WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL RESEARCH

Review Article

2025
Volume: 02
Issue: 05
Page: 77-97

A COMPREHENSIVE REVIEW ON BONE RELATED DISEASE AND EFFICACY OF MEDICINAL PLANTS

Neha[1]*, Hanumanthachar Joshi[1] and P. K. Kulkarni[2]

[1,2]Department of Pharmacognosy, Sarada Vilas College Of Pharmacy, K M Puram, Mysuru.

Received: 10 April 2025 **Revised: 30 April 2025** **Accepted: 18 May 2025**

Corresponding Author: Neha

Address: Department of Pharmacognosy, Sarada Vilas College Of Pharmacy, K M Puram, Mysuru.

ABSTRACT

This article explores the relationship between various diseases of bones and joints and the use of medicinal plants in their treatment. Bone disorders such as osteoporosis, osteoarthritis and fractures are prevalent worldwide, significantly impacting quality of life. Traditional medicine systems, particularly Ayurveda and Traditional Chinese Medicine(TCM), have a long utilized herbal remedies to support bone health and enhance healing processes. Research highlights several effective plants, *including Cassia occidentalis, Willow bark, Devil's claw, Cissus quadrangularis ,tinospora* etc…known for their anti-inflammatory and bone strengthening properties.Some of the plants have shown promise in improving bone mineral density.

INTRODUCTION

Bone diseases and disorders, such as osteoporosis, osteoarthritis, and fractures are widespread conditions that significantly impact human health and mobility. These aliments can arise due to genetic factors, aging, nutritional deficiencies, or autoimmune conditions, often leading to pain, reduced bone density and joint dysfunction. While conventional treatments like medications and surgery are common, the use of medicinal plants has gained attention as a complementary approach for managing these conditions.[1]

Herbs such as *Cassia occidentalis, Willow bark, Devil's claw, Cissus quadrangularis,, tinospora* have shown promising results in improving bone strength, reducing inflammation and accelerating fracture healing. This article delves into the causes and types of bone

diseases while highlighting the therapeutic potential of plant based remedies in supporting bone health and alleviating joint pain.[2]

1 OSTEOPOROSIS

Osteoporosis is a condition that affects the bones, causing them to become weak and brittle. It occurs due to reduction in bone mass and structural deterioration of bone tissue, leading to an increased risk of fractures, especially in the hip, spine, and wrist.

Even it is considered as a SILENT DISEASE. With over 8.9 million fractures per year, osteoporosis is a global health hazard that is only getting worse [(1)]. Patients frequently do not realize they are osteoporotic until after suffering a fragility fracture since bone loss happens gradually and without noticeable symptoms.

Over the course of 39 months, 507 patients who had suffered a fragility fracture were sent to the BHC (Bone health clinic). To record osteoporosis evaluation attendance rates and demographic characteristics (age, gender, race, area deprivation index, insurance type, and fracture kind), a retrospective chart review was carried out. Attendance for osteoporosis examination was defined as a follow-up appointment with the BHC or another physician after a fracture during which osteoporosis was identified in the assessment. One year from the date of the fracture was the cutoff point for nonattendance.

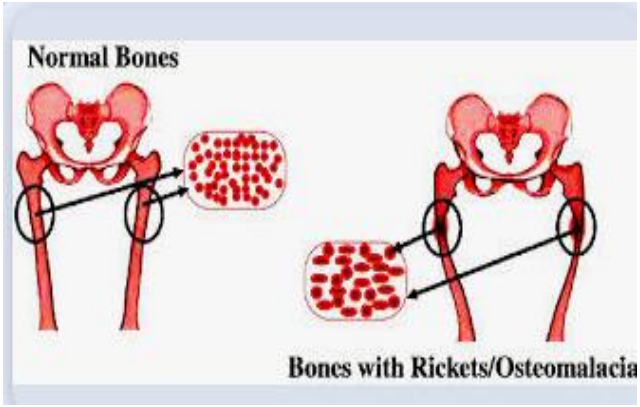
Patients who are older or have experienced a hip fracture may find it more difficult to attend post-fracture checkups, thus inpatient evaluation and therapy for osteoporosis should be explored.[3]

RISK FACTORS ASSOCIATED

- Estrogen deficiency and glucocorticoid use, are associated with reduced BMD(BONE MINERAL DENSITY)[4]
- Gene by gender interaction[5]
- Lifestyle changes
- Medical condition and medication

2 OSTEOMALCIA

Osteomalacia is a medical condition characterized by the softening of bones due to impaired bone mineralization. This typically occurs as a result of deficiencies in vitamin D, Calcium, Phosphate which is essential for bone formation. In children, this condition is known as rickets.[6] Vitamin D can be acquired from dietary sources as well as through skin exposure to ultraviolet light. Once in the body, it is hydroxylated in the liver to produce 25-hydroxycholecalciferol.At one point, it is believed that this compound is most active metabolite of vitamin D.[7]



Nine adults with primary hypophosphatemic osteomalacia were the subjects of the study. This rather uniform condition manifests clinically as bone pain, muscle weakness, and frequently significant height reduction as a result of vertebral collapse. The prevalence is completely sporadic, and there is no history of rickets or any other childhood illness.

