



## A Comparative Study of the Effect of Thyme and Calcium with Vitamin D3 in Treatment of postmenopausal Women with Osteoporosis

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**Abstract :** Osteoporosis is a condition of skeletal fragility due to progressive loss of bone mass. It occurs in the elderly of both sexes but is most pronounced in postmenopausal women . The aim of this study was to assess the efficacy of Thyme in treatment of postmenopausal women with osteoporosis and compare it's effect with Calcium plus Vitamin D3 .Forty postmenopausal women with osteoporosis were randomly divided into two groups( each group include twenty women) .The duration of treatment was 6 months . First group was given Thyme capsule 500mg twice daily, second group was given Calcium plus Vitamin D3(Calcium 600mg plus Vitamin D3 500 I.U.) once daily .The following parameters were measured for two groups at baseline and at 6 months intervalsbone mineral density(BMD)and t score except ESR and serum ionized calcium were measured at baseline and at 2 months interval . There were a significant increase in BMD, t score in group treated with Thyme after 6 months as compared with baseline and with group treated with Calcium plus Vitamin D3 . Also there were a significant reduction in mean serum ionized calcium and mean ESR in group treated with Thyme and group treated with Calcium with vitamin D3 after 2,4,6 months as compared with baseline(P<0.05).

**Keywords :**Thyme, BMD, Calcium, Vitamin D3, Osteoporosis, t score.

### Introduction

Osteoporosis is a serious disease that decreases both the quality and quantity of life (1,2). The disease enhances morbidity and mortality, and it affects hundreds of millions of persons worldwide (3,4). Osteoporosis is a progressive bone disease that is characterized by a reduce in bone mass and density which can cause an increased risk of fracture(5). In osteoporosis, the bone mineral density (BMD) is decreased, bone microarchitecture deteriorates, and the quantity proteins in bone are changed. A recent meta-analysis showed reduce rates of fracture in older women with 80% or greater adherence to calcium supplementation(6) . A daily intake of calcium at least 1,200 mg is recommended for all women suffer from osteoporosis(7, 8) .Recent study has shown that supplementation of 800 mg of calcium per day may helpful to prevent bone loss in postmenopausal women, and the information from clinical trials also show that such supplementation may prevent vertebral and hip fractures in the elderly(9,10 ) .The combination of calcium (1.2 g/day) with vitamin D<sub>3</sub> (800 IU/day) has been used to prevent fractures in elderly women, Daniel obtained that the total number of non vertebral fractures was 32% lower and the number of hip fractures was 43% lower among women treated with calcium and vitamin D<sub>3</sub> than among those who take placebo(11,12) . Enhanced intake of calcium from natural sources, especially low-fat dairy products, such as cheese , ice cream , yogurt , , and milk, may also help prevent or reduce the progress of osteoporosis, although the influences are notgreat(13,14). One review

recorded that sage, thyme extract, rosemary, and other plants, appear to inhibit osteoclast activity, increasing bone density in animals, but more study is needed in humans(15). The essential oil of thyme (*Thymus vulgaris*), contains 20–54% thymol(16). Essential oil of Thyme also contains a range of additional compounds, like linalool, myrcene, p-Cymene, and borneol (Chemical Composition of Thyme Essential Oil). Thymol, an antiseptic, is the major active component in several commercially produced mouth washes like Listerine(17). Before the discovery of modern antibiotics, thyme oil was used to medicate bandages(18). Thymol has also been noted to be effective against different fungi that commonly infect toenails(19). Thymol can also be present as the active component in some natural, alcohol free hand sanitizers. In One study introduced by Leeds Metropolitan University recorded that thyme may be helpful in treating acne (20, 21).

## **Patients, Materials, and methods**

### **Patients**

This is a randomized prospective clinical trial study. It was conducted in Merjan Teaching Hospital in DEXA unit which present in Rheumatology department. The study was conducted between March 2014 and March 2015. The study was approved by ethical committee at Al- Nahrain University/Faculty of Medicine.

### **Sample size**

The sample of the study include (40 postmenopausal women suffering from Osteoporosis). They divide into two groups, each group include 20 patient. The duration of treatment is 6 months.

