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ORIGINAL ARTICLE

Protective Effect of Fucoxanthin on Ovariectomy-Induced Osteoporosis in Rats

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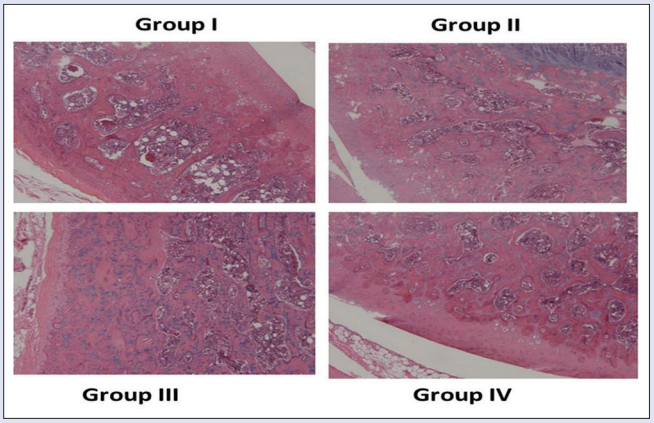
ABSTRACT

Background: The necessity for development of antiosteoporotic drug is receiving increased attention because of high mortality and morbidity rates arising globally. The natural herbal-based compounds such as fucoxanthin possessed greater therapeutic potentials in biomedical field. **Objective:** We planned to investigate the therapeutic effect of fucoxanthin on ovariectomy-stimulated osteoporosis in experimental rats. Hence, the study is conducted to evaluate the protective effect of fucoxanthin against ovariectomy-induced osteoporosis in female Sprague Dawley (SD) rats. **Materials and Methods:** Healthy adult female SD rats weighing about 230–245 g were randomized into four groups of six animals each. Group I served as sham-operated control. Group II served as model (ovariectomized [OVX]) rats. OVX rats were administered with fucoxanthin at a dose of 20 mg/kg and 40 mg/kg orally for 16 weeks which served as Group III and Group IV, respectively. **Results:** A significant increase in body weight and decrease in uterine index was observed in OVX rats, whereas treatment with fucoxanthin substantially reverted the body weight and uterine mass. Bone turnover markers (Ca, P, and osteocalcin), levels of estrogen and 1,25-dihydroxycholecalciferol $1,25(OH)_2D_3$, osteoprotegerin and receptor activator of nuclear factor-κB ligand, and inflammatory markers were reverted back to a significant extent by treatment with fucoxanthin. The biomechanical stability of bones was significantly increased with administration of fucoxanthin. The findings were also substantiated by histopathological analysis. **Conclusion:** Based on the outcome of the results, it can be concluded that fucoxanthin showed better protection against osteoporosis by improving bone mineral content and bone density in addition to biomechanical parameters.

Key words: Bone loss, fucoxanthin, inflammation, osteoporosis, ovariectomy

SUMMARY

- Osteoporosis is a multifactorial and chronic disease of bone which progresses unnoticeably until advanced stage but with complex pathophysiology.
- Fucoxanthin is a marine carotenoid, where numerous studies have reported that various antioxidants and carotenoids available in abundance in fruits and vegetables are associated with reduced risk of bone fracture and/or ensuing osteoporosis.



Abbreviations used: OVX: Ovariectomized; E2: Estrogen; OPG: Osteoprotegerin; RANKL: Receptor activator of nuclear factor-κB ligand; ERT: Estrogen replacement therapy.

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INTRODUCTION

Osteoporosis is a multifactorial and chronic disease of bone which progresses unnoticeably until advanced stage but with complex pathophysiology.[1,2] It is mainly characterized by decreased bone density and mass which eventually results in increased fracture and fragility of bones.[3-5] It is one of the major health problems of concern with higher incidence rate among postmenopausal and elderly women.[6] Menopause in those women is associated with increased risk of osteoporosis which occurs as a result of imbalance between the osteoclast formation and resorption capacity of bones due to loss of estrogen (E2).[7] Decreased E2 acts as an effective initiator of loss of bone density and ensuing osteoporosis.[8]

Estrogen replacement therapy (ERT) or hormone replacement therapy (HRT) has been proven to be beneficial in preventing bone loss in postmenopausal and elderly women.[9,10] Unfortunately, long-term usage of HRT results in undesirable side effects, and it predisposes users to risk of developing ovarian, breast, and endometrial cancers.[11] Maintaining

