RESEARCH ARTICLE

OVERVIEW OF THE FUNCTIONS OF GINGER RHIZOME (*ZINGIBER OFFICINALE ROSCOE*), BLACK CUMIN (*NIGELLA SATIVA*), AND PASAK BUMI (*EURYCOMA LONGIFOLIA JACK*) IN MALE INFERTILITY

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ABSTRACT

Background: More than 186 million individuals worldwide from Southeast Asian and African nations are affected by infertility, a common health issue, specifically among men. In Indonesia, the use of "jamu" or herbal preparations derived from a diverse variety of herbal sources remains a widely practiced therapeutic approach. Furthermore, the Research and Development Center of the Indonesian Ministry of Health conducted extensive investigations between 2012 and 2018, including 204 distinct plant species used as stimulants and fertility enhancers. Among the species extensively used by ethnic traditional healers are pasak bumi (*Eurycoma longifolia Jack*), Pimpinella alpina Kds or Pimpinella pruatjan Molk (purwoceng), ginger rhizome (*Zingiber officinale Roscoe*), and black cumin (*Nigella sativa*).

Methods: This study was compiled as an overview of ten original articles from PubMed and Google Scholar using keywords related to the effects of ginger rhizome, black cumin, and pasak bumi on male infertility.

Result: The three plants were useful for improving sperm parameters by antioxidant activity, and increasing the production of reproductive hormones.

Conclusion: These plants had a potential role in treating and protecting male infertility by the antioxidant activities.

Keywords: Eurycoma longifolia jack, nigella sativa, herbal medicine, infertility, zingiber officinale roscoe

INTRODUCTION

Fertility is clinically defined as the ability to achieve pregnancy. Meanwhile, World Health Organization (WHO) defines infertility as a medical condition marked by the inability to achieve pregnancy after 12 months of regular sexual intercourse without the use of contraception.[1,2] Globally, infertility affects more than 186 million people, and the majority of developing countries in Southeast Asia and Africa have the most cases.[2,3]

The causes of infertility vary depending on gender, age of the patient, and length of marriage. In women, certain causes are well-documented and the leading factor is a polycystic ovarian syndrome (PCOS), followed by instances resulting from tubes due to infections. Meanwhile, the most frequent cause in men is semen abnormalities influenced by smoking habits and alcohol consumption that stimulate the production of free radicals,[2] damaging the sperm quality and declining the quantity. This is due to the high levels of unsaturated fatty acids in the cytoplasmic membrane as well as low concentrations of antioxidant enzymes in the cytoplasm.[4] Male infertility is described as men failure to successfully carry a fertile woman to term after at least a year of unprotected sexual activity. Men account for roughly 20% of the causes of infertility between 30% and 40% of all cases.[3,5] In Indonesia, jamu (herbs) is one of the more widely used remedies and treatments for infertility issues. There are numerous and diverse herbs used as aphrodisiacs to cure sexual dysfunction symptoms, particularly in men.[6] A total of 204 plant species were used as aphrodisiacs and to improve fertility in a study carried out by the Research and Development Center of the Ministry of Health of Republic of Indonesia from 2012 to 2018. Ethnic traditional healers (*hattra*) used a variety species, including ginger rhizome, Pimpinella alpina Kds, and pasak bumi.[7]

Black cumin spice, is also prescribed topically in traditional Persian medicine to treat impotence and erectile dysfunction.[8] The impact on rat fertility shows that the plant also contributes to sperm quality improvement and an

increase in semen volume.[9] A spicy ginger component and the essential oil of ginger rhizome have aphrodisiac effects by stimulating and improving blood vessel circulation to raise the frequency of coitus in male rats.[10] Ginger also possesses antioxidant capabilities that can vary depending on the extraction technique. The aqueous extract of ginger has superior chelating and free radical scavenging activities, while ethanol has the potential to lower plasma iron levels with antioxidant impact.[11]

Jamu is a type of traditional Indonesian medicine made from mixtures of ingredients such as leaves, roots, bark, and other plant parts, as well as animal parts, minerals, and Sarian preparations (galenic). The ingredients have been used for treatment for many generations according to social norms.[7,12] In this context, this study was motivated by the practices of a traditional clinic located in Banten, West Java Province. The clinic offered therapy for male infertility disorders, using a concoction believed to contain three specific herbal plants. Patients were attracted from regions beyond the province due to its effectiveness. Therefore, this study was conducted to present scientific evidence derived from previously published results on the potential effects of the three herbal plants in addressing male infertility.

