

Review

Exploring the Role of Onion Derived Polyphenols in Bone Health: A Systematic Review of In Vitro to Human Studies

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Abstract

Background: We evaluated certain factors relative to onion (*Allium* spp.) and onion-derived polyphenols. **Methods:** We searched PubMed, Scopus, and Google Scholar from 2010 to 20 October 2025 without language limits. Eligible designs comprised of in vitro, animal, and human studies assessing onion, onion extracts, or isolated onion-derived polyphenols with bone outcomes. Two reviewers independently screened, extracted, and assessed risk of bias (RoB 2 for RCTs; SYRCLE for animals). **Results:** We included X studies (a in vitro, b animal, and c human RCTs; N samples). In vitro limitations included the following: heterogeneous models, short human follow-up, small samples, and moderate-to-serious risk of bias in animals. Reports included improvements in bone mineral density (BMD), bone mineral content (BMC), bone turnover markers, and osteoclast/osteoblast activity. Onion extracts consistently inhibited RANKL-induced osteoclastogenesis while sparing osteoblast function. In animals, onion or quercetin/kaempferol preserved BMD and improved mineral content and (in several models) fracture healing. In one small RCT of onion juice (8 weeks), antioxidant status improved with a trend to attenuated BMD loss; a resveratrol RCT was excluded/included as a benchmark. **Conclusions:** Pre-clinical evidence suggests anti-resorptive and osteogenic effects of onion-derived polyphenols; human evidence is limited and characterized by low certainty. Longer RCTs are needed to define effective doses and clinical relevance.

Keywords: *Allium cepa* L.; quercetin; kaempferol; osteoporosis; bone mineral density; systematic



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1. Introduction

Bone health is a central component of overall musculoskeletal integrity, particularly among aging populations. Osteoporosis—a progressive skeletal disorder characterized by reduced bone mineral density (BMD) and microarchitectural deterioration—leads to fragile bones and heightened fracture risk [1,2]. Primary osteoporosis typically arises post-menopause (Type I) or with aging (Type II), whereas secondary osteoporosis may develop from endocrinological disorders, alcohol abuse, certain medications, or prolonged immobilization [3,4]. Because osteoporosis often remains asymptomatic until fractures occur, early detection through clinical assessment, biochemical markers, bone densitometry, and imaging is essential for prevention and management [3,5]. The standard treatment

combines lifestyle strategies—including weight-bearing exercise and adequate calcium and vitamin D intake—with pharmacotherapy tailored to patient age and fracture risk [6,7]. Despite these advances, a substantial treatment gap persists, highlighting the need for safe, accessible, food-based interventions to support lifelong bone health.

Dietary phytochemicals have emerged as promising modulators of bone remodelling, and onions (*Allium cepa* L.) represent a widely consumed, low-cost source of bioactive compounds with potential skeletal benefits. Onions contain essential minerals (e.g., potassium, zinc) and diverse phytochemicals, including organosulfur compounds and flavonoid polyphenols—particularly quercetin and kaempferol [8–11]. Onion peels, often discarded as ‘agro waste’, are especially rich in total phenolics, quercetin, and related flavonoids with established antioxidant, anti-inflammatory, cardioprotective, neuroprotective, and chemo preventive properties [9]. Polyphenols exert strong free-radical-scavenging activity, modulate inflammatory signalling, and can influence pathways relevant to bone turnover. Chronic oxidative stress and inflammation accelerate bone loss by stimulating osteoclastogenesis and impairing osteoblast function; thus, antioxidant polyphenols may help counteract these processes [6]. Notably, quercetin exhibits both potent antioxidant action and phytoestrogenic activity, while kaempferol has been shown to enhance osteoblast survival and function [12,13].

Allium cepa is particularly relevant for bone-health research due to its exceptionally high flavonols content—270–1917 mg/kg fresh weight, predominantly quercetin derivatives—far exceeding those of many vegetables [14]. Epidemiological evidence shows that daily onion consumption is associated with higher spine and hip BMD and an over 20% reduction in hip-fracture risk in older women. The preclinical studies align around these findings: onion flavonoid extracts significantly improve BMD, trabecular microarchitecture, and biochemical markers in ovariectomized rats, with effects comparable to standard osteoporosis drugs [15,16]. In vitro, onion extracts enhance osteoblast proliferation and mineralization while suppressing RANKL-induced osteoclastogenesis via MAPK, NF- κ B, and OPG/RANKL pathways [15,17]. Compared with other plant polyphenols such as green tea catechins, berry flavonoids, and soy isoflavones, onion polyphenols share similar antioxidant and anti-inflammatory mechanisms but offer unique advantages due to their high bioactive content, anthocyanin-rich red varieties, and synergy with sulfur compounds and minerals [18,19].

Underlying Study Novelty

Despite growing evidence, the bone-protective potential of onion-derived polyphenols remains fragmented across cellular, animal, and human studies. This systematic review integrates findings across all research levels to evaluate the mechanisms, efficacy, and translational potential of onion-derived nutrients and polyphenols in promoting bone health. Particular attention is given to varietal differences, bioavailability, and the valorisation of onion byproducts as sustainable sources of functional ingredients targeting osteoporosis prevention.

2. Materials and Methods

2.1. Study Design and Selection

This systematic review was conducted in accordance with the PRISMA 2020 guidelines for transparent reporting as shown in PRISMA 2020 flow diagram of study selection (Figure 1). We included peer-reviewed studies published between 2010 and 2025 that investigated the relationship between onion (*Allium cepa* L.) or its derived polyphenolic compounds and any aspect of bone health. As to protocol registration, the study was not

registered in PROSPERO; as a justification, the study involved the scoping of a rapidly evolving literature; forward registration is planned for a subsequent update.

2.2. Eligibility Criteria

The review encompassed Onion derived polyphenols (e.g., resveratrol) unless pre-specified as comparators for mechanistic context; such studies were narratively referenced but not included in evidence synthesis. We included primary studies evaluating *Allium onions* (e.g., *Allium cepa* L., *A. fistulosum*) or polyphenols isolated from onion (e.g., quercetin/kaempferol from onion matrices), reporting bone outcomes (BMD/BMC, strength, histomorphometry, turnover markers, and osteoclast/osteoblast activity). We excluded non-*Allium* species marketed as “onion” (e.g., *Eleutherine bulbosa*), and trials not involving onion.

2.3. Search Strategy

Comprehensive searches were performed in Google Scholar, PubMed, and Scopus (last search conducted June 2025). The searches were restricted to English-language publications ranging from 2010 to 2025.

PubMed (Run: 1 October 2025)

Filters: 2010-2025. (“*Allium cepa* L.”[MeSH] OR onion*[tiab] OR “*Allium fistulosum*”[tiab]) AND (quercetin[tiab] OR kaempferol[tiab] OR polyphenol*[tiab] OR extract*[tiab]) AND (bone[tiab] OR “Bone Density”[MeSH] OR osteoporos*[tiab] OR osteoclast*[tiab] OR osteoblast*[tiab]))

Scopus and Google Scholar: Corresponding searches.

For each included study, data were extracted on the study design, sample characteristics, intervention details (type of onion-derived compound, dose, and duration), and key bone health outcomes measured. Outcomes of interest included BMD, bone mineral content (BMC), bone length and weight, bone calcium or phosphorus levels, biomechanical strength, bone histology or morphology, and cellular markers of bone turnover (e.g., osteoblast activity, osteoclast number/function, and relevant biochemical markers like alkaline phosphatase or osteocalcin). Given the diverse nature of studies, a meta-analysis was not performed; instead, a qualitative synthesis is presented. The main results are organized into three categories (in vitro, in vivo animal, and human clinical evidence) to facilitate comparison across different research models. The results are tabulated for clarity, and a narrative summary is provided to highlight consistent findings and mechanistic insights.

