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SHORT REVIEW

Herbal Remedies for Osteoporosis

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Abstract

Osteoporosis is a widespread concern that poses significant health risks. In the past, it was commonly thought that women would naturally undergo this condition as they age, especially during menopause when hormonal imbalances heighten the risk. Osteoporotic fractures affect approximately one in three women and one in five men over the age of 50 during their lifetimes. The mature skeleton constantly undergoes a remodelling process that involves both bone formation and resorption. However, when bone resorption exceeds bone growth, osteoporosis develops. Both men and women need to prioritize their bone health throughout their lives. Addressing factors that impact bone health at every stage becomes crucial in preventing osteoporosis. To combat the rising incidence of osteoporotic fractures, it is crucial to implement effective preventive measures aimed at maximizing peak bone density, limiting accelerated bone loss, and reducing the risk of falls. Present therapy goals primarily focus on stopping further bone loss and fractures, preserving bone mass, and utilizing medications like bisphosphonates, Selective Estrogen Receptor Modulators (SERMs), anabolic steroids, strontium, and Hormonal Replacement Therapy (HRT). However, it's worth noting that some of these treatments, such as HRT, bisphosphonates, SERMs, and anabolic steroids, may have negative side effects. As a result, there is an urgent need to identify effective, affordable, natural, and less harmful compounds to manage osteopenia/osteoporosis effectively. The search for safer alternatives is crucial in combating this condition and promoting better bone health.

Keywords: Bone Formation, Bone Resorption, Herbal Remedies, Osteoporosis

1. Introduction

Osteoporosis can be diagnosed when a person has reduced bone density in addition to a degraded bone structure. This results in bones that are weakened and more prone to fractures[1]. The quantity of bone loss and peak bone mass in an individual, measured in grams of mineral content for every square centimetre or cubic inch, is used to calculate bone density. To put it another way, bone density can be defined as the amount of bone mineral that is contained within bone tissue. Denser and less likely to fracture are bones that contain a greater proportion of certain minerals. The quality of the bone is determined by several elements, including the mineralization of the bone, the accumulation of injury (such as microfractures), bone turnover, and general architecture[2].

Osteoporosis, the most common form of chronic metabolic bone disease, is defined by a steady decline in bone strength, which results in increased bone fragility and an increased susceptibility to fractures. The development of this condition is influenced by several variables, including menopause and the natural process of ageing. This condition causes the tissue in the bones to deteriorate and can also disturb the microarchitecture of the bones, which can result in a reduction in the bone's overall strength[3]. Even though osteoporosis can strike anyone of any age, gender, or ethnicity, it is most prevalent in Caucasians (those of white race), old women, and women. Osteoporosis is a disease that is increasing in prevalence all over the world as a direct result of an ageing population and longer life expectancies. It is estimated that more than two hundred

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million people are currently coping with osteoporosis in their daily lives. According to recent research conducted by the International Osteoporosis Foundation, one in three women over the age of 50 and one in five males may experience an osteoporotic fracture at some point in their lifetimes. This highlights the tremendous influence that osteoporosis has on fracture risk and emphasizes how important it is to detect osteoporosis early and take preventative treatments[4].

Osteoporosis typically does not present any clinical symptoms until it has caused a fracture. Fractures in men have the potential to be lethal and almost always result in considerable morbidity. In addition, osteoporosis has a negative influence on quality of life, raises life expectancy when adjusted for disability, and places a considerable financial burden on the healthcare systems that are responsible for treating those who are impacted by the condition. When it comes to the prevention of osteoporosis, early detection, accurate assessment of bone mineral content, and prompt treatment are all extremely important factors[5].

2. Pathogenesis

The disorder known as osteoporosis is characterized by brittle bones that are more prone to breaking than healthy bones. The fragility of skeletal tissue can be affected by several circumstances, including the following: (a) Inadequate accomplishment of the required size and strength of the skeleton throughout development; (b) Accelerated bone decay leading to lower bone density and damaged bone microarchitecture; and (c) Insufficient growth in response to increased destruction during bone remodelling. The frequency and pattern of falls, particularly those that involve the hip and wrist, play a key influence in the development of fragile fractures. These fractures can be caused by several different factors. A disruption in bone remodelling causes increased bone resorption and inadequate bone production, both of which ultimately contribute to skeletal fragility caused by the disruption[6].

