Efficacy of OST-6, a polyherbal formulation in the management of osteoporosis in postmenopausal women

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ABSTRACT
A clinical study was conducted to study the safety and efficacy of a polyherbal preparation, OST-6 in postmenopausal women with osteoporosis. Thirty seven women completed the 6-month study. All the participants were on OST-6, an herbal anti-osteoporotic drug, at a dose of 2 tablets twice daily. Bone densitometry studies using an ultrasound bone densitometer were done to evaluate the percentage of bone loss before and after treatment. A complete blood investigation was also done before and after treatment. On evaluation of the patients following 6 months of treatment, the bone density was significantly increased when matched to young adults, by 2.97% when matched to young adults and, by 3.13% when matched to age. Bone loss was also reduced by 1%. The ‘T’ score reduced by –0.263 and the ‘Z’ score reduced by –0.178. There was also an increase in the serum calcium and a decrease in serum phosphorous and alkaline phosphatase levels. The biochemical parameters including kidney function tests were normal before and after treatment. The study revealed that OST-6 is a safe and effective therapy in postmenopausal women with osteoporosis.

INTRODUCTION
Osteoporosis affects all women during the perimenopausal period. Osteoporotic fractures are more common in older postmenopausal women and account for significant morbidity and mortality. Although age is an independent risk factor for fractures, bone mineral density (BMD) is one of the strongest predictors of fractures. Women often are unaware that they have osteoporosis until they experience an unexpected and painful fracture, usually when they are in their postmenopausal period. The first indication of osteoporosis may be a broken wrist or hip caused by a minor fall. Osteoporotic fractures, particularly those of the hip and spine, often lead to significant pain and disability. The fracture of the wrist often heals with little residual deformity. Studies have also shown that women lose more trabecular bone at a higher rate than men.

Prevention of bone loss with hormone replacement therapy (HRT) has been shown to reduce the incidence of vertebral and hip fractures. However, HRT is associated with increased risks of breast cancer, thrombo-embolism and hypertension, which are well documented.
Withdrawal bleeding together with increased risk factors limits the acceptability of long-term (hormonal estrogen) treatment.\textsuperscript{7,8}

Recent evidence suggests that the rate of bone loss and the degree of bone resorption may be important factors in predicting future fractures.\textsuperscript{9} In elderly women, bone resorption is markedly increased\textsuperscript{10}. This results in uncoupling of the bone-remodeling unit.\textsuperscript{11}

OST-6 is a herbomineral formulation comprising of *Terminalia arjuna*, *Withania somnifera*, *Commiphora wightii*, *Sida cordifolia*, *Vanda roxburghii*, Godanti bhasma and Kukkutandatvak bhasma that are well known for their bone remineralization properties. *Terminalia arjuna* is extensively used to treat osteoporosis and other bone related disorders as it improves the synthesis and secretion of female hormones.\textsuperscript{12} *Withania somnifera* is considered a rejuvenator in Ayurveda. It helps in relieving pain associated with osteoporosis, nervous exhaustion and muscular pains.\textsuperscript{13} *Commiphora wightii* helps in remineralization of the bones, thus reversing the process of osteoporosis.\textsuperscript{14} *Sida cordifolia* has natural phytosterol and phytoestrogens. *Vanda roxburghii* possesses anti-inflammatory properties and relieves joint pains in osteoporosis. Godanti bhasma and Kukkutandatvak bhasma are rich natural forms of calcium. Kukkutandatvak bhasma has an additional adaptogenic property, which is useful in relieving general debility in postmenopausal women.

### MATERIALS AND METHODS
Forty post-menopausal women who were 5 to 30 years post menopause were recruited in the study. The minimum age was 48 and the maximum was 72 years. Women on estrogen therapy were excluded from the trial. All of them were subjected to detailed physical examination and laboratory baseline investigations. The laboratory investigations included complete haemogram including haemoglobin, total and differential white cell count, erythrocyte sedimentation rate, kidney function test (serum creatinine and BUN), serum calcium, phosphorous and blood urea. All the patients were subjected for ultrasound bone densitometry to assess the bone loss before starting drug therapy.

A written informed consent was obtained from all the women prior to trial drug administration.

All women were recommended OST-6 twice daily for 6 months. Their daily dietary calcium intake did not exceed 1 g, as demonstrated by a dietary questionnaire administered at baseline. They were followed up every month for 6 months and subsequently re-examined at one year. Participants were questioned about adverse events at each visit, which were reported in the follow-up proforma.

Bone mineral density was measured at the calcaneum before treatment and after 6 months of treatment with OST-6. The instrument used in the study was LUNAR ACHILLES EXPRESS BONE ULTRASONOMETER.

The patients bone loss ranged from 5% to 57%. The ‘T’ score ranged from –5.240 to -0.6310. When these patients were compared and matched with a 25-year-old young adult there was bone loss of 43% to 95%.
Statistical Analysis
Statistical analyses were done using repeated ANOVA measures using Graph Pad Prism 3.0 software.

RESULTS
Thirty-seven women completed 6 months of treatment with OST-6, 3 patients however, did not complete the trial due to unexplained reasons and were dropped from the study. There was excellent compliance to OST-6 and symptoms of bone pain was significantly reduced, and the bone densitometry result showed significant improvement. The ‘T’ score which was $-3.061$ was reduced to $-2.798$ ($p<0.0042$), the ‘Z’ score, which was $-1.619$ was reduced to $-1.441$ ($p<0.0042$) (Figure 1). There was increase in the bone mineral density by 1%. The mean bone loss before treatment was 32.05% and after 6 months of treatment it was reduced to 31% ($p<0.0024$) (Figure 2). The bone density of these post menopausal women when compared to a young adult female of 25 years increased by 2.97% ($p<0.0031$) and bone density when matched to an adult female of that age group increased by 3.13% ($p<0.0037$). The serum calcium, which was 9.24 mg% before treatment increased to 9.549 mg% ($p<0.0005$). Serum phosphorous was 3.802 mg% before treatment and was reduced to 3.519 mg% ($p<0.0002$) after treatment (Table 1). The routine blood examination, kidney function tests and the blood sugar were not altered after treatment, indicating that OST-6 is safe in women with postmenopausal osteoporosis.

