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# Potential of Combined *Curcuma zedoaria* and *Piper crocatum* Leaf Extracts as Natural Male Antifertility Agents: an Experimental Study in Mice

Sukarjati[1*], Mitha Novia Sari[1]

[1] Department of Biology, Faculty of Teknik and Sains, Universitas PGRI Adi Buana Surabaya, Surabaya, Indonesia.

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Corresponding Author:
Sukarjati
sukarjati@unipasby.ac.id

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**Abstract:** *Curcuma zedoaria* and *Piper crocatum* are indigenous Indonesian herbal plants containing various bioactive compounds. *C. zedoaria* is known to contain curcumin, tannins, saponins, and flavonoids, while *P. crocatum* contains piperine, tannins, saponins, flavonoids, alkaloids, and triterpenoids. This study aimed to investigate the effects of white turmeric extract, red betel leaf extract, and their combination on the spermatogenic cells of male mice. Extracts were obtained using the maceration method. A total of 30 male mice, aged 3 months and weighing 25–30 grams, were randomly divided into four treatment groups with three replications each: control, white turmeric extract, red betel extract, and a combination of both extracts. The extracts were administered orally at doses of 50, 100, and 150 mg/kg BW for individual extracts, and 25:25, 50:50, and 75:75 mg/kg BW for the combined treatment, over 35 days. Histological sections of the testis were prepared following standard laboratory protocols. One-way ANOVA showed a significant decrease ($p < 0.05$) in all cell types in treated groups, with the most substantial reduction observed at the 75:75 mg/kg BW combination dose. The conclusion of this study is that the combined extract of *C. zedoaria* and *P. crocatum* has the potential as an antifertility

**Keywords:** Antitertility; *Curcuma zedoaria*; *Piper crocatum; Mus musculus*; Spermatogonium; Spermatocyte; Spermatids

## Introduction

High population growth rates remain a major challenge to public health development, particularly in developing countries like Indonesia. Despite the long-standing family planning program, male participation in contraceptive use remains low. According to the Indonesian Demographic and Health Survey (IDHS), contraceptive use by men remains far below that of women (only around 7.3%). The main reasons for refusing methods such as condoms and vasectomy are concerns about reduced virility and comfort (Najah & Yuni, 2024).

On the other hand, the use of synthetic contraceptives often causes side effects and is not environmentally friendly (Abbe et al., 2020). Therefore, efforts are needed to develop natural-based antifertility agents that are effective, safe, and socially acceptable (Verma & Yadav, 2021).

The use of medicinal plants as antifertility agents has long been an alternative in traditional medicine (Mishra et al., 2019). Herbal plants contain secondary metabolites that can affect fertility through various mechanisms, including disruption of spermatogenesis, decreased reproductive hormone levels, and histological changes in reproductive organs (Upadhyay, 2024). This strategy is considered cheaper, has fewer side effects, and is more acceptable to the community.

Two plants with antifertility potential are white turmeric (*Curcuma zedoaria*) and red betel leaf (*Piper crocatum*). *Curcuma zedoaria* contains curcumin, essential oils, saponins, and flavonoids. Several studies have shown that its extract can reduce testicular and seminal vesicle weight and reduce spermatozoa count, motility,

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and viability (Winarti et al., 2021). *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two extracts can reduce sperm motility, morphology, viability, and concentration in mice (Sukarjati & Pratama, 2019). The methanol-water fraction of *Piper crocatum* extract is known to be most effective in reducing spermatozoa quality and quantity. Research shows that administering *Curcuma zedoaria* extract leads to a decrease in the number of spermatogenic cells in the seminiferous tubules (Anggeriani, 2019) and a reduction in the number of mitoses in the testes (Gharge et al., 2021). *Curcuma zedoaria* also has the potential to interfere with testosterone synthesis in Leydig cells. This can disrupt Sertoli cell function, leading to degeneration and malnutrition of spermatogenic cells. Furthermore, *Curcuma zedoaria* can cause changes in the structure of the seminiferous tubules, a decrease in spermatogonia, spermatocytes, spermatids, and spermatogenic cells overall, along with reduced sperm motility and viability (Fatrin et al., 2017).

*Piper crocatum* contains piperine, a compound traditionally used for contraceptive purposes, which has shown significant potential as a reversible male contraceptive based on scientific studies. Piperine has a disruptive effect on spermatogenesis by decreasing the synthesis of testicular hormones, including testosterone, FSH (*Follicle Stimulating Hormone*), and LH (*Luteinizing Hormone*), which leads to decreased sperm production and quality. There is a disruption of the testicular antioxidant system, an increase in *Reactive Oxygen Species* (ROS) and hydroxyl radicals, which damage testicular cells and spermatogenesis. Histopathological evidence shows damage to testicular tissue and germ cells, supporting an antifertility effect. These effects were shown to be reversible after withdrawal of piperine treatment, with hormone levels and sperm parameters returning to normal (Chinta et al., 2017). Docking and molecular dynamics simulations revealed that piperine binds to androgen-binding proteins and androgen receptors, potentially blocking the activity of natural androgens required for sperm production and male fertility (Chinta et al., 2015). In vitro studies confirm that piperine inhibits the effects of dihydrotestosterone at nanomolar concentrations, further supporting its male contraceptive action at the molecular level (Chinta et al., 2015). Piperine also negatively impacts epididymal sperm count, motility, viability, and seminal vesicle function, with reversible effects. The overall picture is that piperine supports Leydig cell maturation and androgen synthesis but simultaneously suppresses spermatogenesis. This may occur through hormonal imbalance (high testosterone but low FSH) and a direct effect on the testes (Chen et al., 2018). Thus, piperine from *Piper crocatum* acts through hormonal and molecular mechanisms to decrease spermatogenesis and sperm quality, suggesting it may be a potential reversible male oral contraceptive.

