Study of the effect of ginger and turmeric on osteoporosis in female rats

Eman G. Mohamed1*, Zenab M. Mosa1, Samah M. Esmail1 Adel Bakeer Khloussy2, Sahar O. Ahmed3 and Naglaa A. Abdelkader4

1-Nutrition and Food Sciences, Home Economics Dept., Fac. of Education. Ain-Shams
2- Pathology Dept., Fac. of Veterinary, Cairo University.
3- Food Technology Research Institute.
4- Surgery, Anaesthesiology and Radiology Dept., Fac. of Veterinary, Cairo University

*Email; eman.gamal.mohamed.gs@sedu.asu.edu.eg

ABSTRACT

Osteoarthritis is the most common form of arthritis, involving inflammation and major structural changes of the joint, causing pain and functional disability. Pain and stiffness, particularly after exercise, are the major symptoms, resulting in considerable impact on ability to perform activities of daily living. There is discordance between symptoms and radiographic changes, with some sufferers not experiencing symptoms, but showing osteoarthritic changes on X-ray. The present study was performed to examine the effect of ginger and turmeric consumption on liver function (ALT, AST), phosphorus, total calcium, ionized calcium, x-ray and histopathology on osteoporosis rats induced by prednisone acetate at a dose of 4 mg / kg bw three time a week for three weeks. On the other hand, the chemical constituent’s moisture, protein, fat, crude fibre, total digestible nutrients, ash, carbohydrate, phosphorous, calcium was determined for the tested ginger and turmeric. In addition to, volatile compounds and analysis of phytochemicals was determined for the tested ginger and turmeric.

This work was carried out on 48 non-pregnant female albino rats (age 6 to 8 weeks and about 160 to 210g body weight) classified into two main groups. The first main group (6) fed on basal diet and the second main group (42 rats) injected with prednisone acetate at a dose of 4 mg / kg bw three time a week for three weeks to cause osteoporosis and divided into seven subgroups such as each group consists of (6 rats). Then fed on basal diet containing 10% -15% ginger, 10% -15% turmeric and 10% -15% ginger and turmeric. Results revealed that all osteoporosis groups administrated with different levels of ginger and turmeric (10-15%) had significant decrease liver function (ALT, AST), phosphorus, total calcium, ionized calcium comparing with the positive control group. On the other hand, x-ray and histopathology of the positive control group after two months revealed bone loss of different part such as fibula, tibia and femur in addition to bone demineralization and femoral fracture and fibula bone trabeculae showed dystrophy and resorption and osteoporosis. These findings revealed that ginger and turmeric treatment attenuated and treated degrees to osteoporosis in compare to positive control group.

Keywords: Medicinal Herbs, Osteoporosis, Ginger, Turmeric Rhizome, Phytochemicals Analysis, Biochemical Analysis.

INTRODUCTION

Osteoarthritis (OA) is the most common form of arthritis, involving inflammation and major structural changes of the joint, causing pain and functional disability. Pain and stiffness, particularly
after exercise, are the major symptoms, resulting in considerable impact on ability to perform activities of daily living. There is discordance between symptoms and radiographic changes, with some sufferers not experiencing symptoms, but showing osteoarthritic changes on X-ray. It is known that OA is more common in women than in men, and the prevalence of OA increases steeply with age (Busija et al., 2010). Osteoporosis is worldwide defined as a systemic skeletal disease characterized by low bone density and micro architectural deterioration of bone tissue, which leads to increased bone fragility and risk of fracture (Genant et al., 1999; Anbinder et al., 2006).

In healthy rats, both simvastatin and fenofibrate treatment showed a negative effect on the trabecular bone located at the level of femoral diaphysis. These results are consistent with other studies which concluded that to a certain extent, statins inhibit bone resorption and promote bone formation (Chang et al., 2011; Gradosova et al., 2011). Glucocorticoids act directly on bone cells and one of their principal actions is to reduce osteoblasts function and number by apoptosis (Chang et al., 2009). The Bax expression by osteoblasts increase in the glucocorticoid-induced osteoporosis (GIO) as showed by (Lucinda et al., 2013). It’s well known that apoptosis is regulated by an intrinsic process involving activation of genes that can promote cell death (Bras et al., 2005).

