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Herbal flavonoids in preserving testicular physiology under oxidative stress: A bibliometric analysis of systematic reviews

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Abstract

Herbal antioxidants have gained attention recently as possible treatments for disorders of male reproductive function linked to oxidative stress because of their ability to neutralize free radicals. The investigation into herbal flavonoids for preserving oxidative stress-impaired testicular physiology has been effectively conducted through the visualization of bibliometric analysis. Bibliometric data of published papers collected from the PubMed and Scopus databases in 2018-2023. Network visualization was performed using VOSviewer software on the set keywords that occur (n=15). The literature review was conducted according to the research trends identified by the clusters that appeared in the network visualization. The result revealed that a total of 266 records have been published based on the specified search set keywords since 2018. Through the analysis of keywords, inclusion and exclusion criteria, and the relevant content of papers, 11 articles were identified as suitable for conducting a literature review. Network visualization revealed that the research falls into two general categories: (1) toxicity to the testicles caused by oxidative stress and (2) prevention of oxidative stress impact on tissue through herbal medicine. Examination of the paper's content revealed that certain antioxidant compounds from plants can stabilize free radicals in the testicles. These antioxidants include vitexin, diosmin, hesperidin, phenolic acids, naphthoquinones, fisetin, pachypodol, sciadopitysin, carvacrol, and morin. However, further research is needed to compare active antioxidant content in different herbal plants and identify optimal concentrations for therapeutic effects.

Keywords: Bibliometric, herbal, flavonoid, reactive oxygen species (ROS), testicle

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Introduction

The reactive oxygen species (ROS) signaling molecules play a crucial role in the physiological processes of male fertility, such as maintaining cellular homeostasis, capacitation, and hyperactivation (Fatima, 2018; Simith & Kehrer, 1994). However, ROS can be a double sword because, despite their role as crucial signaling molecules, their overproduction, which overwhelms the body's antioxidant defenses, is believed to negatively impact normal male fertility development (Fatima, 2018). The imbalance of excessive generation of free radicals and reactive oxygen species (ROS) appears to be a significant problem that can harm deoxyribonucleic acid (DNA), proteins, and lipids and lead to the pathogenesis and pathophysiology of several diseases (Banerjee et al., 2018; Simith & Kehrer, 1994). Pathophysiological abnormalities caused by an imbalance in ROS cause increasing oxidative damage and cell death, one of them is damage to the reproductive system cells. Moreover, the testicular tissue and male reproductive system are particularly susceptible to oxidative stress due to the low level of oxygen pressure and a severe cell competition for oxygen (Asadi et al., 2017).

Nowadays, antioxidants are a well-known compound expected to stop oxidative stress. By locating the primer free radicals, these antioxidants can permanently halt an oxidation chain through stabilizing metal radicals such as copper and iron to prevent various diseases (Bahmani et al., 2015; Nasri & Rafieian-Kopaei, 2014; Szabo et al., 2007). Numerous natural compounds are powerful antioxidants that protect chronic diseases from oxidative damage (Banerjee et al., 2018). Among the compounds present in herbal plants that have potent antioxidant properties are flavonoids (Shen et al., 2022).

Flavonoids are widespread polyphenol compounds found ubiquitously, representing a diverse category of natural substances (Mutha et al., 2021). According to recent research, flavonoids derived from herbal plants have been produced to lessen the harmful effect of oxidative stress. Therefore, further investigation into the impact of active antioxidant substances in herbs on the body tissue is necessary (Zulkifli et al., 2020). This special review, aiming to explore herbal flavonoids for maintaining oxidative stress-impaired testicular physiology, presents a collection of articles on flavonoid compounds in herbal medicine that reduce testicular damage related to oxidative stress. This research uses a systematic literature review scheme and a bibliometric analysis.

Materials and Methods

Literature search

The background information of herbal plants' antioxidants to protect the physiology of the testicular against oxidative stress impact presented in the forms of relevant articles and literature published from 2018-2023 were narrowed and gathered through conducting preliminary searches from various search engines such as Scopus and PubMed. Most accurate results were produced by specifying the keywords of the literature articles such as: “herbal phenolic and flavonoid”, “phenol ROS testicular”, “flavonoid ROS testicular”, “phenol oxidative stress testicular”, and “flavonoid oxidative stress testicular”. The title and abstract of the resulting studies were thoroughly evaluated to ensure the level of relevance to the main study. The authors utilized Publish or Perish, VOSviewer, and ASReview Lab to process all the references in this systematic literature review. Biblio.

