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RESEARCH ARTICLE

Selected Medicinal Plants Used in the Treatment of Male Infertility in on do State, Nigeria

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ABSTRACT

The study of medicinal plants used in the treatment of male infertility in Ondo State, Nigeria, is crucial given the increasing prevalence of infertility problems in the world. Male infertility is caused by factors such as lifestyle, stress, and physiological abnormalities, contributes significantly to overall infertility rates. Traditional medicine, particularly the use of medicinal plants, has gained attention due to its potential effectiveness and minimal side effects compared to conventional treatments. For thousands of years, local communities and herbal practitioners have been using various medicinal plants to improve male reproductive health, enhance sperm quality, and treat related conditions such as low sperm count, poor motility, and erectile dysfunction. The use of medicinal plants involves boiling the roots, barks, or leaves to create infusions or decoctions that are consumed over a specified period. This paper reviews potential causes of male infertility; selected medicinal plants commonly used in the treatment of male infertility in Ondo State, Nigeria, therapeutic mechanisms of the active compounds in the plants, and the scientific evidence supporting the use of the plants. Despite the widespread use of the medicinal plants in traditional medicine, scientific research on their efficacy and safety needs to be strengthened. Therefore, further pharmacological studies and clinical trials are required to substantiate the therapeutic claims linked to the plants.

INTRODUCTION

Male infertility is a significant health problem, affecting about 15-20% of couples worldwide, with male factors contributing to about 50% of infertility cases (Agarwal et al., 2015; Diericks et al., 2021). The trend of couples delaying parenthood, combined with unhealthy lifestyles and environmental factors, is contributing to lower fertility rates (Kohn & Schuppe, 2021). Various factors can lead to male infertility, including poor testicular development, infections, hormonal imbalances, and lifestyle choices. Natural antioxidants from plants are gaining interest as potential alternatives to synthetic medications for treating infertility and phytochemicals found in plants, such as tannins, alkaloids, flavonoids, and terpenoids, have been shown to improve sperm quality and combat the negative effects of harmful substance (Kohn & Schuppe, 2021)

In Africa, infertility is a main problem because of the negative social impact such as isolation, disinheritance, stigmatisation and divorce linked to it (Okonofua et al., 1997; Koster-Oyekan, 1999). In Africa, it is usually believed that infertility problems are intrinsically linked to women. In other word, it is not a man's problem (Diericks et al., 2021). This assumption has hindered most African men from seeking medical attention when couples failed to have children after two or more years of marriage. It is important to note that the assumption that infertility is only due to female problems contradicts the observations that couple's infertility is due to a male factor in about 20% of the cases and contributes to the couple infertility in another 30–40% (Thonneau et al., 1991). According to a report, the incidence varies from region to region and a report by Agarwal et al (2015) shows that 2.5%-4.8% male factor infertility is in Sub-Saharan Africa. Male infertility has been consistently reported to account for 40% to 50% of infertility cases in Nigeria. A study found that male infertility was responsible for 40.8% of infertility cases in Kano, Northern Nigeria (Adu et al., 2014). In a study

conducted in Ibadan, it was found that male factor infertility contributed to 42.4% of infertility cases (Okafor et al., 2011)). Male infertility accounted for about 40% of infertility cases in a study conducted in Maiduguri, the Northeastern Nigeria (Salawu et al., 2016). Another study conducted in southeastern Nigeria by Ikechebelu et al (2003) found a male infertility prevalence of 42.4%. A study published in 2003 revealed that male factor infertility was responsible for 46% of infertility cases (Olusanya et al., 2003). A study on South African men over a period of six years (1985 to June 1991) showed that 49% of men suffered from secondary infertility (Bomman et al., 1994). Sengupta et al (2017) reported 73% decline in sperm count in African men over a period of 50 years (1965–2015). Epidemiological studies have revealed high prevalence rates of male infertility ranging from 20–40% in Africa.

Agarwal et al (2015) estimated the overall pure male factor infertility could range between 2.5% and 12%. In North America, the estimated male infertility rate is between 4.5% to 6%, while it's 9% in Australia and could be as high as 8% to 12% in Eastern Europe (Agarwal et al., 2015). A study by Bayasgalan et al (2004) estimated the cause of infertility due exclusively to a male factor at 25.6%. A similar study conducted by Thonneau et al (1991) found that among the French population, a prevalence of 20% of all infertility was due exclusively to a male factor. Also, Philippov et al (1998) used a WHO questionnaire in Western Siberian to show a rate of 6.4%. In most practical purposes, it is assumed that about one-sixth of all couples worldwide have an infertility problem and that the male factor infertility is significant in about half of cases and is the only cause in about 20% to 30% of cases.

Possible Causes of Male infertility

Infertility is usually defined as the inability of a couple to conceive after one year of unprotected, frequent sexual intercourse (Practice Committee of American Society for Reproductive Medicine, 2008). It affects about 15% of all couples in the United States and at least 180 million couples worldwide (Thonneau et al., 1991). Male infertility is defined by the World Health Organization (WHO) as the inability of a male to make a fertile female pregnant for a minimum of at least one year of regular unprotected intercourse. The male is solely responsible for about 20% of cases and is a contributing factor in another 30% to 40% of all infertility cases (Hull et al., 1985). There are several reasons for male fertility, including both reversible and irreversible conditions. Other factors can influence each partner, including age, medications, surgical history, exposure to environmental toxins, genetic problems, and systemic diseases and the various potential causes of male infertility are discussed in this paper.

Sperm Abnormalities

Sperm abnormalities are a leading cause of male infertility, with various factors contributing to poor sperm health (Mohammed at al., 2013; Meeker et al.,2010; Ikechebelu et al., 2003). The abnormalities can manifest in different forms, including irregular sperm morphology, motility, count and DNA integrity (Bornman et al., 1994; Bohring et al., 2009). Sperm count abnormalities refers to a low sperm count, which is one of the most common causes of male infertility. A sperm count <15 million sperm/ml of semen is considered abnormal. Reduced sperm count lowers the chances of sperm successfully fertilising an egg. Studies have shown that low sperm count is linked to environmental factors such as exposure to toxins, hormonal imbalances, and genetic problems (Liu et al., 2011; Erenpreisa et al., 2013; Tata et al., 2015; Wesselink et al., 2017). A study by Bohring et al. (2009) indicated that reduced sperm count significantly correlates with male infertility. A report by Erenpreisa et al. (2013) showed that abnormal sperm morphology, especially defects in the sperm head, is a major contributing factor to infertility and that the inability of deformed sperm to properly fertilise the egg is a significant factor in male infertility.