2.4. Risk of Bias Assessment

Risk of bias was evaluated independently by two reviewers using tools specific to the study design, in accordance with Cochrane recommendations. Human randomized controlled trials were appraised with the Cochrane Risk of Bias 2 (RoB 2) tool, covering five domains—(1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) outcome measurement, and (5) selection of the reported result—and receiving an answer through discussion or arbitration by a third reviewer. Summary traffic-light plots and weighted bar plots were generated with the robvis web application (version 0.3.0) and are presented in Figures 2 and 3. Overall judgements included “low risk”, “several concerns”, or “high risk”. Non-randomized human studies would have been assessed with RoBINS-I; however, none met the inclusion criteria. Animal experiments were assessed with the SYRCLE RoB tool, which adapts RoB 2 to pre-clinical settings across ten domains (e.g., allocation concealment, random housing, blinding, and selective outcome reporting). Each domain was rated as “low”, “unclear”, or “high” risk. Disagreements were resolved.

3. Results

3.1. Study Selection and Characteristics

Across the 12 included studies, interventions ranged from whole onion powder or juice to onion skin extracts, isolated onion compounds (like quercetin), and even other polyphenols (resveratrol, kaempferol) for comparison. The study outcomes collectively provide insights into how onion-derived polyphenols influence bone health indicators. Below, we present the findings separated by in vitro studies, in vivo animal studies, and human clinical studies. Key details of study design, sample, intervention, and outcomes are summarized in Tables 1–3.

Studies were excluded if they did not investigate onion or its polyphenols, or if they lacked quantifiable bone-related outcomes. After removal of duplicates, titles and abstracts of 120 records identified through database searches were screened for relevance. From among these, 32 articles were deemed relevant and underwent full-text screening. Ultimately, 12 studies meeting all inclusion criteria were included in this review for data extraction and analysis. Figure 1 presents the PRISMA flow diagram of the study selection process.

The search yielded 120 records after removal of obvious duplicates. Two reviewers independently screened titles/abstracts for relevance, then evaluated full texts of the 32 studies that passed initial screening. Any disagreements were resolved by consensus. In total, twelve studies were included in the review: among these, two were in vitro studies using cell cultures, nine were in vivo animal studies (in rats, rabbits, or other models), and one was a human clinical study (additionally, one of the human studies also incorporated an in vitro component). The characteristics and findings of these studies are summarized in tables by category (in vitro, animal, and human).

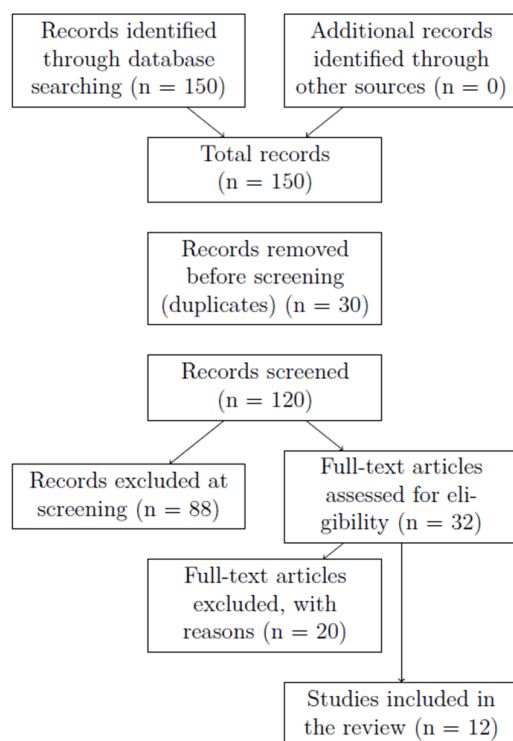


Figure 1. PRISMA 2020 flow diagram of study selection. Studies were eligible if they were peer-reviewed, published between 2010 and 2025, and examined onion (*Allium cepa* L. or *A. fistulosum*) or onion-derived polyphenolic compounds (e.g., quercetin, kaempferol) with quantifiable bone-related outcomes, including BMD, BMC, bone strength, histomorphometry, turnover markers, or osteoclast/osteoblast activity.

3.2. *In Vitro* Studies of Onion-Derived Polyphenols and Bone Cells

The investigation of *in vitro* studies shown in Table 1 demonstrates how onion-derived compounds affect bone cell activities in controlled laboratory settings (cultured cell lines or primary cells). These studies help uncover mechanisms, such as the molecular pathways by which onion-derived polyphenols influence osteoclast (bone-resorbing cell) and osteoblast (bone-forming cell) functions. Table 1 summarizes key *in vitro* investigations, demonstrating the direct cellular actions of onion-derived bioactive compounds on bone-forming and bone-resorbing cells. Early work by Wetli et al. [20] identified a unique sulfur-containing onion peptide, γ -L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide (GPCS), using primary osteoclasts isolated from neonatal rat long bones. Both purified GPCS and hydrophilic onion fractions significantly suppressed osteoclast-mediated bone resorption, and this inhibitory effect was consistent with the reduced *ex vivo* resorption following dietary onion supplementation in rats, indicating that naturally occurring onion compounds exert potent antiresorptive actions. Expanding on these findings, Tang et al. [17] evaluated a crude aqueous onion extract across multiple bone-relevant cell models—including rat bone marrow stromal cells, RAW 264.7 macrophages, rabbit osteoclasts, and human osteoblast-like MG-63 and hFOB cells. Their results revealed profound suppression of osteoclast differentiation and resorptive activity, accompanied by inhibition of key RANKL-induced signaling pathways (ERK, p38 MAPK, and NF- κ B), demonstrating that onion components disrupt essential molecular drivers of osteoclastogenesis. More recently, Zhang et al. [15] assessed an onion flavonoid extract (OFE) in human MG-63 osteoblast-like cells and RAW 264.7 osteoclast precursors. OFE enhanced osteoblast proliferation, alkaline phosphatase activity, and mineralization, while upregulating the OPG/RANKL ratio at the gene level. Simultaneously, OFE inhibited RANKL-stimulated osteoclast differentiation by reducing TRAP activity and the expression of osteoclast-specific markers. Collectively, these studies show that onion-derived compounds—including specific peptides, crude extracts, and flavonoid-rich fractions—effectively promote osteoblast anabolic activity and suppress osteoclast formation and function through modulation of major regulatory pathways such as MAPKs, NF- κ B, and OPG/RANKL. This *in vitro* evidence strongly supports the mechanistic basis for the bone-protective effects observed in preclinical and epidemiological studies.

Table 1. In vitro studies on onion-derived polyphenols and bone cells.