Table 1: Hematological and Biochemical Parameters (Mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (%)</td>
<td>15.71 ± 0.8591</td>
<td>15.68 ± 0.7237</td>
</tr>
<tr>
<td>Total cholesterol (cu.mm.)</td>
<td>7611.00 ± 854.80</td>
<td>7688.00 ± 892.00</td>
</tr>
<tr>
<td>Random blood sugar (mg/dl)</td>
<td>94.24 ± 22.85</td>
<td>111.8 ± 29.78</td>
</tr>
<tr>
<td>Blood urea (mg/dl)</td>
<td>22.47 ± 4.62</td>
<td>22.14 ± 3.87</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.8326 ± 0.09694</td>
<td>0.8334 ± 0.09096</td>
</tr>
<tr>
<td>Serum calcium (mg/dl)</td>
<td>9.247 ± 0.5323</td>
<td>9.549 ± 0.5416</td>
</tr>
<tr>
<td>Serum phosphorous (mg/dl)</td>
<td>3.802 ± 0.5369</td>
<td>3.519 ± 0.5155</td>
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DISCUSSION

OST-6 addresses two factors associated with healthy bone architecture: adequate calcium supplementation and appropriate hormonal balance. Earlier studies with OST-6 demonstrate a dose-dependent increase in the bone mineral content and density. OST-6 treatment shows desired effect on inhibitors on bone reabsorption and stimulators of bone formation in experimental studies, thereby indicating a potential therapeutic usefulness as an anti-osteoporotic agent\(^\text{15}\). It consists of *Terminalia arjuna, Withania somnifera, Commiphora wightii, Sida cordifolia, Vanda roxburghii*, Godanti bhasma and Kukkutandatvak bhasma. Godanti bhasma and Kukkutandatvak bhasma present in OST-6 are the rich natural sources of calcium that are present in adequate levels required for the management of osteoporosis. *Sida cordifolia* and *Withania somnifera* present in OST-6 contain phytoestrogens, which influences bone mineral density. Phytoestrogens are naturally occurring compounds found in many medicinal herbs with a historical use in conditions that are now treated by estrogens. The majority of phytoestrogens found in plants can be classified into two major categories: isoflavones and lignans. After consumption of the plant lignans and isoflavone precursors, metabolic conversions occur in the gastrointestinal tract resulting in the formation of heterocyclic phenols that are similar in structure to estrogens.\(^\text{16}\) Phytoestrogens have a diphenolic ring in chemical structure that is very similar to endogenous estrogens, estradiol and diethylstilbestrol, accounting for their weak estrogen-like effects. Most phytoestrogens contain at least one aromatic ring with a hydroxyl group, similar to those of estrogens, and have been found to bind to the two subtypes of estrogen receptors, but more strongly to the beta-receptors.\(^\text{17}\)

Phytoestrogens are therefore considered as natural selective estrogen receptor modulators, as they appear to be estrogen agonists for the cardiovascular system, bone and brain, while having either no agonist or, perhaps, antagonist effects for the mammary gland and uterus.\(^\text{18}\) As steroidal estrogens are of benefit in preventing osteoporosis, phytoestrogens also have a protective effect in the postmenopausal woman.\(^\text{19}\)

Recent studies conducted on phytoestrogen effect on bone mineral density in hypercholesteremiic post menopausal women showed significant increase in bone mineral density and bone mineral content in the lumbar spine.\(^\text{20}\) *In vitro*, isoflavone can stimulate osteoblast-like cell formation and also suppress osteoclast formation and induce osteoclast apoptosis.\(^\text{21}\) Isoflavone also slows bone reabsorption and stimulates collagen synthesis in bone.\(^\text{22}\) There is evidence from animal studies that phytoestrogens preserve bone mineral density.\(^\text{23}\) Studies conducted with isoflavone derivative ipriflavone have found that it reduces bone loss in postmenopausal women.\(^\text{24}\)

This study confirms the benefits of OST-6 in postmenopausal osteoporosis. There is evidence from this study that OST-6 protects against fractures and slows or reverses bone loss. OST-6 provides benefits in women with associated risk of coronary heart disease. In this study it was seen that the ‘T’ score was reduced by –0.263 within 6 months of treatment. The ‘Z’ score also was reduced by –0.178. The total bone loss was reduced by 1%. The bone mineral density when matched with that of a young adult of 25 years increased by 2.97% and when matched for that particular age in healthy postmenopausal women there was an increase of 3.13%. There was also an increase in serum calcium and simultaneous decrease in serum
phosphorous and alkaline phosphatase. This showed that OST-6 prevents bone loss during the menopausal period. The common symptoms such as backache and leg pain also reduced. This may be attributable to Commiphora wightii, which has a potent anti-inflammatory property. Additional natural forms of calcium, through Kukkutandatvāk and Godanthi bhasmas provide adequate calcium required to prevent osteoporosis.

CONCLUSION
We report that OST-6 prevents bone loss in postmenopausal women primarily by slowing bone resorption. OST-6 provides 362.4 mg of calcium/tablet. Hence, administering 4 tablets/day provides 1449.6 mg calcium, which is in the range of recommended calcium for the osteoporotic patients.

This is a short-term study on a small population of women, the efficacy of OST-6 can be further evaluated in a larger population of women with a longer follow-up.

REFERENCES