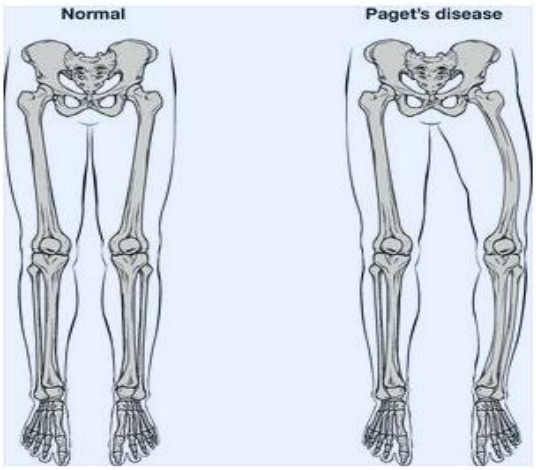
The biochemical and radiological data are consistent with the sex-linked variant of "vitamin D resistant" osteomalacia, which is characterized by prolonged hypophosphatemia brought on by high renal phosphate clearance, normal plasma and urine calcium, and variable elevated alkaline phosphatase. Furthermore, regular paper chromatography can easily detect elevated urine glycine excretion in many cases.

This illness is treated with high doses of vitamin D and oral phosphate supplements, perhaps for life. During the healing period, which lasts for about a year, calcium supplements are also beneficial. Diarrhea, in particular, can make the essential phosphate treatment more difficult. Our current beginning regimen consists of 5 mg of vitamin D2, 10 g of dibasic sodium phosphate (Na2HPO4.10H2O) per day (or its equivalent, such as "Phosphate Sandoz"), and a calcium supplement that contains about 1000 mg per day. It is possible to stop using calcium supplements after about a year or two, and the maintenance dose of vitamin D is less than 2 mg daily.[8][9]

RISK FACTORS ASSOCIATED

- Vitamin D deficiency[10]
- Limited sunexposure
- Dietary factors

3 PAGET'S DISEASE



Paget's disease of bone is a chronic condition that disrupts the normal process of bone remodeling.It causes bones to become larger,weaker,and structurally abnormal due to excessive breakdown by osteoclasts followed by rapid ,disorganized rebuilding by osteoblasts.The disease commonly affects areas like the pelvis,skull,spine and long bones such as femur and tibia.[11]

One or more bone fragments may be affected by the condition, which results in deformities, elevated indicators of bone remodelling, pain in the affected bone, and distinctive imaging characteristics. Complications from the chronic disease activity include arthropathies, cracks or fractures, neurological compressions, and, in rare cases, osteosarcomatous transformation of a pagetic lesion. Strong bisphosphonates have demonstrated their ability to effectively lower disease activity and symptoms.[12]

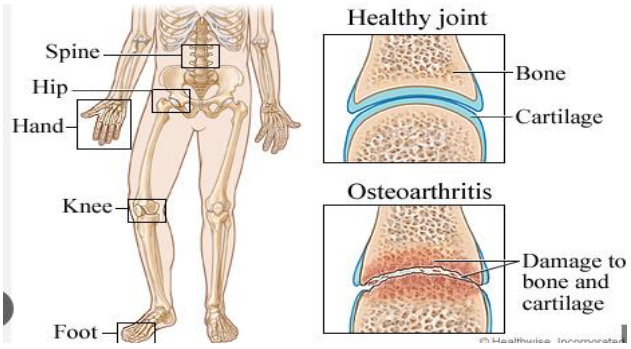
RISK FACTORS ASSOCIATED

- Genetic factors
- Acquired factors

Numerous anomalies in the production of osteoclasts in Paget's disease have been found by marrow culture investigations. In marrow cultures from patients with Paget's disease, osteoclast-like multinucleated cells developed more quickly, generated higher amounts of interleukin-6 (IL-6), and expressed more IL-6 receptors than normal. Patients with Paget's disease also had higher levels of IL-6 in their peripheral blood and bone marrow. Furthermore, osteoclast precursors from Paget's disease patients exhibit hyper responsiveness to calcitonin and 1,25-dihydroxyvitamin D3 (1,25(OH)2D3).