However, the literature search was conducted online through PubMed, Scopus, Web of Science, Google Scholar, ScienceDirect, SpringerLink, DOAJ, as well as national repositories (Garuda, Neliti) and institutional repositories, no research has explicitly examined the combination of these two extracts as an antifertility agent. Previous studies have focused solely on the effects of single extracts of *Curcuma zedoaria* and *Piper cocatum*. There has been no study examining the synergism or antagonism of the combination of these two plants as an antifertility agent. No research has specifically compared the effects of the combination with those of the single extracts on histological structure and spermatogenic parameters.

This study aimed to analyze the effects of *Curcuma zedoaria* extract, *Piper cocatum* leaf extract, and a combination of the two extracts on spermatogenic cell count using a mice model. This research is important because current male contraceptives only include condoms and vasectomy. Therefore, herbal antifertility treatments offer the opportunity for more varied, practical, and reversible male contraceptives that are safe and have minimal side effects. The novelty of this study is the evaluation of the combination of *Curcuma zedoaria* and *Piper crocatum* as a natural antifertility agent. This combination has the potential to become a base ingredient for a locally sourced phytopharmaceutical-based male contraceptive with minimal side effects and a sustainable approach, contributing to the development of herbal male contraceptives, which are currently very limited.

## Method

*Curcuma zedoaria* and *Piper crocatum* leaves were obtained from Sidomulyo Village, Kedungadem District, Bojonegoro Regency.

### *Experimental Animals*

Thirty male mice (*Mus musculus*), 3 months old, with an average weight of 25-30 grams, were obtained from the Center for Veterinary Research (PUSVETMA) Surabaya. The mice were acclimatized to their cages for 7 days. The cages used measured 40 cm x 30 cm x 12 cm, with a wire mesh cover and a drinking bottle. Food and water were provided daily according to laboratory standards.

### *Extract Preparation*

*Curcuma zedoaria*

*Curcuma zedoaria* extract is prepared by thoroughly washing the *Curcuma zedoaria*, slicing it thinly, and then *Curcuma zedoaria* leaf is prepared by thoroughly washing and then air-drying. Once dry, it is blended and then

sieved. 100g of the powdered herb is macerated with 1000ml of 80% ethanol for 3 days and left at room temperature, stirring daily. Then, the extract is filtered. The filtrate is separated from the solvent using a rotary evaporator for approximately 8 hours at a maximum temperature of 50°C.

*Piper crocatum*

*Piper crocatum* leaf extract is prepared by thoroughly washing and then air-drying. Once dry, blend the leaves and sift them through a sieve. 100g of the powdered plant is macerated with 1000ml of 80% ethanol for 3 days at room temperature. Stirring is performed daily. The resulting filtrate is then filtered and separated from the solvent using a rotary evaporator for approximately 8 hours at a maximum temperature of 50°C (Sukarjati & Syahputra, 2025).

*Treatment*

The mice were divided into 4 groups (Group A, B, C, D). A. Control Group (0 mg/KgBW). Groups B, C, and D were each divided into 3 groups. Treatment B1: *Curcuma zedoaria* extract at a dose of 50 mg/KgBW; B2: *Curcuma zedoaria* extract at a dose of 100 mg/KgBW; B3: *Curcuma zedoaria* extract at a dose of 150 mg/KgBW. C1: *Piper crocatum* leaf extract at a dose of 50 mg/KgBW; C2: *Piper crocatum* leaf extract at a dose of 100 mg/KgBW; C3: *Piper crocatum* leaf extract at a dose of 150 mg/KgBW. D1: Combine ectract, *Curcuma zedoaria* extract: *Piper crocatum* leaf extract = 25 mg/KgBW: 25mg/KgBW, D2: Combine extract, *Curcuma zedoaria* extract: *Piper crocatum* leaf extract = 50 mg/KgBW: 50 mg/KgBW, and D3: Combine extract, *Curcuma zedoaria* extract: *Piper crocatum* leaf extract = 75 mg/KgBW: 75mg/KgBW. All treatments were repeated 3 times. The extract was administered for 35 days.

*Preparation of Mice Testicular Histology Slides*

On day 36, all mice were euthanized, and both testicles were removed for histology slides. Testicular histology slides were prepared according to laboratory standards. Observations were made by counting the number of spermatogonia, spermatocytes, and spermatids in the seminiferous tubules using a microscope.