Hematopoietic precursors often interact with cells of the osteoblastic lineage to stimulate the transformation into osteoclasts, the first step in bone transformation, also known as Bone Multicellular Units (BMUs). Howship lacunae, which are seen on the surface of trabecular bone, and Haversian networks, which are found in the cortical bone, are two different manifestations of BMUs. Short periods of breakdown and reversal precede lengthy periods of the osteoblastic rebuilding of bone during the remodelling process. As a result, if bone remodelling were sped up, the bone mass would be lost. In addition, the bone can become fragile if there are more Howship lacunae and haversian canals than normal. If resorption rates are too high, the trabecular scaffolding that supports new bone development can be lost entirely[7]. As a result, many different factors have the potential to contribute to bone fragility by promoting osteoclastic resorption. On the other hand, increased resorption levels do not necessarily result in bone loss during some stages of life, such as during a pubertal growth spurt. As a result, the development of osteoporosis significantly contributed to an inadequate formation response that occurs during remodeling[8].

3. Conventional Therapy for Osteoporosis

In recent years, major therapeutic breakthroughs have been made in the management of osteoporosis as a direct result of the progress that has been made in our understanding of bone biology. The treatment of osteoporosis has been shown to significantly reduce the occurrence of fractures in those who are at risk of such fractures by roughly 70 per cent[9]. This is a great achievement. In addition, it has been demonstrated that the implementation of secondary prevention strategies for fractures can reduce the risk of death as well as the risk of fracture in patients who have a previous history of hip fracture[10-12]. This article provides an overview of the medications that rheumatologists most frequently prescribe, as well as the potential risks associated with their utilization. Antiresorptive medications are used for the treatment of osteoporosis. These drugs work by inhibiting the activity of osteoclasts, which stops the progression of bone loss. Denosumab, selective estrogen receptor modulators, and bisphosphonates are considered to be the three most effective antiresorptive medicines currently available[13]. On the other hand, anabolic medications hasten the process of bone formation and increase its growth. Teriparatide is distinguished by the fact that it was the first anabolic medicine to be approved for the treatment of

osteoporosis[14]. Teriparatide is a chemically similar version of Parathyroid Hormone (PTH)[14]. In mature bone, where they make up 90–95 % of all bone cells, osteocytes perform a critical role in controlling bone metabolism. They regulate osteoclast and osteoblast activity in a coordinated effort to remodel bone. Osteocytes act as mechanosensors, detecting areas of microdamage and microcracks and sending signals to osteoclasts to repair the area. Osteoblasts' use of the Wnt signalling pathway is crucial to bone development. Initiating bone formation, this mechanism is stimulated by bone morphogenetic protein and PTH. However, this mechanism is controlled by endogenous inhibitors such as sclerostin and Dickkopf WNT signalling pathway inhibitor 1 (DKK1). Osteocytes and bone tissue express sclerostin, which affects the Wnt signalling pathway, particularly in reaction to mechanical damage and other metabolic changes[15]. On the other hand, bone resorption is heavily dependent on the pathway that involves the receptor activator of the nuclear factor-kB ligand (RANKL). It is essential for the development, activation, and maturation of osteoclasts for RANKL to be released from the surface of osteoblasts, where it then binds to RANK, which is already present on osteoclasts. Osteoprotegerin (OPG) functions as a decoy receptor for RANKL, preventing the interaction between RANKL and the RANK receptor that is found on osteoclasts. This is done to prevent excessive bone resorption. As a result, the process of osteoclast-driven bone resorption is controlled by the maintenance of a balance between RANK and RANKL as well as OPG[16].