An elevated rate of osteoclast development and anomalies in osteoclast precursors and the marrow microenvironment have been shown by investigations into the cell biology of osteoclasts in Paget's disease. Increased bone turnover at uninvolved areas further from the pagetic lesion may be explained by increased IL-6 production by osteoclasts in Paget's disease, which may also intensify the enhanced osteoclast development already present in the pagetic lesion.[13]

4 Osteoarthritis



Osteoarthritis (OA) is a degenerative joint condition that occurs when the cartilage cushioning the joints deteriorates over time, leading to time, leading to pain, stiffness and reduced mobility. Prostaglandins, cartilage matrix fragments, neuropeptides, reactive oxygen intermediates, proteolytic enzymes, protease inhibitors, cytokines, growth factors, and other pathophysiological processes are all dysregulated in OA, a disease affecting the entire joint. When these variables are dysregulated, a cycle of cartilage, bone, ligament, and synovial degradation begins, which is followed by an inflammatory response and sensitization of the peripheral and central nervous systems.[14]

RISKS FACTORS ASSOCIATED(15)

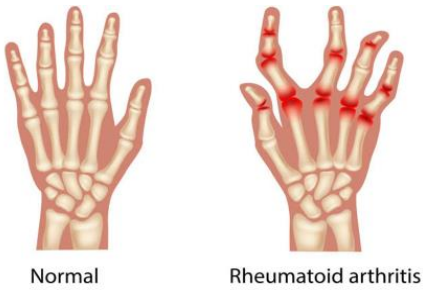
- Genetics
- female sex
- past trauma
- advancing age
- Obesity

Joint replacement is an effective treatment for symptomatic end-stage disease**,** although functional outcomes can be poor and the lifespan of prostheses is limited.[16]

At every stage of the disease, a patient-centered approach suggests that the patient actively participates in the creation of the treatment plan and timely, well-informed decision-making. Patient education, physical activity, therapeutic exercise, and weight control for patients who are overweight or obese form the cornerstone of treatment. In daily patient care, self-care by the patient and their family is essential. Physical therapies, walking sticks, and other technical aids, as well as basic analgesics, opium alkaloids, and anti-inflammatory medications, have proven to be effective in reducing pain, enhancing physical function, and improving quality

of life. Their use is also clearly indicated in the treatment of osteoarthritis. When certain patients' therapeutic objectives are not met, conservative surgery and joint replacement are recommended.[17]

5 Rheumatoid arthritis



Rheumatoid arthritis (RA) occurs in about 5 per 1000 people and can lead to severe joint damage and disability. Significant progress has been made over the past 2 decades regarding understanding of disease pathophysiology, optimal outcome measures, and effective treatment strategies, including the recognition of the importance of diagnosing and treating RA early.

A chronic inflammatory illness, rheumatoid arthritis (RA) is typified by varying extra-articular symptoms and gradual destruction to synovial-lined joints. In the early stages of the disease, tendon and bursal involvement are common and frequently clinically dominant.[18] Although RA can affect any joint, it typically affects the wrists, knee, proximal interphalangeal, metacarpophalangeal, and metatarsophalangeal joints.

RISKS ASSOCIATED[19]

- bone damage
- Fatigue
- feveret
- weight loss
- Malaise

About 25% of patients have acute or subacute RA onset, but other presentation patterns include palindromic onset, extra-articular synovitis (tenosynovitis, bursitis), polymyalgia-like onset, palindromic onset, and general symptoms (malaise, fatigue, fever, weight loss). While the polymyalgic-like onset may be clinically identical to polymyalgia rheumatica in older

people, the palindromic onset is defined by recurring bouts of oligoarthritis with no residual radiologic damage. Symmetric erosive illness is a hallmark of RA. The distal interphalangeal, sacroiliac, and lumbar spine joints are rarely afflicted, though any joint, including the cricoarytenoid joint, may be. In the morning, the symptoms of synovitis are very noticeable. A common symptom of RA is morning stiffness in and around the joints that lasts for at least an hour before getting better. Since it is a subjective symptom, the patient must be thoroughly educated on the distinction between stiffness and pain.[[20]

Other disease/disorder associated with bones/joints

Disease/Disorder	Associated with	Definition
Gout	Inflammatory arthritis caused by the accumulation of uric acid crystals	An accumulation of uric acid in the body causes gout, a form of inflammatory arthritis that frequently affects the big toe and causes painful, inflamed joints.[21]
Osteonecrosis	Often affects the hip and can lead to joint collapse	Avascular necrosis, another name for osteonecrosis, is the loss of bone tissue brought on by a shortage of blood flow, which may result in joint injury and bone collapse.[22]
Osteomyelitis	Infection of bone can results from surgery or spread from other areas of the body	Osteomyelitis is a bacterial infection of the bones that can be either acute or chronic. If treatment is not received, it can cause pain, inflammation, and even irreversible bone destruction.[23]
Osteogenesis Imperfecta	Known as brittle bone disease, genetic disorder results in fragile bones that break easily due to defect in collagen production	A hereditary condition called osteogenesis imperfecta (OI), sometimes referred to as brittle bone disease, makes bones brittle and prone to breaking, frequently with little to no damage. The phrase "osteogenesis imperfecta" literally translates to "imperfect bone formation.[24]
X linked hypophosphatemia	Genetic condition causing low phosphate levels, leading to weak bones and rickets like symptoms	A uncommon hereditary condition called X-linked hypophosphatemia (XLH), sometimes referred to as X-linked hypophosphatemic rickets, is characterized by low blood phosphorus levels brought on by aberrant kidney processing, which can cause issues with bones and teeth.[25]

