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Indonesian medicinal plants that have the potential to affect testicular function: A Review

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Abstract

The testes are two glandular organs in the male reproductive system responsible for producing gametes called sperm and synthesizing androgen hormone called testosterone. The two functions of the testes are used as parameters for fertility and sexual performance in males. This paper presents the results of research to find plant-derived ingredients that are potential to treat disorders related to testicular function carried out in Indonesia in the last two decades. The inclusions criteria of the papers compiled are: containing the results of research conducted in Indonesia, by Indonesian researchers; have been published both in national and international journals that can be accessed using Google search engine. The results indicated there are numerous plant species that were revealed to have potentials to be developed as contraceptive or anti-fertility agent, pro-fertility ingredient and sexual activity enhancer herbs in males. Given fertility, infertility, and sexual behavior in males are all determined by the function of testes, it can be concluded that the Indonesian medicinal plants studied are containing active substance that have an effect on the testes.

Keywords: Medicinal Plant; Plant Extract; Testicles; Spermatogenesis; Testicular Function; Male Fertility; Sexual Behavior

1. Introduction

The testes are the principal and vital organs in the male reproductive system. There are three main functions of these glandular organs namely: produces spermatozoa, synthesizes testosterone--male sex hormone and participate with the hypothalamus-pituitary unit in regulating reproductive function. Regulation of testicular function involves a feedback loop in which the secretion of pituitary gonadotropins which stimulated by gonadotropin-releasing hormone (GnRH) from the hypothalamus and modulated by testicular hormones. In male vertebrates, in addition to affect fertility, the testicular function plays a central role in the expression of numerous sexually selected traits such as musculature, aggression and sexual behavior [1, 2].

The understanding of the regulation and control mechanism of testicular function is the basis for the development of medicinal materials and techniques to address fertility and sexual problems in males. Currently researches on better management of male reproductive function, especially fertility and sexual problems, are still continuous all over the world [3-5]

The major theme of studies related to testicular function is the search for natural materials, especially those derived from plants, which can be used to control fertility, libido, and sexual behavior. Such research is mostly carried out in developing countries including Indonesia. Apart from its pharmacological benefits, studies conducted by researchers in

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developing countries have contributed a lot of information about the types of plants that have the potential to be used to control the reproductive function of animals and humans [6-9].

Indonesia is one of the tropical countries which is rich in plants that have the potential to be developed as medicinal ingredients [10]. This article presents the results of research on medicinal plants that have the potential to be used as medicinal ingredients to control testicular function in males.

2. Methodology

The terms used in searching papers via internet are: medicinal plant, plant extract, testicles, spermatogenesis, testicular function, male reproductive system, male fertility, sexual behavior. The inclusions criteria of the papers retrieved are that have been published both in national and international journals that can be accessed using Google search engine. All indexing journal databases (Google Scholars, Science Direct, PubMed, Scopus, SCI, DOAJ) were considered, but none of which is prioritized. Only papers containing the results of research conducted in Indonesia, by Indonesian researchers, which were published within the last 20 years (2004 -2023) were compiled.

3. Results and discussion

Research to find plant-derived medicinal ingredients to control male testicular function conducted in Indonesia can be sorted into three types. First, researches aimed to look for herbs having contraceptive or anti-fertility properties. Second, researches intended to look for ingredients that can increase male fertility (pro-fertility). Third, researches with purposes to find bioactive substances that can treat sexual dysfunction disorders in male.

3.1. Plants with anti-fertility properties in male

Medicinal plants that found by Indonesian researchers in the last two decades that having potentials to be developed as contraception agents in male are listed in Table 1.

Table 1 Indonesian medicinal plants suspected of having male contraceptive (anti-fertility) properties

Plant species	Plant family	Preparation	Test animal	Observed effects	Reference
<i>Piper nigrum</i> L	Piperaceae	Fruit ethanol extract	Male wistar rats	Increase serum fsh level Decrease serum lh and testosterone levels Decrease number of spermatocytes, spermatozoa, and motility	11
<i>Imperata cylindrica</i> L.	Poaceae	Rhizome ethanol extract	Male Mice of ddy strain	Decrease serum testosterone levels Disrupt testis interstitial area and seminiferous tubules, Decreased epididymal sperm quality	12
<i>Andrographis paniculata</i> (Burm.f.) Nees	Acanthaceae	Whole plant aqueous extract	Male mice	Decrease sperm normal morphology	13
		Leaf ethanol extract	Male mice	Interfere spermatogenesis in seminiferous tubules, Decrease number of spermatogonium, spermatocyte, spermatid, and spermatozoa	14
<i>Centella asiatica</i>	Mackinlayaceae	Leaf and petiole ethanol extract	Male mice	Decrease spermatogenic cells of seminiferous tubules	15

