



## Aphrodisiac Activity of Ethanol Extract of *Cratoxylum sumatranum* (Jack) Blume Stems on Isolated Rat *Corpus cavernosum*

Sjarif Ismail<sup>1,2</sup>, Meiliati Aminyoto<sup>3</sup>

<sup>1</sup> Research Center on Drugs and Public Health Mulawarman University, Indonesia

<sup>2</sup> Pharmacology Laboratory, Faculty of Medicine Mulawarman University, Indonesia

<sup>3</sup> Public Health Laboratory, Faculty of Medicine Mulawarman University, Samarinda

\*Corresponding author email: [ismail@fk.unmul.ac.id](mailto:ismail@fk.unmul.ac.id) and [ismail8997@yahoo.com](mailto:ismail8997@yahoo.com)

### ABSTRACT

*Cratoxylum sumatranum* (Jack) Blume of the Hypericaceae family is known as “Bentaleng” by Dayak Benuaq. In ethnobotany, *Cratoxylum sumatranum* stems (CSS) is used as energy drink or aphrodisiac, but its effect has not been scientifically proven. The objective of this research was to evaluate the aphrodisiac activity of CSS extract by screening the aphrodisiac activity *in vitro*. CSS was collected from Kutai Kertanegara Regency, East Kalimantan Province. Extraction was by maceration with ethanol solvent for three days. Remaceration was done twice. *In vitro* screening of aphrodisiac activity used isolated rat *corpus cavernosum*. The organ was placed into a 10 mL chamber containing *Krebs-Henselheit* solution at pH 7.4, 37°C and aerated with carbogen gas. After acclimation, a contraction test was performed with phenylephrine solution and after reaching the peak of contraction at plateau the Control (solvent extract) or CSS ethanol extract was administered at cumulatively increased concentration. Vasodilation activity was known if the contraction response was decreased after the extract’s administration and expressed in percent contraction with negative value. The result of this study showed that CSS ethanol extract induce vasodilatory response on rat *Corpus cavernosum* blood vessels. Vasodilation activity was increasing with increasing concentration of extract given compared to Control. This study concluded that CSS ethanol extract has aphrodisiac activity and it act directly through the vasodilatation of blood vessels in the rat *corpus cavernosum*.

**Keywords:** *Cratoxylum sumatranum*, aphrodisiac, *in vitro*, *corpus cavernosum*, vasodilation

---

Submitted on: 3 January 2018

Accepted on: 16 July 2018

---

DOI: <https://doi.org/10.25026/jtpc.v4i3.150>

### INTRODUCTION

Erectile dysfunction (ED) is a sexual dysfunction disorder on men due to

the inability to achieve and maintain an erection of the penis for a satisfactory sexual relationship [1]. Prevalence of ED

in the world is estimated at about 2% in adult men <40 years old and reaches 86% in older men >80 years [2]. There are many options to deal with ED, phosphodiesteration inhibitor under the name sildenafil is most widely used but its raw materials are still imported and the price is expensive so the national pharmaceutical industry is difficult to develop. The global drug market for erectile dysfunction through 2020 is promising because it will reach a market size of 4 billion dollars and sildenafil (Viagra®) dominates the market by 47% in 2014 [3,4]. Research for invention of new drug's raw material to overcome ED is urgently needed for the sake of national pharmaceutical needs in order to compete and enlarge its market share.

A potential plant to be studied is *Cratoxylum sumatranum* (Jack) Blume (*C. sumatranum*) from the Hypericaceae family, which is a wild plant and in abundance in East Kalimantan secondary forest around Suharto Hill, Kutai Kertanegara Regency. Their other name are *C. clandestinum* Blume, *C. floribundum* (Turcz.) Fern. Vill., *C. hornschurchii* Blume, *C. hypericinum* Merr., *C. racemosum* Blume [5]. Its local name are Haremeng and Ki remeng (Sundanese); Arong, Klampet, Lampet, Marong, Urang-urangan (Javanese); Bentalong (Ethnic Dayak Benuaq, East Kalimantan). Medicinal plants *Cratoxylum sp.* ethnobotanically are used to treat abdominal pain (bark), burns (leaves), scabies and ulcers (exudat), fever (leaves and stems) [6]. From ethnobotanic search in East Kalimantan, *C. sumatranum* stems were used to increase male virility or aphrodisiac [7], but this effect has not been scientifically proven. The aim of this research was to study the aphrodisiac activity of *C. sumatranum* stem extract by screening for its aphrodisiac activity *in vitro*.

## EXPERIMENTAL SECTION

### Chemicals and Materials

Ethanol, Calcium chloride, Glucose, Magnesium chloride, Potassium chloride, Potassium dihydrogen phosphate, Sodium chloride, Sodium bicarbonate, Potassium chloride, and DMSO from Merck; Phenylephrine (PE) and Methacholine (META) from Sigma-Aldrich. All other reagents used in the study were of analytical grade.

