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Review Article

A Review Article of Polyherbal Tablet for the Management of Osteoporosis

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ABSTRACT

Osteoporosis is an aging problem. The declining bone mineral density (BMD) enhances the chances of fractures during minor falls. Effective pharmaceuticals are available for a rapid improvement of BMD. Osteoporosis is an enormous and growing public health problem. Once considered an inevitable consequence of ageing, it is now eminently preventable and treatable. Ironically, despite tremendous therapeutic advances, there is an increasing treatment gap for patients at high fracture risk. In this Series paper, we trace the evolution of drug therapy for osteoporosis, which began in the 1940s with the demonstration by Fuller Albright that treatment with oestrogen could reverse the negative calcium balance that developed in women after menopause or oophorectomy. We note a watershed in osteoporosis drug discovery around the year 2000, when the approach to developing novel therapeutics shifted from one driven by discoveries in animal studies and clinical observations (eg, oestrogen, calcitonin, and teriparatide) or opportunistic repurposing of existing compounds (eg, bisphosphonates) to one driven by advances in fundamental bone biology (eg, denosumab) coupled with clues from patients with rare bone diseases (eg, romosozumab, odanacatib). Despite these remarkable advances, concerns about rare side-effects of anti-resorptive drugs, particularly bisphosphonates, and the absence of clear evidence in support of their long-term efficacy is leading many patients who could benefit from drug therapy to not take these drugs. As such, there remains an important clinical need to develop ways to enhance patient acceptance and compliance with these effective drugs, and to continue to develop new drugs that do not cause these side-effects and have prolonged anabolic effects on bone. Such changes could lead to a true reversal of this potentially devastating disease of ageing.

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INTRODUCTION

Dependence of human beings on plants dates back to the origin of the human race. The basic needs of life for human being are shelter, clothing, food, lavors and fragrances and not the least, medicines. Plants are a common source of medicine. Plants have shaped the creation of reined traditional medicine structures among which are Ayurvedic, Unani and Chinese are common. In Indian, Egyptian, Chinese, Roman and the Greek civilizations.¹

Bone is the most rigid tissue in the human body. Yet, it is the most dynamic and ever-changing tissue apart from blood. From birth until around age 20 years, the bone

grows and stores up its Calcium reserve. At the same time and under all circumstances, every bone unit is undergoing continuous changes of breakdown and restoration. These rapid, continuous changes are required for the control of calcium metabolism and to maintain the healthy state of the bone. Special cells called osteoblasts are responsible for the build-up of the bone unit, while other special cells called osteoclasts are responsible for the breakdown.² Build-up and breakdown are kept at a harmonized speed, so that there is good balance between the two mechanisms that are kept at a dynamic state. The balance is affected most commonly when the breakdown mechanism supersedes the restoration process and the causes behind could be aging, nutritional, disuse, vitamin D deficiency (no sunlight), and

disease conditions. Given good health, good nutrition, and freedom from major diseases, aging becomes the most unquestionable cause of bone loss.⁵

There are many ways to assess the physiological state of bone in the living individual, including clinical tests, imaging, and biochemical tests, of which imaging to detect the bone mineral density (BMD) has become the most accepted simple and reliable investigation.⁴

The past 30 years have witnessed remarkable developments in our understanding of the pathogenesis of osteoporosis and the availability of new drugs to treat the disease. Osteoporosis is characterized by low bone mass with susceptibility to fracture. It may only be discovered when fractures of the osteoporotic bone have occurred. Prevention and early treatment of osteoporosis are important to avoid its complications. Some of the commercially available antiosteoporotic drugs are associated with serious side effects.⁵

Osteoporosis a metabolic skeletal disorder “It is a progressive systemic skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture This disease is characterized by low bone mass and structural deterioration of bone tissue has a huge impact on public health through high morbidity, mortality and economic burden.

