

Here are some significant studies and research areas from the sources that include or focus on older adults:

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Study on Hemoglobin-to-Red Cell Distribution Width Ratio (HRR) and Bone Health: One study utilized a nationally representative sample of 9,128 elderly Americans to investigate the relationship between HRR and Bone Mineral Density (BMD), as well as the correlation between HRR and the occurrence of osteoporosis¹. This was noted as the first study to specifically investigate the link between HRR and bone density, concluding that HRR could be a crucial indicator for assessing bone health, bone density, and the risk of osteoporosis in the elderly¹².

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Clinical Trial on Nanomicelle Curcumin, Nigella Sativa Oil, and their Combination: A randomized, double-blind, placebo-controlled trial included 303 patients diagnosed with osteopenia (n=194) or osteoporosis (n=109). These conditions are commonly observed in older adult populations. Participants received weekly alendronate tablets plus daily calcium-vitamin D supplements as standard treatment regimens, in addition to the study interventions. A total of 115 patients completed the follow-up³⁴.

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Women's Health Initiative (WHI) Data-Based Investigations on Menopausal Hormone Therapy (MHT): Investigations based on WHI data, including a parallel analysis for the UK population using a Markov cohort simulation model for women aged 50 and older, confirmed the cost-effectiveness of MHT. These studies encompassed women from Sweden, the United States, and the United Kingdom. The cost-effectiveness of MHT was largely influenced by the severity of menopausal symptoms⁵.

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Systematic Review and Meta-Analysis on Osthole for Osteoporosis: This meta-analysis included 13 randomized controlled studies focusing on the use of osthole in the treatment of osteoporosis in rats, with some studies inducing osteoporosis by senility⁶⁷. The analysis concluded that osthole significantly increased BMD in osteoporotic rats, with varying effects depending on dose and duration⁸. While these are animal studies, they contribute to the understanding of age-related osteoporosis.

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Systematic Review and Meta-Analysis on Xianling Gubao Capsule (XLGB) for Osteoporosis: A comprehensive systematic review and meta-analysis included 20 randomized controlled trials (RCTs) published between 2009 and 2020, involving a total of 1,911 participants. Many of these

studies examined the effect of XLGB combined with Alendronate (ALE) on postmenopausal osteoporosis and senile osteoporosis⁹¹⁰. The review suggests that adding XLGB to bisphosphonate medications is an effective and safe strategy for treating osteoporosis patients¹¹. Another related review included 52 RCTs with a total of 4,899 participants, among whom 3,312 had senile osteoporosis and 1,577 had postmenopausal osteoporosis, with a mean age of 64.8 ± 6.4 years¹².

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can i get a bit more detail of the outstanding observations for each.

Here are more detailed outstanding observations for each of the studies mentioned, drawing from the provided sources:

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Study on Hemoglobin-to-Red Cell Distribution Width Ratio (HRR) and Bone Health

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This study was highlighted as the first to specifically investigate the relationship between HRR and bone density¹. It utilized a nationally representative sample of 9,128 elderly Americans aged 50 and above¹.

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A significant positive correlation was found between HRR and T-scores at various femoral sites ($P < 0.05$)¹. This indicates that higher HRR values are associated with better bone density in this elderly population¹.

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Conversely, HRR exhibited a negative correlation with the occurrence of osteoporosis ($P < 0.05$)¹. This suggests that higher HRR values are associated with a lower risk of developing osteoporosis¹.

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The findings underscore that HRR could be a crucial indicator for assessing bone health, evaluating bone density, and predicting the risk of osteoporosis in the elderly, offering a more comprehensive perspective than traditional whole blood indices like hemoglobin (Hb) or Red Cell Distribution Width (RDW) alone¹².

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Clinical Trial on Nanomicelle Curcumin, Nigella Sativa Oil, and their Combination

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This randomized, double-blind, placebo-controlled trial included 303 patients diagnosed with osteopenia (n=194) or osteoporosis (n=109), conditions commonly observed in older adults³. A total of 115 patients completed the follow-up³.

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The study demonstrated beneficial effects of the combination of nanomicelle curcumin and Nigella sativa oil (CUR-NS) on improving certain bone turnover biomarkers⁴.

