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A review on common Ayurvedic herbs as adjuvant therapy in Osteoporosis for Children

Ravi Dhaliya[1], Aman Kumar[2]

[1]*Ph.D Scholar, Assistant professor, Dept of Agada Tantra, Babe ke Ayurvedic Medical College & Hospital, Daudhar, Moga, Punjab, India.*

[2]*Post Graduate Scholar, Dept of Kumarbhritaya, Babe ke Ayurvedic Medical College & Hospital, Daudhar, Moga, Punjab, India.*

ABSTRACT

Osteoporosis is a phenomenon where weaken and porous bones are formed by decreasing the bone density. Decreased bone mass increases the risk of bone and joint related disorder which is most frequent health illness among the women, old aged peoples as well as paediatric population. The osteoporosis in children is not directly mentioned in Ayurveda but general principle of management is usually followed for children. Further *Acharya Charak* has mentioned about the general principles for the treatment of diseases in children and advised the use of Herbs with sweet taste (*Madhur Rasa)*, Tasty, Palatable and Good smelling medicines with milk in small doses. He says that diseases of adults, also affect the children as *Dosha* and *Dushya* are the same and hence their treatment and herbs should be similar with certain modification in dosage. *Asthi Kshaya and Asthi Saushariya* are the two conditions explained in Ayurveda for decrease in bone tissue and later as porous bones which allies with the modern condition like osteoporosis in which the bones become porous, brittle and weak. It is bone health is been directly depended upon *Vataja Dosha* health status as well as *Dhatu Poshan* (Nutrition of tisssues). The line of treatment adopted mainly is always a holistic, multidimensional, balancing three doshas, improving *Agni* (metabolism) and functioning and cleaning of *Srotas* (channels) and also with specific herbs which work directly on *Asthi Dhatu* (Bone) like *Asthi Shrinkala*. Principle of treatment adopted is always by *Shaman Aushadhis* (pacifying herbs and formulations) and *Shodhana* (bio-purification) by *Pancharkarma*. Thus, it prevents *Asthi Dhatu Kshaya* (loss) and strengthens the *Asthi Dhatu* – bone tissues. All these drugs are easily available, simple for administration and devoid of any adverse reactions. This article will be useful for food and drug companies to produce safe herbal products for children.

Key words: *Ayurveda, Asthi Dhatu, Arjun, Asthishrinkala, Vata Dosha, Osteoporosis.*

INTRODUCTION

Osteoporosis is a phenomenon where weaken and porous bones are formed by decreasing the bone density. Decreased bone mass increases the risk of bone and joint related disorder which is most frequent health illness among the women, old aged peoples as well as paediatric population and improving bone intensity will definitely reduce these bone related disorders. It is a skeletal condition of compromised bone strength accompanied by an increased risk of fracture.[1] It is a result of low calcium, protein, or hereditary causes. Thus, the body does not form sufficient bone mass, or reabsorbs existing bones into the body. Osteoporosis is a disease that is characterized by low bone mass, deterioration of bone tissue, and disruption of bone microarchitecture: it can lead to compromised bone strength and an increase in the risk of fractures[2] Bone strength reflects both bone density and bone quality. According to the International Society for Clinical Densitometry, osteoporosis in the paediatric population is defined as the presence of both a clinically significant fracture history and a bone

Address for correspondence:
Dr. Ravi Dhaliya
Ph.D Scholar, Assistant professor, Dept of Agada Tantra, Babe ke Ayurvedic Medical College & Hospital, Daudhar, Moga, Punjab, India.
E-mail: drravidhaliya@gmail.com

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mineral density (BMD) Z-score ≤ -2.0. A clinically significant fracture history includes: Two or more long bone fractures by the age of 10 years. Three or more long bone fractures by the age of 19 years.[3]

Possible Aetiology

Paediatric bone health is determined by genetics, diet, mobility, and exercise, but it can also be affected by medications and chronic disease. Although a diagnosis of osteoporosis may inspire thoughts of the geriatric population, some children are also vulnerable. Physicians providing care to both paediatric and adult populations should particularly note the major differences in the diagnosis and management of osteoporosis in children.[4]

