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Potential of White Oyster Mushroom to Improve Male Fertility : A Systematic Review

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ABSTRACT

Infertility in men is a health problem that is quite often experienced these days. One of the causes of idiopathic infertility in men is oxidative stress (SO). Several previous research results have previously been presented which prove that poor sperm quality is associated with an increase in reactive oxygen species (ROS) due to SO. White Oyster Mushroom (*Pleurotus ostreatus*) is a mushroom that is rich in antioxidants which has great potential to reduce the occurrence of reactive oxygen species (ROS) which reach high levels of SO so it is thought to be useful in improving sperm quality.
Keyword: Infertility, Sperm, *Pleurotus ostreatus*.

ABSTRAK

Infertilitas pada pria merupakan masalah kesehatan yang cukup sering dialami saat ini. Salah satu penyebab infertilitas idiopatik pada pria adalah stres oksidatif (SO). Beberapa hasil penelitian terdahulu telah dipaparkan sebelumnya yang membuktikan bahwa kualitas sperma yang buruk berhubungan dengan peningkatan spesies oksigen reaktif (ROS) akibat SO. Jamur Tiram Putih (Pleurotus ostreatus) merupakan jamur yang kaya akan antioksidan yang berpotensi besar dalam menurunkan terjadinya spesies oksigen reaktif (ROS) yang mencapai kadar SO tinggi sehingga diduga bermanfaat dalam meningkatkan kualitas sperma.
Kata kunci : Infertilitas, Sperma, Pleurotus ostreatus

1. Introduction

Infertility is a worldwide problem. This affects 15% of couples who have intercourse without contraception. For men have a contribution of 30-40%. This data is an accumulative result from around the world [1]. Infertility in men in Indonesia is caused by internal body factors (58%), external body factors (32%) and other factors (10%) [2]. We can see from the percentage of male infertility factors in Indonesia, it boils down to general factors and special factors. Common factors include age, frequency of sex and length of time trying. Specific factors, pretesticular and posttesticular problems, immunological reactions and environmental factors, namely exposure to alcohol, cigarettes, heavy metals and drugs [3].

The global prevalence of infertility varies between 2.5%-15%, correlating with at least 30 million infertile men worldwide [4]. The prevalence of infertility in the Asian region shows that male infertility has increased in all Asian regions. The highest increase was found in South Asian men (with an average rate of change of 48.4 per 100,000 men) [5]. Meanwhile, the prevalence of infertility in Indonesia is 12% - 15% of 40 million couples of childbearing age, with 40% of infertility in men having no known cause [6], but this infertility has been associated with several emotional, physical and sociocultural problems [7].

The diagnosis of infertility in men is mainly based on semen analysis [8]. Sperm quality parameters are determined by: sperm morphology, sperm motility, and the number of sperm undergoing apoptosis [9]. Infertility in men is related to several factors including smoking, consuming alcohol, lifestyle and a Body

Mass Index (BMI) < 19 or > 29 [10]. Age over 40 years, uncomfortable work environment, excessive and heavy workload [11], hormonal disorders, physical activity, lifestyle, psychology, sexual problems, chromosomal abnormalities and single gene defects [8], including oxidative stress (SO) [12].

White Oyster Mushroom (Pleurotus ostreatus) is a mushroom that can be consumed, has many benefits, and is also widely cultivated [13]. White oyster mushrooms (Pleurotus ostreatus) contain protein, fat, phosphorus, Vitamins B1, B2, C and E. There are also 20 amino acids that resemble protein derivatives in animal flesh but do not contain cholesterol [13]. These amino acids include methionine, tyrosine, histidine, lysine and tryptophan, which generally function as antioxidants [13]. Methionine is a sulfur-containing antioxidant amino acid with clinically relevant antioxidant properties [14]. Methionine sulfoxide reductase (Msr) has an important role in repairing protein damage and improving oxidative stress caused by ROS (reactive oxygen species) [15].