Recent years have seen significant research into osteoporosis, resulting in better treatment choices. Treatments available today have proven successful in raising BMD and decreasing fracture risk. Recent advances in drug research have provided clinicians with multiple effective treatment options for osteoporosis, including sequential/combination therapy and goal-driven therapy[13]. However, standard treatments may have unintended consequences. Consequently, the quest for natural therapies that are both cost-effective and have fewer adverse effects in the treatment of osteoporosis and osteopenia should be prioritized.

3.1 Herbal Remedies for Osteoporosis

Evidence suggests that nearly every ancient society employed plants for treating ailments and repairing biological functions, making herbal therapy one of the oldest forms of healthcare in the world. Herbs are more important than ever before because of the shockingly clear repercussions of processed diets and heavy medication. Herbs are being used in more and more modern beverages, cosmetics, and foods[17]. The concept that herbs and other plants have great therapeutic potential reflects a broader push toward improvements in lifestyle. The treatment of osteoporosis18 has been proven to benefit from several unconventional medicinal sources, including plant extracts and their crude forms[18]. Numerous plants are believed to have the potential to address osteoporosis, including:

3.1.1 *Salvia miltiorrhiza*

Red sage, also known as *Salvia miltiorrhiza* (Lamiaceae), is a natural remedy indigenous to China, commonly referred to as Chinese sage. It thrives abundantly in the slopes and riverbanks of the western and southwestern provinces of China and Japan. *Salvia miltiorrhiza* comprises approximately 70 different compounds, categorized as hydrophilic and lipophilic compounds. Studies have indicated its ability to inhibit the RANKL signalling pathway induction of Tumor Necrosis Factor Receptor Associated Factor 6 (TRAF6) and Nuclear Factor of Activated T-cells, cytoplasmic 1 (NFTAc1), as well as uncontrolled cathepsin K and calcitonin receptor, which contribute to promoting osteoclast differentiation. It was earlier reported that SML (Ethanolic Extract combination of *S. miltiorrhiza* and Liquid Calcium) demonstrated protective mechanisms against bone loss caused by estrogen deficiency[19]. The inclusion of *Salvia miltiorrhiza* in more than 30% of traditional clinical studies that effectively treated osteoporosis has generated significant interest in exploring and characterizing the specific components of this herb[20].

3.1.2 *Trifolium pretense*

Red clover, scientifically known as *Trifolium pratense*, is a flowering herbaceous plant belonging to the Fabaceae family. While it originates from Europe, Northwest Africa, and Western Asia, it has been widely cultivated and naturalized in various other regions. Red Clover (*Trifolium pratense* L.) is a plant component known for its high content of isoflavones and has been traditionally used to alleviate menopausal

symptoms. The most prevalent form of osteoporosis occurs due to bone loss resulting from decreased ovarian hormones after menopause. Diets containing phytoestrogenic isoflavones have been associated with a reduced incidence of osteoporosis and menopausal symptoms. In rat studies, ovariectomy led to reduced bone minerals, femoral weight, femoral volume, tibial stiffness, increased levels of bone-specific alkaline phosphatase in the blood, and an elevated number of osteoclasts in femur sections compared to sham operations. The studies suggest that ovariectomy stimulates both bone growth and resorption[21]. However, isoflavone therapy significantly improved bone minerals, tibial stiffness, femoral weight, and femoral volume, and reduced the increase in serum alkaline phosphatase levels. Additionally, the isoflavone treatment resulted in a noteworthy decrease in the number of osteoclasts compared to control rats with ovariectomies. These findings indicate that red clover isoflavones are beneficial in reducing bone loss caused by ovariectomy, likely by regulating bone turnover through the suppression of bone resorption. Research suggests that isoflavone extract from red clover, when administered in sufficient amounts, can effectively help maintain bone mass in rats with ovariectomies[22].

3.1.3 *Equisetum arvense*

Horsetail, scientifically known as *Equisetum arvense*, has a rich history as an herbal remedy dating back to ancient Roman and Greek civilizations. This slender perennial plant has a rhizomatous stem that bears a resemblance to a horse's tail. Horsetail is particularly abundant in the mineral silicon, which is well-known for its bone-strengthening properties. A clinical trial involving 122 Italian women found that those who consumed horsetail showed higher bone densities[23]. Collagen, the body's most abundant protein, plays a vital role in supporting tendons, skin, cartilage, and muscles, and it contains a significant amount of silica[24].