## Result and Discussion

*Spermatogonia*

Research data on the potential of *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two extracts on spermatogonia cell counts was analyzed using one-way ANOVA and LSD. The statistical analysis revealed an effect of *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two extracts at various doses on spermatogonia cell counts (p=0.000). The average spermatogonia count data is presented in Figure 1.

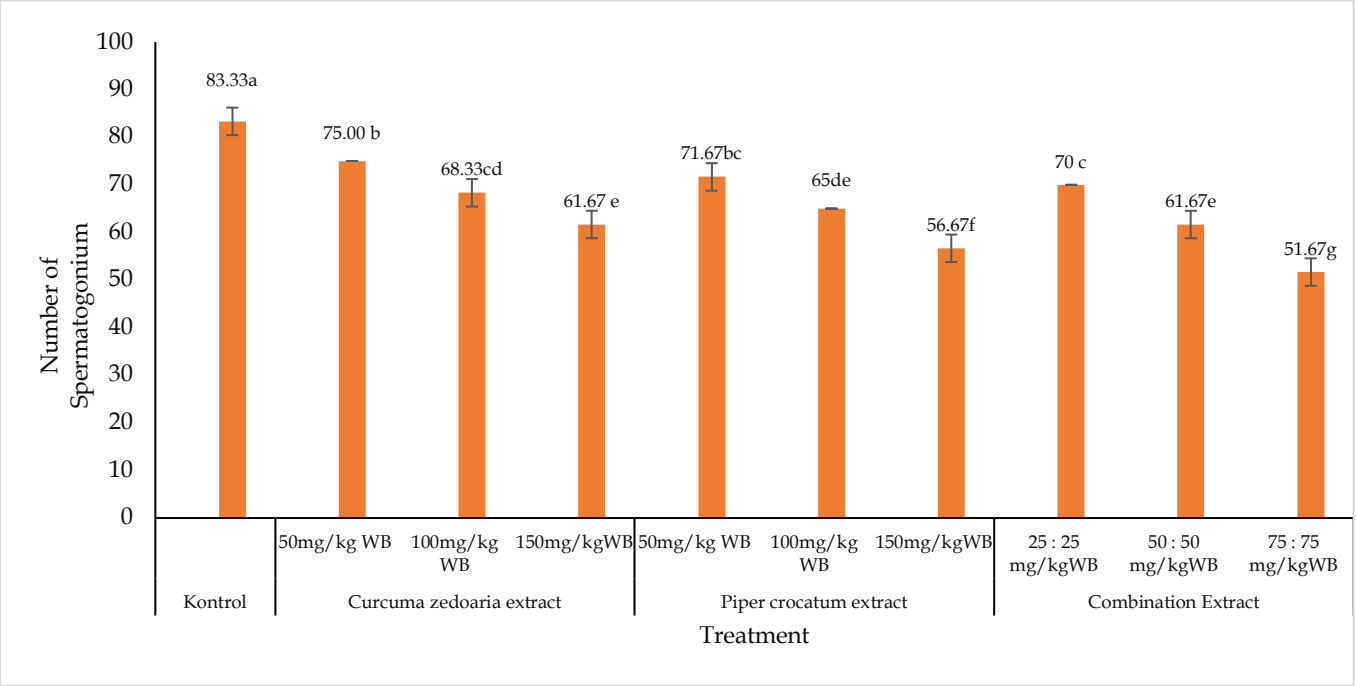


**Figure 1.** Diagram of Spermatogonium on Different Extract and Doses Notation for the same letters is not significantly different

The Figure 1 shows that the average number of spermatogonia cells in the treatment group with

*Curcuma zedoaria* extract, *Piper crocatum* extract, and a combination of the two extracts was lower than in the control group.

*Spermatocytes*

The results of a study on the potential of *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two extracts on spermatocyte counts were analyzed using one-way ANOVA. The results showed that various doses of the extracts significantly affected spermatocyte counts (p=0.000). Spermatocyte count data are presented in Figure 2.

