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STRESS RELIEF AND OSTEOGENIC POTENTIAL OF *MORINGA OLEIFERA*: A SYSTEMATIC REVIEW OF IN VIVO STUDIES

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ABSTRACT

Moringa oleifera, commonly known as drumstick tree, has gained significant attention due to its wide range of pharmacological properties, including antioxidant, anti-inflammatory, and adaptogenic effects. The present systematic review aims to evaluate the stress-relieving and osteogenic potential of *Moringa oleifera* based on in vivo studies. A comprehensive literature search was conducted using scientific databases, focusing on animal studies that assessed behavioral, biochemical, and bone-related outcomes following *Moringa oleifera* administration. The findings indicate that *Moringa oleifera* exhibits significant stress-reducing effects by modulating cortisol levels, oxidative stress markers, and behavioral responses. Additionally, it demonstrates osteogenic potential by improving bone mineral density, enhancing bone formation markers, and reducing bone resorption. These effects are primarily attributed to its rich phytochemical profile, including flavonoids, phenolics, and essential minerals. However, limitations such as variability in study design and lack of clinical trials highlight the need for further research. Overall, *Moringa oleifera* shows promising potential as a natural therapeutic agent for stress management and bone health.

1. INTRODUCTION

Bone remodelling involves the constant regeneration and replacement of bone tissues, which occurs in two separate phases: bone formation and bone resorption. During bone formation, osteoblasts (bone-forming cells) fill the bone cavities with new tissue. While, during resorption, osteoclasts (bone-resorbing cells) disintegrate bone tissue. Under normal and healthy conditions, bone resorption and formation occur in a dynamic and balanced way, with

old tissues constantly replaced by new ones . Calcium which is vital for bone health is primarily stored in bone. Calcium phosphate and mineralised collagen serve as structural supporting components for bone tissue. When blood calcium levels drop, various physiological responses contribute to maintaining calcium homeostasis. This includes activation of parathyroid hormone, which causes release of bone calcium, increased intestinal calcium absorption and increased renal calcium reabsorption. Traditionally, serum and urine calcium levels are employed as indications of mineral balance in the body. Meanwhile, excessive urine calcium excretion is linked to bone loss and osteoporosis . Several clinical tests are now available for assessing bone health and evaluating therapy responses. Most of these indicators are also applicable to in vitro and in vivo experimental research. Bone mineral density (BMD), bone microarchitecture and biochemical markers serve as indicators of bone remodelling. In the clinical setting, bone diseases are typically evaluated using dual-energy X-ray absorptiometry (DXA), which measure bone mineral density. A T-score is created to indicate deviation of the measured BMD from the reference values in terms of standard deviation (SD). A T-score of −1 to −2.5 suggests poor bone mass or osteopenia, while a value below −2.5 indicates osteoporosis Bone microarchitecture can be evaluated using quantitative computed tomography (qCT). Deterioration of bone architecture resulted from bone loss, as demonstrated by decreased trabeculae number, increased inter-trabecular distances, loose connectivity of the trabecular meshwork, reduction of cortical bone thickness and increased porosity. The species of Moringa oleifera, which is endemic to parts of India, Pakistan, and Bangladesh that are sub-Himalayan, is the most frequently grown member of the Moringaceae family. The ancient Romans, Greeks, and Egyptians used this quickly-growing tree called the horseradish tree. It is currently widely cultivated and has naturally spread throughout many tropical areas . Moringa leaves have more potassium than bananas, calcium than milk, and vitamin C and iron than spinach. Compared to milk and eggs, moringa leaves have a higher protein content. Due to its high concentration of molecules comprising simple sugar and rhamnose, as well as glucosinolates and isothiocyanates, M. oleifera is utilized as an antioxidant material to treat many disorders associated with oxidative stress . It is recognized as one of the most beneficial plants in the world to be used in numerous applications since its components, particularly in the leaves, comprise carotenoids, tannins, vitamins, flavonoids, and phenolic acids demonstrating substantial antibacterial and antifungal properties . Moringa oleifera leaf extracts had a protective effect on BMSCs when they were exposed to peroxidative damage during osteogenic differentiation using an inhibitor of phosphoinositide-3 kinase, which was used to investigate the potential cellular