3.1.4 *Thymus vulgaris*

Thymus vulgaris is a flowering plant that is a member of the family Lamiaceae and is indigenous to southern Europe. Its natural range extends from the western Mediterranean to the southern tip of the Italian peninsula. This widely used medicinal herb includes a significant quantity of volatile compounds and essential oils, both of which have demonstrated a possible role in reducing bone loss[25]. There have been no reports of any adverse effects or digestive issues brought on by eating the essential oil molecules[26]. These molecules are also biodegradable and feature antimicrobial capabilities. Thymol, carvacrol, terpinene, and caryophyllene are the primary components that make thyme essential oil[27]. The presence of phenolic compounds, in particular thymol and carvacrol, is responsible for the majority of the biochemical effects that are caused by *Thymus vulgaris*. Thyme has been prized for its antibacterial and antispasmodic qualities for a significant portion of human history. It possesses anti-inflammatory properties and multiple benefits for bone development, which enables it to be an effective inhibitor of bone resorption. These benefits can be found in the bone formation process. Additionally, thyme has a variety of antibacterial, antifungal, and antiviral activities, in addition to having antioxidant properties[28].

3.1.5 *Curcuma longa*

Curcumin, a vibrant yellow compound derived from the *Curcuma longa* variety of plants, is commonly known as turmeric, which belongs to the Zingiberaceae family of ginger plants. Turmeric contains curcumin as its primary curcuminoid, serving as the main active component. Within traditional Chinese medicine, turmeric has a well-established history of being used as an anti-inflammatory remedy[29]. Prolonged use of glucocorticoid medication can lead to osteoporosis. Nevertheless, studies have indicated that curcumin offers protective effects against bone loss caused by ovariectomy and reduces osteoclast genesis in mouse models[30,31]. Additionally, research by Yang *et al.,* demonstrated that curcumin enhances bone microarchitecture and mineral density in APP/PS1 transgenic mice[32].

Curcumin has proven its effectiveness in preventing osteoporosis induced by dexamethasone both *in vivo* and *in vitro*. Studies have revealed that curcumin restores bone mineral density and the levels of bone metabolic biomarkers, such as osteocalcin and collagen type-I fragments, in rats. Additionally, it regulates the bone differentiation process and the proteins associated with bone maturation in crucial bone-forming cells. Furthermore, curcumin has been observed to reactivate the Wnt/β-catenin signalling pathway, which may

contribute to its bone-protective properties. Based on these findings, it is strongly suggested that curcumin offers protection against glucocorticoid-induced osteoporosis[29].

3.1.6 *Glycine max*

Soy, scientifically known as *Glycine max* and belonging to the Fabaceae family, is highly esteemed for its nutritional advantages. It offers a range of health benefits, including potential positive effects on breast cancer, prostate cancer, menopausal symptoms, heart disease, and osteoporosis. Soybeans are a rich source of protein, isoflavones, dietary fibre, and fatty acids, especially alpha-linolenic acid. These active components serve diverse biological functions, such as promoting bone health, improving lipid metabolism, preventing cancer, and displaying estrogenic and hypocholesterolemia actions. One notable active ingredient found in soy is isoflavone[33].

3.1.7 *Withania somnifera*

In *Ayurveda*, an Indian traditional medical practice that dates back thousands of years, one of the most important medicinal herbs is ashwagandha, which has the scientific name of *Withania somnifera* and is a member of the family Solanaceae. It has been utilized for ages as a Rasayana, which is renowned for its myriad of beneficial effects on one's health. Ashwagandha is known to contain several bioactive compounds, some of which are known as withanolides, withaferin, cuscohygrine, anahygrine, tropine, pseudo tropine, and anaferine. Withanolides are one of them and are most commonly found in withania root extract. Because of the estrogen-like effects that withanolides have on bones, this extract has the potential to be used as a treatment for osteoporosis. The excellent influence that Ashwagandha extract has on bone health was highlighted in a study conducted on ovariectomized rats. The researchers found that the Ashwagandha extract led to increased ash weight, ash calcium, ash phosphorus, and ash magnesium in the tibia and femur bones[34].