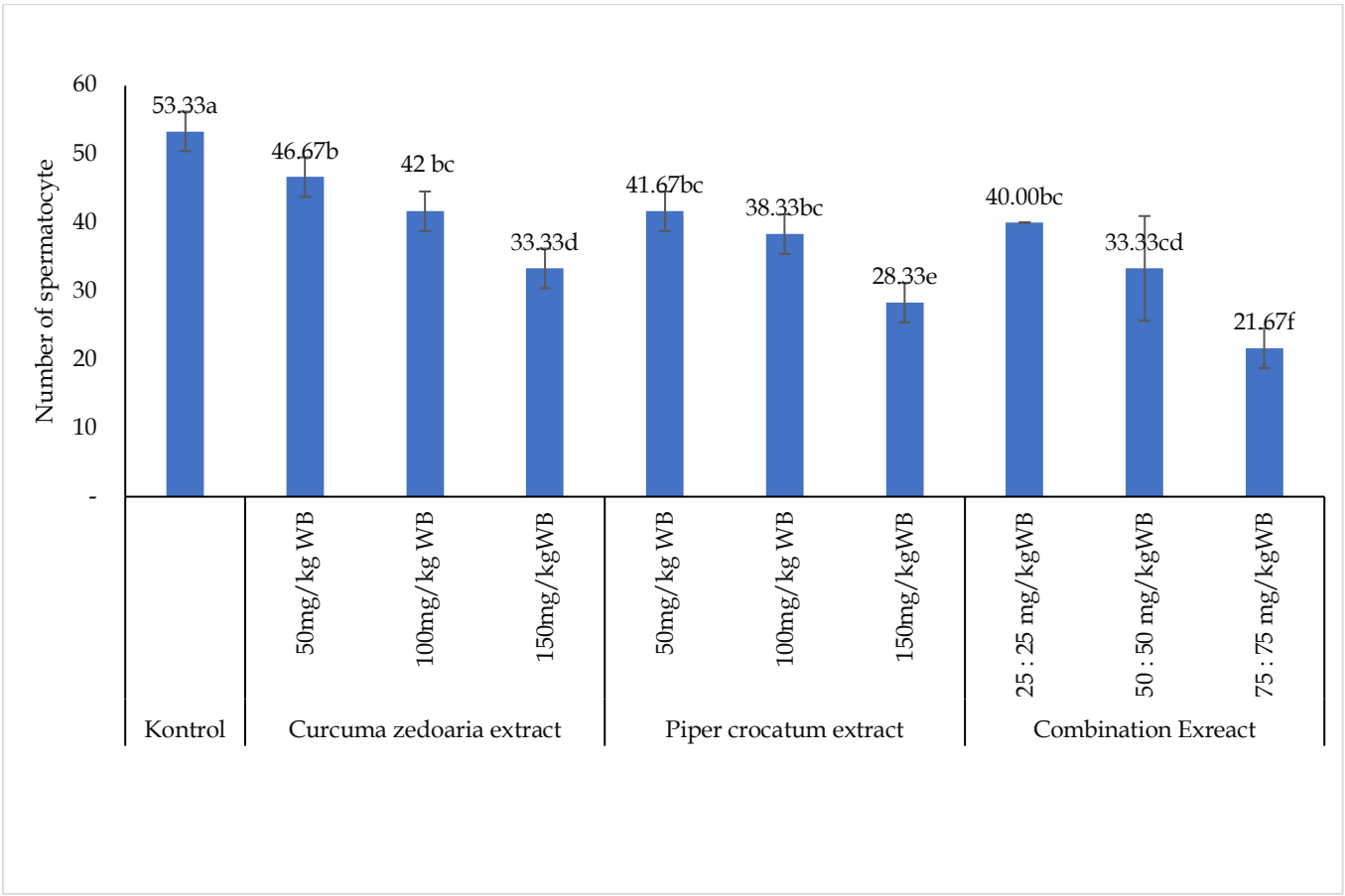


**Figure 2**. Diagram of Spermatocytes Different Extract and Doses Notation for the same letters is not significantly different

The Figure 2 shows that the average number of spermatocyte cells in the treatment group with *Curcuma zedoaria* extract, *Piper crocatum* extract, and a combination of the two extracts was lower than in the control group.

*Spermatids*

The results of the research and analysis of the potential of *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two extracts on spermatid cell count were analyzed using one-way ANOVA. The results showed that various doses of the extracts significantly affected spermatids count (p=0.000). Spermatids count data are presented in Figure 3.

Figure 3 shows that the average spermatid count in the *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and the combination of the two extracts was lower than in the control group.