Study (Author, Year)	Cell Models (Sample)	Intervention	Main Findings
Wetli et al., 2005 [20]	Primary osteoclasts are isolated from newborn rat long bones (femurs, tibias).	<p>Tested various onion fractions and a purified compound in vitro on osteoclast resorption assays. Also tested whole onion in the diet of rats (ex vivo effect). Specific concentrations tested:</p> <ul style="list-style-type: none"> • Hydrophilic Fraction A: 1, 10, and 30 mg/mL. • GPCS (γ-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide): 2, 4, and 8 mM. • Whole onion 1 gm in the rat feed 	Identified a unique onion peptide, γ -L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide (GPCS), that significantly inhibited osteoclast activity in culture ($p < 0.05$). When 1 g of onion was added to rat feed, it markedly inhibited bone resorption in vivo (reduced tritium release from prelabeled bone). This indicates onion contains compounds (like GPCS) that directly suppress osteoclast-mediated bone breakdown.
Tang et al., 2009 [17]	Multiple cell types: rat bone marrow stromal cells, RAW264.7 murine macrophages (osteoclast precursors), rabbit mature osteoclasts, and human osteoblast-like cells (MG-63 and hFOB lines).	Cells were treated with a water extract of onion (crude powder) at concentrations of 150–300 μ g/mL. Osteoclastogenesis was assessed by TRAP staining; osteoblast activity by alkaline phosphatase (ALP), collagen, osteocalcin, and osteopontin levels. Western blotting measured signaling (MAPKs, NF- κ B), and NF- κ B activity was measured via a reporter assay.	The onion water extract profoundly inhibited osteoclast development and activity: it decreased RANKL + M-CSF-induced osteoclast differentiation from bone marrow cells and RAW264.7 macrophages. It also reduced mature osteoclasts' bone resorption activity. Mechanistically, onion extract blocked RANKL-induced activation of ERK, p38, and NF- κ B signaling pathways in osteoclast precursors, pathways essential for osteoclastogenesis.
Zhang et al., 2024 [15]	Human osteoblast-like MG-63 cells and mouse RAW 264.7 cells.	OFE (Onion flavonoid extract) at 6.25–100 μ g/mL for MG-63 cells (proliferation, ALP, mineralization); 12.5–50 μ g/mL with RANKL (50 ng/mL) for RAW 264.7 cells (osteoclastogenesis).	Promoted MG-63 proliferation, ALP activity, mineralization, upregulated OPG/RANKL mRNA. Inhibited RANKL-induced osteoclastogenesis in RAW 264.7, reduced TRAP activity, downregulated osteoclast marker mRNA. Suggests OFE ameliorates osteoporosis via enhancing osteoblast function and inhibiting osteoclastogenesis through OPG/RANKL pathway.

3.3. In Vivo Animal Studies

As shown in Table 2, despite the diversity of animal models and conditions, the in vivo evidence consistently supports the positive role of onion-derived substances in bone health. Table 2 synthesizes the extensive in vivo evidence demonstrating the bone-protective and osteoanabolic potential of onion-derived polyphenols and related *Allium* bioactives across diverse animal models. Several studies using ovariectomized (OVX) or glucocorticoid-treated rodents—a standard model of postmenopausal or secondary osteoporosis consistently reported that onion flavonoids or onion bulb extracts mitigate bone loss and enhance skeletal recovery. In glucocorticoid-induced osteoporotic rats, kaempferol prevented declines in bone mineral density (BMD), preserved trabecular microarchitecture, and significantly accelerated fracture healing [13]. Similarly, Dayak onion (*Eleutherine bulbosa*) extract administered to OVX rats improved bone calcium content, bone length, and bone weight, with the highest dose producing effects comparable to tamoxifen. When Dayak onion extract was combined with cowpea—a daidzein-rich phytoestrogen source—the synergistic intervention further enhanced tibial calcium content, bone weight, and reduced marrow adiposity, outperforming single-agent treatments. Studies in younger and growing animals also demonstrate growth-promoting actions. Welsh onion extract restored femur and tibia growth suppressed by a high-fat diet in weanling rats and activated IGF-1 and TGF- β signaling pathways, yielding bone growth comparable to growth hormone administration [20,21]. A combined extract of green onion root and oat (GOO) dose-dependently improved longitudinal bone growth and BMD, with the highest dose producing tibial lengths like those of growth hormone-treated controls [22]. Beyond rodents, dietary onion extract enhanced tibial morphometrics, mineral content, and bone strength indicators in broiler chickens without compromising growth or meat quality, indicating consistent bone benefits across species [23]. Dietary interventions in adult rats further revealed enhanced tibial calcium and other mineral concentrations following onion powder supplementation, independent of background fat composition [24–26]. Finally, onion flavonoid extract (OFE) in OVX rats dose-dependently improved BMD, trabecular microstructure, serum estradiol, and mineral homeostasis while reducing bone turnover markers and marrow fat accumulation [15]. Collectively, these findings demonstrate that onion-derived polyphenols promote bone formation, inhibit bone loss, and support mineral metabolism across multiple physiological and pathological contexts.

Table 2. In vivo animal studies on onion-derived polyphenols and bone health.

Study (Author, Year)	Animal Model (Sample)	Intervention	Main Findings
Adhikary et al., 2018 [13]	Adult female Sprague–Dawley rats (OVX + glucocorticoid-induced bone loss model; $n = 10$ per group). Also included a bone injury sub-model.	Four groups: (1) Control (no treatment), (2) Methylprednisolone (MP, 5 mg/kg/day s.c.) to induce osteoporotic changes, (3) MP + Kaempferol (5 mg/kg/day orally), (4) MP + human PTH (positive control). Duration, 4 weeks; a drill-hole defect was created in femur of some rats to assess fracture healing, with kaempferol given for 14 days post-injury.	Glucocorticoid (MP) treatment caused bone loss—lowering BMD and deteriorating bone microarchitecture. Kaempferol co-treatment prevented these osteoporotic effects: rats given kaempferol preserved BMD and improved bone microarchitecture compared to MP alone. Kaempferol also enhanced fracture healing, as evidenced by significantly better callus formation at the injury site versus MP-only group.
Bahtiar and Annisa, 2018 [24]	Ovariectomized (estrogen-deficient) female Sprague–Dawley rats ($n = 36$).	Six groups: (1) Sham surgery (no OVX, baseline control), (2) OVX negative control, (3) OVX + Tamoxifen (positive drug control), (4–6) OVX + Dayak onion (<i>Eleutherine bulbosa</i>) bulb extract at low, medium, and high doses (8, 12, and 18 mg per 200 g body weight) for 21 days.	The highest dose of Dayak onion extract (18 mg/200 g) produced significant improvements in the bone parameters of OVX rats. It significantly increased bone calcium content, bone weight, and bone length compared to untreated OVX controls. These gains approached those observed with estrogenic treatment (tamoxifen), suggesting that onion bulbs contain bioactives that mitigate estrogen-deficiency bone loss.
Bahtiar and Dewi, 2019 [25]	Ovariectomized female Sprague–Dawley rats ($n = 32$).	Eight groups: (1) Sham control, (2) OVX negative control, (3) OVX + Raloxifene (reference osteoporosis drug), (4) OVX + Cowpea extract (rich in daidzein, a phytoestrogen), and (5–8) OVX + Combination of Dayak onion bulb extract + cowpea at four dose ratios. Treatment lasted 28 days post-OVX.	The combination of Dayak onion extract with cowpea yielded the best outcomes. The combo groups showed significantly greater increase in tibial bone calcium levels and bone weight in comparison. Combination treatment also reduced bone marrow fat accumulation in osteopenic rats to a greater extent than single-agent treatment.
Ko et al., 2019 [21]	Weanling male Sprague–Dawley rats (3 weeks old; $n = 50$).	Seven groups on different diets for 4 weeks: (1) Standard diet (normal control), (2) High-fat diet (growth-suppression control), (3) High-fat + Welsh onion (<i>Allium fistulosum</i>) extract—low dose, (4) High-fat + Welsh onion—high dose, (5) High-fat + Purslane (<i>Portulaca oleracea</i>) extract—low dose, (6) High-fat + purslane—high dose, (7) High-fat + Growth Hormone (GH) injection (positive control). Low and high doses of plant extracts corresponded to ~20 mg/day and 50 mg/day equivalents.	Both Welsh onion (WO) and purslane (PO) supplementation promoted bone growth in the young rats. Notably, the high-dose Welsh onion group (WO-H) showed significant increases in femur and tibia lengths, comparable to the growth hormone-treated group. Mechanistically, WO-H activated IGF-1 and TGF- β signaling pathways in bone tissue, correlating with greater longitudinal growth.