1. There are many possible causes for OP in children - most are secondary to other illnesses or treatments, especially glucocorticoid (GC) use.
2. The most common primary bone disorder leading to OP is osteogenesis imperfecta (OI), a structural genetic defect in the quantity or quality of bone type 1 collagen production. Primary osteoporosis in the paediatric population occurs due to an intrinsic skeletal defect of genetic or idiopathic origin. Osteogenesis Imperfecta (OI) is the most common condition, with an incidence of 1 in 25,000 births[5] Osteogenesis Imperfecta has several subtypes ranging from mild forms to that which causes intrauterine foetal death. The family history, the blue, purple, or Gray sclera commonly found in OI, radiographic findings, and in some cases, bone biopsy help determine the diagnosis. Other primary bone causes of OP include idiopathic juvenile osteoporosis (IJO).[6]
3. Secondary osteoporosis in children is due to either the effects of a chronic disease process on the skeleton or its treatment. With medical advances resulting in improved survival rates and long-term outcomes, complications such as secondary osteoporosis are on the rise in children with chronic diseases. In healthy children, 80% of fractures occur in the upper extremities. Risk factors for fractures include age, gender, previous fractures, genetic predisposition, poor nutrition, total body mass, vigorous physical activity and, equally, lack of physical activity.[7]
4. In non-ambulatory, disabled children, 70% of fractures are in the lower extremities, with over 50% occurring at the distal femur. Prevalence of osteoporosis in children with cerebral palsy (CP) is up to 50%. CP) is the most common chronic paediatric disability associated with paediatric osteoporosis. The prevalence of osteoporosis in children with CP is up to 50%, and the annual fracture rate in patients with CP is approximately 5%, double that of a normal age-matched population.[8]
5. Neurological disorder has a high risk of developing diseases with low done density and number of risk factors poor nutrition, decreased exposure to sunlight can cause low bone density mineral density.
6. Calcium is absorbed into the body and in some circumstances, bone loses some part of calcium from it (called bone re-absorption). As child grow, the bones naturally become thinner. The changes start to happen in middle age itself. There should always be a balance between bone formation and bone re-absorption by the body which is quite normal before we attain middle age, i.e., during active growth. After childhood age, the more of the existing bone cells are reabsorbed by the body in comparison to the new bone being made. This means to tell that as we age further, the bone formation will become less in comparison to bone re-absorption.

Some important causes for Osteoporosis / osteopenia

- Genetics (family disposition to osteopenia and / or osteoporosis, family history of early bones and other genetic disorders)
- Hormonal (decreased oestrogen or testosterone)
- Eating disorders and metabolism problems that do not allow the body to take in and use enough minerals and vitamins

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- Chemotherapy or certain medicines (ex. corticosteroids and anti-seizure medications)
- Mal-absorption due to conditions like celiac sprue
- Chronic inflammation due to medical conditions such as Rheumatoid arthritis
- Exposure to radiation
- Being thin (Thin frame of body)
- Being white or Asian
- Limited or less physical activity (Immobility)
- Excessive beverage drinks

Diagnosis

The diagnosis of osteoporosis in children is different than in adults. For adults, a dual energy x-ray absorptiometry (DXA) or bone mineral densitometry (BMD) test with a *t*-score less than −2.5 standard deviations from the mean indicates osteoporosis. For children, it is more complex. DXA scans can be performed on children, but *t*-score measures are not reported. Instead, a BMD *z*-score utilizing standardized bone density with respect to age, gender, bone age, height, and weight is needed.[9]

Ayurvedic View

The osteoporosis in children is not directly mentioned in Ayurveda but general principle of management is usually followed for children. Further *Acharya Charaka* has mentioned about the general principles for the treatment of diseases in children and advised the use of sweet, tasty, palatable and good smelling medicines with milk in small doses. He says that diseases of adults, also affect the children as *Dosha* and *Dushya* are the same and hence their treatment should be similar with certain modification in dosage.[10]

Formation of *Asthi Dhatu* - Bone System

Ayurveda a holistic traditional and oldest medicinal system of India which describe herbal treatment approach. Osteo means bones and is the fifth dhatu in the body as per Ayurveda. *Asthi* i.e., the bone gives the solid structure to the body. The formation of the bones of the body, teeth are formed through the *Dhatu Poshan* (nutrition) from *Ahara Rasa (*food). In the process of *Dhatus* formation after the digestion by *Agni* forms two *Dhatus* i.e., *Sthayi Dhatu* (nutrition to *Dhatu* which is already present in body) and *Poshya Dhatu* (precursors for next *Dhatu)* and produces *Kitta Bhaga* (waste product). All the seven *Dhatus* are formed in sequence like from *Rasa Dhatu* to *Rakta* to *Mamsa Dhatu* to *Meda Dhatu* to *Asthi Dhatu* to *Majja Dhatu* to *Shukra Dhatu*. Thus, formation of *Asthi Dhatu* depends upon previous *Dhatu* (precursor from *Meda Dhatu*) and in this *Dhatu* formation process, produces the waste product (*Mala*) i.e., hair and nails.