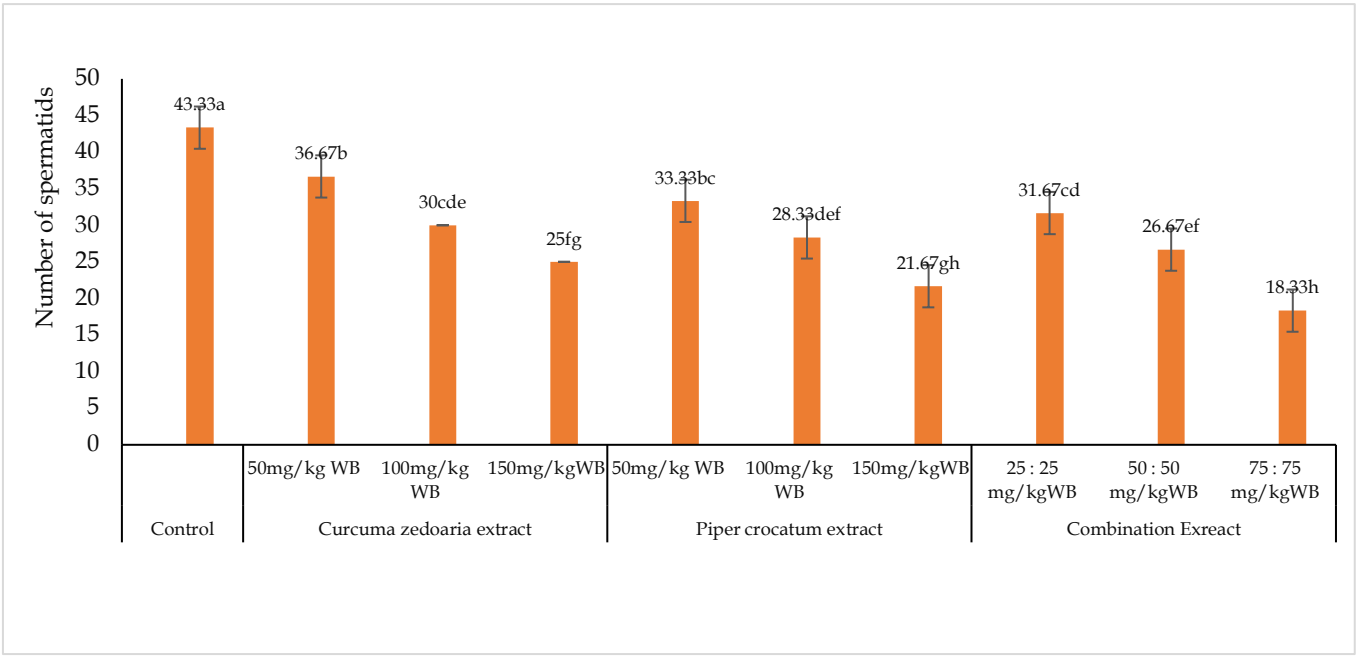


**Figure 3**. Diagram of Spermatids Different Extract and Doses Notation for the same letters is not significantly different

Visualization of testicular histology in each treatment is presented in Figure 4.