Eligibility Criteria

The inclusion criteria for this study were any published journal articles from PubMed and Scopus, between 2018 to 2023, that reported the role of flavonoids in improving testicular physiology damaged due to oxidative stress. Included studies were analyzed by the authors to generate a new conclusion. However, the exclusion criteria were: (1) No original results reported; secondary only, (2) not relevant,

(3) publication has not been peer-reviewed, (4) no available full text (e.g. conference abstracts), (5) not includable, (6) ROS-free, (7) oxidative stress-free, (8) meta-analysis, (9) reviews, (10) mini-reviews, (11) case reports, and (12) non-English text).

Data Selection and Strategy

All available data were extracted to probe the role of flavonoids in improving testicular physiology damaged due to oxidative stress. To ensure the relevance and reliability of all information gathered from the selected studies, the screening of the articles was divided into two phases: the first phase of the screening began with all authors filtering journals based on the exclusion and inclusion criteria and the second phase of the screening was completed by four authors (1st, 2nd, 9th, 10th, and 11th) who finalized and approved the relevant articles to the studies.

During this screening phase, research titles, abstracts, methods, and results were carefully examined. The name(s) of the author(s), the publication date, the phenol and flavonoid herbal compounds, the extraction method, and the overall percentage of phenol and flavonoid compounds are all included in the set of data for this systematic review. For future use, all of the data were extracted and put into Microsoft Excel spreadsheets.

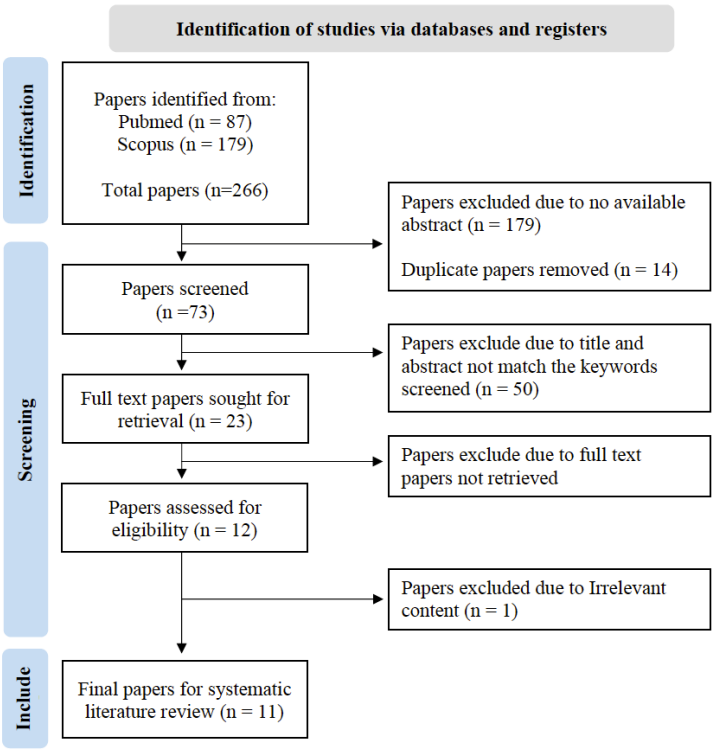

Figure 1. Flowchart illustrating the extraction process of bibliometric data from reports, encompassing the analysis of keywords, inclusion and exclusion criteria, and relevant content of papers.

Results and Discussion

Study of co-occurrence frequency based on the keywords

Bibliometric analysis has become well-established as a specialized scientific practice and is an integral component of research evaluation methodology, particularly in scientific and applied fields (Ellegaard & Wallin, 2015). Nowadays, bibliometric studies are extensively employed for conducting literature review assessments (Zulkifli et al., 2023). The outcomes of the analysis of published articles, considering keywords and the relevance of the articles to the inclusion and exclusion criteria, are detailed in Table 1. Additionally, summaries of reports on the utilization of herbal flavonoids for maintaining testicular physiology impaired by oxidative stress are provided in Table 2.

