

Medicinal Plants for the Treatment of Postmenopausal Osteoporosis

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Osteoporosis is a metabolic bone disorder which causes bone loss in course of time leading to increasing the fracture risk. The disease is often silent and known only when fractures occur. Both men and women are equally affected. But women are more susceptible to osteoporosis. The main cause of fragility fractures in women is due to the estrogen deficiency. For the treatment of Osteoporosis the potential biological use of traditional medicines have been exposed to logical assessment since synthetic medications are considered to have a wide range of side effects and they lack efficacy. Hence broad research is to be done to examine the therapeutic plants to be utilized as an option for the treatment of Osteoporosis. The present survey work demonstrates the data on medicinal plants with their common name, phytochemical constituents, reported pharmacological activities and their Osteoporotic action.

Keywords : Osteoporosis, medicinal plants, estrogen replacement therapy, phytochemical constituents, postmenopausal.

Osteoporosis is a major public health problem globally. It is characterized as a skeletal disorder due to decreased bone strength prompting an expanded danger of fractures (The Royal Australian College of General Practitioners and Osteoporosis Australia., 2017). Osteoporosis literally means “porous bones” and is characterized by decreased mineral density of the bones. It is frequently seen in aging population and is considered as a modern day epidemic. Osteoporosis makes the bones weak and fragile increasing the chances of getting them fractured with trivial trauma. Such a kind of fractures may lead to pain, deformity and disability (The Royal Australian College of General Practitioners and Osteoporosis Australia., 2017). Osteoporosis and related fractures are the major noteworthy reason for morbidity and mortality of the elderly population. From the age of 50 the remaining lifetime risk of

fractures is evaluated to be 50% in women and 30% in men (Nguyen, Ahlborg, Eisman, & Nguyen, 2007). According to WHO “Osteoporosis is a disease characterized by low bone mass and micro architectural destruction of the bone tissue leading to fragility and sequential increase in fracture risk resulting in fractures with minimal trauma”. (Soelaiman, Das, Shuid, Mo, & Mohamed, 2013).

Osteoporosis has risen as one of the leading health issue worldwide. It is often considered as silent since it is known only when it causes bone fracture (Res, 2013). Due to increased longevity of life in the Indian population Osteoporosis has become the major cause of morbidity and mortality when compared to the western countries (National & Journal, 1996). The predominance of Osteoporosis increases with age in women and not in men. It was reported that 22% of the population will have Osteoporosis by 2025 and 33% in 2050 (Mithal,

Bansal, Kyer, & Ebeling, 2014). In women decline in Ovarian estrogen generation is the significant reason for bone loss which results in higher bone turn over between bone development and bone resorption(Ji & Yu, 2015). The most widely recognized sites of fractures in postmenopausal women include the vertebrae , forearm and hip. Due to aging the incidence of hip fractures increases leading to increased cost burden(Shirwaikar, Khan, Kamariya, Patel, & Gajera, 2010). For the development of human skeleton adequate amount of nutritional intake is required. Nutrition is being considered as an important factor in the prevention of osteoporosis(Ahmadiéh & Arabi, 2011). The role of calcium and vitamin D has been very well established due to their increasing bone mineral capacity and fracture prevention status(Sunycz, 2008). In addition to vitamin and calcium studies have shown that fruits and vegetables have shown a positive effect on bone mineral status(Prynne et al., 2018)(Tucker et al., 1999). Most current treatments for osteoporosis center around inhibiting bone resorption and reducing bone remodelling(Jolly, Chin, & Soelaiman, n.d.). The anabolic therapy to treat osteoporosis is the parathyroid hormone derivatives(Reginster, Pelousse, & Bruye, 2013). The present treatments have demonstrated to improve the bone mineral density by reducing the fracture risk , yet their long term use has brought in some serious side effects (Khajuria, Razdan, & Mahapatra, 2011)(Solomon, Rekedal, & Cadarette, 2009). So the search of a new drug has led to the advancement in the phytomedicine to convert herbal plants into treatment for disease like Osteoporosis(Herbs, n.d.).

Plant based remedies can be a safe alternative to estrogen therapy for the counteractive action and treatment of postmenopausal osteoporosis. The present review has been composed to include the therapeutic plants which have been accounted for their Osteoprotective activity. From the data obtained from the literatures the plants having the Osteoprotective activity have been listed in the Table 1.

MATERIALS AND METHODS

The computerized data bases such as PUBMED , SCOPUS and google scholar were extensively used. Hint words such as osteoporosis

, postmenopausal osteoporosis , medicinal plants , ovariectomized rat , medicinal plants , herbs and plant medicine was used while searching the titles. The paper satisfies a) studies on anti-osteoporotic activity conducted in animals and or cell lines , b) extractions from plants or compounds isolated from them.

