Aphrodisiac Effects of Areca Fruit in Erectile Dysfunction Rat Model
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ABSTRACT

Background
Erectile Dysfunction (ED) cases are quite high in both women and men and increase with age. Areca fruit, ginseng and purwoceng are plants that have been traditionally used to increase male vitality.

Objective
To analyze the efficacy of areca fruit, ginseng and purwoceng in sexual activity and hormonal level in erectile dysfunction rat model.

Methods
This is in vivo experimental research study with pre and post-test control group design located in the laboratory of animal house and the biomolecular laboratory Faculty of Medicine Sriwijaya University. The subjects of this study were albino rats (Rattus norvegicus), Wistar strains, divided into 6 groups are negative control, Sildenafil, Areca Fruit Extract (AFE) 50 mg/kgBW, AFE 100 mg/kgBW, Combination of Areca Fruit, Ginseng and Purwoceng (AGP) 50 mg/kgBW and AGP 100 mg/kgBW. Female rat was injected by giving 500 mg/100 g of subcutaneous progesterone and 10 μg/100 g of BB benzoate 48 hours before mating so that female mice enter the esterus phase.

Results
It was found that Combination of Areca fruit, Ginseng and Purwoceng (AGP) group 50mg/kgBW significantly improved testosterone levels compared to sildenafil, while single areca fruit (AFE) dose 50mg/kgBW increased FSH and LH levels as well as sildenafil statistically.

Conclusion
The combination of areca fruit, ginseng and purwoceng is effective as treatment for erectile dysfunction.

Keywords: areca fruit, erectile dysfunction, FSH, ginseng, LH, purwoceng, testosteron

Introduction
Sexual needs support happiness for a partner throughout his life. Then every disturbance of sexual life will surely interfere with the happiness and life of the couple. Various diseases such as illness, age, tiredness and life stress often cause disruption in sexual life so that the couple's inability to achieve sexual satisfaction appears. This disorder is called sexual dysfunction.
The results of research by Edward O. Laumann, et al. (1999) conducted in the United States stated that 14.8% of men aged 18-59 years experience a lack of sexual desire. Whereas 30.6% experience a climax that is too fast which can be caused by premature ejaculation. As many as 10.2% feel difficulty in achieving or maintaining an erection, commonly called erectile dysfunction (ED). Sildenafil is an oral medication to treat erectile dysfunction, which is quite successful, but there are still many side effects. Sildenafil increases sensitivity to light, blurred vision, color blindness (blue-green) in 3-10% of patients. In addition, for patients who consume drugs that contain organic ingredients, if taken together with Sildenafil will increase the risk of systemic hypotension that endangers the lives of consumers. So that another alternative treatment is needed using traditional medicine. Areca fruit (Areca catechu) is a plant that has been traditionally used to increase male vitality. In addition, purwoceng plants (Pimpinella priatjan) and ginseng (Javanese Som) are also known to the community for their ability to spur spermatogenesis and efficacy to increase male vitality.

The combination of several types of herbs has been started by the ancient Indonesian ancestors with a powerful herb known as "herbal medicine". In this study, it was further developed a combination of 3 types of herbs that would be tested experimentally at the preclinical level, followed by the determination of the active molecular formula and could be accounted for and finally formulated in a product formulation of a tested herbal drug (fitopharmaca) which could be consumed accordingly the indication.

**Method**

The research design is an in vivo experimental study with pre and post test with control group. The subject of study was Male Rattus norvegicus Wistar strain, divided into 6 groups (5 rats each group) were negative control, Sildenafil, Areca Fruit Extract (AFE) 50 mg/kgBW, AFE 100 mg/kgBW, Combination of Areca Fruit, Ginseng and Purwoceng (AGP) 50 mg/kgBW and AGP 100 mg/kgBW. It was injected by testosterone 5 mg/KgBW for 21 days to induce erectile dysfunction. The female rats was injected injected by giving 500 mg/100 g of subcutaneous progesterone and 10 μg/100 g of BB benzoate 48 hours before mating so that female mice enter the esterus phase.
Simplisia was obtained from Gandus Plantations and Natural Herbal Medika Yogyakarta. Aquous extract is made by infusion method from simplicia from each medicinal plant, and evaporated it by rotary evaporator.

