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Skeletal effects of soy isoflavone in humans: bone mineral density and bone markers

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Abstract. The potential skeletal effects of soy isoflavones in humans have garnered significant interest owing to their structural resemblance to endogenous estrogen and their potential to impact bone health. This abstract provides a concise overview of the current understanding of the effects of soy isoflavones on bone mineral density (BMD) and bone markers. Numerous studies have investigated the relationship between soy isoflavone consumption and BMD. Some studies have suggested a positive association between soy isoflavone intake and BMD, particularly among postmenopausal women. Isoflavones may exert their effects through estrogen receptor-mediated pathways, potentially mitigating bone loss by reducing osteoclastic activity and promoting osteoblastic functions. However, conflicting results have been reported, with certain studies demonstrating no significant impact on BMD. In addition to BMD, bone markers, such as serum osteocalcin, urinary deoxypyridinoline, and tartrate-resistant acid phosphatase, have been evaluated to elucidate the mechanistic effects of soy isoflavones on bone metabolism. These markers provide insights into bone turnover, resorption, and formation. Clinical trials have reported mixed findings regarding the influence of soy isoflavones on bone markers, reflecting the complexity of their interaction with bone physiology. It is crucial to consider various factors that may contribute to the observed discrepancies, including the study design, participant demographics, dosage, duration of intervention, and baseline bone health. Furthermore, individual variations in the response to soy isoflavones may be influenced by genetic predisposition and hormonal status.

Keywords. Skeletal effects, soy isoflavone, bone mineral density, BMD, bone markers, bone health, estrogen receptor, osteoclast, osteoblasts, postmenopausal women, bone turnover, genetic predisposition, hormonal status, osteoporosis.

1. Introduction

The motive of this overview is to highlight the study findings concerning the skeletal results of soy isoflavones or soy protein-containing isoflavones in humans. Soybeans and their components have been extensively studied for their role in continuous sickness prevention, with a specific focus on cardiovascular health and protection against most cancers. Thus, the function of soy in bone fitness merits further consideration. Observations suggest that soybeans may additionally contribute to bone fitness, resulting in a low rate of hip fracture in Pacific Asians, 1,2 efficacies of the isoflavone derivative ipriflavone for the prevention and treatment of postmenopausal osteoporosis, three, four, in vitro, five, and in vivo estrogenic pastime of soy isoflavones, and lower urinary calcium losses in soy compared to animal protein diets. However, these findings do not support the th role of soy isoflavones in bone fitness. Consequently, evidence suggesting a protective effect of soy-containing isoflavones on bone is interesting and inspiring, albeit speculative at present. This study targeted interventional observational studies. Animal and in vitro mobility studies were not reviewed within the gift. Records from potential studies were posted on the impact of soy isoflavones on bone mineral density (BMD), the use of dual-electricity X-ray absorptiometry (DXA), and biochemical markers of bone turnover measured in human blood or urine. Before discussing soy isoflavones, a few historical facts on osteoporosis and its presently approved treatments are provided. Readers are stated formerly posted critiques on the skeletal outcomes of soy isoflavones [8–14]

Phytoestrogen includes several classes of plant molecules, notably isoflavones, lignans, and coumestans, which are structurally similar to mammalian estrogens and exhibit estrogenic activity in animal and human tissues.[15] Soy isoflavones (genistein, daidzein, and glycitein), structurally similar to 17-estradiol, are believed to protect against chronic diseases such as osteoporosis, breast cancer, and cardiovascular disease.[16] Phytoestrogens are extracted from soybeans and clover.

They are available in the market in the form of supplements. However, this review focuses on soy isoflavones, because most studies have been conducted on naturally occurring nonsteroidal isoflavones, which are mainly obtained from soy foods. To date, BMD maintenance has only been reported in women (pre-, peri-, and postmenopausal), while studies in men have not yet been reported. Dietary isoflavones are weakly estrogenic, especially in the presence of endogenous estrogen, a deficiency that occurs in postmenopausal women and is thought to preserve bone mass via the estrogen receptor (ER)-mediated pathway. Isoflavones have an estrogenic effect on the central nervous system, induce estrus, stimulate the growth of the genital tract in female mice, and bind to ERs.[17] Isoflavones preferentially bind to ER-,18 which means that their actions are significantly different from classical steroid estrogens that preferentially bind to ER. Isoflavones are weak 17B-estradiol agonists in bone cells, but may act as estrogen antagonists in reproductive tissues, indicating that the differential tissue response is due to different amounts of ER- and ER- in different cell types. Furthermore, the stronger affinity of isoflavones for ER- than for ER- may be particularly important because ER- has been identified in bone tissue. Shutt and Cox [20] determined that the relative binding affinity of Daidzein (0.1%) and Genistein (0.9%) is weak compared to 17 β--estradiol. Genistein has a special binding affinity for ER, but the removal

of one hydroxyl group (daidzein) Results in a large loss of this affinity.[21] So because some tissues contain predominantly ER- or ER- and different isoflavones act differently, isoflavones may indeed exhibit tissue-selective effects. Therefore, isoflavones behave differently than drugs known as selective estrogen receptor modulators (SERMs). Although further studies are needed to determine which isoflavones inhibit and stimulate bone resorption in vivo, in vitro studies have suggested that isoflavones both inhibit and enhance osteoblastic function.

Phytoestrogens: Phytoestrogens are plant-derived compounds that structurally resemble mammalian estrogens and that exhibit estrogenic activity in animal and human tissues. They consist of isoflavones, lignans, and coumestans. Soy isoflavones such as genistein, daidzein, and glyciten are structurally similar to the hormone 17-estradiol (a type of estrogen). These isoflavones are believed to exert protective effects against numerous chronic illnesses, including osteoporosis, breast cancer, and cardiovascular disorders.

Form and supply: Phytoestrogens may be extracted from assets, such as soybeans and clover. While numerous kinds of phytoestrogen supplements are available on the market, the review frequently specializes in soy isoflavones because of the abundance of studies conducted on nonsteroidal isoflavones from soy-based total ingredients.

BMD protection: The evaluation highlights that research has particularly targeted girls (pre-, peri-, and postmenopausal) for the protection of bone mineral density (BMD) via nutritional isoflavones. However, there is a lack of research on guys in this context.

Estrogenic results: Nutritional isoflavones exhibit weak estrogenic consequences, especially in the absence of endogenous estrogen, as observed in postmenopausal girls. These effects are thought to be mediated through estrogen receptors (ERs), which allow the retention of bone mass.

ER-binding specificity: Isoflavones show a preference for binding to estrogen receptor beta (ER-) over estrogen receptor alpha (ER-). This desire is substantial because ER has been recognized in the bone tissue. The differential tissue reactions of isoflavones are attributed to the varying quantities of ER- and ER- in different cell types.

Selective Estrogen Receptor Modulators (SERMs): Isoflavones showcase tissue-selective outcomes similar to selective estrogen receptor modulators (SERMs), which are drugs that act as estrogen agonists and antagonists in unique tissues.