Plants which are related to bone /joints disease/disorder

1 Cassia Occidentalis

Cassia occidentalis is a regularly used plant that is extensively dispersed. Alkaloids, anthocyanosides, phenolics, proteins, phlobatannins, steroids, tannins, flavonoids, anthroquinone, saponins, terpenes, resins, balsams, amino acids, carbohydrates, sugars, and cardiac glycosides were among the several chemical groups it contains. Numerous pharmacological benefits of *Cassia occidentalis* included wound healing, antibacterial, anthelmintic, insecticidal, antioxidant, antianxiety, antidepressant, and antimutogenic antidiabetic properties.[26]

It exhibit its property by:

Mass cell degranulation inhibition which is crucial in reducing allergic and inflammatory responses[27]

⬇

It stablizes HRBC membranes, which helps in preventing heat and hypotonic induced lysis, thereby indicating lysis, thereby indicating anti-inflammatory activity.

⬇

Carrageenan induced inflammation reduction: The extract significantly reduces carrageenan induced paw edema in mice, further supporting its anti inflammatory extracts(28)

2 Devil's Claw (Harpagophytum Procumbens)

Devil's claw contains several active constituents but the most notable are iridoid glycosides, particularly harpagoside and harpagide. These compounds are believed to have strong anti-inflammatory and analgesic properties, contributing to the plant's traditional use in treating conditions like arthritis ,muscle pain, and inflammation.[29]

Other bioactive compounds include phenolic glycosides, flavonoids, phytosterols, and amino acids.

Devil's claw extracts inhibit the release of proinflammatory cytokines such as TNFα, IL-6 and IL-1β as well as prostaglandin E_2(PEG_2) which are key players in inflammation.[30]

⬇

The extract prevents the activation of the AP-1 transcription factor, which is involved in the expression of genes related to inflammation.

⬇

Harpagoside has been found to supress the action of cytokines, molecules known to promote inflammation.

Devil's claw extracts inhibit the expression of cyclooxygenase-2 (COX-2), an enzyme involved in the production of pro-inflammatory prostaglandins.[30]

3 Willow bark

Willow bark contains Salicin as its primary active constituent. Salicin is metabolized in the body into salicylic acid, which is responsible for its anti-inflammatory and analgesic effects. In addition to salicin, *willow bark* also contains polyphenols and flavonoids, which contribute to its anti-oxidant and anti-inflammatory properties by inhibiting pro-inflammatory cytokines, COX-2, and NF-Kb pathways.[31]

This inhibits pro-inflammatory cytokines such as TNFα and COX-2 which are involved in inflammation[32][33]

Which enhances the anti-oxidant activity through polyphenols and flavonoids, which help reduce oxidative stress and inflammation.(34)

⬇

This reduces leukocytic infiltration by suppressing the migration of white blood cells to the site of inflammation.[34]

4 Cissus quadrangularis

Cissus quadrangularis (Hadjod) explore its potential for bone healing, pain relief, anti-inflammatory, and antioxidant effects, with studies examining its phytochemical composition includes flavonoids(quercetin, genisten, daidzein),stilbenes(quadrangularin-A, resveratrol, piceatannol), triterpenoids (friedelin, α/β-amyrins), phtosterols, iridoids and vitamins and minerals[35] [36] [37]

Inhibition of Pro-inflammatory cytokines the plant extract reduces the expression of cytokines like TNF-α, IL-1β, AND IL-6 which are key mediators of inflammation.[38]

⬇

The suppression of matrix metalloproteinases (MMPs) it inhibits MMPs which degrade cartilage and exacerbate inflammation in conditions like arthritis(39)

⬇

Cissus quadrangularis downregulates the p38 MAPK signalling pathway, reducing inflammatory responses and promoting chondrocyte survival and cartilage regeneration.

⬇

It inhibits both cyclooxygenase (COX) and lipoxygenase pathways, reducing prostaglandin and leukotriene production, which are involved in acute inflammation.[40]

The extract decreases oxidative stress markers, further mitigating inflammation.[41]

5 Tripterygium wilfordii

Tripterygium wilfordii contains several acc including terpenoids(triptolide, celastrol, wilforlide A, sesquiterpenes) which have anti-inflammatory and immunosuppressive along immune suppressive properties, alkaloids including sesquiterpene and indole alkaloids which have anti-inflammatory,antiviral and immunosuppressive properties,glycosides, flavonoids, ligans (42)

This down regulates the expression of pro-inflammatory cytokines like IL-6 and IL-17 by inhibiting the IL-6/STAT 3 pathway, which is crucial in reducing inflammation in conditions like colitis[43]

⬇

Tripterygium wilfordii reduces the differentiation of T helper 17 (Th17) cells, which are involved in inflammatory responses, and promotes the differentiation of regulatory T cells (Tregs), enhancing immune regulation