3.1.8 *Cissus quadrangularis*

Cissus quadrangularis (CQ), also known as Asthishrinkala, is a traditional medicinal herb with potential osteoprotective effects. This perennial climber, belonging to the Vitaceae family, thrives in the hot regions of India and is commonly known as "hadjod". In India, it is widely used to enhance bone health and has been studied extensively for its anti-osteoporotic properties, targeting various pathways and mechanisms. CQ contains natural matrices with well-known bioactivity, making it valuable in protecting against conditions such as osteoporosis, stiffness, and gastric ulcers. As per the definition of Asthi Shrinkhala as Asthiyuka, it supports and sustains the integration of Asthi Dhatu, preventing age-related bone degeneration. The active component in CQ, ketosterone, contributes to several beneficial actions: (a) It promotes optimal bone health and acts as an antagonist to glucocorticoid receptors; (b) It exhibits anabolic steroid characteristics, aiding in fracture repair and leading to increased intramuscular creatinine levels; (c) It stimulates the growth of new muscles by countering the detrimental effects of cortisol on muscular tissue; (d) It significantly inhibits the development of harmful free radicals, such as DPPH, superoxide, and lipid peroxide in erythrocytes; (e) It exerts a calming effect on the central nervous system; (f) Its antisecretory and cytoprotective effects safeguard the stomach mucosa against ulcers; (g) It facilitates the recruitment of fibroblasts and chondroblasts to damaged tissues, accelerating the process of regeneration and (i) It provides benefits for back and spine issues[35,36].

3.1.9 *Terminalia arjuna*

Terminalia arjuna, commonly known as *Arjuna*, is a plant native to the Indian subcontinent and belongs to the Combretaceae family. It can also be found in Sri Lanka's southwest and Myanmar to the east. Apart from being a source of lumber, fuel, tannin, and sericulture, it is a widely used medicinal plant in various indigenous systems of medicine, including the *Ayurveda*, Siddha, Unani, and Yunnan systems of medicine. The tree holds cultural significance due to its association with astrology and Hindu mythology. References to the name "Arjuna" appear only a few times in the Rig Veda and Artharva Veda. The Charka Samhita mentions the use of Arjuna bark powder as an astringent and diuretic[37]. The bark of *Terminalia arjuna* (Roxb.) Wight and Arn. holds significant therapeutic importance due to its diverse compounds. The ethanol extract contains glycosides, a substantial

amount of calcium carbonates, tannins, and lower levels of aluminium and magnesium. Flavonoids like arjunolone, arjunone, gallic acid, and quercetin, along with terpenoids such as arjumin, arjunic acid, arjunolic acid, and terminic acid, are among the components found in bark[38]. Additionally, other compounds like tannins, pyrocatechols, punicallin, punicalagin, terchebulin, and casurinin have been isolated from the bark[39]. The high flavonoid content in the bark powder has been found to positively impact the antioxidant status of individuals with coronary heart disease. Furthermore, the bark is believed to possess properties that are anticancer, hypolipidemic, and cardiotonic. Studies on ovariectomized rats have demonstrated the anti-osteoporotic effects of *T. arjuna*, which closely resemble the signs of postmenopausal osteoporosis observed in humans. Due to its ability to enhance the production and release of female hormones, the bark is well-regarded for its capacity to remineralize bones, making it a commonly used remedy for osteoporosis and other bone-related conditions, providing relief for postmenopausal women experiencing discomfort. The application of *T. arjuna* ethanol extract has been shown to inhibit osteoclast development and has proven to be advantageous, safe, and effective in managing osteoporosis[40,41].