L-carnitine is a beneficial antioxidant where L-Carnitine plays a major role in sperm motility and sperm morphology [16]. In addition, men who received antioxidant supplements for a period of 3 months experienced significant improvements in conventional semen parameters, sperm concentration, normal morphology and seminal oxidation reduction potential (ORP). So, antioxidants play an important role in improving sperm quality, especially regarding morphology [17]. ω-3 fatty acids have a very important role regarding sperm concentration in men [16]. One source also states that Coenzyme-Q10 has a better effective treatment for sperm concentration [17].Vitamin E has a good influence on men's metabolism. The addition of antioxidant compounds such as Vitamin E can increase the number and quality of male sperm [18], reducing the destructive effects of SO on sperm. These antioxidant properties can increase sperm parameters, one of which is sperm count [19].

Flavonoids have great potential to reduce the occurrence of reactive oxygen species (ROS) caused by high levels of SO [20]. One of the herbal plants that contains flavonoid compounds is the Moringa plant (Moringa oleifera Lam.) which contains high antioxidants [21].

Several previous research results have previously been presented proving that poor sperm quality is associated with increased ROS due to SO. Where the formation of SO can be inhibited by antioxidants. On the other hand, white oyster mushrooms contain several nutrients that function as antioxidants, but the results of previous research have not provided much information on the influence of white oyster mushrooms on the quality (morphology, motility and quantity) of sperm, especially in experimental animals for infertility induced with Cyclophosphamide [22].

2. Materials and Methods

This systematic review was conducted in accordance with The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.1 Literature search strategy

A systematic literature search was conducted in the Mendeley database for intervention studies of white male Wistar rats investigating the effect of P. ostreatus intake on sperm quality. For the literature search, the following Medical Subject Heading (MeSH) terms were used: ((“edible mushrooms” OR “culinary mushrooms” OR “pleurotus ostreatus” OR “oyster mushrooms”) AND “Sperm quality” OR “Sperm Count” OR “ Sperm Morphology” OR “Sperm Motility”). Two filters were applied: English and male white Wistar rat species. The database search, performed by one reviewer (Y.F.), was completed on November 28, 2023. Eligible articles published up to that date were considered for inclusion. In addition, the reference lists of included studies were perused to identify further studies of relevance that had not been previously identified in the Mendeley database.

2.2 Inclusion and Exclusion Criteria

This review focuses on intervention studies investigating the efficacy of P. ostreatus extract to improve sperm quality in male white Wistar rats. Studies were included if they investigated (1) the effect of P. ostreatus as a whole mushroom extract; (2) sperm quality parameters (e.g. number, morphology, motility); (3) healthy subjects, subjects have no abnormalities either anatomical or physiological.

Studies were excluded for the following reasons: (1) treatment with other edible fungi other than P. ostreatus ; (2) treatment with natural extraction ingredients from P. ostreatus which are enriched with vitamins or functional ingredients; (3) discussing other topics (e.g., effects for other diseases)

2.3 Study Selection, Data Extraction and Risk of Bias Assessment

Three independent reviewers (Y.F., D.A., M.I.) identified relevant studies by analyzing records using a home-made Excel template that considered pre-specified eligibility criteria. First, all items were screened based on title and/or abstract to exclude contributions that met the exclusion criteria. Afterwards, all remaining studies were assessed for eligibility by reading the full-text articles. Any differences in the selection process were discussed until consensus was reached. Finally, studies deemed eligible were included in this systematic review.

3. Results

After a systematic literature search, 4 records were retrieved from Mendeley database and another were retrieved 55 record from Google Scholar. After the removal of duplicates, 57 records remained. Based on titles and/or abstracts, 55 records were excluded (reasons: intervention with other mushrooms than P. ostreatus, n = 7; intervention with isolated substances from P. ostreatus, n = 4; considering other topics not related to human health, e.g., cultivation conditions, n = 15; considering biomarkers related to other diseases than cardiometabolic disorders, e.g., cancer, n = 1; no interventional study design, n = 12; investigating HIV-infected individuals under antiretroviral therapy, n = 5; full-text article not available, n = 11). After reading the full-text articles, a further publication was excluded which used another Pleurotus sp. Than P. ostreatus for treatment. Finally, two studies which were included in the present review. A flow diagram of the identification and selection of studies is shown in **Figure 1**.