Table 1. The results of the investigation for articles that align with the study criteria's relevance.

Author	Year publish	Title	Source	GS Rank
Muhammad Umar Ijaz, Arfa Tahir, et al.	2022	Chemoprotective effect of vitexin against cisplatin-induced biochemical, spermatological, steroidogenic, hormonal, apoptotic and histopathological damages in the testes of Sprague-Dawley rats	Saudi pharmaceutical journal	21
Elçin Bakır, Serpil Sarıözkan, et al.	2020	Cherry laurel fruit extract counters dimethoate-induced reproductive impairment and testicular apoptosis	Arhiv za higijenu rada i toksikologiju	13
Aishat O Olatunji, Joseph O Ayo, et al.	2022	Effect of daflon-500®, a flavonoid compound on chlorpyriphos-induced oxidative changes in the hypophysis and testes in adult male rats	Toxicological research	18
Davood Nasiry, Ali Reza Khalatbary, et al.	2021	Effects of *Juglans regia* L. leaf extract supplementation on testicular functions in diabetic rats	Biotechnic & histochemistry	19
Muhammad Umar Ijaz, Saqlain Haider, et al.	2023	Mechanistic insight into the protective effects of fisetin against arsenic-induced reproductive toxicity in male rats	Scientific reports	13
Muhammad Umar Ijaz, Ayesha Rauf, et al.	2022	Pachypodol attenuates Perfluorooctane sulphonate-induced testicular damage by reducing oxidative stress.	Saudi journal of biological sciences	26
Dhekra Grami, Kaïs Rtibi, et al.	2020	Protective Action of *Eruca sativa* Leaves Aqueous Extracts Against Bisphenol A-Caused In Vivo Testicular Damages.	Journal of medicinal food	22
Mai M Anwar, Ibrahim M Ibrahim Laila	2023	Protective and restorative potency of diosmin natural flavonoid compound against tramadol-induced testicular damage and infertility in male rats.	Natural product research	20
Muhammad Umar Ijaz, Mohammad Qamer, et al.	2023	Sciadopitysin mitigates spermatological and testicular damage instigated by paraquat administration in male albino rats.	Scientific reports	11
Hamed Shoorei, Arash Khaki, et al.	2019	The ameliorative effect of carvacrol on oxidative stress and germ cell apoptosis in testicular tissue of adult diabetic rats.	Biomedicine & pharmacotherapy	26
Ebenezer Tunde Olayinka, Ayokanmi Ore, et al.	2019	The role of flavonoid antioxidant, morin in improving procarbazine-induced oxidative stress on testicular function in rat.	Porto biomedical journal	43

Table 2. Study the effect of antioxidants in all included studies.

Author, Year	Herb	Phytochemical compound	Significant findings
Muhammad Umar Ijaz, Arfa Tahir, et al., 2022	Hawthorn (*Crataegus pinnatifida*)	Flavonoid (vitexin)	Vitexin acts as a therapeutic agent against cisplatin-induced male reproductive dysfunction. Vitexin plays a role in