### Animal

Young male Wistar rats (4-6 month old) weighing 200-250 g were obtained from the Animal House Unit, Faculty of Medicine, Mulawarman University. The animal had free access to food and drinking water, and were kept at room temperature of  $25 \pm 1^\circ\text{C}$ . Study protocol was reviewed and approved by the institutional ethics committee of Faculty of Medicine Mulawarman University before the start of the work.

### Plant material and extraction

*C. sumatranum* stems was picked from Soeharto Hill, Kutai Kertanegara Reagency of East Kalimantan Province and authenticated by the taxonomist of Forestry Faculty of Mulawarman University. Specimen samples were stored at Pharmacology Laboratory, Faculty of Medicine Mulawarman University repository with specimen number CS01/XI/2016. The stems were washed, cut in small pieces and dried in an oven at  $60^\circ\text{C}$ , then ground into powder. Extraction was by maceration using ethanol solvent with a ratio of 1:4 for three days. Remaceration was done twice. The extract was dried in a vacuum evaporator at  $50^\circ\text{C}$  until a constant yield of 17.1% on repeated weighing was obtained.

### Effects of CSS ethanol extract on *corpus cavernosum*

Six male albino rats were used in this experiment. The animals were anesthetized with Ketamine (100 mg/kg). The rat's isolated *corpus cavernosum* was prepared according to the method described by Keegan *et al.* (1999) and Paskaloglu *et al.* (2004) [8,9]. The penises were removed and the *corpus cavernosa* was carefully dissected in a dish containing chilled *Krebs-Henselheit* solution at pH 7.4 and aerated with carbogen gas (95% O<sub>2</sub> + 5% CO<sub>2</sub>). Each *corpus cavernosum* yielded a single strip of 2x2x15 mm. Strips of rat *corpus cavernosum* placed in a 10 mL organ chamber. Tissue baths containing *Krebs-Henselheit* solution at pH 7.4 and 37°C, aerated with carbogen gas. The rat *corpus cavernosum* strips were connected to isometric force-displacement transducers (model 7003, Ugo Basile), and changes in the tension were recorded continuously by using an octal bridge amplifier and Power Lab/16 SP digital recorder (AD Instrument). Data acquisition and processing were carried out with Chart v.5 software (AD Instrument). Tissues were preloaded with 1 g of tension and allowed to equilibrate for 90 min in *Krebs-Henselheit* solution that was changed at 15 min interval. Each strip was submaximally contracted with PE (10<sup>-5</sup> M). After the contractile response due to PE has stabilized, relaxation responses to the different treatment were assessed as a percentage of the PE-induced contractile responses = ((submaximal contraction with PE only - contraction in the presence of extract) / submaximal contraction with PE only) x 100.

### Data analysis

The results obtained were expressed as mean ± standard error of mean (SEM), data were analyzed statistically using student's *t*-test at significance level of *p*<0.05.

### Result and Discussion

The addition of PE (10<sup>-5</sup> M) to the strip of rat *corpus cavernosum* produced contraction responses. The extracts solvent containing DMSO-ethanol 10% was used as Controls. On the other hand, the *C. sumatranum* stems extract elicited a concentration-dependent vasodilation responses on the PE-precontracted rat *corpus cavernosum* (Fig 1). As the concentration of the extract put into the chamber increased, the vasodilation activity of the *corpus cavernosum* was also increased.

