucidation mechanism. Turmeric can decrease ovarian cell death and support the development of atretic follicles due to its antioxidant content (Sak *et al.* 2013). Another plant that supports women fertility is bean sprouts. Bean sprouts contains vitamin C and vitamin E that function as antioxidant and it is able to reduce free radical's effect. Antioxidant components in bean sprouts have been proven to increase the level of FSH and estrogen (Fatmaningrum and Ningtyas 2019). Other than antioxidant compound, bean sprouts also contain phytoestrogen. Phytoestrogen has a structure and functions that are similar to estrogen, so it can stimulate the ovulation process in women (Ariyanti and Apriliana 2016).

This study was conducted to explore the combination of basil, turmeric and bean sprouts in enhancing fertility and maintaining health during pregnancy. This study is expected to provide an overview related to the potential of the combination of basil, turmeric and bean sprouts as fertility stimulator and support for pregnancy health. In addition, this study is expected to be used as a basis of consideration of the use of the combination as fertility and health stimulator for pregnant women.

MATERIALS AND METHODS

Preparation of Basil, Turmeric, and Bean Sprouts Extract

Basil leaves *(Ocimum basilicum),* tumeric *(Curcuma longa),* and bean sprouts (*Vigna radiata)* were collected from Bogor. A 100 g of basil leaves, 100 g of turmeric and 100 g of fresh bean sprouts were coarsely ground in a mortar and mixed well. The mixture was put into an Erlenmeyer tube, and added with 100 mL of distilled water at a temperature of 100° C. The extract was then cooled at room temperature, filtered through a 100-um mesh sieve to gain a stock solution, and stored in the refrigerator at a temperature of 4-5° C. The extraction was conducted 3 times a day. The extraction of basil, turmeric and bean sprouts was carried out at Laboratory Animal Management Unit of School of Veterinary Medicine and Biomedics, IPB University.

Ethical Clearance

The usage of rats in the study had suited research ethics rules of Animal Ethics Commission, School of

Veterinary Medicine, IPB University in accordance with ethical clearance certificate Number. 007/KEH/SKE/I/2020.

Administration of Combination of Basil, Turmeric and Bean Sprouts Extract to Rat

Female *Sprague Dawley* rats, aged 8 weeks with body weight of 220-230 g were obtained from the Laboratory Animal Management Unit of School of Veterinary Medicine and Biomedics IPB University. Rats were put inside animal cages made from plastic boxes measuring 55 x 37 x 17 cm with wire covers on the top of the cages. The base of the cages was covered with wood husk. Feed and drinking water were provided *ad libitum.* Before treatment, the rats were climatized for 7 days in order to adapt to the new cage conditions and to reduce the stress level.

A total of 15 rats were divided into 3 groups based on the treatment dose. Each group consisted of 5 rats. The rats in control group (K) did not given extract combination, while the rats in group KKT 1% and KKT 5% received combination of basil, turmeric and bean sprouts extract at dose of 1% and 5%, respectively, for 20 days.

Blood Analysis

Blood sampling was carried out on the 21st day. Rats were anesthetized using ketamine (100 mg/kg BW) and xylazine (3 mg/kg BW) via intraperitoneal and blood was drawn through intracardial route. Four mL blood was taken from each rat, 1 mL was inserted into the EDTA (Hematology) tube, and 3 mL was inserted into plain tube. Hematology test was carried out using a Mindray BC-2800 hematology analyzer (PT. Mindray Medical Indonesia. The parameters observed in the complete blood count were the number of erythrocytes (RBC), hematocrit (HCT), hemoglobin (Hb), leukocytes (Leu), lymphocytes, differential leukocytes (monocyte, neutrophils, eosinophils and basophils), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and platelet distribution width (PDW). Blood chemical test was performed using UV spectrophotometer. Blood chemical test parameters included liver function tests, which were Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxsaloasetic Transaminase (SGOT), and kidney function (Ureum and creatinine).

Data Analysis

The data were tabulated using Microsoft Excel 2019 and Minitab 19. Data analysis was conducted using one-way analysis of variance (ANOVA) and subjected to Tukey test.

RESULTS AND DISCUSSION

Effect of the Administration of Basil, Turmeric and Bean Sprouts Extraction on Hematological Parameters.