⬇

Active constituents such as triptolide and celastrol exhibit potent anti-inflammatory effects by inhibiting COX-2 and other inflammatory mediators, contributing to its efficacy in treating autoimmune diseases like rheumatoid arthritis and systemic lupus erythematosus.[44]

⬇

The plant acts synergistically on multiple signaling pathways, including MAPK and PI3K/AKT, to alleviate inflammation and maintain immune homeostasis.[45]

Other Plants

List Of Plants	Its action	ACC
Astragalus membranaceus	Acts on inflammation by reducing pro-inflammatory cytokines like TNF-α, inhibiting COX-2 and suppressing NF-KB activation	Polysaccharides, triterpenoids (like astragalosides), isoflavones (like kumatakenin, calycosin, and formononetin), and their glycosides and malonates are among the chemical components of the roots (Radix Astragali) The saponin cycloastragenol is present in it(46)(47).
Curcuma domestica	*Curcuma domestica* acts on inflammation by inhibiting inflammatory mediators such as IL-1β, IL-6, TNF-α, and NF-κB, while also suppressing enzymes like COX-2 and iNOS. Additionally, it modulates immune cells, particularly dendritic cells and T cells, helping to maintain immune homeostasis and reduce inflammatory responses.	The main active ingredients that were separated from C. longa were curcumin, curcuminoids, ar-turmerone, α-turmerone, β-turmerone, and (z) β-ocimene, α-phellantrene, terpinolene, 1,8-cinceole, undecanol, and p-cymene(48).
Erythrina Fusca	*Erythrina fusca* exhibits anti-inflammatory activity by reducing inflammatory mediators such as COX-2, PGE2, TNF-α, IL-1β, and IL-6, and significantly inhibiting paw edema in carrageenan-induced inflammation models, likely due to its bioactive compounds like flavonoids and phenolics.	Erysotrine, erythraline, erysodine, erysovine, and erysopine are some of the prominent alkaloids found in Erythrina fusca, along with flavonoids, pterocarpans, and other substances(49).

Moringa oleifera	*Moringa oleifera* acts on inflammation by suppressing the expression of pro-inflammatory cytokines such as IL-6, IL-1, TNF-α, and NF-κB, thereby inhibiting inflammatory pathways. Its bioactive compounds, including polyphenols and flavonoids, contribute to these anti-inflammatory effects, making it beneficial for conditions like inflammatory bowel disease.	high concentrations of fatty acids, amino acids, minerals, vitamins, and other bioactive substances like carotenoids, phenols, and flavonoids[50][51].
Frankincense	*Frankincense*, derived from Boswellia resin, acts on inflammation by inhibiting 5-lipoxygenase (5-LOX) and cyclooxygenase enzymes, reducing leukotriene synthesis, and modulating immune responses. Its active compound, boswellic acid, reprograms inflammatory enzymes to produce anti-inflammatory substances.	*acid resins (boswellic acids), gum, and essential oils, including terpenes like α-pinene and limonene*[52].
Tinospora cordifolia	*Tinospora cordifolia* acts on inflammation by suppressing pro-inflammatory cytokines like IL-6, IL-1β, TNF-α, and IL-17, inhibiting NF-κB activation and COX-2 expression, and reducing p38 MAPK phosphorylation. These mechanisms contribute to its anti-inflammatory effects in models of arthritis and carrageenan-induced inflammation	The shrub contains various classes of compounds such as alkaloids, glycosides, aliphatic compounds, polyphenols, lactones, steroids, and terpenoids[53][54].
Zingiber Officinale	*Zingiber officinale (*ginger) acts on inflammation by inhibiting NF-κB activation, reducing pro-inflammatory cytokines like TNF-α, IL-6, and IL-1β, and suppressing COX-2 and PGE2 production. Its active compounds, such as gingerol, shogaol, and zingerone, also provide antioxidant effects that complement its anti-inflammatory properties	monoterpenoids, sesquiterpenoids, phenolic compounds and its derivatives as well as aldehydes, ketones, alcohols, and esters[55][56].

DISCUSSION

The discussion surrounding diseases related to bones particularly osteoporosis and other metabolic bone disorders, highlights the significant role that herbal remedies can play in their management. As traditional medicine continues to gain recognition for its holistic approach,

various plants have emerged as effective alternatives or complements to conventional treatments.

Research indicates that many herbal remedies possess properties that can positively influence bone health. Medicinal plants has been shown to enhance bone mineral density and improve overall bone metabolism by modulating this activity, thereby reducing bone resorption. Similarly herbs like *cissus quadrangularis, Devil's claw, willow bark* through their active compounds, which promote osteoblast differentiation and inhibit osteoclast formation.

CONCLUSION

Despite the promising results, it is essential to approach the integration of herbal remedies with caution with caution. While many plants have demonstrated efficacy in preclinical trials are necessary to establish their safety and effectiveness in diverse populations.