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standard levels of calcium (Ca) and Vitamin D helps in prevention of osteoporosis. In addition to this, regular exercise, avoiding smoking, and caffeine and alcohol intake also act as preventive actions from developing osteoporosis.[12] Adequate intake of nutrients in diet along with necessary Ca and Vitamin D helps in minimizing bone loss and density.[13-15] Loss of bone in postmenopausal women arises mainly as a result of oxidative stress which occurs from overproduction of free radicals and altered or lowered action of antioxidants and ensuing inflammation. Oxidative stress increases bone differentiation and osteoclastic function of bones, thus resulting in loss of bones.[16-18]

At present, osteoporosis has developed as a major threat to humankind and it results in lack or reduced physical activity, quality of life is lowered, and mortality rate increased devastatingly.[6] Almost nearly 200 million people are affected.[19] Increased aging population and poor life quality worldwide have increased the risk of osteoporosis in those populations.[20] Thus, osteoporosis results in overall socioeconomic burden, increased mortality, and fractures.[21] However, pathological events that lead to the development of osteoporosis are poorly elucidated. Therapeutic regimens available for osteoporosis include HRT, modulation of E2 receptor, Vitamin D, and mineral supplementation in addition to various antiosteoporotic drugs.[22] Apart from this, the ovariectomy procedure was performed to women globally to maintain the homeostatic balance between bone resorption and formation. However, the methodologies adopted for treating osteoporosis is reported with adverse side effects such as bone or muscle pain, nausea, difficulty in swallowing, and heartburn.[23]

Thus, effective treatment strategies including intake of healthy nutrients in diet and proper physical activity might reduce the risk of osteoporosis.[24,25] Therefore, further investigation is needed to find alternative approaches that might minimize the osteoporotic bone loss. In such scenario, treatment using nonhormonal methodologies or compounds derived from natural products might be of great importance in preventing osteoporosis.[26]

Fucoxanthin is one such marine carotenoid which is extracted from brown seaweeds. Fucoxanthin has attracted attention because of its wide range of beneficial properties which include its antioxidant, anticancer, antidiabetic, cardioprotective, anti-inflammatory, anti-malarial, hepatoprotective, and its protective effects in brain, bones, eyes, and skin.[27] Bone resorption, suppressed osteoclast formation, and apoptosis in *in vitro* have been reported.[28,29] Fucoxanthin has been reported to be safe for animal consumption which makes it a promising medicinal agent for treating wide range of pathologies.[30,31] In view of this, the present study assessed the efficacy and mechanism of fucoxanthin action using ovariectomy-induced osteoporotic rats.

MATERIALS AND METHODS

Healthy female Sprague Dawley rats weighing about 230–245 g were used in this study. The animals were purchased and maintained under standard animal house conditions in air-conditioned environment with adequate light. The rats were fed with commercially procured standard pellet diet and allowed free access to water throughout the experimental period. The experiments were carried out according to the guidelines approved by the Institutional Animal Ethical Committee (Approval number: 2019-1016).

The rats used for the experimental study were randomized into four groups of six animals each. Group I was sham (SHAM) which were fed with standard pellet diet. Group II rats were ovariectomized (OVX) and maintained for 3 weeks after operative procedure. Group III rats were OVX and administered fucoxanthin (20 mg/kg body weight) orally for 16 weeks. Group IV rats were OVX and administered fucoxanthin (40 mg/kg body weight) for 16 weeks.

After the end of the treatment period, the animals were anesthetized with ketamine inhalation and sacrificed, and blood was collected by cardiac puncture for biochemical analysis. The body weight of all the rats was measured from day 0 till the final day of the experiment, and the alterations in their weight gain were calculated. The uteri were isolated and measured at the end of the experimental period.

The uterine horns were dissected following anesthesia and weighed. Following centrifugation, serum was obtained and maintained at −80°C for further analysis. Femurs were also dissected from all experimental groups and wrapped in cotton gauze soaked in saline and stored at −20°C for biomechanical examination.

