



## RESEARCH ARTICLE

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## Effect of Extract Meat Dates (*Phoenix dactylifera L.*) to Oxytocin Levels in Pregnant Mice (*Mus musculus L.*)

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### ABSTRACT

The process of spontaneous labor is sensitive to the oxytocin hormone that causes uterine smooth muscle contraction as a receptor for the start of labor. Dates contains source of carbohydrates are simple sugars, iron, potassium, selenium, calcium, and flavonoids. The purpose of this study was to determine the effect of date's extracts (*Phoenix dactylifera L.*) to the oxytocin hormone day 19 of gestation age of mice (*Mus musculus L.*). This experiment devide dose of date extract into four groups, group I : control (no treatment), group II: 3 dates (3.12 mg/kg), group III 5 dates (5.2 mg/kg), and group IV 7 dates (7.28 mg/kg) to the oxytocin hormone. The research method is done by extracting palm ajwa with methanol. Treat made orally at the age of 14-19 days gestation. Measurement of oxytocin levels using ELISA at the age of pregnancy 19 days, showed the average number of levels of the oxytocin hormone in group I in the amount of 126.494 ng / L, the second group is equal to 124.169 ng / L, group III amounting to 129.041 ng / L, and group IV is equal to 132.252 ng / L. Overall extract dates with various doses of the treatment led to increased levels of the oxytocin hormone in mice. However, these increases did not show a significant effect, although the hormones oxytocin on uterine tissue of mice kept rising.

**Keywords:** Dates extract, Oxitocin levels, Pregnant mice

### INTRODUCTION

Labor is the process expulsion of conception from the uterus when uterine contractions became more frequent and lower uterine segment (cervical) thinner and having regular contractions every 2-5 minutes. Factors of labor is the power of the mother, fetal position, passeege of birth , and hormonal. Hormonal factors is mainly a decrease in estrogen and progesterone levels 1-2 weeks before delivery, can increase oxytocin and prostaglandins levels. Spontaneous labor very sensitive to the oxytocin hormone (Oxorn & Forte, 2010). Many the ending of progress labor with cesarean section. This risk can minimalizer with eating and drinking during labor procces (Lowe, 2007).

Oxytocin is a hormone produced by the posterior pituitary (neurohypophysis). The oxytocin is also known as the love hormone, this hormone is secreted during sexual activity, male and female orgasm, labor and breastfeeding. At the start of delivery of the hormone oxytocin can cause uterine smooth muscle contraction. Oxytocin receptors in the uterus are 100 times more in late pregnancy. Labor begins with the dilated cervix and then neural reflex will begin stimulates oxytocin release and caused uterine contractions. When production of the hormone oxytocin during labor decreases, resulting in birth mother experiencing his or abnormal uterine inertia (uterine contractions) inadequate. If this condition is not immediately get proper treatment can have an impact on both the mother and the death of the fetus (Saifuddin, et al., 2010). The hormone oxytocin in normal labor is very important.

There are times when the pregnancy to be terminated on medical indications including induction of labor and caesarea section. Section caesarea in Indonesia 2006 by 25-30% in the Government hospital and 30-80% in the private hospital of total deliveries. Immanuel Hospital in Bandung in 2010 is the highest indication of uterine inertia (42.8%) in 2012 at the Hospital of Semarang in 2012 the incidence of uterine inertia that is

40.04%. Induction of Labor can occur 15% to 25% of the number of pregnancies on medical indications pregnancy through time due to inadequate uterine contractions or uterine inertia (Manuaba, 1998).

*Phoenix dactylifera L.* or palm fruit are one source of carbohydrates, which contained simple sugars such as glucose, fructose and sucrose. Besides the palm fruit also contain iron, potassium, selenium, calcium, and vitamins such as vitamin C, B1, B2, A, riboflavin, niacin, flavonoids which are antioxidants. Palm fruit also contain saturated fatty acids and unsaturated such as oleic acid and linoleic acid which affect the production of prostaglandins (Kordi, et al., 2014). Palm fruit has much glucose can used to source of production energy during labor.