			antioxidant, anti-apoptotic, and androgenic potential.
Elçin Bakır, Serpil Sarıözkan, et al., 2020	Cherry laurel (*Laurocerasus officinalis* Roem.)	Flavonoid	Cherry laurel extract showed protective effects against dimethoate-induced reproductive damage in rats, which is similar to vitamin C.
Aishat O Olatunji, Joseph O Ayo, et al., 2022	*Rutaceae aurantiae*	Flavonoid (diosmin and hesperidin)	Pre-treatment with Daflon-500® induced the ateration of oxidative stress and biochemical parameters caused by the insecticide Chlorpyrifos. The flavonoid compounds contained in the *Rutaceae aurantiae* plant is the basic ingredient of Daflon-500®.
Davood Nasiry, Ali Reza Khalatbary, et al., 2021	*Juglans regia* L.	Phenolic acids, naphthoquinones and flavonoids	*Juglans regia* L. leaf extract exerts preventive effects against diabetic dysfunction in the testis by decreasing the malondialdehyde level, improved antioxidant status, and normalized testosterone levels in the diabetic rats.
Muhammad Umar Ijaz, Saqlain Haider, et al., 2023	Chamomile, lime blossom, cucumber, onion, lotus root, tomato, apple, kiwi, persimmon, peach, red grapes, white grapes, strawberries, tea, and Anacardiaceae plants	Flavonoid (fisetin)	Treatment with fisetin leads to enhanced effectiveness against male reproductive toxicity induced by arsenic.
Muhammad Umar Ijaz, Ayesha Rauf, et al., 2022	Blanco (*Pogostemon cablin*)	Flavonoid (pachypodol)	Perfluorooctane sulfonate exposure disturbed the biochemical profile by altering the oxidant balance. The pachypodol treatment potently alleviated all the impairments in testes due to perfluorooctane sulfonate exposure.
Dhekra Grami, Kaïs Rtibi, et al., 2020	*Eruca sativa* (*Brassicaceae* family)	Flavonoids and glucosinolates	*Eruca sativa aqueous* extracts administration at lower doses improved testicular histological and biochemical injuries induced by toxicity of bisphenol.
Mai M Anwar, Ibrahim M Ibrahim Laila, 2023	Citrus fruit	Flavonoid (diosmin)	Diosmin is a naturally occurring flavonoid that is safe to use. It has anti-inflammatory and antioxidant properties that help reduce testicular damage caused by tramadol toxicity by inhibiting oxidative stress.
Muhammad Umar Ijaz, Mohammad Qamer, et al., 2023	Chinese yew (*Taxus chinensis*)	Flavonoid (sciadopitysin)	The flavonoid sciadopitysin has shown promise in mitigating the effects of paraquat, a herbicide that causes toxicity to the testicles by generating reactive oxygen species.
Hamed Shoorei, Arash Khaki, et al., 2019	Essential oil family *Lamiaceae* (thyme, summer savory, and marjoram)	Phenolic monoterpene (carvacrol)	In diabetic rats, carvacrol treatment reduces the amount of damage to testicular tissue, reduced the rate of germ cell apoptosis, raised B-cell lymphoma 2 (Bcl-2) and decreased Bcl-2-associated X protein (BAX).

Ebenezer Tunde Olayinka, Ayokanmi Ore, et al., 2019	White mulberry, red Wine, almond, sweet chestnut, Acridocarpus orientalis, and fruits	Flafonoid (morin)	Procarbazine significantly increased the level of malondialdehyde and significantly decreased the levels of ascorbic acid and glutathione in the testes. The examination of rats administered procarbazine and morin demonstrates the protection against testicular and sperm toxicity attributed to the beneficial impact of morin on enhancing the testicular antioxidant system.