Table 2. Cont.

Study (Author, Year)	Animal Model (Sample)	Intervention	Main Findings
Mohamed et al., 2011 [26]	Adult male Sprague–Dawley rats (dietary intervention model).	Rats were fed semi-purified diets with 8% of either flaxseed oil or olive oil (high in unsaturated fats) instead of corn oil, for 28 days. Within each oil group, half the rats' diets were supplemented with 2% onion powder (others with 2% garlic or no allium as controls). This resulted in diet containing different fat compositions, with or without onion supplementation. After 4 weeks, liver and bone minerals were measured.	Including onion in the diet significantly increased mineral concentrations in bone (tibia), regardless of oil type. Specifically, rats receiving onion supplementation had higher levels of calcium and other minerals in the tibia compared to those on the same base diet without onion. Onion (and, similarly garlic) also enhanced mineral content in the liver, suggesting improved mineral uptake or reduced mineral loss. The effect was notable in both the flaxseed and olive oil groups, suggesting that the benefits of onion supplementation are consistent across different background diets.
Wong and Rabie, 2008 [12]	New Zealand White rabbits with surgically created cranial bone defects (critical size $\sim 5 \times 10$ mm in parietal bone). Nine rabbits with 2 defects each (18 defects total).	Three treatment groups for the bone defects: (1) Defects filled with quercetin solution mixed into a collagen matrix (6 defects), (2) Defects filled with collagen matrix alone as material control (6 defects), and (3) Empty defects (no fill) as negative control (6 defects). Rabbits were sacrificed after 14 days and new bone formation in the defects was quantified by histomorphometry.	Quercetin dramatically stimulated new bone formation in the defect sites. Defects treated with quercetin + collagen showed 556% more new bone area than those filled with collagen matrix alone. Empty defects exhibited essentially no bone regeneration. The quercetin group's robust osteogenesis indicates quercetin can act locally to enhance bone formation, likely by recruiting osteoprogenitor cells or stimulating osteoblastic activity.
Wu et al., 2023 [22]	Weanling male Sprague–Dawley rats ($n = 50$)—model of nutritional intervention to promote growth.	Five groups ($n = 10$ each) for 4 weeks: (1) Normal diet control, (2) Positive control with daily growth hormone injections, (3) Low-dose GOO (Green onion + oat) supplementation (50 mg/kg/day), (4) Mid-dose GOO (200 mg/kg), (5) High-dose GOO (500 mg/kg). GOO = combined extract of green onion root and oat given orally. Outcomes: tibia and femur length, bone mineral density (DXA for spine and leg bones), serum levels, metabolic parameters, and gut microbiota analysis.	Green onion root + oat (GOO) supplementation dose-dependently enhance the bone growth and density. The high-dose GOO group had tibia lengths relative to the growth hormone-treated group after 4 weeks. GOO also significantly increased BMD of the lumbar spine and hindlimb bones relative to controls.

Table 2. Cont.

Study (Author, Year)	Animal Model (Sample)	Intervention	Main Findings
Malematja et al., 2023 [23]	200 one-day-old, unsexed Ross 308 broiler chicks (in vivo study).	Broiler chickens were fed diets including onion extracts at concentrations of 0, 5, 10, 15, or 25 g/kg in a complete broiler diet for 42 days. Growth performance, carcass characteristics, sensory evaluation, and bone morphometrics were assessed.	Onion extract supplementation did not affect ($p > 0.05$) growth performance (feed intake, FCR, weight gain) or meat sensory evaluation (juiciness, flavor, tenderness). However, it significantly increased ($p < 0.05$) meat shear force in some groups. Onion extracts improved ($p < 0.05$) bone morphology in terms of tibia weight, diameter, calcium, and phosphorous contents, suggesting enhanced bone growth and strength in broiler chickens.
Zhang et al., 2024 [15]	Included 48 female Sprague–Dawley rats (12 weeks old, 250–270 g).	Onion flavonoid extract (OFE) at 25, 50, 75 mg/kg oral gavage daily for 8 weeks in OVX (ovariectomized) rats.	OFE improved bone mineral density (BMD) and bone microstructure in OVX rats' dose-dependently, increased serum estradiol (E2), calcium (Ca), and phosphorus (P), and decreased Alkaline phosphatase (ALP) and tartrate-resistant acid phosphatase (TRAP), in addition to reducing fat vacuoles.

3.4. Human Clinical Studies

Table 3 shows that two randomized–controlled human trials provided preliminary clinical evidence. Law et al. [27] enrolled 24 healthy middle-aged and post-menopausal volunteers who ingested 100 mL/day of freshly prepared yellow-onion juice or a flavor-matched placebo for 8 weeks. Dual-energy X-ray absorptiometry (DXA) revealed that onion juice attenuated the loss of lumbar-spine and femoral-neck bone mineral density (BMD) by approximately 1–2%, while antioxidant capacity (TEAC) increased and systemic free-radical levels declined, signalling a shift toward an osteoprotective redox milieu. Bo et al. [28] randomised 192 adults with type 2 diabetes, with participants receiving resveratrol 500 mg, resveratrol 40 mg, or placebo capsules daily for 6 months in a double-blind trial. High-dose resveratrol prevented the ~3% whole-body BMD and bone mineral content (BMC) decline observed in the placebo arm and improved serum phosphorus and alkaline phosphatase; the low-dose arm showed no effect. Both studies support a modest bone-sparing role for polyphenols in humans, yet the interpretation of these results is tempered by the short follow-up, small sample size in the onion-juice trial, and population specificity (diabetes) in the resveratrol study.

Table 3. Human clinical studies on polyphenols (onion juice/resveratrol) and bone health.

Study (Author, Year)	Participants	Intervention	Main Findings
Law et al., 2016 [27]	Thirty healthy adults (12 men, 18 women) aged 40–80, including 3 postmenopausal women. Randomized into two groups (15 each).	Onion juice trial: One group consumed 100 mL of fresh onion juice daily for 8 weeks; the other group consumed a placebo drink. In addition, the study included an in vitro component using RAW264.7 pre-osteoclast cells treated with onion extracts to assess anti-osteoclastogenic effects.	Onion juice supplementation showed a protective effect on bone and oxidative status. Subjects who drank onion juice had significantly improved antioxidant activity—e.g., increased total antioxidant capacity (TEAC) and reduced levels of oxidative stress markers (free radicals). They also showed favorable changes in bone turnover markers such as alkaline phosphatase (ALP), compared to placebo.
Bo et al., 2018 [28]	A total of 192 outpatients with type 2 diabetes (mean age ~60, both genders). Randomized into 3 arms.	Resveratrol dose–response trial: Double-blind RCT over 6 months with daily doses of 500 mg resveratrol (Resv500), 40 mg resveratrol (Resv40), or placebo. All patients continued standard diabetes care. Bone outcomes: whole-body BMD and BMC (by DXA), and serum calcium, phosphorus, vitamin D, and alkaline phosphatase, measured baseline and 6 months. (Note: Resveratrol is a polyphenol from grapes; it is included here due to its similar mechanisms on bone and to broaden human evidence on polyphenols.)	High-dose resveratrol (500 mg/day) effectively prevented bone loss in diabetic patients, whereas a low dose (40 mg) did not differ from placebo. Over 6 months, the placebo group experienced significant decreases in BMD and BMC, reflecting ongoing bone loss with diabetes. The Resv40 group also had BMC loss. In contrast, the Resv500 group maintained their BMD and BMC, with no significant losses. The difference was significant: the adjusted mean change in whole-body BMD in Resv500 vs placebo was +0.01 vs −0.03 g/cm ² ($p = 0.001$).