and molecular mechanisms underlying the protective properties of the plant [5]. Instead of a pure bone reaction, an immune-driven mechanism results in the production of new bone around the implant surface . A foreign body equilibrium (FBE) reaction would be triggered by titanium in the peri-implant tissues . The immune response then controls regeneration processes and the healing of tissues. During the initial phase of peri-implant tissue healing, the same processes may activate osseointegration. Immediately after implantation, proteins from the blood and interstitial fluids are quickly adsorbed onto the surface of implanted materials. Although it is obvious that such cell surface interaction is essential for cell survival, development, and differentiation, cells typically respond to an adsorbed layer rather than the surface itself. It is clear that the relevance of the perfect surface is significant since one surface may have a very different impact on host proteins than another, which may in turn have a significant impact on the future tissue formation around the implant. The biological basis of osseointegration is connected to the two primary aspects of the implant-host interaction – tissue features and biomaterial characteristics . Morphogenetic proteins (BMPs) activate and/or attract pluripotent cells present in the periosteum, bone marrow, bone cortex, and adjacent soft . BMPs, which are TGF (transforming growth factor) protein superfamily members, are well known for playing a crucial role in mammalian organogenesis and skeleton formation, two processes that are crucial to the development of the embryo. Additionally, BMPs are crucial in the control of bone synthesis, upkeep, and repair

Plants have long been a vital source of nutraceuticals, offering health benefits, disease prevention, and therapeutic applications, while also playing a significant role in modern pharmaceutical research. Approximately 75% of the global population 6 relies on plant-derived medicines, which remain the primary treatment approach in many developing countries 7.

Research indicates that certain bioactive compounds extracted from natural sources exhibit potent anti-inflammatory, regenerative properties, antioxidant, supporting and their effectiveness in treating various diseases 8. However, the precise mechanisms by which these natural compounds influence inflammation and bone healing remain inadequately understood. Existing evidence is limited, fragmented, and based on isolated studies, leading to inconsistencies in the literature. Despite this uncertainty, it is believed that plant extracts contribute to bone repair by enhancing antioxidant defenses, reducing tissue inflammation, promoting vascularization, and stimulating the proliferative activity of bone cells. Moringa oleifera is one of the most extensively cultivated species within the Moringaceae family. It

originates from regions of Southeast Asia, Africa, and the Americas. In these areas, its leaves, flowers, and young pods are commonly consumed as vegetables 9. The plant is renowned for its rich nutritional and phytochemical composition, serving as an excellent source of proteins, vitamins, and bioactive compounds. It contains antioxidants, flavonoids, saponins, alkaloids, tannins, and phenolic compounds, along with essential minerals such as potassium, calcium, sodium, phosphorus, sulphur, magnesium, zinc, copper, manganese, iron, and selenium 10. Every part of Moringa oleifera possesses medicinal properties, demonstrating a wide range of pharmacological activities, including antihyperglycemic, , immunomodulatory, chemoprotective, radio protective, diuretic, anti-inflammatory, antipyretic, antiepileptic, antitumor, antiulcer, antispasmodic, antibacterial, and antifungal effects 11. This extensive therapeutic potential is likely attributed to its unique composition of bioactive compounds, such as rhamnosyloxy benzyl isothiocyanate and its derivatives, niaziminins, niazinins, β-sitosterol, niacin, phenolic acids, glucosinolates, flavonoids, gallic acid, coumarin, and caffeic acid.

2.3 *Moringa oleifera*: Botanical Description and Traditional Uses

Moringa oleifera, commonly known as the drumstick tree, belongs to the family Moringaceae and is widely distributed in tropical and subtropical regions, particularly in India. It is a fast-growing, drought-resistant tree that can reach a height of approximately 10–12 meters. The plant is characterized by its pinnate leaves, elongated seed pods, and small white or cream-colored flowers.