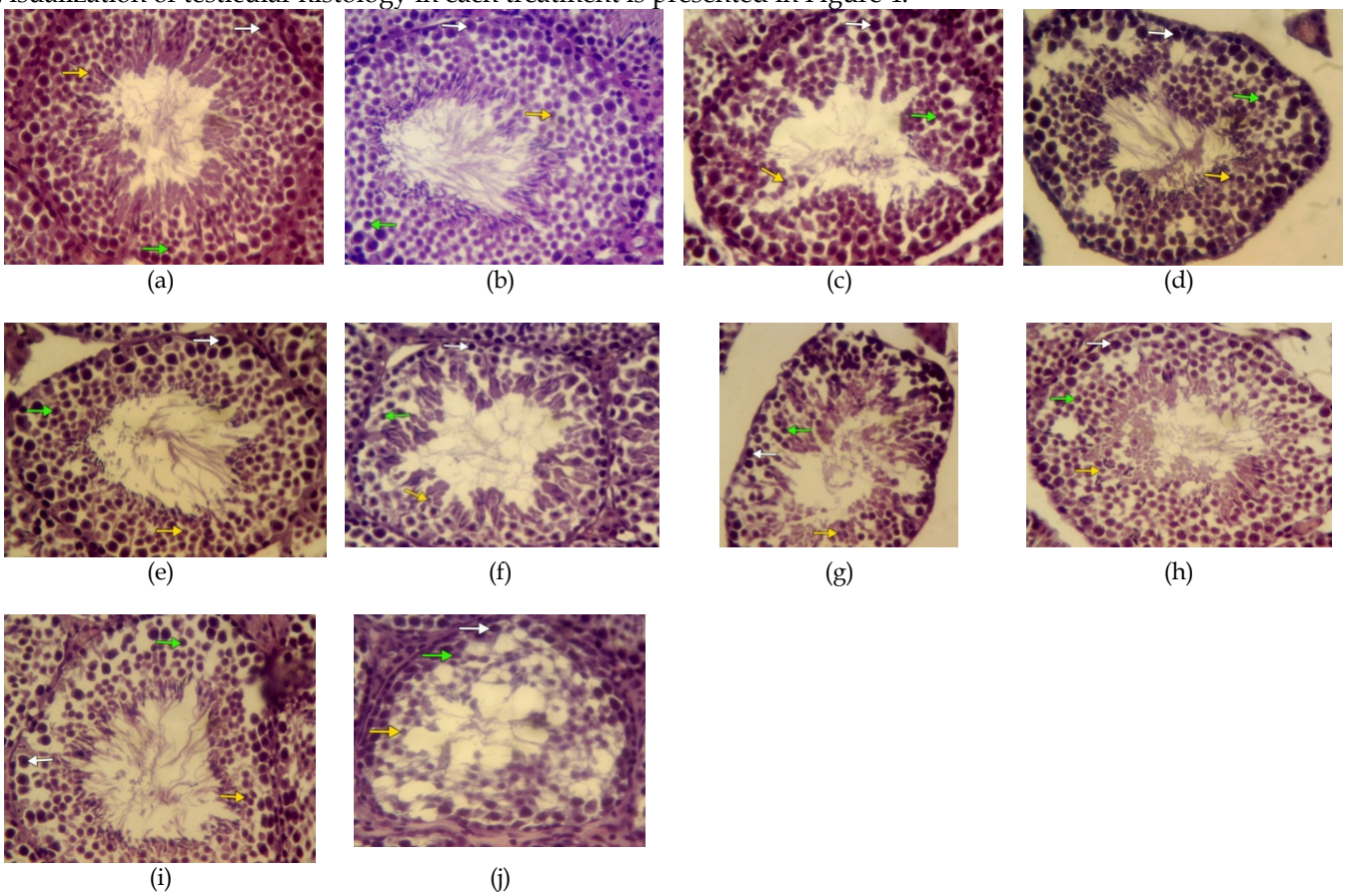


**Figure 4.** Testicular histology in each treatment: (a) Control; (b) Curcuma zedoaria 50mg/kgWB; (c) Piper crocatum 50mg/kgWB; (d) Combination 25:25mg/kgWB; (e) Curcuma zedoaria 100gmg/kgWB; (f) Piper crocatum 100mg/kgWB; (g) Combination 50:50mg/kgWB; (h) Curcuma zedoaria 150gmg/kgWB; (i) Piper crocatum 150mg/kgWB; and (j) Combination 75:75mg/kgW

*Discussion*

*Spermatogonia*

The results of this study showed that administration of *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two resulted in a decrease in the number of spermatogonia compared to the control group.

The control group showed the highest average spermatogonia count, at 83.33 cells, reflecting normal spermatogenesis without active ingredient treatment. The 50 mg/kgBW dose resulted in an average spermatogonia count of 75 cells for the *Curcuma zedoaria* extract, 71.67 cells for the *Piper crocatum* leaf extract, and 70 cells for the combination extract. Therefore, the decrease in spermatogonia count was not significant. This indicates that at low doses, the active compounds in the extracts do not have a strong toxic effect on spermatogonia. However, early disruption of spermatogenesis began to appear, particularly with the combination extract treatment. A study by (Fatrin et al., 2017) showed that *Curcuma zedoaria* extract contains flavonoids and alkaloids, which can interfere with spermatogonia proliferation through the mechanisms of oxidative stress and inhibition of testosterone hormone.

Treatment of extract administration with a dose of 100 mg/kgBW, the average number of spermatogonia decreased further, namely in the treatment of *Curcuma zedoaria* extract: 68.33 cells, *Piper crocatum* leaf extract: 65 cells, Combination extract: 61.67 cells. This decrease indicates the cytotoxic effect of the extract on germ cells. The flavonoid and tannin content of *Piper crocatum* is known to be able to induce apoptosis of germ cells at high doses through activation of the ROS (*Reactive Oxygen Species*) pathway. A study by Gofur & Lestari (2018) supports this, where *Piper crocatum* leaf reduces the number of spermatogenic cells in rheumatoid arthritis model mice due to high oxidative stress that damages the spermatogonia plasma membrane.

Treatment of extract administration dose of 150 mg/kgBW, obtained results at the highest dose (150 mg/kgBW), there was a drastic decrease, namely in the treatment of *Curcuma zedoaria* extract: 61.67 cells, *Piper crocatum* leaf extract: 56.67 cells, Combination extract: 51.67 cells. The strongest effect occurred in the combination extract group, indicating a toxic synergism between the bioactive components of the two plants. This is in line with research (Ongko et al., 2019), which reported that administration of 300 mg/kgBW *Curcuma zedoaria* extract causes degeneration of seminiferous tubules and loss of spermatogenic cells. In addition, flavonoids in both plants can also suppress Leydig cell activity, reducing testosterone production needed to maintain the spermatogonia population. This effect is exacerbated by saponins and phenolic compounds that have hormone-like activity, disrupting the hypothalamic-pituitary-testicular axis.

The hypothalamic-pituitary-testicular (HPT) axis is a key neuroendocrine system that governs male reproductive function, including the process of spermatogenesis, which is the production of sperm cells from spermatogonia (Li et al., 2024; Yadav, 2024). Spermatogonia are the foundational germ cells in the testes from which spermatozoa develop. They serve as stem cells that self-renew and differentiate into mature sperm through a series of stages during spermatogenesis (Diao et al., 2022). This process takes place in the seminiferous tubules of the testes and progresses through spermatocytes and spermatids to form mature spermatozoa (Zhang et al., 2024). Proper functioning and regulation of spermatogonia are essential for continuous sperm production and male fertility (Liu et al., 2024).

Proper functioning and regulation of spermatogonia are essential for continuous sperm production and male fertility (Maroto et al., 2025). Disruption of the HPT axis can negatively impact spermatogonia function and thus impair spermatogenesis (Hasan et al., 2022; Martins & Anderson, 2022). This can occur through various mechanisms such as inflammation, hormonal imbalances, or environmental insults (Tesarik, 2025; Mansour, 2025). Testosterone, produced by Leydig cells in the testes under the stimulation of luteinizing hormone (LH) from the pituitary, plays a crucial role in maintaining spermatogenesis, including the function of spermatogonia (Lei et al., 2025; Li et al., 2024). Sertoli cells, which support and nourish developing germ cells, are also regulated by hormones from the HPT axis (Cannarella et al., 2024; Shah et al., 2021). In summary, the hypothalamic-pituitary-testicular axis regulates spermatogonia through hormonal signals that promote their proliferation and differentiation into mature sperm. Disruption of this axis can impair spermatogonia function and result in male infertility due to defective spermatogenesis.

