Original Research Paper

Volume - 13 | Issue - 10 | October - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Ayurveda

EFFECT OF ASHWAGANDHA ON BONE MINERAL DENSITY IN ANIMAL MODELS: A NARRATIVE REVIEW

Simran Obhrai* Ph.D. Scholar, MYAS-Department of Sports Sciences and Medicine, Guru Nanak Dev University, Amritsar *Corresponding Author

Dr. Shweta Shenoy Devraj Professor, Head and Dean, MYAS-GNDU Department of Sports Sciences and Medicine, Faculty of Sports Medicine and Physiotherapy, Guru Nanak Dev University, Amritsar

Dr. Minaxi Arora Principal, Head of the Department and Professor, Shree Lakshmi Narayan Ayurvedic College & Hospital, Amritsar

ABSTRACT Osteoporosis is a prevalent health issue characterized by reduced bone strength and an increased risk of fractures. Current treatments for osteoporosis have limitations and associated side effects, necessitating the exploration of alternative therapies. Ashwagandha, a medicinal herb with a long history in traditional Indian medicine, has gained attention for its potential health benefits, including its effects on bone health. This narrative review aims to provide an up-to-date overview of the existing knowledge on the effects of ashwagandha on bone mineral density (BMD) in animal models. The findings suggest that ashwagandha supplementation can improve bone density parameters, such as tibia bone weight, tibia ash weight, and tibia calcium and phosphorus content, enhance calcium retention and gene expression related to bone development. Additionally, studies demonstrated that ashwagandha can prevent bone loss induced by ovariectomy and calcium deficiency. These discoveries imply that ashwagandha could emerge as a promising natural remedy for osteoporosis and related skeletal ailments. Nonetheless, it is imperative to emphasize that additional investigations, encompassing clinical trials involving human subjects, are indispensable to substantiate these initial findings and ascertain ashwagandha's effectiveness and safety in managing osteoporosis. Furthermore, delving into the intricate mechanisms underpinning ashwagandha's actions and exploring the spectrum of potential adverse effects is a crucial avenue for future exploration.

KEYWORDS : ashwagandha, bone mineral density, osteoporosis, OST-6, ayurveda, herbal drugs

INTRODUCTION

Osteoporosis, a global health challenge characterized by weakened bones and an increased fracture risk, primarily afflicts the elderly population [1]. With the aging population, the prevalence of osteoporosis is on the rise, posing significant morbidity and mortality concerns, particularly in India [2]. The condition often remains undetected until fractures occur, making it a pressing issue in a country with increasing life expectancy [3,4].

The cessation of ovarian function, particularly the decline in estrogen after menopause, leads to an imbalance between bone formation and resorption, resulting in net bone loss [5]. A recent study also underscores the role of oxidative stress in postmenopausal osteoporosis [6]. Declining ovarian hormone levels in postmenopausal women hinder the body's ability to counteract oxidative stress and maintain healthy bone remodeling, ultimately leading to bone deformities [7]. Current treatments primarily target bone resorption [8], but they are associated with side effects such as hypercalcemia and an increased risk of cancer [9,10,11]. Newer estrogen therapies like selective estrogen receptor modulators (SERMs) and low-dose estrogens show promise in treating osteoporosis with fewer side effects [12].

Amid these challenges, interest is growing in exploring herbal remedies for osteoporosis treatment [13]. Herbal drugs offer a holistic approach, aiming to improve symptoms, restore balance, and enhance overall well-being. These drugs are considered safe and effective, serving as complementary options to conventional medicines. One such herbal remedy is Indian ginseng, known as Ashwagandha. Root extracts of Ashwagandha [14] have been used for centuries in traditional Indian medicine due to its adaptogenic effects [15] and potential to strengthen the nervous system [16]. Rich in bioactive compounds [17], it has gained attention for various potential health benefits, including stress management, cognitive function, and physical performance [18].

Although the impact of Ashwagandha on bone mineral density remains a relatively underexplored area, its prospective advantages in the realm of bone health merit an extensive exploration. Prior to embarking on human trials, a thorough examination of studies conducted on animals is imperative to lay down a robust groundwork. Animal studies serve as invaluable preclinical tools, shedding light on underlying mechanisms, possible adverse effects, and the broader therapeutic promise.

The utilization of herbal treatments adheres to the principles of Ayurvedic medicine, providing viable and economically feasible choices, particularly in remote regions of developing nations. Phytoestrogens sourced from soy, mirroring the effects of hormone replacement therapy (HRT) in mitigating menopausal symptoms, unveil a hopeful path for addressing postmenopausal osteoporosis devoid of substantial adverse outcomes [19,20].