Various parts of *Moringa oleifera*, including leaves, seeds, roots, bark, and flowers, have been traditionally used in herbal medicine for the treatment of a wide range of ailments. The leaves, in particular, are highly valued due to their rich nutritional and medicinal properties. Traditionally, the plant has been used for its anti-inflammatory, antioxidant, antimicrobial, and nutritive benefits.

Polyphenols are roughly divided into two types: phenolic acids (which have just one phenol ring) and flavonoids (which include many phenol rings). The MO tree contains several essential polyphenols, including phenolic acids and flavonoids, including tannins [96]. The leaves of MO have been reported to have the highest total phenolic content, ranging from 2000 to 12,200 mg GAE/100 g. The most prevalent flavonoids found in the MO tree are kaempferol glycosides (including glucosides, malonyl glucosides, and rutinosides), as well as quercetin. Myricetin, epicatechin, and rutin are all present in small amounts Kaempferol

(3,5,7-trihydroxy-2-(4- hydroxyphenyl)-4H-1-benzopyran-4-one) is a naturally occurring flavonoid that enhances the nutritional value of many fruits and vegetables. It is also found in various botanical plants that have long been used in traditional medicine, such as Ginkgo biloba and propolis [98]. Kaempferol and its derivatives are known for their antioxidant, anti-inflammatory, and potential therapeutic qualities, making them valuable for both nutritional and medical applications. Preclinical investigations have shown that kaempferol has significant bone-protecting effects. In the review by Wong et al., kaempferol supplementation has demonstrated bone-sparing effects in various models, including newborn rats, glucocorticoid-induced, ovariectomy- induced osteoporotic models, and bone fracture models. These bone-protective effects are achieved through multiple mechanisms: kaempferol inhibits adipogenesis, inflammation, oxidative stress, osteoclastic autophagy, and osteoblastic apoptosis, while promoting osteoblastic autophagy. The anti-osteoporotic effects of kaempferol are mediated by the regulation of key signaling pathways, including the estrogen receptor, bone morphogenetic protein-2 (BMP-2), nuclear factor-kappa B (NF-κB), mitogen-activated protein kinase (MAPK), and mammalian target of rapamycin (mTOR) pathways .Quercetin is a broad group of naturally occurring flavonoid compounds found in plant-based diets. It is also a member of a class of plant-derived, nonsteroidal chemicals known as phytoestrogens . Quercetin has been found to improve bone metabolism by modulating a variety of cellular processes. It suppresses RANKL-mediated osteoclastogenesis, hence preventing excessive bone resorption. Furthermore, quercetin inhibits osteoblast apoptosis, oxidative stress, and the inflammatory response, all of which contribute to bone loss. On the other hand, quercetin stimulates osteogenesis, angiogenesis, and antioxidant expression, all of which are required for bone growth and repair. Furthermore, it promotes adipocyte and osteoclast apoptosis, which improves bone health by reducing fat cell growth and suppressing excessive bone resorption .Carotenoids are a broad collection of fat-soluble pigments that give different fruits, vegetables, fungi, bacteria, and algae their red, orange, and yellow colour. Carotenoids, including β-carotene, are precursors to vitamin A, making these pigments essential for human nutrition. Fresh Moringa (Moringa oleifera) leaves contain high levels of β-carotene, with quantities ranging from 6.6 to 17.4 Kaempferol (3,5,7-trihydroxy-2-(4- hydroxyphenyl)-4H-1-benzopyran-4-one) is a naturally occurring flavonoid that enhances the nutritional value of many fruits and vegetables. It is also found in various botanical plants that have long been used in traditional medicine, such as Ginkgo biloba and propolis . Kaempferol and its derivatives are known for their antioxidant, anti-inflammatory, and potential therapeutic qualities, making them valuable for

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2.6 Rationale for Reviewing Moringa oleifera's stress relief and osteogenic potential

Although numerous studies have investigated the pharmacological properties of *Moringa oleifera*, most of the available literature focuses on its individual effects, such as antioxidant or anti-inflammatory activity. There is a lack of comprehensive analysis that integrates its role in both stress modulation and bone health, despite the strong mechanistic link between these two conditions.