Ovariectomy procedure

Either rat was anesthetized and bilateral ovariectomy procedure was performed by making incisions dorsolaterally using scissors under ketamine anesthesia. The dorsal muscles and the skin of the rats were cut, and the fat tissues around the ovary were removed. The junction between the uterine horn and fallopian tubes was clamped, and the cut was made to remove the ovary. After the removal of ovary, the skin was closed by suture. The method of ovariectomy was carried out as described previously.[32] In SHAM control rats, the procedure was performed, but the ovaries were exposed.

Assessment of serum concentration of inflammatory markers, bone turnover markers, estrogen, 1,25-dihydroxycholecalciferol, osteoprotegerin, and receptor activator of nuclear factor-κB ligand

Concentration of inflammatory markers such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and IL-1β and bone turnover marker osteocalcin (OC) and the levels of E2 and $1,25(OH)_2D_3$, osteoprotegerin (OPG),[33] and receptor activator of nuclear factor-κB ligand (RANKL)[34] in serum sample were assayed using ELISA kits (Thermo Fisher Scientific Inc., MA, USA), and the procedure was performed according to the protocol given by the supplier.

Blood samples collected by cardiac puncture were left to clot for about 10 min. Then, the serum was collected by centrifuging blood for 5 min at 12000 rpm. Serum Ca and phosphorus (P) concentrations were determined colorimetrically using specific diagnostic kits (Thermo Fisher Scientific Inc., MA, USA), and the absorbance was measured spectrophotometrically.[35,36]

Assessment of bone mineral content and bone mineral density

Bone mineral content (BMC) and mineral density of the bones (BMD) of the left femur of control and OVX rats were measured at the end of the experimental period using lunar prodigy advance dual-energy X-ray absorptiometry which is equipped with specific software for assessing bone density in rats.[37] The results were represented as g and g/cm^2.

Biomechanical examination of femur (bending test)

The femurs which were stored at −20°C were thawed and brought to room temperature to examine the biomechanical stability using MTS 858 Mini Bionix testing machine. The procedure was performed as instructed by the manufacturer. The length and diameter of the femur were calculated before testing by caliper. The biomechanical stability of the femur was determined at a rate of 2 mm/min and the load–deformation curve calculated.[38] Calculating the load–deformation curve helps in determining the energy absorption, stiffness, young modulus, and maximum load and stress.

Histopathological examination of femur

The sections of femur were excised and fixed in phosphate-buffered formaldehyde solution for 24 h and then decalcified for 3 weeks in formic acid. The tissues were cut using a microtome longitudinally at 5 µm and stained with hematoxylin and eosin (H and E) for histological examination.[39]

Statistical analysis

The data were represented as mean ± standard deviation. Comparisons between the groups were made statistically using one-way analysis of variance, and the intercomparison between the groups was made using least significant difference method. Statistical analysis was done with SPSS software (version 21 (SPSS Inc., Chicago, IL, USA)) which was used for data processing, and the level of significance was represented as $P < 0.05$.

RESULTS

Effect of fucoxanthin on body weight and uterine index of sham-operated control and experimental rats

The body weight analysis of control and experimental animals revealed that OVX rats have gained more body weight than the sham-operated control animals [Figure 1a]. OVX rats treated with fucoxanthin at 20 mg/kg and 40 mg/kg showed a significant ($P < 0.05$) decrease in body weight in comparison to that of untreated Group II OVX rats. Figure 1b portrays the uterine index of control and OVX experimental rats. Ovariectomy in rats resulted in a significant decrease in uterine index than the sham control rats (Group I). Fucoxanthin-administered OVX rats displayed an increase in uterine weight than OVX rats.

Effect of fucoxanthin on serum concentration of inflammatory markers, bone turnover markers, estrogen, 1,25-dihydroxycholecalciferol ($1,25(OH)_2D_3$), osteoprotegerin, and receptor activator of nuclear factor-κB ligand

The concentration of IL-6, TNF-α, and IL-1β in serum were increased concomitantly in the OVX-induced group (Group II) when compared to sham-operated control rats [Figure 2]. However, intervention with fucoxanthin was downregulated the expression of pro-inflammatory cytokines in Group III and Group IV animals to a significant extent ($P < 0.05$) as compared to OVX Group II animals in a dose-dependent manner.