Incorporating phytoestrogens and exploring herbs like Ashwagandha in osteoporosis treatment can complement existing options. A thorough review of the constituents and polyherbal preparations with potential anti-osteoporotic properties is crucial for advancing research in this area. The authors aim to stimulate global interest in herbal remedies, encouraging the development of novel anti-osteoporotic agents that can enhance current treatments.

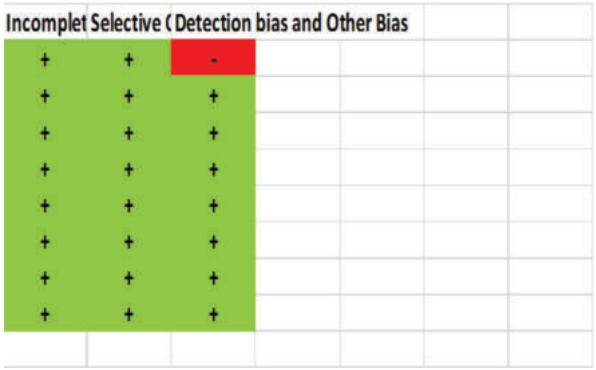
In conclusion, osteoporosis emerges as a formidable global health concern, particularly as our population ages. The realm of herbal remedies, such as Ashwagandha, emerges as a promising avenue, drawing upon age-old knowledge and the bounty of natural compounds. By delving into the intricacies of oxidative stress and venturing into the domain of multi-herbal concoctions, we embark on a path toward innovative therapeutic modalities that fortify skeletal health and present alternative dimensions to conventional interventions. Through comprehensive research, collaboration, and the integration of herbal approaches, the battle against osteoporosis can gain new momentum.

METHODS

A systematic search was conducted to identify relevant studies investigating the impact of ashwagandha on BMD parameters in animals. The search strategy included electronic databases (PubMed, Google Scholar), conducted using the keywords "ashwagandha" or “Withania” with "bone density" or “osteoporosis”, and "animals" and manual screening of reference lists. Studies published till 29 February 2023 were included. The search focused on animal studies examining the effect of ashwagandha on bone density. The paper includes a) studies on ashwagandha in the bone density of animals, b) studies on extractions from ashwagandha plant and herbal mix comprising ashwagandha as a key component in the bone density of animals. Studies that fulfilled the predetermined inclusion criteria underwent a meticulous assessment, wherein their methodologies, outcomes, and constraints were subjected to rigorous scrutiny.

The information obtained were compiled and reviewed systematically and a risk of bias (RoB) was conducted using SYRCLE's RoB to improve transparency and applicability of the study.

Assessment Of Bias Risk In Animal Studies Using SYRCLE's Tool



RESULT AND DISCUSSION

Experimental Studies On The Effects Of Ashwagandha On Bone Health In Animal Models

Ashwagandha has been the subject of several studies investigating its effects on bone density parameters. One study by examined the effects of dietary supplementation with ashwagandha root extract on laying hens [21]. The results showed that ashwagandha supplementation led to an increase in egg production and a decrease in egg weight during the second two weeks of the experiment. However, no significant effects were observed on egg shell thickness and yolk weight. Interestingly, ashwagandha supplementation significantly improved the retention of calcium (Ca) and phosphorus (P) in the tibia bone. This suggests that ashwagandha may have beneficial effects on bone density parameters in birds.

Another study investigated the effect of ashwagandha extract on bone density in ovariectomized rats [22]. The results showed that ovariectomized rats exhibited bone loss, but treatment with ashwagandha extract prevented these changes. This suggests that ashwagandha may have potential as a treatment agent for osteoporosis.

Furthermore, a study focused on a compound called withaferin A (WFA) found in ashwagandha [23]. The researchers found that WFA acts as a proteasomal inhibitor, which has a positive effect on bone formation. WFA increases the growth and differentiation of osteoblasts and decreases the activity of osteoclasts. WFA also reduces inflammation in bone cells and improves bone health in mice.

Another study in ovariectomized adult female Balb/c mice showed that WFA treatment enhanced bone health by increasing new bone formation, improving bone structure, and enhancing bone strength [24]. It achieved this by suppressing the expression of genes related to bone resorption, including Tartrate Resistant Acid Phosphatase and Receptor Activator of Nuclear Factor κ B. Furthermore, WFA treatment reduced the elevation of bone turnover marker Osteocalcin and the inflammatory cytokine Tumor Necrosis Factor-alpha caused by ovariectomy. These effects were similar to those of alendronate and 17-beta-estradiol treatment. Importantly, histomorphometric analysis of the uterus confirmed that WFA did not lead to estrogenic or anti-estrogenic effects, indicating that its positive influence on bone health wasn't associated with hormonal disruptions [24]. On a cellular level, WFA played a role in promoting the differentiation of Bone Marrow Cells (BMCs) and increasing mineralization by stimulating the expression of genes involved in bone formation.

