

Potassium: A Frontier in Osteoporosis

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ABSTRACT

Osteoporosis is a significant public health concern, particularly in aging populations, leading to fractures, decreased mobility, and reduced quality of life. While calcium and vitamin D have long been recognized as essential for bone health, emerging research suggests that potassium may play a crucial role in maintaining bone density and preventing osteoporosis. This manuscript explores the relationship between potassium and osteoporosis, delving into the mechanisms, epidemiological evidence, and potential therapeutic implications of potassium in bone health. Furthermore, the manuscript discusses the sources of dietary potassium, its impact on bone metabolism, and the future directions in research and clinical practice regarding potassium's role in osteoporosis management.

Introduction

Osteoporosis is a systemic skeletal disorder characterized by low bone mass, structural deterioration of bone tissue, and an increased susceptibility to fractures. It is a major global health concern, particularly as the aging population continues to grow [1]. Osteoporosis is often referred to as the “silent disease” because it progresses without symptoms until a fracture occurs. The primary hallmark of osteoporosis is reduced bone density and altered bone microarchitecture, leading to bones becoming fragile and prone to fractures, especially in the hip, spine, and wrist [2].

Epidemiology

Osteoporosis is a global health issue affecting both men and women. According to the International Osteoporosis Foundation, it is estimated that worldwide, one in three women over the age of 50 and one in five men will experience an osteoporotic fracture during their lifetime. The prevalence of osteoporosis varies across re-

gions, with higher rates observed in postmenopausal women and the elderly [3, 4].

Causes and Risk Factors

Osteoporosis results from an imbalance in bone remodeling, a continuous process involving bone resorption by osteoclasts and bone formation by osteoblasts. Several factors contribute to this imbalance [5–7]:

- Aging: Osteoporosis is more common in older adults due to the natural aging process, which leads to decreased bone density.
- Hormonal Changes: Postmenopausal women are at a higher risk of osteoporosis due to a decline in estrogen levels, which plays a crucial role in bone health.
- Genetics: A family history of osteoporosis can increase one's risk.
- Nutrition: Inadequate intake of calcium and vitamin D can impair bone formation and maintenance.

- **Physical Activity:** Sedentary lifestyles contribute to bone loss while weight-bearing exercise helps maintain bone density.
- **Medications and Health Conditions:** Certain medications (e. g., glucocorticoids) and health conditions (e. g., rheumatoid arthritis) can increase osteoporosis risk.

Diagnosis

Accurate diagnosis is crucial for effective management. The cutting-edge diagnostic tools to detect fractures and osteoporosis with advanced technology include ► **Fig. 1**.

- **Bone Density Testing:** Dual-energy X-ray absorptiometry (DXA) scans measure bone mineral density and are used for diagnosis. Bone densitometry is a reliable method to know the prognosis of osteoporotic conditions. It is conventional to use either of the methods to calculate and diagnose the osteoporotic condition which is T-Score or Z-Score. T-Score is where standard deviations are compared with a young healthy individual's mean bone density [4]. Z-Score is calculated by comparing standard deviations with mean bone mineral density of individuals of identical age, gender and size [8]. World Health Organization suggested T Score or Z Score value – 1.0 to – 2.5 as low mineral density indicating osteopenia and below – 2.5 indicates porous bone that may tend to fracture, that is, osteoporosis [9, 10].
- **Fracture Risk Assessment:** FRAX (Fracture Risk Assessment Tool) calculates the ten-year risk of hip and major osteoporotic fractures. For the detection of fractures suggested technology of use is Dual Energy X-ray Absorptiometry. Another technique to know bone mass is high-resolution computed tomography. Ultrasound can predict the fracture by diagnosing the bone firmness [9]. A bone biopsy is another method to determine the occurrence of osteoporosis [10].
- **Change in Biomarkers:** Serum osteocalcin and bone-specific alkaline phosphatase serve as indicators of bone formation, whereas urinary type I collagen C-telopeptide and urinary pyridinoline and deoxypyridinoline serve as indicators of bone resorption. Alterations in these biomarkers are linked to rapid bone loss. Strontium absorption tests determine calcium absorption through the intestine [8, 9].
- **Clinical Evaluation:** A comprehensive assessment of medical history and risk factors helps identify those at risk [11].

Prevention

Preventing osteoporosis is essential, and lifestyle modifications can significantly reduce the risk [12–14]:

- **Diet:** Adequate calcium and vitamin D intake through diet or supplements is crucial.
- **Physical Activity:** Weight-bearing exercises help maintain bone density and strength.



► **Fig. 1** Advanced technologies for fracture and osteoporosis detection.

- **Lifestyle Choices:** Avoiding smoking and excessive alcohol consumption can reduce osteoporosis risk.
- **Medication:** In some cases, medication may be prescribed to prevent or treat osteoporosis.