The parameters examined include testosterone, FSH and LH by the sandwich ELISA method. Examination of testosterone, FSH and LH levels was carried out 2 times, namely pre-treatment and post-treatment.

Result

**Effectiveness on Testosterone, FSH and LH Level Post Treatment**

Testosterone, FSH and LH levels were examined before and 14 day post treatment, results were obtained there are significant differences in testosterone, FSH and LH levels before and after treatment in all groups (p < 0.05).

However, the highest testosterone levels were found in the AGP 50mg/kgBW group, the highest FSH level in the AFE 50mg/kgBW group and the highest LH level increase in the AFE 50mg/kgBW group.

| Parameter | Group                  | Pre Treatment | Post Treatment | p value |
|-----------|------------------------|---------------|----------------|---------|
| Testosteron | Negative Control       | 0.43 ± 0.016  | 0.517 ± 0.018  | 0.001   |
|           | Sildenafil             | 0.41 ± 0.007  | 0.624 ± 0.034  | 0.000   |
|           | AFE 50mg/kgBW          | 0.43 ± 0.019  | 0.639 ± 0.044  | 0.000   |
|           | AFE 100mg/kgBW         | 0.44 ± 0.023  | 0.626 ± 0.011  | 0.000   |
|           | AGP 50mg/kgBW          | 0.42 ± 0.010  | 0.873 ± 0.017  | 0.000   |
|           | AGP 100mg/kgBW         | 0.41 ± 0.016  | 0.789 ± 0.019  | 0.000   |
| FSH       | Negative Control       | 0.33 ± 0.019  | 42.47 ± 1.175  | 0.000   |
|           | Sildenafil             | 0.31 ± 0.012  | 10.43 ± 1.175  | 0.000   |
|           | AFE 50mg/kgBW          | 0.33 ± 0.030  | 84.97 ± 1.749  | 0.000   |
|           | AFE 100mg/kgBW         | 0.34 ± 0.016  | 38.47 ± 1.094  | 0.000   |
|           | AGP 50mg/kgBW          | 0.32 ± 0.023  | 59.03 ± 3.439  | 0.000   |
|           | AGP 100mg/kgBW         | 0.31 ± 0.028  | 75.22 ± 2.112  | 0.000   |
| LH        | Negative Control       | 0.24 ± 0.031  | 1.468 ± 0.141  | 0.000   |
|           | Sildenafil             | 0.21 ± 0.008  | 2.397 ± 0.227  | 0.000   |
|           | AFE 50mg/kgBW          | 0.22 ± 0.012  | 2.493 ± 0.221  | 0.000   |
|           | AFE 100mg/kgBW         | 0.23 ± 0.015  | 2.013 ± 0.126  | 0.000   |
|           | AGP 50mg/kgBW          | 0.20 ± 0.039  | 1.788 ± 0.149  | 0.000   |
|           | AGP 100mg/kgBW         | 0.24 ± 0.020  | 2.013 ± 0.170  | 0.000   |

*Paired T Test*
Figure 1. Testosteron Level Pre and Post Treatment

Figure 2. FSH Level Pre and Post Treatment
Comparison of Effectiveness on Testosteron, FSH and LH Level Post Treatment

Testosteron Level

Testosteron, FSH and LH levels between groups were then compared. By conformity test using Post hoc showed that there was no difference in testosterone levels in the sildenafil group with AFE 50mg/kgBW and AFE 100mg/kgBW.