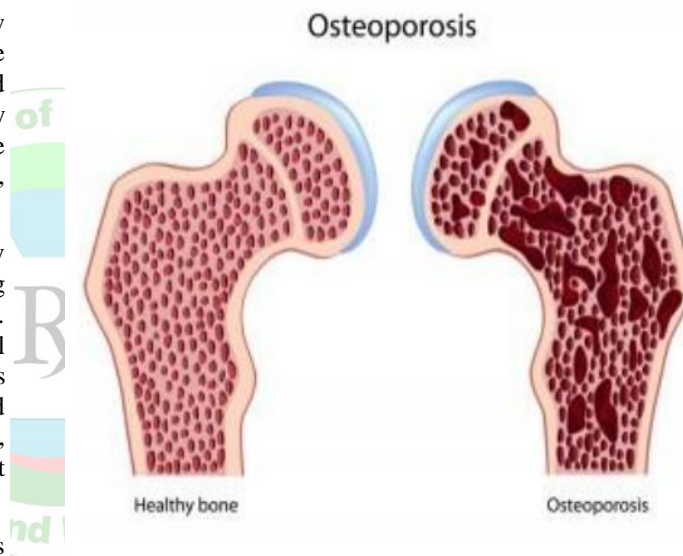
It is also described by low bone mass and underlying decay of bone tissue enormously affects general wellbeing through high dismalmness, mortality and economic burden. Bone strength reduction and micro architectural deterioration occur that lead to increased fracture risk.⁶ It is an exponentially increasing disease entity with aging and especially, post-menopause Mostly occur in women, affecting one in three women and one in twelve men at some point in their lives.

World Health Organization (WHO) defines osteoporosis as bone density (BD) that is 2.5 Standard Deviation (SD) or more below the young adult mean value (T score < - 2.5). Bone density decreases with age as the fracture risk rises rapidly. Every 1 SD decrease in BMD increases fracture risk two to three fold. Osteoporosis is second only to cardiovascular disease as a leading health care problem, according to the World Health Organization. It is now considered as major health care problem in India with an estimated 50 % of healthy women and 36% men over 50 years of age having low bone mass. Occurrence of osteoporosis is 10 years earlier in Indian people than in the West. A quiet sickness that reflects just in low bone thickness, till a break happens,much in the way that asymptomatic conditions, for example, hypertension and dyslipidemia incline to stroke and myocardial localized necrosis, individually .

The estimation of bone mineral density and bone mineral content can diagnosed by peripheral quantitative computed tomography (pQCT) or Dual energy X-ray absorptiometry (DXA). The common sites of fracture among postmenopausal women include the vertebrae, forearm and hip. The projected cost of osteoporotic fractures in white

postmenopausal women during the next 10 years in the United States alone is expected to be more than \$45 billion. It has been assessed that there are around 200 million osteoporotic subjects on the planet and that one of two ladies over age 50 will endure an osteoporotic break in the course of their life .⁷

It has been assessed that there are around 200 million osteoporotic subjects on the planet and that one of two ladies over age 50 will endure an osteoporotic break in the course of their life. Further, in ladies more than 45, osteoporosis represents a larger number of days spent in clinic than numerous different illnesses, including diabetes, myocardial dead tissue and bosom malignant growth. The assessed instances of osteoporosis in the U.S. alone are at 10 million, with one more 34 million people in danger of crack because of low bone mass. Roughly 3/4 of the total populace lives in Asia where the populace is quickly expanding and maturing. The picture of healthy bone and osteoporosis bone shown below in figure:1.⁸⁻⁹



Consequently osteoporosis is a developing general wellbeing worry across this district. The level of the older (matured 65 years or more) subjects in Asia was about 5.3% of the complete populace in 1995, and has been projected to increment to 9.3% in 2025, which addresses a 75% expansion. Financially savvy methods for recognizing and treating patients at high danger of hip crack are consequently, essential India, the second most populous country in the world, is home to an exceptionally huge populace, of osteoporosis patients; however, there is no solid epidemiological information to help this.