Several studies review the benefits of dates and delivery of which is the provision of syrup of palm honey effectively accelerate the process of opening the active period or start opening 4 through the birth process, so that the normal birth process may take more (Kordi and Colleagues, 2010). Palm fruit consumption effect can also be seen in post matur pregnancy. pregnant with gestational age of 36 weeks consumption of dates has a significant effect in cervical dilatation compared with those not taking the palm fruit and significant results were also obtained on the time of rupture of membranes, in women who consume dates compared with no consumption (Al-Kuran, et al., 2011). Besides being able to speed up the process of opening the labor consumption of dates also can reduce the incidence of postpartum hemorrhage. Research by Khadem, et al. (2007) using 50 grams of dates which is equivalent to 7 gram of date palm fruit can prevent bleeding in women after childbirth. This study will be varied dosing palm fruit extract 3 seeds (3.12 mg / kg in mice), 5 seeds (5.2 mg / kg in mice) and 7 seed (7.28 mg / kg mice) and visible influence on the hormone oxytocin in pregnant mice (*Mus musculus L.*)

## METHODS

### Materials

Dates ajwa, methanol, methylene blue, NaCl 0.9%, Thermoscientific Stirring Hot Plate, Thermo-Heratherm Oven, Heidolph Rotary Evaporator Hei-VAP Advantage Hand lift G3, Giemsa, vaccutainer red, micropipette (0.5  $\mu$ L - 1000  $\mu$ L) Biopetee, Thermo Centrifuge, ELISA (Biochrom) EZ Read 400, Microplate Strip Washer 80-4000-10, Laboratory freezer TSC1390D Heraeus, mouse oxytocin kit (Bioassay Technology Laboratory), Binocular microscope Nikon E100.

### Preparation

Initial treatment is the selection of dates ajwa has good quality (black and round shape). Date palm fruit is separated from the seeds. A date will be cut into small pieces to increase the surface area and dried at room temperature until the water content is reduced by 8-10%. Next procedure is blend date palm until smooth.

### Extraction

A dates that already has a constant weight extracted with methanol at temperature 80°C. The extraction process is during for 3x24 hours. Results of the extraction was filtered with Whatman 41. Furthermore, the solvent was evaporated by using a rotary evaporator with the temperature and pressure in order to obtain extracts of dates. Palm fruit extract was analyzed by FT-IR and GC-MS to determine the compounds contained in the extract.

### Treatment

Pregnant mice divided into four groups contains 6 female mice/groups. Dates extract solution orally using a needle sonde with a volume of 0.2 ml administered daily at 14 days of age pregnancy up to 19 days, with variation extract concentrations. Group I is a control group that was not treated, the second group is a group that was treated 3.12 mg / kg extract dates, group III was treated 5.2 mg / kg of dates extracts, Group IV was treated 7.28 mg / kg of dates extracts.

### Analysis

On the day of gestation to 19 mice were dissected and blood was taken intracardiac. The blood tested with ELISA use mouse oxytocin kit from Bioassay Technology Laboratory and analyzed by ANOVA.

## RESULTS

Ajwa palm extraction results were analyzed by FTIR to see the functional groups present in the extract and GC-MS to determine the content of the compounds contained in extracts of dates ajwa. FTIR spectra are shown in Table 1 and Figure 1.

Table 1. Peaks extracts of dates ajwa

No	Functional Group	Wavenumber (Cm <sup>-1</sup> )	Intensity
1	Alkohol (-OH)	3650-3200	Wide
2	Alkana (sp <sup>3</sup> C-H)	2960-2850	Sharp
3	Alkena (C=C)	2119,17	Sharp
4	Karbonil (C=O)	1635,9	Sharp
5	C-C (sp <sup>3</sup> )	1384,10	Wide
6	C-O eter	1257,11	Wide