Based on the result of the study, it was found that the administration of extract combination did not affect any hematological parameters of the rats (Table 1). This was shown by the result of the measurement of hematological parameters in rats administered with the combination of basil, turmeric and bean sprouts that did not show any significant difference compared to the control group ($P>0.05$).

Measurement of the toxicity of a natural substance can be identified through blood testing. Hematological examination is able to provide information on the effects of the test compound on blood and blood-forming tissues (Hidayat *et al.* 2017). One of the methods of measuring blood components is complete blood count (CBC). A substance that is toxic will affect the number of red bloods, white blood and other blood components. According to Pizzorno (2015), the number of erythrocytes, leukocytes and platelets tend to decrease when being exposed to toxins. All hematological parameters observed in this study were within the normal range. This was proven by the absence of significant differences ($P<0.05$) from the treated groups compared to the control group.

Numerically, the result showed that the number of erythrocytes, leukocytes and platelets in treated rats were higher than the control group. This is might be due to the curcumin compound in turmeric acts as a

Table 1. Effect of the administration of combination of basil, turmeric and bean sprouts extract on hematological parameters

Parameters	Control	KKT 1%	KKT 5%
RBC (10^6/L)	5.28±1.00	5.88±0.81	5.63±0.96
HCT (%)	42.28±3.68	40.85±2.35	41.69±1.98
Hb (g/L)	13.93±2.40	14.92±2.55	15.39±2.41
LEU (10^9/L)	3.50±1.37	4.08±2.05	4.65±2.34
Lymp (10^9/L)	3.17±1.57	4.00±0.95	2.54±1.59
Monosit (10^9/L)	0.04±0.02	0.03±0.02	0.03±0.02
NEU (10^9/L)	1.41±0.48	0.75±0.47	1.02±0.62
EOS (10^9/L)	0.11±0.08	0.14±0.04	0.13±0.06
BAS (10^9/L)	0.01±0.01	0.01±0.01	0.02±0.01
MCV (fl)	65.70±2.29	65.77±3.43	65.27±2.43
MCH (pg)	25.87±4.58	20.21±2.79	23.37±3.95
MCHC (g/L)	36.18±4.31	34.30±3.51	34.33±4.07
RDW(%)	13.41±0.26	14.55±0.67	13.95±0.78
PDW (%)	6.76±0.02	6.80±0.04	6.81±0.03

hematopoietic. According to Prihardini and Basuki (2015), turmeric has been shown to have an antianemia effect by increasing erythrocyte levels because it contains curcumin compounds. The results of calculation of white blood cell parameters in 1% and 5% combination groups showed an increase compared to the control group. The number of leukocytes has a major role in immune function by protecting the body from invading antigens. The increase in the number of leukocytes will support the mother's immune system during pregnancy, so that there will be no transplacental infection from mother to fetus (Khasanah *et al.* 2016). Hematological parameters showed that the treatments did not have any negative effect on the blood profile of the rats.

Administration Effect of The Combination of Basil, Turmeric, and Bean Sprouts on Blood Biochemistry Test

Measurement of blood biochemistry test was conducted to observe the effect of administration of the extract combination on the organs inside the body. The parameters used for blood biochemistry test were Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloasetic Transaminase (SGOT), blood urea nitrogen and creatinine. Based on the result of the study, it was found that the administration of the combination did not have any effect on blood biochemistry test (Table 2). The SGPT, SGOT, Ureum, and creatinine values in KKT 1% and KKT 5% groups did not differ significantly as compared to the control group ($P>0.05$). All of the parameters observed were still within the normal range.