***Trifolium pratense* – red clover**

Trifolium pratense , the red clover is a herbaceous type of the flowering plant having a place in the family of Fabaceae , widely seen in Europe , Western Asia and Northwest Africa(Rosso & Pagano, 2005). Red clover contains a few chemical compounds but they are more rich in isoflavones , flavones and flavonols(Booth et al., 2006). It was reported that Red clover extract contains significant amount of estrogenic isoflavones like genistein , daidzein , biochanin A and formononetin(Booth et al., 2006). These isoflavones are utilized as alternatives instead of Hormone replacement therapy as selective estrogen modulators and in the administration of postmenopausal osteoporosis (Dornstauder et al., 2001). It is used as fodder crop due to its nitrogen fixation capacity which is essential for the soil and hence it is used as manure crop. Blossoms have been made into ointments for the treatment of ulcers , but traditionally it has been used for respiratory ailments and anti-cancer therapy (Booth et al., 2006) . It was noted that red clover extracts accelerated the uterine weight and vaginal cell cornification in Ovariectomized rats. The studies showed that Isoflavones from the extract when given in optimal doses was found to maintain the bone mass effectively (Al et al., 2007).

***Salvia miltirrhiza*– red sage**

Salvia miltirrhiza named as Danshen is a Chinese medicinal herb. It is sometimes described as Chinese sage or simply the red sage. It is widely distributed in China and Japan along the slopes and the stream banks in the west and southwest province. Nearly some seventy compounds have been isolated from *Salvia miltirrhiza* and have been separated as hydrophilic and lipophilic compounds. Some of the hydrophilic compounds isolated are rosmarinic acid , ursolic acid , baicalin , stigmasterol and some lipophilic compounds isolated are tanshinone I , IIA , IIB, V, VI, salviol , miltirone(B. Wang, 2010). It is reported for its anticancer activity , anti-inflammatory ,

antimicrobial, antiviral and antioxidant (B. Wang, 2010). Bongkyun Park et al. reported that SML (Combination of ethanolic extract of *S. miltiorrhiza* and liquefied calcium) had defensive mechanism on estrogen deficient bone loss through blocking of the RANKL signaling pathway induced expression of TRAF6 and NFTAcl as well as the unregulated cathepsin K and calcitonin receptor to support osteoclast differentiation (Park et al., 2017).

***Eucommiaulmoides*– du – zhong**

Eucommiaulmoides commonly called as Du Zhong belongs to the family of Eucommiaceae cultivated in the central china. Nearly 112 compounds have been segregated from this plant which includes lignans, iridoids, steroids and monooxylignans (Hussain et al., 2016). It is generally used to fortify the muscles and lungs, lower the blood pressure, prevent premature deliveries, improve the tone of liver and kidneys and increase longevity (R. Zhang et al., 2009). Zang et al. reported that day to day oral administration of the cortex extract for 16 weeks in adult ovariectomized rats stopped estrogen deficiency induced bone loss and destruction of trabecular microarchitecture finally maintaining the biomechanical competence of bone (R. Zhang et al., 2009). Fei Li et al. reported that the water extract of Du Zhong given orally for a period of 12 weeks in a female ovariectomized rat prevented estrogen deficiency induced bone loss simultaneously increasing the Serum osteocalcin and E2 levels. They even reported that 6.0g/kg/d of the water extract was progressive in increasing the Bone mineral density of the femur in comparison with the other dosages.

***Urticadioica*– Stinging nettle**

Urticadioica commonly called as stinging nettle is a perennial plant widely distributed throughout the temperate and tropical areas around the world (Krystofova, Adam, Babula, Zehnalek, & Beklova, 2010). The chemical compounds isolated from this plant include phytosterols, saponins, flavonoids, tannins, amino acids and vitamins (Rutto, Xu, Ramirez, & Brandt, 2013). Traditionally it has been used for the treatments such as anti-oxidant (Bemgümeçi, Tu, & Özü, 2004), anti-ulcer (Faculty, 2004) rheumatoid arthritis (Y, Behnke, & Y, 1999), hepatoprotective activity (Akbar, Basaran, & Basaran, 2003), anti-cancer (Sak, Jürisoo, Raal, Sak, & Ju, 2014)

and cardiovascular effects (Legsyyer et al., 2002). Ramiji et al. reported that the oral administration of the extract for two months significantly re-established the decreased serum calcium and phosphorous concentrations induced by ovariectomy to normal levels (Ramji Gupta, Singh, Kumar, Kumar, & Singh, 2014).