The results of serum bone turnover markers in control and OVX-induced experimental animals are represented in Figure 3. The results indicated that the levels of OC were increased to a significant level in OVX rats when compared to sham control animals. OVX rats which were supplemented with fucoxanthin (20 mg/kg and 40 mg/kg) in a dose-dependent manner markedly reduced the levels of OC in serum of Group III and Group IV rats when compared to Group II. In contrast, serum levels of Ca and P were found to be lowered in OVX rats than control animals. Ca and P levels were upregulated by supplementation of fucoxanthin to OVX rats, which are represented in Group III and Group IV rats.

The serum levels of E2 and $1,25(OH)_2D_3$ in different groups of rats were represented in Table 1. The findings indicated that the serum levels of E2 and $1,25(OH)_2D_3$ in OVX rats were increased to a marked level compared to sham-operated control animals. OVX animals treated with fucoxanthin showed a significant improvement in serum levels of E2 and $1,25(OH)_2D_3$ in Group III and Group IV animals. Interestingly, fucoxanthin treatment has increased the levels of E2 and $1,25(OH)_2D_3$ in a dose-dependent manner.

Osteoporotic OVX rats (Group II) displayed a noticeable elevation in the levels of RANKL, whereas OPG levels were lowered in serum with respect to Group I animals [Figure 4]. Oral supplementation of fucoxanthin (20 and 40 mg/kg) to OVX rats portrayed a marked reduction in RANKL and increase in OPG levels (Groups III and IV), respectively, when compared to Group II.

Effect of fucoxanthin on bone mineral content and bone mineral density

BMC and BMD of sham-operated control and experimental animals are represented in Figure 5. Ovariectomy significantly decreased the BMC and BMD in Group II animals compared to the sham control

Table 1: Effect of fucoxanthin on the serum levels of E2 and $1,25(OH)_2D_3$ of sham-operated control and experimental animals

Group	E2 (ng/L)	$1,25(OH)_2D_3$ (ng/ml)
Group I	346.94	0.833333
Group II	576.89#	2.763333#
Group III	473.6633*	1.836667*
Group IV	398.9633*	1.11*

Values are expressed as mean±SD for six animals in each group. #Control versus other groups; *Group 2 versus Group 3, 4, and 5. Values are statistically significant at the level of $P<0.05$. Group I: Control animals; Group II: Ovariectomy-induced animals; Group III: Ovariectomy-induced and 20 mg/kg of fucoxanthin-treated animals; Group IV: Ovariectomy-induced and 40 mg/kg of fucoxanthin-treated animals; SD: Standard deviation; E2: Estrogen

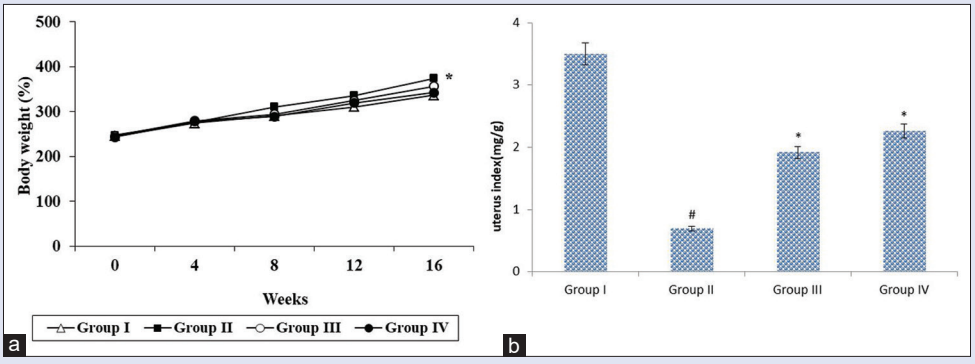

Figure 1: Effect of fucoxanthin on body weight (a) and uterus index (b) of sham-operated control and experimental animals. Values are expressed as mean ± standard deviation for six animals in each group. #Control versus other groups, *Group II versus Group III and IV. Values are statistically significant at the level of $P < 0.05$