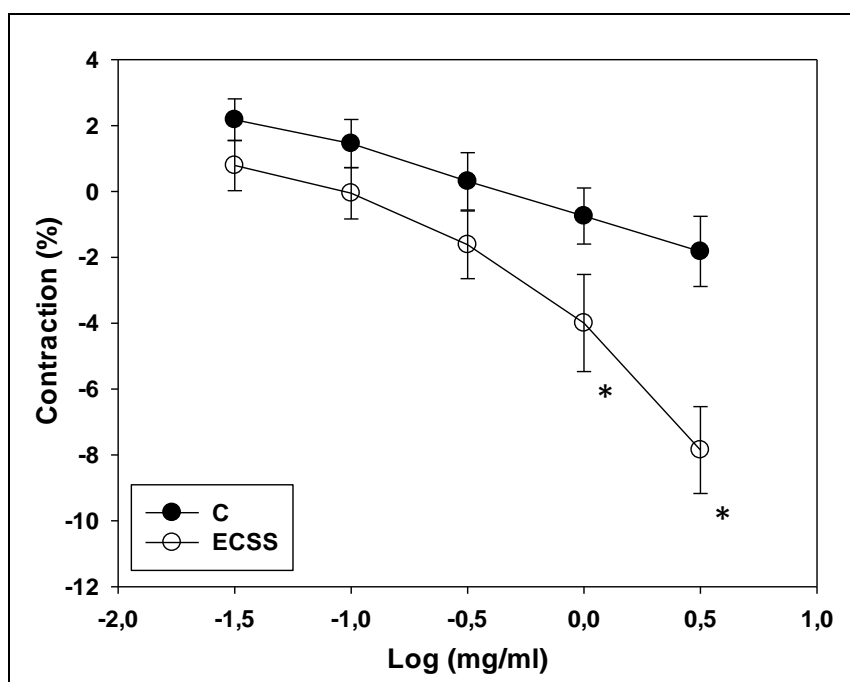
The test results of the effects of Control and *C. sumatranum* ethanol extract on strip of rat *corpus cavernosum* can be seen in the Figure 1. The extract solvent could induce percent contraction with a small negative value. Increasing concentration of the solvent that were put into the chamber containing strip of rat *corpus cavernosum* could cause percent contraction with increasing negative value and at Control concentration which was equivalent to extract concentration of 3 mg/ml, a (-1,82 ± 0.53)% response was obtained. This indicated that the extract solvent could cause mild vasodilation on blood vessels in the *corpus cavernosum*.

*C. sumatranum* stems ethanol extracts could cause percent contraction with a mild negative value. Increasing concentration of extracts administered into the chamber containing the strip of rat *corpus cavernosum* could cause percent contraction with an increasingly negative value and at extract's concentration of 3 mg/ml a response of (-7.85 ± 0.66)% was obtained. This indicated that the extract of *C. sumatranum* stems could cause vasodilation on blood vessels in the *corpus cavernosum*.

The result of statistical test by *t*-test with *p*>0.05 at concentrations of 0.03, 0.1, and 0.3 mg/ml showed no significant difference between the control group and

the *C. sumatranum* stems extract group at the same concentration. The result of statistical test by *t*-test with  $p < 0.05$  at concentration of 1 and 3 mg/ml showed

significant different result between the control group and the *C. sumatranum* stems extract group at the same concentration.



**Figure 1:** Concentration dose curve of CSS extract effect compared to control on an isolated *corpus cavernosum*

Description:  $n=5$  rats. Data is expressed in mean  $\pm$  SEM. Negative results indicates vasodilation response. C = Control (DMSO-ethanol 10%). ECSS = extract of *Cratoxylum sumatranum* stems. \**t*-test was significantly different with  $p < 0.05$  if percent contraction in *corpus cavernosum* was compared with control at same concentration.

Erection on penis occurs due to the helicin arterioles vasodilatation in the *corpus cavernosum* such that the arterial blood flows faster to fill the lacunar spaces on the *corpus cavernosum* causing the penis to become tense. When the helicin arterioles in the *corpus cavernosum* contracts, it causes the arterial blood flow into the lacunar space to be inhibited and so the penis becomes flaccid. The balance between factors affecting vasodilation or vasoconstriction in the lacunar cavities and arteriole smooth muscles in the *corpus cavernosum*

will determine if the penis will be in an erect or flaccid state [10]. Nitric oxide (NO) plays an important role in the erection response, it was released from the vascular endothelium or from the non-adrenergic non-cholinergic neurons (NANC) from the central or peripheral nervous system [11,12]. Nitric oxide synthase (NOS) is an enzyme that converts L-arginine to NO and L-citrulline. NOS is present in the endothelium (eNOS), neuronal tissue (nNOS), and epithelial tissue within the pelvic and urogenital structures of males

[13,14]. eNOS activation by an agonist in the vascular endothelium will produce NO which can diffuse easily into the blood vessels' smooth muscle in the *corpus cavernosum*. NO activates soluble *guanylate cyclases* (sGS) such as those present in the blood vessels which induce *guanosine triphosphate* (GTP) conversion to cyclic *guanosine monophosphate* (cGMP). cGMP stimulates calcium ions out from the blood vessels smooth muscle in the *corpus cavernosum*, resulting in blood vessels vasodilation that causes penis erection.

NO can also be released if there is sexual stimulation or the influence of drugs. Decreased calcium ions in the blood vessels' smooth muscle in the *corpus cavernosum* can also be caused by inhibition of the *phosphodiesterase* (PDE) enzyme. This enzyme converts cyclic *adenosine monophosphate* (cAMP) and cGMP to AMP or GMP. Inhibition of PDE enzyme will cause cGMP levels to remain high such that the blood vessels in the *corpus cavernosum* remain in a state of relaxation that results in more blood coming into the *corpus cavernosum* and the penis will remain erect or tense [15].