3.5. Included Studies Describing Polyphenol Studies

The polyphenols studies summarized in Table 4 synthesize 12 investigations published between 2005 and 2023 that examined onion-associated polyphenols in progressively rigorous research settings—two in vitro cell studies, seven animal experiments, and three human trials.

Quercetin emerges as the principal compound, reported either in purified form or within onion extracts in nine studies. Kaempferol appears in three studies, while mixed flavanol matrices or peptide fraction account for the remaining investigations. One study included resveratrol as an external benchmark.

Table 4. Polyphenols studied in the included studies.

Study	Model	Polyphenol(s)
Witli et al., 2005 [20]	In vitro—osteoclast pit assay	Onion peptide (GPCS)
Tang et al., 2009 [17]	In vitro—rat bone marrow stromal cells, RAW264.7 murine macrophages (osteoclast precursors), rabbit mature osteoclasts, and human osteoblast-like cells (MG-63 and hFOB lines).	Onion crude extract (quercetin-rich)
Zhang et al., 2024 [15]	In vitro—Human osteoblast-like MG-63 cells and mouse RAW 264.7 cells. Animal—female Sprague–Dawley rats	OFE (Onion flavonoid extract)
Adhikary et al., 2018 [13]	Animal—Adult female Sprague–Dawley rats (OVX + glucocorticoid-induced bone loss model; $n = 10$ per group). Also included a bone injury sub-model.	Kaempferol
Bahtiar and Annisa 2018 [24]	Animal—Ovariectomized (estrogen-deficient) female Sprague–Dawley rats.	Dayak onion bulb extract (quercetin, kaempferol)
Bahtiar and Dewi 2019 [25]	Animal—Ovariectomized (estrogen-deficient) female Sprague–Dawley rats.	Dayak onion extract + Cowpea (daidzein)
Ko et al., 2019 [21]	Animal—Weanling male Sprague–Dawley rats.	Welsh onion extract (flavonols)
Mohamed et al., 2011 [26]	Animal—Adult male Sprague–Dawley rats (dietary intervention model).	Onion powder (quercetin)
Wong and Rabie 2008 [12]	Animal—New Zealand White rabbits with surgically created cranial bone defects (critical-size $\sim 5 \times 10$ mm in parietal bone).	Quercetin
Wu et al., 2023 [22]	Animal—Weanling male Sprague–Dawley rats (model of nutritional intervention to promote growth).	Green onion root extract (quercetin) + oat
Malematja et al., 2023 [23]	Animal—200 one-day-old, unsexed Ross 308 broiler chicks.	Onion extract
Law et al., 2016 [27]	Human—Healthy adults (aged 40–80), including 3 postmenopausal women.	Onion juice (quercetin, kaempferol)
Bo et al., 2018 [28]	Human—outpatients with Type 2 Diabetes (mean age ~ 60 , both genders).	Resveratrol (reference polyphenol)

3.6. Overall Certainty and Interpretation

Human clinical efficacy was very low for BMD, and low for turnover markers—the evidence is preliminary, short-term, and imprecise. The mechanistic plausibility was moderate (in vitro suppression of osteoclastogenesis). The translational preclinical signal was low (beneficial direction across models, but risk of bias and indirectness limit confidence). Footnotes and decisions include the following: (1) The resveratrol RCT (grape-derived

polyphenol) is not included in the onion evidence synthesis and is retained only as contextual polyphenol evidence. (2) This SoF treats the onion juice RCT as the sole human efficacy study.

Table 5 shows the PICO. The population is composed of adults (general, non-osteoporotic) and preclinical models relevant to osteoporosis mechanisms. The intervention comprised onion or onion-derived polyphenols (e.g., quercetin/kaempferol from onion matrices; onion juice/extract). The comparator utilized was placebo/no onion, usual diet. Primary outcomes included the following: BMD change; bone turnover markers; mechanistic outcomes (animal BMD/microarchitecture; in vitro osteoclastogenesis).

Table 5. Summary of findings (GRADE). onion/onion-derived polyphenols and bone outcomes.

Outcome	Participants (Studies)	Follow-Up	What the Studies Show	Certainty of the Evidence (GRADE)	Reasons for Rating
BMD change (DXA)	24–30 adults, 1 RCT (onion juice 100 mL/day)	8 weeks	Onion juice attenuated BMD loss by ~1–2% at lumbar spine/femoral neck vs placebo; effect small and imprecise; antioxidant capacity improved. No fracture outcomes.	Very low ●○○○	Downgraded for risk of bias (allocation concealment/protocol not reported), imprecision (small N, short duration), and indirectness (surrogate outcome, healthy volunteers).
Bone turnover markers (e.g., ALP)	1 RCT	8 weeks	Directionally favorable changes (increased ALP; antioxidant shift) suggesting osteoblast-leaning turnover; magnitude uncertain.	Low ●●○○	Downgraded for imprecision (small N) and risk of bias; not upgraded (no large effect, no dose–response).
In vitro osteoclastogenesis	2 studies (multiple cell systems)	Hours–days	Onion fractions/extract inhibit RANKL-induced osteoclast differentiation and resorption (ERK/p38/NF-κB blockade), while sparing osteoblast activity; consistent across systems.	Moderate ●●●○	Mechanistic indirectness prevents “high”; otherwise, consistent with plausible mechanism and coherence across models.
Animal BMD/microarchitecture (OVX, steroid-induced, growth models)	≥7 studies	3–6 weeks (typical)	Onion/kaempferol preserved BMD, mineral content, and microarchitecture; some models showed fracture-healing enhancement; effects often comparable to positive controls in model context.	Low ●●○○	Downgraded for risk of bias (SYRCLE domains frequently unclear/high), indirectness (animal-to-human), and inconsistency in species/dosing regimens.
Fracture healing (local quercetin application)	1 rabbit study	14 days	Marked increase in new bone area with quercetin-treated defects vs controls (≈five- to six-fold); local delivery and species limit applicability.	Very low ●○○○	Downgraded for indirectness (local biomaterial, rabbit), imprecision (single small study), and risk of bias reporting.

3.7. Risk of Bias Across Studies

Figure 2 summarizes domain-level judgements for the two human randomized trials. The larger, double-blind resveratrol trial [28] was rated overall **low risk of bias**, whereas the smaller onion-based trial—principally due to insufficient information on allocation concealment and lack of a pre-registered protocol—remained at low risk for missing data and outcome measurement. The juice trial [27] showed **several concerns**.

Figure 3 displays SYRCLE assessments for the nine animal studies. Reporting of sequence generation, allocation concealment, and blinding was rare, leaving these domains predominantly **unclear risk**. Only two studies explicitly described random housing and blinded outcome evaluation. Consequently, seven animal studies were rated **high or unclear risk** in at least three domains, reflecting a moderate-to-high overall risk of bias within the pre-clinical evidence base. These methodological limitations should be considered when interpreting the consistency of positive bone-protective effects observed across animal models.