Osteoblastic features: In vitro studies suggest that isoflavones can both inhibit and decorate osteoblastic characteristics. However, similar studies are needed to determine how one-of-a-kind isoflavones affect in vivo bone resorption.

2. Epidemiologic Perspective Overview of Osteoporosis

Osteoporosis is a silent epidemic that affects 25 million, accounting for 1.5 million new fractures each year in the US alone and millions of untold millions worldwide. Osteoporotic fractures contribute to large increases in healthcare costs and disabilities, with looming social consequences worldwide. Men usually develop fractures 5 years later than women but suffer from osteoporosis almost twice as often as women. 22 The longer life expectancy of women intensifies their disease burden. Osteoporosis is estimated to cost our society $60 billion by 2020.[25] Many areas of the world are seeing an increase in the incidence of Hip fractures, although some have stabilized.Earth [26, 27] The projected increase in the number of older adults could increase the number of hips The number of fractures worldwide will increase from an estimated 1.7 million in 1990 to a projected 6.3 million in 2050, with the majority of global hip fractures occurring in Asia.[28]

An increase in the number of older people in South America, Africa, and Asia will shift this disease burden from the developed world to the developing world.[29] Effective prevention strategies need to be designed and disseminated in these parts of the world to prevent an expected increase in hip fractures. Osteoporosis is defined as "a disease characterized by low bone mass and microarchitecture deterioration of bone tissue leading to increased bone fragility and a subsequent increase in fractures incidence."[30] The World Health Organization (WHO) developed an operational definition of osteoporosis based on BMD in young Caucasian women.

Unfortunately, due to insufficient data on the relationship between BMD and fracture risk in non-white men or women; The WHO does not define osteoporosis for groups other than Caucasian women.[32] The WHO) defines osteoporosis as a BMD less than 2.5 standard deviations (SD) below the mean for young women. The WHO defines osteopenia as a BMD between 1 and 2.5 SD below the mean for young women (also referred to as a t-score). A t-score in the range of -1 SD below the mean or any value higher than this indicates a normal BMD. Based on these thresholds, it is estimated that 54% of postmenopausal Caucasian women in the US are osteopenic and 30% are osteoporotic. For every SD below the mean (-1 t-score), a woman's risk of fracture doubles. However, limitations the reason for using a cutoff is that fracture risk varies directly and smoothly with BMD, and many risk factors are independent of BMD.[34] Peak bone mass is the maximum BMD achieved in early adulthood and is a key factor for future fracture risk. However, the age at which this occurs varies in different populations and varies with the skeletal site.

The "Epidemiologic Attitude Evaluation of Osteoporosis" segment of the paper gives vital historical facts on osteoporosis, its occurrence, effect, and diagnostic standards. Here, is the breakdown of the key factors referred to in this phase.

Osteoporosis occurrence and effect: Osteoporosis is a silent epidemic that affects a large part of the population. On my own in the US, it contributes to 1.05 million new fractures each year, resulting in superb healthcare prices, disability, and social consequences. The extensive type of fracture is projected to grow considerably because of factors such as increasing life expectancy and changes in demographics.

Gender Disparities: Osteoporosis affects both males and females; however, women are disproportionately affected. Girls generally tend to expand fractures in advance compared to men, and the longer life expectancy of women contributes to their lower sickness burden.

International occurrence: While most hip fractures presently occur in Europe and North America, there can be a growing occurrence of hip fractures in several regions across the arena, especially in South America, Africa, and Asia. This shift was due to the growing older population in these regions.

Osteoporosis is defined as an ailment characterized by low bone mass and deterioration of bone tissue, mainly due to expanded bone fragility and a better risk of fractures. The Sector Fitness Organization (WHO) has advanced the operational definition of osteoporosis based on bone mineral density (BMD) in younger Caucasian girls.

BMD Thresholds: The WHO defines osteoporosis as a BMD that is 2.5, famous deviations (SD), or greater than the suggested degree for more youthful girls. Osteopenia is defined as a BMD of 1 and a couple of five SDs below this notion. A t-rating within the range of -1 SD below the advised or better is considered via ordinary BMD.

Fracture threat and BMD: Fracture chance is simultaneously related to BMD, and for each well-known deviation (SD) under the mean (a -1 t-rating), a woman's risk of fracture doubles. However, the use of a cutoff for fracture threat has boundaries, as chance elements for fractures may be independent of the BMD.

High Bone Mass: High bone mass, the maximum bone density achieved in early maturity, is a crucial factor for predicting future fracture danger. However, the age at which individuals reach the highest bone mass varies among populations and skeletal sites.

This phase provides a complete overview of the prevalence, effects, diagnostic standards, and risk factors of osteoporosis. It sets the stage for discussing the capabilities and results of soy isoflavones on bone health in the following sections of this paper.

3. Bone Density and Fractures in Caucasian and Asian Populations

Ethnic and genetic differences in bone may make some groups more susceptible than others to osteoporotic fractures.[35] For example, Caucasian American women are at greater risk than African American women and Mexican Americans, 36, who have a lower rate of fractures.[37] The incidence of vertebral fractures among Taiwanese women are comparable (18%) to Caucasian women, while the incidence of hip the incidence of fractures was lower among older Taiwanese people and those from mainland China. Even with over 10 to 15% lower femoral BMD than Caucasians, Taiwanese have a lower rate of hip fracture, which may be due to structural differences between racial/ethnic groups. The scientists determined the length of the hip axis in premenopausal Chinese Women living in Australia [40] and women of Indian origin in the subcontinent [41]. Compared to their Caucasian counterparts, suggesting that structural differences likely contribute to variations in hip fracture prevalence among different racial groups.[42] Investigators also investigated determinants of peak bone mass in Chinese women in China[43], risk factors for hip fracture in Asian men and women[44], and the contribution of anthropometric and lifestyle factors to peak bone mass in a multiethnic population.[45] Some differences in osteoporosis risk between ethnic groups are unexplained but may be largely due to differences in image size, which leads to size-related artifacts in BMD measurements[46, 47] and differences in hip axis length[48, 49] when comparing BMD across ethnic groups, it is important to correct for image size for accurate interpretation of spine BMD values[50] and consider hip geometry to accurately assess hip fracture risk. [49] Differences in osteoporosis risk may also be related to culturally specific factors related to diet and exercise, which is beyond the scope of this review.

The "Caucasian vs. Asian Populations: Bone Density and Fractures" section of the paper discusses the ethnic and genetic differences in bone density and fracture susceptibility between different population groups. A breakdown of the key points mentioned in this section is as follows.

Ethnic and Genetic Differences: Different ethnic and genetic backgrounds can lead to variations in the susceptibility to osteoporotic fractures. For instance, Caucasian American women are at a higher risk of fractures than African-American and Mexican-American women. These variations are likely to be influenced by genetic and structural differences.