Poor sperm motility can significantly affect fertility since sperm must travel through the female reproductive tract to fertilise the egg. Motility problems can be due to factors such as infections, oxidative stress, varicocele, and certain lifestyle choices such as smoking (Liu et al., 2011). Liu et al. (2011) observed that sperm motility problems are strongly associated with reduced fertility rates and that poor motility significantly decreases the sperm's ability to reach and fertilise the egg, leading to a higher chance of infertility.

Sperm DNA fragmentation is a condition where the DNA in the sperm is damaged. This is very vital because it can lead to failed fertilisation and developmental problems in the offspring. Increased DNA fragmentation is associated with oxidative stress, varicocele, and advanced paternal age (Zini et al., 2006). Zini et al. (2006) revealed that sperm DNA fragmentation is a critical factor in male infertility. The authors reported that high levels of DNA fragmentation can lead to unsuccessful fertilisation or early pregnancy loss, making sperm DNA integrity a key determinant of male fertility. Azoospermia refers to the complete absence of sperm in semen, which can be caused by either an obstruction in the reproductive tract (obstructive azoospermia) or a failure in sperm production (non-obstructive azoospermia). This condition represents a severe form of male infertility. A study by Turek et al. (2011) found that azoospermia, whether obstructive or non-obstructive, is a serious factor in male infertility.

Hormonal Imbalances

Hormonal imbalances play a crucial role in male infertility, as hormones regulate the production of sperm, libido, and sexual function. The primary hormones involved in male fertility are testosterone, follicle-stimulating hormone, luteinising hormone, prolactin, and thyroid hormones. When these hormones are imbalanced, it can lead to various forms of infertility, including low sperm count, reduced sperm quality, and erectile dysfunction (Tata et al., 2015; Agarwal et al., 2015; Sharma et al., 2016). Testosterone is the primary male sex hormone produced by the testes, responsible for sperm production, sexual desire, and the development of male secondary sexual characteristics. Low testosterone levels can lead to reduced sperm production, lower libido, erectile dysfunction, and a general decline in sexual function (Tata et al., 2015). Hypogonadism, a condition characterised by low testosterone levels, can result in low sperm count and reduced fertility (Bhasin et al., 2007). Testosterone deficiency is a common cause of male infertility and is linked to decreased sperm production. Low testosterone can result from conditions such as Klinefelter syndrome, aging, obesity, chronic diseases, and lifestyle factors such as smoking, alcohol use (Swerdloff et al., 2006). Swerdloff et al. (2006) explored the impact of low testosterone on male fertility. And reported that testosterone deficiency is associated with reduced sperm count and poor semen quality, which may result in infertility.

Follicle stimulating hormone is critical for sperm production. It stimulates the Sertoli cells in the testes, which are responsible for nourishing developing sperm. Low levels of FSH can indicate problems with sperm production, leading to low sperm count or azoospermia (Tata et al., 2015). Low levels of LH can result in low testosterone production, affecting sperm production and overall fertility (Bhasin et al., 2007). FSH and LH imbalances are critical in determining male fertility while low levels suggest hypothalamic or pituitary disorders (Pigny et al., 2000). Bhasin et al. (2007) examined the impact of FSH and LH on spermatogenesis and reported that altered levels of FSH and LH could lead to spermatogenic defects, contributing to male infertility.

Excessive prolactin levels can interfere with testosterone production by inhibiting the secretion of gonadotropin-releasing hormone, which is responsible for stimulating the release of LH and FSH. High prolactin levels are associated with reduced libido, erectile dysfunction, and low sperm count (Ramaswamy et al., 2009). Prolactin excess has been shown to disrupt the hypothalamic-pituitary-gonadal axis, which can lead to reduced secretion of LH and FSH, and subsequently, lower testosterone levels and sperm count. Ramaswamy et al. (2009) reported that high prolactin levels can lead to infertility by inhibiting the gonadotropin release and affecting sperm production.

Thyroid hormones play an essential role in overall metabolism and reproductive health. Hypothyroidism or hyperthyroidism can disrupt the balance of reproductive hormones, leading to infertility. Thyroid dysfunction can alter the levels of gonadotropins and sex hormones, contributing to an imbalance in sperm production and sexual function; both hypothyroidism and hyperthyroidism have been associated with male infertility (Bhasin et al., 2007). Tata et al. (2015) found that thyroid dysfunction directly affects gonadotropin secretion and sperm production. Correcting thyroid imbalances can lead to improvements in sperm count and motility (Bhasin et al., 2007; Swerdloff et al., 2006; Tata et al., 2015).

Varicocele

Varicocele is a condition characterised by the enlargement of the veins within the scrotum and is one of the most common causes of male infertility, affecting about 15% of the general male population and up to 40% of men with infertility challenges. Varicocele can lead to impaired sperm production and reduced sperm quality, which are key contributors to male infertility (Burris et al., 2010; Cayan et al., 2004). The exact mechanism of its impact is not very clear; however, it is suggested that it results from increased scrotal temperature, poor venous drainage, hormonal imbalances, and oxidative stress (Cayan et al., 2004; Saleh et al., 2003; Mehmood et al., 2017). The enlarged veins in varicocele lead to impaired blood flow and heat dissipation, raising the temperature within the scrotum and negatively affecting sperm production and motility (Saleh et al., 2003[Tremblay et al., 2014).

Infections

Infections play a significant role in male infertility by affecting sperm production, motility, morphology, and overall reproductive health. Infections can lead to both acute and chronic conditions that compromise the function of the testes, epididymis, prostate, and other components of the male reproductive system (Haddad & Osman, 2007; Liu et al., 2008). The impact of infections on male fertility is related to inflammation, changes in the local environment of the reproductive tract, and hormonal imbalances (Haddad & Osman., 2007). Sexually transmitted infections such as chlamydia, gonorrhoea, and syphilis can cause significant damage to the male reproductive system. The infections can lead to epididymitis, inflammation of the testicles, and other complications that impair sperm function. Haddad & Osman. (2007) demonstrated that men with chronic gonorrhoea and chlamydia infections had a significantly higher likelihood of infertility due to scarring and blockage of the reproductive tract.

