

# **EFFECTS OF $\omega$ -3 FATTY ACIDS AND ESTROGEN REPLACEMENT THERAPY ON OVARIECTOMY INDUCED OSTEOPOROSIS IN FEMALE ALBINO RATS**

Thesis  
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## **Abstract**

Fatty acids especially omega 3 unsaturated fatty acids has known anti-inflammatory effects. And there are different mechanisms by which dietary fatty acids may affect bone, but there protective effect against postmenopausal osteoporosis remains a controversial issue. This study was applied on 50 female albino rats that were divided into 5 equal groups: sham operated group, ovariectomy group, ovariectomy + flaxseed oil group (0.4 g per day), ovariectomy + fish oil administered group (0.4 g per day) and ovariectomy + estrogen replacement therapy group (30 µg/kg 5 days a week). The study proceeded for 12 weeks then femurs bone mineral density (BMD) were measured with dual-energy X-ray absorptiometer (DXA) scan and serum osteoprotogerin (OPG), bone specific alkaline phosphatase (ALP-b) and tumour necrosis factor alpha (TNF- $\alpha$ ) were measured. There was a significant increase in the BMD of the treated groups compared with the ovariectomy group ( $p < .01$ ). There were a significant differences in the means of serum bone markers measures of the treated groups versus the ovariectomy group in the form of significant increase in OPG ( $p < .001$ ) and a significant decrease in ALP-b ( $p < .001$ ) and TNF- $\alpha$  ( $p < .001$ ) of the treated groups compared with the ovariectomy group. This study showed a significant negative correlation between BMD and ALP-b ( $r = - 0.375$ ,  $p < .001$ ). According to this study the chronic administration of omega 3 fatty acids (flaxseed oil - fish oil) has a preventive effect against osteoporosis and suppression of bone turn over process appears to have a role in this preventive effect.

**Key Words :** Osteoporosis - Omega 3 fatty acids - Bone mineral density - Osteoprotogerin - Tumour necrosis factor alpha - Alkaline phosphatase

# List of Contents

<b>Introduction .....</b>	<b>1</b>
<b>Review of literature.....</b>	<b>5</b>
<b>Bone physiology.....</b>	<b>5</b>
<b>Osteoporosis .....</b>	<b>37</b>
<b>Fatty acids.....</b>	<b>45</b>
<b>Materials and methods .....</b>	<b>52</b>
<b>Results .....</b>	<b>67</b>
<b>Discussion.....</b>	<b>91</b>
<b>Summary .....</b>	<b>104</b>
<b>References .....</b>	<b>106</b>

## List of Tables

Number	Subject	Page
Table 1	Major growth factors in bone formation and fracture repair	15
Table 2	Diagnostic criteria for primary osteoporosis	38
Table 3	Causes of secondary osteoporosis	39
Table 4	Bone Mineral Density (gm/cm <sup>2</sup> ) in studied groups	68
Table 5	The effect of 12 weeks administration of flaxseed oil (0.4 g per day), fish oil (0.4 g per day) & estrogen (30 µg/kg 5 days a week) on bone mineral density (BMD) measured by (gm/cm <sup>2</sup> ) in ovariectomized female rats	69
Table 6	Serum osteoprotegerin (pg/ml) in studied groups	74
Table 7	Comparison between the effects of 12 weeks administration of flaxseed oil (0.4 g per day), fish oil (0.4 g per day) & estrogen (30 µg/kg 5 days a week) on serum osteoprotegerin (OPG) measured by (pg/ml) in ovariectomized female rats	75
Table 8	Serum tumor necrosis factor (TNF-α) (pg/ml) in studied groups	78
Table 9	Serum tumour necrosis factor (TNF-α) measured by (pg/ml) in ovariectomized female rats after 12 weeks administration of flaxseed oil (0.4 g per day), fish oil (0.4 g per day) & estrogen (30 µg/kg 5 days a week)	79
Table 10	Serum bone specific alkaline phosphatase (ALP-b) (U/L) in studied groups	82