Co-occurrences of all keywords

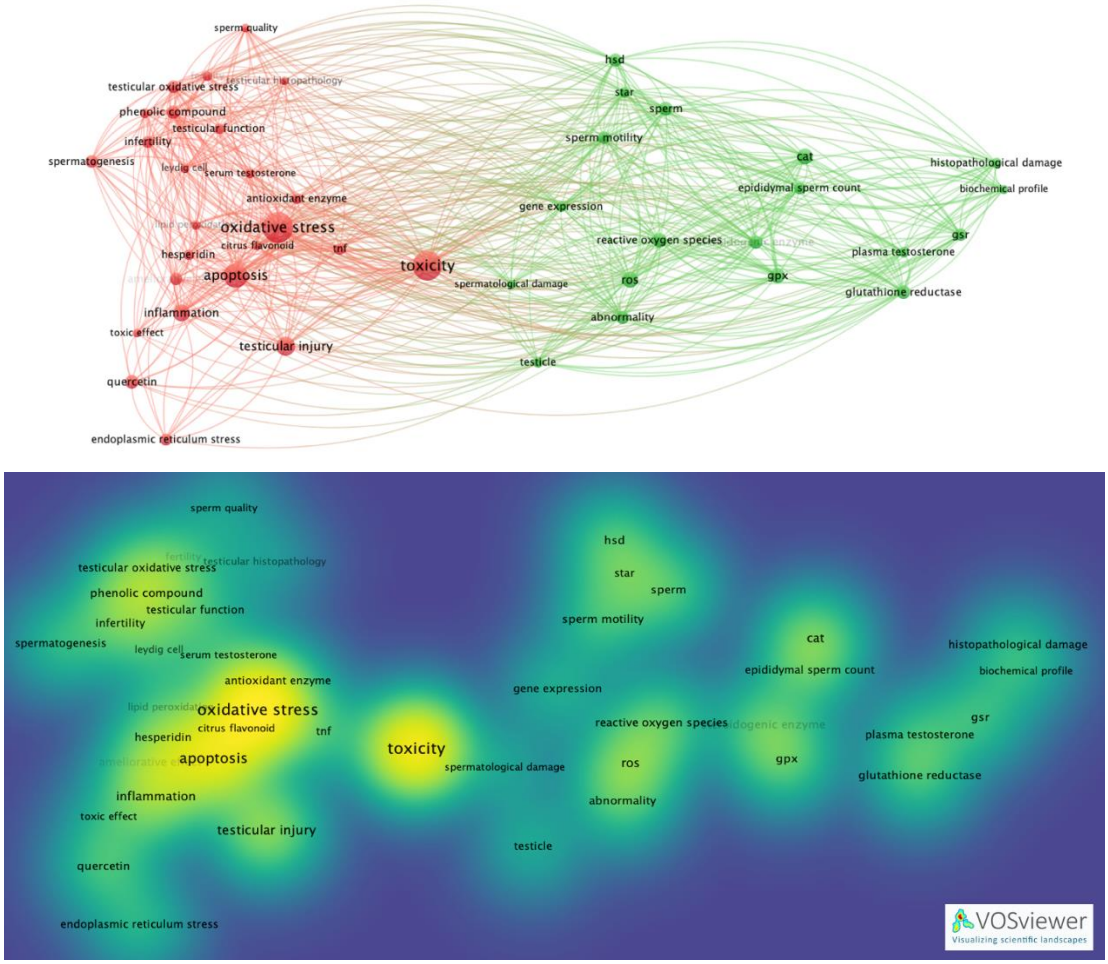

Figure 2. Top: network visualization of all keywords. Nodes with the same color represent a research cluster; Bottom: density visualization of all keywords. Both picture weights: occurrences. Visualization is performed using the VOSviewer software program.

The network and density visualizations of all the keywords' co-occurrences are shown in Figure 2. Figure 2 displays the network visualization and density visualization of all the co-occurrences of each keyword. In order to better analyze the co-occurrences of the keywords, some limitations were established in implementation. In this case, the minimum number of keyword occurrences that might appear was 10. The number of Total Link Strengths (TLS), which represents the total strength of a keyword's co-occurrence links to other

keywords, was used to determine which keyword was most frequently used. 103 keywords out of 2620 that were found in the metadata satisfied the criterion. Consistent with the most commonly occurring keywords, 'oxidative stress' (TLS=381) was the most used keyword across all article literature research, followed by 'toxicity' (TLS=309), 'apoptosis' (TLS=216), 'inflamation' (TSL=112), 'phenolic compound' (TSL=83), tnf (TSL=80) 'testicular injury' (TLS=78), and 'testicular oxidative stress' (TSL=72). Only these eight keywords—which together account for slightly more than 50,8% of all other keywords—passed 60 TLS.

The colors shown in the network visualization indicated the closeness of certain keywords to a research cluster (Figure 2). There were two clusters found in the bibiliometric analysis in herbal flavonoids for maintaining oxidative stress-impaired testicular physiology, distinguished by their color. These clusters were comprised of keywords associated to 'the impact of reactive oxygen species on abnormalities in tissue and testicular cell homeostasis' (green) and 'Oxidative stress is affected by natural treatments that contain flavonoids' (red). The density visualization indicates how other keywords revolve around a given keyword by using different colors for different keywords (Figure 2). 'oxidative stress' and 'toxicity' were the keywords with the highest density, where all other keywords revolved around other keywords.

Discussion

Oxidative stress factors on the testicle

The physiological phenomenon of oxidative stress is caused by the accumulation of reactive oxygen species (ROS) that reaches disproportionately high levels, either due to excessive production or due to the insufficiency of the antioxidant capability to detoxify these reactive molecule products (Forcados et al., 2017; Johansen et al., 2005; Pizzino et al., 2017). These reactive oxygen species are byproducts of cellular metabolism and play essentially in all signaling pathways of metabolism, homeostasis, metabolic regulation, and memory formation through DNA methylation. However, ROS can disrupt biomolecules and trigger oxidative damage in several diseases such as neurodegenerative anomalies, atherosclerosis, cancer, benign, and other disorders (He et al., 2017; Rhee, 1999; X. Zhou et al., 2016).