Blood biochemistry test can help to determine the safety of the extraction against vital organs such as the liver and kidneys. Kidneys function as a place to excrete substances out of the body and a toxic substance will affect the performance of the kidneys. The performance of kidneys can be measured through the level of ureum and creatinine in the blood. On the other hand, liver has a crucial function on metabolic process and detoxification of any drugs and foreign substances inside the body. Therefore, the liver is often exposed to foreign substances that can be toxic and very susceptible to damage and tend to leave traces of damage (Christina *et al.* 2016). On the measurement of the performance of the liver, the enzymes that were measured were SGOT and SGPT. The levels of SGPT and SGOT is supposed to be at the normal range because the enzymes reside inside hepatocyte cells. But, if tissue damage happens, the cells will rupture and the enzymes will be unraveled out of the hepatocytes and enter the blood circulatory system. Thus, the levels will increase above the normal range (Suryaningsih *et al.* 2017). The result of the study showed that the level of SGPT and SGOT in all treatment groups were still within the normal range for female *Sprague Dawley* rats, which are 60-139 U/L for SGOT and 14-30 U/L for SGPT (He *et al.* 2017). This proved that there wasn't any liver damage on the rats. Based on research conducted by Liu *et al.* (2014), bean sprouts were proven to have hepatoprotective effect on the liver, even on livers that were already damaged in rats. This might be due to the flavonoid component found in bean sprouts which play a role as antioxidant. Other than bean sprouts, turmeric also has a potential as a hepatoprotective agent. Turmeric has a strong antioxidant effect and anti-inflammation effect; thus, it has a potential as hepatoprotective agent.

Parameters used to observe the performance of kidneys were ureum and creatinine. Ureum or blood urea nitrogen (BUN) is a unit that expresses the level of ureum in the blood. The increase of ureum level may indicate decreased kidney function due to toxin exposure. Kidneys have the ability to clean up blood from toxic substances, which cause accumulation of metabolic substance in the blood, such as ureum (Setyaningsih *et al.* 2013). Kidneys that experience damage or decreasing function cause urea not to be excreted along with urine (Griffin *et al.* 2019). In other words, the measurement of the performance of kidneys can be done with measuring the level of blood creatinine. Creatinine is a breakdown product from creatine that provides energy to the muscle. Creatinine is a substance that is produced from normal muscle contraction and is release into blood, then passes the kidneys to be excreted. Elevation of creatine level is an indication that the kidneys are not able to excrete creatinine normally (Ningsih *et al.* 2021). The result of the study showed that the ureum and creatinine levels were still within the normal range. Normal range for ureum level on female *Sprague Dawley* rats is in the range of 5.56-12.67 mmol/L, on the other hand, the level of normal creatinine for female *Sprague Dawley* rats are in the range of 34.91-59.67 mmol/L (Liu *et al.* 2014). The creatinine level in rats given 1% and 5% of the combination tend to decrease. This may be due to the kidney protective effect of turmeric and basil. Based on the research conducted by Thadani (2015), basil has been proven to decrease ureum and creatinine level significantly on rats in 8 weeks. This is due to the phenolic compound inside basil that has free radical effect and high antioxidant activity (Arif and Suryani 2020). Thus, it can be concluded that the administration of the combination of basil, turmeric and bean sprouts does not have any negative effect on the liver and kidney.

Tabel 2. Effect of the administration of combination of basil, turmeric and bean sprouts extract on blood biochemistry profile

Parameters	Control	KKT 1%	KKT 5%
SGPT (U/L)	24.80±3.35	20.60±4.88[a]	20.20±6.18
SGOT (U/L)	93.80±13.88	86.80±10.62	98.60±27.92
Ureum (mmol/L)	9.62±2.64	9.84±1.89	7.33±1.28
Creatinine (mmol/L)	49.89±8.46	44.82±8.14	47.33±7.85

CONCLUSION

The combination of basil, turmeric and bean sprouts at dose of 1% and 5% do not adversely affect hematology profile and blood biochemistry of rats. This indicates that the extract combination does not cause any toxicity effects on the rats and has a potential to enhance the health of the female rats before pregnancy.

ACKNOWLEDGEMENT

Researchers thank the team that had been involved from the beginning of the research until the process of writing this academic research paper. Researchers also thank all the people that had been involved in helping the research and the process of writing this academic paper.

REFERENCES

Ahinkorah BO, Seidu AA, Armah-Ansah EK, Budu E, Ameyaw EK, Agbaglo E, *et al*. 2020. Drivers of desicer for more children among childbearing women in sub-Saharan Africa: Implications for fertility control. *BMC Pregnancy and Childbirth*, 20(778):1-11.

Akbar. 2019. Faktor penyebab abortus di Indonesia tahun 2010-2019: Studi meta analisis. *Jurnal Biomedik*, 11(3):182-191.