<b>Table 11</b>	<b>The effect of 12 weeks administration of flaxseed oil (0.4 g per day), fish oil (0.4 g per day) &amp; estrogen (30 µg/kg 5 days a week) on serum bone specific alkaline phosphatase (ALP-b) measured by (U/L) in ovariectomized female rats</b>	<b>83</b>
<b>Table 12</b>	<b>Pearson's correlation coefficient (<i>r</i>) between studied parameters (BMD, OPG, TNF-<math>\alpha</math> and ALP-b) in all cases studied</b>	<b>85</b>

## List of Figures

Number	Subject	Page
Figure 1	Parts of a long bone	5
Figure 2	Cambium layer near the periosteal surface	6
Figure 3	Compact and cancellous bone	7
Figure 4	Woven bone seen on hematoxylin and eosin and with polarized light	8
Figure 5	Lamellar bone as seen on H&E-stained slide and with polarization	9
Figure 6	Cross sections of cortex with circumferential, concentric, and interstitial lamellae	10
Figure 7	The osteocyte lacuno-canalicular network	17
Figure 8	Mechanism of osteoclastic bone resorption	24
Figure 9	Bone remodeling	24
Figure 10	Mechanisms of action for OPG, RANKL, and RANK	26
Figure 11	Signaling pathways essential for osteoclastogenesis in pathologic bone disorders	27
Figure 12	Classification of primary osteoporosis	38
Figure 13	Major cytokines in the bone microenvironment that regulate osteoclast function	44

<b>Figure 14</b>	<b>The metabolic pathway of biosynthesis of EPA, docosapentaenoic acid, and DHA</b>	<b>46</b>
<b>Figure 15</b>	<b>Overview of eicosanoid and docosanoid biosynthesis</b>	<b>47</b>
<b>Figure 16</b>	<b>Scheme for the maresin pathway</b>	<b>50</b>
<b>Figure 17</b>	<b>Dilution of standard</b>	<b>60</b>
<b>Figure 18</b>	<b>Lunar Prodigy dual-energy X-ray absorptiometer</b>	<b>63</b>
<b>Figure 19</b>	<b>Comparison of BMD among studied groups control, OVX, OVX-FX, OVX-FS and OVX-E</b>	<b>70</b>
<b>Figure 20</b>	<b>DXA scan on lower end of the femur in one of the control group</b>	<b>70</b>
<b>Figure 21</b>	<b>DXA scan on lower end of the femur in one of the OVX group</b>	<b>71</b>
<b>Figure 22</b>	<b>DXA scan on lower end of the femur in one of the OVX-FX group</b>	<b>71</b>
<b>Figure 23</b>	<b>DXA scan on lower end of the femur in one of the OVX-FS group</b>	<b>72</b>
<b>Figure 24</b>	<b>DXA scan on lower end of the femur in one of the OVX-E group</b>	<b>72</b>
<b>Figure 25</b>	<b>Comparison of OPG serum levels among studied groups control, OVX, OVX-FX, OVX-FS and OVX-E</b>	<b>76</b>
<b>Figure 26</b>	<b>Comparison of TNF-<math>\alpha</math> serum levels among studied groups control, OVX, OVX-FX , OVX-FS and OVX-E</b>	<b>80</b>
<b>Figure 27</b>	<b>Comparison of ALP-b serum levels among studied groups control, OVX, OVX-FX, OVX-FS and OVX-E</b>	<b>84</b>