The main intracellular source of the majority of this oxidant is the mitochondrion, which is produced when electron transport and oxidative phosphorylation occur to create ATP. If this unbalanced electron reacts with oxygen (O2), it can create superoxide anions (•O2), which then react with Fe2+ to produce other reactive species (RS) such as the hydroxyl radical (•OH), hydrogen peroxide (H2O2), and organic peroxides that resulting in serious pathological scenarios (Pisoschi & Pop, 2015; Turrens, 2003). These three molecules (•O2, •OH, and H2O2) are referred to as reactive oxygen species. Free radicals are frequently referred to as O2• and HO•. These molecules can react with organic substances to form intermediate species that can produce more ROS (Collin, 2019; Neta et al., 1990).

Latest research has discovered that ROS, particularly hydroxyl and superoxide radicals, react with numerous biomolecules such as amino acids (cysteine, histidine, tryptophan, methionine, and tyrosine), proteins, lipids, and simple peptides, altering their function and structure (Collin, 2019; Hohn et al., 2014; Monroy Maria & Mejia, 2013; Weber et al., 2015). The interaction of ROS with fatty acids, lipoproteins, and phospholipids generates lipid peroxidation, which results in the accumulation of intermediates/products such as 4-hydroxynonenal, hydroperoxide lipid, and malondialdehyde. These chemical molecules disrupt the plasma membrane, and they can spread into other cells inside the organism, producing inflammation and inducing apoptosis through the interaction of the oxidized low-density lipoprotein receptor (Liou & Storz, 2010; Monroy Maria & Mejia, 2013). Testicular cells and

spermatozoa are among the most susceptible cells in the body to ROS damage, which disrupts sperm formation and contributes to male infertility (Nash & Rahman, 2019). This statement aligns with a previous study that emphasized that fertilization requires spermatozoa of high quality supported by compact DNA integrity for transmitting accurate genetic information (Agarwal & Said, 2003; Akmal et al., 2016).

Numerous research studies have investigated the unbalancing of ROS molecules that might cause harm to the sperm DNA and promote lipid peroxidation in the male reproductive system (Rahim et al., 2013; Wu et al., 2015). Cell membranes, such as those that build the sperm, are highly sensitive to ROS (Sahreen et al., 2013). The abnormal production of ROS in the reproductive organ can disrupt the membrane fluidity of the sperm as well as the DNA integrity in the nucleus, which leads to spermatogenic malfunction and toxicities to the sperm (S. Zhou et al., 2016). Another study presents that excessive ROS production and oxidative stress have adverse effects on spermatozoa, leading to alteration of morphological and dynamic cellular components and reduced fertilization (Mannucci et al., 2021). This statement ties well with previous studies wherein testicle ROS has serious impacts and causes pathological conditions that lead to degeneration of Leydig cells, decreased testosterone synthesis, disrupted sperm differentiation process, and infertility. These conditions are closely related to men's hypogonadism increased age-related cause due to decreased plasma testosterone levels (Chung et al., 2018; Nasr, 2017; Pavin et al., 2018). In aged Leydig cells, the cellular alterations in the steroidogenic pathway are followed by reducing testosterone production. This process causes decreased cyclic adenosine monophosphate (cAMP) luteinizing hormone-stimulated and then suppresses the production of steroidogenic acute regulatory (StAR), CYP11A1 gene in the mitochondria, and CYP17A1 gene in the endoplasmic reticulum (ER) (Noh et al., 2020).

Most of the theories are widely considered that ROS not only damage sperm but also renders it ineffective by interfering with their signal transduction pathways, such as Adenylate cyclase (AC). AC is an enzyme molecule utilized extensively in signaling pathways. Cyclic adenosine monophosphate (cAMP), which is produced by the AC-catalyzed reaction, is an essential second messenger in sperm and plays a crucial role in sperm capacitation and initial acrosome response (Bin et al., 2015).