The exploration of herbal remedies for bone health presents a valuable opportunity to enhance treatment options for individuals suffering from bone diseases. By combining traditional knowledge with modern scientific validation, there is potential not only to improve patient outcomes but also to faster a more integrative approach to healthcare. Traditional medicine has long utilized various plants to aid in bone healing, demonstrating their efficacy in reducing pain, inflammation and promoting recovery.

The integration of ethnobotanical research could pave the way for novel treatments that leverage the benefits of these natural compounds.

ABBREVATION USED:

TCM: Traditional Chinise Medicine
BHC: Bone Health Clinic
BMD: Bone Mineral Density
OA: Osteoarthritis
RA: Rheumatoid arthritis
ACC: Active constituents
PGE2: Prostaglandin E2
COX2: Cyclooxygenase-2
IL: Interleukin
NF-Kb: Nuclear factor kappa light chain enhancer of activated B cells

TNF: Tumor Necrosis Factor

LOX: Lipoxygenase enzyme

T Cell: Thymus derived lymphocytes

INOS: Inducible nitric oxide synthase

MAPK: Mitogen Activated Protein Kinases

P13K: Phosphatidylinostitol 3-kinase

AKT: Protein kinase B

MMPS: Matrix Metalloproteinases

REFERENCES

1. Han J, Lv X, Zhao Z, Liu Y, Wan D. Natural products, medicinal foods, herbal medicines, bone metabolism diseases, bone-related tumor diseases. Frontiers in Pharmacology, 2024 May 15; 15: 1421115.
2. Karimi SM, Bayat M, Rahimi R. Plant-derived natural medicines for the management of osteoporosis: A comprehensive review of clinical trials. Journal of Traditional and Complementary Medicine, 2024 Jan 1; 14(1): 1-8.
3. Seyok T, Collins JE, Hodys C, Erikson SJ, Perez Menendez S, Earp BE, Charles JF. Factors Associated With Nonattendance for Osteoporosis Evaluation Following Fragility Fracture. Journal of Osteoporosis, 2024; 2024(1): 5602020.
4. Frost ML, Blake GM, Fogelman I. Quantitative ultrasound and bone mineral density are equally strongly associated with risk factors for osteoporosis. Journal of Bone and Mineral Research, 2001 Feb 1; 16(2): 406-16.
5. Karasik D, Ferrari SL. Contribution of gender-specific genetic factors to osteoporosis risk. Annals of human genetics, 2008 Sep; 72(5): 696-714.
6. Rosa J. Osteomalacie [Osteomalacia]. Vnitr Lek. 2023 Summer; 69(4): 254-260. Czech. doi: 10.36290/vnl.2023.048. PMID: 37468295.
7. Stanbury SW. Osteomalacia. Clinics in Endocrinology and Metabolism, 1972 Mar 1; 1(1): 239-66.
8. Dent CE, Stamp TC. Hypophosphataemic osteomalacia presenting in adults. QJM: An International Journal of Medicine, 1971 Apr 1; 40(2): 303-29.
9. Morgan B. Osteomalacia, renal osteodystrophy, and osteoporosis. (No Title). 1973.
10. Bhan A, Rao AD, Rao DS. Osteomalacia as a result of vitamin D deficiency. Endocrinol Metab Clin North Am., 2010 Jun; 39(2): 321-31, table of contents. doi: 10.1016/j.ecl.2010.02.001. PMID: 20511054.

11. Appelman-Dijkstra NM, Papapoulos SE. Paget's disease of bone. Best Pract Res Clin Endocrinol Metab., 2018 Oct; 32(5): 657-668. doi: 10.1016/j.beem.2018.05.005. Epub 2018 May 26. PMID: 30449547.
12. Kravets I. Paget's Disease of Bone: Diagnosis and Treatment. Am J Med., 2018 Nov; 131(11): 1298-1303. doi: 10.1016/j.amjmed.2018.04.028. Epub 2018 May 10. PMID: 29752905.
13. Reddy SV, Menaa C, Singer FR, Demulder A, Roodman GD. Cell biology of Paget's disease. Journal of bone and mineral research, 1999 Nov 1; 14(S2): 3-8.
14. Krasnokutsky S, Samuels J, Abramson SB. Osteoarthritis in 2007. Bulletin of the NYU hospital for joint diseases, 2007 Oct 1; 65(3).
15. Sinusas K. Osteoarthritis: diagnosis and treatment. American family physician, 2012 Jan 1; 85(1): 49-56.
16. Glyn-Jones S, Palmer AJ, Agricola R, Price AJ, Vincent TL, Weinans H, Carr AJ. Osteoarthritis. Lancet, 2015 Jul 25; 386(9991): 376-87. doi: 10.1016/S0140-6736(14)60802-3. Epub 2015 Mar 4. PMID: 25748615
17. Vargas Negrín F, Medina Abellán MD, Hermosa Hernán JC, de Felipe Medina R. Tratamiento del paciente con artrosis [Treatment of patients with osteoarthritis]. Aten Primaria. 2014 Jan; 46 Suppl 1(Suppl 1):39-61. Spanish. doi: 10.1016/S0212-6567(14)70043-5. PMID: 24467960; PMCID: PMC8171423.
18. Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. European journal of radiology, 1998 May 1; 27: S18-24.
19. Ragan C, Farrington E. The clinical features of rheumatoid arthritis: prognostic indices. Jama., 1962 Aug 25; 181(8): 663-7.
20. Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. European journal of radiology, 1998 May 1; 27: S18-24.
21. Busso N, So A. Gout. Mechanisms of inflammation in gout. Arthritis research & therapy, 2010 Apr; 12: 1-8.
22. Pavelka K. Osteonecrosis. Best Practice & Research Clinical Rheumatology, 2000 Jun 1; 14(2): 399-414.
23. Schmitt SK. Osteomyelitis. Infectious Disease Clinics, 2017 Jun 1; 31(2): 325-38.
24. Rowe DW. Osteogenesis imperfecta. Principles of bone biology, 2002 Jan 1: 1177-93.
25. Harrell RM, Lyles KW, Harrelson JM, Friedman NE, Drezner MK. Healing of bone disease in X-linked hypophosphatemic rickets/osteomalacia. Induction and maintenance