### **Study Groups**

Group I:- received Thymecapsule 500mg twice daily.

Group II:- received Calcium with Vitamin D3 (Calcium hydrogen Phosphate 600mg and Vitamin D3 500I.U.) one tablet daily.

All the following parameters were measured for all groups at baseline and at 2 months interval for 6 months duration except BMD, t score was measured before treatment and 6 months of treatment, parameters include ESR, Serum ionized calcium.

### **Data collection**

The method of collecting information depend on direct (personal) interview in a specific room attached to unit DEXA measurement. The data were collected through the used of developed questionnaire and the structured interview technique patients. Data were collected from the patients in organized fashion and individually with all the patients. The interview lasted for about (30) minutes, knowing that the data collection was only every Monday and Wednesday from every week, begin at 8:00 am. and continue until 2:00 pm.

### **Statistical analysis**

Statistical analyses were performed using SPSS 16.0 for windows. Inc. An expert statistical advice was consulted for tests used. Data of quantitative variables were expressed as mean  $\pm$  SEM. Differences in each variable through treatment intervals in the same group were compared using paired-sample Student's t-test. Analysis of Variance (ANOVA) followed by post-hoc tests using LSD method were used for the multiple comparisons among all groups. In all tests,  $P < 0.05$  was considered to be statistically significant unless another levels were stated.

## **Results**

### **Anthropometry**

Between the two groups included in this study, there were no significant difference in anthropometric data as shown in table (1).

**Table 1: Anthropometric data for all included patients in this study**

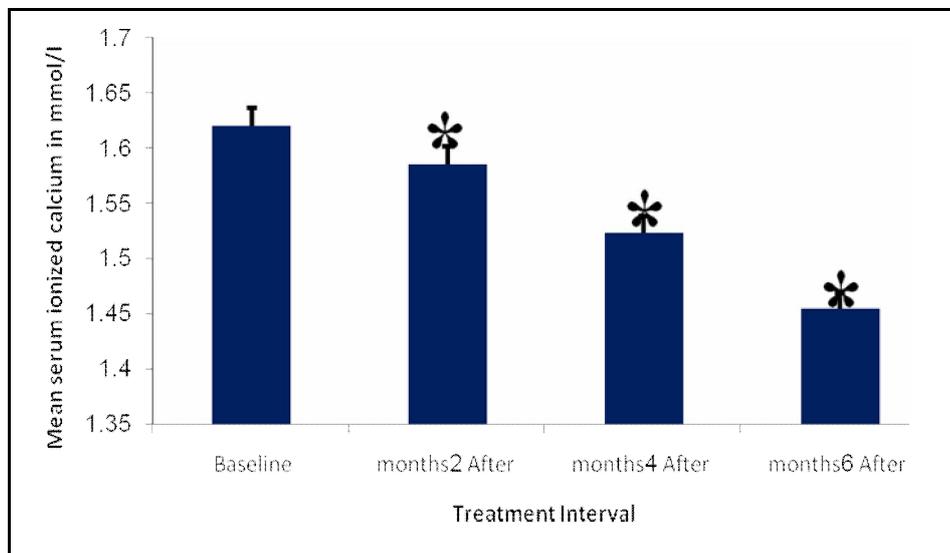
Anthropometric data	Mean±SEM (Group I)	Mean±SEM (Group II)
Age(year)	57.15±1.96	60.9±1.96
Weight(kg)	82.2±2.49	83.95±4.06
Height(cm)	153.4±1.19	155.6±1.56