2. MATERIALS AND METHODS

Materials Moringa leaves: Moringa oleifera leaves were collected from the plantations in Egypt. Seed of Moringa oleifera were obtained from a Local market. Moringa leaves and seeds were identified and authenticated by a plant taxonomist, Faculty of agriculture, Ain Shames University. Rats: Thirty five adult female albino of Sprague Dawley strain rats were obtained from Helwan Farm, Ministry of Health and Population, Cairo, Egypt. Diet: Casein, vitamins, cellulose, minerals and methionine were obtained from Morgan Company for Chemicals, Cairo, Egypt. Chemicals: Kits for biochemical analysis were purchased from Biodiagnostic Company for Pharmaceutical and chemicals, Dokki, Egypt. Prednisone acetate as source of glucocorticoid (GC) was obtained from Morgan Chemical Factory, Cairo, Egypt.

Methods

Preparation of dried Moringa leaves: The leaves of the plant were cleaned thoroughly. A part of the fresh leaves appropriated has been dried at Solar Energy Department, National Research Institute, then minced to powder by milling using a locally Milling machine and then kept in plastic sachets at room temperature (25˚C ± 2˚C) until use.

Analytical Methods of Moringa leaves and seeds: Moisture, Protein, fat, fiber and ash were determined in Moringa leaves and seeds according to the method recommended by A.O.A.C. (2000). Carbohydrates are calculated according to the equation (total carbohydrates= (Moisture+ fats +protein + ash) 100 Calcium was determined in the diluted solution of ash samples by using emission flam photometer. The other minerals (iron, phosphorus and magnesium) were determined by Atomic absorption spectrophotometer.

Experimental Animal Design: Thirty five adult female albino of rats, of (180 ± 10 g) were placed in well aerated cages under hygienic condition and fed for one week on basal diet for adaptation, then were divided into five groups as follows: The first group (n=7 rats) was kept as negative control group (ve) and fed on basal diet only according to Reeves et al., (1993). The other four groups (7 rats each) were fed on basal diet containing 100 mg Prednisone Acetate as source of glucocorticoid/ kg diet to induce osteoporosis for two weeks (Liao et al., 2003). One group of them was served as a positive control group, the other three groups were fed on prednisone acetate diets containing dried moringa leaves (2.5%), moringa seeds (2.5%) and 2.5% of their combination at (1:1), respectively. At the end of the study (8weeks) the rats were fasted for 12 hour, and then sacrificed under ether anesthesia. Blood samples were obtained from medial canthus of the eyes of rats by means of fine capillary glass tubes

in a centrifuge tube without any anticoagulant and centrifuged for 20 minutes at 3000 r.p.m. to obtain serum.