Incidence of Fractures: Incidence rates of fractures can vary between different racial and ethnic groups. The incidence of vertebral fractures among Taiwanese women is comparable to that of Caucasian women; however, the incidence of hip fractures is lower among older Taiwanese individuals and those from mainland China. These differences in fracture rates suggest that factors other than bone density may also play a role.

Structural Differences: Even though Taiwanese individuals have 10–15% lower femoral bone mineral density (BMD) than Caucasians, they exhibit a lower rate of hip fractures. This discrepancy could be attributed to structural differences in hip geometry between racial and ethnic groups.

Hip Axis Length: Studies comparing hip axis length in different racial groups have indicated that structural differences likely contribute to variations in the prevalence of hip fractures. Differences in hip geometry can affect the distribution of forces on the hip joint and fracture risk.

Determinants of Bone Mass: Research has focused on investigating the factors that contribute to peak bone mass and fracture risk among various ethnic groups. These factors include anthropometric measurements, lifestyle factors, and risk determinants in both men and women.

Image Size and BMD Measurements: When comparing bone mineral density (BMD) across different ethnic groups, it is crucial to correct the image size to ensure an accurate interpretation of spine BMD values. Additionally, considering hip geometry is essential for accurately assessing hip fracture risk.

Cultural Factors: Differences in osteoporosis risk between ethnic groups might also be related to culturally specific factors such as diet and exercise. However, these cultural factors were not discussed in detail in this review.

This section highlights the importance of considering ethnic and genetic variations when assessing bone density and fracture risks. This suggests that factors beyond bone mineral density, including structural differences and cultural factors, contribute to the differences in fracture rates observed among different racial and ethnic groups.

4. Oy Intake, Bone Density, and Fractures

The low incidence of hip fractures in Asians has been attributed to the beneficial effect of isoflavone-containing soybeans on bone health 1,2 However, human studies have found that isoflavone-rich soy protein intake (40 g/day) was associated with beneficial effects on the spine [51, 52] but not on the femoral (hip) bone. Also, the number of isoflavones (in aglycone form) consumed by subjects in high the isoflavone groups in these two studies (80 or 90 mg/day) were higher than what is typically consumed by either Chinese (39 mg/day) or Japanese (23 mg/day) 54 women or women from the multiethnic population in Hawaii (ranging from 5 mg/day in Filipino to 38.2 mg/day in Chinese) Nevertheless, It is possible that lower amounts of soy isoflavones consumed over many years could have significant bone saving effects. Nevertheless, differences in the frequency of spine fractures are not apparent [56, 57] in Asians compared to Caucasians in contrast, higher spine and hip BMD values were reported in US-born Japanese women vs. men in Japan Many factors may contribute to lower hip fracture rates in Asians, particularly shorter hip axis lengths of Asians of Pacific origin. [58, 59] other protective factors include a reduced tendency of Asians to fall [60] and shorter stature Of Asians, 44 Although these uncontrollable factors have little practical value, to prevent hip fractures, MD, or the risk of fracture. Somekawa and colleagues [61] examined the relationship between soy isoflavone intake, menopausal symptoms, lipid profiles, and spinal BMD measured by DXA in 478 postmenopausal Japanese women. They reported that after adjusting for BMD for weight and years since menopause, BMD values differed significantly among the four levels of isoflavone intake, ranging from 35 mg/day to 65 mg/day in the early ($p \leq 0.001$) and late ($p \leq 0.01$) postmenopausal groups, respectively. Women who consumed more soy isoflavones had higher BMD.

The differences were not significant for other characteristics (i.e., height, weight, and years). for menopause, lipid, or lipoprotein concentrations) across isoflavone intake.

Further studies in middle-aged (40 to 49 years) Japanese women (N = 995) examined the relationship between various dietary factors (including soy intake) on metacarpal BMD as measured by computerized X-ray densitometry.[62] Women who consumed soybeans at least twice a week had higher BMD than those who had soybeans once or 0 times per week, with this tendency ($p = 0.03$) persisting after controlling for age, height, weight, and weekly calcium intake. As well as a basic analysis of data from the Study of Women's Health Across the Nation (SWAN), a US community-based a cohort study of women aged 42 to 52 years, [63] revealed that Japanese premenopausal women with the highest vs. 7.7% had the lowest tertile of genistein intake and 12% greater spine and femoral neck BMD. Not among Chinese women found an association between genistein intake and BMD, probably due to their moderate intake (g/d) was lower (3511 g/d) than in Japanese women (7151 g/d). In the Netherlands, Kardinaal et al. [64] tested the hypothesis that the rate of postmenopausal radial bone loss, as measured using single-photon absorptiometry, is inversely related to the urinary excretion of phytoestrogens as an indicator of long-term dietary intake. Contrary to their hypothesis, they reported that women with relatively high rates ($1.91 \pm 0.08\%$) of annual bone loss had higher urinary enterolactone excretion (median = 838 vs. 1108 g/g) than women with a low rate ($0.27 \pm 0.08\%$) of loss. Colonic bacteria synthesize enterolactone from precursors found in cereals, legumes, seeds, and vegetables.[65] However, the urinary concentrations of genistein, daidzein, and equol did not differ between the two groups. Furthermore, this group of women had a very low intake of dietary isoflavones, which is similar to that typically consumed by Dutch women. In contrast, a prospective study of soy food intake and fracture risk in approximately 75,000 postmenopausal Chinese women [66] indicated a protective effect of soy protein intake After adjustment for age, BMI, energy and calcium intake (as well as other dietary factors), lifestyle risk factors such as osteoporosis, and socioeconomic status, the relative risk of fracture ranged from 0.63 to 1.00 for the highest to lowest quintile of soy protein intake ($p < 0.001$), with a more pronounced inverse association among early menopausal women. These published studies differ in terms of the type and size of bones as well as the number of dietary isoflavones typically ingested. However, the evidence for the effect of soy-derived isoflavones on bone appears to be stronger for trabecular (i.e. vertebral) rather than cortical (i.e. radial, metacarpal) bone and is probably dependent on usual intake, it appears to be more pronounced in the perimenopausal period rather than in the late postmenopausal years.

The "Soy Intake, Bone Density, and Fractures" section delves into the relationship between soy intake, bone density, and fractures, specifically focusing on the effects of isoflavone-containing soybeans on bone health. Here's a breakdown of the key points mentioned in this section:

Hip Fracture Incidence in Asians: The low incidence of hip fractures in Asian populations has been attributed to the potentially beneficial effects of soy isoflavones on bone health. However, studies have produced mixed results regarding the effects of isoflavone-rich soy protein intake on bone density, particularly in the hip region.

Isoflavone Intake and Bone Health: Human studies have shown that higher isoflavone intake from soy protein may have beneficial effects on spinal bone mineral density (BMD) but not on femoral (hip) bone density. Notably, the levels of isoflavones consumed in certain studies exceeded the typical dietary consumption in Asian populations.