Thus, in this study, there was a linear decrease in the number of spermatogonia with increasing extract doses. The effect of the combined extract was stronger than that of the single extract, indicating the potential synergistic antifertility effect. *Curcuma zedoaria* extract tended to have a moderate effect, while *Piper crocatum* leaf was more toxic to spermatogonia at high doses. The combination extract of 75 mg/kgBW: 75 mg/kgBW caused a decrease of almost 37% from the control, which was very biologically significant.

*Spermatocytes*

The results of this study indicate that administration of *Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two at graded doses (50, 100, and 150 mg/kgBW) reduced the number of spermatocytes compared to the control

group. The control group had the highest average spermatocyte count, at 53.33 cells, indicating optimal testicular physiological condition. At a dose of 50 mg/kgBW, a decrease in spermatocyte count occurred in all three treatment groups (*Curcuma zedoaria* extract: 43.33 cells; *Piper crocatum* leaf extract: 41.67 cells; Combination extract: 40 cells). The decrease in spermatocyte count was most significant at a dose of 100 mg/kgBW and was lowest at a dose of 150 mg/kgBW, particularly in the combination extract group (*Curcuma zedoaria* + *Piper crocatum* leaf = 75 mg/kgBW+ 75 mg/kgBW), with only 21.67 spermatocytes. These results indicate that both *Curcuma zedoaria* extract and *Piper crocatum* leaf extract have antispermatogenic effects, and the strongest effect was found in the administration of a combination of extracts, namely *Curcuma zedoaria* + *Piper crocatum* leaf = 75 mg/kgBW + 75 mg/kgBW, indicating a synergistic effect.

*Curcuma zedoaria* extract is reported to contain curcuminoids, sesquiterpenes, and flavonoids that have mild cytotoxic effects on testicular cells. Administration of Curcuma zedoaria extract can cause a decrease in the size of the seminiferous tubules and a reduction in the number of spermatocytes (Ongko et al., 2019). This occurs because the extract has antiandrogenic activity that inhibits testosterone synthesis in Leydig cells, thereby disrupting Sertoli cell function. Disrupted Sertoli cells cannot provide optimal nutrition to germ cells, causing degeneration and death of spermatogenic cells through a pro-apoptotic mechanism. Disruption or dysfunction of Sertoli cells results in their inability to provide optimal nutrition and support to germ cells, which leads to degeneration and death of spermatogenic cells through pro-apoptotic mechanisms. Sertoli cells produce lactate and other metabolites essential for nurturing developing germ cells, including spermatids, and they also maintain the blood-testis barrier (BTB), creating a protective microenvironment for spermatogenesis. When Sertoli cells are impaired, lactate metabolism is downregulated, their phagocytic capacity decreases, and mitochondrial function is reduced, contributing to germ cell apoptosis and defective spermatogenesis (Yokonishi et al., 2020).

*Curcuma zedoaria* contains bioactive compounds such as curcumin that can interfere with sperm function and reduce fertility in men, supporting the plant's potential as a natural male contraceptive (Bhardwaj et al., 2025). Other bioactive compounds found in *Curcuma zedoaria*, such as essential oils, saponins, flavonoids, alkaloids, and polyphenols, may contribute to its antifertility properties by affecting hormone secretion and spermatogenesis (Naz, 2011). *Curcuma zedoaria* was found to cause a concentration-dependent decrease in sperm motility and fertilization ability in vitro, and in vivo administration caused a significant and reversible decrease in fertility. Curcumin also exhibits spermicidal and microbicidal properties, making it a promising non-steroidal contraceptive candidate with the added benefit of preventing infection (Naz & Lough, 2014).

*Piper crocatum* Leaves contain eugenol, flavonoids, saponins, and tannins, which are known to have antiandrogenic and mild cytotoxic properties, especially against spermatogenic cells. (Salehi et al., 2019) showed that Piper species, including *Piper crocatum*, contain compounds that inhibit steroidogenesis enzymes such as 5-α-reductase, which is important in testosterone production. Piper extracts can cause testicular tissue damage through increased ROS and decreased Bcl-2 (an antiapoptotic protein) expression. Piperine compounds from other Piper genera, such as *Piper nigrum*, are known to inhibit spermatogenesis, including reducing spermatid count, through mechanisms such as decreased FSH hormone and increased oxidative stress in the testes. These effects are reversible after discontinuation of administration (Chen et al., 2018). Piper nigrum (black pepper) and its active alkaloid piperine are known to inhibit spermatogenesis, including reducing spermatid count, through several mechanisms. Studies in rats and mice show that piperine treatment leads to degenerative changes in the seminiferous tubules, such as loosening of the germinal epithelium, intraepithelial vacuolation, giant cells formation, and disorganized spermatids (Chen et al., 2018).