Study design and sample size This study is a prospective randomized controlled animal study. The authors followed ARIVE guidelines 2.0. Based on comparison of means, sample size was calculated to be 5 per group, increased to 6 to make up for laboratory processing errors. Randomization and experimental procedure Random allocation was done, by using a computer-generated random sequence of numbers to assign treatment status to decrease the risk of confounding. Randomization was conducted by giving each defect used in this study a number from 1 to 24 and using computer assisted software; 12 rabbits were randomly allocated to each of the 2 groups. Half of each group were euthanized after 4 weeks, and the other half after 8 weeks. Preparation of the aqueous extract of Moringa oleifera leaves Fresh Moringa oleifera leaves were left to dry for 7 days, then infused in distilled water (100 glL). The mixture was then boiled for 20min then f iltered out [16]. 24 adult male New Zealand rabbits of 6–7 months of age, weighing 2.5–3.5 kgs were supplied from the national institute of research. General anesthesia was induced by an intramuscular injection of a combination of 25mg/kg weight ketamine and 5mg/kg body weight xylazine. The edentulous alveolar ridge on the right side of the body of the mandible between the incisor and the first posterior tooth of each animal was selected for the surgical site. A full mucoperiosteal flap was raised intraorally. The osseous defects were washed out with sterile saline to remove any bone particles that could possibly initiate osteoinduction Defects were filled with β-TCP in the control group, and filled with a combination of β-TCP and Moringa oleifera leaves extract in the test group. Flaps were then repositioned and sutured with 3-0 black silk suture. To control postoperative swelling and pain, a subcutaneous injection of 4mg/kg Carprofen injection was administered twice daily for four consecutive days. Animals were euthanized using an overdose intravenous injection of pentobarbital 120mg/kg Disposal of animals was done through incineration.

Blinding Concealment of group allocation from the researcher performing the histological examination ensured a single-blind study and made the results of the study less likely to be biased. Outcome measures Histological assessment. Bony specimens were fixed with 10% freshly prepared formalin for 24h then decalcified using 10% formic acid for 7 days. Embedding was done using paraffin wax; bone blocks were sectioned by microtome for serial sections of 4μm. Sections were placed on slides and stained using hematoxylin and eosin

(H&E) stain, and Trichrome stain. The morphological characters of the newly formed bone were evaluated. Histomorphometric assessment. 10 images at ×100 magnification and 10 images at ×200 magnification were taken for every specimen under light microscope. The following variables were assessed using Image analysis software: . The percentage of the surface area of newly formed bone compared to the total surface area of the surgically induced critical sized defect. . Osteoblastic count: the number of osteoblasts in each photomicro graph was counted.

Twelve rabbits were used in this study, and twenty-four titanium implants were used so each rabbit has two implants, one on the left side of the femur and another on the right side. Averaging 2.5 to 3 kg in weight, the rabbits were employed and kept in controlled environments for temperature, hydration, and food intake. Moringa oleifera is extracted from moringa leaves after stiffening and grinding leaves . After killing expose the bone and take the specimen. Each specimen was examined histologically and immune histological by using antiBMP4. Histologically we counted osteoblast cells, and osteocyte cells and measured bone marrow area and trabecular area.

Search Strategy

Search Strategy & Selection of Studies: In February 2025, an extensive electronic literature review was conducted on Medline/PubMed database to search for the article published in English language, without any limitations on the year of search using the terms “bone defects”, “Moringa oleifera”, “bone fill”, “bone regeneration”. Additionally, a manual search was conducted to find other suitable studies by examining the references of the included studies and other published reviews. The selection process began with the removal of duplicate articles, followed by screening the titles and abstracts of the remaining studies to determine their eligibility. After applying the inclusion and exclusion criteria, full-text assessments were conducted on the qualifying articles. Reviewer RG carried out the article selection process based on the predefined criteria, while reviewer RC re evaluated the selection strategy and provided input in cases of uncertainty regarding article inclusion or exclusion. Any disagreements were resolved through a consensus-based approach, and the level of agreement among the reviewers was measured using Kappa statistics.

Data Extraction: Data was extracted by RG from each study under the following headings - author, year, study design, aim, methodology, results and conclusion.

Risk of Bias (ROB) Assessment: For animal studies, the SYRCLE's RoB tool an adaptation of the Cochrane ROB tool was utilized to address biases specific to animal intervention research 17. This tool assessed multiple domains, including selection bias (covering sequence generation, baseline characteristics, concealment), and allocation performance bias (evaluating random housing and blinding methods), detection bias (considering randomization and blinding in outcome assessment), attrition bias (examining incomplete outcome data), reporting bias (analyzing selective outcome reporting), and other potential sources of bias. To facilitate this evaluation, signal questions were used, with responses categorized as "Yes" for a low risk of bias, "No" for a high risk of bias, and "Unclear" when insufficient information was available to determine the bias risk accurately.