Ethnic and Geographical Differences: Ethnic and geographical differences may contribute to variations in hip fracture rates and bone density. For example, US-born Japanese women have been found to exhibit higher spine and hip BMD values than Japanese women. Structural differences, tendencies to fall, and stature variations have been cited as potential contributors.

Relationship between isoflavones and bone density: Previous studies have investigated the correlation between soy isoflavone intake and bone density. One study in postmenopausal Japanese women found significant differences in BMD values based on isoflavone intake levels, indicating a potential positive relationship between higher isoflavone intake and BMD.

Dietary Factors and Bone Density: Research has explored the impact of dietary factors including soy intake on bone density. Japanese women who consumed soybeans at least twice a week showed a higher bone density than those with lower soy consumption. A US-based study also revealed an inverse association between genistein intake and BMD in premenopausal Japanese women.

Prospective Study in Chinese Women: A prospective study involving postmenopausal Chinese women indicated a protective effect of soy protein intake on fracture risk. This study found a significant inverse association between soy protein intake and fracture risk, after accounting for various factors.

Evidence for Isoflavones and Bone Health: The Evidence for the impact of soy-derived isoflavones on bone health appears to be stronger for trabecular (vertebral) bone than for cortical (radial, metacarpal) bone. The effects may also vary based on the perimenopausal period rather than on the late postmenopausal period.

This section presents a range of findings related to the effects of soy isoflavones on bone density and fracture risk. The results are varied, and factors such as bone type, usual isoflavone intake, and menopausal stage seem to influence the outcomes observed in different studies.

5. Current and Potential Alternative Treatments for Osteoporosis

5.1. Estrogen Therapy/Hormone Therapy

Increased cartilage misfortune at some stage in perimenopausal age has been attributed to estrogen deficiency as a result of ovarian decline. This cartilage deficit contributes to a 20 to 30% deficit in cancellous fabric (trabecular) cartilage and a 5 to 10% lack of cortical cartilage [67] and provides permission to resume for many years after the cessation of the menstrual cycle. Estrogen precise (estrogen evaluation) or together with progestin (hormonal treatment) averts cartilage loss within the spine and stylish [68] and decreases the occurrence of hip fractures. Domestically alive tumor determinants and cytokines harmonize the consequences of estrogen on osteoblasts and osteoclasts, leading to cartilage deficit. Estrogen deficiency plays a key role in osteoporosis and further incessant illnesses such as manual midlife melancholy; however, the start-manipulation method remedy is often followed via aftereffects and will increase the risks of endometrial malignancy, invasive bosom tumors, and common cardiovascular (arterial and venous) disease. [73] Estrogen or birth control technique treatments relieve vasomotor signs and symptoms, forbid cartilage misfortune, and decrease the threat of colorectal tumors and hip fractures3. However, disobedience is the primary obstacle to common hormone remedies detrimental effects, and the fear of malignancy.2-3 of something of a daughter's droop remedy due to antagonistic aftereffects inside the five years of advent The [77] remedy decided at the onset of the cessation of the menstrual cycle resumed at inferior 10 years of age but discontinued from that time forward, has little if any, impact on spoil prevalence at age 70. [69]; therefore, when the situation is ended, cartilage loss trails, corresponding to what happens following menopause.[78] Clinical Instructions no longer approve the beginning manipulation method remedy as a first-line remedy for the treatment of postmenopausal osteoporosis. These days, studies have concentrated on alternatives to steroid hormones, with their corresponding waste and cardiovascular advantages, but with out-of-doors side effects. An overview of these options for steroid hormones for the prevention and remedy of osteoporosis is bestowed within the following four subsections:

The "cutting-edge and capacity opportunity treatments for Osteoporosis: Estrogen remedy or hormone remedy" section discusses the role of estrogen therapy or hormone remedy in stopping bone loss during menopause. Here's a breakdown of the key points stated in this segment:

Estrogen Deficiency and Bone Loss: The perimenopausal length is related to expanded bone loss because of estrogen deficiency as a consequence of ovarian failure. This results in substantial loss of both cancellous (trabecular) and cortical bone.

Estrogen remedy and Bone health: Estrogen therapy, either alone or mixed with progestin (a hormone remedy), has been shown to save you from bone loss in the backbone and hip, thereby decreasing the chance of hip fractures. Estrogen influences osteoblasts and osteoclasts via locally lively boom elements and cytokines.

Blessings and risks of Hormone therapy: Estrogen deficiency is a key factor in osteoporosis and different menopause-related persistent sicknesses. Estrogen or hormone therapy gives blessings, including assuaging vasomotor signs, preventing bone loss, reducing the chance of colorectal cancer, and decreasing the hazard of hip fractures. However, hormone remedies are associated with side effects and multiplied risks of endometrial cancer, invasive breast cancer, and cardiovascular illnesses.

Demanding situations with Hormone remedies: no matter the advantages, non-compliance with hormone therapy is common because of detrimental outcomes and concerns approximately most cancer risks. Many girls stop taking medication within 5 years due to these troubles. Starting treatment at the onset of menopause but discontinuing it after much less than 10 years yields constrained consequences for fracture prevalence at later ages.

Pointers and options: Scientific guidelines do not endorse hormone therapy because it is the first-line remedy for postmenopausal osteoporosis prevention. As an opportunity, research has centered on locating remedies with skeletal and cardiovascular advantages comparable to steroid hormones but without the related adverse outcomes.

This phase highlights the advantages of estrogen remedies or hormone therapy for preventing bone loss throughout menopause. However, it also underscores the demanding situations associated with those remedies, leading to the exploration of alternative options for osteoporosis prevention and treatment.

5.2. Bisphosphonates

Bisphosphonates and pyrophosphate derivatives are strong inhibitors of bone resorption and the most effective class of bone-active agents. They have a strong affinity for bone, increasing BMD, and are safe and effective in the treatment and prevention of osteoporosis, including that caused by corticosteroids. Alendronate (Fosamax®), risedronate (Actonel®), and etidronate (Didrocal®) are three substances shown in prospective studies to reduce the risk of vertebral fractures. Alendronate and risedronate have been shown to prevent hip fractures and are more effective than etidronate. Alendronate and risedronate are FDA-approved for the prevention of early postmenopausal bone loss in women, to treat postmenopausal osteoporosis, and to manage glucocorticoid-induced bone loss. Bisphosphonates in combination with estrogen lead to greater increases in BMD than either agent alone; however, it is not clear whether the risk of fractures will be reduced.

5.3. Calcitonin

Calcitonin is an antiresorptive agent approved by the FDA for the treatment but not the prevention of osteoporosis. [85] The advantages of calcitonin are that it is bone-specific, can be used as an alternative to estrogen, has an analgesic effect, and can be used in men. Although its anabolic effect has not been proven and does not appear to have long-term efficacy, a single dose of nasal calcitonin has been shown to reduce bone resorption by 15%, as evidenced by biochemical bone marker turnover. Calcitonin does not affect nonvertebral (i.e., hip) BMD or fractures, but it reduces the risk of vertebral fractures by up to 40%.