Pathophysiology

Bones are dynamic living tissue; which constantly decaying and rebuilding. The process of rebuilding is slow rather than the decaying. If the *Jatharagni* (digestive fire) and *Bhutagni* (particularly *Parthivagni*) are affected than there will be lack of *Poshana* of *Asthi* means less nutrition supply to bones which leads to *Asthi Kashaya* or Osteoporosis. *Vata Dosha* is commonly located in Bones and the bone density of *Vata* body type people commonly get affected in *Vata* phage of life i.e., after 45-50 years.

Vata Dosha and *Asthi-Vata Dosha* contributes largely for occurrence of *Asthi* related diseases because of unique relationship of *Vata* and *Asthi*. *Gambhira Dhatu* (deep-seated tissue), *Svabhava Balapravritta Vyadhi* (natural phenomenon due to old age) and *Bhedawastha* (complicated stage) make this disease *Asadhya* (incurable). Management of established bone porosity is difficult. Hence, prevention of the condition becomes all important. This disease can become *Yapya* by intervention at proper level, followed with *Pathyapathaya*. Prevention of *Asthisaushirya* should be commenced at the level of *Asthi-Majjakshaya*, which is precursor of *Asthisaushirya* (bone porosity).[11]

Treatment Approach

To nourish the *Asthi Dhatu* it is important to nourish previous four *Dhatus* i.e., *Rasa* - *Plasma*, *Rakta* - *Blood*, *Mamsa* - Muscles/flesh, *Medha* - Adipose, *Asthi* - Bone. Bones are formed from the nutrient supply by *Medha Dhatu* through *Asthivaha* Channels

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(*Srotas*). *Vayu, Agni & Prithvi Mahabhutas* bring compactness and hardness among the nutrients, which form *Asthi* /Bones. *Asthi* give strength and structure to body like tree stem as all muscles, tendons, ligaments etc. are attached to *Asthis*.

Ayurveda recommends holistic treatment for osteoporosis which involves avoiding factors that lead to the vitiation of *Vata Dosha* that ultimately lead to worsening of the condition and second medicinal approach with principal management of treatment.

Shamana therapy

It is a palliative therapy to normalize the *Doshas* rather than expelling them from the body. *Shamana* can be external treatment (*Bahya Samshamana*) like application of herbal pastes, showering with medicinal liquids, tub bath in medicinal liquids, herbal oil massage, oil pooling over the head, oral rinsing, gargling, oil pulling etc. It can also be mild internal treatment (*Aabhyantara Samshamana*) like medicines that *Dosha* pacifying, digestives, fat scraping procedures, aphrodisiacs, anti-inflammatory, anti-bacterial, antioxidants, anti-toxins to nullify poisonous effects, immune modulation, bone strengthening etc.[12],[13]

Arjun - Terminalia arjuna

Terminalia arjuna (Roxb.) Wight & Arn. bark is considered to be the most important constituent from medicinal point of view. The ethanol extract contains tannins, a glycoside, a large quantity of carbonates of calcium and smaller amounts of aluminium and magnesium.[14],[15] The bark of this plant is well known for their bone remineralization of properties and extensively used to treat osteoporosis and their bone related disorder. Articular elastase (ELA) level in the arthritic tissue was measured as a marker for neutrophil infiltration. Terminalia arjuna bark extract administration significantly inhibited the increase in paw thickness induced by immunization with collagen as compared to CIA-control animals. Further, it attenuated the fall in tissue SOD and GSH levels and mitigated the increase in tissue nitrites and TBARS levels as compared to CIA-control animals. Tissue ELA levels, which were significantly increased in the CIA-control animals as compared to normal animals were also significantly reduced by *Terminalia arjuna* bark extract (TABE) administration. Results of the study showed the antioxidant and antiarthritic activity of *Terminalia arjuna* bark extract (TABE) in collagen-induced arthritis (CIA) in rats. We believe that TABE could find clinical application in the management of rheumatoid arthritis and associated disorders.[16]