with phosphorus and calcitriol. The Journal of clinical investigation, 1985 Jun 1; 75(6): 1858-68.

26. Sreejith G, Latha PG, Shine VJ, Anuja GI, Suja SR, Sini S, Shyamal S, Pradeep S, Shikha P, Rajasekharan S. Anti-allergic, anti-inflammatory and anti-lipidperoxidant effects of Cassia occidentalis Linn.
27. Al-Snafi AE. THE THERAPEUTIC IMPORTANCEOF CASSIA OCCIDENTALIS-AN OVERVIEW.
28. Sreejith G, Latha PG, Shine VJ, Anuja GI, Suja SR, Sini S, Shyamal S, Pradeep S, Shikha P, Rajasekharan S. Anti-allergic, anti-inflammatory and anti-lipidperoxidant effects of Cassia occidentalis Linn.
29. Gxaba N, Manganyi MC. The fight against infection and pain: Devil's claw (Harpagophytum procumbens) a rich source of anti-inflammatory activity: 2011–2022. Molecules, 2022 Jun 6; 27(11): 3637.
30. Fiebich BL, Muñoz E, Rose T, Weiss G, McGregor GP. Molecular targets of the antiinflammatory Harpagophytum procumbens (devil's claw): inhibition of TNFα and COX-2 gene expression by preventing activation of AP-1. Phytotherapy Research, 2012 Jun; 26(6): 806-11.
31. Ishikado A, Sono Y, Matsumoto M, Robida-Stubbs S, Okuno A, Goto M, King GL, Blackwell TK, Makino T. Willow bark extract increases antioxidant enzymes and reduces oxidative stress through activation of Nrf2 in vascular endothelial cells and Caenorhabditis elegans. Free Radical Biology and Medicine, 2013 Dec 1; 65: 1506-15.
32. Bonaterra GA, Heinrich EU, Kelber O, Weiser D, Metz J, Kinscherf R. Anti-inflammatory effects of the willow bark extract STW 33-I (Proaktiv®) in LPS-activated human monocytes and differentiated macrophages. Phytomedicine, 2010 Dec 1; 17(14): 1106-13.
33. Lin CR, Tsai SH, Wang C, Lee CL, Hung SW, Ting YT, Hung YC. Willow bark (Salix spp.) used for pain relief in arthritis: A meta-analysis of randomized controlled trials. Life, 2023 Oct 14; 13(10): 2058.
34. Khayyal MT, El-Ghazaly MA, Abdallah DM, Okpanyi SN, Kelber O, Weiser D. Mechanisms involved in the anti-inflammatory effect of a standardized willow bark extract. Arzneimittelforschung, 2005 Nov; 55(11): 677-87.
35. Sundaran J, Vasanthi M, Kamalapathy M, Bupesh G, Sahoo U. A short review on pharmacological activity of Cissus quadrangularis. Bioinformation, 2020 Aug 31; 16(8): 579.