In light of 2001 evaluation, roughly 163 million Indians were over the age of 50 and this number was required to increment to 230 million by 2015. Indeed, even traditionalist appraisals propose that, of these, 20% of ladies and around 10-15 percent of men would be osteoporotic. A portion of the emergency clinic information recommend that hip breaks are regular in India and that, men are likely more ordinarily influenced than ladies generally as a result of ladies' feeling of prosperity, the quiet bleakness load that they convey and the absence of admittance to wellbeing merchandise and ventures.¹⁰⁻¹⁴



Causes of Osteoporosis

Traditional Medicines

The treatment of injury or disease by plants or plant material, either in the crude or processed state, is known as traditional herbal medicine. The medicinal plants with ethnomedicinal values are currently being screened for their therapeutic potential. The ethnopharmacological approach toward the understanding and appraisal of traditional and herbal medicines is characterized by the inclusions of the social as well as the natural sciences. Anthropological field-observations describing the local use of nature-derived medicines are the basis for ethnopharmacological enquiries. Herbal product has been used abundantly over the years in curing several diseases. Natural products and related structures are essential sources of new pharmaceuticals, because of the immense variety of functionally relevant secondary metabolites of microbial and plant species.¹⁵⁻¹⁸

Herb-Herb Combinations

Herb-herb combinations also known as polyherbal therapy have been used in Chinese medicine practice for thousands of years, yet scientific evidence of their therapeutic benefits is lacking.⁸ Drug combination often produces a promising effect in treatment of diseases over a single drug. The concept of drug combination has been well established in Western medicine and remarkable success has been achieved over the decades. In recent years, drug combination therapies in cancer and infectious diseases have offered new hope to patients. Naturally occurring herbs and herbal ingredients organized into certain formula have been shown to have potential interaction effects. These include mutual enhancement, mutual assistance, mutual restraint and mutual antagonism. In the Ayurvedic system of medicine mainly polyherbal compounds are used for treatment of various infections. Bharangyadi polyherbal is a mixture of *Clerodendrum serratum*, *Hedychium spicatum* and *Inula racemosa*. *Indukantha Ghritha* (IG) is a polyherbal preparation consisting of plant components widely prescribed by ayurvedic physicians for various ailments. The Unani system of medicine is also gaining global acceptance due to the amazing clinical efficiency of the formulations. Although Unani medicines have long

been used, there is negligible documented evidence regarding their safety and effectiveness. The lack of evaluation has, in turn, slowed down the development of regulations and legislations. Majoon Suranjan (MS) is a polyherbal formulation consisting of *Lawsonia inermis*, *Foeniculum vulgare*, *Capparis spinosa*, *Terminalia chebula*, *Ipomoea turpethum*, *Apium graveolens*, *Zingiber officinale*, *Convolvulus scammony*, *Colchicum luteum*, *Cassia angustifolia*, *Piper nigrum*, *Coriandrum sativum*, *Rosa damascus*, *Origanum vulgare*, *Pyrethrum indicum*, *Plumbago zelanicum*, *Verbascum thapsus*, *Ricinus communis* oil used in Unani system of medicine for the treatment of rheumatoid arthritis (RA). A successful attempt has been made using *Cissus rotundifolia* leaf extracts, *Cassia abbreviate* bark extract, *Zanthoxylum chalybeum* bark extract and *Zanthoxylum chalybeum* leaf extract form the polyherbal formulation and further evaluated for *in-vitro* studies.¹⁹

Polyherbal Formulation

Studies showed that selected individual plants contained abundant quantity of phenolics and flavonoids and their polyherbal combination with green tea was found to produce best antioxidant activity among all individual extracts.¹⁶ In majority of traditional systems, diabetes is better managed by the herbs combination (Polyherbal) instead of single herb because of synergism and less side effects. Diabetic wound cream prepared by using polyherbal formulation was found to be effective as well as safe in healing diabetic foot ulcers like the standard silver sulphadiazine cream.¹⁸ The anti-inflammatory activity of the polyherbal formulation Entox consists of *Allium cepa*, *Allium sativum*, *Aloe vera*, *Cajanus cajan*, *Coccinia indica*, *Caesalpinia bonducella*, *Ficus bengalensis*, *Gymnema sylvestre*, *Momordica charantia*, *Ocimum sanctum*, *Pterocarpus marsupium*, *Swertia chirayita*, *Syzgium cumini*, *Tinospora cordifolia* and *Trigonella foenum graecum* was investigated in rats for acute and sub-acute models of inflammation using carrageenan-induced rat paw edema and cotton pellet granuloma methods respectively at a dose of 300 mg/kg and 600 mg/kg administered orally. The formulation showed a significant anti-inflammatory activity in both the experimental models and the activity was comparable to that of the standard drug, indomethacin. BHUX, a patented polyherbal formulation consisting of the aqueous fraction of five medicinal plants of the ayurvedic system, has significant anti-inflammatory properties through inhibition of cyclooxygenase-2 and lipoxygenase. The polyherbal formulation "RIPARE" containing ingredients such as *Boswellia serrata*, *Commiphora mukul*, *Cissus quadrangularis*, *Vitex negundo*, *Centella asiatica*, *Tinospora cordifolia*, *Curcuma longa*, *Euphorbia hirta* and *Piper nigrum*. This formulation is known to possess antiarthritic activity.²¹ List of some important polyherbal formulations worldwide is mentioned in table 1. Table 1 represents publications on Polyherbal formulation in different countries since 2010 till now whereas Species list of number of publications on polyherbal formulation, evaluated in treatment of different diseases or pharmacological activities in year 2015.²⁰