***Lepidiummeyenii*– maca**

Lepidiummeyenii commonly called as maca belonging to the family of Brassicaceae grown in the Peruvian central andes (Gonzales, 2012) (Lee, Kim, & Lee, 2017). There are a lot of primary and secondary chemical constituents isolated from maca like alkaloids, sterols, glucosinolates and their derivatives, macaene and macamides (Y. Wang, Wang, Mcneil, & Harvey, 2007). Traditionally it is used to increase fertility and sexual function (Yongzhong Zhang, Yu, Ao, & Jin, 2006) (Oshima, Gu, & Tsukada, 2003). It was reported for its anti-fatigue property (Jieying Li et al., 2017), memory and learning enhancer (Rubio et al., 2011). Yongzhong et al. reported that *Lepidiummeyenii* improved bone mass, re-established trabecular system in the lumbar vertebrae in Ovariectomized rats which recommends that it is possibly valuable for postmenopausal osteoporosis (Yongzhong Zhang et al., 2006).

***Cissusquadrangularis*– hadjod ,pirandai , nalleru**

Cissusquadrangularis commonly called as hadjod, pirandai, nalleru in different languages is a perennial plant having a place with the family vitaceae (Siddiqua & Mittapally, 2017). Found extensively in India, srilanka and Bangladesh. Studies have demonstrated that the plant is rich in constituents like flavonoids, triterpenoids, vitamin C, stilbene derivatives, sitosterol, amyryl and amyryl (Mehta, Kaur, & Bhutani, 2001). It has been reported for its anti-oxidant and free radical scavenging activity (Prabhavathi, Prasad, & Jayaramu, 2016), anti-microbial and anti-bacterial activity (Basker, Yassir, & Kottamparambath, 2013), anti-ulcer activity (Mag, Jainu, Vijaimohan, & Kannan, 2010), anti-helmintic activity ("A REVIEW ON CISSUS QUADRANGULARIS AND EVALUATION OF ITS IN-VITRO ANTHELMINTIC ACTIVITY," 2014), and bone healing activity (Mishra, Srivastava, & Nagori, 2010). Jameela et al. reported that *Cissusquadrangularis* can reduce Ovariectomy

induced bone loss and it does this in the long bones in a site-specific manner with more effects on the cancellous bone of femur followed by tibia. *Cissusquadrangularis* probably reduces bone resorption primarily by down regulating proinflammatory cytokines that are often increased after ovariectomy. The beneficial effects of *Cissusquadrangularis* are probably due to the flavanoids present (Banu et al., 2012).

Allium cepa– onion

Allium cepa generally called as onion is a multipurpose food plant consumed for its nutritional and health benefits (Article, 2008). Belonging to the family of Liliaceae it is grown in India and other sub-tropical countries. A wide range of chemical compounds like phenols, flavonoids, anthocyanins, vitamins and minerals and is rich in sulphur amino acids (D et al., 2018) (Marrelli, Amodeo, Statti, & Conforti, 2019). It is used as an anti-bacterial agent (Bakht, Khan, & Shafi, n.d.), anti-cancer, cardio-protective, anti-parasitic, anti-microbial, antihyperlipidemic (R. K. Upadhyay, 2016). Tsang et al reported that high onion rich diets were able to decrease ovariectomy induced osteoporosis and declining of the biomechanical strength (T. Huang et al., 2008).

Erythrinavariegata– coral tree, Indian coral tree

Erythrinavariegata commonly called as coral tree, tigers claw belonging to the family of Fabaceae is a local plant in the ancient westward to Zanzibar and eastward to eastern Polynesia (Kumar, Lingadurai, Jain, & Barman, 2010). The plant contains alkaloids, flavonoids, pterocarpanes, steroids, stable oils, fatty acids and lecithin (Kumari & Kumari, 2017). Has been reported for its anti-oxidant, analgesic, anti-inflammatory, cardiovascular and smooth muscle relaxant property (Kumar et al., 2010). Yang et al established the useful effects of orally given *Erythrinavariegata* extract on skeletal tissues in an animal models of estrogen deficiency. The proof plainly shows that *Erythrinavariegata* could be considered as a natural alternative to hormone replacement therapy for the treatment of bone loss in postmenopausal women (Yao & Wong, 2007).