**Effect of the two treatment regimen on BMD, t score, serum ionized calcium, ESR**

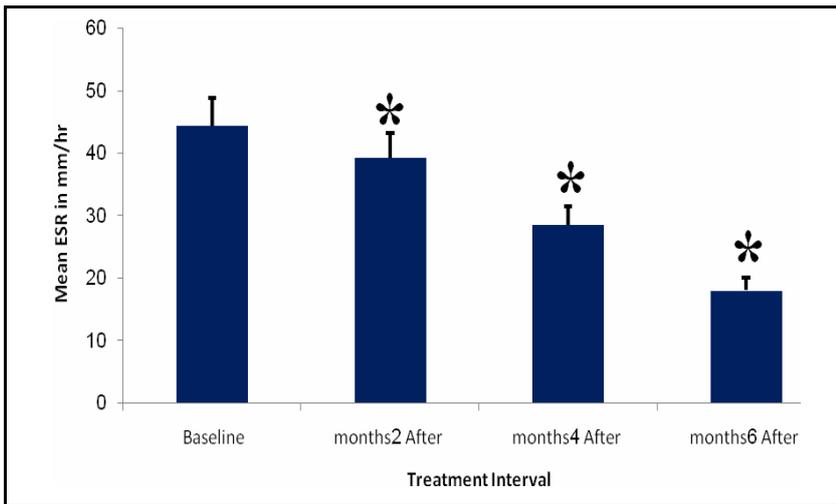
There were a significant reduction in mean serum ionized calcium, ESR in group treated with thyme after 2,4,6 months(P<0.05) as compared with baseline as shown in figure(1,2), also there were a significant increase in mean t score, BMD after 6 months(P<0.05) as compared with baseline as shown in figure(3,4). There were a significant reduction in mean serum ionized calcium, ESR in group treated with Calcium plus Vitamin D3 after 2,4,6 months(P<0.05) as compared with baseline as shown in figure(5,6), also there were a significant increase in mean t score, BMD after 6 months(P<0.05) as compared with baseline as shown in figure(7,8). In multiple comparison thyme more efficacious than calcium plus vitamin D3 in treatment of postmenopausal osteoporosis than as shown in table(2).

**Table(2) percentage of patients remain osteoporosis, become osteopenia or normal after end of treatment**

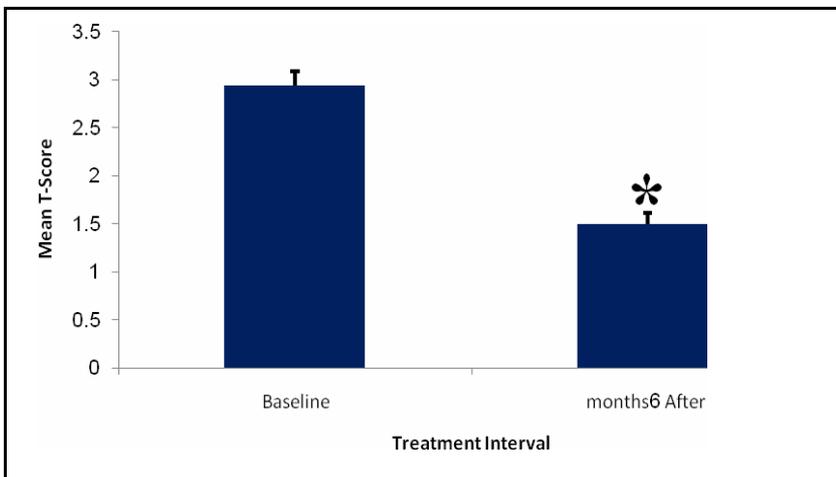
Osteoporosis (No. ,%)	Osteopenia (No. ,%)	Normal (No. ,%)	Group
2, 10%	11, 55%	7, 35%	Thyme
5, 25%	10, 50%	5, 25%	Calcium with Vitamin D3



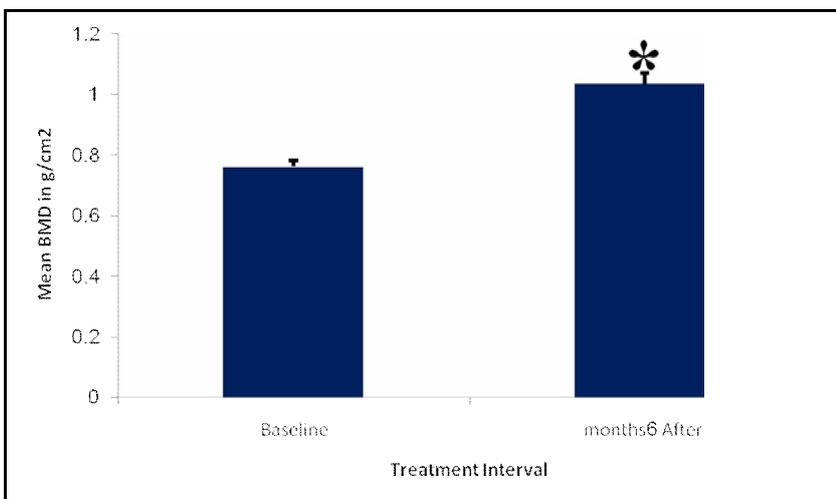
**Figure(1):-A comparative effect of Thyme on mean ionized calcium at different time interval (\*) :- Mean there is a significant difference**



