

# Chapter I

## Introduction

### 1.1. Introduction.

Osteoporosis (OP) is a bone metabolic disease characterized by low bone mineral density (BMD) with high risk of fractures. It occurs when there is an imbalance between bone resorption and bone formation during the bone remodeling process (Nazrun *et al.*, 2011). Lau and Guo (2011) defined OP as "a multifactorial skeletal disorder characterized by decreased bone mass and deteriorated microarchitecture that lead to increase risk of fracture. Incidence of OP is elevated worldwide as populations age increase. Women are generally affected four times more likely than men, and fracture rates among women are approximately twice as high as men (Kanis *et al.*, 2008). Greer *et al.* (2008) estimated the prevalence of OP for Saudi Arabian women aged 50-70 years to be approximately 23%.

The most common type of OP is bone loss associated with ovarian hormone deficiency (Occhiuto *et al.*, 2007), which can result from naturally or surgically induced menopause and endocrine disorders that reduce estrogen secretion in premenopausal women. Estrogen deficiency influences osteoclast which enhances bone loss by stimulating bone resorption (NAMS, 2002). There are clear bone-related benefits of hormone replacement therapy (HRT) (Atkinson *et al.*, 2004), although HRT helps to prevent the development of pathologies in post-menopause

women, however, because a greater incidence of breast and endometrial cancer has been linked to some forms of HRT, increased attention has been placed on finding viable and safe alternatives. Many women are turning to botanical and dietary supplement products for the prevention or treatment of these health issues (**Mahady et al., 2002 and Geller and Studee, 2006**).

Treatment with natural herbs is likely to be fraught with lesser side effects compared to the presently used synthetic drugs (**Tenpe and Yeole, 2009**). Of all the natural alternatives currently under investigation phytoestrogens, which appear to offer the most potential for the prevention of bone loss and have attracted new attention as a possible agent to prevent and treat postmenopausal osteoporosis (PMO), cancer preventive, cardio-protective, as well as their ability to relieve menopausal symptoms (**Chen et al., 2003 and Yatkin and Daglioglu, 2011**).

Red clover (RC) (*Trifolium pratense* L.) is a perennial herb growing in all temperate and subtropical areas around the world. In several cultures, it is used a traditional medicine (**Booth and Piersen, 2006**). RC botanical dietary supplements have received much attention recently for their potential use in maintenance/improvement of bone and cardiovascular health. It contains four important estrogenic isoflavones mainly (daidzein, genistein, formononetin and biochanin A) and coumestans (**Sabudak and Guler, 2009**). Supplements of RC have been the subject of much interest for the reduction of menopausal symptoms and conditions related to aging because of their high concentrations of phytoestrogens (**Piersen et al., 2004 and Beck et al., 2005**). Red clover isoflavones (RCI) are increasingly used in dietary supplements for their purported estrogenic effect in *vivo* and *vitro* assays (**Engelmann et al., 2009**), hypolipidemic (**Geller and Studee, 2006**), and is hypothesized to be of potential use as a natural form of HRT (**Occhiuto et al., 2007**).

## **1.2. Aim of the study.**

The present study aims to investigate the effectiveness of RCI (*Trifolium pratense* L.) on the progression of bone loss induced by estrogen deficiency in ovariectomized (OVX) female rats.

## **1.3. Objectives of the study.**

**The present study is design to assess the effect of RCI on the following:**

- 1- Biological evaluation in OVX rats.
- 2- Some biochemical bone marker enzymes in OVX rats.
- 3- Some bone homeotasis hormones in OVX rats.
- 4- Bone densitometry (DEXA; BMD and BMC) in OVX rats.
- 5- Bone histological and histochemical changes in OVX rats.