Asparagus racemosus–shatavari

Asparagus racemosus commonly called as Shatavari belonging to the Asparagaceae family is an indigenous medicinal plant grown in North India (Sachan, Das, Dohare, & Shuaib,

2012) (Thakur et al., 2009). The major bioactive constituents present in the plant are steroidal saponins mainly shatavarin I – VI apart from that copper, zinc, manganese, cobalt, potassium, calcium and selenium are found (Shaha & Bellankimath, 2017). It is used in the treatment of anti-cancer, antifungal, anti-bacterial, anti-ulcer, anti-coagulant and anti-dysenteric activity (Journal, Khulbe, & Pradesh, 2015). Chitmeet all reported that the methanolic extract of *Asparagus racemosus* is **more dynamic in conserving** the animals from osteoporosis than aqueous extract. The observed effects from the study were similar to estrogen treatment (Chitme, Muchandi, & Burli, 2009).

Ciceraritenium- chick pea

Ciceraritenium commonly called as chick pea adapted to the family of Fabaceae is a plant grown in many countries like India, Middle east, Cyprus, Jordan and Lebanon (Al-snafi & Medicine, 2016). The phytochemical evaluation showed the presence of many constituents like amino acids, methionine, glycine, aldehydes, hydrocarbons, terpenoids, esters, ketones and few phytoestrogen compounds like diadzein and genistein (Linn, 2009). It was reported for its anti-oxidant activity (Tiwari, Sahana, & Zehra, 2013), anti-diabetic activity (Y. Yang et al., 2007), anti-inflammatory activity (Al-snafi, 2018a), hepatoprotective activity (Kaur & Kaur, 2019), anticancer (Al-snafi & Medicine, 2017), diuretic and anti-nephrolithiasis effects (Al-snafi, 2018b). Sohair et al reported the *Ciceraritenium* extract activates OPG synthesis and reduced RANKL expression in osteoblast, producing an increase of the OPG / RANKL ratio and slow down the process of osteoclast differentiation. These results suggested that the extract not only benefits osteoblast differentiation but also up regulates OPG and downregulates RANKL secretion in osteoblasts, finally preventing bone loss. The phytoestrogen compounds genistein and diadzein could be responsible for the osteoporotic activity (Fahmy, Soliman, Sayed, & Marzouk, 2015).

Zingiberofficinale– ginger

Zingiberofficinale commonly called as ginger belonging to the family of Zingiberaceae is indigenous to the warm tropical climates and grown in Asia, Africa, India, Jamaica, Mexico and Hawaii (Zadeh & Kor, 2014). The chemical composition of ginger includes gingerols,

paradols , di-acetyl derivatives of gingerols , zingiberene , phellandrene and methyl ether derivatives(Press, 2015).It was reported for its activity on gastrointestinal tract , anti-microbial effects(Sebiomo, Awofodu, Awosanya, Awotona, & Ajayi, 2011) , cardiovascular activity(Nabeel, Hassan, Afridi, & Houghton, 2005) , anti-oxidant property(Stoilova, Krastanov, & Stoyanova, 2007) , hypoglycemic activity(Communication, 2010), anti-inflammatory property(Ojewole, 2006), anti-cancer activity(Taylor et al., 2011) and platelet aggregation (Liao, Leu, Chan, Kuo, & Wu, 2012). Mohamed et al reported that cadmium chloride is poisonous to bone and causes osteoporotic changes which was more marked and exaggerated in bilateral ovariectomized rat. Ginger improved the osteoporotic effect of bilateral ovariectomy and cadmium chloride through its composition and strong anti-oxidant properties(Mustafa, Mahmoud, & Hussein, 2013).

***Moringaoleifera*– drumstick**

Moringaoleifera commonly called as drumstick belonging to the family of Moringaceae is a native to the sub-himalayan tracts of India , Pakistan , Bangladesh and Afghanistan(P. Upadhyay et al., 2015).The phytochemical composition consists of glucosinolates , flavonoids, phenolic compounds,moringine , vanillin , beta-sitosterol,ascorbic acid ,moringine , niazimiciniazirin(Paikra & Gidwani, 2017). They are reported for their anti-oxidant activity(Sreelatha & Padma, 2009), anti-inflammatory activity(Ciiceresa et al., 1992),anti-diabetic(Rajnish Gupta et al., 2012), anti-cancer(Guevara, Vargas, Sakurai, & Fujiwara, 1999) , anti-fertility(Publishers & Mathur, 1988) and anti-asthmatic activity(Articles & Report, 2008).Chirag et al reported that *Moringaoleifera* components are having specific effect on Osteoblastic cells.The flower extract was found to boost the number of Osteoblastic cells , while the fruit extract had more deliberative effect as it increased ALP (Alkaine phosphatase activity) , induced bone formation , increased collagen content and bone mineral development(Patel, Rangrez, & Parikh, 2013).