Table 2. Conformity Test of Testosteron Level Post Treatment

|               | Negative | Sildenafil | AFE 50 | AFE 100 | AGP 50 | AGP 100 |
|---------------|----------|------------|--------|---------|--------|---------|
| Negative      | 0.000    | 0.000      | 0.000  | 0.000   | 0.000  | 0.000   |
| Sildenafil    | 0.009    | 0.946      | 1.000  | 0.971   | 0.000  | 0.000   |
| AFE 50        | 0.000    | 0.971      | 0.000  | 0.000   | 0.000  | 0.000   |
| AFE 100       | 0.000    | 1.000      | 0.000  | 0.000   | 0.000  | 0.000   |
| AGP 50        | 0.000    | 0.000      | 0.000  | 0.000   | 0.000  | 0.000   |
| AGP 100       | 0.000    | 0.000      | 0.000  | 0.000   | 0.000  | 0.000   |

*Post Hoc Test
FSH Level

In addition, there were results of differences in FSH levels between the sildenafil group and all treatment groups, both single areca fruit or combination of areca fruit, ginseng and purwoceng.

Table 3. Conformity Test of FSH Level Post Treatment

|                | Negative | Sildenafil | AFE 50 | AFE 100 | AGP 50 | AGP 100 |
|----------------|----------|------------|--------|---------|--------|---------|
| Sildenafil      |          | 0.000      | 0.000  | 0.039   | 0.000  | 0.000   |
| AFE 50         | 0.000    |            | 0.000  |         | 0.000  | 0.000   |
| AFE 100        | 0.039    | 0.000      |        | 0.000   |        | 0.000   |
| AGP 50         | 0.000    | 0.000      | 0.000  |         |        | 0.000   |
| AGP 100        | 0.000    | 0.000      | 0.000  | 0.000   | 0.000  |         |

*Post Hoc Test

LH Level

The next parameter is the LH level. In this study, there was no difference LH level between the sildenafil and AFE 50mg/kgBW. In addition, there was no difference in LH levels in the AFE 100mg/kgBW with AGP 50 mg/kgBW and AGP 100mg/kgBW.

Table 4. Conformity Test of LH Level Post Treatment

|                | Negative | Sildenafil | AFE 50 | AFE 100 | AGP 50 | AGP 100 |
|----------------|----------|------------|--------|---------|--------|---------|
| Sildenafil      |          | 0.000      | 0.000  | 0.000   | 0.081  | 0.001   |
| AFE 50         | 0.000    |            | 0.953  | 0.024   | 0.000  | 0.024   |
| AFE 100        | 0.001    | 0.024      | 0.003  |         | 0.003  |         |
| AGP 50         | 0.081    | 0.000      | 0.000  | 0.365   | 0.365  | 1.000   |
| AGP 100        | 0.001    | 0.024      | 0.003  | 1.000   | 0.365  |         |

*Post Hoc Test

Discussion

In this study showed that there was no difference in testosterone levels in the sildenafil group with Areca fruit extract (AFE) 50mg/kgBW and 100mg/kgBW. This result accordance with Reena's research which shows that ethanol extract of young areca fruit seeds (Areca cathecu) at a dose of 150 mg/kg BW increases libido/sexual activity in male white rats. However, the highest testosterone levels were found in the combination of Areca fruit, Ginseng and Purwoceng (AGP) group 50mg/kgBW, this condition shows the effectiveness of the
combination of Areca fruit, Ginseng and Purwoceng (AGP) group 50mg/kgBW is better in increasing testosterone levels than sildenafil.

In a condition of decreased libido (sexual arousal) testosterone deficiency occurs or in postmenopausal conditions (women) or andropause (men over 60 years) characterized by a decrease in some sex hormones including testosterone. Areca fruit (Areca cathecu) is a plant that has been traditionally used to increase male vitality. In addition purwoceng plants (Pimpinella pruatjan) and ginseng (Javanese Som) are also known to the community for their ability to spur spermatogenesis and efficacy to increase male vitality. For the FSH and LH parameters, the highest increase in the Areca fruit extract (AFE) 50mg/kgBW group and statistically there was no difference in LH level between sildenafil and Areca fruit extract (AFE) 50mg/kgBW. However, for FSH levels all groups were different from sildenafil.

**Conclusion**

Combination of Areca fruit, Ginseng and Purwoceng (AGP) group 50mg/kgBW significantly improved testosterone levels compared to sildenafil, while single areca fruit (AFE) dose 50mg/kgBW increased FSH and LH levels as well as sildenafil statistically.

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