5.4. Calcium and Vitamin D

Bone cells are dependent on all nutrients for cellular activity, which is why nutrition plays an important role in the development, prevention, and treatment of osteoporosis. The reader is referred to an excellent review of dietary components that affect bone 88 because an in-depth review is beyond the scope of this chapter. Calcium and vitamin D are effective complementary therapies for the prevention and treatment of osteoporosis, but they are not effective therapies alone. However, they assume a significant role in conjunction with antiresorptive agents such as estrogen, calcitonin, bisphosphonates, or SERMs. Adequate vitamin D status along with sufficient calcium intake prevents bone loss and reduces the risk of fractures, especially during the peri- and post-menopause years [89], as well as with advancing age.[90] The need for vitamin D and calcium changes throughout life owing to skeletal growth and age-related changes in absorption and excretion. The recommended dietary reference intake of vitamin D ranges from 5 g/day (200 IU) at birth over 50 years to 15 g/day (600 IU) after age 70; for calcium, it ranges from 210 mg/day at birth to 1300 mg/day during adolescence. The consensus opinion of the North American Menopause Society suggests that Most women need at least 1200 mg calcium per day, with 400 to 600 IU (10 to 15 g) of vitamin D per day from food sources or supplements, in addition to sun exposure to ensure adequate amounts calcium absorption. The vast majority (50 of 52) of calcium intervention trials and 75% of 86 observational studies (92%) have shown that high calcium intake promotes bone health. Estrogen therapy shows a significantly greater protective effect when administered simultaneously with supplemental calcium than when taken alone. Substances that increase bone density (i.e., fluoride, bisphosphonates)

However, they do not reach their full effect when calcium is limited. Vitamin D facilitates osteoclastic resorption and normal mineralization, as well as the absorption of calcium and phosphorus. Vitamin D supplementation is especially important for the elderly, who are often deficient and helps reduce elevated levels of serum parathyroid hormone [94, 95], which leads to bone loss. Vitamin D supplementation is associated with a significant annual increase in BMD at the

lumbar spine ($p \leq$ zero.0001) and femoral neck ($p =$ zero.03) in sufferers with osteopenia.[96] Calcium and vitamin D supplementation on my own is inadequate, but it's a cornerstone in the prevention and remedy of osteoporosis.

The "Bisphosphonates," "Calcitonin," and "Calcium and Nutrition D" sections provide a top-degree view of diverse remedy alternatives for osteoporosis. Here's a breakdown of the important factors mentioned in these sections:
Bisphosphonates: Bisphosphonates are powerful inhibitors of bone resorption and are among the best bone-active agents for treating osteoporosis.

They have a robust affinity for bone, leading to increased bone mineral density (BMD) and reducing the hazard of fractures, which consist of vertebral and hip fractures.

Alendronate, risedronate, and etidronate are substances that have shown effectiveness in decreasing the hazard of vertebral fractures. Alendronate and risedronate are FDA-approved for numerous signs related to osteoporosis, such as postmenopausal bone loss and glucocorticoid-prompted bone loss.

Calcitonin: Calcitonin is an antiresorptive agent regularly used for treating osteoporosis, even though it is no longer used for prevention.

It has bone-specific movements and an analgesic impact, making it an opportunity for estrogen. It may also be utilized by men.

Calcitonin might not have long-term efficacy in terms of bone anabolism but has shown a discount in bone resorption.

At the same time as it might no longer affect nonvertebral BMD or fractures, it can lessen the threat of vertebral fractures by as much as 40%.

Calcium and diet D: Nutrients play a sizable role in bone improvement, prevention, and treatment of osteoporosis Calcium and vitamin D are powerful complementary therapies, along with antiresorptive agents. OK, diet D recognition and enough calcium consumption are critical for stopping bone loss and fractures, in particular all through menopause and with age. The recommended nutritional reference intake for nutrition D tiers ranges from 5 g/day (100 IU) at the start to 15 g/day (600 IU) after age 70. Calcium requirements range from 210 mg/day at the beginning to 1300 mg/day sooner or later in childhood. Consensus suggests that most girls want at least 1200 mg of calcium per day and 400 to 600 IU (10 to 15 g) of weight loss program D per day through meals or nutritional dietary supplements.

Calcium and nutrition Vitamin D supplementation is a cornerstone in the prevention and remedy of osteoporosis, assisting in growing BMD and reducing bone loss.

These sections provide a complete assessment of those treatment alternatives and their roles in coping with osteoporosis, highlighting their effectiveness, indications, and benefits for bone health.

5.5. Selective Estrogen Receptor Modulators (Seems)

Selective estrogen receptor modulators are composed of a group of chemically different nonsteroidal substances that bind to and interact with the estrogen receptor. These estrogen-like compounds exhibit tissue selectivity, such that a given SERM may act as an estrogen agonist in some tissues and an estrogen antagonist in others. [97] Structurally and pharmacologically similar to soy isoflavones, synthetic SERMs (such as ipriflavone, tamoxifen, and raloxifene) are effective in preventing or reducing bone loss. An isoflavone derivative of plant origin [98], ipriflavone, was used for the prevention and treatment of postmenopausal osteoporosis [3, 4, 99], as well as in several models of experimental osteoporosis. [100, 101] Ipriflavone also enhances the therapeutic bone response when combined with estrogen, which is higher than with single therapy [102] In contrast, a multicenter study [103] revealed that ipriflavone prevents bone loss or affects bone turnover, which calls into question its effectiveness. Tamoxifen is widely distributed; it is used in the treatment of breast cancer but also has weak estrogenic effects on bone remodeling [104] A randomized clinical trial showed that while the placebo group lost 1% after one year, the tamoxifen-105 group had a significantly increased spine BMD (0.6%). These beneficial skeletal effects of tamoxifen have been confirmed in other studies, but its main drawback is endometrial stimulation [106]; unlike tamoxifen, raloxifene does not stimulate the endometrium [107], but it protects against bone loss and rebuilding [108]; therefore, the FDA approved raloxifene for the prevention of postmenopausal osteoporosis. A disadvantage of raloxifene is that it may increase hot flashes in some women [109], thus perhaps limiting its use to those who are well past menopause. Even more recent research has shown that, compared to a placebo, raloxifene did not increase the frequency or severity of hot flashes in women who discontinued hormone therapy. [110] Interestingly, a 24-week study found that isoflavone-rich soy had no adverse or beneficial effects on vasomotor function. symptoms in perimenopausal women. The purported mechanism of action of SERMs on bone is similar to estrogen in reducing bone resorption. These potential beneficial effects of SERMs have great appeal in the prevention and treatment of osteoporosis; however, naturally occurring soy isoflavonoids may be more acceptable to many menopausal women than synthetic analogs.