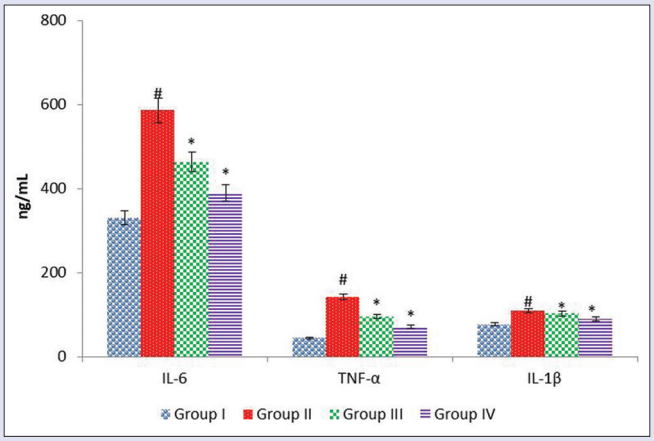

Figure 2: Effect of fucoxanthin on the concentration of serum levels of inflammatory markers in sham-operated control and experimental animals. Values are expressed as mean ± standard deviation for six animals in each group. #Control versus other groups, *Group II versus Groups III and IV. Values are statistically significant at the level of $P < 0.05$

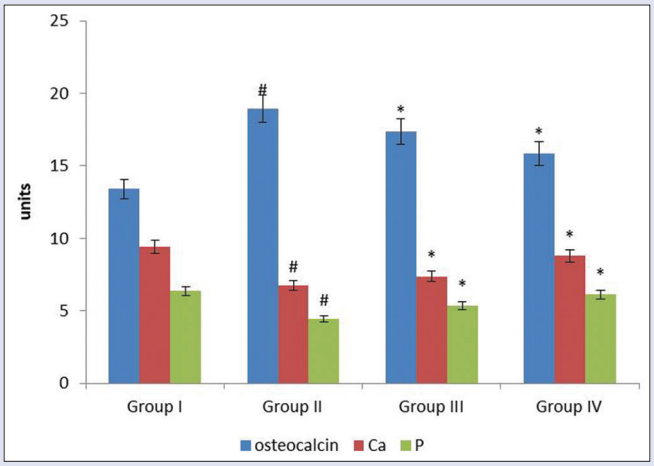

Figure 3: Effect of fucoxanthin on serum bone turnover markers (osteoclastic factors) of sham-operated control and experimental animals. Values are expressed as mean ± standard deviation for six animals in each group. #Control versus other groups, *Group II versus Groups III and IV. Values are statistically significant at the level of $P < 0.05$

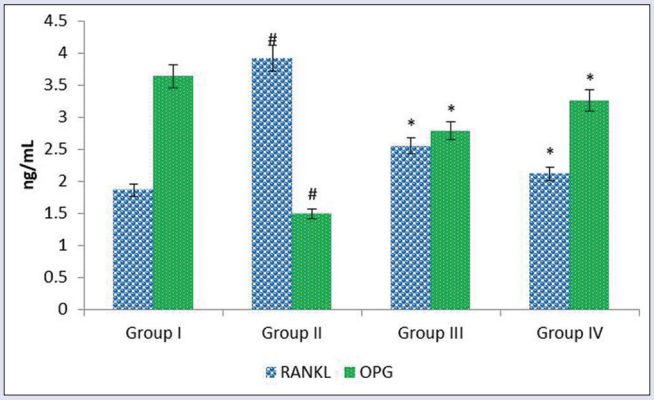

Figure 4: Effect of fucoxanthin on osteoprotegerin and receptor activator of nuclear factor-κB ligand levels in the serum of sham-operated control and experimental animals. Values are expressed as mean ± standard deviation for six animals in each group. #Control versus other groups, *Group II vs. Groups III and IV. Values are statistically significant at the level of $P < 0.05$

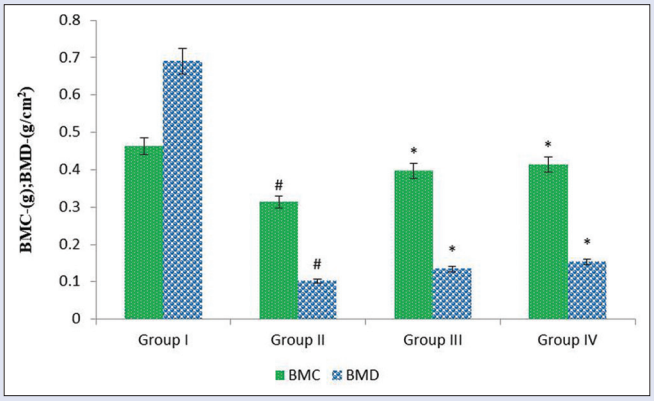

Figure 5: Effect of fucoxanthin on bone mineral content (a) and bone mineral density (b) in the femur of sham-operated control and experimental animals. Values are expressed as mean ± standard deviation for six animals in each group. #Control versus other groups, *Group II versus Groups III and IV. Values are statistically significant at the level of $P < 0.05$