<i>Azadirachta indica</i> A. Juss	Meliaceae	Aqueous seeds extract	Male Mice of ddy strain	Decrease spermatogenic cells count	16
<i>Pluchea indica</i> L.	Asteraceae	Leaf extract	Male mice	Decrease spermatid cells count	17
<i>Hibiscus rosasinensis</i> Linn.	Malvaceae	Flower methanol extract	Male mice	Decrease in spermatozoacount, motility, normal morphology andviability	18
<i>Psidium guajava</i> L.	Myrtaceae	Leaf ethanol extract	Male Mice of ddy strain	Decrease spermatozoacount, motility, normal morphology andviability	19
<i>Momordica charantia</i> L.	Cucurbitaceae	Ethanol extract	Male mice	Decrease in spermatogenic cells count	20
<i>Carica papaya</i> L.	Caricaceae	Seed ethanol extract	Male albino mice	Decrease viability, motility and normal morphology of spermatozoa.	21
<i>Ceiba pentandra</i> G.	Bombacaceae	Ethanol extract of seeds	Male wistar rats	Increased the expression of p53 protein Reduced the number of leydig cells	22

Based on the data in Table 1 above, there are 11 plant species reported by 12 researchers in Indonesia which exhibit anti-fertility properties in males. Although using different types of plants, the twelve studies have much in common in terms of materials and methods. The extracts that were applied were all crude extracts using more or less the same solvents, namely polar solvents (water, methanol, and ethanol).

The observed and measured research parameters were also almost the same namely: spermatogonia, spermatocytes, spermatids and spermatozoa count, as well as sperm motility, viability, and normal morphology. Only a few measured endocrinological parameters such as serum LH, serum FSH, and serum testosterone as was done by Ekaputri et al. (2018) Widyastuti et al. (2020) [11,12]; and enzymatic parameters as performed by Hendrawan et al. (2019) [22].

Thus the results of the studies presented above are clearly still far from sufficient in terms of quality and utility. One aspect that is important for further and thorough research on medicinal ingredients that are suspected of having anti-fertility properties is the toxicity and side effects of the active ingredients. In-vivo testing of this drug substance is also not sufficient only in animals, but needs to be continued in clinical trials. In addition, the chemical properties of materials, apart from their biological properties, also need to be studied in depth [47, 48]

3.2. Plants with pro-fertility properties in male

Plants that were assumed to have potentials to be developed as enhance and maintain fertility in male can be seen in Table 2.

Table 2 Indonesian medicinal plants having potentials to be used as pro-fertility ingredients

Plant species	Plant family	Preparation	Test animal	Observed effects	Reference
<i>Ficus deltoidea</i>	Moraceae	Ethanol extract of leaves	Male mice	Increase the level of testosterone, LH and FSH, protein, cholesterol, Increase activity of testicular enzymes, Increase activity of the enzyme superoxide dismutase	23
<i>Zingiber officinale</i> var. <i>rubrum</i>	Zingiberaceae	Rhizome extract combined with zinc	Male albino rats	Increase serum testosterone levels, Increase sperm count, viability and motility	24
<i>Hylocereus</i> sp.	Cactaceae	Ethanol extract of leaves	Male albino rats	Enhance the androgen concentration; Increases primary spermatocyte spermatid and spermatozoa count, sperm viability, sperm motility,	25
<i>Lunasia amara</i> Blanco	Rutaceae	Woodaqueous extract	Male albino rats	Increased the sperm count, progressive motility, and seminiferous tubules diameter	26
		Woodaqueous extract added with andromed® diluent	Belgian blue crossbreeds bull	Increase motility and viability of spermatozoa	27
<i>Zingiber officinale</i> Roxb	Zingiberaceae	Rhizome extract	Aging male mice	Increase pre-leptotene and pachytene spermatocytes, and spermatids Increase sperm count, viability, motility and normal morphology	28
<i>Piper nigrum</i> L	Piperaceae	Ethanol extract of fruits	Male albino rats	Increase serum testosterone level, Increase weight of epididymis tubules Increase spermatozoa, spermatocyte and spermatid count	29
<i>Neptunia plena</i>	Fabaceae	Methanol extract of leaves	Male rats	Increase the spermatogenesis activity	30

<i>Barringtonia racemosa</i>	Lecythidaceae	Leaf aqueousextract	Male rats	Increase sperm count, motility, viability, normal morphology	31
<i>Coriandrum sativum</i> Lour	Apiaceae	Seed-ethanol extract	Diabetic male rats	Increase sperm viability and motility	32
<i>Vigna radiate</i>	Fabaceae	Bean sprouts extract	Male mice	Increase spermatozoa percentage of morphology and motility	33
<i>Caesalpinia sappan</i> . L	Leguminosae	Wood ethanol extracts	Male rats	Improve sperm motility, viability and sperm concentration	34
<i>Bischofia javanica</i> Blume	Euphorbiaceae	Ethanol extract	Hyperglycemic male rats	Improve testes volume, sperm concentration and sperm motility	35
<i>Garcinia mangostana</i> L.	Cluciaceae	Fruit pee ethanol extract	Male mice	Improve motility, normal morphology and viability of spermatozoa	36
<i>Lycopersicum esculentum</i> L.	Solanaceae	Fruit ethanol extract	Male rats	Increase the number of Sertoli and spermatogenic cells in seminiferous tubules.	37
<i>Citrus limon</i>	Rutaceae	Fruit juice extract	Male mice	Improve sperm count, motility and normal morphology	38
<i>Phaleria macrocarpa</i> (Scheff.) Boerl	Thymelaeaceae	Fruit pericarp methanol extract	Streptozotocin and nicotinamide-induceddiabetic male rats	Improve sperm count, spermatogenic score, seminiferous tubule epithelial thickness, Sertoli and Leydig cell's number and testicular MDA level	39
<i>Smilax rotundifolia</i> L.	Smilacaceae	Leaf ethanol extract	White male rats	Increase fertility index	40
<i>Peperomia pellucida</i> L. Kunth)	Piperaceae	Whole plant ethanol extract	Alloxan –induced hyperglycemic male mice	Ameliorate sperms count, viability, motility, and morphology	41