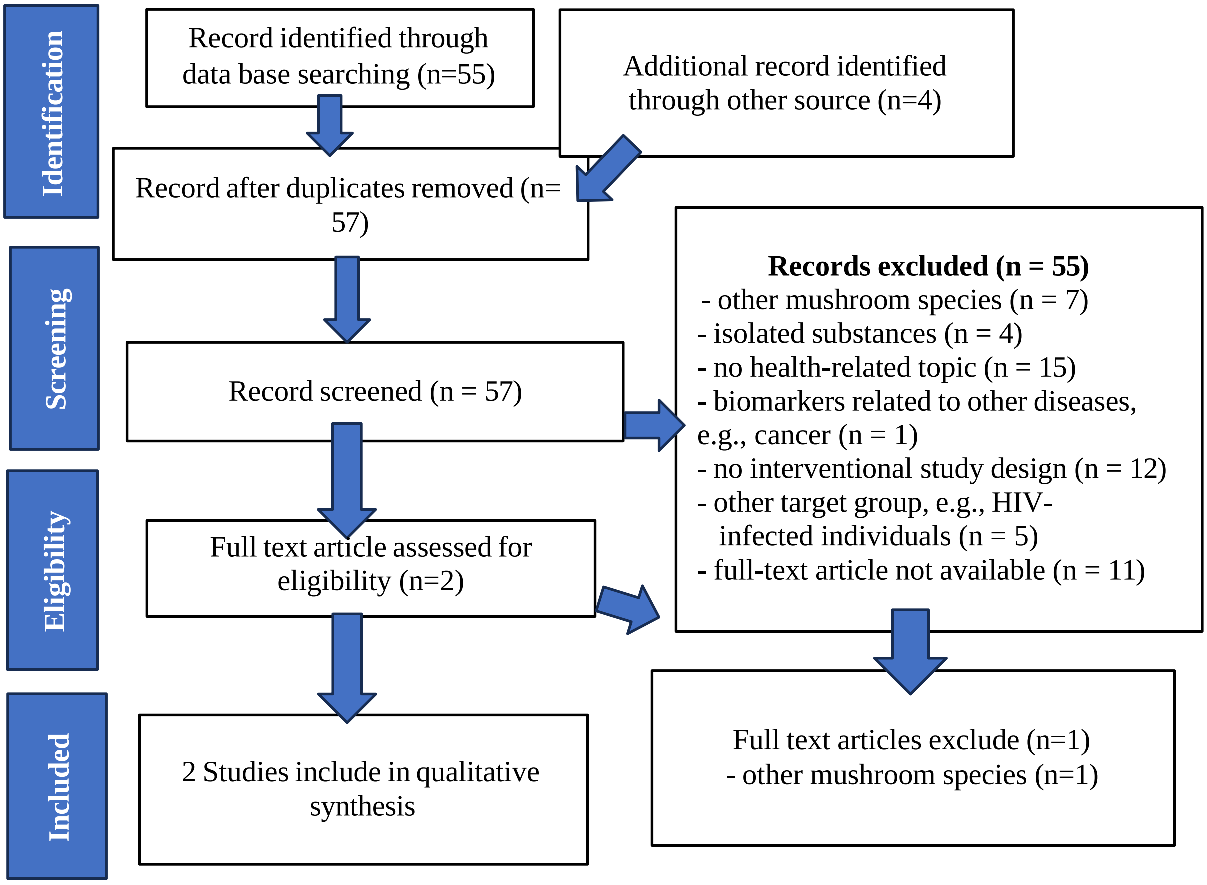

Figure 1. Flow-diagram of study selection process according to the preferred reporting items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