<b>Figure 28</b>	<b>A scatter plot illustrates the correlation between serum bone specific alkaline phosphatase (ALPbone) (U/L) and serum TNF-<math>\alpha</math> (pg/ml)</b>	<b>85</b>
<b>Figure 29</b>	<b>A scatter plot illustrates the correlation between bone mineral density in the lower end of the femur (BMD) (g/cm<sup>2</sup>) and serum bone specific alkaline phosphatase (ALPbone) (U/L)</b>	<b>86</b>
<b>Figure 30</b>	<b>A scatter plot illustrates the correlation between serum osteoprotogerin (OPG) (pg/ml) and serum TNF-<math>\alpha</math> (pg/ml)</b>	<b>87</b>
<b>Figure 31</b>	<b>A scatter plot illustrates the correlation between serum osteoprotogerin (OPG) (pg/ml) and serum bone specific alkaline phosphatase (ALPbone) (U/L)</b>	<b>88</b>
<b>Figure 32</b>	<b>A scatter plot illustrates the correlation between bone mineral density in the lower end of the femur (BMD) (g/cm<sup>2</sup>) and serum osteoprotogerin (OPG) (pg/ml)</b>	<b>89</b>
<b>Figure 33</b>	<b>A scatter plot illustrates the correlation between bone mineral density in the lower end of the femur (BMD) (g/cm<sup>2</sup>) and serum TNF-<math>\alpha</math> (pg/ml)</b>	<b>90</b>

## List of Abbreviations

<b>3<math>\beta</math>-HSD</b>	<b>3<math>\beta</math>-hydroxysteroid dehydrogenase</b>
<b>15-S-HETE</b>	<b>15S-hydroxyeicosatetraenoic acid</b>
<b>17<math>\beta</math>-HSD</b>	<b>17<math>\beta</math>-hydroxysteroid dehydrogenase</b>
<b>17-HDHA</b>	<b>17-hydroxydocosahexaenoic acid</b>
<b>18-HEPE</b>	<b>18-hydroxyeicosapentaenoic acid</b>
<b>AA</b>	<b>Arachidonic acid</b>
<b>ALA</b>	<b>Alpha-linolenic acid</b>
<b>ALP-b</b>	<b>Bone specific alkaline phosphatase</b>
<b>ALX</b>	<b>Lipoxins receptor</b>
<b>BCAR1</b>	<b>Breast cancer anti-estrogen resistance protein 1</b>
<b>BMD</b>	<b>Bone mineral density</b>
<b>BMP</b>	<b>Bone morphogenetic protein</b>
<b>Cbfa1</b>	<b>Core-binding factor alpha 1</b>
<b>COX</b>	<b>Cyclooxygenase</b>
<b>CRP</b>	<b>C-reactive protein</b>

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*List of Abbreviations*

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<b>CYP</b>	<b>Cytochrome P450</b>
<b>DBD</b>	<b>DNA-binding domain</b>
<b>DDH</b>	<b>Death domain homologous</b>
<b>DHA</b>	<b>Docosahexaenoic acid</b>
<b>DHEA</b>	<b>Dehydroepiandrosterone</b>
<b>DNA</b>	<b>Deoxyribonucleic acid</b>
<b>DPA</b>	<b>Docosapentaenoic acid</b>
<b>DXA</b>	<b>Dual-energy X-ray absorptiometry</b>
<b>EDTA</b>	<b>Ethylenediaminetetraacetic acid</b>
<b>EFA</b>	<b>Essential fatty acids</b>
<b>EGF</b>	<b>Epidermal growth factor</b>
<b>ER</b>	<b>Estrogen receptor</b>
<b>ERK</b>	<b>Extracellular-signal-regulated kinase</b>
<b>EPA</b>	<b>Eicosapentaenoic acid</b>
<b>FA</b>	<b>Fatty acid</b>
<b>FasL</b>	<b>Fas ligand</b>

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*List of Abbreviations*

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<b>FDA</b>	<b>Food and drug administration</b>
<b>FGF</b>	<b>Fibroblast growth factor</b>
<b>GM-CFU</b>	<b>Granulocytic-macrophage colony-forming unit</b>
<b>H&amp;E</b>	<b>Hematoxylin and eosin stain</b>
<b>HPETE</b>	<b>Hydroperoxy-eicosatetraenoic acids</b>
<b>IGF</b>	<b>Insulin-like growth factor</b>
<b>IJO</b>	<b>Idiopathic juvenile osteoporosis</b>
<b>I<math>\kappa</math>B<math>\alpha</math></b>	<b>nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor alpha</b>
<b>IKKs</b>	<b>inhibitor of nuclear factor kappa-B kinase</b>
<b>IL</b>	<b>Interleukin</b>
<b>ITAM</b>	<b>Immunoreceptor tyrosine-based activation motif</b>
<b>JNK</b>	<b>c-jun N-terminal kinase</b>
<b>LA</b>	<b>Linoleic acid</b>
<b>LBD</b>	<b>Ligand- binding domain</b>
<b>LDLs</b>	<b>Low density lipoproteins</b>
<b>LOX</b>	<b>lipoxygenase</b>