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Specifically, a significant reduction in the mean differences of Alkaline Phosphatase (ALP) was observed in the Nigella sativa (NS) group and the CUR-NS group compared to baseline (p=0.008 and p=0.003, respectively)⁵.

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In between-group analysis, a significant reduction in ALP was detected in the NS group (p=0.029) and CUR-NS group (p=0.015) compared with the placebo⁵. After adjusting for multiple covariates (including baseline values, physical activity, age, BMI, gravida, menopausal age, and lumbar spine BMD), a significant reduction in ALP was only detected in the CUR-NS group compared to both placebo (p=0.004) and curcumin (CUR) alone (p < 0.05)⁵⁶.

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Both nanomicelle curcumin and Nigella sativa oil appeared safe at the doses used for postmenopausal women⁴. The study recommended further research on the effects of these compounds on osteopenia and osteoporosis separately, or on secondary osteoporosis, and suggested that future studies could compare the CUR-NS combination with alendronate³.

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Women's Health Initiative (WHI) Data-Based Investigations on Menopausal Hormone Therapy (MHT)

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Re-analyses of original observational studies, utilizing advanced pharmacoepidemiological methods, demonstrated results that were more aligned with those from randomized trials regarding MHT, by better accounting for confounding factors⁷.

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MHT has the capacity to mitigate the risk of bone loss and fractures⁸.

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Beyond skeletal benefits, MHT is also effective in alleviating menopausal symptoms⁸.

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The sources indicate that MHT should be viewed as a first-line treatment for women who have recently entered menopause, particularly if the primary therapeutic goal is preserving skeletal health and they present a low risk of cardiovascular disease (CVD), thromboembolic disease, and breast cancer⁸.

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Systematic Review and Meta-Analysis on Osthole for Osteoporosis

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This meta-analysis included 13 randomized controlled studies that evaluated the use of osthole in treating osteoporosis in rats⁹¹⁰. Some studies induced osteoporosis by senility¹¹.

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The most significant finding was that osthole significantly increased Bone Mineral Density (BMD) in osteoporotic rats (Standardized Mean Difference [SMD] = 3.08, 95% CI = 2.08-4.09, $p < 0.00001$)¹²¹³.

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Subgroup analysis revealed that the increase in BMD varied with the dose and duration of osthole treatment¹⁰.

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Beyond BMD, osthole also significantly improved bone biomechanical parameters, including increasing maximum load, maximum deflection, and maximum stiffness in femoral shaft samples during three-point bending tests¹⁴.

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While effects on osteoblast proliferation varied among studies, almost all studies demonstrated that osthole can promote osteoblast differentiation¹⁵, possibly by activating Wnt/ β -catenin pathways and up-regulating BMP2 expression¹⁵.

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Systematic Review and Meta-Analysis on Xianling Gubao Capsule (XLGB) for Osteoporosis

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One meta-analysis reviewed 20 Randomized Controlled Trials (RCTs) involving 1,911 participants¹⁶, many of whom had postmenopausal osteoporosis and senile osteoporosis¹⁷.

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A key observation was that XLGB combined with Alendronate (ALE) remarkably increased Bone Mineral Density (BMD) ($p < 0.001$) at the lumbar spine, femoral neck, and Ward's area¹⁶.... It also significantly improved Bone Gla Protein (BGP), serum Calcium (S-Ca), and serum Phosphorus (S-P) levels, and the total effective rate in patients with primary osteoporosis (POP)¹⁶....

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The combination treatment also significantly decreased Alkaline Phosphatase (ALP) and Visual Analogue Scale (VAS) scores ($p < 0.001$ for both), indicating effective pain relief¹⁶....

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Crucially, XLGB combined with ALE did not markedly increase the rate of adverse drug reactions (ADR) compared to ALE alone ($p = 0.499$), suggesting that it is a relatively safe and well-tolerated treatment strategy for osteoporosis patients¹⁶....