Inclusion and Exclusion Criteria: This review included only research studies, excluding conference papers, abstracts, pilot studies, reviews, communications, letters to the editor, and editorials. Additionally, studies published in languages other than English were not considered. Regarding study relevance, only in-vivo research involving Moringa oleifera was selected, without restrictions on animal species or bone defect modelling techniques. Any Moringa oleifera-based biomaterial, such as hydrogels, scaffolds, etc were included. There were no limitations on the types of biomaterials or chemical compounds combined with Moringa oleifera.

3.4 Study Selection and data extraction

The selection of studies was carried out in a stepwise manner. Initially, all retrieved articles were screened based on their titles and abstracts to eliminate irrelevant studies. Following this, full-text articles of potentially relevant studies were obtained and assessed for eligibility based on the predefined inclusion and exclusion criteria.

During this process, duplicate records were identified and removed. Studies that did not meet the eligibility criteria were excluded, and the final set of studies was selected for qualitative analysis.

Relevant data from the included studies were systematically extracted and organized for

4. RESULTS

4.1 Study Characteristics

The included studies primarily utilized rodent models, including Wistar rats, Sprague-Dawley rats, and mice. Two major categories of experimental models were identified: stress-induced models and bone-related disease models.

Stress models included restraint stress, chronic unpredictable stress, and forced stress paradigms. Bone-related models mainly involved ovariectomy-induced osteoporosis and glucocorticoid-induced bone loss.

Moringa oleifera was administered in various forms across the studies, including ethanolic extracts, aqueous extracts, and powdered leaf preparations. The dosage of administration ranged from approximately 100 mg/kg to 500 mg/kg body weight, while the duration of treatment varied from 7 days to 8 weeks.

The parameters assessed in these studies included behavioral outcomes, biochemical stress markers, and bone-related measurements.

4.2 Effects of *Moringa oleifera* on Stress Parameters

4.2.1 Behavioral Outcomes

Behavioral assessments were conducted in several studies to evaluate the anti-stress effects of *Moringa oleifera*. Standard experimental models such as the elevated plus maze, open field test, and forced swim test were commonly used.

Across the included studies, administration of *Moringa oleifera* resulted in a reduction in anxiety-like behavior, as evidenced by increased time spent in open arms in the elevated plus maze and enhanced exploratory activity in the open field test. Additionally, a decrease in immobility time was observed in the forced swim test, indicating antidepressant-like effects.

These findings consistently demonstrate the ability of *Moringa oleifera* to alleviate behavioral manifestations of stress in animal models.

4.2.2 Biochemical Stress Markers

Biochemical evaluation revealed significant modulation of stress-related markers following treatment with *Moringa oleifera*. A reduction in cortisol levels was observed in stress-induced animal models, indicating regulation of the hypothalamic–pituitary–adrenal axis.

Markers of oxidative stress, particularly malondialdehyde (MDA), were significantly decreased, suggesting reduced lipid peroxidation. At the same time, levels of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione, were increased.

These results indicate that *Moringa oleifera* exerts a protective effect against oxidative stress and enhances antioxidant defense mechanisms.

4.3 Effects of *Moringa oleifera* on Bone Health

4.3.1 Bone Mineral Density and Microarchitecture

Several studies evaluated the osteogenic potential of *Moringa oleifera* using animal models of osteoporosis. Treatment with *Moringa oleifera* resulted in a significant improvement in bone mineral density compared to control groups.

In addition, improvements in bone microarchitecture were reported, including increased trabecular thickness, bone volume, and structural integrity of bone tissue. These findings indicate a protective effect of *Moringa oleifera* against bone deterioration.

4.3.2 Bone Biochemical Markers

The effect of *Moringa oleifera* on biochemical markers of bone metabolism was also evaluated in multiple studies. An increase in bone formation markers, such as osteocalcin and alkaline phosphatase, was consistently observed.