group (Group I). Fucoxanthin administration to OVX rats resulted in a marked increase ($P < 0.05$) in BMC and BMD in Group III and Group IV animals. Treatment with fucoxanthin to OVX rats improved BMC and BMD in a dose-dependent manner.

Effect of fucoxanthin on biomechanical parameters of control and experimental animals

Table 2 illustrates the potent efficacy of fucoxanthin on biomechanical parameters (bending test) in left femur diaphysis of control and experimental animals. The levels of all biomechanical parameters such as energy absorption, maximum load and stress, and stiffness were reduced significantly in Group II (OVX) rats compared to sham-operated animals. However, fucoxanthin administration in a dose-dependent manner increased the levels of all biomechanical parameters to a marked extent in Group III and Group IV.

Effect of fucoxanthin on histological examination of femur in control and experimental animals

The representative histopathological images of femur of control and experimental animals are shown in Figure 6. The architecture of the bone was analyzed using H and E stain. Sham-operated control rats displayed a normal density of the diaphysis and normal trabeculae (Group I). OVX rats showed abnormal thinning of the trabeculae with increased interspace in trabeculae (Group II). Group III animals treated with 20 mg/kg fucoxanthin exhibited minimal changes, along with uniform interstitial trabecular space together with mild bone mineralization, whereas Group IV rats supplemented with 40 mg/kg fucoxanthin resulted in a complete reversal of normal bone architecture and trabecular formation noticed which was similar to that of sham-operated Group I animals.

Table 2: Effect of fucoxanthin on biomechanical parameters (bending test) in left femur diaphysis of sham-operated control and experimental animals

Group	Group I	Group II	Group III	Group IV
Energy (N)	55.47±7.36	43.14±4.28#	49.63±5.14*	51.74±5.96*
Maximum load (N)	113.41±10.21	83.61±8.47#	102.87±9.65*	108.32±9.30*
Stiffness (N/mm)	188.28±21.66	167.56±17.50#	174.97±19.36*	181.69±20.03*
Young Modulus (MPa)	6741.77±798.19	5839.49±764.87#	6124.33±767.99*	6452.49±786.94*
Maximum stress (MPa)	215.23±24.88	167.83±19.64#	194.68±21.94*	202.61±22.51*

Values are expressed as mean ± standard deviation for six animals in each group. #Control versus other groups, *Group II versus Groups III and IV. Values are statistically significant at the level of $P < 0.05$

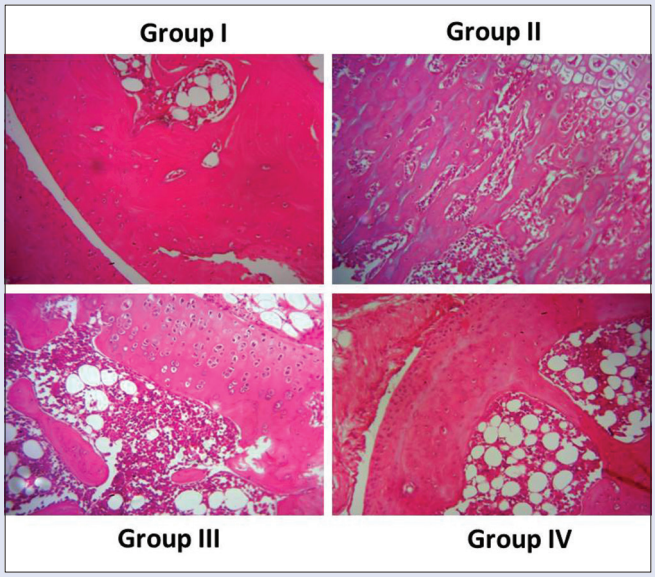

Figure 6: Histopathological examination of femur of sham-operated control and experimental animals. Femur tissue histology of control and ovariectomized rats with/without treatment with fucoxanthin (H and E, ×400)