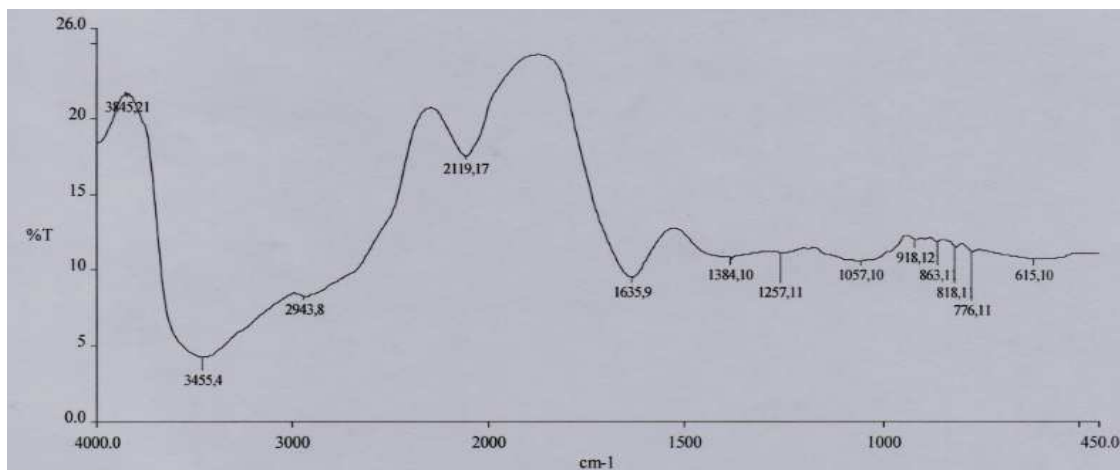


Figure 1. FTIR spectra extracts of dates ajwa

FTIR spectra of the extracted compounds showed characteristic for several functional groups, in the wave number 3650-3200 cm<sup>-1</sup> with a widened showed absorption peaks characteristic stretching vibration of functional groups hydroxy (OH), wave numbers of 2960-2850 cm<sup>-1</sup> shows a typical absorption stretching vibration aliphatic CH functional groups on the methyl and methylene, wave number of 2119 cm<sup>-1</sup> shows a typical absorption of functional groups alkene C = C be supported absorption at wave number 918.12 cm<sup>-1</sup>, 863.1 cm<sup>-1</sup>, 818.1 cm<sup>-1</sup>, 776.11 cm<sup>-1</sup> in the area of finger print that indicates vibration buckling = CH, wavenumber of 1635.9 cm<sup>-1</sup> shows a typical absorption stretching vibration of the carbonyl functional group C = O, waves numbers of 1384.10 cm<sup>-1</sup> shows a typical absorption C-C (sp<sup>3</sup>) functional group it is supported by the presence of functional groups aliphatic CH, wavenumber on 1257.11 cm<sup>-1</sup> shows a typical vibration absorption buckling CO ether functional groups. From the analysis of the functional groups can be predicted that the extract contained flavonoid or phenolic compounds. It is characterized by the uniqueness of the phenolic compounds or flavonoids have O-H groups and some aromatic rings which is characterized by the functional group C = C. Functional groups FTIR data is used as supporting data for subsequent analysis in the determination of the active compounds contained in extracts of dates ajwa.

The results of the analysis blood to the oxytocin hormone levels with various doses treatment using ELISA can be seen in Table 2.

Table 2. Effect of extract dates (*Pheonix dactylifera L*) against oxytocin hormone levels in pregnant mice (*Mus musculus L*).

No	Group I: Control	Group II: 3,12 mg/kgBB	Group III: 5,20 mg/kgBB	Group IV: 7,28 mg/kgBB	$\rho$
1	104.294	105.955	130.204	128.543	0,792
2	131.200	121.567	125.221	161.760	
3	133.193	114.924	130.204	105.291	
4	124.889	143.490	124.224	113.595	
5	121.567	133.525	141.830	142.162	
6	143.823	125.553	122.564	142.162	
$\Sigma$	126.494 <sup>a</sup>	124.169 <sup>a</sup>	129.041 <sup>a</sup>	132.252 <sup>a</sup>	

*P.value* oxytocin hormone levels ng/L

<sup>a</sup> = Show Significanci from ANOVA

A relationship date extracts doses 3.12; 5.20; 7.28 mg / kg with of the oxytocin hormone levels can be Seen on Figure 2.