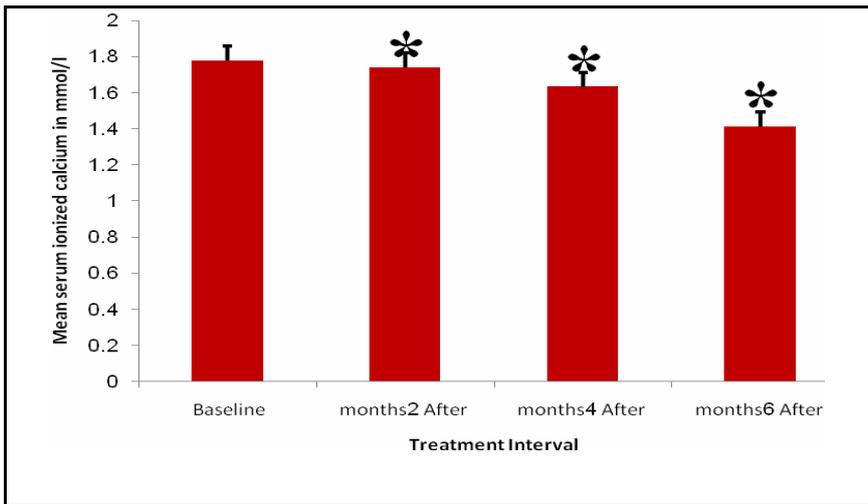
**Figure(2):-A comparative effect of Thyme on mean serum ESR at different time interval (\*) :- Mean there is a significant difference**



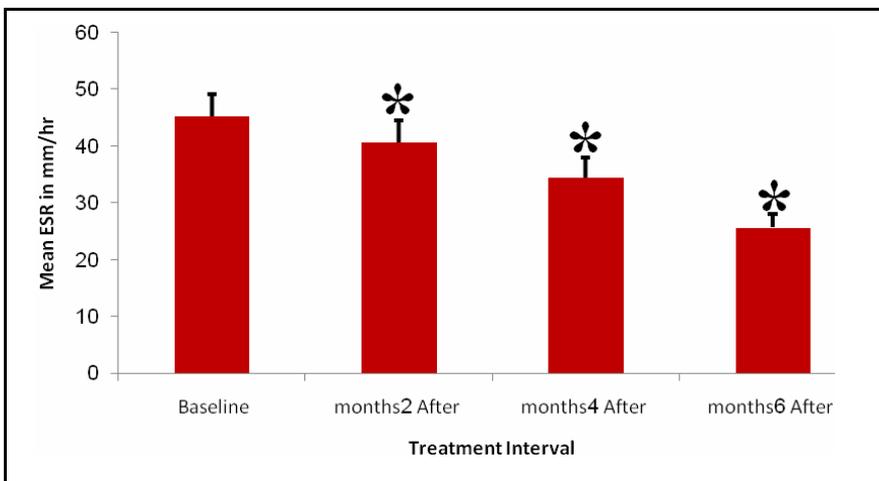
**Figure(3):-A comparative effect of Thyme on mean T-score at different time interval (\*) :- Mean there is a significant difference**