DISCUSSION

Aging is typically accompanied by deterioration of bone architecture, composition, and function, thus resulting in osteoporosis. Bone is highly prone to age-related loss and fragility, and the research areas at present are mainly focusing on age-related bone loss.[40,41] In postmenopausal women, deficiency of ovarian hormone E2 acts as an important risk factor in development of osteoporosis. A well-established model of animals in osteoporosis research is the ovariectomy procedure. OVX rats show several similarities with that of bone loss in postmenopausal condition, and it is recommended to study the effectiveness and safety of therapies involved in treating osteoporosis.[42,43] Ovariectomy in rats results in a significant decrease in weight of uterus, BMC, and density and alteration in various other biomechanical and biochemical parameters which are due to deficiency of E2.[44]

Fucoxanthin is a marine carotenoid isolated from brown seaweeds, and it has been reported with numerous beneficial therapeutic properties. Literature evidence has described that fucoxanthin possesses a potent promising application relating to human health. Fucoxanthin is reported to suppress the osteoclast formation and differentiation and induce apoptosis in *in vitro* cell lines.[45] It is also reported to be beneficial in prevention of rheumatoid arthritis and osteoporosis.[30] Bone remodeling and mineralization is maintained mainly by the action of E2 which acts by regulating homeostasis among osteoclast and osteoblast.[46] Hence, the present study was conducted to evaluate whether the fucoxanthin was effective in preventing bone loss in ovariectomy-induced osteoporosis in rats.

Body weight gain is a more prominent phenomenon observed in both OVX rats and in women who attained menopause.[24] The results also revealed that OVX-induced osteoporotic rats showed a significant increase in body weight and decrease in uterine index compared with the sham-operated control group. The reduction in uterine weight in OVX rats might be due to deficiency of E2 which is supported by earlier evidence[47] that showed a significant increase in body weight and decrease in uterine weight in OVX rats. Fucoxanthin administration alleviated the excess body weight gain and improved uterine index in the OVX rats. Fucoxanthin even at lower doses was shown to be beneficial in lowering the body weight gain, fat accumulation, and visceral fat[48-50] which correlates with our present findings.

Osteoporosis mainly results from an imbalance or homeostasis which occurs between bone resorption and formation. Therefore, we investigated further the bone turnover and inflammatory markers in serum samples of sham control and experimental animals. Ovariectomy causes increased accumulation of ROS resulting in oxidative stress and increases the production of inflammatory cytokines that promote generation of osteoclasts and bone loss. A sufficient intake of Ca and Vitamin D is associated with lowered incidence of osteoporosis.[51] Cholecalciferol-D3 plays a major role in absorption of Ca and P in the body which are essential for the development of bones.[15] Ca and P also holds an important role as a marker of bone mineralization. Ca and P levels in serum are lowered significantly in OVX rats compared to sham control animals which might be because of E2 deficiency observed commonly in OVX rats.[52,53] Markers of bone formation such as OC are synthesized by the osteoblasts, and they directly correspond to their specific functions.[54] Increased or upregulated levels of bone formation indicate osteoporosis in menopausal women, which is in agreement with our present findings.[55,56] In the present study, the increase in the serum level of OC in OVX rats could possibly be due to osteoblast formation in order to compensate bone loss caused due to E2 deficiency.[57]

RANKL/OPG axis is a vital pathway in regulating the homeostatic balance between bone formation and resorption.[58,59] They also serve as crucial factors in mediating differentiation of osteoclasts. OPG produced by the lineage of osteoblasts has an inhibitory effect on bone formation, whereas elevated RANKL is mainly related to fracture of bones, thus resulting in increased osteoclast formation.[60,61] Thus, the ration between OPG and RANKL is essential to determine the bone density and integrity.[62] We also assessed the concentration of OPG and RANKL in serum of control and experimental animals. We found that in OVX rats, serum OPG level is decreased, whereas RANKL level is increased. Fucoxanthin-supplemented animals displayed a significant increase in OPG and decrease in RANKL levels in serum of OVX rats. Thus, the results specify that fucoxanthin protects rats against ovariectomy-induced bone loss through upregulating the ratio

of OPG/RANKL in experimental animals. Thus, the study supports that fucoxanthin supplementation could be effective in prevent bone loss in postmenopausal women.