Asthi Shrunkala (*Cissus Quadrangularis*)

Cissus. Quadrangularis acts by the stimulation of metabolism and increased uptake of the mineral's calcium, sulphur, and strontium by the osteoblasts in fracture healing. Certain amino acids such as lysine help in absorption of calcium. Cissus also contains Vitamin A and C that is effective in the formation of collagen.[17-19] The pharmacological properties of *C. quadrangularis* are antioxidant, free radical scavenging potential, antibacterial activity, antiosteoporosis activity, antitumor activity, antiulcer activity, analgesic activity, antiobesity activity, antipyretic activity, and bone fracture healing activity.[20-22] The phytoestrogen–rich fraction (IND–HE) from aerial parts of *C. quadrangularis* has shown presence of phytoestrogen–rich fraction. Treatment with IND–HE (75 and 100mg/kg) showed statistically significant increase in bone thickness, bone density and bone hardness in ovariectomised in rats. IND–HE and estrogen treatment significantly increased serum estradiol, serum vitamin D3 and serum calcium compared to control. Alkaline phosphatase was significantly reduced. Results of Histopathology studies indicated that IND–HE (75 and 100mg/kg) prevented bone loss.[23] In another experimental study, ethanol extract of *Cissus quadrangularis* at two different dose levels of 500 and 750mg/kg per day showed a definite antiosteoporotic effect.[24] The petroleum-ether extract at the dose of 500mg/kg, for 3 months reduced bone loss, as evidenced by the weight gain in femur, and also reduced the osteoclastic activity there by facilitating bone formation in experimental animals.[25] *Asthishrunkhala* contains anabolic and phytogenic steroids like Ketosteroids, sitosterol, alpha amayrin, alpha ampyrone and tetracyclic

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triterpenoids.[26] These anabolic and steroidal components showed a marked influence on fracture–healing. Ketosteroid acts as antagonists to the glucocorticoid receptor and promotes good bone health. It mobilizes fibroblast and chondroblasts to an injured tissue and enhances regeneration. The anabolic steroidal component of *Asthishrunkhala* showed a marked influence in the rate of fracture healing by influencing early regeneration of all connective tissues of mesenchyme origin, namely the fibroblasts, the chondroblasts and osteoblasts involved in the healing and quicker mineralization of the callus.[27]

Guduchi (Tinospora cordifolia (Thunb.)

Effects of alcoholic extract of *Tinospora cordifolia* on the proliferation, differentiation and mineralization of bone like matrix was studied on human osteoblast–like cells MG–63 and primary osteoblast cells isolated from femur of rats. The extract at a dosage of 25µg/ml stimulated the growth of osteoblasts, increased the differentiation of cells into osteoblastic lineage and increased the mineralization of bone like matrix on both the osteoblast model systems used in the study. Cell morphology studies clearly indicated the increase in cell numbers and absence of adverse change in the cell morphology on treatment with the extract. 21(cells SAOS–2). It was observed that ethanolic extract stimulated proliferation of osteoblasts at a dosage of 25µg/ml but, the aqueous extract showed no influence on cell proliferation. The extract also elicited pro-stimulatory effects on osteoblasts.

Probably with this insight, the fermented form of medication is recommended for therapeutic purposes in Ayurveda.) Aqueous and alcoholic extracts were evaluated for osteogenic effect using a widely employed in vitro model system for human osteoblasts (human osteoblast like cells SAOS–2). It was observed that ethanolic extract stimulated proliferation of osteoblasts at a dosage of 25µg/ml but, the aqueous extract showed no influence on cell proliferation. The extract also elicited pro-stimulatory effects on osteoblasts.[28]

Haridra (Curcuma longa)