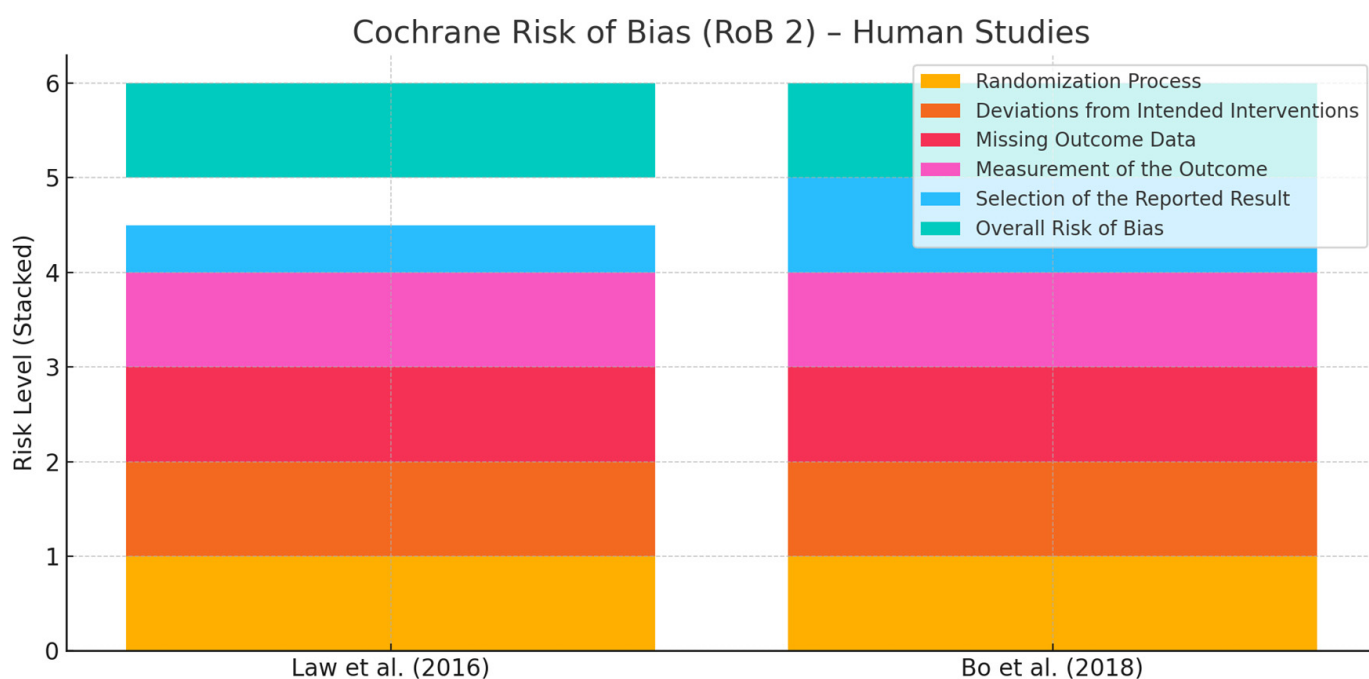


Figure 2. Cochrane Risk of Bias (RoB 2)—Human Studies [27,28].

Figure 2 illustrates domain-level judgements of bias for the included human randomized trials according to the Cochrane RoB 2 tool. The figure displays weighted bar charts and traffic-light indicators across five domains: (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result. Colors correspond to the RoB 2 categories (“low risk”, “several concerns”, or “high risk”). These visual outputs are automatically generated through the robvis application and reflect the risk-of-bias judgements that underpin the certainty of evidence in this review.

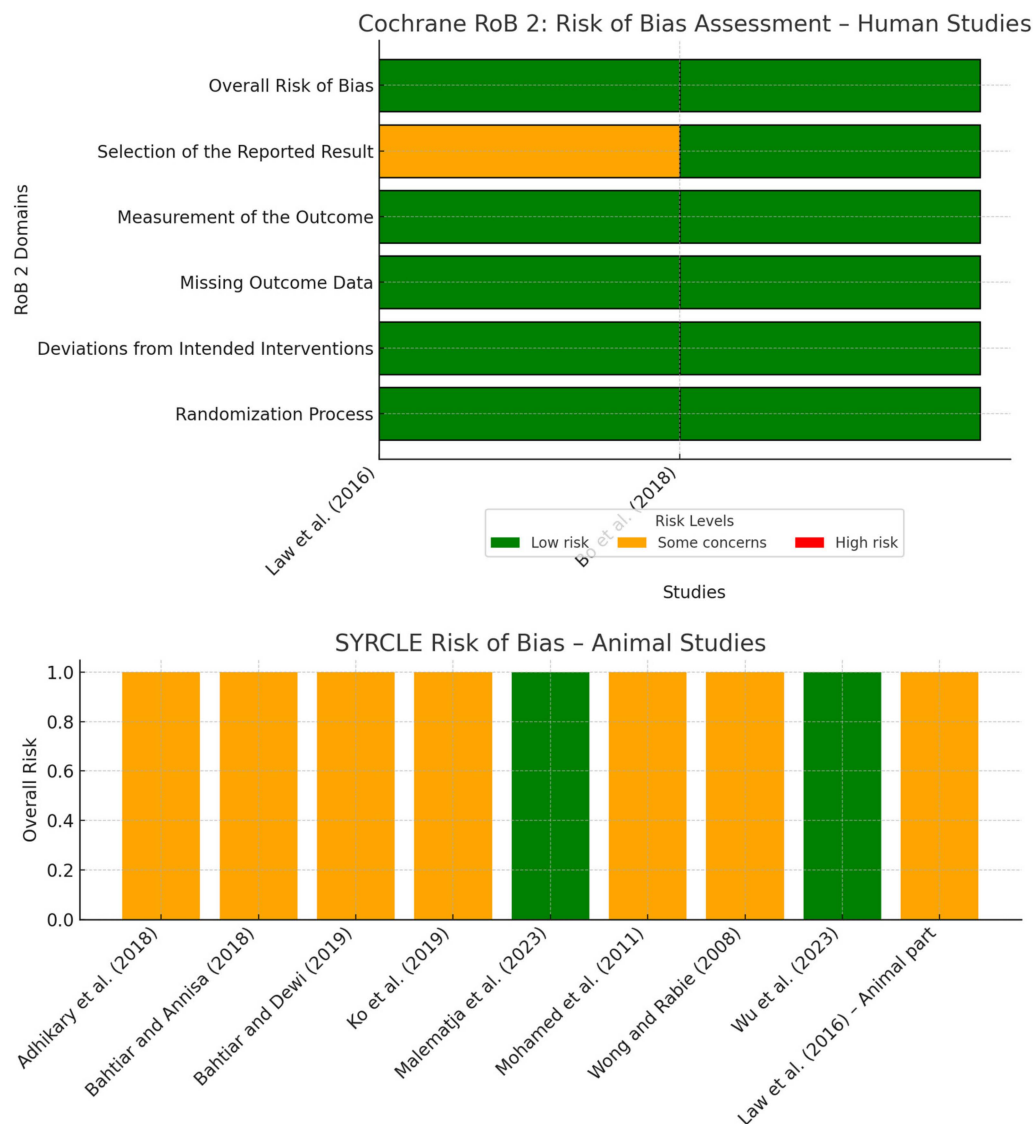


Figure 3. SYRCLE Risk of Bias—Animal Studies [12,13,21–27].