Treatment

Several medications are available for osteoporosis management [15–17]:

- **Bisphosphonates:** Alendronate, risedronate, and others inhibit bone resorption.
- **Hormone Replacement Therapy (HRT):** Estrogen therapy can help maintain bone density in postmenopausal women.
- **Denosumab:** A monoclonal antibody that reduces bone resorption.
- **Teriparatide and Abaloparatide:** Anabolic agents that stimulate bone formation.
- **Calcitonin:** Reduces bone resorption and may be used for pain relief.
- **Emerging Therapies:** Novel treatments are under investigation, including sclerostin inhibitors and romosozumab.

Potassium and Bone Health

Mechanisms of Action

Potassium is an essential mineral known primarily for maintaining electrolyte balance and cardiovascular health. However, emerging evidence suggests that potassium may have a positive impact on bone health through several mechanisms [18].

Potassium's Role in Acid-Base Balance and Bone Buffering

Potassium plays a critical role in maintaining acid-base balance in the body. It acts as an alkaline buffer by neutralizing excess acid, which is produced during metabolic processes. This acid-base balance is intimately connected with bone health [19].

Recent studies have highlighted the following key points:

- **Acidosis and Bone Resorption:** Acidosis, characterized by elevated blood acidity, has been associated with increased bone resorption. The body releases calcium from bones to neutralize excess acid, potentially leading to reduced bone density [20]. Frassetto et al., found that reducing dietary acid load through increased potassium intake can mitigate bone loss [21].
- **Potassium's Alkaline Effect:** Potassium-rich foods, such as fruits and vegetables, have an alkalizing effect on the body. Alkaline diets have been linked to a lower risk of osteoporosis. Hannan et al., demonstrated that a diet rich in potassium from fruits and vegetables was associated with a higher bone mineral density (BMD) in older adults [22].

Influence of Potassium on Bone Turnover Markers

Potassium has been shown to influence bone turnover markers, providing insights into its direct impact on bone remodeling.

- **Serum Alkaline Phosphatase (ALP):** Elevated serum ALP levels are associated with increased bone formation. Daw-

son-Hughes et al., reported that higher potassium intake was positively associated with lower serum ALP levels, suggesting a potential role in regulating bone formation [23].

- **Markers of Bone Resorption:** Potassium's alkaline properties may also affect markers of bone resorption. Macdonald et al., illustrated that increased fruit and vegetable consumption, rich in potassium, was associated with lower urinary excretion of markers of bone resorption [24].

Interaction with Calcium and Vitamin D in Bone Remodeling

Potassium's interaction with calcium and vitamin D is crucial for bone health.

- **Calcium Absorption:** Adequate potassium levels may enhance calcium absorption in the intestines. Lu et al. showed that potassium supplementation improved calcium retention, potentially promoting bone health [25].
- **Vitamin D Activation:** Potassium may also play a role in vitamin D metabolism. Research carried out by Kim et al., suggests that potassium may influence the conversion of vitamin D to its active form, which is essential for calcium absorption and bone remodeling [26].

A simplified representation of the mechanisms of potassium in osteoporosis is illustrated in ► **Fig. 2**.

Cellular Mechanisms

The cellular mechanisms underlying osteoporosis involve a delicate balance between bone formation by osteoblasts and bone resorption by osteoclasts. Emerging research suggests that potassium, an essential mineral, plays a significant role in regulating these cellular processes in bone tissue.

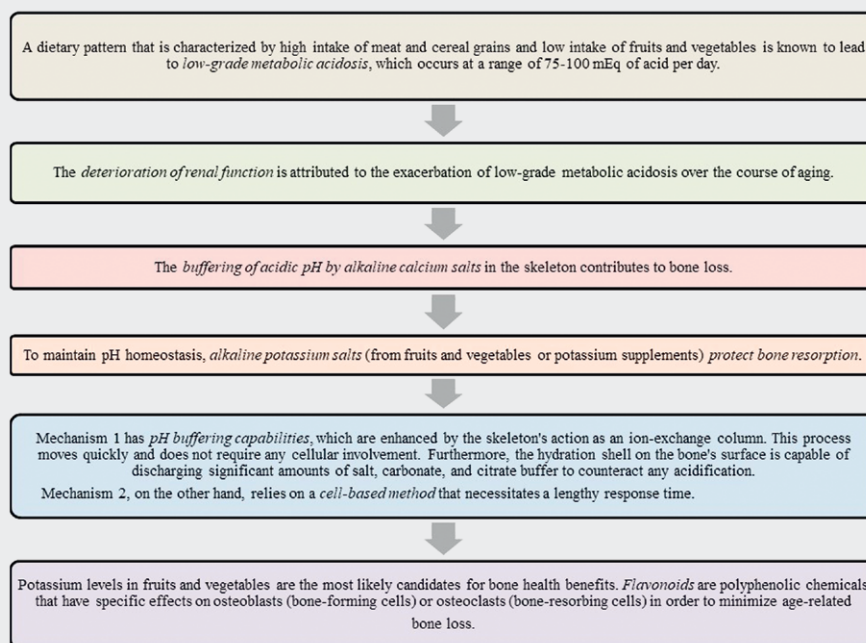
Effects of Potassium on Osteoblasts and Osteoclasts

Recent studies have demonstrated that potassium levels can modulate the activity of both osteoblasts and osteoclasts, thereby affecting bone health. Potassium exerts its effects through potassium channels present on the cell membranes of these bone cells [18].