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Another broader systematic review and meta-analysis included 52 RCTs with a total of 4,889 participants (mean age 64.8 ± 6.4 years)²⁶. This larger review indicated that combining herbal medicine (HM) with supplements (calcium and/or vitamin D variants) tended to be more effective in improving BMD in primary osteoporosis than supplements alone^{26,27}. Specifically, XLGB combined with Ca and Vit.D variants improved lumbar spine BMD score²⁸. However, this review noted limitations due to substantial heterogeneity and potential publication bias in many included studies^{26,29}.

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what are the top 5 studies testing herbs on elderly humans.

Based on the sources and our conversation, here are five prominent studies or meta-analyses that focus on testing herbs or herbal compounds on elderly human populations for osteoporosis or bone health:

1. Xianling Gubao Capsule (XLGB) Meta-analysis for Primary Osteoporosis

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Outstanding Observations: This comprehensive review analyzed 20 randomized controlled trials (RCTs) involving 1,911 participants, many of whom had postmenopausal osteoporosis (1,577) and senile osteoporosis (3,312), with a mean age of 64.8 ± 6.4 years [Previous response, 312]. The study found that XLGB, when combined with Alendronate (ALE), remarkably increased Bone Mineral Density (BMD) ($p < 0.001$) at the lumbar spine, femoral neck, and Ward's area [Previous response]. It also significantly improved bone turnover markers such as Bone Gla Protein (BGP), serum Calcium (S-Ca), and serum Phosphorus (S-P) levels, and was associated with a decrease in Alkaline Phosphatase (ALP) and Visual Analogue Scale (VAS) scores, suggesting pain relief [Previous response, 313]. Importantly, the combination did not markedly increase the rate of adverse drug reactions (ADR) compared to ALE alone ($p = 0.499$), indicating its relative safety and effectiveness as an add-on strategy [Previous response]. XLGB is a Traditional Chinese Medicine (TCM) formula composed of six herbs: *Herba Epimedii*, *Radix Dipsaci*, *Fructus Psoraleae*, *Rhizoma Anemarrhenae*, *Radix et Rhizoma Salviae*, and *Radix Rehmanniae*¹. Specific compounds like luteolin, kaempferol, anhydroicaritin, and diosgenin from these herbs are believed to contribute to its anti-osteoporosis effects².

2. Clinical Trial on Nanomicelle Curcumin, Nigella sativa Oil, and their Combination

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Outstanding Observations: This was a randomized, double-blind, placebo-controlled trial that included 303 postmenopausal women diagnosed with osteopenia (n=194) or osteoporosis (n=109) [Previous response, 47]. Participants received weekly alendronate tablets plus daily calcium-vitamin D supplements as standard care, in addition to daily nanomicelle curcumin, Nigella sativa oil, or a combination (CUR-NS) [Previous response]. The study revealed beneficial effects of CUR-NS on improving certain bone turnover biomarkers [Previous response, 49]. Specifically, a significant reduction in Alkaline Phosphatase (ALP) was observed in both the Nigella sativa group and the CUR-NS group compared to baseline [Previous response]. After adjusting for various factors, a significant reduction in ALP (a bone formation biomarker) was uniquely detected in the CUR-NS group compared to both placebo and curcumin alone ($p = 0.004$) [Previous response, 48]. Both nanomicelle curcumin and Nigella sativa oil were found to be safe at the administered doses for postmenopausal women [Previous response, 49].

3. Clinical Trial on Epimedium-derived Phytoestrogen Flavonoids

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Outstanding Observations: This was a 24-month randomized, double-blind, and placebo-controlled trial specifically on late postmenopausal women³. The intervention involved a Traditional Chinese Medicine formula containing *Herba epimedii*, *Fructus ligustri lucidi*, and *Fructus psoraleae*, with a focus on Epimedium-derived phytoestrogen flavonoids³⁴. The key finding was that the herbal formula increased spine and hip BMD by 0.69% and 0.21%, respectively⁴. In contrast, the placebo group showed a significant decrease in spine (0.61%) and hip (0.52%) BMD over the same period⁴. This trial provided strong clinical evidence for the antiosteoporotic potential of these plant-derived compounds, demonstrating their beneficial effect in preventing bone loss in this elderly female population³⁵.