Ginger (Zingiber officinale Roscoe, Zingiberaceae) is widely used around the world in foods as a spice. For centuries, it has been an important ingredient in Chinese Ayurvedic and Tibb-Unani herbal medicines for the treat-ment of catarrh, rheumatism, nervous diseases, gingivitis toothache, asthma, stroke, constipation and diabetes (Awang, 1992; Wang and Wang, 2005; Tapsell et al., 2006). The constituents of ginger are numerous and vary depending on the place of origin and whether the rhizomes are fresh or dry. The odor of ginger depends mainly on its volatile oil, the yield of which varies from 1% to 3%. Over 50 components of the oil have been characterized and these are mainly monoterpenoids. Some of the oil components are converted into less odor-defining compounds on drying (Langner et al., 1998; Evans, 2004). The pungency of fresh ginger is due primarily to the gingerols, which are a homologous series of phenols. Ginger and compounds isolated there from include immuno-modulatory, anti-tumorigenic, anti-inflammatory, anti-apoptotic, anti-hyperglycemic, anti-lipidemic and anti-emetic actions. Ginger is a strong anti-oxidant substance and may either mitigate or prevent generation of free radicals. It is considered a safe herbal medicine with only few and insignificant adverse side effects (Badreldin et al., 2008).

Turmeric has anti-inflammatory (Jurenka, 2009) and anti-cancer (Ravindran et al., 2009) properties, which have been mainly attributed to curcumin, a diarylheptanoid compound. However, turmeric oil containing ar-turmerone, turmerone and curlone showed antioxidant effects and may provide an explanation for their antimutagenic action (Jayaprakasha et al., 2002). This turmeric oil also has antibacterial activity (Negi et al., 1999). Turmeric is a rich source of various volatile oils, including turmerone, atlantone, zingerone, and other constituents such as sugars, proteins, resins, lignin, salts, resins. The root contains 10% resin which is a glucoside (Dulbecco et al., 2014). Phytochemical studies of turmeric have shown the presence of curcumin, demethoxy curcuminbisde methoxy curcumin, zingerene, curcumeno, curcumol, eugenol, tetrahydrocurcumin- triethylcurcumin, turmerin, turmerones, and turmeronols. Turmeric is made up three
curcuminoids: 75% diferuloyl methane (also called curcumin), 16% demethoxy curcumin, and 8% bisdemethoxy curcumin. The present data revealed that most of the therapeutic effects of Turmeric are due to presence of curcumin. Curcumin is also the component that gives turmeric its yellow colour. Curcumin, a polyphenol compound with a molecular formula C21H20 O6, can exist in two tautomeric forms: a keto form (an aldehyde) and a stable enol form (an alcohol) (Balaji and Chempakam, 2010).

Based on ginger and turmeric data from white ginger (rhizome root and leaf), yellow ginger (rhizome, root and leaf) and turmeric (rhizome and leaf released to the NCBI database), we selected putative mono- and sesquiterpene synthases and cloned and expressed them with GPP and FPP as substrates in E. coli or yeast. Although many of these enzymes were found to be insoluble when expressed in these systems, we were able to identify the functions for some of them. We also analyzed why some that are paralogs produce different products even though their sequences are very similar according to protein structural modeling. Both ginger and turmeric produce α-zingiberene and β-sesquiphellandrene. However, only turmeric synthesize α-turmerone, β-turmerone, which is also described, astumerone and curlone, respectively, in some papers (Hiserodt et al., 1996). Curcuma-containing products consistently demonstrated statistically significant improvement in osteoarthritis-related endpoints compared with placebo, with one exception. When compared with active control, curcuma-containing products were similar to nonsteroidal anti-inflammatory drugs, and potentially to glucosamine (Kimberly et al., 2017). The research aimed at study of effect of ginger and curcumin on osteoporosis in rats.

**MATERIALS AND METHODS**

**Materials:**
The fresh ginger and turmeric rhizomes were purchased from herbal market, the ginger and turmeric were dried and powdered in the air temperature. The betamethasone (4mg/1kg bw) three times a week for three weeks was purchased from Pharmaceutical industries El Obour City- in Egypt, Dexaglobe Ampoules.