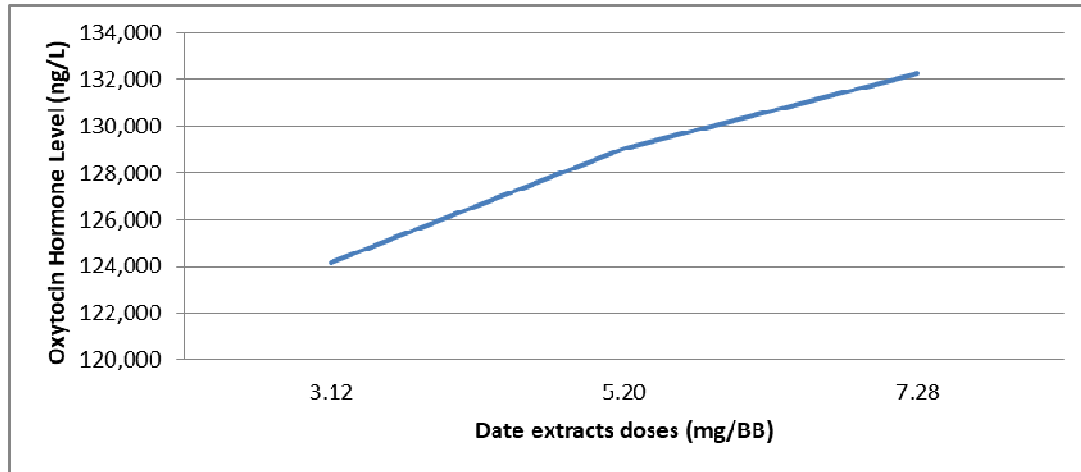


Figure 2. A relationship date extracts doses with of the oxytocin hormone levels

The results of the analysis oxytocin hormone levels using ELISA has displayed on Table 1 and Figure 1 indicates that the control group had an average value of the oxytocin hormone levels 126.494 ng/L, group II (3.12 mg / kg) had an average value of the oxytocin hormone levels 124.169 ng / L, group III (5.20 mg / kg) had an average levels of the oxytocin hormone levels 129.041 ng/L, and group IV (7.28 mg / kg) had an average levels of the oxytocin hormone levels 132.252 ng / L. If the views of the average value oxytocin levels in the blood of the mice in each dose treatment group showed an increase. After that, the data is processed by using SPSS to determine the normality of the data, the Kolmogorov-Smirnov test was used, the results show P value  $0.552 > \alpha$  it shows that the data obtained normal distribution. Then to determine the homogeneity of the data using homogeneity test, the result P.value  $0.13 > \alpha$  it shows that the data is homogen. Therefore is used of Oneway ANOVA test, results the value of  $p > 0.792$  it shows that there is no significant difference between the treatment groups.

## DISCUSSION

Based on the results of the ELISA test, extract dates with various doses 3.12; 5.20 and 7.28 mg / kg body weight mice to the oxytocin hormone levels continue to rise, this can be seen in Figure 1. Various dose extract dates that increased the levels of the oxytocin hormone is a sign that not achieving the optimum dose extract. The optimum dose is reached when there is no more change in the concentration levels of the oxytocin hormone to increasing doses of the extract a date given in mice. To determine the optimum dose of the extract of a date on the levels of the hormone oxytocin need a wider dose range.

The analysis test showed no significant difference between the treatment groups, it relates to the regulatory role of the oxytocin hormone in the body. There are several factors that can affect hormone levels in the blood that is the half-life of the oxytocin in the blood that is only about 20 minutes, the loss of hormones in the blood circulation can be caused by the process of destruction metabolic by target tissues, binds to the target tissue, in excreted by the liver into bile, and excreted by the kidneys into the urine. The hormone sometimes degraded the target cells via the enzymatic process that causes endocytosis of hormone receptor complex on the cell membrane. These hormones then undergoes metabolism in the cells and its receptor is usually reused by the cell membrane.

Hormones are bound to plasma proteins disappear from the bloodstream longer and it is possible to remain in circulation for a few days. In this case the hormone oxytocin works in a way bound by the target cell receptor that is on the uterus. Hormonal receptor is a protein-size in each cell usually has 2000 to 100,000 receptors (Al-Kuran, et al., 2011). Each of these receptors also have a specificity at single hormone. Target tissue oxytocin hormone in this study is muscular uterine cells whose activity is strongly influenced by the oxytocin hormone. So it could be possible that the oxytocin hormone, which is produced by the posterior pituitary gland directly binds to receptors on the surface of cells in the uterine tissue, so that the oxytocin hormone which is dissolved in the blood results were not significant (Khadem, et al., 2007).

The concentration of the hormone needed to regulate the process of metabolism and endocrine function of labor is very small. The concentration in the body ranges between 1 picogram. Usually the secretion of

hormones measured in micrograms or milligrams per day. Once in production, and into the blood circulation (Kordi dan Collegues, 2010). Number of hormone receptors in target cells is usually not constant every day or even every minute. Receptor proteins themselves are usually inactive or destroyed during these receptors function. And on the other hand these receptors can also be reactive or can be reshaped with the formation mechanism of the protein inside the cell. The increase concentration of hormones and increased binding of hormone to the target cell receptors can sometimes lead to a reduced number of receptor activation. But there are also some hormones which can lead to increased regulation of intracellular signaling proteins (Rahmadi, 2010). Which can induce hormonal stimulation higher than normal formation of the receptor. Or it can lead to a greater ability of the receptor to interact with hormones, causing the target tissue progressively more sensitive to the effects of hormone stimulation. This is why there are some mice in the treatment group IV with treated dose (7.28 mg / kg body weight mice) experienced a spontaneous birth dates before the specified time. So basically the hormones oxytocin on uterine tissue of mice increased, although in very small quantities and with varying levels of very little anyway, because the activity of a hormone in order to carry out its function only requires 1 picogram only (Guyton & Hall, 2006).

### CONCLUSION

Measurement of oxytocin levels using ELISA at the age of pregnancy 19 days, showed the average number of levels of the oxytocin hormone in group I in the amount of 126.494 ng / L, the second group is equal to 124.169 ng / L, group III amounting to 129.041 ng / L, and group IV is equal to 132.252 ng / L. Overall extract dates with various doses of the treatment led to increased levels of the oxytocin hormone in mice. However, these increases did not show a significant effect, although the hormones oxytocin on uterine tissue of mice kept rising.

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