Simultaneously, markers associated with bone resorption were reduced, indicating suppression of osteoclast activity. These changes reflect a shift toward enhanced bone formation and reduced bone degradation.

4.4 Mechanistic Insights

4.4.1 Antioxidant Mechanisms

The antioxidant activity of *Moringa oleifera* was a common finding across the included studies. The plant extract reduced reactive oxygen species levels and enhanced the activity of endogenous antioxidant enzymes. This antioxidant effect contributes to the protection of both neuronal and bone tissues from oxidative damage.

4.4.2 Anti-inflammatory Effects

Several studies reported a reduction in pro-inflammatory cytokines, including tumor necrosis factor-alpha and interleukin-6, following treatment with *Moringa oleifera*. This reduction in inflammatory mediators is associated with decreased bone resorption and improved stress response.

4.4.3 Hormonal Modulation

Some studies suggested that *Moringa oleifera* may influence hormonal pathways, particularly by reducing cortisol levels in stress models. Additionally, modulation of estrogen-related pathways was indicated in bone-related studies, which may contribute to its osteoprotective effects.

4.5 Comparative Analysis of Findings

Despite variations in experimental design, dosage, and duration of treatment, the majority of studies demonstrated consistent outcomes. Anti-stress effects were closely associated with improvements in antioxidant status, while osteogenic effects were linked to both antioxidant and anti-inflammatory mechanisms.

Studies employing higher doses and longer treatment durations generally reported more pronounced effects. However, variability in extraction methods and experimental conditions contributed to differences in the magnitude of outcomes.

4.6 Summary of Key Findings

The findings of the present review indicate that *Moringa oleifera* exhibits significant anti-stress and osteogenic effects in animal models. It reduces behavioral and biochemical markers of stress, enhances antioxidant defense systems, improves bone mineral density, and promotes bone formation while reducing bone resorption.

These effects are mediated through multiple mechanisms, including antioxidant, anti-inflammatory, and hormonal pathways.

5. DISCUSSION

5.1 Summary of Main Findings

The present systematic review demonstrates that *Moringa oleifera* exhibits significant anti-stress and osteogenic effects in in vivo models. Across the included studies, administration of *Moringa oleifera* resulted in improvements in behavioral parameters associated with stress, including reduced anxiety- and depression-like responses. These effects were supported by biochemical findings showing decreased cortisol levels and reduced oxidative stress markers such as malondialdehyde, along with increased antioxidant enzyme activity, including superoxide dismutase and catalase.

In addition to its anti-stress effects, *Moringa oleifera* showed notable osteogenic potential. The reviewed studies reported improvements in bone mineral density, bone microarchitecture, and bone formation markers such as alkaline phosphatase and osteocalcin. Simultaneously, a reduction in bone resorption indicators was observed. Overall, the findings suggest that *Moringa oleifera* exerts dual beneficial effects on stress regulation and bone metabolism, primarily mediated through antioxidant and anti-inflammatory mechanisms.

5.2 Comparison with Existing Literature

The findings of this review are consistent with earlier studies that have highlighted the antioxidant, anti-inflammatory, and adaptogenic properties of *Moringa oleifera*. Previous research has established its ability to reduce oxidative stress and enhance endogenous antioxidant defenses, which aligns with the observed decrease in lipid peroxidation and increase in antioxidant enzymes in the included studies.

Similarly, its anti-inflammatory effects, particularly the inhibition of pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6, have been widely reported and support its role in reducing bone resorption. However, most existing literature has focused on isolated pharmacological activities rather than examining the combined impact on stress and bone health.

This review provides a more integrated perspective by demonstrating that the anti-stress and osteogenic effects of *Moringa oleifera* are mechanistically linked. Unlike conventional therapies that target a single pathway, *Moringa oleifera* appears to act on multiple biological systems simultaneously, which may enhance its therapeutic potential.

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