Curcuma longa L. Curcumin is considered as a potential treatment in numerous diseases, including osteoporosis. Curcumin has been reported to be beneficial in osteoclastogenesis and osteoblast proliferation and activity in vitro.[29] Extracts prepared from *Curcuma longa* L., containing bioactive phenolic curcuminoids was evaluated for bone-protective effects in a hypogonadal rat model of postmenopausal osteoporosis. The curcuminoid enriched turmeric prevented up to 50% of ovariectomized induced loss of trabecular bone and also preserved the number and connectedness of the strut–like trabeculae.[30] Treatment with curcumin was able to reverse all the ovariectomy–induced deteriorations. The high dose of curcumin treatment was not only able to reduce the osteoclast number but also increase the osteoblast count.[31] Curcumin administration ameliorates oxidative stress–induced apoptosis in osteoblasts by preserving mitochondrial functions and activation of Akt–GSK3β signalling. These data provide experimental evidence supporting the clinical use of curcumin for prevention or treatment of osteoporosis.[32]

Shigru (*Moringa oleifera* Lam.)

In an in-vivo study, methanolic extracts of *Moringa oleifera* components showed a positive effect on osteoblast cell line SaOS2. Flower and fruit were found to have significant osteoblast stimulating property. Flower extract was found to be increasing the number of osteoblastic cells; while the fruit extract was having more elaborative effect as it increased ALP activity, induced bone formation, increased hydroxyproline content and bone mineral formation.[33]

Regenerative effect of *Moringa oleifera* extract on haematological parameters and bone marrow of adult Wistar rat is reported.[34]

Ethanolic extract at the dose of 600 mg/kg, significantly reduced urinary calcium excretion and significantly increased calcium content of bones in ovariectomised rats. The osteoprotective effect was

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comparable with estradiol.[35] Ethanolic extract of leaves at the dose of 100, 200, and 300ng/ml enhanced osteogenic differentiation capacity of porcine bone marrow derived mesenchymal stem cells as demonstrated by increased alkaline phosphatase staining and alkaline phosphatase activity.[36]

Tila (*Sesamum Indicum Linn.*)

Sesame seed is an ancient food containing health benefitting nutrients like essential fats, minerals, antioxidants, and vitamins. Sesame seed is considered to be helpful for its potential to provide recommended daily allowance (RDA) of certain nutrients like calcium, phosphorus, iron, magnesium, and potassium. As a study revealed that sesame seed provides 100% of the recommended daily allowance (RDA) for manganese and potassium, 57%-65% of the RDA of phosphorus and iron, and 13%-35% for zinc, calcium, and copper while its recommended daily intake is 25 to 50 grams.[37] Lignan glycosides have naturally potential against oxidation as antioxidant which is rich in sesame seed. This antioxidant ability helps to prevent bone inflammation consequently prevent bone resorption and increase bone formation.[38]

In an experimental study, feeding of 10% sesame oil reduced the significantly altered alkaline phosphatase activity and tartrate resistant acid phosphatase activity in ovariectomized rats. The test drug also reduced disruptive, lytic bone trabeculae and improved bone microarchitecture.[39]

Nimba (*Melia azedarach* Linn)

In an in vitro study, it has been reported that, the root extracts of M. azedarach, could be used as medicines for osteoporosis. The extract s inhibited osteoclast proliferation and induced apoptosis by up–regulation of caspase activity and increase of mitochondrial pro–apoptotic proteins expression. Furthermore, the extracts enhanced differentiation, but did not affect proliferation of both osteoblasts and chondrocytes. The osteo–inducible effect was also observed in cultured primary bone marrow cells.[40]

Krishna Jeeraka (*Nigella sativa* linn.)

In an experimental study, ovariectomized rats showed significant decrease in plasma Ca+2, accompanied by a significant increase in plasma ALP, amino terminal collagen type 1 telopeptide, MDA, nitrates, TNF–α and IL–6. These changes were reversed by supplementation of test drug.[41] *Nigella sativa* seed oil improved the micro architecture and biomechanical properties of the femur in male diabetic rats to a level equivalent to that achieved with parathyroid hormone treatment.[42] In a clinical study, effects of *Nigella sativa* supplements were evaluated on the bone markers of postmenopausal women. The test drug failed to cause any significant changes in the bone markers levels, when supplemented for the duration of 3 months to these postmenopausal women. The sample size of the study was only 15 and the duration of study was not longer to obtain the readings of bone markers at several time points and any changes in the bone mineral density. So, a long-term study with larger sample size may give more convincing results.

Dadima (*Punica granatum* L.)