<table>
<tr><th>Judul jurnal</th><th>Study, Country</th><th>Design</th><th>na</th><th>Participants</th><th>Interventions</th><th>IP (d)</th><th>Results</th><th>Annotations</th></tr>
<tr><td>Protective effect of ethanolic extract of white oyster mushroom on morphological rat sperm damage due to cigarette smoke exposure</td><td>Bandung, Indonesia</td><td>Experimental studi</td><td>40</td><td>The inclusion criteria were male, healthy and active Wistar rats, with body weight of 175-250 grams and age of 2-3 months

The exclusion criteria in this study were died rat during the adaptation period or lost more than 10% body weight.</td><td>The experiment was carried out in a completely randomized design. Rats were divided into five groups consisting of groups I, II, III, IV and V. Group I was a normal control, rats were only get standarized food and drink, carboxymethyl cellulose (CMC) and not induced by cigarette smoke. Group II is a negative control, given cigarette smoke without treatment. Groups Ill, IV and V were treatment groups 1, 2 and 3.
Each group was given cigarette</td><td>14 days</td><td>Table 1. Average percentage of sperm morphology of Wistar strain male rats exposed to cigarette smoke and ethanolic extract of white oyster
<table>
<tr><th rowspan="2">Group</th><th colspan="2">Sperm Morfologi</th></tr>
<tr><th>Normal</th><th>Abnormal</th></tr>
<tr><td>Normal Control</td><td>79 ± 0.79</td><td>21 ± 0.76</td></tr>
<tr><td>Negative Control</td><td>39 ± 0.55</td><td>61 ± 0.55</td></tr>
<tr><td>Treatment 1</td><td>56 ± 0.15</td><td>44 ± 0.15</td></tr>
<tr><td>Treatment 2</td><td>65 ± 0.54</td><td>35 ± 0.54</td></tr>
<tr><td>Treatment 3</td><td>66 ± 0.21</td><td>34 ± 0.21</td></tr>
</table></td><td>-</td></tr>
</table>

<table>
<tr><td></td><td></td><td></td><td></td><td></td><td>smoke induction 30 minutes per day/group and ethanol extract of white oyster mushroom at doses of 125 mg, 250 mg and 500 mg/kg body weight (BW)/rat/ day for 14 days. On the 15th day, the rats were executed and the sperm were examined.</td><td></td><td></td><td></td></tr>
<tr><td>Effects of graded doses of ethanol extract of Pleurotus ostreatus (Oyster mushroom) on the sperm quality and haemo-biochemical parameters of the male Wistar rats</td><td>Nigeria</td><td>Eksperimental studi</td><td>25</td><td>Twenty-five adult male albino rats (Wistar strain)</td><td>The twenty-five experimental rats were assigned into five groups (A-E), each group having 5 rats (n=5). They were administered with oral dose of ethanol extract of Pleurotus ostreatus constituted with propylene glycol at dosage rate of</td><td>14 days</td><td>Table 2. Semen characteristics of male albino rats in different groups at 2 weeks post-treatment.
<table>
<tr><th>Parameters</th><th>A (200 mg/kg)</th><th>B (400 mg/kg)</th><th>C (600mg/kg)</th><th>D (800 mg/kg)</th></tr>
<tr><td>Sperm motility (%)</td><td>95.50 ± 6.29^{b}</td><td>96.00 ± 5.48^{b}</td><td>98.00 ± 2.45^{b}</td><td>99.00 ± 4.00^{b}</td></tr>
<tr><td>Sperm liveability (%)</td><td>95.00 ± 3.08^{a}</td><td>95.20 ± 2.40^{a}</td><td>95.20 ± 2.40^{a}</td><td>96.20 ± 0.73^{a}</td></tr>
<tr><td>Sperm count ($x10^{6}$ spermatozoa/ml)</td><td>142.75 ± 6.33^{b}</td><td>145.20 ± 5.15^{b}</td><td>155.80 ± 3.06^{b}</td><td>160 ± 6.45^{b}</td></tr>
</table>
^{a,b,c}Mean(±SEM) with same superscript are not significantly different at 0.05 level along the rows.</td><td>-</td></tr>
</table>

					200, 400, 600, 800 mg/kg bodyweight respectively for 2 weeks. Animals in groups A, B, C and D received 200, 400, 600 and 800 mg/kg of ethanol extract of *Pleurotus ostreatus* respectively while group E received 0.2 ml propylene glycol serving as the control. Samples were collected from all the animals at 2 weeks (14 days) post-treatment.				