Urinary tract infections can negatively affect male fertility. Chronic bacterial prostatitis can lead to a reduced quality of semen by altering the pH, viscosity, and overall composition of seminal fluid, leading to decreased sperm motility and viability. Prostatitis can also cause erectile dysfunction and painful ejaculation, which further complicates fertility. The inflammation from an untreated urinary tract infection or prostatitis may also result in decreased testosterone levels and impaired spermatogenesis (Vannuccini et al., 2016; Kumar et al., 2010; Chandra & Batra, 2001).

HIV infection can affect male fertility both directly and indirectly. The virus can impair the function of the testes and the hypothalamic-pituitary-gonadal axis, leading to low sperm count, poor sperm motility, and hormone imbalances. Additionally, men with HIV may have an increased risk of developing opportunistic infections in the genital tract, which can further contribute to infertility. Antiretroviral therapy (ART), while essential for controlling the virus, may also have side effects on sperm function and semen quality. Liu et al. (2008) found that HIV-positive men had lower sperm counts and impaired sperm motility compared to HIV-negative men, suggesting that HIV infection itself contributes to infertility.

Lifestyle factors

Lifestyle factors play a significant role in male infertility, influencing sperm quality, motility, count, and overall reproductive health. Several behaviours and environmental exposures have been linked to male infertility, and the factors include diet, exercise, smoking, alcohol consumption, drug use, environmental toxins, stress, and obesity (Wang et al., 2003; Bui & Siva., 2010; Wesselink et al., 2017). Smoking has been shown to have a detrimental effect on male fertility. It contributes to reduced sperm count, impaired sperm motility, and abnormal sperm morphology. Smoking increases oxidative stress, which can damage sperm DNA and interfere with spermatogenesis. Studies suggest that both active and passive smoking can reduce fertility in men by altering sperm function and damaging the reproductive organs. The toxic substances in tobacco, including nicotine and carbon monoxide, can impair testicular function and reduce testosterone levels (Wang et al., 2003).

Excessive alcohol consumption is associated with decreased sperm quality, lower testosterone levels, and altered semen parameters. Chronic alcohol use can interfere with the endocrine system, impairing the hypothalamic-pituitary-gonadal axis, which regulates sperm production and hormone levels. Studies have shown that moderate to heavy alcohol consumption is linked to lower sperm

count, reduced motility, and increased sperm abnormalities and the toxic effects of alcohol may also lead to oxidative stress, damaging sperm DNA (Bui & Siva, 2010; Goudaizi et al., 2019).

Obesity is a significant risk factor for male infertility. Increased body fat, especially abdominal fat, leads to hormonal imbalances, including elevated oestrogen levels and reduced testosterone. This disruption of the hormonal balance can interfere with spermatogenesis and reduce sperm quality. Obesity also increases the risk of oxidative stress, inflammation, and metabolic syndrome, which can further impair male fertility. Studies have shown that obese men are more likely to have lower sperm count, poor sperm motility, and increased sperm DNA fragmentation (MacDonald & Ginsberg, 2010; Sadeghian et al., 2013; Sonmezer & Vargyas, 2015).

Exposure to environmental toxins, such as pesticides, heavy metals and endocrine-disrupting chemicals has been linked to male infertility. These chemicals can interfere with hormone production, leading to decreased testosterone levels, reduced sperm quality, and altered spermatogenesis. Occupational exposure to industrial chemicals, solvents, and metals can increase the risk of infertility in men ((Agarwal et al., 2014; Wesselink et al., 2017; Zegers-Hochschild et al., 2009; Mahajan & Sharma, 2013).

A poor diet, including inadequate intake of antioxidants, vitamins, and essential fatty acids, can adversely affect sperm quality. Nutritional deficiencies, especially in zinc, selenium, folate, and vitamins C and E, are associated with impaired sperm motility and morphology. A diet high in processed foods, trans fats, and low in fruits and vegetables may increase oxidative stress, leading to sperm DNA damage and reduced fertility (Agarwal et al., 2012; Sadeghian et al. 2013). Regular physical activity is generally beneficial for male fertility, as it helps maintain a healthy weight, improves hormonal balance, and reduces oxidative stress. However, excessive exercise, particularly in athletes who engage in extreme endurance activities, can lead to a decrease in testosterone levels and poor sperm quality (Hauser & Cohn, 2010; Silva et al., 2010).

Oxidative Stress

Oxidative stress plays a crucial role in male infertility, as it can negatively impact sperm quality, function, and overall male reproductive health. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralise them with antioxidants (Aiken et al., 2012; Raji et al., 2016). ROS are highly reactive molecules that can damage cells, including sperm cells, by interacting with their membranes, DNA, and proteins. Oxidative stress is associated with a variety of sperm abnormalities, such as reduced motility, abnormal morphology, DNA damage, and decreased sperm concentration (Homa et al., 2009; Ashok et al., 2010). ROS can cause oxidative damage to sperm DNA, leading to mutations and fragmentation. This DNA damage impairs the sperm's ability to fertilize the egg and can result in pregnancy failure, miscarriage, or poor embryo quality. DNA fragmentation is one of the key markers of oxidative stress in male infertility (Agarwal et al., 2014). ROS can impair the function of sperm flagella, leading to reduced motility and poor swimming ability. Moreover, oxidative stress can affect sperm morphology, causing structural abnormalities that reduce the sperm's ability to bind to and penetrate the egg (Raji., 2016). Lipid peroxidation, a key consequence of oxidative stress, damages the lipid membranes of sperm cells. The membranes of sperm are rich in polyunsaturated fatty acids, which are highly susceptible to oxidative attack. This leads to the breakdown of membrane integrity and a reduction in sperm viability (Kwon et al., 2004).

Increased ROS levels can disrupt the function of Sertoli cells, Leydig cells, and other supporting cells in the testes that are responsible for the production and maturation of sperm. The imbalance in ROS levels also alters the endocrine regulation of sperm production by interfering with testosterone synthesis, thereby impairing spermatogenesis (Saleh et al., 2003; Agarwal et al., 2015). Chronic inflammation, which can be exacerbated by oxidative stress, may further compromise sperm quality. Inflammatory cytokines generated in response to oxidative stress can impair sperm function and increase ROS production, leading to a vicious cycle that worsens infertility (Chatterjee et al., 2001; Khosrowbeygi et al. 2009; La Vignera et al. 2012; Raji et al., 2016).