Several potential mechanisms can be hypothesized that the active ingredients in *Piper crocatum* leaves reduce the number of spermatocytes by the mechanism (1). Disrupting Spermatogenesis in general, namely *Piper crotatum* extract, is suspected of having active compounds that can cause oxidative stress and damage germ cells in the seminiferous tubules. (2) Disrupting reproductive hormones, namely the active compounds in *Piper crotatum*, may reduce testosterone hormone levels, which are important for spermatid development and sperm maturation, thereby inhibiting the development of spermatids into mature spermatozoa. (3) inducing Germinal Cell Apoptosis, namely that several bioactive compounds in *Piper crotatum* have the potential to induce apoptosis (programmed cell death) in germ cells, including spermatocytes, thereby reducing the number of developing spermatocytes. (4) Damaging the Structure of Seminiferous Tubules, namely that toxic effects on Sertoli cells and the structure of the seminiferous tubules can disrupt the microenvironment needed by spermatocytes to develop properly. The combination extract of two plants with high flavonoids can increase proapoptotic activity and suppress spermatogenesis more strongly than each single extract (Parveen et al., 2021).

*Spermatids*

This study showed that administration of *Curcuma zedoaria*, *Piper crocatum* leaf, and a combination of the

two extracts caused a dose-dependent decrease in spermatid counts. This decrease in spermatid count indicates the potential antifertility effects of all three treatments, especially at high doses.

In the control group (0 mg/kgBW), the highest average number of spermatid cells was recorded at 43.33 cells, which is a reference for normal physiological conditions. After administering the extract treatment at a dose of 50 mg/kgBW, a significant decrease occurred in all treatment groups, where the combination extract group showed the largest decrease of 31.67 cells, followed by *Piper crocatum* leaf extract at 33.33 cells and *Curcuma zedoaria* extract at 36.67 cells. This decreasing trend continued at doses of 100 mg/kgBW and 150 mg/kgBW. At the highest dose of 150 mg/kgBW, the lowest number of spermatid cells was recorded in the group given the combination extract of *Curcuma zedoaria* +*Piper crocatum* leaf = 75 mg/kgBW: 75 mg/kgBW at 18.33 cells, compared to *Piper crocatum* leaf extract at 21.67 cells and *Curcuma zedoaria* extract at 25 cells. This indicates a synergistic effect of the combination of the two extracts on suppressing spermatogenesis.

The underlying mechanism of action for this decline is likely related to the bioactive compounds in both plants, such as flavonoids, tannins, saponins, and essential oils. In very high dose, Flavonoids and phenolic compounds are known to increase oxidative stress in testicular tissue, thereby disrupting spermatogenesis. Furthermore, curcuminoids in Curcuma are reported to have antiandrogenic effects that can affect Sertoli cell function and spermatid maturation (Arwansyah et al., 2014).

The sharper decrease in spermatid count in the combined extract group compared to the single extract group indicates the presence of additive or synergistic phytochemical interactions, which may enhance the inhibitory effect on spermatogenesis. This finding is in line with the study by Zhou et al. (2016), which stated that the combination of herbal compounds with mutually supporting pharmacological activities can enhance biological effects, including antifertility effects, by acting on various hormonal or cellular targets in the reproductive system.

Interestingly, although both single extracts demonstrated significant antifertility effects, *Piper crocatum* leaf extract appeared to have a stronger effect than *Curcuma zedoaria* extract at high doses. At a dose of 150 mg/kgBW, *Piper crocatum* leaf extract resulted in 21.67 spermatid cells, while *Curcuma zedoaria* extract resulted in 25 spermatid cells. This suggests that *Piper crocatum* may be more effective in disrupting the spermatogenic pathway.

Overall, these findings support the potential use of herbal plants as alternative antifertility agents for men, which are relatively safer than synthetic contraceptives, which often cause systemic side effects (Samarghandian et al., 2017).

## Conclusion

*Curcuma zedoaria* extract, *Piper crocatum* leaf extract, and a combination of the two extracts have the potential to reduce the number of spermatogonia, spermatocytes, and spermatids in a mice model (*Mus musculus* L.). The combined extract treatment at a dose of 75 mg/kgBW:75 mg/kgBW was the treatment that most significantly reduced the number of spermatogonia, spermatocytes, and spermatids. Therefore, the combined extract of *Curcuma zedoaria* and *Piper crocatum* leaf at a dose of 75 mg/kgBW:75 mg/kgBW has the potential as an alternative herbal antifertility agent for men. The conclusion of this study is that the combined extract of C. zedoaria and P. crocatum has the potential as an antifertility However, further research is needed to evaluate the reversibility, hormonal modulation, and long-term safety of these extracts.

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**Author Contributions**
Conceptualization, S.; methodology, S; software, M.; validation, S and M.; formal analysis, S.; investigation, S and M.; resources, S and M.; data curation, S, writing—original draft preparation, S and M.; writing—review and editing, S ; visualization, S and M.; supervision, S; project administration, S and M.; funding acquisition, S and M. All authors have read and agreed to the published version of the manuscript.

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**Conflicts of Interest**
The authors declare no conflict of interest

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