Potassium Channels in Bone Cells

Potassium channels, specifically the inwardly rectifying potassium (Kir) channels and voltage-gated potassium (Kv) channels, have been identified in osteoblasts and osteoclasts. These channels are involved in regulating membrane potential and intracellular calcium levels, which are crucial for cellular functions [19].

- **Osteoblasts:** High extracellular potassium concentrations have been shown to enhance the differentiation and mineralization of osteoblasts. Activation of Kir channels in osteoblasts can lead to membrane hyperpolarization, triggering calcium influx and promoting osteoblast maturation [3].
- **Osteoclasts:** In contrast, increased extracellular potassium levels inhibit osteoclast activity. High potassium concentrations can hyperpolarize osteoclasts, reducing their resorptive capacity. This effect is mediated through voltage-gated potassium channels, which influence calcium signaling in osteoclasts [16].



► Fig. 2 Mechanisms of potassium in osteoporosis.

The Role of Potassium in Collagen Synthesis

Collagen is a major component of the bone matrix and is essential for bone strength. Potassium has been linked to collagen synthesis in osteoblasts. Research suggests that optimal potassium levels are necessary for collagen production, contributing to bone quality and integrity [16, 18].

Epidemiological Evidence

Epidemiological studies have provided supportive evidence for the role of potassium in osteoporosis prevention [16]. Li et al., reported that higher dietary potassium intake was associated with increased bone mineral density (BMD) in postmenopausal women [27]. In another study Larsson et al., showed that potassium-rich diets were associated with a lower risk of osteoporotic fractures in elderly men [28].

Population Studies

Population studies play a crucial role in understanding the relationships between dietary factors and bone health.

Correlations Between Dietary Potassium Intake and Bone Mineral Density (BMD) Several population-based studies have investigated the association between dietary potassium intake and BMD:

- **NHANES III Study:** The National Health and Nutrition Examination Survey III found that higher dietary potassium intake was positively associated with BMD in older adults [29]. Increased potassium intake was linked to higher spine and hip BMD, indicating a potential protective effect on bone density.
- **The Framingham Osteoporosis Study:** Research from this longitudinal cohort study revealed that higher dietary potassium intake was associated with greater hip BMD in older

men and women [30]. These findings suggest a potential role for potassium in preserving bone health with age.

Longitudinal Studies on Potassium-Rich Diets and Fracture Risk

Population-based longitudinal studies have explored the relationship between potassium-rich diets and fracture risk:

- **The Nurses' Health Study:** This prospective cohort study found that postmenopausal women with higher potassium intake had a lower risk of hip fractures [31]. The protective effect of potassium was particularly evident in women who consumed diets rich in fruits and vegetables.
- **The Osteoporotic Fractures in Men (MrOS) Study:** In this study of older men, those with higher dietary potassium intake had a reduced risk of hip fractures [32]. The results support the notion that potassium-rich diets can contribute to fracture prevention in both genders.

Impact of Potassium on Bone Health Across Different Age Groups

Understanding the effects of potassium on bone health across various age groups is essential:

- **Adolescents and Young Adults:** A cross-sectional study conducted by Whiting et al., indicated that higher dietary potassium intake was associated with greater bone mass in adolescents. This suggests that potassium-rich diets during youth may contribute to optimal peak bone mass [33].
- **Elderly Populations:** Research from Harding et al., demonstrated that higher potassium intake was associated with reduced risk of hip fractures in older women. These findings under-

score the importance of potassium in maintaining bone health in the elderly [34].

Clinical Trials

Potassium Supplementation and Bone Health Outcomes

Clinical trials have examined the impact of potassium supplementation on bone health outcomes, with promising results. A randomized controlled trial carried by Dawson-Hughes et al., investigated the effects of potassium bicarbonate supplementation on bone mineral density (BMD) in postmenopausal women. The study found that potassium supplementation led to significant improvements in BMD at the lumbar spine [29]. Another clinical trial conducted by Orchard et al., explored the effects of potassium citrate supplementation in individuals with osteopenia. The results indicated that potassium citrate supplementation was associated with reduced bone resorption and improved bone microarchitecture [35]. A randomized controlled trial conducted by Nasri et al., investigated the effects of potassium supplementation on bone health in postmenopausal women. The study found that daily potassium supplementation led to improved bone mineral density (BMD) at the lumbar spine and hip over a one-year period. This suggests that potassium supplementation may have a positive impact on bone density [36].