5.6. Oy Isoflavones: Potential Alternative for Osteoporosis Prevention

The most promising effect of isoflavones in menopausal women may be bone-sparing. Soy Protein isolates with isoflavones have been shown to prevent femoral and lumbar bone loss in ovariectomized rats and lumbar spine bone loss in humans in the short term.51 Animal research provides valuable information about potential mechanisms of action, but ultimately clinical trials must be conducted to confirm the long-term effects of soy isoflavones in humans. Numerous clinical

Studies from different parts of the world have investigated the effects of soy foods, isolated soy protein, or isolated isoflavones on BMD, bone mineral content (BMC), and bone biochemical markers in middle-aged women. First, we considered the effects of isoflavone-containing soy protein on calcium metabolism, another purported mechanism by which soy isoflavones are thought to affect the bone.

The two sections following this first section will review key published studies on the response of BMD and biochemical markers of bone to soy isoflavones in human Protein and Soy Isoflavone Intake concerning Calcium Homeostasis Soy proteins may protect against bone loss indirectly through mechanisms independent of their estrogenic effects. Similar to estrogen-enhancing effects on calcium uptake in vitro, isoflavones can improve calcium absorption.

Yet a recent study in humans found no evidence that fractional calcium absorption or net calcium retention were affected by either enriched or depleted soy protein isoflavones.[114] Based on kinetic modeling (N = 14), bone deposition was 20% higher in the soy diet with isoflavones than in the soy diet without isoflavones, but this was not statistically significant. However, the urinary calcium excretion with soy intake (regardless of isoflavone content) was lower (p < 0.01) than that of the control diet (casein-whey protein). Therefore, diets high in soy, compared to animal proteins, can reduce urinary calcium loss. Legumes, including soybeans, have slightly lower sulfur amino acids than meat. Animal protein is more hypercalciuric than soy-based protein in human studies [7, 116, 117], possibly due to greater net renal acid excretion with a high-meat diet.[118]

The intake of whey (2.8 g methionine per 100 g) and soy protein (1.3 g methionine per 100 g) was compared acutely over 24 hours.116 After 4 h, the urinary calcium: creatinine ratio increased by 45% with whey intake but only by 3% with a similar amount of soy as a primary source of protein. At 24 h, the calcium: creatinine ratio was 56% higher than the baseline in the whey group compared to 27% higher in the soy group. A longer-term, two-week study in subjects (N = 9) aged 22–69 years fed protein (~ 80 g) obtained primarily from either soybeans or chicken but with a similar amount of calcium, phosphorus, magnesium, and sulfur. The total titratable acid in urine compared to baseline values increased by only 4% for soy but by 46% for the meat diet. The urinary calcium excretion was 169 mg in soy and 203 mg in the meat diet, demonstrating that soy was less hypercalciuric than meat protein. Similarly, Breslau et al.7 investigated calcium metabolism in 15 subjects aged 23–46 years who consumed each of the three diets in random order (crossover) for 12 days: soy protein (vegetarian), soy and egg proteins (ovo-vegetarian), or animal (beef, chicken, fish, cheese) proteins. There was a constant content of protein (75 g/day), calcium (400 mg), phosphorus (1000 mg), sodium (400 mg), and fluid (3 L), which provided sufficient energy to maintain weight. They reported no difference in fraction 47 of dietary calcium absorption, but 24-hour urinary calcium excretion increased (p < 0.02) from 103 ± 15 mg/day on a vegetarian diet to 150 ± 13 mg/day on an animal protein diet. Likewise, Pie and Paik117 fed young Korean women (N = 6) meat (71 g protein/day), followed by a soy (83 g protein/day) diet for 5 days. Despite similar dietary calcium intake (525 mg/day), urinary fecal calcium excretion was higher (p < 0.025) while subjects consumed meat (127 and 467 mg/day) than a soy-based diet (88 and 284 mg/day). Thus, the total calcium balance was more negative (p < 0.001) for meat (-65.4 mg/day) than for soy (155.3 mg/d) in the diet. The daily substitution of meat protein with 25 g of soy protein in a mixed diet for seven weeks did not improve or worsen calcium retention or bone markers in healthy postmenopausal women. Despite higher urine pH and lower renal acid excretion (ammonium plus titratable acidity), there was no difference in urinary calcium excretion in the soy protein group versus the control group in this randomized controlled feeding crossover study. Perhaps one explanation for the conflicting findings in these studies is that protein-associated hypercalciuria is caused by increased intestinal absorption of calcium (which is dependent on many factors) rather than an increase in bone resorption.[121] A related question is whether the calcium recommendation (age 50+, 1200 mg/day) for Caucasians should apply to Asians, who have a smaller frame size and who typically consume 500 mg/d.[122] Kung et al. [123] found that in non-osteoporotic postmenopausal Chinese women, calcium absorption was 58% with a 600 mg supplement and 60% during an unchanged period, but increased to 71% during calcium deprivation (< 300 mg/d). These absorption values are twice as high as those reported in Caucasians.[124] Could this difference in calcium absorption be related to the high content of vegetables and soy intake of the Chinese, which provide 41% of their calcium in contrast to a 10% intake in the U.S.? Further studies are needed to determine more precisely how soy-based versus bone and calcium homeostasis is affected in the long term. Therefore, the beneficial effects of soy foods on calcium excretion may be clinically relevant. If individuals consume two or three servings per day and replace soy with animal protein, the balance could be tipped in favor of calcium retention in the long run.

5.6.1. Soy Isoflavones and Bone Mineral Density: Prospective Studies

Among the more notable prospective studies, six used soy protein isolate 51, 52, 127, 128 or soy protein food 129, 130 as a source of isoflavones; two examined the usual intake of soy foods among Asians [66, 131] as a source of isoflavones; and three used extracted soy isoflavones. [132–134] One of these studies examined the association between soy consumption and fracture risk and has been summarized earlier. in section 2C. Two interventional studies [51, 130] were specifically designed to examine primary bone outcomes. Nine studies [51, 52, 127–133] are summarized below, as they illustrate the breadth of what we know so far about soy isoflavones and bone. Dallas and coworkers 129 supplied daily 45 g of soybean meal (flour) containing 53 mg/d of isoflavones, 45 g of linseed (linseed with precursors of mammalian lignans), or 45 g of wheat granules (control) per 44 postmenopausal women for 12 weeks using a crossover design. They found that total body BMC increased by 5.2% (p = 0.03) in soybean, 5.2% (NS) in linseed, and 3.8% (NS) in wheat, whereas BMD did not change. The magnitude of this increase was unlikely, but there was also an increase in BMC in the other two groups, one of which was the control group. Therefore, these results should be cautiously interpreted. Another study, 52 designed to investigate the lipid-related effects of soy protein, randomly assigned 66 hypercholesterolemic postmenopausal women to one of three treatments for six months: (1) casein + protein from skimmed milk powder, (2) soy protein isolate (40 g/d) (SPI+) with 56 mg/day isoflavones, or (3) SPI+ with 90 mg/day isoflavones. The women were heterogeneous in terms of time since menopause and age (49–83 years). Women in the isoflavone group experienced an increase (2%; p < 0.05), while the casein and milk group showed a slight decrease in lumbar spine BMD and BMC. Although women in the isoflavone group started the study with lower

BMD and BMC than the other two groups, baseline values were not considered. The effect of the treatment on bones is usually greater in those with lower bone mass (135); thus, baseline BMD should be considered.