4. Resveratrol Clinical Trial on Postmenopausal Women

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Outstanding Observations: A randomized, placebo-controlled trial investigated the effects of resveratrol supplementation on bone health in postmenopausal women⁶⁷. Regular supplementation with resveratrol (75 mg, twice daily) was found to positively augment BMD in both the lumbar spine and femoral neck⁶⁷. Beyond increasing bone density, the supplementation also led to a 7.24% reduction in C-telopeptide of type I collagen (CTX), a key marker of bone resorption⁶. The study also projected that the observed increase in femoral neck BMD could contribute to a reduction in the 10-year probability of hip fracture risk, highlighting resveratrol's significant bone-strengthening effects in postmenopausal women⁶.

5. Trifolium pratense (Red Clover) Clinical Trial

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Outstanding Observations: Clinical studies have investigated the effect of Trifolium pratense (red clover) extract on bone health in menopausal women⁸⁹. One such study involved supplementation with 150 mL red clover extract containing 37.1 mg isoflavones daily for 12 weeks⁸. The results indicated that this intervention improved bone health in menopausal women, as evidenced by positive changes in BMD and T-score⁸. This study supports the potential of phytoestrogens, naturally occurring compounds in plants like red clover that can mimic estrogen, to provide a protective effect against osteoporosis, especially in the context of menopause-related bone loss⁹....

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list any interactions observed during these 5 studies, if any. any interactions, are they safe.

Here's a detailed look at the observed interactions, and their safety, within the top five studies testing herbs on elderly humans for bone health, drawing from the provided sources and our conversation history:

1. Xianling Gubao Capsule (XLGB) Meta-analysis for Primary Osteoporosis

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Observed Interactions: This meta-analysis specifically evaluated the effects of Xianling Gubao Capsule (XLGB) when combined with Alendronate (ALE), a conventional anti-osteoporosis drug¹. This combination demonstrated remarkable beneficial interactions:

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It significantly increased Bone Mineral Density (BMD) at the lumbar spine, femoral neck, and Ward's area¹.

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It improved bone turnover markers such as Bone Gla Protein (BGP), serum Calcium (S-Ca), and serum Phosphorus (S-P) levels¹.

◦

It also significantly decreased Alkaline Phosphatase (ALP) and Visual Analogue Scale (VAS) scores, indicating pain relief¹.

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Safety of Interactions: Crucially, the combination of XLGB with Alendronate did not markedly increase the rate of adverse drug reactions (ADR) compared to Alendronate alone ($p = 0.499$)¹. The most frequently reported adverse events in the combined treatment group were mild, including gastrointestinal discomfort, liver function damage, and menstruation disorders or amenorrhea, with no severe adverse impacts observed². This suggests that XLGB can be safely and effectively combined with Alendronate as an add-on therapy¹³.

2. Clinical Trial on Nanomicelle Curcumin, Nigella sativa Oil, and their Combination

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Observed Interactions: This trial investigated the combination of nanomicelle curcumin (CUR) and Nigella sativa oil (NS)⁴. All participants also received standard treatment with weekly alendronate tablets plus daily calcium-vitamin D supplements⁵.

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A significant beneficial interaction was observed: a significant reduction in the mean differences of Alkaline Phosphatase (ALP), a bone turnover biomarker, was only detected in the CUR-NS combination group after adjusting for covariates, compared to both placebo and curcumin alone ($p = 0.004$)⁴. This indicates a synergistic or enhanced effect of the two herbal compounds when used together⁶.

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Safety of Interactions: Both nanomicelle curcumin and Nigella sativa oil were found to be safe at the doses used for postmenopausal women^{4,7}. Safety assessments, including evaluation of renal and hepatic biomarkers (urea, creatinine, aspartate transaminase (AST), and alanine transaminase (ALT)), showed no significant intergroup differences, indicating an absence of toxicity at the administered doses^{8,9}. The sources also highlight that Nigella sativa oil is "generally recognized as safe" (GRAS) by the U.S. Food and Drug Administration, and curcumin has shown no toxic effects even at high doses in other studies⁹.

3. Clinical Trial on Epimedium-derived Phytoestrogen Flavonoids

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Observed Interactions: This study utilized a Traditional Chinese Medicine (TCM) formula containing *Herba epimedii*, *Fructus ligustri lucidi*, and *Fructus psoraleae* [Previous response]. The "interaction" here refers to the intended synergistic action of these multiple herbal components within the formula, aiming to collectively promote bone health. The formula successfully increased spine and hip Bone Mineral Density (BMD) compared to the placebo group [Previous response].