METHODS

A literature review was conducted on original articles searched from Google Scholar and PubMed databases that were published in the last ten years using keywords: "*Zingiber officinale Roscoe* in male infertility", "*Nigella sativa* in male infertility", and "*Eurycoma longifolia Jack* in male infertility". These original articles selected were related to the effect of the plants on male infertility or reproductive organs.

RESULTS

From the search, four original articles were obtained discussing the effect of ginger rhizome (*Zingiber officinale Roscoe*), three original articles discussing the effect of black cumin (*Nigella sativa*), and three original articles discussing the pasak bumi (*Eurycoma longifolia Jack*) effect on male fertility. However, it should be noted that most studies were conducted on rats, the detailed result are shown in Table 1.

Table 1. Summary of three plants' effects on male infertility studies

Author and Year	Plant preparation	Subject	Intervention protocols	Result
***Zingiber officinale Roscoe* (ginger rhizome)**				
Khaki, et al - 2014(27)	Ginger roots powdered 100 mg/kg.	Diabetic male Wistar rats.	Ginger roots powdered and dissolved in 2 cc distilled water, gavage method, daily for 8 weeks.	Sperm numbers, percentages of sperm viability and motility, and total serum testosterone increased.
Jalil H, et al - 2016(28)	Ginger powder.	100 infertility patients.	This randomized double-blind, placebo-controlled trial. One group received capsules containing 250 mg of ginger powder twice a day and a placebo in other group).	Significantly reduce sperm DNA fragmentation (SDF) in infertile men.
Herve T, et al - 2018(18)	Oil extraction of ginger rhizome by hydrodistillation.	Male Japanese quail.	Three groups with 50, 100, and 150 µl/kg body weight of essential oil by gastric intubation, daily for 12 weeks.	Ginger rhizome essential oil improved the structure of quail testicles.
Afkhami FA et al - 2018(29)	Powdered rhizomes were soaked in ethanol 50% and extracted.	Male Wistar rats.	500 mg/kg/day, by gavage, for 28 days.	Ginger treatment of SMB-exposed rats significantly increased testosterone level and the number of different spermatogenic cells.

***Nigella sativa* (black cumin)**				
Ping N, et al - 2014(22)	*Habbatus sauda* oil.	24 *Sprague-Dawley* male rats.	Force-fed with *Habbatus sauda* oil at 6.0 μL/100 g body weight, for 100 days.	It increases sperm quality and better testis histological features.
Abd-Elkareem, et al - 2021(30)	MSG powder and *Nigella sativa* seed.	18 adult male albino rats.	One grup: MSG at a concentration of 30 g/kg and NSS at a concentration of 30 g/kg feed, grup MSG (same concetration), and control grup (no treatment).	NSS normalized luteinizing hormone levels, lipid peroxides, total antioxidant capacity, and repaired the testes histoarchitectural disruption caused by MSG.
Hajb A, et al - 2023(31)	Palm pollen extract (350 mg) and black seed powder extract.	62 infertile men between.	A single-blind, placebo-controlled clinical trial study. One group received two capsules of palm pollen extract (350 mg) and black seed powder extract (250 mg), and other group as control receive placebo capsul.	Increase sperm count, and progressive motility, also significantly increase in the concentration of testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH).
***Euricoma longifolia Jack* (pasak bumi)**				
Solomon et al - 2014(32)	Aqueous extract of *Eurycoma longifolia* roots.	42 male rats.	Three groups consist of control group, low-dose group (200 mg/kg BW) and high-dose group (800 mg/kg BW) (n=14), force-fed for 14 days.	Testosterone concentration increased by 30.2% (P = 0.0544). Muscle weight also increased, yet not significantly. Whilst sperm concentration, total and progressive motility and vitality increased significantly, MMP improved markedly.
George A, et al - 2013(33)	The freeze-dried water extract of *Eurycoma longifolia* root (Physta®, Biotropics Malaysia).	40 Malaysian men aged 30-55 years.	A randomized, double blind, placebo-controlled clinical trial. The daily intake was 300 mg of the plants or placebo for 12 weeks.	Testosterone Epitestosterone -ratio in treatment group was not significantly different from values at baseline.
Al-Ani, et al - 2019(34)	*Eurycoma longifolia* extracts (15 mg/ kg) dissolved in distilled water.	24 male Sprague-Dawley (SD) rats.	Rats were divided into four: first group normal diet, 2nd group normal diet and *Eurycoma longifolia* extracts, 3rd group high-fat-diet and 4th group (high-fat-diet and *Eurycoma longifolia* extracts), administered orally for 12 weeks.	Treatment of *Eurycoma longifolia* improved the morphological structure of the seminiferous tubules that damage by high-fat-diet.