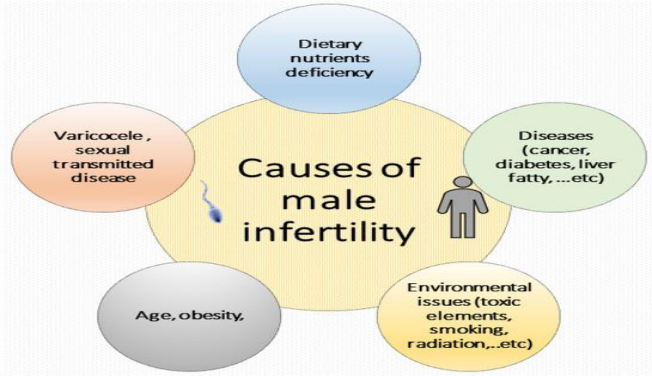

Figure 1: Interconnection between the factors that cause male infertility (MDPI, 2024)

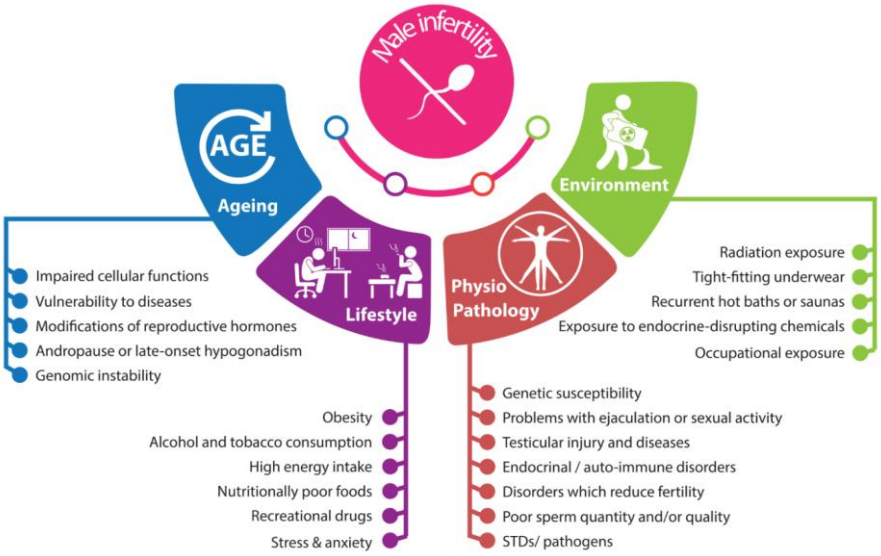

Figure 2: Causes of male infertility (Sadeghian et al., 2013)

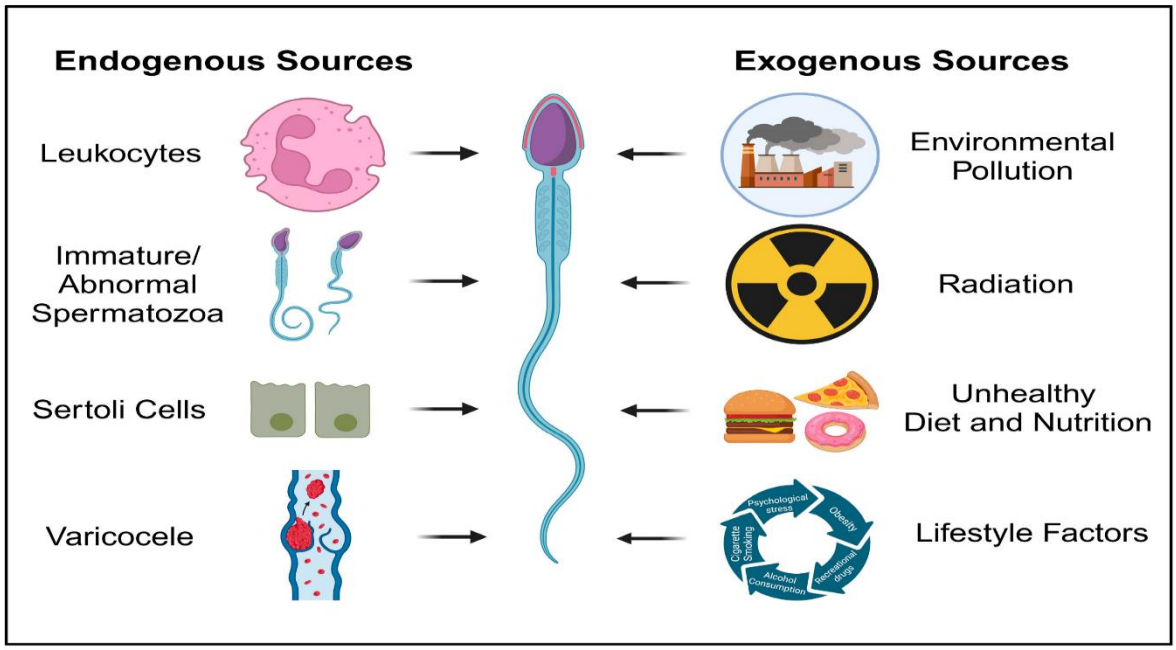

Figure 3: Oxidative stress-associated male infertility (Agarwal et al., 2015)

Traditional use of medicinal plants in male infertility treatment in Ondo State

In many developing regions, including Nigeria, traditional medicine, the use of medicinal plants, plays an important role in addressing health challenges, including infertility. Ondo State, located in southwestern Nigeria, is home to diverse ethnic groups, each with distinct practices in herbal medicine (Oluwole et al., 2018). The people of Ondo State have a rich tradition of using herbal medicine to address various health issues, including male infertility. These plants are often used in the form of decoctions, teas, or powders. Some of the commonly used medicinal plants in Ondo State are discussed in this paper.

Kalanchoe pinnata

Kalanchoe pinnata has been used to treat male infertility by enhancing sperm production and improving overall reproductive health. Studies suggest that this plant has antioxidant properties that protect sperm from oxidative damage. (Akinmoladun et al., 2020; Akinmoadun et al., 2021). The biological activity of the plant can be attributed to various bioactive compounds such as flavonoids, terpenoids, alkaloids, and phenolic compounds. The compounds contribute to its broad therapeutic properties. Ethnobotanical studies have documented the traditional use of Kalanchoe pinnata in treating various health conditions, including those related to male reproductive health. Its use suggests a potential role in addressing fertility issues. While much of the research on Kalanchoe pinnata focuses on its general therapeutic effects, recent studies have explored its potential use in the treatment of male infertility. The plant has potent antioxidant effects due to the presence of flavonoids and phenolic compounds. The antioxidants help scavenge free radicals and reduce oxidative stress, which is a common underlying factor in many diseases, including male infertility. Chia et al. (2018) studied the impact of oxidative stress on male infertility and reported that antioxidants could reduce oxidative damage to sperm cells, improving semen quality. Saha et al. (2017) demonstrated that various plant-based extracts, including those from Kalanchoe pinnata, could improve sperm quality and motility in infertile males by reducing oxidative stress.