Table 1: List of Commercially Available Polyherbal Product

Commercial Name	Formulation With Scientific Names	Country	Pharmacological Activity	Evaluation
Diabrid	Gymnema sylvestre, Momordica charantia, Eugenia Jambolana, Trigonella graecium	India	Anti-diabetic	Clinical trial Phase-1
Hepax-A	Plumbago zeylanica, Picrorrhiza kurroa, Piper nigrum, Zingiber officinale, Sodii carbonas impura, Phyllanthus emblica, Terminalia chebula, Calcii oxidum Potassii carbonas impura.	India	Hepatoprotective	In-vivo
Majoon	Lawsonia inermis, Foeniculum vulgare,	India Pakistan	Antiarthritic activity	In-vivo
Suranjan	Capparis spinosa, Terminalia chebula, Ipomoea turpethum, Apium graveolens, Zingiber officinalis, Convulvulus scammony, Colchicum luteum, Cassia angustifolia, Piper nigrum, Coriandrum sativum, Rosa damascus, Origanum vulgare, Pyrethrum indicum, Plumbago zelanicum, Verbascum thapus, Ricinus communis oil			
Praneem	Azadirachta indica (Neem) along with purified Saponins from Sapindus mukerosi and Mentha citrata oil	India	Vaginal microbicides	Clinical trial Phase-2
Zylamend	Ocimum sanctum, Curcuma longa, Zingiber officinale, Camellia sinensis, Rosmarinus officinalis, Polygonum cuspidatum, Berberis vulgaris, Origanum vulgare, Scutellaria baicalensis and Coptis chinensis	the United State of America	Prostate cancer	In-vitro
Ovoutoline	Glycyrrhiza glabra, Saraca indica, Symplocos racemosa, Tinospora cordifolia, Asparagus racemosus, Valeriana walchii and Holarrhena antidysenterica	India	post-menopausal symptoms	In-vitro
Okudiabet	Stachytarpheta angustifolia, Alstonia congensis bark and Xylophia aethiopia fruits extract	Nigeria	Anti-diabetic	In-vivo

CONCLUSION

Traditional practitioners emphasize on the clinical responses of individual patients. They are not totally supportive of RCTs which insist on group analysis and uniform treatment. Indeed, traditional practitioners prefer treating their patients according to their syndrome presentation, i.e. the “clinical pattern” apparent to the attending clinician. They are looking forward to a balancing effect rather than an abrupt effective control of the problem. In the situation of osteoporosis, current clinical practice has chosen BMD measurement as a convenient tool of Assessment. The time taken to achieve an observable improvement in BMD while using herbal supplement is expected to be longer and the intensity of improvement is also expected to be milder since the nature of treatment is not specific. Modern pharmaceuticals aim at quick and specific responses. The popular pharmaceutical agents elevate BMD within a short period for the need of those people at high risk. However, a proportion might respond too well to give rise to over hardening of cortical components of the long bone, which might lead to odd fractures at unusual sites. On the other hand, herbal treatment is supportive and slow. It offers prevention and maintenance rather than over-active treatment. Although polyherbal formulation is commonly used in many parts of the world, but the scientific evidence is still lacking. Many herbal therapies are still under in-vivo evaluation and have not been evaluated by clinical trials. Moreover, safety evaluations such as toxicological studies have not

performed. here is need of time to evaluate polyherbal formulation using scientific methods such as clinical trial, possible bioactive compounds and mechanism of action for the future world.

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