4. Discussion

Reactive oxygen species (ROS) are compounds that contain reactive oxygen, so they easily form new compounds with other molecules around them [16]. Exogenous ROS, such as pollutants, cigarette smoke, xenobiotics and radiation. Endogenous ROS are generated through many mechanisms, mainly mitochondria, peroxisomes, endoplasmic reticulum and NADPH oxidase (NOX) complexes in cell membranes. Mitochondria are the main site for producing endogenous ROS [16]. At low to moderate dose levels, ROS is considered important for the regulation of normal physiological functions such as cell cycle progression and proliferation, differentiation, migration and cell death. ROS also play an important role in the immune system, maintaining the oxidation-reduction balance and are involved in the activation of various cellular signaling pathways. Excessive levels of cellular ROS can cause damage to proteins, nucleic acids, lipids, membranes and organelles, leading to activation of cell death processes such as apoptosis. ROS play a central role in cell signaling as well as regulation of key pathways of apoptosis mediated by mitochondria, death receptors, and the endoplasmic reticulum (ER) [23].

Male infertility and oxidative stress (OS) are closely related, as reported in several papers [24]. OS is associated with many infertility risk factors, such as varicocele, inflammation, metabolic changes, endogenous or exogenous toxins and radiofrequency [24]. Somewhat surprisingly, cells such as spermatozoa, which are rich in substrates suitable for preventing oxidative stress and its actions, produce large amounts of ROS. To balance the effects of ROS, spermatozoa are endowed with several antioxidant enzymes, although in low concentrations. ROS have an important role as signal transductors in several cell types, but in spermatozoa, the processes mediating ROS make spermatozoa capable of fertilization: capacitation, hyperactivation, and acrosome reaction. A decisive, but often overlooked, role played by ROS in spermatozoa is the regulation of apoptosis.

Spermatozoa are highly susceptible to oxidative damage due to various factors intrinsic to the structural characteristics of these specialized cells, but also due to the complex mechanisms of the structural characteristics of these specialized cells, but also due to the complex mechanisms of differentiation (i.e., spermatogenesis) and maturation required for achieving full fer- differentiation (i.e., spermatogenesis) and maturation necessary to achieve full fertilization utilization capacity. Although spermatozoa primarily rely on glycolysis for their energy catabolism, oxidative phosphorylation (OXPHOS) in mitochondria is essential in supplying spermatozoa with sufficient energy for their movement. Paradoxically, although spermatozoa have all the susceptibility factors to oxidative damage, OS is still required and cannot eliminate these factors. Spermatozoa are not only exposed to the ROS they produce, but also ROS contained in seminal plasma. One of the ingredients in oyster mushroom ethanol extract is vitamin C [25]. Mice given vitamin C had significantly higher sperm concentrations than mice given Cyclophospamide. This is because vitamin C is a strong antioxidant and is known to have a protective effect on genotoxicity and cytotoxicity in mice [26]. In his research, he found that giving vitamin C supplements to white mice had a positive effect on spermatozoa and hormone concentrations. In addition, vitamin C was found to be efficacious in increasing the motility and normal morphology of white rat spermatozoa [27][28].

5. Conclusion

All studies included in this systematic literature review looked at the effects of white oyster mushroom extract with its benefits related to physiological functions, namely sperm quality in male white Wistar rats. With several studies, white oyster mushrooms have many benefits for humans. However, evidence regarding this impact is still low because the amount of research is insufficient. Therefore, the current findings regarding the efficacy of white oyster mushroom extract on sperm quality parameters can only be considered as a suggestion of a beneficial effect. Therefore, further clinical trials with well-controlled research designs are needed.

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