The effectiveness of herbal plant compounds in reducing oxidative stress on testicle

Various herbal extracts and plant-derived purified compounds have been proven to have protective benefits in a variety of disorders, including those that affect the reproductive system (Askaripour et al., 2018; Rahmouni et al., 2019). The amount of bioactive components of herbal compounds, such as phenolic acids, tannins, and flavonoids, varies with plant species, environmental conditions, and growth stage (Hübner & Arendt, 2013; Laura et al., 2019; Shahidi & Naczk, 2003). In addition, herbal compounds possess antioxidant properties and have also been shown to influence fertility and sexual development (Al Mamari, 2021; Ly et al., 2015).

The articles gathered extensively elaborate on the efficacy of herbal flavonoids in preserving testicular physiology affected by oxidative stress. Among these findings is an explanation regarding the significant effect of vitexin as a naturally occurring flavonoid, which exhibits remarkable antioxidant properties against cisplatin. Cisplatin, a widely utilized antineoplastic drug, has demonstrated efficacy in treating various malignancies and male reproductive dysfunction (Qi et al., 2019). The impacts include detrimental effects on the biochemical profile, such as a decrease in the activity of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase

(GPx), and glutathione reductase (GSR), accompanied by an increase in malondialdehyde (MDA) and ROS levels. Cisplatin also adversely affects sperm characteristics, including motility, viability, the number of hypo-osmotic tail-swelled spermatozoa, and epididymal sperm count, along with an increase in sperm morphological anomalies. Furthermore, it induces a decrease in luteinizing hormone, follicle-stimulating hormone, and plasma testosterone levels. Histopathological damage in testicular tissues is another consequence of cisplatin administration. Notably, vitexin counteracts these detrimental effects on testicular parameters, attributed to its antioxidant and androgenic potential (Ijaz, Tahir, et al., 2022).

In another study on herbal flavonoid antioxidants, the findings indicated that cherry laurel fruit extract effectively mitigated numerous dimethoate-induced adverse effects on testicular apoptosis. This included the preservation of reproductive organ weight, semen parameters, the oxidant-antioxidant balance, sperm DNA integrity, testicular apoptosis, and histological structure (Bakır et al., 2020). Previous studies on morin, a flavonoid antioxidant, showed a significant protective effect against testicular and sperm toxicity induced by procarbazine (Olayinka et al., 2019). A recent study on diosmin also provided evidence that it has effects as anti-inflammatory and antioxidant properties, reducing testicular damage caused by tramadol toxicity through the inhibition of oxidative stress (Anwar & Laila, 2023).

Testicular dysfunction is also a consequence of complications arising from diabetes mellitus (DM). The study conducted by Nasiry et al. (2021) revealed a reduction in malondialdehyde (MDA) levels and an imbalance in antioxidant status in the testes of diabetic rats, conditions that were alleviated by the administration of *Juglans regia* L. leaf extract. The diabetic rats exhibited a significant decrease in antioxidant biomarkers and testosterone levels, all of which were restored to normal levels following the administration of *Juglans regia* L. leaf extract. The application of *Juglans regia* L. leaf extract was associated with a decrease in MDA levels and an improvement in antioxidant status in the testes of diabetic rats (Nasiry et al., 2021). A similar study of carvacrol (a phenolic monoterpene), reveals substantial therapeutic effectiveness in diabetic rats. Carvacrol treatment resulted in diminished activity of SOD, GPx, and MDA, along with the restoration of testicular tissue damage. Additionally, at the gene and protein expression levels, carvacrol's antioxidant properties significantly lowered the rate of germ cell apoptosis, elevated B-cell lymphoma 2 (Bcl-2), and decreased Bcl-2-associated X protein (BAX) (Shoorei et al., 2019).

Another promising study on flavonoid compounds has uncovered valuable information regarding the effectiveness of these components in mitigating the harmful effects of herbicides and pesticides. Prior research suggests that the flavonoid sciadopitysin, found in *Taxus chinensis*, has the potential to mitigate the impact of paraquat, a herbicide known to induce testicular toxicity through the generation of reactive oxygen species (Ijaz, Qamer, et al., 2023). Furthermore, the investigation of Olatunji et al. (2022) article also indicated that Daflon-500, a flavonoid compound, demonstrated a comparable protective effect against pesticide toxicity in testicular cells. This study revealed that pre-treatment with Daflon-500® mitigated cisplatin-induced alterations in oxidative and biochemical parameters, likely attributed to the antioxidant properties of the flavonoid compound.