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Safety of Interactions: The provided excerpts for this specific trial do not detail safety outcomes or adverse events. However, *Herba epimedii* is a component of the Xianling Gubao Capsule (XLGB)1011. As noted in point 1, the meta-analysis on XLGB combined with Alendronate did not show a marked increase in adverse drug reactions¹², suggesting that Epimedium as part of a multi-herb formula can be safely used alongside conventional anti-osteoporosis medication.

4. Resveratrol Clinical Trial on Postmenopausal Women

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Observed Interactions: This trial focused on the effects of resveratrol supplementation alone [Previous response]. The provided sources do not describe any specific interactions with other drugs or between multiple herbal compounds within this particular study. However, other sources mention resveratrol in various combinations in different contexts:

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A mixture of curcumin, polydatin, and quercetin, including resveratrol, was found to be a safe bioactive compound with synergistic effects in promoting osteoblast differentiation¹².

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Conversely, a dietary combination of vitamin D, resveratrol, quercetin, and genistein was found to be not as effective as zoledronic acid in a postmenopausal rat model, possibly due to the relatively low doses of phytochemicals not producing a sufficiently potent effect or the study duration¹².

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Safety of Interactions: The excerpts for this specific resveratrol trial do not explicitly report adverse events or detailed safety observations. The study observed positive outcomes like increased BMD and a reduction in a bone resorption marker (CTx)¹³.

5. Trifolium pratense (Red Clover) Clinical Trial

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Observed Interactions: This study investigated the effects of Trifolium pratense (red clover) extract, focusing on its isoflavone content [Previous response]. The provided sources do not specify any interactions with other drugs or other herbal compounds within this particular trial.

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Safety of Interactions: The excerpts for this specific Trifolium pratense trial do not detail explicit safety observations or adverse events. However, a systematic review on phytoestrogens (a class of compounds found in red clover) generally noted that long-term consumption of phytoestrogens did not significantly increase severe side effects such as endometrial hyperplasia or various cancers. Nonetheless, it could lead to elevated rates of gastrointestinal side effects¹⁴. It also specifically noted that "high doses of genistein [an isoflavone] can cause gastrointestinal complications"¹⁴. This implies that while generally considered safe, the potential for dose-dependent gastrointestinal issues exists.

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Did any one or more human participants show amazing results in herbal studies?

Based on the sources and our conversation history, while none of the studies explicitly highlight individual human participants showing "amazing" or "miraculous" results, they do report statistically significant and notably positive outcomes at the group level for elderly human participants. These group-level improvements often occurred with a favorable safety profile.

Here's a breakdown of the most positive observations and safety considerations from the studies involving human participants:

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Xianling Gubao Capsule (XLGB) Meta-analysis for Primary Osteoporosis: This meta-analysis of 20 randomized controlled trials (RCTs) found that XLGB, when combined with Alendronate (ALE), "remarkably increased Bone Mineral Density (BMD)" at the lumbar spine, femoral neck, and Ward's area ($p < 0.001$)¹. It also "overtly decreased" Alkaline Phosphatase (ALP) and Visual Analogue Scale (VAS) scores, indicating pain relief¹. The combination treatment did not markedly increase the rate of adverse drug reactions (ADR) compared to ALE alone ($p = 0.499$), with reported adverse events being mild, such as gastrointestinal discomfort, liver function damage, and menstruation disorders or amenorrhea [389, Previous response]. This "remarkable" improvement in BMD and pain reduction, coupled with the lack of significantly increased ADRs, represents a very positive outcome for the patient groups.

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Clinical Trial on Nanomicelle Curcumin, Nigella sativa Oil, and their Combination: This randomized, double-blind, placebo-controlled trial observed "beneficial effects of CUR-NS on the improvement of some bone turnover biomarkers"². Specifically, a "significant reduction in Alkaline Phosphatase (ALP) was only detected in the CUR-NS group" compared to both placebo and curcumin alone ($p = 0.004$)³. This highlights a synergistic or enhanced effect of the combination. Both nanomicelle curcumin and Nigella sativa oil were deemed safe at the administered doses for postmenopausal women, with no significant intergroup differences in renal or hepatic biomarkers [58, Previous response].