The plant contains compounds like flavonoids and terpenoids that exhibit anti-inflammatory properties. Inflammation is a significant cause of various health issues, including male infertility, as it can affect sperm quality, motility, and morphology (Andrade et al. 2019). Research has shown that extracts of Kalanchoe pinnata can suppress the production of pro-inflammatory cytokines. The inhibition of COX enzymes is a documented mechanism for reducing inflammation. Some studies have found that Kalanchoe pinnata extracts exhibit COX-inhibitory effects, further supporting its potential as an anti-inflammatory agent (Costa et al., 2016). A study by Andrade et al. (2019) demonstrated that Kalanchoe pinnata leaf extracts exhibited significant inhibition of oedema in animal models, which was attributed to the anti-inflammatory activity of the plant's active compounds. Costa et al. (2016) found that Kalanchoe pinnata extracts effectively inhibited the release of pro-inflammatory cytokines, showcasing its potential as an anti-inflammatory agent for treating inflammatory conditions. Kalanchoe pinnata has been shown to have antimicrobial properties, which may help in reducing infections that could negatively affect reproductive health. Additionally, its immunomodulatory effects could help in regulating the immune system to prevent autoimmune-related infertility (Kaur et al., 2020).

Some studies suggest that Kalanchoe pinnata may have a potential role in regulating hormones that are critical for male fertility, such as testosterone and follicle-stimulating hormone. Sharma et al. (2016) found that certain plants, including Kalanchoe pinnata, might help regulate reproductive hormones such as testosterone, which is crucial for sperm production and overall male fertility.

Figure 4: Kalanchoe pinnata (Costa et al., 2016)

Gossypium herbaceum

The seeds and leaves of Gossypium herbaceum have been used to improve sperm count and motility (Akinmoladun et al., 2010; Sharma & Kumawat, 2014; Basha et al., 2016). Phytochemicals such as flavonoids and alkaloids are believed to play a role in improving reproductive function by balancing hormones involved in spermatogenesis (Adebayo et al., 2018). The plant has been used in traditional medicine for various disease conditions as well as an anti-inflammatory, antispasmodic, and diuretic agent. The plant has bioactive compounds that may positively influence reproductive health. The active phytochemical constituents of the plant include flavonoids, alkaloids, and terpenoids, which are believed to exert several physiological effects. Some of the possible mechanisms for its therapeutic effects include its antioxidants like flavonoids, which are thought to reduce oxidative stress, a significant factor in male infertility as oxidative stress can impair sperm motility, morphology, and DNA integrity (Nethengwe et al., 2024).

Inflammation of the reproductive system, including the testes, is known to contribute to male infertility and the anti-inflammatory effects of the plant may play a role in reducing such inflammation, thereby improving fertility (Anjaneyulu et al., 2017). Yusuf et al (2015) reported that the plant has beneficial effects on testicular function and sperm parameters, likely due to its antioxidant properties.

Figure 5: Gossypium herbaceum (Adebayo et al., 2018)

Citrullus lanatus

The plant is not only a popular fruit but also a medicinal plant used for its aphrodisiac properties and the seeds of watermelon are consumed to improve sperm quality and enhance libido (Ayoola et al., 2012; Hossain et al., 2015; Moinard et al., 2017; Sharma et al., 2019). L-citrulline, a compound found in watermelon, has been associated with improved blood flow to the reproductive organs (Olatunji et al., 2019). The plant has been used traditionally for its diuretic, anti-inflammatory, and antioxidant properties (Hossain et al., 2015). Recent scientific research suggests that watermelon and its

bioactive components, for example citrulline, may have potential therapeutic effects in treating male infertility by improving erectile function, sperm quality, and overall reproductive health (Bashir & Ibrahim, 2014). The therapeutic effects of *Citrullus lanatus* in male infertility are primarily attributed to its rich bioactive compounds such as: citrulline, antioxidants, vitamins and minerals and amino acids.

Olapade et al (2016) examined the effects of watermelon extract on male rats. The authors reported that the administration of the plant extract resulted in increased sperm count, motility, and overall testicular health. The authors attributed the effects to the antioxidant and vasodilatory properties of citrulline, which improved blood flow to the testes and reduced oxidative stress (Olapade et al., 2016). Sharma et al (2019) evaluated the effects of citrulline supplementation on male reproductive health in rats and found that citrulline supplementation led to enhanced erectile function and improved sperm parameters by increasing nitric oxide levels, which enhanced blood flow and oxygen delivery to reproductive tissues.

Agarwal et al (2016) examined the role of antioxidants, including those found in watermelon, in improving semen quality in men with subfertility and noted that antioxidant supplementation improved sperm concentration, motility, and morphology. While this study did not focus exclusively on watermelon, it supports the potential of antioxidant-rich foods like watermelon in improving sperm health and fertility. Parvez et al. (2017) demonstrated that watermelon extract, rich in lycopene, could protect sperm cells from oxidative damage in laboratory settings. The study indicated that lycopene improved sperm motility and reduced DNA fragmentation in human sperm cells.

Figure 6: Citrullus lanatus (Hossain et al., 2015)

Azadirachta indica

The leaves and seeds have been used in many African cultures for fertility-enhancing properties. The plant is believed to possess anti-inflammatory, anti-bacterial, and antioxidant effects, which could promote healthy sperm production and improve sexual function (Daramola et al., 2017; Singh et al., 2017). The plant has been used in traditional medicine to treat various of health challenges such as skin disorders, fever, and infections. In recent years, it has attracted attention for its potential role in improving male fertility, due to its antioxidant, anti-inflammatory, and hormonal regulatory effects (Agarwal et al., 2005; Shivanand et al., 2016).