Potassium-Rich Diets and Bone Density Changes

Clinical trials have assessed the relationship between potassium-rich diets and changes in bone density. A study carried by Wu et al., examined the dietary potassium intake of elderly women and its association with changes in BMD over time. The research suggested that higher dietary potassium intake was linked to slower BMD decline, supporting the potential benefits of potassium-rich diets in preserving bone density [37]. In a prospective cohort study reported Macdonald et al., researchers assessed the relationship between dietary potassium intake and bone health. The study included a large sample of postmenopausal women and found a positive association between higher dietary potassium intake and increased BMD at the hip and lumbar spine. These findings suggest that potassium-rich diets may support bone density maintenance [38].

Combination Therapy with Potassium, Calcium, and Vitamin D

Clinical trials have explored combination therapies involving potassium, calcium, and vitamin D for optimizing bone health. A clinical trial reported by Saadi et al. investigated the effects of a combination therapy involving calcium, vitamin D, and potassium citrate in postmenopausal women. The study demonstrated that this combination therapy had a positive impact on BMD and reduced the risk of fractures [39]. A multicenter randomized trial conducted by Weaver et al. investigated the effects of combination therapy with potassium, calcium, and vitamin D on bone health in older adults. The trial demonstrated that participants receiving the combination therapy exhibited greater improvements in BMD compared to those receiving calcium and vitamin D alone. This highlights the potential synergistic effects of potassium when combined with other bone-boosting nutrients [40].

The findings from these clinical trials have significant therapeutic implications for bone health. Potassium supplementation, particularly in the form of potassium citrate or potassium bicarbonate, may offer a non-pharmacological approach to enhance bone mineral density in postmenopausal women and individuals with osteopenia. Encouraging potassium-rich diets may be a simple and accessible strategy for preserving bone density in aging populations. Combination therapies involving potassium, calcium, and vitamin D may have synergistic effects on bone health, reducing the risk of fractures and improving bone microarchitecture.

Dietary Guidelines

Diet plays a crucial role in maintaining bone health and overall well-being. In addition to calcium and vitamin D, potassium is an essential nutrient that has garnered attention for its potential role in preventing osteoporosis and maintaining overall health. This article explores dietary guidelines related to potassium intake, potassium-rich foods, and the importance of balancing potassium and sodium intake, supported by recent evidence [41].

Recommendations for Potassium Intake in Osteoporosis Prevention

The recommended daily intake of potassium varies by age, sex, and individual health status. However, there are general guidelines provided by health organizations, such as the World Health Organization (WHO) and the U.S. Department of Agriculture (USDA). These guidelines typically recommend a daily intake of around 4700 milligrams (mg) of potassium for adults [41–43].

Recent evidence has shown that maintaining adequate potassium intake can be beneficial for bone health and may contribute to osteoporosis prevention. A study carried by Li et al., found that higher dietary potassium intake was associated with increased bone mineral density (BMD) in postmenopausal women, suggesting that meeting recommended potassium levels may support bone health [27].

Potassium-Rich Foods and Their Role in Bone Health

Consuming potassium-rich foods is an effective way to meet daily potassium requirements and support bone health. Key potassium-rich foods include [43, 44]:

- i. **Fruits:** Bananas, oranges, and avocados are rich sources of potassium. These fruits not only provide essential potassium but also contain other nutrients, such as vitamin C and folate, which contribute to overall bone health.
- ii. **Vegetables:** Spinach, sweet potatoes, and tomatoes are examples of vegetables high in potassium. They are also packed with vitamins and minerals like vitamin K, which plays a crucial role in bone metabolism.
- iii. **Legumes:** Beans, lentils, and peas are excellent sources of potassium and provide protein and dietary fiber, which are beneficial for bone health.
- iv. **Dairy Products:** Dairy items like yogurt and milk contain potassium along with calcium, which is vital for maintaining strong bones.

Balancing Potassium and Sodium Intake for Overall Health

Maintaining a proper balance between potassium and sodium (salt) intake is essential for overall health, as both minerals have significant impacts on heart health and blood pressure regulation. High sodium intake is associated with hypertension, which can increase the risk of heart disease and stroke. Recent studies emphasize the importance of reducing sodium intake and increasing potassium intake to mitigate these risks [45].

A potassium-rich diet can help counteract the negative effects of excess sodium by promoting healthy blood pressure levels. In fact, the Dietary Approaches to Stop Hypertension (DASH) diet, which is high in potassium-rich foods and low in sodium, has been shown to reduce blood pressure and improve overall cardiovascular health [46].

Potassium Supplementation

Potassium is an essential mineral that plays a crucial role in various bodily functions, including maintaining proper nerve and muscle function, regulating heart rhythm, and balancing fluid levels. Supplementation with potassium may be necessary in certain situations, particularly for at-risk populations and older adults.