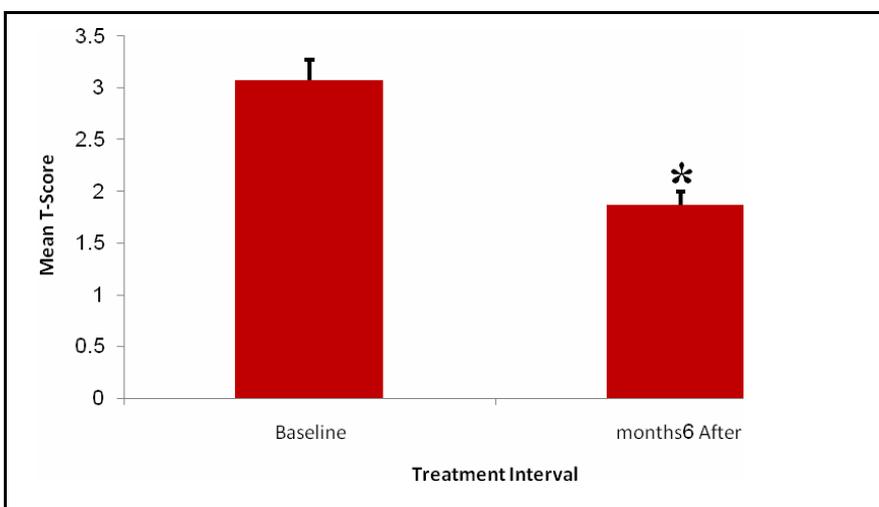
**Figure(4):-A comparative effect of Thyme on mean BMD at different time interval (\*) :- Mean there is a significant difference**



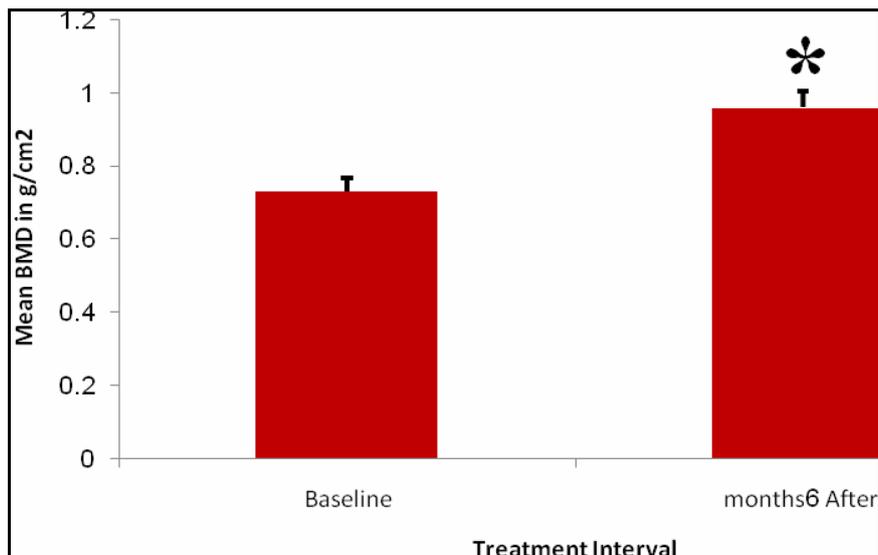
**Figure(5):-A comparative effect of Calcium with vitamin D3 on mean ionized calcium at different time interval (\*) :- Mean there is a significant difference**



**Figure(6):-A comparative effect of Calcium with vitamin D3 on mean ESR at different time interval (\*) :- Mean there is a significant difference**



**Figure(7):-A comparative effect of Calcium with vitamin D3 on mean T-Score at different time interval (\*) :- Mean there is a significant difference**



**Figure(16):-A comparative effect of Calcium with vitamin D3 on mean BMD at different time interval (\*) :- Mean there is a significant difference**

## Discussion

Osteoporosis is a bone disease in which the quantity of bone is reduced and the structural integrity of trabecular bone is disturbed. Cortical bone becomes more porous and thinner. This renders the bone very weak and more likely to fracture. Osteoporosis is characterized by reduce bone mineral density (BMD) and enhanced likelihood of bone fracture ( 22) . Fracture sequela include pain psychiatric distress, stature changes, raise morbidity and mortality, and increased hospitalization (23, <http://www.hindawi.com/journals/jos/2014/909153/-B324>) .However, pharmacotherapy is efficacious in maintaining skeletal health, slowing bone loss, and reducing fracture risk. Common treatment include bisphosphonates such as sodium alendronate and selective estrogen receptor moderators (SERMs), such as raloxifene, also calcitonin . These antiresorptive drugs decrease bone turnover by suppressing osteoclastic activity, thus enhancing BMD and bone microarchitecture (25) .