***Emblicaofficinalis*– amla**

Emblicaofficinalis generally called as amla belongs to the family of Euphorbiaceae has been used for centuries for its wide spread medicinal properties(Jain, 2015). From various

analysis it was found that the plant contains tannins , flavonoids , vitamin C, emblicanin A , B , Chlorogenic acid , quercetin , phyllaemblicin –A , B and C , and corilagin(Ying-jun Zhang, Abe, Tanaka, Yang, & Kouno, 2001)(Variya, Bakrania, & Patel, 2016). It is reported for its activity on anti-diabetic activity , anti-hyperlipidemic activity , cardio-protective , anti-cancer , anti-mutagenic , hepato-protective(Jose & Kuttan, 2000) and anti-inflammatory(Asmawl, Kankaanranta, Moilanen, & Vapaatalo, 1993).Srinivasa et al reported on the combined effect of *Cissiusquadrangularis* and *Embilcaofficinalis*. The aqueous extract of *Embilcaofficinalis* completely alleviates the ovariectomy induced osteoporotic bone damage (Sirasaganandla, Sreedhara Ranganath Pai, & Bhat, 2013).

***Angelica sinensis*- dong quai / Female ginseng**

Angelica sinensis commonly called as female ginseng or dong quai belonging to the family of Umbelliferae is found in China , Korea and Japan(Constituents, 2004). Some of the main compounds isolated from *Angelica sinensis* are coniferylferulate , E-Coniferin , Butanal , Limonene , â-terpinene ,methane -3-ol apart from these it also contains vitamin A,E , B12 , valine and many more are present(Wei, Zeng, Gu, Qu, & Huang, 2016). The plant is reported for its anti-inflammatory(Jian Li et al., 2016), anti-platelet activity(Hang & Ang, 2009) , anti-oxidant activity(Lin-yan et al., 2015) and cerebral infarction(Wu & Hsieh, 2011).Dong et al reported that the extract of *Angelica sinensis* can avert ovariectomy induced bone loss with increased potency comparable to that of estrogen. The findings also suggested that the extract could be an efficient natural alternative for the prevention of postmenopausal osteoporosis(Lim & Kim, 2014).

***Rubiaccordifolia*– manjishta**

Rubiaccordifolia commonly called as manjishta belonging to the family of Rubiaceae is widely distributed throughout India especially on the northwest Himalayas(Meena, Pal, Panda, Sannd, & Rao, 2010).Different bioactive compounds have been isolated such as glycosides , naphthoquinones , glycosides , terpenes , bicyclic hexapeptides , iridoids(Siril, 2014).The plant is reported for its anti-arthritis property(Monitor, 2017) , anti-cancer activity, anti-microbial, anti-oxidant(Barlow, Barnes, Campbell, & Nigam, 2016) , hepato-

protective(Chaudhary, Kamboj, Singh, & Kalia, 2010), diuretic activity(Divakar, 2009) and neuro-protection(Rawal, Muddeshwar, & Biswas, 2004). Kasabi et al described that the administration of the ethanolic extract of *Rubiocordifolia* increased the biomechanical strength, high osteoblastic activity and minimal osteoclastic activity estimated to be responsible for the bone formation(Shivakumar, Mukund, & Rabin, 2012).

***Punicagranatum*– pomegranate**

Punicagranatum commonly called as pomegranate belonging to the family of Punicaceae is grown in Cyprus, Egypt, Morocco, Spain, Tunisia and Turkey(Maurya & Asthana, 2018). It consists a variety of flavonoids like genistein, diadzein alkaloids such as isopelletierine, pseudopelletierine, N-methylisopelletierine, anthocyanidins, ellagotannins, gallic acid and ellagic acid(Reza, Arastoo, & Nasser, 2012). It is reported for its activity on Alzheimer's disease(Hartman et al., 2006), obesity(Lei et al., 2007), erectile dysfunction(Azadzoi, Schulman, Aviram, & Siroky, 2005), male infertility(Aydin, Yu, & Gu, 2008), bacterial infections(Machado et al., 2002), diabetes(T. H. Huang et al., 2006), hypertension(Stowe, 2011) and atherosclerosis(Ignarro, Byrns, Sumi, Nigris, & Napoli, 2006). Melanie et al demonstrated that Pomegranate peel extract metabolites can precisely balance bone cell differentiation, leading to an enhanced formation ratio together with anti-inflammatory and anti-oxidative effects in the bone microenvironment. This put forwards that pomegranate consumption could be a promising substitute and complementary therapeutic agent for the prevention of osteoporosis(Spilmont et al., 2015).