Potassium Supplements for At-Risk Populations

- Hypokalemia Risk:** Potassium supplementation is often recommended for individuals at risk of hypokalemia, which is a condition characterized by low potassium levels in the blood. At-risk populations may include people with kidney disease, certain gastrointestinal disorders (e.g., chronic diarrhea), and those taking specific medications such as diuretics, which can lead to potassium loss [47].
- Recommended Dosage:** The appropriate dosage of potassium supplements varies depending on individual needs and medical conditions. Typically, healthcare providers prescribe potassium supplements in the form of tablets or capsules, with dosages ranging from 20 mEq to 100 mEq per day. However, the dosage should be determined by a healthcare professional after considering the patient's specific circumstances [48, 49].
- Forms of Potassium Supplements:** Common forms of potassium supplements include potassium chloride, potassium citrate, and potassium gluconate. The choice of supplement depends on factors like the patient's tolerance, the presence of underlying conditions, and the potential for drug interactions [49, 50].

Considerations for Supplementation in Older Adults

- Age-Related Changes:** Older adults may be at an increased risk of potassium deficiency due to age-related changes in kidney function and reduced dietary intake. Therefore, they may benefit from potassium supplementation to maintain healthy potassium levels [50].
- Caution with Medications:** Older adults are more likely to be taking medications that can interfere with potassium levels, such as diuretics or certain blood pressure medications. Healthcare providers should carefully consider the interaction

between these drugs and potassium supplements to avoid adverse effects [51].

- Individualized Assessment:** Supplementation in older adults should be individualized and based on their specific health status, dietary habits, and medication use. Regular monitoring of potassium levels is essential to prevent both deficiency and excess [52, 53].

Monitoring Potassium Levels and Potential Side Effects

- Regular Blood Tests:** People who are prescribed potassium supplements should undergo regular blood tests to monitor their potassium levels. This is crucial to ensure that supplementation is effective but not leading to hyperkalemia (excess potassium in the blood) [51, 52].
- Potential Side Effects:** Excessive potassium intake can lead to hyperkalemia, which can cause muscle weakness, irregular heart rhythms, and in severe cases, cardiac arrest. Therefore, it is essential to monitor for symptoms of hyperkalemia and adjust the dosage as needed [47, 54].
- Consultation with Healthcare Provider:** Anyone considering potassium supplementation, especially those with underlying health conditions, should consult with a healthcare provider who can provide guidance on the appropriate dosage and monitor for any adverse effects [55].

Interdisciplinary Approaches in Management and Prevention of Osteoporosis

Interdisciplinary approaches have gained prominence in managing and preventing osteoporosis as they leverage the expertise of various healthcare professionals to address the multifactorial nature of the condition. The present review delves into three key interdisciplinary approaches in osteoporosis prevention:

Collaborative Efforts between Nutritionists, Endocrinologists, and Bone Specialists

Nutrition plays a pivotal role in bone health, and collaborative efforts among nutritionists, endocrinologists, and bone specialists can provide comprehensive care for individuals at risk of osteoporosis. Nutritionists can assess dietary intake and formulate personalized nutrition plans to optimize calcium and vitamin D intake, which are critical for bone health. Endocrinologists can identify hormonal imbalances that may contribute to bone loss, such as hormonal deficiencies or excesses, while bone specialists can evaluate bone density and assess fracture risk [27]. A study reported by Ceglia et al., demonstrated that collaborative care involving nutritionists, endocrinologists, and bone specialists resulted in significant improvements in bone health markers in postmenopausal women [56].

Personalized Nutrition Plans for Osteoporosis Prevention

Personalized nutrition plans tailored to an individual's specific needs and risk factors can be highly effective in osteoporosis pre-

vention. These plans consider factors such as age, gender, dietary preferences, and existing medical conditions. They aim to optimize calcium and vitamin D intake, as well as other nutrients like potassium, magnesium, and protein. Additionally, dietary plans may consider the avoidance of excessive sodium and caffeine consumption, as they can contribute to bone loss. A meta-analysis carried by Tang et al., concluded that personalized dietary interventions had a positive impact on bone mineral density, particularly in postmenopausal women [57].

Addressing the Potassium-Calcium Balance in Dietary Guidelines

Potassium and calcium are vital minerals for bone health, and maintaining an appropriate balance between them is crucial. High sodium intake, which is common in many Western diets, can lead to excessive calcium excretion in the urine and increase the risk of osteoporosis. Interdisciplinary teams can work together to develop dietary guidelines that emphasize potassium-rich foods (e. g., fruits and vegetables) and recommend reducing sodium intake to improve the potassium-calcium balance. A study conducted by Tucker et al., 1999 found that a higher dietary potassium-calcium ratio was associated with a lower risk of osteoporosis-related fractures in older adults [30].