36. Singh G, Rawat P, Maurya R. Constituents of Cissus quadrangularis. Natural product research, 2007 May 20; 21(6): 522-8.
37. Jain S, Kohli S. Isolation and evaluation of chemical constituents of Cissus quadrangularis. In3rd International Conference and Exhibition on Pharmacognosy, Phytochemistry & Natural Products, 2015 Oct 26.
38. Kumar R, Gupta YK, Singh S, Arunraja S. Cissus quadrangularis attenuates the adjuvant induced arthritis by down regulating pro-inflammatory cytokine and inhibiting angiogenesis. Journal of Ethnopharmacology, 2015 Dec 4; 175: 346-55.
39. Kanwar JR, Samarasinghe RM, Kumar K, Arya R, Sharma S, Zhou SF, Sasidharan S, Kanwar RK. Cissus quadrangularis inhibits IL-1β induced inflammatory responses on chondrocytes and alleviates bone deterioration in osteotomized rats via p38 MAPK signaling. Drug design, development and therapy, 2015 Jun 5: 2927-40.
40. Panthong A, Supraditaporn W, Kanjanapothi D, Taesotikul T, Reutrakul V. Analgesic, anti-inflammatory and venotonic effects of Cissus quadrangularis Linn. Journal of ethnopharmacology, 2007 Mar 21; 110(2): 264-70.
41. Kumar R, Gupta YK, Singh S, Arunraja S. Cissus quadrangularis attenuates the adjuvant induced arthritis by down regulating pro-inflammatory cytokine and inhibiting angiogenesis. Journal of Ethnopharmacology, 2015 Dec 4; 175: 346-55.
42. Wang L, Wang Z, Yang Z, Yang K, Yang H. Study of the active components and molecular mechanism of tripterygium wilfordii in the treatment of diabetic nephropathy. Frontiers in Molecular Biosciences, 2021 Jun 7; 8: 664416.
43. Song CY, Xu YG, Lu YQ. Use of Tripterygium wilfordii Hook F for immune-mediated inflammatory diseases: progress and future prospects. Journal of Zhejiang University-Science B., 2020 Apr; 21(4): 280-90.
44. Hong Y, Wang D, Qian H, Jiang X, Wang Y, Liang X, Gao S, Hua C. Exploring the molecular mechanism of Tripterygium Wilfordii Hook F in treating systemic lupus erythematosus via network pharmacology and molecular docking. Clinical Rheumatology, 2025 Feb 11: 1-21.
45. Wang Z, Xu Y, Liang S. Network pharmacology and molecular docking analysis on the mechanism of Tripterygium wilfordii Hook in the treatment of Sjögren syndrome. Medicine, 2024 Apr 5; 103(14): e37532.
46. D'Avino D, Cerqua I, Ullah H, Spinelli M, Di Matteo R, Granato E, Capasso R, Maruccio L, Ialenti A, Daglia M, Roviezzo F. Beneficial effects of Astragalus membranaceus

(Fisch.) Bunge extract in controlling inflammatory response and preventing asthma features. International Journal of Molecular Sciences, 2023 Jun 30; 24(13): 10954.

47. Zhang X, Liang T, Yang W, Zhang L, Wu S, Yan C, Li Q. Astragalus membranaceus injection suppresses production of interleukin-6 by activating autophagy through the AMPK-mTOR pathway in lipopolysaccharide-stimulated macrophages. Oxidative Medicine and Cellular Longevity, 2020; 2020(1): 1364147.
48. Peng Y, Ao M, Dong B, Jiang Y, Yu L, Chen Z, Hu C, Xu R. Anti-inflammatory effects of curcumin in the inflammatory diseases: status, limitations and countermeasures. Drug design, development and therapy, 2021 Nov 2: 4503-25.
49. Nhung TT, Quoc LP. Exploring the therapeutic potential of ethanol extract of Erythrina fusca Lour. roots as an analgesic, antipyretic, and anti-inflammatory agent in experimental animals.
50. Chiș A, Noubissi PA, Pop OL, Mureșan CI, Fokam Tagne MA, Kamgang R, Fodor A, Sitar-Tăut AV, Cozma A, Orășan OH, Hegheș SC. Bioactive compounds in Moringa oleifera: mechanisms of action, focus on their anti-inflammatory properties. Plants, 2023 Dec 20; 13(1): 20.
51. Xu YB, Chen GL, Guo MQ. Antioxidant and anti-inflammatory activities of the crude extracts of Moringa oleifera from Kenya and their correlations with flavonoids. Antioxidants, 2019 Aug 9; 8(8): 296.
52. Efferth T, Oesch F. Anti-inflammatory and anti-cancer activities of frankincense: Targets, treatments and toxicities. InSeminars in cancer biology 2022 May 1 (Vol. 80, pp. 39-57). Academic Press.
53. Hussain L, Akash MS, Ain NU, Rehman K, Ibrahim M. The analgesic, anti-inflammatory and anti-pyretic activities of Tinospora cordifolia. Advances in Clinical and Experimental Medicine., 2015; 24(6): 957-64.
54. Philip S, Tom G, Vasumathi AV. Evaluation of the anti-inflammatory activity of Tinospora cordifolia (Willd.) Miers chloroform extract–a preclinical study. Journal of Pharmacy and Pharmacology, 2018 Aug; 70(8): 1113-25.
55. Boarescu I, Boarescu PM, Pop RM, Bocșan IC, Gheban D, Bulboacă AE, Buzoianu AD, Bolboacă SD. Zingiber officinale root capsule extract synergistically enhance the anti-inflammatory effects of diclofenac sodium in experimental acute inflammation. International Journal of Molecular Sciences, 2024 Feb 1; 25(3): 1781.

56. Szymczak J, Grygiel-Górniak B, Cielecka-Piontek J. Zingiber officinale roscoe: The antiarthritic potential of a popular spice—preclinical and clinical evidence. Nutrients, 2024 Jan; 16(5): 741.