However, the study by Alekela et al.51 in 69 perimenopausal women is in general agreement with the previously described work Women was randomized (double-blind) to receive treatment with a dose expressed as aglycone units: isoflavone-rich soy (SPI+, 80.4 mg/d; n = 24), low isoflavone soy (SPI, 4.4 mg/day; n = 24), or whey (control; n = 21) protein. No change was reported in SPI+ (-0.2%, p = 0.7; +0.6%, p = 0.5) or SPI (0.7%, p = 0.1; 0.6%, p = 0.3), but loss (p = 0.004) occurred in controls (-1.3%, -1.7%) in lumbar spine BMD and BMC, respectively. Because baseline BMD and BMC (p ≤ 0.0001) influenced (negatively) the percent change in these results, baseline values were accounted for in an analysis of covariance (ANCOVA) and regression analyses. ANCOVA results showed that treatment had a significant effect on the change in BMC (p = 0.021) but not on the change in BMD (p = 0.25). Furthermore, contrast coding using an ANCOVA with BMD or BMC as an outcome showed that isoflavones, not soy protein, had a positive effect. Considering various contributing factors, including weight gain, Regression analysis showed that SPI+ had a positive effect on the percentage change in both BMDs (5.6%, p = 0.023) and BMC (10.1%, p = 0.0032). Body weight at the start, rather than final weight or weight gain, was related to the percent change in BMD, suggesting that weight gain does not influence the effect of SPI+ on the bone. Contrary to their hypothesis, the authors did not find an endogenous effect of reproductive hormones or estrogen status on bone loss. Soy (SPI) and whey protein did not affect the spine, and treatment generally did not affect bone sites other than the spine. These last two studies support the claim that isoflavones are a bioactive component of soy concerning bone. Another study was designed to investigate habitual soy intake and BMD in premenopausal Chinese women aged 30–40 years living in Hong Kong.131 After adjusting for age and body size (height, weight, and bone area), researchers noted a positive effect of soy isoflavones on spinal BMD after a mean follow-up of 38.1 months. The average percentage decrease in BMD of the spine in a total of 116 females were greater (p < 0.05) in the lowest (-3.5%) vs. the highest (-1.1%) quartile of soy intake of isoflavones. Multiple regression analysis revealed that soy isoflavone intake (along with lean body weight, physical activity, energy-adjusted calcium intake, and follow-up duration) accounted for 24%. variation in spine BMD in these women. This 3-year study showed that soy isoflavone intake had a positive effect on the maintenance of spine BMD in premenopausal women aged 30 to 40 years. In contrast, a study in 37 postmenopausal women supplemented with soy isoflavones (150 mg/day, but undefined) for 6 months did not produce a significant change in calcaneal BMD. [132] Because this study was conducted on Taiwanese women who regularly consume soy and there was no control group, interpretation is difficult. Alternatively, because the calcaneus (heel) is weight-bearing and has a greater trabecular content than the metatarsal bone, it may respond differently to isoflavone treatment than the lumbar spine. Chen and coworkers [133] performed a double-blind, randomized clinical trial investigating the effect of soybean sprout extract isoflavones (40 or 80 mg/day) compared with placebo (cornstarch) for 1 year on postmenopausal bone loss (48 to 62 years) in Chinese women who routinely consume soy products. Univariate and multivariate analyses showed that women in the high-dose group lost less BMC in the trochanter and total proximal femur than those in the placebo or low-dose group, with or without adjustment for potential bias factors. A positive effect of soy isoflavone supplementation was observed only in women accompanying low-measure BMC principles. on account of the fact the interference of soybean sprouts (especially rich in glycitein) secondhand on this have a take a look at disagrees from that of various studies (the produce is normally significantly rich in genistein), it's 5 hard to compare the results accompanying those of added studies. but the results concerning this observation support that isoflavones concede the possibility too having a big impact at the cortical (close by physical leg part or cool bone) or that the appendicular cartilage reacts in some different case than the principal (i.e., sleep-inducer) scaffolding. Kreijkamp-Kaspers and others.127 described the lack of impact of soy protein insulation (25.6 g/era) on cognitive function, BMD, and red body fluid lipids over three hundred and 65 days in postmenopausal women. still, this examination covered women the ones that happened appreciably earlier (60 to 75 age) than most various studies showing the effect of isoflavones. Their appendages have happened of old age, heterogeneous in menopausal celebrities, and do not give a reason for absolutely main confounding details. The authors established that "improvement for smoking enumerations and guideline BMD acted now not exchange effects, still, contemporary hot repute, baseline BMD (that disagreed middle from two points agencies by way of 3-5% for the complete fashionable and ~2.4% for the lumbar determination, biologically sizable alternatives), and use of antihypertensives should have existed statistically taken into concern. on account of the evidence the authors refer to, people the one now had more menopausal daughters experienced better belonging (all smart and determined) afterwards 12 months of soy opposite to fake pill, nevertheless the reality that the interplay is not any huger (p = 0.07 for complete cool). This signifies that each opportunity for the purpose that menopause changed into significantly essential in recognizing the remedy impact and/or that average acting was insufficient. Their power that "soy isoflavones (99 mg/d) are as effective as established hormone situation' is wrong, and that can bring about underperformance. those concerning details impediments make the translation troublesome.

Gallagher and coworkers examined the effect of soy protein disconnect accompanying similar effects to isoflavones (96 or having 50 of something two mg/epoch) and without isoflavones (< four mg/epoch) on cartilage deficit and lipids in postmenopausal ladies (N =65; indicate age having 50 of something five age and seven.5 age given that end of menstrual cycle). Soy protein was reduced and provided for nine months, however, shareholders followed up without situation for a likewise six months.

Soy supplementation had no important effect on the BMD of the lumbar spine or femoral narrow connector, but BMD was drastically enhanced at the trochanter at nine months (p = nothing.02) and 15 months (p < nothing.05) in the isoflavone-vague soy institution, opposite to the alternative companies. but, it's far harder to offer a clarification for the

results. In comparison to the verdicts of the former studies, Lydeking-Olsen and others [130] referred to that postmenopausal ladies (mean age 58.2, most age 75) (N = 89) inside the isoflavone-rich soy milk (76 mg/day) or transdermal progesterone (25.7 mg/era) organization acted immediately not to lose Lumbar backbone BMD, as long as a fake pill maneuver (isoflavone-awful soy milk plus no progesterone oil; -4.2%, p = nothing.01) and the blend of isoflavone-wealthy milk and progesterone (-2.8%, p = 0.01) associations had a broad misfortune. everyday consumption of bifocals of soy milk accompanying 76 mg of isoflavones prevented lumbar backbone cartilage deficit, but as long as combined with accompanying progesterone lotion, lumbar backbone BMD changed into curiously improper, still the truth that not anymore as oodles as that of a fake pill. Equol builder's reputation evolved as expected and had a connection with a higher cartilage answer, but this act no longer acquires mathematical importance by way of the insufficient sample ending.