Limitations of Current Research

Variability in Study Methodologies and Populations

Numerous studies examining the association between potassium intake and bone health have employed different methodologies, including cross-sectional studies, cohort studies, and randomized controlled trials (RCTs). These studies often have varying methodologies for assessing potassium intake and bone health outcomes. For example, a meta-analysis performed by Lanham-New et al. found significant heterogeneity among studies investigating the association between dietary potassium intake and bone mineral density, highlighting the variability in methodologies and populations [58]. Variability in study designs and methodologies can lead to inconsistent findings and make it difficult to draw definitive conclusions about the relationship between potassium intake and bone health [59].

The Need for Randomized Controlled Trials (RCTs)

While there is evidence from observational studies suggesting a positive association between higher potassium intake and better bone health, the gold standard for establishing causation is RCTs. RCTs involve randomly assigning individuals to different levels of potassium intake and observing the impact on bone health outcomes. RCTs help control for confounding variables and provide stronger evidence for causation [60]. Identifying the optimal range of potassium intake that promotes bone health without causing harm requires more research, including RCTs and long-term studies. A meta-analysis reported by Lambert et al. concluded that both low and high potassium intakes may be associated with a higher risk of osteoporosis, emphasizing the need for further research to determine optimal levels [61]. The scarcity of RCTs specifically designed to assess the effects of potassium supplementation on bone

health limits our ability to make definitive conclusions regarding the causal relationship.

Identifying Optimal Potassium Levels for Bone Health

There is a lack of consensus regarding the optimal level of potassium intake for promoting bone health. Some studies suggest that higher potassium intake is associated with improved bone density and reduced risk of fractures, while others find no significant association or even potential adverse effects at very high potassium levels. Optimal potassium levels may vary depending on an individual's overall diet and other factors [62]. The lack of a clear consensus on the optimal potassium intake for bone health makes it challenging to provide specific dietary recommendations.

Potential Risks

Monitoring potassium levels in individuals with renal issues and balancing potassium intake with medications are important considerations in healthcare to prevent potential risks associated with potassium imbalances.

Monitoring Potassium Levels in Individuals with Renal Issues

Potassium is an essential mineral that plays a critical role in various bodily functions, including nerve function, muscle contractions, and maintaining heart rhythm. However, the kidneys are responsible for regulating potassium levels in the body by excreting excess potassium through urine. In individuals with renal (kidney) issues, such as chronic kidney disease (CKD), the kidneys may not function properly, leading to a potential risk of high potassium levels in the blood (hyperkalemia). Hyperkalemia can have serious consequences, including cardiac arrhythmias and muscle weakness, which can be life-threatening if not properly managed [63, 64].

Balancing Potassium Intake with Medications

Some medications can affect potassium levels in the body. For example, certain medications, like potassium-sparing diuretics (e. g., spironolactone), can increase potassium levels, while others, like certain diuretics (e. g., furosemide), can decrease potassium levels. It is crucial to balance dietary potassium intake with medications to prevent either hyperkalemia (high potassium) or hypokalemia (low potassium). Imbalances in potassium levels can lead to adverse health effects. High potassium levels can cause heart rhythm disturbances, and low potassium levels can result in muscle weakness and irregular heartbeat [65, 66].

Future Research Areas

Potassium is an essential mineral in the human body, primarily known for its role in maintaining electrolyte balance and regulating blood pressure. However, emerging evidence suggests that potassium may also play a significant role in bone health by influencing bone microarchitecture, including bone density and structure. Conducting longitudinal studies to investigate the association between dietary potassium intake and bone microarchitecture. These studies could include advanced imaging techniques like high-res-

olution peripheral quantitative computed tomography (HR-pQCT) to assess bone quality. Examining the potential mechanisms through which potassium affects bone microarchitecture. This might involve in vitro studies using bone cell cultures to understand the cellular processes involved [67].

Genetic factors can play a crucial role in determining an individual's potassium metabolism and, by extension, their bone health. Identifying specific genes and genetic variations associated with potassium metabolism and bone health can provide valuable insights into personalized medicine and interventions. Genome-wide association studies (GWAS) to identify genetic variants associated with potassium metabolism and bone health outcomes such as bone mineral density and fracture risk. Investigating gene-environment interactions to understand how genetic factors and dietary potassium intake interact to influence bone health [68].

To understand how potassium influences bone health at the cellular level, mechanistic studies are essential. These studies can provide insights into the signaling pathways and cellular processes involved in potassium's impact on bone cells. Conducting in vitro studies using bone cell cultures to investigate how potassium influences osteoblast (bone-forming cell) and osteoclast (bone-resorbing cell) activity. This could involve exploring potassium's effects on cell proliferation, differentiation, and mineralization [69].