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*List of Abbreviations*

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<b>LPS</b>	<b>Lipopolysaccharide</b>
<b>LRP</b>	<b>Lipoprotein receptor-related protein</b>
<b>LX</b>	<b>Lipoxin</b>
<b>MAPK</b>	<b>Mitogen-activated protein kinases</b>
<b>M-CFU</b>	<b>Macrophage colony-forming unit</b>
<b>M-CSF</b>	<b>Macrophage colony-stimulating factor</b>
<b>miR-21</b>	<b>MicroRNA 21</b>
<b>MMP-13</b>	<b>Matrix metalloproteinase 13</b>
<b>MSCs</b>	<b>Mesenchymal stem cells</b>
<b>MUFA</b>	<b>Monounsaturated fatty acid</b>
<b>NFATc1</b>	<b>Nuclear factor of activated T cell c1</b>
<b>NF-<math>\kappa</math>B</b>	<b>Nuclear Factor kappa B</b>
<b>OI</b>	<b>Osteogenesis imperfecta</b>
<b>OPG</b>	<b>Osteoprotegerin</b>
<b>OSCAR</b>	<b>Osteoclast-associated receptor</b>
<b>OVX</b>	<b>Ovariectomy group</b>

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*List of Abbreviations*

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<b>OVX-E</b>	<b>Ovariectomy + Estrogen</b>
<b>OVX-FS</b>	<b>Ovariectomy + Fish oil group</b>
<b>OVX-FX</b>	<b>Ovariectomy + Flaxseed oil group</b>
<b>P450aro</b>	<b>Aromatase enzyme</b>
<b>P450scc</b>	<b>Cholesterol side-chain cleavage enzyme</b>
<b>PDGF</b>	<b>Platelet-derived growth factor</b>
<b>PG</b>	<b>Prostaglandins</b>
<b>PGE2</b>	<b>Prostaglandin E2</b>
<b>PGI</b>	<b>Prostacyclins</b>
<b>PI3K</b>	<b>Phosphatidyl inositol 3 kinase</b>
<b>PLC<math>\gamma</math></b>	<b>Phospholipase C<math>\gamma</math></b>
<b>PPAR<math>\gamma</math></b>	<b>Peroxisome proliferator-activated receptor-<math>\gamma</math></b>
<b>PTH</b>	<b>Parathyroid hormone</b>
<b>PTHrP</b>	<b>Parathyroid hormone-related protein</b>
<b>PUFA</b>	<b>Polyunsaturated fatty acid</b>
<b>RANK</b>	<b>Receptor Activator of Nuclear Factor kappa B</b>

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*List of Abbreviations*

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<b>RANKL</b>	<b>Receptor activator of nuclear factor kappa B ligand</b>
<b>RBC</b>	<b>Red blood cell</b>
<b>RGD</b>	<b>Arginyl-glycyl-aspartic acid sequence</b>
<b>ROS</b>	<b>Reactive oxygen species</b>
<b>RUNX2</b>	<b>Runt-related transcription factor 2</b>
<b>SFA</b>	<b>Saturated fatty acid</b>
<b>Spry1</b>	<b>Sprouty Homolog 1</b>
<b>TGF-<math>\beta</math></b>	<b>Transforming growth factor beta</b>
<b>TNF-<math>\alpha</math></b>	<b>Tumor necrosis factor alpha</b>
<b>TRAF</b>	<b>TNF receptor-associated factor</b>
<b>TREM</b>	<b>Triggering receptor expressed in myeloid cells</b>
<b>TX</b>	<b>Thromboxanes</b>
<b>VEGF</b>	<b>Vascular endothelial growth factor</b>
<b>Wnt</b>	<b>Wingless-related integration site</b>