In conclusion, WFA displayed potential for preserving bone health by both inhibiting bone resorption and promoting new bone formation, even before the onset of osteoporosis. It demonstrated comparable efficacy to alendronate (ALD) and 17-beta-estradiol (E2) in preventing bone loss. This suggests that WFA could be an effective strategy for maintaining bone mineral density in animals, as it addresses multiple aspects of bone health without causing uterine hyperplasia.

In another study, the researchers examined the use of ashwagandha root extract incorporated into biodegradable chitosan microparticles to enhance the biodegradation of materials and facilitate the controlled release of bioactive molecules [25]. The inclusion of the extract led to an increase in the growth and differentiation capabilities of pre-osteoblasts, suggesting its potential to improve the bioactivity of hydroxyapatite-based ceramic biomaterials.

Additionally, the herbomineral preparation OST-6, which contains ashwagandha, has been studied for its effects on bone density parameters. One study tested OST-6 in rats to prevent bone loss induced by ovariectomy and calcium deficiency [26]. The results showed that OST-6 significantly prevented the increase in serum alkaline phosphatase and urinary excretion of calcium and phosphorus observed in ovariectomized rats. It also prevented bone resorption and maintained the calcium to phosphorus ratio in the femur bone.

Another study investigated the effects of OST-6 on bone loss induced by ovariectomy in rats [27]. The results showed that treatment with OST-6 improved markers of bone loss, including bone mineral content, serum alkaline phosphatase levels, urinary calcium and pyridinium cross-links levels, and histological changes in the bones.

Furthermore, a study examined the effectiveness of OST-6 in treating rickets in rats [28]. The results showed that a diet deficient in vitamin D, calcium, and phosphorus led to rickets, but when the rats were fed a diet containing OST-6, the rickets were completely reversed. This suggests that OST-6 may be a natural way to prevent bone loss, may be an effective treatment for osteoporosis and may be an effective treatment for rickets.

In the assessment of the included studies using SYRCLE's Risk of Bias tool for animal studies, it was observed that most of the studies (6 out of 8) exhibited a low risk of bias concerning baseline characteristics and random assignment. This indicates that these studies effectively described the characteristics of the study subjects and implemented randomization techniques, contributing to the methodological rigor. However, a notable limitation across all studies was the lack of clarity regarding allocation cover-up, implying a high risk of bias in this aspect. This underscores the need for enhanced transparency in future research to ensure proper allocation processes. Additionally, there was a consistent deficiency in random housing and blinding evaluation in all studies, which poses a high risk of experimental bias. This highlights the significance of implementing random housing and blinding procedures in animal studies to enhance methodological robustness. Furthermore, it's noteworthy that all studies reported low risk of bias in terms of incomplete outcome data and selective outcome reporting. However, concerning detection bias and other bias, the majority of studies (7 out of 8) demonstrated low risk, with only one study showing a high risk of bias in this regard. This emphasizes the importance of maintaining vigilance against detection bias in animal studies to ensure the reliability of research outcomes.

The studies reviewed in this paper indicate positive effects on bone density parameters, calcium retention, and gene expression, while also preventing bone loss from ovariectomy and calcium deficiency. Compounds like WFA and the herbomineral mix OST-6 show promise in enhancing bone density. However, the studies are limited, necessitating further research in animals and humans to evaluate ashwagandha's potential as a natural treatment for low bone density conditions.

CONCLUSION

In summary, the collective body of research examined in this review underscores the potential advantages associated with ashwagandha and its bioactive components in the context of bolstering bone health. These insights hint at the possibility that ashwagandha supplementation, particularly concerning compounds like WFA within ashwagandha and herbomineral formulations containing ashwagandha, may contribute to improving various aspects of bone density. Furthermore, it appears that ashwagandha can potentially counteract bone loss stemming from factors such as ovariectomy and calcium deficiency, while also exerting positive effects on the genetic processes associated with bone formation and resorption. Additionally, the integration of ashwagandha extract within chitosan

microparticles shows promise for enhancing the biodegradation of biomaterials and fostering pre-osteoblast differentiation. Nonetheless, it is crucial to acknowledge that while these initial findings are encouraging, the pursuit of more comprehensive research, encompassing both animal models and eventually human clinical trials, remains imperative in substantiating ashwagandha's effectiveness and safety as a prospective natural intervention for conditions characterized by diminished bone density and bone loss.

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