Marketed Products of Potassium

Potassium supplements are available in many salt forms like Potassium gluconate, Potassium Chloride, Potassium Citrate, Potassium Aspartate, Potassium Iodide, Potassium Magnesium Citrate, Potassium Magnesium Aspartate, Potassium Bicarbonate in various brand names for different indications like Nephrotic stones, hypokalemia, Hypertension, Arrhythmia, Thallium toxicity, Hyperthyroidism, Sporotrichosis [70]. Potassium bicarbonate cannot be given orally since it releases carbon dioxide that could impart a deleterious effect on gastric mucosa [71].

Some Potassium Supplements Products that are Available in the Market

Although the branded products of potassium listed (► **Table 1**) below are just a few examples of potassium supplements, they are also a prescription medication that is available in tablet, capsule, powder form. Low blood potassium levels are treated or prevented using this medication. Only use prescription drugs as directed by a healthcare professional.

Other Products

Twinlab Potassium Caps, Country Life Target-Mins Potassium, Solgar Potassium Tablets, Nature's Way Potassium Chelate, Bluebonnet Nutrition Chelated Potassium, Douglas Laboratories Potassium 99 mg Chelated, Life Extension Potassium Caps, Solaray Potassium Aspartate, Pure Encapsulations Potassium Magnesium Citrate, Doctor's Best High Absorption Magnesium & Potassium, GNC Potassium Magnesium Aspartate, Now Foods Potassium Citrate Powder, Himalayan Organics Potassium Citrate Tablets, Jarrows Potassium Citrate Tablets, Source Naturals Potassium Iodide.

Adverse Reactions, Drug Interactions and Contraindications to Potassium Supplements

To guarantee the safety and efficacy of the medication, potassium contraindications or potential drug interactions should be carefully reviewed and assessed prior to usage. Potassium is contraindicated in hyperkalemia and it tends to interact with Angiotensin-Converting Enzyme (ACE) Inhibitors, Angiotensin Receptor Blockers (ARBs) [72] and Potassium-Sparing Diuretics (Triamterene, Amiloride, Spironolactone) causing hyperkalemia [73], gastrointestinal adverse drug reactions [74], esophageal obstruction [75], Perforation of Small Bowel [76], ulcer, and stenosis [77].

The National Academies of Sciences describes the Dietary Reference Intakes (DRIs) for potassium as guidelines established by the National Academies of Sciences, Engineering and Medicine to help people maintain a healthy diet and avoid nutrient deficiencies. The article specifically focuses on the potential toxicity of potassium, providing recommendations for safe intake levels and potential adverse effects of consuming too much potassium. Although not consistently, high, acute potassium intakes have been linked to symptoms of neuromuscular dysfunction such as weakness, paralysis, nausea, vomiting and diarrhea [78].

Potassium overdose is also related to morbidity as mentioned in one of the case studies by Guillermo et al., where a deliberate ingestion of 100 extended release potassium chloride pills, 50 mg of clonazepam, and an unknown quantity of ethanol by a woman (42 years of age) resulted in hyperlactatemia, metabolic acidosis, and sinus tachycardia within two hours. No particular procedures were required after the patient originally received therapy with activated charcoal and gastric lavage. She did, however, need to have a transcutaneous pacemaker implanted. Her medical history led to the suspicion of a pharmacobezoar, which was treated with an endoscopy to eliminate 99 pills of potassium that had developed concretions [79].

Afshar et al., demonstrated that the BALB/c fetal mice developed their eyes with substantial abnormalities as a result of long-term potassium benzoate ingestion. The detected consequences included ocular malformations and structural abnormalities, suggesting that potassium benzoate may be teratogenic. The level of potassium benzoate exposure and the severity of the anomalies were associated [80].

Safe Dose of Potassium

It seems that adding around 2500 mg/day (64 mmol/day) of potassium in regular meal for a brief period is not risky for individuals who are generally in good health [78].

A study conducted Goyal et al., in 2012 revealed that individuals who suffer from Acute Myocardial Infarction displayed a lower incidence of mortality if their potassium levels in serum lie within range of 3.5 mEq/l and <4.5 mEq/l conversely to potassium levels that were higher or lower. Therefore, it is plausible to deduce that healthy serum potassium values may fall within the range of 3.5 mmol/l and 5.0 mmol/l. Levels that fall beyond this range could potentially result in death due to various complications [81].

A reference daily intake (RDI) for potassium is set by the Food and Drug Administration (FDA). RDI refers to 'the quantity of a nu-