**Biological experiment**

**Animal, housing and diets:**

48 non-pregnant female albino rats (age 6 to 8 weeks and about 160 to 210g body weight) were obtained from the animal house in Agriculture Research Center, Cairo, Egypt were housed (6 rats per cage) in the animal room under controlled lighting (12-hour light:12-hour darkness) and temperature (20°C ± 2°C) conditions and had free access to laboratory food and tap water. They were kept under normal healthy conditions and fed on the commercial diet (Table 1) without any treatment for one week for acclimatization. Experimental diet (Table 2) and water were offered ad libitum all over the experimental period. The first group of rats, the control (-) fed on commercial diet for 8 weeks (total period of experimental). The remained 42 rats were injected with beta methasone at a dose of 4 mg / kg bw three time a week for three weeks to cause osteoporosis then divided to 7 groups of six rats each (Liao et al., 2003). The second group after injected fed on commercial diet (control +). The third and fourth groups after injected fed on 10 and 15% of ginger, respectively. Fifth and sixth groups after injected fed on 10 and 15% of turmeric, respectively. Seventh and eighth groups after injected fed on mixture of 10 and 15% ginger and turmeric, respectively.
Table 1: Composition of commercial diet.

| Ingredients                        | Percentage % |
|------------------------------------|--------------|
| Protein: [soy flour meal + sun flower meal + gluten] | 21.00        |
| Fat                                | 03.26        |
| Crude fibre                        | 03.29        |
| Dl. Methionine                     | 00.40        |
| Vitamins mixed                     | 01.00        |
| Minerals mixed                     | 04.00        |
| Carbohydrates                      | 67.05        |

Table 2. Composition of Experimental diet as follows:

| Groups         | Experimental diets                                                                 |
|----------------|-------------------------------------------------------------------------------------|
| Frist          | Commercial diet (control (-) group)                                                 |
| Second         | Beta methasone + Commercial diet (control (+) group)                                |
| Third          | Beta methasone + commercial diet contain 10% of the ginger.                         |
| Fourth         | Beta methasone + commercial diet contain 15% of the ginger.                         |
| Fifth          | Beta methasone + commercial diet contain 10% of the turmeric.                       |
| Sixth          | Beta methasone + commercial diet contain 15% of the turmeric.                       |
| Seventh        | Beta methasone + commercial diet contain 10% of ginger and turmeric                 |
| Eighth         | Beta methasone + commercial diet contain 15% of ginger and turmeric                 |
| Nineth:        | were injected with Beta methasone at a dose of 4 mg / kg bw three time a week to three a week then slaughtering |

At the end of the experiment after 8 weeks the rats mended before slaughtering and all the blood done from each rat separately after anesthesia and conduct a blood centrifuge to get the serum. Blood samples were withdrawn from orbital plexus venous by using fine capillary glass tubes. Blood samples were collected into plain tubes without anticoagulant and allowed to clot. Blood samples were centrifuged at 3000 rpm for 10 min at 4°C, to obtain clear serum. Blood samples were centrifuged at 3000 rpm for 10 min at 4°C, to obtain clear serum. Serum was frozen at -18°C until analyzed. The animals were anesthetized with ether and sacrificed. Liver, kidney, and femoral bone will be separated from each rat and will be weighed to calculate the percentage of increase in organ weight. These organs were weighed and then kept until histological investigations.

Methods:
Chemical analysis

Moisture, protein, fat, crude fibre, total digestible nutrients and ash were determined according to the method of AOAC (2007). All determinations were done in triplicate. Phosphorous, calcium, atomic absorption spectrophotometer according to the method of AOAC (1998). All determinations were done in triplicate. The carbohydrate contents were tested quantitatively by the phenol–sulphuric acid method (Chaplin and Kennedy, 1986).

The absorbance was measured at a wavelength of 490 nm using UV-Vis Shimadzu Spectrophotometer (UV-1601 PC).

Volatile compounds
Hydro distillation (Extraction of essential oil)

About 100 g of cleaned and dried plant material was powdered using metal mortar and placed in a round bottom flask fitted with condenser hydro distilled for about 3hrs at atmospheric pressure and constant temperature. The strongly aromatic oil was separated from the water layer using
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diethyl ether and the solvent was removed by sodium sulfate anhydrous and concentrated by rotary evaporator.

**Phytochemicals Analysis:**

Phytochemical analysis for qualitative detection of alkaloids, tannins, saponins, flavonoids and phenol was performed on the powder of ginger and turmeric rhizome as follows:

Total tannins content in the lyophilized plant extract was determined by a modified method of Polshettiwar et al., (2007). The total phenolic content was determined using Folin-Ciocalteau reagent (Mc-Donald et al., 2001). The total flavonoids in the beverage were determined using aluminium chloride colorimetric method (El-Olemy et al., 1994). Alkaloids and Saponins were determined using method of Oloyed (2005).