***Ficuscarica*– fig**

Ficuscarica commonly called as fig belonging to the family Moraceae is grown extensively in Africa, Asia, Europe, Australia and America(Al-snafi, 2017). Preliminary phytochemical investigation demonstrated that the fruits contained alkaloids, tannins, glycosides, flavonoids, saponins, coumarins, sterols, terpenes, carbohydrates, phenols and proteins(Mawa, Husain, & Jantan, 2013). It is reported for its anti-oxidant activity(Polat, 2011), anti-cancer activity(Rubnov, Kashman, Rabinowitz, Schlesinger, & Mechoulam, 2001),

anti-bacterial and anti-fungal activity(Al-snafi, 2017), anti-diabetic activity(Serraclara et al., 1998), anti-inflammatory and antipyretic (Patil & Patil, 2011), anti-pyretic(V, Bhangale, & Patil, 2010) and anti-platelet(Schwarz, Dorner, Turecek, & Bioscience, 2002). Norfarah et al reported that *Ficuscarica* showed Osteo-protective effect and it can be used as a potential anti-osteoporotic agent to replace Estrogen replacement therapy with lesser side effects (R, M, Dzulkhairi, Ma, & Me, 2019).

***Curcuma longa*– turmeric**

Curcuma longa commonly called as turmeric belonging to the Zingiberaceae family is a commonly used plant in the Indian subcontinent(Niazi, Poonia, Gupta, & Kaur, 2010). The active constituents of turmeric are the flavonoid curcumin, various volatile oils like tumerone, atlantone and zingiberone(“Kumar and Sakhya,” 2013) rich sources of polyphenolic curcuminoids like curcumin, demethoxycurcumin and bisdemethoxycurcumin are also present(Govindarajan & Stahl, 2009). It is reported for its anti-oxidant activity(Khan, 2016), anti-inflammatory and anti-arthritic activity(Soleimani, 2018), anti-diabetic(Weisberg, Leibel, & Tortoriello, 2008), anti-thrombotic activity(Printed, 1985), anti-fungal activity(Ungphaiboon & Supavita, n.d.), anti-cancer(Kuttan, Sudheeran, & Josph, 1987) and Alzheimer's(F. Yang et al., 2005). Laura et al reported that the curcuminoid enhanced turmeric stopped up to 50% of Ovariectomy induced bone loss of trabecular bone and also preserved the trabecular bone structure.(Unk, 2010).

***Dioscoreaalata*– purple yam**

Dioscoreaalata commonly called as purple yam belonging to the family of Dioscoreaceae is popular in Sri Lanka and grown in all the ecological zones of the country(Foods, Nutrition, Publishers, Science, & Lanka, 1994). The main constituents present in purple yam are dioscorin, saponins and dioscin(Nabawiyati et al., n.d.). It is reported for its anti-inflammatory activity(Dey, Chowdhuri, & Sarkar, 2016), anti-hypertensive(Liu et al., 2014), anti-carcinogenic, anti-thrombotic, anti-mutagenic and immunomodulatory activities(Nabawiyati et al., n.d.). Kang et al reported that Dispo85E regulated the mesenchymal stem cells differentiation into an osteogenic lineage rather than adipogenic lineage and ameliorates osteoporosis in the mouse model and it holds as a **rare** therapeutic drug treatment