► Table 1 An overview on marketed products of potassium.								
En-try	Brand	Manufacturer	Marketed by	Category	Dose	Dosage form	Formulation technology	Reference
1.	Klor-Con® (USP)	Upsher-Smith Laboratories, LLC	Upsher Smith Laboratories, LLC	Potassium Chloride	600 mg, 750 mg	ER Tab	Wax Matrix Tablet	RxList [85]
2.	Klor-Con®M 10/15/20 (USP)	Upsher-Smith Laboratories, LLC	Upsher Smith Laboratories, LLC	Potassium Chloride	750 mg, 1125 mg, 1500 mg	ER Tab	ME	Dailymed [86]
3.	KCl Cure (I.P.)	Pharma Cure Laboratories/Curetech Formulations (P) Ltd	Hargun Biotech	Potassium Chloride	1500 mg in 10 mL	Liquid Injection	Not Specified	Pharmaceutical Laboratories [87]
4.	K-TAB (USP)	AbbVie LTD	AbbVie Inc.	Potassium Chloride	600 mg, 750 mg, 1500 mg	ER Tab	Film sealed tablet	Food and Drug Administration [88]
5.	Slow-K (USP)	Novartis Pharmaceutical Corporation	Novartis Pharmaceutical Corporation	Potassium Chloride	600 mg	ER Tab	Wax Matrix	RxList [89]
6.	Sando-K	Alturix Limited	Sandoz	Potassium Chloride (Ph.Eur.), Potassium Bicarbonate (USP)	600 mg + 400 mg	ER Tab	Not Specified	Medicines [90]
7.	Micro-K ExtenCaps (USP)	KV Pharmaceutical	Ther Rx Corporation	Potassium Chloride	600 mg, 750 mg	ER- HGCap	ME	RxList [91]
8.	K-Dur (USP)	Key Pharmaceuticals Inc.	Key Pharmaceuticals Inc.	Potassium Chloride	750 mg, 1500 mg	ER Tab	ME	Drugs [92]
9.	Urikind-K Oral Solution (USP)	Cris Pharma (India) Ltd	Mankind Pharmaceuticals	Potassium Citrate	1100 mg	Oral Solution	Not Specified	1 mg [93]
10.	Urocit-K	Mission Pharmaceutical	Allmed Labs	Potassium Citrate	1080 mg	ER Tab	Wax Matrix Tablets	Urocit-K [94]
11.	Bone Up	Jarrow Formulas	Jarrow Formulas	Potassium Citrate	99 mg	Capsule	Not Specified	Jarrow [95]
12.	Klotrix	Bristol-Myers Squibb Company	Bristol-Myers Squibb Company	Potassium Chloride	750 mg	ER Tab	Film-Coated Wax-Matrix Tablet	Drugs [96]
ER Tab: Extended Release Tablets; ER-HG Cap: Extended Release Hard Gelatin Capsules; ME: Microencapsulation.								

trient thought to be enough to fulfill the needs of most healthy people on a daily basis'. According to the FDA, potassium RDI is 4700 milligrams per day indicated to individuals over the age of 14. However, certain populations may require different amounts, such as pregnant or lactating women [82].

As per National Institute of Health Adequate intake (AI) of potassium recommended for 14 to 18 years of age is 3000 mg (male) and 2300 mg (female), 19 to 50 years of age and above 3400 (male) 2600 mg (female). For pregnant ladies of age 14 to 18 years AI of potassium recommended is 2600 mg and 19 to 50 years is 2900 mg whereas for lactating mothers recommended AI for the age between 14 to 18 years is 2500 mg and for 19 to 50 years is 2800 mg. This recommended AI is not applicable for patients with any renal condition [83].

Around 90 % of the potassium consumed, which amounts to 60–100 mEq, is eliminated through urine, 10 % of the body's waste is passed in the stool, and some is lost through perspiration. Despite this, uncertainty exists regarding the bioavailability of potassium from dietary sources, and its impact on health outcomes remains largely unknown [84].

Summary and Conclusion

In the ever-evolving landscape of bone health research, potassium emerges as a frontier with immense potential to reshape our understanding of osteoporosis. The journey of exploring the role of this essential mineral in bone microarchitecture, deciphering genetic factors influencing potassium metabolism, and unraveling mechanistic insights into its effects on bone cells has opened a world of possibilities. As we navigate the complexities of osteoporosis, the evidence amassed from studies linking potassium intake to improved bone mineral density and reduced fracture risk in postmenopausal women and older adults cannot be overlooked. The tantalizing prospect of potassium as a modifiable dietary factor brings hope for preventive strategies and personalized interventions. Furthermore, genetics adds a layer of complexity and intrigue to the potassium-bone health equation. Genetic factors influence not only our potassium metabolism but also our predisposition to bone-related disorders. By delving into the genetic determinants of potassium and bone health, we may unearth the keys to personalized osteoporosis management and treatment.

Mechanistic studies at the cellular level have unveiled glimpses of how potassium interacts with bone cells, from osteoblasts to osteoclasts. These investigations shed light on the intricate molecular pathways that underlie the effects of potassium on bone remodeling. Such insights hold promise for the development of targeted therapies that can harness potassium's potential to strengthen bones.

In conclusion, the exploration of potassium's role in osteoporosis represents an exciting frontier in bone health research. It beckons us to venture further, to probe deeper, and to seek answers that may ultimately transform the way we approach osteoporosis prevention and treatment. With continued dedication and scientific rigor, potassium may well become a cornerstone in our efforts to fortify the foundations of bone health for generations to come.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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