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Clinical Trial on Epimedium-derived Phytoestrogen Flavonoids: This 24-month randomized, double-blind, placebo-controlled trial on late postmenopausal women found that an herbal formula containing *Herba epimedii*, *Fructus ligustri lucidi*, and *Fructus psoraleae* "increased spine and hip BMD" by 0.69% and 0.21%, respectively⁴. In contrast, the placebo group experienced a significant decrease in spine (0.61%) and hip (0.52%) BMD⁴. This result provides "strong clinical evidence for the antiosteoporotic potential" of these compounds [Previous response]. The sources for this specific trial do not provide details on observed adverse events or safety profiles⁴⁵.

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Resveratrol Clinical Trial on Postmenopausal Women: Regular supplementation with resveratrol (75 mg, twice daily) was found to "positively augment BMD in both the lumbar spine and femoral neck" and led to a "7.24% reduction in C-telopeptide of type I collagen (CTX)," a marker of bone resorption⁶. The study also projected that the observed increase in femoral neck BMD could contribute to a "reduction in the 10-year probability of hip fracture risk," which is a significant clinical benefit⁶. The specific excerpts for this trial do not detail safety outcomes⁶.

-

Trifolium pratense (Red Clover) Clinical Trial: Clinical studies indicated that Trifolium pratense (red clover) extract, particularly 150 mL containing 37.1 mg isoflavones daily for 12 weeks, "improved bone health in menopausal women, as evidenced by positive changes in BMD and T-score"⁷⁸. While generally considered safe due to their phytoestrogen content, a systematic review noted that long-term consumption of phytoestrogens "elevated the rates of gastrointestinal side effects"⁹, particularly with "high doses of genistein"⁹. The provided excerpts for this specific trial do not detail observed side effects during the study period⁷.

In conclusion, while no individual patient's results were described as "amazing," the collective efficacy demonstrated in these studies, using terms like "remarkably increased," "significantly reduced," "positively augmented," and "improved bone health," suggests highly beneficial outcomes at the population level. These positive effects, often achieved with good safety profiles (some with noted mild gastrointestinal side effects for phytoestrogens in general), indicate promising therapeutic potential for these herbal interventions in elderly human populations for bone health.

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list studies that indicate bone regeneration as an outcome.

The sources provide evidence from various studies, including those on herbal compounds, that indicate outcomes related to bone regeneration in both animal models (rats, mice, zebrafish) and, in some cases, human participants. While "bone regeneration" specifically implies the regrowth of lost or damaged bone tissue, these studies also include interventions that promote bone formation, osteogenesis, fracture healing, improved bone microstructure, and restoration of bone mass, all of which contribute to or are aspects of bone regeneration.

Here are studies from the sources that indicate or strongly suggest bone regeneration as an outcome:

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Gastrodin: A review indicates its future application in "bone regeneration" and "implant osseointegration"¹. Specifically, sequential gastrodin release composite scaffolds were shown to improve osteogenesis and angiogenesis in in vivo and in vitro studies². Its effects on

"organizational engineering" included improving hydrophilic properties and promoting nerve regeneration in vivo and in vitro, and for "implant osseointegration," it led to an increase in "trabecular microstructure around implant" in vivo in rats³.

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Icariin (from Epimedium):

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Icariin-loaded porous scaffolds were investigated for bone regeneration through the regulation of osteogenesis and osteoclastic activity².

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Studies showed that icariin can promote bone formation and osteogenic differentiation⁴.... It was found to stimulate osteoblast differentiation and bone formation by activating the cAMP signaling pathway in primary cilia of osteoblasts in growing rats⁵.

-

It promoted osteogenic differentiation of bone marrow stromal cells and prevented bone loss in ovariectomized (OVX) mice⁸, and was noted to promote proliferation and osteogenic differentiation of bone-derived mesenchymal stem cells in patients with osteoporosis and type 2 diabetes by upregulating GLI-1⁹.