Investigations in several other articles also provide results that flavonoid compounds in herbal plants do have maintenance properties for the balance of antioxidants in the testicles. A study by Ijaz, Haider, et al. (2023) showed fisetin treatment resulted in improvements in the efficacy of antioxidant, antilipoperoxidative, anti-apoptotic, and androgenic levels against arsenic-induced male reproductive toxicity. In a different study, perfluorooctane sulfonate exposure

was found to disrupt the biochemical profile by affecting the oxidant balance. Treatment with pachypodol effectively alleviated all the impairments in the testicles caused by perfluorooctane sulfonate exposure (Ijaz, Rauf, et al., 2022). Furthermore, a more targeted investigation based on the article by Grami et al. (2020) demonstrated that the administration of Eruca sativa aqueous extracts at lower doses improved testicular histological and biochemical injuries induced by the toxicity of bisphenol.

Another finding of herbal plants' antioxidant

In recent years, plant extracts have been proven to increase semen quality, androgen status, fertility index, and have a beneficial impact on sperm in males (Fakher et al., 2019; Park et al., 2017). Excessive ROS and decreased cellular antioxidants lead to redox imbalance, decreased sperm motility, and DNA damage in sperm. Due to the abundance of unsaturated fatty acids in their cell membranes, spermatozoa are extremely susceptible to the damaging effects of ROS. ROS promotes the peroxidation of lipids, resulting in an intracellular oxidative hindrance. The chain of events consists of lipid peroxidation, loss of membrane integrity with increased permeability, decreased sperm motility, DNA damage, and lead sperm apoptosis (Henkel & Schill, 1998; Sanocka-Maciejewska et al., 2005; Schuppe et al., 2008). Several internal and external factors have been related to the increased prevalence of oxidative stress in the male reproductive system (Alahmar, 2019).

Natural antioxidants that can neutralize free radicals have attracted much interest as potential treatments for oxidative stress and hormone function disorders (Mvondo et al., 2017; Sm & Mahaboob Basha, 2017). Antioxidants can directly bind reactive oxygen species (ROS), inactivate them, and recover the harm they cause (Smits et al., 2018). Furthermore, their ability to imitate endogenous estrogen actions, inhibit hormone actions, and improve hormone production resulted in a wide range of sciences and discovery (Mvondo et al., 2017). Numerous studies have frequently been established to analyze the antioxidant activity of phenolic compounds, flavonoids, and diets high in these compounds. Some herbal research objectives were to look into the effects and the mechanisms of different plant extracts and natural products on the reproductive system. The latest research reveals that plants have been used to cure infertility thousands of years ago (Agbodjento et al., 2021; Heo & Lee, 2005). Prior research has indicated that extracts derived from banana peels, particularly kepok banana peel extract, could have the potential as herbal medicine to support male reproductive health and restore the physiological function of Leydig cells (Zulkifli et al., 2022).

In modern societies, natural plants are used as an alternative medicine to treat several ailments and have also been shown to increase reproductive function. Natural products are created from plants, animals, and fungus, and they come in various forms, including compounds, extracts, and various recipes. Other research has revealed structural and functional improvements in the reproductive system and unique mechanisms of action due to the implementation of natural plants as alternative medicine. However, there have been reports of negative consequences associated with the use of several natural products (Noh et al., 2020). In light of such results, antioxidants have often been administered to infertile men with the expectation of enhancing the quality of the semen profile. There have been very few properly controlled double-blind crossover trials conducted in this context. Nevertheless, in cases where these conditions have been met, the results have been exceptionally promising.

Conclusion

Exploration of herbal flavonoids for maintaining oxidative stress-impaired testicular physiology has been successfully observed using bibiliometric analysis. The exploration of herbal flavonoids for

maintaining oxidative stress-impaired testicular physiology can be categorized into two aspects: (1) toxicity to the testicles caused by oxidative stress and (2) prevention of oxidative stress impact on tissue through herbal medicine. Herbal antioxidants with the ability to neutralize free radicals have attracted considerable attention as potential treatments for male reproductive function disorders caused by oxidative stress. However, additional research is necessary to compare the content of active antioxidant substances across various herbal plants and determine the appropriate concentrations that can exert a healing impact on the body.

Conflict of interest

There is no conflict of interest in this study.

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