Figure 3 summarizes SYRCLE risk-of-bias domains for animal studies (sequence generation, baseline characteristics, allocation, housing, blinding, outcome assessment, incomplete data, selective reporting, and ‘other’). Predominant ‘unclear’ reflects underreporting. Visuals were auto generated by robvis. Onion-derived polyphenols (e.g., quercetin, kaempferol) exhibit low oral bioavailability due to first-pass metabolism and extensive glucuronidation/sulfation; high plasma protein binding and potential UGT/CYP interactions may limit free concentrations. Peptide/sulfur derivatives (e.g., GPCS) are polar and likely poorly absorbed without delivery vectors. Transporter effects (P-gp, OATP) and possible pro-oxidant activity at high doses should be considered. These pharmacokinetic and safety factors contextualize the translational gap between in vitro signals and clinical efficacy, emphasizing dose, formulation, and chronic administration.

4. Discussion

This systematic review examined evidence from cell culture experiments, animal models, and human trials to elucidate the role of onion-derived polyphenols in bone health. Across these diverse study designs, a consistent theme emerges onion-derived polyphenols (like quercetin, kaempferol, and related flavonoids) exert beneficial effects on bone by reducing bone resorption and supporting bone formation. The mechanisms

underlying these effects are multifaceted, involving antioxidant and anti-inflammatory actions, modulation of signaling pathways in bone cells, and even hormonal or growth-factor-related effects. In this section, we integrate the findings, discuss the biological mechanisms in detail, and interpret the significance of outcomes such as improved BMD, bone growth, and bone cell activity.

4.1. Antioxidant Effects and Reduction of Oxidative Stress

One well-supported mechanism is the antioxidant properties of onion-derived polyphenols [17,27] and their impacts on bone remodeling. Oxidative stress—an imbalance between reactive oxygen species (ROS) and antioxidants—has deleterious effects on the skeleton, promoting osteoclast formation and inducing osteoblast apoptosis. Onion-derived polyphenols, particularly quercetin, are potent free-radical scavengers. The *in vitro* study by Tang et al. [17] showed that onion extract prevented activation of NF- κ B and MAPK pathways in osteoclast precursors, pathways often triggered by oxidative stress and inflammatory cytokines. By suppressing these pathways, the onion extracts effectively blunted osteoclastogenesis. *In vivo*, onions' antioxidant effects were evident in the human trial: daily onion juice significantly increased total antioxidant capacity [27] and lowered markers of oxidative damage in participants. This biochemical improvement correlated with a trend toward higher BMD in onion-treated individuals. We can infer that onion-derived polyphenols protect bones by creating a more antioxidative environment, thereby preserving osteoblast function and dampening osteoclast activation. Quercetin's dual role as an antioxidant and a phytoestrogen [12] further underscores its value: it may simultaneously neutralize ROS and mimic estrogen's bone-preserving effects. Indeed, oxidative stress and estrogen deficiency often synergize to cause bone loss; quercetin, abundant in onions, targets both issues (reducing oxidative stress and possibly engaging estrogen receptors).

4.2. Anti-Inflammatory and Osteoclast Inhibition

Chronic inflammation is a key contributor to bone loss as pro-inflammatory cytokines (like TNF- α , IL-1, IL-6) stimulate osteoclast formation [17] and activity. Onion compounds have known anti-inflammatory properties. Although the studies reviewed did not always measure inflammatory markers, the outcomes strongly suggest the anti-resorptive effect of onion-derived polyphenols. For example, in multiple animal models, onion supplementation led to reduced indices of bone resorption [17,25], which is a direct demonstration of anti-inflammatory/anti-resorptive action, since RANKL is upregulated by inflammatory signals. Mechanistically, quercetin has been shown in other research to inhibit NF- κ B activation in immune cells; our review confirms a similar inhibition in bone cells. By downregulating NF- κ B, onion-derived polyphenols are likely to reduce the production of osteoclastogenic cytokines and the differentiation of osteoclasts. This aligns with the findings of Wetli et al. [20], which identified γ -L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide (GPCS (γ -L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide)) as a potent inhibitor of osteoclast resorptive activity—whether it was fewer osteoclasts (noted histologically in several studies) or lower bone marrow fat (an indicator of osteoporotic change). The suppression of RANKL-induced osteoclastogenesis was achieved by onion extract. In human terms, these anti-inflammatory effects could suggest that diets rich in onions mitigate the low-grade inflammation associated with aging and menopause, thereby indirectly protecting bone. It is noteworthy that the diabetic patients in Bo et al. [28] who took high-dose resveratrol had no bone loss over 6 months. Since diabetes involves oxidative and inflammatory stress, the polyphenol's success in preventing bone density decline reinforces the way controlling inflammation and oxidation can stabilize bone turnover.

4.3. Osteogenic and Anabolic Actions

Beyond preventing bone breakdown, onion-derived polyphenols appear to actively promote bone formation. Several lines of evidence support this osteogenic role. In the rabbits with bone defects, quercetin application resulted in a five-fold increase in new bone formation [12], indicating a strong osteo inductive capacity, at least locally. Quercetin may recruit osteoprogenitor cells or upregulate growth factors in the healing milieu. In cultured osteoblasts, kaempferol prevented steroid-induced apoptosis [13] and elevated markers of osteogenesis, which suggests onion flavonoids can directly enhance osteoblast survival and function. The increase in alkaline phosphatase (ALP) observed in humans consuming onion juice could indicate stimulated osteoblast activity, as ALP is a marker of bone formation. Furthermore, multiple animal studies reported increased bone calcium content and improved bone mass with onion treatments. For instance, Dayak onion extract in OVX rats significantly raised bone calcium and weight [12,24]. Daidzein, present in cowpea and referenced in the combination study, likely played a role, but onion itself contains eleutherinol and other compounds with selective estrogen receptor modulator (SERM)-like activity. This could explain why onion and cowpea together demonstrate synergistic benefits—both provided estrogen-like stimulation to bone, resulting in significant anabolic outcomes, an outcome that implied not just anti-resorption but also enhanced mineral deposition (since simply slowing resorption in estrogen deficiency usually is not enough to increase absolute bone mass without several anabolic input). It is plausible that organosulfur compounds or flavonoids in onion have mild estrogenic effects on osteoblasts, activating pathways that lead to collagen matrix production and mineralization.

4.4. Hormonal and Growth Factor Pathways

One striking finding is the ability of onion compounds to influence systemic hormonal regulators of bone growth. The study by Wu et al. [22] revealed that supplementing rats with green onion root (plus oat) raised their endogenous growth hormone (GH) levels and enhanced IGF-1 signaling in bone. GH and IGF-1 are critical stimulators of bone formation and longitudinal growth. The high-dose onion supplementation matching the effect of administered growth hormone on bone length is remarkable. This suggests that onion may contain bioactive nutrients capable of stimulating the pituitary GH axis or improve GH sensitivity. One hypothesis is that improvements in gut microbiota (like the increased *Lactobacillus* and *Akkermansia* observed in that study) could indirectly modulate hormone levels—a burgeoning field known as the gut–bone axis. Additionally, onions are rich in prebiotic fibers that can benefit gut health, which in turn can influence nutrient absorption and inflammatory status, potentially affecting bone. In another study, Welsh onion extract in high-fat-diet rats activated TGF- β signaling and IGF-1 in osteoblasts [21]. TGF- β [25], which could hint at alternative pathway activation (perhaps via ER α receptors on osteoblasts or by providing substrates for IGF-1 production). and IGF-1 are key growth factors in bone matrix production and growth plate chondrogenesis. Therefore, onion's effect on these pathways positions it as a functional food that can mimic or enhance the body's anabolic signals for bone. For older adults who have lower IGF-1 levels, regular intake of onion might help maintain a more youthful bone remodeling balance. It is worth noting that estrogen deficiency also reduces IGF-1 in bone; by several mechanisms, onion extract in OVX rats still managed to increase bone metrics.