The therapeutic effects of the plant are attributed to its rich phytochemical composition, which includes azadirachtin, flavonoids and alkaloids, triterpenoids and terpenoids, vitamins and minerals. A major active compound found in neem is azadirachtin which has been shown to exhibit anti-inflammatory, antioxidant, and immunomodulatory effects (Rajasekaran et al., 2013; Shivanand et al., 2016). Azadirachtin is believed to have an impact on reducing oxidative stress, which is known to damage sperm cells and negatively affect male fertility (Das set al (2014). The plant contains flavonoids such as quercetin, kaempferol, and catechins, which are potent antioxidants that help reduce free radical-induced damage to sperm cells. The compounds have anti-inflammatory and

antioxidant properties that may protect sperm cells from oxidative damage and improve sperm motility and morphology (Parmar et al., 2014). Chandrashekhar et al. (2018) examined the effects of the bark extract on male rats with induced infertility. The results demonstrated an increase in sperm count and motility, along with enhanced testosterone levels. Parmar et al. (2014) examined the general health benefits of the plant in men and reported that its antioxidant and anti-inflammatory effects may contribute to improved sperm health, although additional specific research on its direct impact on male infertility is needed. Das et al (2014) demonstrated that the leaf extract, when applied to human sperm cells, reduced oxidative stress induced by hydrogen peroxide and suggested that the extract could enhance sperm viability and motility by acting as an antioxidant.

Figure 7: Azadirachta indica (Singh et al., 2017)

Ficus Exasperate

Is a plant species belonging to the genus Ficus, used in various African and Asian traditional medicine practices for its wide range of therapeutic properties. It is believed that its high content of tannins and flavonoids can improve sperm count and motility by regulating the male reproductive hormones (Nchinda et al., 2017; Ajala et al., 2021). The plant has been shown to possess antioxidant properties, which could be beneficial in combating oxidative stress, a major factor contributing to male infertility (Ajala et al., 2021). Its anti-inflammatory effects could help in reducing inflammation within the male reproductive organs (Sofowora et al., 2016). A few studies suggest that the plant could act as an aphrodisiac, improving libido and sexual function, possibly through its effects on the hormonal balance and overall vitality (Owu & Ukpabi, 2017).

A study by Ajiboye et al. (2018) in male rats was linked the plant to improved reproductive health due to its antioxidant and anti-inflammatory effects. The study suggested that this could result in better sperm motility and count, though it did not directly measure these outcomes. Nchinda et al (2017) reported that the plant exhibited strong antioxidant activity and suggested that its antioxidant compounds could help protect sperm from oxidative damage, a major factor in male infertility. Sofowora et al (2016) explored the effects of the plant on testicular toxicity in rats and indicated that the plant extract could alleviate testicular damage induced by toxic substances, potentially supporting its use in treating male infertility.

Figure 8: Ficus exasperate (Ajala et al., 2021)

Carpolobia lutea

The plant, native to West Africa, has been used in ethnomedicine for various therapeutic purposes, including as an aphrodisiac agent and for improving male reproductive health (Ogunyemi et al., 2017; Oduola & Olaleye, 2014). The root of this plant, obtained from Ijare near Akure in Ondo State, has been studied for its effects on sperm parameters, capacitation, acrosome reaction, seminal fructose levels, and sperm chromatin integrity in male Wistar rats and its effect may be due to its potential ability to influence hormonal balance and improve overall vitality (Oduola & Olaleye, 2014). Ogunyemi et al. (2017) examined the effects of the plant on reproductive health in male rats and noted that its extract improved sperm quality, including sperm count and motility, likely due to its antioxidant and anti-inflammatory properties.

Inflammation is a known factor that contributes to male infertility, therefore. the anti-inflammatory properties of the plant could play a role in reducing inflammation in the male reproductive system, improving sperm health and function (Ogunyemi et al., 2017). Its antioxidant activity appears to help in combating oxidative stress-induced damage to sperm cells, improving sperm quality and motility (Alabi & Oladipo, 2018). Oduola et al. (2014) investigated the antioxidant effects of the plant and its potential in improving male fertility and observed that the extract had significant antioxidant activity, which may help in protecting sperm cells from oxidative damage. Alabi and Oladipo. (2018) examined the effects of the plant on testicular function and testosterone levels in rats and reported that the extract of the plant increased testosterone levels, suggesting its potential role in improving male fertility and sexual health.

Figure 9: Carpolobia lutea (Oduola et al., 2014)

Aspilia africana

Is a plant native to tropical Africa; it is widely used in traditional medicine for various therapeutic purposes. The plant is known for its medicinal properties, including its antioxidant, anti-inflammatory, and aphrodisiac effects, which may contribute to improving male reproductive health (Olanipekun et al., 2016; Okunade & Olorunfemi, 2017; Dike et al., 2017). An ethnobotanical survey in the Akoko region of Ondo State identified 36 plant species from 29 families used in treating women's health issues, including reproductive problems. The parts of the plants used include roots, stems, leaves, and stem barks (Olanipekun et al (2016).

One of the primary therapeutic properties of the plant is its antioxidant potential. Oxidative stress is a significant factor in male infertility, leading to sperm damage, decreased motility, and compromised DNA integrity. Therefore, its rich-antioxidant content could help in neutralising free radicals, thus protecting sperm cells from oxidative damage (Giday et al., 2010; Dike et al., 2017). The plant has demonstrated strong anti-inflammatory properties, which can help reduce inflammation and improve reproductive health. The plant is traditionally used as an aphrodisiac to enhance libido and sexual performance (Sanni et al., 2016; Kassim et al., 2018). There is some evidence suggesting that the plant may have a positive impact on male hormonal levels, particularly testosterone, which is crucial for sperm production and sexual function (Olaleye et al., 2017). A study by Oduola et al. (2019) found that the extract of the plant increased sperm motility and count in rats, possibly due to its

antioxidant and anti-inflammatory effects. The study suggested that the plant could be beneficial in the treatment of infertility. Okunade et al. (2017) explored the protective effects of the plant against testicular damage caused by toxins in rats and reported that the plant extract had protective effects on the testes, improving sperm quality and function by reducing oxidative stress and inflammation.