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Icariin was also linked to inducing osteogenic differentiation in vitro in a BMP- and Runx2-dependent manner⁶.

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Its therapeutic potential in bone tissue engineering due to its osteoinductive potential has been discussed⁶.

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A semisynthetic molecule, icaritin, which is related to icariin, stimulated osteogenic differentiation and inhibited adipogenesis of mesenchymal stem cells¹⁰. Icaritin enhanced the differentiation of MC3T3-E1 preosteoblastic cells, leading to mineralization, collagen synthesis, and bone formation⁷. It was found to be beneficial to bone regeneration in animal bone defect models¹¹. A bone-targeting delivery system carrying icaritin prevented osteoporosis in mice¹².

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Naringin: Studies demonstrated that naringin can induce osteogenic differentiation of Bone Marrow Stromal Cells (BMSCs), which promotes bone formation and improves osteoporosis¹³¹⁴. It also promotes osteogenic proliferation and differentiation to ameliorate osteoporosis development by inactivating JAK2/STAT3 signaling¹⁴¹⁵. Its potential for novel orthopedic biotherapies has been highlighted¹⁶. Improvements in bone microstructure (BV/TV, BMD, Tb.Th, Tb.N) and increased mineral apposition rate (MAR) and number of osteoblasts per bone surface (N.Ob/BS) were observed in OVX mice treated with quercetin, indicating bone formation and improved structure¹⁷¹⁸.

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Resveratrol (RSV):

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RSV increased osteoblast bone formation and possibly due to reduced inflammation in animal models¹⁹²⁰.

-

It preserved long bone mass, microstructure, and strength in hindlimb-suspended old male rats²¹.

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Resveratrol was shown to positively augment Bone Mineral Density (BMD) in both the lumbar spine and femoral neck and reduced a bone resorption marker (CTx) in postmenopausal women [Previous conversation].

-

It has effects on osteogenic differentiation of rat and human adipose-derived stem cells in a 3-D culture environment²²²³. It also prevents alveolar bone loss in an experimental rat model of periodontitis²⁴.

-

Moringa oleifera (MO): A study on glucocorticoid-induced osteoporosis in rat jawbones showed that MO had significant bone healing ability²⁵. It resulted in a significant upregulation of BMD, marked healing of jawbone micro-anatomy, and a significant increase in bone area percentage²⁵²⁶.

-

Modified Bu-Shen-Yi-Qi Decoction (MBSYQ): This herbal formula restored femur and L1 bone mass and microstructure damage in chronic smoke-exposed rats²⁷. Quantitative analysis showed that MBSYQ partially attenuated the decrease in BMD and reversed phenomena related to lower bone microstructural parameters, suggesting effective treatment for bone microstructure damage²⁷.

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BushenHuoxue formula (BSHX): This formula effectively improved trabecular bone and reticular structure and promoted the osteogenic differentiation of BMSCs in an osteoporosis model²⁸.

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Qing`e Pill: This traditional Chinese medicine inhibits osteoblast ferroptosis (a type of cell death) via the ATM and PI3K/AKT pathways in primary osteoporosis, which contributes to maintaining bone cell viability²⁹.

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Achyranthes bidentata Root Extract (ABBRE): A systematic review and meta-analysis concluded that ABBRE increased bone biomechanical parameters and played a role in promoting bone tissue strength in osteoporotic rats³⁰.

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Pinoresinol Diglucoside (PDG): PDG was shown to mitigate dexamethasone-induced impairment of bone mineralization in zebrafish^{31,32}, indicating a protective effect on bone formation.

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Various Traditional Chinese Medicine (TCM) compounds:

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Rehmannia glutinosa Libosch extracts enhance osteoblastic bone formation³³.

-

Curculigoside improves osteogenesis of human amniotic fluid-derived stem cells and stimulates osteogenic differentiation of MC3T3-E1 cells^{34,35}.

◦

Er-Xian Decoction promotes MC3T3-E1 cell proliferation and osteogenic differentiation and exerts estrogen-like osteoprotective effects⁴³⁶.

◦

Salidroside protects against osteoporosis and promotes osteogenesis in ovariectomized rats³⁶.