Akbaribazm M, Goodarzi N, Rahimi M. 2021. Female fertility and herbal medicine: An overview of the new findings. *Food Science & Nutrition*, 9(10):5869-5882.

Arif NZ, Suryani D. 2020. Pengaruh protektif ekstrak daun kemangi *(Ocimum sanctum)* terhadap fungsi ginjal tikus wistar jantan yang diinduksi aspartam. *Jurnal Pandu Husada*, 1(3):16-166.

Ariyanti H, Apriliana E. 2016. Pengaruh fitoestrogen terhadap gejala menopause. *Majority*, 5(5):1-5.

Askari K. 2017. Effect of hydroalcoholic extract of *Vitex Agnus-castus* fruit on fertility and estrous cycle in letrozole-induced polycystic ovary (PCOS) in rat. *Razi Journal of Medical Sciences*, 24(156):42-48.

Borght MV, Wyns C. 2018. Fertility and infertility: definition and epidemiology. *Clinical Biochemistry*, 62:2-10.

Christina I, Setyawati AN, Tjahjono K. 2016. Pengaruh ekstrak daun dewa *(Gynura divaricata)* terhadap kadar SGOT dan SGPT (Studi eksperimental pada tikus *Sprague Dawley* betina model kanker payudara). *Jurnal Kedokteran Diponegoro*, 5(4):1013-1025.

Dhyani IAD, Kurniawan Y, Negara MO. 2020. Hubungan antara faktor-faktor penyebab infertilitas terhadap tingkat keberhasilan IVF-ICSI di RSIA Puri Bunda Denpasar pada Tahun 2017. *E-Jurnal Medika Udayana*, 9(5):23-29.

Fatmaningrum W, Ningtyas WS. 2019. Mung bean sprout extract suppresses monosodium glutamate (MSG) effect on the reproductive hormones (FSH and estrogen) in female Wistar rats. *Majalah Obstetri & Ginekologi*, 27(1):24-27.

Griffin BR, Faubel S, Edelstein CL. 2019. Biomarkers of drug-induced kidney toxicity. *Therapeutic Drug Monitoring*, 41(2):213-226.

Hartini NNSM, Nugraha B, Priyadi A. 2021. Analisis tingkat pengetahuan, persepsi dan sikap wanita usia subur (WUS) pengguna non-MKJP terhadap MKJP di Kecamatan Cigugur Kabupaten Kuningan Indonesia. *Jurnal Farmagazine*, 3(1):1-7.

He Q, Su G, Liu K, Zhang F, Jiang Y, Gao J. 2017. Sex-specific reference intervals of hematologic and biochemical analytes in *Sprague-Dawley* rats using the nonparametric rank percentile method. *PloS One*, 12(2):1-18.

Hidayat M, Prahastuti S, Dewi E, Safitri D, Farah S, Soemardji AA. 2017. Uji toksisitas subkronis kombinasi ekstrak kedelai dan jati belanda terhadap hematologi) tikus Wistar. *Jurnal Ilmu Kefarmasian Indonesia*, 5(1):114-119.

Hillard TS, Modi DA, Burdette JE. 2013. Gonadotropins activate oncogenis pathways to enhance proliferation in normal mouse ovarian surface epithelium. *International Journal of Molecular Sciences*, 14(3):4762-4782.

Indarwati I, Hastuti URB, Dewi YLR. 2017. Analysis of factors influencing female fertility. *Journal of Maternal and Child Health*, 2(2):150-161.

Khasanah MN, Harjoko A, Candradewi I. 2016. Klasifikasi sel darah putih berdasarkan ciri warna dan bentuk dengan metode *K-Nearest Neighbor* (K-NN). *Indonesian Journal of Electronics and Instrumentation Systems*, 6(2):151-162.

Lengkong GT, Langi FLFG, Posangi J. 2020. Faktor-faktor yang berhubungan dengan kematian bayi di Indonesia. *Jurnal Kesehatan Masyarakat*, (4):41-47.

Liu T, Yu XH, Gao EZ, Liu XN, Sun LJ, Li HL. 2014. Hepatoprotective effect of active constituents isolated from mung beans (*Phaseolus radiatus* L.) in an alcohol-induced liver injury mouse model. *Journal of Food Biochemistry*, 38(5):453-459.