3.1.10 Punica granatum L

Punica granatum L, commonly known as the pomegranate plant, is native to Iran, Afghanistan, India, and Mediterranean countries. Its primary source of origin is believed to be Iran. Pomegranates are also found naturally in specific regions of India, specifically in the Western Himalayan states of Jammu and Kashmir, Himachal Pradesh, and Uttarakhand[42]. Pomegranate seeds contain a diverse array of active compounds, including tannins like ellagic acid and gallotannic acid, as well as alkaloids, glycosides, phenols, saponins, coumarins, flavones, and resins. Among these compounds, ellagic acid has been found to have a beneficial effect on reducing bone loss by promoting bone mineralization through osteoblast activity. In a study using a rodent model of osteoporosis, an ethanolic extract of *P. granatum* L. with high tannin content and ellagic acid demonstrated the ability to prevent bone loss. The anti-osteoporotic properties of the *P. granatum* seed extract containing ethanol were even more pronounced in rats that had undergone ovariectomy (OVX). Administration of the ethanol extract of *P. granatum* (L) seeds effectively mitigated the average body weight gain caused by OVX in the rats. Furthermore, the *P. granatum* seed extract, administered at different doses (100, 300, and 500 mg/kg), exhibited significant restorative effects, characterized by improved ossification, mineralization, increased osteoclastic activity, and reduced bone resorption. These findings suggest that this extract has the potential to facilitate bone recovery with essential characteristics resembling normal bone in the treated rats[43].

3.1.11 Tinospora cordifolia

Tinospora cordifolia (Willd.) Miers ex Hook. F. and Thoms, a massive deciduous climbing shrub with a potential height of up to 300 meters, falls under the Menispermaceae family and is extensively found across India, especially in tropical regions, and certain parts of China. It is commonly known as Giloy in Hindi and Guduchi in Sanskrit[44]. The effects of an alcoholic extract of *Tinospora cordifolia* on human osteoblast-like cells MG-63 and primary osteoblast cells from rat femurs were investigated to understand its impact on bone growth, differentiation, and mineralization of bone-like matrix[45]. The extract, when administered at a dose of 25 g/ml, demonstrated positive effects on osteoblast proliferation in both cell model systems, promoted cell differentiation into osteoblastic lineage, and enhanced the mineralization of bone-like matrix. Cell morphology studies also revealed that the extract increased cell counts without any adverse effects on cell morphology[46]. In another study using human osteoblast-like cells sarcoma osteogenic SAOS2, both aqueous and alcoholic extracts were tested for their ability to promote bone formation. The ethanolic extract, at a dosage of 25 g/ml, showed increased osteoblast proliferation, while the aqueous extract had no impact on cell growth. The extract also exhibited pro-stimulatory effects on osteoblasts[47]. The fermented version of this medicine is suggested for healing purposes in *Ayurveda*, possibly due to these findings[45].

3.1.12 Nigella sativa

Nigella sativa, an herb belonging to the Ranunculaceae family, has been used as an herbal remedy for various acute and chronic diseases since ancient times. It is

commonly known as black cumin or *habatus sauda*, and its active components are mainly found in the seeds[48]. *Nigella sativa* seed oils are a good source of essential fatty acids, surpassing regular vegetable oil in this aspect. The seeds and oil extracts of *Nigella sativa* have been used for various health benefits, including anticancer, antioxidant, antimicrobial, antifungal, antiparasitic, and anti-asthmatic properties. Thymoquinone (TQ), the primary active component of *Nigella sativa*, has shown potential benefits in bone and joint health[49]. Both *Nigella sativa* and Thymoquinone possess anti-oxidative and anti-inflammatory properties, which contribute to their antiosteoporotic actions. *Nigella sativa* nutritional supplementation is beneficial in preventing decreased glucose levels caused by ovariectomy in rats. The seed oils of *Nigella sativa* contain a higher percentage of unsaturated fatty acids, with linoleic acid and oleic acid being the main non-saturated fatty acids[50]. Oleic acid has been associated with increasing calcium levels and promoting bone health by enhancing nutrient assimilation in the body[51]. Studies have demonstrated that consuming milk fortified with oleic acid and other fortifiers resulted in significant increases in plasma calcium, Vitamin D, and osteocalcin[52]. *Nigella sativa* has shown potential in countering osteoporotic conditions in ovariectomized rats, possibly due to its elevated levels of non-saturated fatty acids, in addition to its antioxidant and anti-inflammatory qualities[53].