Table 1. List of medicinal plants reviewed

| Common Name | Biological source | Chemical constituents | Report |
|----------------------------|----------------------------|--|---|
| Red clover | <i>Trifolium pratense</i> | Estrogenic isoflavones | Competitively bond to ER α and ER β |
| Ginger | <i>Zingiber officinale</i> | gingerols , paradols , di-acetyl derivatives of gingerols , zingiberene , phellandrene and methyl ether derivatives | cadmium chloride is poisonous to bone and causes osteoporotic changes which was more marked and exaggerated in bilateral ovariectomized rat |
| Red sage | <i>Salvia miltirrhiza</i> | rosmarinic acid , ursolic acid , baicalin , stigmasterol and some lipophilic compounds isolated are tanshinone I , IIA, IIB,V,VI, salviol , miltirone | SML(Combination of ethanolic extract of <i>S. miltirrhiza</i> and liquefied calcium) had defensive mechanism on estrogen induced bone loss |
| Onion | <i>Allium cepa</i> | flavonoids , anthocyanins , vitamins and minerals | High onion enhanced diets were able to decrease ovariectomy induced osteoporosis and worsening of the biomechanical strength |
| Maca | <i>Lepidium meyenii</i> | Maca alkaloids , steroids , glucosinolates , isothiocyanates and macamides | Improved bone mass , reestablished trabecular system in lumbar vertebrae in Ovariectomized rats. |
| Drumstick | <i>Moringa oleifera</i> | glucosinolates , flavonoids, phenolic compounds, moringine , vanillin , beta-sitosterol, ascorbic acid, moringine , niazimiciniazirin | Displayed a beneficial outcome on Osteoblastic cells. The fruit extract prompted bone development , elevated collagen content and bone mineral production. |
| Amla | <i>Emblica officinalis</i> | Tannins , alkaloids, vitamin c , Emblicanin A , E | The aqueous extract of <i>Emblica officinalis</i> viably improved Ovariectomy induced bone damage |
| Turmeric | <i>Curcuma longa</i> | flavonoid curcumin , various volatile oils like tumerone , atlantone and zingiberone | Curcuminoid halted nearly 50% of the Ovariectomy induced bone loss saving the trabecular bone structure. |
| Dong quai / Female ginseng | <i>Angelica sinensis</i> | coniferylferulate , E-Coniferin, Butanal , Limonene , α -terpinene, methane -3-ol | The extract of <i>Angelica sinensis</i> can avert ovariectomy induced bone loss with potency compared to that of estrogen. |
| Fig | <i>Ficus carica</i> | alkaloids , tannins , glycosides , flavonoids , saponins , coumarins , sterols , terpenes , carbohydrates , phenols and proteins | Showed Osteo-protective effect and it can be used as an potential anti-osteoporotic agent to replace Estrogen replacement therapy with lesser side effects |
| Chick pea | <i>Cicer arietinum</i> | Amino acids , methionine, glycine, aldehydes , hydrocarbons, terpenoids , esters , ketones and few phytoestrogen compounds like diadzein and genistein | The extract accelerated OPG synthesis and reduced RANKL expression in osteoblast ending in the increase of the OPG / RANKL ratio and declining the osteoclast differerentation. |

| | | | |
|------------------------------------|----------------------|--|--|
| Manjishta | Rubiacordifolia | glycosides , naphthoquinones , glycosides , terpenes , bicyclic hexapeptides , iridoids | The administration of the ethanolic extract of Rubiacordifolia increased the biomechanical strength , high osteoblastic activity and minimal osteoclastic activity accounted for the bone formation |
| Pomegranate | Punicagranatum | Genistein , diadzein alkaloids such as isopelletierine , pseudopelletierine , N-methylisopelletierine , anthocyanidins , ellagotannins, gallic acid and ellagic acid | Pomegranate peel extract metabolites can directly modulate bone cell differentiation, leading to an improved resorption/ formation ratio together with anti-inflammatory and anti-oxidative effects in the bone microenvironment. |
| Shatavari | Asparagus racemosus | Shatavarin I – IV , steroidal saponins , zinc and few minerals | Similar to that of estrogen treatment. |
| Pirandai, Hadjod , devils backbone | Cissusquadrangularis | Flavonoids , triterpenoids , vitamin c , stilbene derivatives , β - sitosterol , α - amyryn and α -amyrone | It reduce Ovariectomy induced bone loss and it does this in the long bones in a site-specific manner with more effects on the cancellous bone of femur followed by tibia. |
| Coral tree , Indian coral tree | Erythrinavariegata | Alkaloids , flavonoids , triterpenes , steroids , lecithin | It can be considered as natural substitute in place of hormone replacement therapy for the obstruction and treatment of bone loss in postmenopausal women |
| Du Zhong | Eucommiaulmoides | Lignans , iridoids, phenolics , steroids | The treatment increased ER expression in the endometrium similar to the E2 treated group. |
| Ashwagandha | Withaniasomnifera | Withanine , Withanone , Sitoindosides X , Withanolide , Withaferin (steroidal lactone) and Withanone | Treatment with Withaniasomnifera restored the metaphyseal bone loss in femur and demonstrated an increase in the biomechanical strength of the tibia in the ovariectomized animals. |
| Stinging nettle | Urticadioica | Phytosterols , saponins , tannins , sterols , carotenoids, fatty acids | Restored the decreased serum calcium and phosphorous concentrations induced by ovariectomy. |
| Purple yam | Dioscoreaalata | dioscorin , saponins and dioscin | Dispo85E regulated the mesenchymal stem cells differentiation into an osteogenic lineage rather than adipogenic lineage and ameliorates osteoporosis in the mouse model and it holds as innovative therapeutic drug treatment for osteoporosis |

for osteoporosis (Peng, Horng, Sung, Huang, & Wu, 2011).