### Effect of Thyme on different parameters of the present study

The present study show a significant reduction in mean serum ionized calcium after 2,4,6 months treatment with thyme as compared with baseline mean serum ionized calcium as shown in figure(1) .These findings were in line with findings of study by Banu et al.,(26) , they were stated that several herbs were had a protective effect on the bone including black cohosh, red clovers, thyme, and good source of calcium , iron, potassium, and enhance the absorption of calcium from the intestine, so they were had a regulatory role in maintain the calcium homeostasis, thus when given to postmenopausal osteoporosis, they were reduce the elevated serum ionized calcium in preclinical studies .

The results of current study show a significant reduction in mean ESR after 2,4,6 months treatment with thyme as compared with baseline mean ESR as shown in figure (2) . These findings were in consistency with findings of study by Saw et al.,(27), Zhang et al.,(28),they were reported that in study on the use of angelica sinensis root extract in experimental model of ovariectomized osteoporosis rat, in osteoporosis Pro-inflammatory cytokines such as interleukin-1 (IL-1), IL-6, and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) are well known regulators of bone metabolism, These cytokines are known as highly potent bone resorption cytokines ,which can mediate increased bone turnover markers, thus ESR was a marker of inflammation was measured and recorded elevated, thus it is hypothesized that the anti-inflammatory action of A. sinensis extract Lim and Kim (29) might have potential anti-osteoporotic effects in an animal model via inhibition of bone turnover markers and ESR was decrease(30) .

The results of current study show a significant increase in mean T score, BMD after 6 months treatment with thyme as compared with baseline mean T score , BMD as shown in figure(3,4) .These findings were had similarity with findings of studies by Setchell and Lydeking-Olsen (31), Zhao et al.,(32) ,they were demonstrated that the phytoestrogens in the herbal preparations, certain flavones, isoflavones, flavanones,

flavonols, coumestans, and lignans, could be playing an important role in the amelioration of postmenopausal bone loss and increase bone mineral density by increase osteoblast activity and decrease osteoclast activity (33,34).

### Effect of Calcium plus Vitamin D3 on different parameters of the present study

The results of current study show a significant reduction in mean serum ionized calcium after 2,4,6 months treatment with calcium + vitamin D3 as compared with baseline mean serum ionized calcium as shown in figure(5). These results were in accordance with the findings of Boonen et al.,(35), Meggan et al.,(36), they were stated that supplementation of calcium with vitamin D3 for postmenopausal women with osteoporosis result in reduction of serum ionized calcium because there is a negative feedback mechanism that maintain the calcium homeostasis and help to remove calcium from the blood to the bone which accomplished by assistant of vitamin D3.

The present study show a significant reduction in mean ESR after 2,4,6 months treatment with calcium plus vitamin D3 as compared with baseline mean ESR as shown in figure(6). These results were in consistency with the results of study by Mundy (37), which was stated that in osteoporosis activated macrophage produce proinflammatory cytokines (TNF  $\alpha$ , interleukin IL-1, IL-6, IL-11, IL-1 and IL-17) which induce osteoclast formation and activation, thus treatment with antiosteoporotic drugs result in decrease ESR which is a marker of inflammation because the osteoclast activity and macrophage activity were reduced due to they were originated from bone marrow(30).

The present study show a significant increase in mean T score, BMD after 6 months treatment with calcium + vitamin D3 as compared with baseline mean T-score, BMD as shown in figure(7,8). This fact were in line with Vonhurst (38) study which stated that nutritional habits had a positive effect on BMD, and in accordance with L'Abbe et al.,(39) study, they were reported that calcium and vitamin D intake are the most important determinants of peak BMD, they also contribute to maximize the bone strength (40).

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