On fucoxanthin supplementation, the serum levels of E2 and $1,25(OH)_2D_3$ were markedly increased in a dose-dependent manner. The study also demonstrated that there was a significant increase in the level of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β in OVX rats than the sham-operated control animals. These pro-inflammatory cytokines are increased in osteoporosis and involved mainly in the regulating turnover of bone by increasing bone resorption.[63] Our results are in correlation with a previous study which inferred that the serum levels of IL-6, IL-1β, and TNF-α were increased significantly in OVX rats than control rats.[64] It has also been reported that the levels of these cytokines are expressed highly in postmenopausal women than those who are undergoing ERT.[65] Increased levels of these cytokines predispose an increased release of free radicals and inhibit bone formation and stimulate bone resorption.[66-68] Treatment of OVX rats with fucoxanthin attenuated the levels of pro-inflammatory cytokines in a dose-dependent manner which is due to antiosteoporotic efficacy of fucoxanthin.[28,29,69]

BMC and density are the important factors that reflect the quality and integrity of bones. Hence, in the present study, we evaluated the BMC and BMD using DEXA. Both BMD and BMC are suppressed to the maximum extent in OVX rats than sham control rats. Previous literature evidences have proved that the BMC and BMD were reduced significantly in OVX-induced osteoporotic rats due to E2 deficiency.[70] Treatment with fucoxanthin for 16 weeks in a dose-dependent manner considerably increased the levels of both BMD and BMC as compared to Group II (OVX) rats. In a recent study, it has been reported that fucoxanthin exhibits bone differentiation property in *in vitro* cells and it displays capability of bone mineralization in *in vivo*.[71]

The biomechanical efficacy of the fucoxanthin was determined by a three-point bending test which portrays the rigidity and tensile strength of bone under stress. The antiosteoporotic efficacy of fucoxanthin is evaluated by the biomechanical characteristics of bone which serves as a more consistent test.[72] All biomechanical parameters such as load, maximum stress, young modulus, energy level, and stiffness were reduced significantly in OVX rats due to increased inflammation which might have triggered the resorption and loss of bones. Administration of fucoxanthin in a dose-dependent manner (20 and 40 mg/kg) to OVX rats increased the biomechanical parameters in a significant manner similar to that sham control rats. Fucoxanthin must have acted on E2 receptor and stimulated synthesis of osteoblasts, thereby preserving the homeostasis of bone as well as bone density and quality. Both doses of fucoxanthin (20 and 40 mg/kg) were found to be potent in mitigating the osteoporosis induced by OVX.

To substantiate the present findings, we further performed histopathological analysis of the bone architecture of OVX rats and sham-operated control rats in femur. The cortical bone thickness, osteoclasts, and resorption of bones in OVX rats were decreased significantly compared to sham control rats. These are major factors which contribute to the pathogenesis of osteoporosis. Fucoxanthin supplementation effectively increased the thickness of cortical bone and the trabecular space in a dose-dependent manner. The results suggest that fucoxanthin has a protective effect in minimizing bone loss in OVX-induced osteoporosis. Our findings were in corroboration with earlier studies which explained a close correlation with E2 deficiency and increased bone resorption.[73,74] Fucoxanthin is a marine carotenoid, where numerous studies have reported that various antioxidants and carotenoids available in abundance in fruits and vegetables are associated with reduced risk of bone fracture and/or ensuing osteoporosis.[75-78]

CONCLUSION

The present investigation clearly shows that treatment with fucoxanthin significantly reduced the body weight gain, uterine index, bone turnover markers (Ca, P, and OC), and inflammatory markers such as TNF-α, IL-6, and IL-1β in OVX rats. In addition to biochemical parameters, fucoxanthin administration also improved BMC and BMD and biomechanical parameters considerably in a dose-dependent manner. Histopathological evidences also confirmed the same. Thus, fucoxanthin can be validated as an alternative therapeutic regimen for treating osteoporosis in postmenopausal women. However, further mechanistic action of fucoxanthin needs to be explored to recommend it as an effective compound in treating osteoporosis.

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Conflicts of interest

There are no conflicts of interest.

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