3.1.13 *Zingiber officinale*

Ginger, scientifically known as *Zingiber officinale* Roscoe and belonging to the Zingiberaceae family, is a rhizome that has been used for more than 3000 years in various countries and regions, including Arab nations, Tibet, Burma, China, Germany, Greece, Indonesia, India, Japan, Sri Lanka, Congo, and the United States of America. It is valued for its medicinal properties, including its astringency, fragrance, use as a dietary supplement and therapeutic benefits[54]. In experimental studies, polyphenols known as gingerols, extracted from *Z. officinale* rhizomes, have shown osteoprotective properties. These extracts are beneficial in protecting bones in cases of arthritis caused by streptococcal cell walls and preventing the loss of bone mineral density, as determined by dual-energy absorptiometry[55]. Gingerol treatment induced osteoblast differentiation in both normal and inflammatory conditions. It facilitated the development of bone-forming cells, leading to increased transcription levels of osteogenic markers, heightened activity of the ALP enzyme, and improved formation of mineralized nodules. Additionally, in TNFa-treated MG-63 cells, gingerol reduced the level of inflammation[56]. Furthermore, garlic oil extract has shown promise in preventing bone damage caused by ovariectomy. Supplementing with garlic oil extract reduced significant changes in serum tartrate-sensitive acid phosphatase activity, serum alkaline phosphatase activity, renal elimination of calcium, phosphate, and hydroxyproline, as well as the ratio of renal calcium to creatinine, which are all associated with ovariectomy-induced bone loss[45].

3.1.14 *Azadirachta indica*

The Meliaceae family includes *Azadirachta indica A. Juss*, a medicinal plant native to the Indian subcontinent. It is commonly known as the neem tree, and it has been extensively used in traditional medicine for centuries, earning it names like the "pharmacy of the village" tree and the miracle tree. Neem tree extracts contain various beneficial compounds, including tannins, limonoids, gallic acid, di- and triterpenoids, and coumarins, which contribute to a wide range of effects, such as anti-inflammatory, anti-arthritic, anti-pyretic, anti-microbial, anti-tumour, and immunomodulatory properties[57]. *In vitro* studies have shown promising results for *Azadirachta indica* root extracts as potential medications for osteoporosis. These extracts demonstrated an increase in caspase enzyme activity and enhanced expression of mitochondrial pro-apoptotic proteins, leading to a reduction in osteoclast proliferation and inducing apoptosis. Furthermore, the extracts promoted cell differentiation, though they did not affect the multiplication of osteoblasts or chondrocytes. The extracts also exhibited an osteo-inductive effect in primary bone marrow cells that were cultured[58].

3.1.15 *Sesamum indicum*

Sesame (*Sesamum indicum*), also referred to as benne, is an annual plant that stands upright and belongs to the Pedaliaceae family. Cultivated since ancient times, it is valued for its edible seeds known for their delightful flavor and fragrance. The sesame plant

thrives in tropical, subtropical, and southern temperate regions across the globe[59]. In a study involving rats with ovariectomies, the administration of 10% sesame oil led to a significant decrease in modified alkaline phosphatase activity and tartrate-resistant acid phosphatase activity. Additionally, the treatment exhibited positive effects on bone microarchitecture by strengthening it and reducing disruptive, lytic bone trabeculae[60].