Figure 10: Aspilia Africana (Oduola et al., 2019)

Gongronema latifolium

This plant is known for its broad therapeutic applications and often used to enhance libido, improve sperm count, and treat erectile dysfunction (Oluwadamilola et al., 2016). The leaves are usually boiled in water, and the resulting extract is consumed daily. It can also be used in combination with other medicinal plants to improve the overall effectiveness. Its biological activities have drawn attention in scientific research, because for its potential in treating male infertility. The plant is known for its antioxidant, anti-inflammatory, and aphrodisiac properties, which may contribute to improving male reproductive health. Nwankwo et al. (2021) evaluated the antioxidant and spermatogenic effects of the plant in male rats and reported that its extract significantly improved sperm motility, count, and morphology, possibly due to its antioxidant activity. The extract has been reported to reduce oxidative stress markers in the testicular tissue, suggesting its potential role in combating oxidative damage that impairs sperm health. Oloyede et al. (2018) examined the effects of the plant on testicular function and testosterone levels in male rats. The authors reported that the plant extract increased testosterone levels and improved sperm count, suggesting that it could be beneficial in treating male infertility related to low testosterone. Iwalewa et al. (2016) reported on the anti-inflammatory effects of the plant and its potential in reducing inflammation in the reproductive organs and noted that the plant extract reduced inflammatory markers in the reproductive tissues, which could help improve male fertility.

Figure 11: Gongronema latifolium (Nwankwo et al., 2021)

Alchornea laxiflora

The plant has been traditionally used for treating male infertility, particularly in increasing sperm production and motility (Oluwatoyin et al., 2016; Ajayi et al., (2017; Oluwole et al., 2018). It is also believed to improve general reproductive health. The roots and barks are boiled to prepare an infusion, which is consumed over a period. Its biological activities such as its antioxidant, anti-inflammatory, and aphrodisiac properties, suggest it may have a role in improving male reproductive health (Abiola et al., 2018). Ibrahim et al. (2019) examined the antioxidant properties of the plant and its effects on sperm health in rats and reported that its extract significantly reduced oxidative stress markers in the testicular tissue, leading to improved sperm count and motility. The extract was found to have a protective effect on sperm DNA integrity, suggesting its potential as a treatment for infertility caused by oxidative stress. Okonkwo et al. (2020) evaluated the effects of the plant on testicular function and testosterone levels in male rats and reported that the plant extract increased testosterone levels and improved sperm production, suggesting that it could be effective in addressing infertility due to hormonal imbalance or low testosterone levels. Oluwole et al. (2018) examined the anti-inflammatory effects of the plant on male reproductive health and reported that it reduced inflammation in the testes and prostate, which could potentially improve sperm production and overall fertility.

Figure 12: Alchornea laxiflora (Okonkwo et al. (2020)

Cucumis sativus

Cucumber, while often considered a food, is also used in traditional medicine to treat male infertility (Oluwadamilola et al., 2020; Jain et al., 2019; Raji et al., 2017; Arif et al., 2018; Singh et al., 2019). It is believed to improve sperm motility and overall reproductive health. Fresh cucumber juice or slices are often consumed to boost reproductive health. Scientific studies suggest that cucumber possesses antioxidant, anti-inflammatory, and hormonal-regulating properties, which may contribute to improving male reproductive health (Singh et al., 2019; Oluwadamilola et al., 2020). There is evidence to suggest that the antioxidant properties of the plant can help improve sperm motility and count. Khazdair et al. (2017) examined the antioxidant properties of the plant extract and its effects on sperm health and reported that the extract significantly reduced oxidative stress markers in sperm cells, which led to improvements in sperm count and motility. The findings suggested that its antioxidant compounds could protect sperm from oxidative damage. Soni et al. (2015) studied the anti-inflammatory properties of the plant in male rats and noted that its extract reduced inflammatory markers in the testes, improved overall sperm quality and reproductive function of the rats. This finding supports the notion that the plant may help in reducing inflammation, a key factor in male infertility. Siddiqui et al. (2020) explored the effect of the plant on hormone and reported an increase testosterone levels in male rats. The increase in testosterone was associated with enhanced spermatogenesis, suggesting that cucumber could help address male infertility caused by low testosterone levels.

Figure 13: Cucumis sativus (Singh et al., 2019)

Pausinystalia Yohimbe

The plant is found in various parts of West Africa, including Ondo State, Nigeria and the bark of the plant is used to improve sexual health and male fertility. It is known to enhance libido and increase blood flow to the genital area, thus improving sperm function and overall male reproductive health (Abdul-Wahab et al., 2012; Ali et al., 2015; Khera et al., 2009). The plant has been studied for its aphrodisiac properties and its ability to treat erectile dysfunction, which is often associated with male infertility. The bark is typically boiled, and the extract is consumed; the active compound in the plant known as yohimbine, has attracted attention for its potential biological activities in the treatment of male infertility (Goulart et al., 2011; Haddad et al., 2015). Botros et al. (2012) examined the effects of the plant on erectile function and its potential use in treating male infertility and observed that the plant significantly improved erectile function in men with erectile dysfunction, which could have an indirect effect on fertility by facilitating natural conception. Ayoob et al. (2014) studied the impact of the plant on sperm motility and testosterone levels in male rats and noted that its supplementation increased testosterone levels and improved sperm motility, suggesting a potential benefit in the treatment of male infertility related to low testosterone. Mann et al. (2015) examined the antioxidant properties of the plant and its potential to protect sperm from oxidative damage and reported the plant could reduce oxidative stress in the testes and improve sperm count and motility, which are critical factors in male fertility.

Figure 14: Pausinystalia yohimbe (Goulart et al., 2011)

Baphia nitida

The bark and leaves are boiled to make a decoction or infusion, which is consumed by men experiencing fertility problems. It is found in tropical West Africa and is believed to possess several bioactive compounds, including alkaloids, flavonoids, and saponins, which contribute to its medicinal properties. In recent years, there has been increasing interest in its potential biological activities, particularly in the treatment of male infertility (Akinmoladun et al., 2014; Lai et al., 2020; Okoro et al., 2018). Through its antioxidant and anti-inflammatory effects, the plant can improve sperm motility, count, and overall sperm health. Akinmoladun et al. (2014) evaluated the antioxidant and spermatogenic effects of the plant in male rats and noted that its extract significantly reduced oxidative stress markers in testicular tissue, leading to improved sperm motility, count, and morphology. The authors concluded that the antioxidant activity of the plant may be beneficial for treating infertility caused by oxidative stress. Adeyemi et al. (2015) examined the anti-inflammatory effects of the plant regarding its effects in male reproductive health and observed that the plant extract reduced inflammation in the testes and prostate, which could contribute to enhanced sperm production and function. In a traditional medicine, the plant has been used to enhance sexual desire. Olubayo et al. (2016) reported that the plant was found to influence testosterone levels in male rats, increasing testosterone production and improving sperm count and that its effect could be useful in cases of male infertility due to low testosterone levels.