This study was still in its early stages to scientifically prove the local ethnic knowledge of local aphrodisiacs. In this study CSS extracts was proved to be aphrodisiacs with direct action mechanisms of causing blood vessels vasodilation in the *corpus cavernosum*. It is necessary to further investigate the action mechanism of blood vessels' vasodilation in the *Corpus cavernosum* on CSS extract's intervention whether it is affected by NO or directly activate sGC and inhibit PDE by administration of NO antagonists or methylene blue as sGC antagonists or PDE antagonists.

## CONCLUSION

The ethanol extract of *C. sumatranum* stems was proven *in vitro* to have an aphrodisiac effect as it could induce vasodilation in the isolated rats *corpus cavernosum*.

## ACKNOWLEDGMENT

The research is entirely funded by the Year 2016 Lecturer Research Grant from Mulawarman University.

## REFERENCES

- [1] NIH Consensus Development Panel on Impotence. 1993. Impotence. *Journal of the American Medical Association*, 270:83-90.
- [2] Prins J, Blanker MH, Bohnen AM, Thomas S, & Bosch JLHR. 2002. Prevalence erectile dysfunction: a systematic review of population-based studies. *International Journal of Impotence Research*, 14:422-432.
- [3] Technavio. 2016. Global erection dysfunction market 2016-2020. SKU: IRTNTR9506, Inviniti Research Limited. Available at: <https://www.technavio.com/report/global-health-and-wellness-global-erectile-dysfunction-market-2016-2020>. Accessed 10/23/2017.
- [4] Grand View Research. 2017. Erectile dysfunction drug market worth \$ 3.2 billion by 2022. Grand View Research Inc. Available at: <http://www.grandviewresearch.com/press-release/global-erectile-dysfunction-drugs-market>. Accessed 10/23/2017.
- [5] The Plant List. 2017. *Cratoxylum sumatranum* (Jack) Blume. The plant list: a working list of all plant species. Available at: <http://www.theplantlist.org/tpl1.1/record/kew-2742440>. Accessed 10/23/2017.

- [6] Heyne K. 1987. Tumbuhan berguna Indonesia. Diterjemahkan oleh Badan Litbang Kehutanan Jakarta. Penerbit: Koperasi Karyawan Departemen Kehutanan. Page 1371-1373.
- [7] Badan Penelitian dan Pengembangan Kalimantan Timur. 2006. Identifikasi dan pengembangan fitokimia tanaman obat unggulan Kaltim. Bidang Ekonomi dan Pembangunan Badan Penelitian dan Pengembangan Provinsi Kaltim. *Laporan Penelitian*.
- [8] Keegan A, Cotter MA, & Cameron NE. 1999. Effects of chelator treatment on aorta and *corpus cavernosum* from diabetic rats. *Free Radical Biology and Medicine Journal*, 27(5-6):536-43.
- [9] Paskaloglu K, Sener G, & Ayançolu-Dülger G. 2004. Melatonin treatment protects against diabetes-induced functional and biochemical changes in rat aorta and *corpus cavernosum*. *European Journal of Pharmacology*, 499(3):345-54.
- [10] Anderson KE. 2011. Mechanisms of penile erection and basis for pharmacological treatment of erectile dysfunction. *Pharmacological Review*, 63:811-859.
- [11] Lue TF. 2000. Erectile dysfunction. *The New England Journal of Medicine*, 342(24):1802–1813.
- [12] Burnett AL. 2006. The role of nitric oxide in erectile dysfunction: implications for medical therapy. *Journal of Clinical Hypertension*, 8(12):53–62.
- [13] Burnett AL, Ricker DD, Chamness SL, Maguire MP, Crone JK, Bredt DS, Snyder SH, & Chang TS. 1995. Localization of nitric oxide synthase in the reproductive organs of the male rat. *Biology of Reproduction*, 52(1):1–7.
- [14] Gonzalez CM, Brannigan RE, Bervig T, Zelner D, Podlasek CA, McKenna KE, & McVary KT. 2001. Protein and gene expression of nitric oxide synthase isoforms I and III in the rat penile shaft. *Journal of Andrology*, 22(1):54–61, 2001.
- [15] Cartledge JS, Minhas I, Eardley, & Morrison JF. 2000. Endothelial and neuronal derived nitric oxide mediated relaxation of corpus cavernosal smooth muscle in a new rat, in vitro model of erectile function. *International Journal of Impotence Research*, 12:213-221.

How to cited this article :

Ismail, S., Aminyoto, M., 2018. Aphrodisiac Activity of Ethanol Extract of *Cratoxylum sumatranum* (Jack) Blume Stems on Isolated Rat *Corpus cavernosum*. *J. Trop.Pharm. Chem.* 4(3); 122-127.