There are 18 plant species reported by 19 researchers in Indonesia suspected to have pro-fertility properties in males. As with the anti-fertility herbal assays listed in Table 1, the pro-fertility assays presented in Table 2 also employ similar preparation and measurement techniques. Test animals were simply treated with plant crude extracts, and the effect parameters observed and measured are also the same. Only two among the 19 researchers that used biochemical parameters in assessing the effects of plant extracts on the testicular function of the test animals. Nugroho et al. (2022) measured serum testosterone, LH and FSH, protein and cholesterol levels. Additionally, the activities of testicular enzymes including alkaline phosphatase, lactate dehydrogenase, and glutamyltransferase, as well as the superoxide dismutase enzymes were also assessed [23]. Sutyarso et al. (2016) in their two studies, in addition to use sperm parameters, they also assessed serum testosterone level [24, 29].

Thus it can be assumed that research on medicinal plants for fertility enhancing ingredients in men, which are presented in Table 2, are all classified as basic research. In order to produce effective, efficacious and safe medicinal ingredients, it

is necessary to carry out further in-depth studies, especially regarding the mechanism of action of the active ingredients in certain potential plants [49].

It is highly recommended for researchers to evaluate several important parameters related to the induction of spermatogenesis such as cAMP-responsive element modulator (CREM) in rat testes. If necessary, reverse transcription polymerase chain reaction (RT-PCR), and Western blot analysis are also performed to test sperm function [50].

3.3. Plants for enhancing sexual activity

The potential efficacy of Indonesian medicinal plants related to testicular function based on parameters of sexual behavior is presented in Table 3.

Table 3 Indonesian medicinal plants which are thought to be useful in maintaining male sexual function

Plant species	Plant family	Preparation	Test animal	Observed effects	Reference
<i>Gigantochloanigrociliata</i>	Poaceae	Bamboo shoots ethanol extract	Male mice	Increase mating behavior parameters, increase spermcount, motility,and viability	42
<i>Moringaoleifera</i>	Moringaceae	Leavesas supplementation	Bali bulls	Increase libido Increase testosterone levels Increase total andprogressive motility of sperm.	43
<i>Piper nigrum</i> Linn.	Piperaceae	Fruit ethanol and water extract	Male swiss albino mice	Enhance courtship activity	44
<i>Pimpinella pruatjan</i>	Apiceae	Root ethanol extract	Male albino mice	Enhance aggressiveness , shorter attacklatency	45
<i>Peperomia pellucida</i> L. Kunth	Piperaceae	Whole plant ethanol extract	Male albino mice	Enhance courtship and mounting activity, Increasing mounting frequency in mating test	46

The selection of plant species tested by Indonesian researchers in an effort to find ingredients to improve male sexual function was generally based on claims of the aphrodisiac properties of plants that have been known by indigenous peoples for generations. Purwoceng (*Pimpinella pruatjan*), black pepper (*Piper nigrum* Linn.), kelor (*Moringa oleifera* Linn.) are examples of plants among 204 species that have long been known to have aphrodisiac effects among indigenous peoples in several regions in Indonesia. [51].

Research on the search for plant-derived ingredients to increase male sexual activity in Indonesia which is presented in Table 3 above is still very basic. In order to develop plant-derived drugs that are not risky to users, then the mechanisms of action, safety profile, and effects of the ingredient on humans need to be intensively studied [52].

This in-depth study is important because the growing trend of searching for drugs made from natural ingredients is triggered by the fact that synthetic sexual drugs cause side effects. Therefore it is important to ensure that the ingredients derived from plants are free from substances that are harmful to humans [53].

4. Conclusion

Research conducted in Indonesia in the last 20 years has succeeded in demonstrating plant species that have pro-fertility, anti-fertility and aphrodisiac properties in male test animals. Given fertility, infertility, and sexual behavior in males are all determined by the function of the gonadal organs called testes, it can be concluded that the Indonesian medicinal plants studied are containing active substance that have an effect on the testes. However, the studies that have been conducted whose results are presented in this article are still largely too basic. It is necessary to carry out more in-depth studies to determine the mechanism of action, toxicity, and side effects of the plant's bioactive substances.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

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