Figure 15: Baphia nitida (Adeyemi et al. (2015)

Xylopia aethiopica

The plant is used to improve male fertility; it is also believed to treat erectile dysfunction and boost sexual stamina (Akinmoladun et al., 2016; Ogunwande et al., 2020). The fruits and seeds are used in powdered form or as part of a herbal mixture to improve sperm quality and count. Its fruit, seeds, and bark contain bioactive compounds that have been shown to possess antioxidant, anti-inflammatory, and aphrodisiac properties, which may contribute to its potential therapeutic role in treating male infertility (Olaleye et al., 2017; Afolabi et al., 2018). Due to its antioxidant and anti-inflammatory effects, the plant has the potential to improve sperm motility, count, and morphology. Akinmoladun et al. (2016) examined the antioxidant properties of the plant and its effects on sperm health in male rats and noted that the extract significantly reduced oxidative stress and improved sperm count and motility. The authors concluded that the plant's antioxidant properties might offer potential for treating infertility caused by oxidative stress. Ajayi et al. (2017) explored the anti-inflammatory effects of the plant on the male reproductive system and observed that the plant extract reduced inflammation in the testes and prostate, leading to an increase in sperm count and motility, suggesting its potential as a fertility-enhancing agent. Ibitoye et al. (2018) evaluated the aphrodisiac and hormonal effects of the plant in male rats and indicated that the plant extract increased testosterone levels and improved sexual behaviour, which could be beneficial for addressing infertility due to hormonal imbalances or low libido. Chukwujekwu et al. (2019) studied the effect of

the plant on sperm motility and count and reported that the plant extract enhanced sperm motility and count in male rats, supporting its use as a potential treatment for male infertility.

Figure 16: Xylopia aethiopica (Chukwujekwu et al., 2019)

Future Studies

Studies on medicinal plants used in the treatment of male infertility in Ondo State, Nigeria, could be of great significance in understanding traditional medicine and their potential in addressing infertility problems. Due to the increasing interest in the use of herbal medicine for fertility treatments, there are several areas where future research could make a meaningful impact. Selected potential research directions for future studies on medicinal plants used in the treatment of male infertility in Ondo State are suggested below:

Future studies should aim to document and record the specific plants used in Ondo State for the treatment of male infertility. This should include working with traditional healers, herbalists, and local communities to identify plants believed to address male reproductive health problems.

Future studies should explore the diversity of plant species in Ondo State that have yet to be studied for their medicinal properties and their roles in reproductive health.

Future studies should aim at understanding the parts of plants that are used and methods of preparation in the treatment of male fertility.

Research should focus on the isolation of bioactive compounds in the plants used for treating male infertility.

Advanced techniques such as HPLC, GC-MS and spectroscopy can help identify and profile the chemical constituents of plants, providing valuable data for standardising their use in fertility treatments.

Future studies should focus on how these plants impact sperm parameters such as as sperm count, motility, morphology, and viability. Animal models could be used to evaluate the efficacy of specific plants in improving these biological factors.

Research should explore the mechanisms of action of the plants on hormones such as testosterone, luteinising hormone and follicle-stimulating hormone.

More detailed future studies should also focus on evaluating the antioxidant and anti-inflammatory properties of plants used in the treatment of male infertility in Ondo State.

It is important to undertake toxicological studies to assess the safety of medicinal plants used for male infertility treatments as such studies would go a long way in helping to establish safe dosages and any potential adverse effects, ensuring that the remedies do not cause harm to clients.

Long-term studies should be undertaking to determine if continuous use of these plants could have any harmful effects on male reproductive health or general well-being.

Clinical trials involving male infertility patients in Ondo State can provide valuable insight into the real-world effectiveness of medicinal plants. The studies should be designed to measure improvements in sperm quality and overall reproductive health.

Clinical trials should compare the effectiveness of plant-based treatments with conventional pharmaceutical treatments for male infertility, to determine their relative efficacy.

Understanding how plants influence the expression of genes related to sperm production and quality would open the door to targeted fertility treatments.

Future studies should focus on ensuring the sustainability of these medicinal plant species.

Research should explore the feasibility of cultivating the plants in controlled environments or on farms to meet growing demand without harming natural ecosystems.

Investigating the cultural significance of male infertility and the associated use of herbal medicine in Ondo State would provide a broader context for understanding how the treatments are perceived and utilised by local populations.

Research should also focus on the economic potential of medicinal plants and their contributions to local economies.

Research should explore the development of guidelines for the preparation, dosage, and quality control of herbal medicines used for male infertility and establishing protocols for plant processing and storage that would enhance the credibility and safety of the treatments.

Future research should work in collaboration with local and national health agencies to create a regulatory framework that ensures the safe and effective use of medicinal plants for male infertility in Ondo State in particular and Nigeria as a whole.

Research should explore approaches to integrate traditional knowledge of medicinal plants with modern medical practices in treating male infertility.

Educating the public on the safe use of medicinal plants for male infertility, through outreach programs, seminars, and health campaigns, could increase awareness and promote responsible use.

CONCLUSION

The review of medicinal plants used in Ondo State, Nigeria, in the treatment of male infertility shows a significant interconnection between traditional practices and contemporary health problems. As male infertility rates rise globally, influenced by lifestyle and environmental factors, the use of medicinal plants is gaining attention. In Ondo State, traditional medicine plays a crucial role in healthcare, with many couples seeking herbal remedies for infertility. Many medicinal plants contain natural antioxidants that combat oxidative stress, a known contributor to male infertility. These plants work by enhancing sperm quality, motility, and overall reproductive health due to their antioxidant and anti-inflammatory as well as hormone-boosting activities. The traditional knowledge of indigenous communities in Ondo State provides valuable insights into the potential therapeutic applications of these plants, contributing to the growing field of ethno pharmacology. While some of these plants have shown promise in preliminary studies, further research is essential to confirm their efficacy and safety. The future of research on medicinal plants used in the treatment of male infertility in Ondo State, Nigeria, offers significant opportunities to bridge traditional knowledge with modern science. Ethnobotanical documentation, scientific investigation of plant compounds, pharmacological evaluation, and clinical trials would provide pathways to better understand the potential of these plants to address male infertility. The increasing prevalence of environmental contaminants affecting male fertility underscores the importance of integrating traditional and modern medical approaches in addressing male infertility. Although traditional remedies are widely used, reliance solely on them without scientific backing may not be the best option. Also, while the plants have been used for centuries in traditional medicine, it is essential for individuals to consult with healthcare professionals before using herbal remedies, especially considering that scientific research on some of the plants is still ongoing.

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