Ningsih SA, Rusmini H, Purwaningrum R, Zulfian Z. 2021. Hubungan kadar kreatinin dengan durasi pengobatan HD pada penderita gagal ginjal kronik. *Jurnal Ilmiah Kesehatan Sandi Husada*, 10(1):202-207.

Panjaitan RF, Manurung E. 2020. Analisis faktor risiko kejadian infertilitas pada perawat di RSU Sembiring. *Biology Education Science & Technology Journal*, 3(2):244-250.

Pizzorno J. 2015. Conventional laboratory tests to assess toxin burden. *Integrative Medicine: A Clinican's Journal*, 14(5):8-16.

Prihardini, Basuki. 2019. Uji aktivitas antianemia ekstrak etanol dan perasan rimpang kunyit (*Curcuma Longa* Linn.) ditinjau dari peningkatan kadar haemoglobin dan eritrosit pada tikus galur wistar dengan pengindukasi $NaNO_2$ secara in vivo. *Jurnal Wiyata*, 6:(2)117-127.

Rahmadiani D. 2021. Ekstrak pollen kurma *(Phoenix dactylifera* L) sebagai terapi infertilitas pada pria. *Jurnal Ilmiah Kesehatan Sandi Husada*, 10(1):31-40.

Sak ME, Soydinc HE, Sak S, Evsen MS, Alabalik U, Akdemir F. 2013. The protective effect of curcumin on ischemia-reperfusion injury in rat ovary. *International Journal of Surgery*, 11:967-970.

Setyaningsih A, Puspita D, Rosyidi MI. 2013. Perbedaan kadar ureum & kreatinin pada klien yang menjalani hemodialisa dengan *hollow fiber* baru dan *hollow fiber re-use* di RSUD Ungaran. *Jurnal Keperawatan Medikal Bedah*, 1(1):15-24.

Shahrajabian MH, Sun W, Cheng Q. 2020. Chemical components and pharmacological benefits of Basil *(Ocimum basilicum):* A review. *International Journal of Food Properties*, 23(1):1961-1970.

Sinaga L, Hardiani, Prihanto PH. 2017. Faktor-faktor yang mempengaruhi tingkat fertilitas di perdesaan (Studi pada Desa Pelayangan Kecamatan Muara Tembesi Kabupaten Batanghari). *Jurnal Paradigma Ekonomika*, 12(1):41-48.

Sirotkin AV, Kadasi A, Stochmalova A, Balazi A, Foldesiova M, Makovicky P. 2018. Effect of tumeric on the viability, ovarian folliculogenesis, fecundity, ovarian hormones and response to luteinizing hormone of rabbits. *Animals*,12(6):1242-1249.

Sunanda P, Panda B, Dash C, Padhy RN, Routray P. 2014. Effect of age and abstinence on semen quality: a retrospective study in a teaching hospital. *Asian Pacific Journal of Reproduction*, 3(2):134-141.

Suryaningsih NM, Dewi IAT, Suksmawati NKA, Putri NPRA, Febrianti NM, Warditiani NK. 2017. Pengaruh kadar SGOT dan SGPT dan morfologi hepar tikus putih betina wistar pada pemberian isolat andrografolid. *Jurnal Farmasi Udayana*, 6(1):34-38.

Thadani S. 2015. Renoprotective effect of *Ocimum sanctum* in comparision with olmesartan medoxomil and pitavastatin in metformin treated diabetic rats. *International Journal of Pharmaceutical Sciences and Research*, 6(10):4433-4441.

Tomao F, Russo GL, Spinelli GP, Stati V, Prete AA, Prinzi N, *et al.* 2014. Fertility drugs, reproductive strategies and ovarian cancer risk. *Journal of Ovarian Research*, 7(51):1-8.

Wicaksono AW, Trilaksana IGNB, Laksmi DNDI. 2013. Pemberian ekstrak daun kenangi *(Ocimum basilicum)* terhadap lama siklus estrus pada mencit. *Indonesia Medicus Veterinus*, 2(4):369-374.

Yanti L. 2018. Faktor determinan kejadian abortus pada ibu hamil: *Case control study*. *Medisains: Jurnal Ilmiah Ilmu-Ilmu Kesehatan*, 16(2):95-100.