Anti–osteoporotic activity of ethanolic extract of *Punica granatum* in ovariectomized rat model of osteoporosis at 100, 300 and 500 mg/kg is reported experimentally. There was significant increase in femur length, weight and density, increase in serum calcium, phosphorus and reduction in alkaline phosphatase, tartrate resistant acid phosphatase, *Dadima - Punica granatum* L. Anti–osteoporotic activity of ethanolic extract of *Punica granatum* in ovariectomized rat model of osteoporosis at 100, 300 and 500 mg/kg is reported experimentally. There was significant increase in femur length, weight and density, increase in serum calcium, phosphorus and reduction in alkaline phosphatase, tartrate resistant acid phosphatase, osteocalcin whereas urine calcium, creatinine and phosphorous levels were significantly decreased. Histology of femur exhibits restorative progress with increased ossification, mineralization and increased osteoclastic activity. Polar fraction of *Punica granatum* (L) peel extract at the doses of 50,

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100, and 200 mg/kg significantly prevented bone loss in ovariectomized rats. These effects were described in increased mineral content of calcium. On histology data shown that fraction could increase osteoblast number.[43] Consumption of pomegranate peel extract was able to significantly prevent the decrease in bone mineral density and bone micro–architecture impairment in ovariectomized mice.[44] The alcoholic extract of fruit peel at the dose of 500mg/kg and 750mg/kg, daily for 90 days showed significant increase in uterine weight, femur BMD and femur hardness. In addition, increased levels of calcium and phosphorus in serum and significant decrease in urine were observed.[45] Exposure of different concentrations (10–100µg/ml) of the ethanolic extract on osteoblastic cells showed characteristic morphological changes and increment in cell number. A significant growth in cell proliferation, ALP activity, collagen contents and matrix mineralization of osteoblasts in a dose dependent manner suggested that extract has a stimulatory effect on osteoblastic bone formation or potential activity against osteoporosis.[46]

Shunti (*Zingiber officinale* roscoe willd)

The osteo–protective effects of structurally related polyphenols (gingerols) isolated from the rhizomes of *Z. officinale* was reported in experimental studies. All the extracts were found bone protective in streptococcal cell wall induced arthritis, preventing bone mineral density loss as determined by dual energy absorptiometry.[47] Treatment with 6–gingerol stimulated osteoblast differentiation in normal and inflammatory settings. This compound induced the differentiation of osteoblast like cells with increased transcription levels of osteogenic markers, upregulated ALP enzyme activity, and enhanced mineralized nodule formation. It also reduced the degree of inflammation in TNF–a–treated MG–63 cells.[48] Oil extract of garlic possibly has a positive role in suppressing ovariectomy induced bone resorption. Garlic oil extract supplementation prevented ovariectomy–induced significant alteration of serum alkaline phosphatase activity, serum tartrate resistant acid phosphatase activity, urinary excretion of calcium, phosphate, hydroxyproline and urinary calcium to creatinine ratio.[49]

Ashwagandha (*Withania somnifera*)

Effect of *Withania somnifera* root ethanolic extract has been evaluated for anti-osteoporotic activity in ovariectomized Sprague–Dawley rats. Extract at the dose of 65 mg/kg for 16 weeks has shown a significant increase in serum alkaline phosphatase levels and urinary calcium and phosphorus excretion. Histological findings have revealed narrowed, and disappearance of trabeculae with widened medullary spaces in the ovariectomized group.[50]

Conclusion

Osteoporosis is the most common metabolic bone disorder characterized by reduced bone mass and osteoporotic fracture in children and needs an effective treatment measure without any adverse effect. The single herbs mentioned in Ayurveda showed significant results in improvement of osteoporotic changes. According to Ayurveda these herbs improves the *Dhatu Gata Agni* -Metabolism, *Sroto Sodhana* - cleaning of nutritive channels, strengthen the tissue indirectly by improving *Rasa Dhatu* to *Meda Dhatu* and directly strengthen the *Asthi Dhatu* by direct *Poshan* (nutrition) with herbs which having *Prithavi Mahabhoot* components (calcium, phosphorus, magnesium etc.). Thus, prevent further *Asthi Dhatu Kshaya* (loss) and strengthens the *Asthi Dhatu* - bone tissues. All these drugs are easily available, simple for administration and devoid of any adverse reactions. The article will be useful for food and drug companies to produce safe herbal products for children.

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