◦

Berberine has therapeutic potential and molecular mechanisms for bone regeneration³⁷³⁸. It can also promote osteogenic differentiation of mesenchymal stem cells³⁹.

◦

Psoralen accelerates bone fracture healing by activating both osteoclasts and osteoblasts⁴⁰.

◦

Astragalin promotes osteoblastic differentiation in MC3T3-E1 cells and bone formation in vivo⁴¹.

◦

Cistanche Deserticola Extract increases bone formation in osteoblasts⁴².

◦

Myricetin ameliorates glucocorticoid-induced osteoporosis by activating the ERK signaling pathway⁴³.

◦

Ginsenoside Rc protects against osteoporosis by increasing the synthesis of type I collagen⁴⁴.

◦

Catalpol promotes osteogenic differentiation of bone marrow mesenchymal stem cells⁴⁵ and accelerates osteoporotic bone repair through osteogenesis-angiogenesis coupling¹⁵⁴⁶.

◦

Dried plum/prunes showed a unique capacity to reverse bone loss and alter bone metabolism in a postmenopausal osteoporosis model⁴⁷.

◦

Quercetin was found to rescue TNF α -impaired BMSC osteogenesis⁴⁸ and promote osteoblast differentiation⁴⁹. It also alleviates ovariectomy-induced osteoporosis by modulating autophagy and apoptosis in rat bone cells⁵⁰⁵¹.

◦

Apigenin promotes osteogenic differentiation of adipose-derived mesenchymal stem cells⁵² and affects bone formation homeostasis in postmenopausal osteoporosis rats⁵³.

◦

Antler and fermented antler extracts stimulated osteoblastic differentiation and mineralization⁵⁴. Deer antler extracts also showed positive effects on an osteoporosis-induced animal model⁵⁵.

◦

Diosgenin stimulates osteogenic activity by increasing bone matrix protein synthesis and bone-specific transcription factor Runx2⁵⁶.

◦

Lycopene influenced osteoblast functional activity and prevented femur bone loss in female rats⁵⁷.

◦

Astragaloside IV has an inhibitory effect on osteoporosis by regulating specific pathways, contributing to bone health⁵⁸. It was also found to promote osteogenic differentiation of bone marrow mesenchymal stem cells⁵⁹.

◦

Salvianolic acid B induced osteogenic differentiation of rat bone marrow stromal stem cells⁶⁰.

◦

Puerarin promotes osteogenesis and inhibits adipogenesis in vitro⁶¹, enhances vascular proliferation⁶², prevents bone loss⁶³, and promotes proliferation and osteoblastic differentiation of human bone marrow stromal cells⁶⁴.

◦

Chrysin upregulated osteogenic proteins and induced mineralized bone tissue formation in dental pulp stem cells in vivo⁶⁵.

◦

Hesperetin in combination with gelatin sponge scaffolds accelerates fracture healing⁶⁶.

◦

(-)-Epigallocatechin-3-gallate (EGCG) enhances healing of femoral bone defects⁶⁷.

◦

Probiotics (e.g., *L. Reuteri* and a mix of *Lactobacillus* strains) were found to prevent or reduce bone loss in animal models and human trials, suggesting a beneficial effect on bone health^{68,69}.

◦

Fructus Ligustri Lucidi (FLL) exerts positive effects on oxidative stress-related osteoporosis⁷⁰ and preserves bone quality⁷¹. Its water extract showed protective effects against oxidative stress-related osteoporosis in vivo and in vitro⁷².

◦

Eucommia ulmoides affected proliferation and differentiation of bone marrow stromal cells⁷³.

◦

Gastrodia elata (Gastrodin) promotes bone formation⁷⁴.

◦

Oleanolic acid stimulates osteoblastic differentiation of bone mesenchymal stem cells⁷².

◦

Antrodia camphorata alcohol extracts recovered osteoporosis through bone regeneration⁷⁵.

◦

Du-Huo-Ji-sheng-Tang and its active component *Ligusticum chuanxiong* promote osteogenic differentiation of human mesenchymal stem cells⁴⁵.

◦

Tanshinone prevents alveolar bone loss⁷⁶.

These studies provide varied and comprehensive evidence of herbal interventions leading to or supporting bone regeneration and related positive bone outcomes.