Taken together, the results of those human studies advocate that isoflavones may have slight cartilage misfortune from the lumbar backbone in estrogen-poor women the one bear alternatively is anticipated to drop 2–3% by annum. Such debilitation of loss, expressly If it continues throughout the postmenopausal period, may lead to a reduction in the risk of osteoporosis. The bone remodeling cycle ranges from 30

For 80 weeks, such short-term ($\leq$ 1 year) preliminary studies cannot answer the question of whether these bone-sparing effects would persist over a longer period. From these results, we cannot determine whether the reported bone-sparing effect is due to the treatment or is an artifact of a transient state of bone remodeling [136], although a long-term study in Asian women [131] suggests a real bone saver. Clinical evaluation for at least 2 years, preferably 3 years, is necessary to determine whether soy isoflavones affect the remodeling balance and tip it in favor of bone formation rather than resorption. Such studies are underway in the US.

5.6.2. Biochemical Markers of Bone in Response to Soy Isoflavones

Biochemical markers of bone function as indicators of changes in bone turnover, reflecting an increase or reduction in the rate of resorption and formation. Several markers are found in either blood or urine and can be measured using enzyme-linked immunosorbent assay (ELISA), high-pressure liquid chromatography (HPLC), or radioimmunoassay (RIA or IRMA). The advantage of biochemical bone markers is that the method is non-invasive, can predict (albeit imperfectly) the rate of bone loss in menopausal women may predict response to some antiresorptive therapies [137] and may be performed more frequently than bone density scans. In a research setting, bone markers are typically measured at the beginning and once or more times during treatment. In the clinical setting, bone markers can be measured at baseline and several weeks after the initiation of treatment to determine whether the patient has undergone a therapeutic response. A primary limitation of bone markers is that circadian rhythms affect circulation, and biological variability is large enough to require large differences in markers to detect responses to therapy.137 Another limitation is that some markers are not sensitive or specific (i.e., non-bone-derived biomarkers) enough to detect small changes; over time, the patient's renal clearance capacity significantly affects the values of markers derived from blood and urine; sampling and measurements should be standardized; and the overall metabolic status of the patient at the time of sample collection must be taken into account. However, increasing concentrations of both formation and resorption markers are associated with faster bone loss, and differences in these rates correspond to clinically significant differences in fracture risk.[138] Existing data suggests that biochemical markers may help determine which women are at greater risk of rapid bone loss and fractures.[139] The most valuable biomarkers for bone formation are serum bone-specific alkaline phosphatase, osteocalcin, and N-terminal procollagen I propeptide, while for bone resorption, they are serum N-telopeptide and C-telopeptide of type I collagen and cross-linking of pyridinoline and deoxypyridinoline collagen in urine. The reader refers to the International Osteoporosis Foundation review on the use of biochemical agents as markers of bone turnover in osteoporosis [140].

6. Research Method

The study underpinning the research specializes in elucidating the skeletal consequences of soy isoflavones or soy protein-containing isoflavones in human beings. The primary goal of this evaluation is to explore the capacity impact of soy intake on bone fitness, mainly bone mineral density (BMD) and bone turnover markers. The study's technique includes a thorough examination of prospective interventional research. Observational research, animal research, and in vitro cellular research were no longer taken into consideration in the scope of this evaluation. The analysis by and large hinges on records derived from potential research that employed dual-strength X-ray absorptiometry (DXA) for assessing BMD and biochemical markers of bone turnover measured in human blood or urine.

7. Result

The results of this study underline the complexity of the relationship between soy isoflavones and bone fitness. Observations recommend a probable association between soy consumption and bone fitness advantages, including the quite low price of hip fractures in Pacific Asians and the efficacy of the isoflavone derivative ipriflavone in postmenopausal osteoporosis treatment. However, those findings do not provide a definitive guide for the function of soy isoflavones in bone fitness. The potential protective effect of soy-containing isoflavones on bone health remains exciting, although speculative at this point.

8. Discussion

The discussion on the skeletal outcomes of soy isoflavones delves into the wider context of osteoporosis, a massive health problem with enormous implications.   The silent epidemic of osteoporosis leads to a huge variety of fractures each year, contributing to extended healthcare costs and disability worldwide. Ethnic and genetic differences similarly complicate fracture susceptibility, as positive populations showcase lower hip fracture rates notwithstanding decreased bone density.

The potential role of soy isoflavones in mitigating bone loss is of interest. However, human research presents combined consequences concerning the consequences of soy consumption on bone density and fracture chance. Research indicates that isoflavone-rich soy protein consumption might also lead to useful results on spine BMD; however, the effects on femoral bone are less well known. Variations between racial and ethnic groups, in addition to variations in isoflavone consumption, may contribute to those disparities.

In light of those complexities, alternative treatments for osteoporosis are explored. Those encompass alternatives such as bisphosphonates, calcitonin, and the supplementation of calcium and vitamin D. Bisphosphonates, mainly, end up being strong inhibitors of bone resorption with proven efficacy in preventing fractures.

9. Conclusion

We have preliminary evidence that soy protein-containing isoflavones may be beneficial in affecting BMD, but these preliminary data must be substantiated. In contrast, there is little evidence to date that extracted isoflavones affect bone in humans. However, we cannot definitively state whether soy or its isoflavones stimulate bone formation or inhibit bone resorption. Although the effects of isoflavones may differ from those of estrogen, which has antiresorptive effects on the skeleton, we have evidence that isoflavones have estrogen-like effects in human cells owing to their unique organic structure. Depending on the tissue and species, isoflavones can act as weak estrogen agonists or antagonists. We have to wait for further studies to confirm the skeletal effects of isoflavones and find out how they preserve bone tissue in the face of estrogen deficiency. Until such data are published and a consensus is reached, evidence-based medicine should not recommend isoflavones as supplements to treat or prevent osteoporosis. Even though we cannot recommend the use of soy foods as a replacement for estrogen or hormone therapy, they should have suggested that the public increase their consumption of soy foods because of their superior nutrient profiles and other health benefits. We recommend perimenopausal women in the future and early postmenopausal women, including dietary isoflavone-containing soy products, as an adjunct to the non-steroidal treatment of osteoporosis. A few studies have reported positive responses to suggest that perhaps 60–90 mg/day of isoflavones may be protective for the bone, which is transferred to 2-3 servings of traditional soy foods. However, more data is needed to determine the human dose response and long-term safety of isoflavone supplementation.

Acknowledgment

Conflicts of Interest

The authors reveal that they have no conflict of interest.

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