***Withaniasomnifera*– ashwagandha**

Withaniasomnifera commonly called as ashwagandha belongs to the family Solanaceae and is grown in India, Srilanka, Afghanistan, Baluchistan and Sind (Uddin, Samiulla, Singh, & Jamil, 2012). The chemical constituents found in the plant Withanine, Withanone, Sitoindosides X, Withanolide, Withaferin (steroidal lactone) and Withanone (Mir, Khazir, Mir, Hasan, & Koul, 2012) (Africa, 1993). It is reported for its anti-oxidant, anti-stress, hepatoprotective, anti-tumor, immunomodulatory, anti-convulsant, antiproliferative and anti-diuretic activity (Ahlawat, Khajuria, Bhagwat, & College, 2012). Prabhakara et al reported that the treatment with *Withaniasomnifera* restored the metaphyseal bone loss in femur and **displayed** an increase in the biomechanical strength of the tibia in the ovariectomized animals (Nagareddy & Lakshmana, 2006).

DISCUSSION

Chemical and biochemical agents like bisphosphonates, estrogen therapy and calcitonin are being considered as the main drugs in the treatment of osteoporosis they have many side effects and they fail to satisfy the fracture complications. Plant sources have always played an important role in the place of the currently available drugs. Clinical practice and folk medicine have shown the possibility of using natural products to redeem the osteoporosis and its symptoms. Many medicinal plants have the ability to regulate bone metabolism in order to reduce the bone loss. Biological, chemical and pharmacological methods can be applied to obtain the active compounds from medicinal plants for the treatment of osteoporosis and its related complications.

Two types of drugs are being used in the treatment of osteoporosis i.e. anti-resorptive drugs and anabolic drugs. Anti-resorptive drugs inhibit the bone resorption and anabolic drugs build up the bone. Drugs like bisphosphonates, estrogen therapy act as bone resorption agents while calcitonin is used to reduce bone loss stabilizing the architecture of the bone finally decreasing the bone turnover. The anabolic drugs available increase the

bone formation but they are very rarely available. Teriparatide a synthetic parathyroid hormone is the only anabolic drug approved for the treatment of osteoporosis by the FDA. Some medicinal plants not only inhibit bone resorption but also increase the bone formation. Finally these plant medicines can be used to increase the osteoblast proliferation activity and improve bone formation. According to the patients need the physician can select anti-resorptive therapy or anabolic therapy or their combination for the treatment of osteoporosis.

Many evidences are available stating that proper nutrition and lifestyle can promote bone health. But still there is no complete cure for the treatment of osteoporosis and other bone related disorders. The drugs available for the treatment come in with a lot of side effects when taken. When medicinal plants are being used few things are to be considered before using them like a) compatibility – the chemical compounds present in the plants must be clear and compatible to use, b) selection – the action of the drug should be selected in such a way that its action specifically binds to the targeted drug surface promoting prompt healing action, c) therapeutic index – developed drug should be optimized to improve the efficacy and reduce the side effects caused by the other drugs and finally d) convenience – drug must be conveniently made such that it should be given orally and not given by any parenteral route.

Plants utilized frequently must be checked for the pharmacological and therapeutic effects in patients with osteoporosis. It is obvious that many plants have the potential to prevent and treat osteoporosis. The biggest drawback is that only a fraction of the plants have been investigated so far. More efficient and reliable assay must be developed to systematically evaluate the anti-osteoporotic activity of the plant extracts to identify the active components. In addition to this many anti-osteoporotic agents from medicinal plants are being considered as prophylactic in nature rather than the therapeutic and clinical trials have not yet been undertaken. If such studies are being encouraged more herbal drugs may be available for human use soon.

CONCLUSION

The combined harm related with aging

is one of the significant issues worldwides. Scientificadvances could be an approach to prevent the ailment occurring with increasing age, for example, osteoporosis and related difficulties which are the primary cause of increased medical cost. On the development of skeletal fragilityinsufficiency of estrogen and its metabolites have real impacts on the skeletal system. Current medications could be an approach to prevent bone loss, like estrogen replacement treatments, however with a few adverse reactions. Healthful procedure like Mediterranean style diet is another methodology for the aversion of osteoporosis. It is likewise revealed that enemy of oxidant and mitigating dynamic supplements could add to bone health. On the other hand the significance of organic exercises of plant inferred mixes is broadly known. Consequently option and correlative prescription could likewise be successful in the treatment of osteoporosis.

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