4.5. Mineral Bioavailability and Bone Quality

Another important observation is the improvement of bone mineral content and quality in animal supplemented with onion. Chickens fed onion extract had higher calcium and phosphorus in their bones, and rats on high-fat diets with onion had more minerals

in bone [26] despite the calcium-leaching effect of certain fats. These findings that onions may enhance mineral absorption or retention. Thus, an onion-rich diet could act similarly to a prebiotic that boosts calcium absorption. Additionally, onion's ability to reduce bone resorption means less minerals are lost from bone. Over time, even a slight tilt favoring formation or reducing resorption results in better bone mineral density and content. The increased shear strength of bones in onion-fed chickens and the improved microarchitecture in kaempferol-treated rats both indicate that onion-derived polyphenols not only increase mineral deposition but also support its integration into a stronger bone matrix. Quality of bone (e.g., collagen cross-linking, microarchitecture) is as important as quantity; antioxidants like quercetin might protect the collagen in bone from oxidative cross-link damage, preserving the toughness of bone. Some compounds contain fructans and sulfur compounds that might increase intestinal calcium absorption. Fructooligosaccharides (FOS), for example, are known to improve mineral uptake in the colon by acidifying the gut environment; several onion varieties are rich in FOS.

4.6. Comparisons of Pharmacological Agents

It is instructive to compare onion's effects with standard osteoporosis treatments seen in the studies. In OVX rats, Dayak onion at a high dose was nearly as effective as raloxifene (a SERM) or tamoxifen in improving bone parameters [25]. This suggests onion-derived polyphenols act along pathways similar to those of SERMs (which bind estrogen receptors) to exert bone-protective effects without actual estrogen. Raloxifene primarily inhibits resorption by estrogen receptor modulation in osteoclasts, and tamoxifen can have estrogen-like effects on bone. Onion's mimicry of these outcomes strengthens the hypothesis that onion compounds have SERM-like activity. Meanwhile, in young rats, the effect of onion was compared to growth hormone [21]. Onion and its polyphenols can thus be viewed as a functional food approach to bone health management—potentially useful as an adjunct to therapy or a preventative measure. Unlike drugs that target one pathway intensely (and often have side effects), onions might gently modulate multiple pathways beneficially, with low risk. The human studies reported no adverse effects of onion juice or resveratrol aside from adherence issues, suggesting good tolerability and feasibility for long-term dietary incorporation.; while not identical, high-dose onion did promote growth comparably in that model. Of course, onions are not as potent as pharmaceuticals per se, but their multifactorial mode of action (a combination of SERM, several antioxidants, several prebiotic effects, etc.) yields a net positive effect on bone health.

4.7. Limitations and Considerations

While the collective evidence is encouraging, interpretation must be tempered by the limitations of the findings. Human data remain sparse—we have one small trial with onion juice and one with resveratrol. The onion juice trial, though randomized, had a short duration and a small sample (especially only 3 postmenopausal women, which is too few to generalize). The BMD changes were modest and not statistically robust due to sample size. Long-term effects of onion consumption on bone (over years) were not directly studied; thus, whether regular dietary onion can meaningfully reduce fracture risk is still hypothetical. Moreover, the effective 'dose' of onion is unclear rodents were often given fairly large extract doses relative to body weight (e.g., 18 mg/200 g BW of onion extract in rats, which would scale to a high intake in humans). For humans, consuming 100 mL of onion juice daily [27] (like oat in [22]) might be one strategy to improve efficacy via synergistic effects (fiber plus polyphenols, etc.). SINCE is quite feasible through diet, but higher doses or concentrated supplements might be needed to replicate several of the animal study outcomes. Another consideration is bioavailability: polyphenols like

quercetin have limited absorption; however, consuming them as part of food (with other flavonoids and ingredients) can enhance their uptake. The combination of onion with other foods can be beneficial.

Inter-species differences also matter. For instance, quercetin markedly healed rabbit bone defects, but rabbits have a faster metabolism and different bone turnover dynamics than humans. Translating such local application results to a clinical use (e.g., a quercetin-based bone graft material) is an intriguing possibility that would need testing in humans. The safety profile of high-dose onion or concentrated onion extract is generally good—onion is a common food—but we should note that extremely high intakes might affect thyroid function or cause gastrointestinal discomfort due to FODMAP content in sensitive individuals. No such effects were reported in the review, but long-term supplementation studies would clarify that possibility.

4.8. Translational Outlook and Future Research

Large, multi-centre RCTs (>12 months) in osteopenic and post-menopausal populations should compare whole-food versus standardised onion-extract supplementation; employ fracture or DXA-BMD change as primary endpoints; explore gut-microbiota and endocrine mediators and establish optimal intake (e.g., ≥ 100 g cooked onion or ≥ 50 mg quercetin day⁻¹). Emerging delivery systems—nano-encapsulated quercetin, onion-skin polyphenol concentrates—warrant evaluation for bioavailability and safety.

4.9. Practical Implications

Integrating $\frac{1}{2}$ –1 medium onion daily (~70–150 g) into habitual diets may provide ≈ 30 –45 mg quercetin glycosides, a dose associated with antioxidative and potential bone-sparing effects. Culinary use of onion skins or aqueous extracts could further enhance flavonol intake with minimal cost.

5. Conclusions

Pre-clinical evidence (low–moderate certainty) supports the anti-resorptive and osteogenic actions of onion-derived polyphenols; human evidence is limited to one short RCT with imprecise BMD effects. Larger, longer RCTs are needed to establish clinically meaningful benefits and dosing.

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Abbreviations

ALP	Alkaline Phosphatase
BMC	Bone Mineral Content
BMD	Bone Mineral Density
BW	Body Weight
DeFENS	Department of Food, Environmental and Nutritional Sciences
DXA	Dual-energy X-ray Absorptiometry

ER α	Estrogen Receptor Alpha
FODMAP	Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols
FOS	Fructooligosaccharides
GH	Growth Hormone
GPCS	γ -L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide (A Gamma-glutamyl Peptide isolated from onion)
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IGF-1	Insulin-like Growth Factor 1
IL-1	Interleukin-1
IL-6	Interleukin-6
MAPK	Mitogen-Activated Protein Kinase
MeSH	Medical Subject Headings
NF- κ B	Nuclear Factor Kappa-B
OVX	Ovariectomized
PICO	Population, Intervention, Comparator, Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RANKL	Receptor Activator of Nuclear Factor Kappa-B Ligand
RCTs	Randomized Controlled Trials
RoB 2	Risk of Bias 2
RoBINS-I	Risk of Bias in Non-randomized Studies - of Interventions
ROS	Reactive Oxygen Species
SERM	Selective Estrogen Receptor Modulator
SoF	Summary of Findings
SYRCLE	Systematic Review Centre for Laboratory Animal Experimentation (Risk of Bias tool)
TEAC	Trolox Equivalent Antioxidant Capacity
TGF- β	Transforming Growth Factor Beta
tiab	Title/ Abstract (PubMed search field)
TNF- α	Tumor Necrosis Factor Alpha

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