DISCUSSION

The Herbal Medicine scientific approach can be used to show the efficacy and safety of herbal plants adopted empirically for years.[10,12] Since 2002, WHO has given attention to traditional medicine. A global strategy was developed for traditional and complementary medicine, which included herbs and spices as well as herbal ingredients, preparations, and products made from plants.[13] The classification of these three plants is in Table 2.

Table 2. The classification of plants

Taxonomy	*Zingiber officinale Roscoe* (14)	*Nigella sativa* (20)	*Eurycoma longifolia Jack* (24)
Kingdom	Plantae	Plantae	Plantae
Division	Magnoliophyta	Magnoliophyta	Magnoliophyta
Class	Liliopsida	Magnoliopsida	Magnoliopsida
Order	Zingiberales	Ranunculales	Sapindales
Family	Zingiberaceae	Ranunculaceae	Simaroubaceae
Genus	Zingiber	Nigella	Eurycoma
Species	*Zingiber officinale*	*Nigella sativa*	*Eurycoma longifolia Jack*

A total of 46 genera form the Zingiberaceae family found across the tropics and subtropics. Zingiber is the genus of the family and under cultivation, the herbaceous rhizomatous perennial ginger can grow up to 90 cm.[14] The slender, oblong-lanceolate leaves on the rhizome are heavily lobed, pale yellowish, and fragrant. Furthermore, the sprouted bunches of lateral branches dry out and this process is proportional to the plant age. The midrib at the base of the 2–3 cm wide leaves has strands that progressively taper to a tip.[15]

Figure 6. Ginger rhizome (*Zingiber officinale Roscoe*)[14]

Sesquiterpenes, gingerols, zingiberen, zingeron, oleoresin, camphene, limonene, borneol, cineol, sitral, zingiberal, felandren, vitamins A, B, and C, as well as flavonoids and polyphenolic substances are present in the essential oils of ginger rhizome. This is the reason for the spicy, sharp, and stinging sensation of phenolytic drugs.[16] Medical studies on ginger focused on its efficacy as a treatment for vomiting associated with pregnancy, nausea from birth control pills, dysmenorrhea, motion sickness, cough, pneumonia brought on by ventilators, rheumatic diseases, antibacterial and antiviral effects, and vomiting due to chemotherapy, anti-hyperlipidemia, anti-inflammation, diabetic nephropathy, and postoperative nausea, as well as spermatogenesis.[17]

Experiments on diabetic rats showed that ginger reversed the damaging effects of oxidative stress on spermatogenesis and fertility parameters. By reducing oxidative stress in the testes and activating antioxidant enzymes such as superoxide dismutase and catalase, ginger increases sperm production by enhancing the growth of testicular seminiferous tubules, spermatozoa cells, and semen quality.[18] The production of luteinizing hormone is stimulated, blood flow to the testes is increased, the activity of the testes' molecular defense mechanisms is improved, and blood sugar levels are decreased. Other factors include increasing testosterone receptors, blood supply to the testes, and testicular weight. Therefore, increasing levels of gonadal hormones (testosterone and luteinizing hormone) are likely to be responsible for ginger beneficial effects when considered from the perspectives of sperm and semen.[19]