3.1.16 Moringa oleifera

The *Moringa genus*, belonging to the Moringaceae family, includes both natural and cultivated varieties, among which *Moringa oleifera* is notable. It is renowned for being one of the most abundant plant sources of vitamins A, B (1, 2, 3, 6, 7), C, D, E, and K. Moreover, Moringa contains essential minerals such as copper, iron, calcium, potassium, magnesium, zinc, and manganese. With over 40 natural antioxidants, it offers a wide range of health benefits. More than 80 countries, including Pakistan, utilize various parts of the Moringa plant, such as leaves, pods, seeds, gums, bark, and flowers, to address deficiencies in minerals and vitamins, promote cardiovascular health, maintain normal blood sugar levels, neutralize free radicals for reduced cancer risk, support anti-inflammatory mechanisms, improve anaemia, and enhance the immune system[61]. Additionally, Moringa has positive effects on bone strength, brain function, and eye health. It is also considered beneficial for women experiencing menopause and individuals dealing with overall weakness and malnutrition. In research involving rats with ovariectomies, *Moringa oleifera* and its various constituents demonstrated a significant role in preventing bone loss[62].

3.1.17 Asparagus racemosus

Recently, a new plant family called Asparagaceae was established to accommodate the *Asparagus genus*, which was previously part of the Liliaceae family's subfamily Asparagae. The Asparagus genus is considered to have medicinal significance due to the presence of steroidal saponins and sapogenins in various parts of the plant. The term "asparagus" originates from the Greek word meaning "stalk" or "shoot." There are approximately 300 different varieties of asparagus found worldwide. In traditional Indian medicine, the most commonly used species of asparagus are *A. racemosus, A. gonoclados, and A. adsendens. A. racemosus* is frequently referred to as a *Rasayana* in *Ayurveda*, which pertains to herbal medicines that enhance cellular vitality or resistance to improve overall well-being[63]. In histopathological examinations, methanolic and aqueous extracts of *Asparagus racemosus* roots significantly influenced mineralization, ossification, and the suppression of osteoclastic activity. The overall ash weight, ash percentage, and calcium content were notably increased. The extract also had a significant effect on lowering serum calcium levels, serum alkaline phosphatase function, and excessive calcium loss in urine caused by ovariectomies. Additionally, it improved biomechanical characteristics, such as the hardness of the fourth lumbar vertebra, its weight, and the length of the femur. *Asparagus racemosus* root contains phytosterols and other active ingredients that may exhibit estrogen-like effects on estrogen receptors, protecting against osteoporosis[64].

3.1.18 Rubia cordifolia

Rubia cordifolia, commonly known as Manjishta and belonging to the Rubiaceae family, is widely distributed in India, particularly in the northwest Himalayas. It contains various bioactive substances such as glycosides, naphthoquinones, terpenes, bicyclic hexapeptides, and iridoids, which contribute to its diverse medicinal properties, including anti-arthritic, anti-cancer, anti-microbial, antioxidant, and hepatoprotective effects[65]. In traditional medicine, several herbal plants have been used to treat osteoporosis, bone hardening, and fractures. The root of *Rubia cordifolia* is known in *Ayurveda* as a bone mender (Sandhaniya) and is used for treating broken bones. Studies have shown that anthraquinones isolated from Morinda officinalis, such as physcion, exhibit anti-osteoporotic effects on both osteoblasts and osteoclasts[66]. According to Kasabi *et al.,* the application of ethanolic extract of *Rubia cordifolia* enhanced biomechanical strength, increased bone formation activity, and reduced bone destruction activity, promoting bone development. In ovariectomized rats, the administration of raloxifene and *Rubia cordifolia* extract at 200 and 400 mg/kg significantly strengthened the bones[67].

4. Conclusion

Osteoporosis is a metabolic bone illness that affects most people. It is distinguished by a decreased bone mass and an increased susceptibility to fractures. Because of the significant influence it has on a person's quality of life, an effective treatment method that does not cause any unwanted consequences is required. Herbal medications derived from the Ayurvedic tradition have demonstrated considerable improvement in osteoporotic alterations and provide a viable therapeutic strategy. These drugs are simple to obtain and simple to administer, and there are no known adverse effects associated with their use. The completion of more clinical research can assist in establishing their position in the osteoporosis treatment process that is both effective and efficient in clinical settings.

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