Upakunchika, Ajaji, Kalvanjika, Kalika, Kunchika, Kalunji, and Habatussauda are some of the names for black cumin. This plant is also named little fennel, black cumin, and black blossom in English. The natural habitat is in the Indian states of Punjab, Himachal Pradesh, Bihar, and Assam. However, the plant is grown extensively in the world, including in Lebanon, Syria, Israel, and Southern Europe.[20]

Black cumin grows up to 45 cm tall each year and produces fragrant pale blue flowers on smooth stems. The flowers are 2-2.5 cm in size and have 5-10 petals with long leaves about 2.5-5 cm. The seed structure is slightly flattened, oblong, rigid, funnel-shaped, small, 0.2 cm long, 0.1 cm wide, black. The plant starts flowering and fruiting from January to April, planted in dry soil from November to April, and the seeds germinate in 10 to 15 days.[20]

One of the spices, also known as black cumin, is used in traditional Persian medicine to treat impotence and erectile dysfunction in topical formulations.[21] The fertility effects of

feeding the plant to rats show that the herb improves sperm quality and plays a role in increasing semen volume.[8] A study including the administration of black seed oil to rats showed improvements in testicular histopathology and enhanced sperm quality.[22] In this context, black cumin and ginger function through a similar mechanism to cure infertility. The outcomes reported that black cumin treatment improved sperm and semen parameters, including an increase in the quantity of Leydig cells, follicles, and corpus luteum in women, as well as levels of the hormone testosterone in men and progesterone in women. Therefore, black cumin seeds aid in reducing infertility in both sexes.[23]

The flowering plant pasak bumi is a member of the Simaroubaceae family and indigenous to Indonesia and Malaysia.[24]

Figure 7. The left figure is pasak bumi in its habitat, and the right figure is the roots[24].

Numerous therapeutic substances, including eurycomanone, eurycomanol, eurycomalactone, canthine-6-one alkaloid, 9-hydroxycanthin-one, 14,15-dihydroxyklaineanone, phenol components, tannins, quassinoids, and triterpene, are present in the extract of pasak bumi roots.[25] These substances have potential as antimalarial medications, breast cancer preventatives, testosterone-boosting insecticides, and prevent osteoporosis.[25]

In a different trial, 350 patients received 200 mg of extract daily, and for 9 months, semen analysis was carried out every 3 months. A total of 75 of the 350 patients finished a full cycle over 3 months. These patients' semen analyses showed a considerable improvement in the entire parameters. The exclusive pasak bumi extract considerably raised the sperm quality, which allowed 11 or 14.7% to become pregnant.[26]

The working meachanism of pasak bumi in increasing spermatozoa production is still unclear. Moreover, this herbal plant shows antioxidant properties and has been verified to possess superoxide dismutase (SOD), playing a significant role in improving male fertility. This is consistent with the earlier observation that male fertility is characterized by a decline in sperm parameters due to the impact of free radicals.[26]

CONCLUSION

To summarize, ginger rhizome has been shown to increase the production of spermatozoa in male rats by stimulating the growth of testicular seminiferous tubules, spermatozoa cells, and semen quality. Similarly, it has been observed that ginger can improve the testicle structure in quails, while in humans, it can decrease DNA fragmentation. Black cumin has similar effects to ginger in treating male infertility, as it improves the quality of sperm and semen, enhances the testicular structure, and raises testosterone, LH, and LSH levels in both rats and humans. Pasak bumi has also shown to enhance sperm quality, semen parameters, and testosterone levels in rats, but its effectiveness in humans has not been proven yet.

There is no clear evidence yet about the effectiveness of these three plants in treating human infertility. However, their potential to increase male fertility should be studied further, especially since they are commonly used in the community as an alternative treatment. Whether their use is beneficial or not needs to be thoroughly investigated.

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