**Histopathology Technique**

Autopsy samples were taken from the liver, kidney and femur bone of rats in different groups and fixed in 10% formal saline for twenty four hours. The bone was decalcified by formic acid. Washing was done in tap water then serial dilutions of alcohol (methyl, ethyl and absolute ethyl) were used for dehydration. Specimens were cleared in xylene and embedded in paraffin at 56 degree in hot air oven for twenty four hours. Paraffin bees wax tissue blocks were prepared for sectioning at 4 microns thickness by slide microtome. The obtained tissue sections were collected on glass slides, deparaffinized, stained by hematoxylin and eosin stain for routine examination through the light electric microscope (Banchroft et al., 1996).

**Scanning X-ray**

Determination the right femurs and LV5 of rats were wrapped with saline-saturated gauze to maintain their moisture and stored at 20C. After thawed at room temperature, the bones were moisturized by soaking them in saline solution with the residual muscle removed. The whole femoral BMD was scanned with Prodigy Dual-Energy X-ray Absorptiometry scanner (GE Healthcare, Little Chalfont, UK) to measure the bone mineral content (BMC, g/cm²) and bone area (BA, cm²). The BMD was calculated as BMC/BA (Bagi et al., 2011).

**Biological Determination**

Biological evaluation of the different tested diets was carried by determination of body weight gain% (BWG %) and organs weight/body weight% according to Chapman et al. (1959). BWG% = (Final weight - Initial weight) / (Initial weight) X 100

Organ weight/ body weight % = (Organ weight / Final weight) X 100

**Biochemical analysis**

Blood samples were withdrawn from orbital plexus venous by using fine capillary glass tubes, placed in centrifuge tubes without anticoagulant and allowed to clot. After the serum prepared by centrifugation (3000 rpm for 15 min), serum samples were analyzed by biodiagnostic kits:

- Alanine aminotransferase (ALT) activities were determined colorimetrically using spectrophotometer (model DU 4700) at 505 nm according to the method of Reitman and Frankel (1975).

- Aspartate Aminotransferase (AST) activities were determined colorimetrically using spectrophotometer (model DU 4700) at 540 nm according to the method of Reitman and Frankel (1975).

- Phosphorus, inorganic and calcium O-cpcaactivities were determined calorimetrically using spectrophotometer at
340 nm according to the method of Young (1990).

- Calcium O-cpc activities were determined calorimetrically using spectrophotometer (model DU 4700) at 540 nm according to the method of Young (1990).

RESULTS AND DISCUSSION

According to the WHO Osteoporosis is a disease characterized by low bone mass and microarchitectural deterioration of bone tissues, leading to enhanced fragility and consequent increase in fracture risk that results in fractures with minimal trauma. There is imbalance between bone formation (osteoblastic activity) and bone resorption process (osteoclastic activity) due to various causes such as deficiency of estrogen hormone as in post-menopausal osteoporosis, aging and oxidative stress (Yan Zhang et al., 2007). Ginger (Zingiber officinale Roscoe) is one of the most commonly consumed dietary condiments in the world. The main active phytochemicals present in ginger are gingerols, shogaols and paradols, and they have strong antioxidant and chemopreventive properties (Halvorsen et al., 2002). The medicinal, chemical and pharmacological properties of ginger has been extensively reviewed (Ali et al., 2008). Ginger extracts have been extensively studied for a broad range of biological activities including antibacterial, anticonvulsant, analgesic, antiulcer, gastric antisecretory, antitumor, antifungal, antispasmodic, antithrombotic, hypcholesterolemic, antiallergic, antiserotanergic, anticholinergic and other beneficial activities (Tchombé et al., 2012).

Turmeric (Curcuma longa) is a dietary spice belonging to the family zingiberaceae. It is a coloring and flavouring agent in foods, and has been reported to possess antioxidant properties both in vitro and animal studies. Aqueous extracts of turmeric showed antioxidant and antimicrobial activity due to the presence of curcumin (5%), a polyphenolic compound. It is known that the phenolic character of curcumin is responsible for its anti-oxidant properties (Varunraj et al., 2011). Fresh root contains good levels of vitamin-C. Other phytochemicals in turmeric include tumerone, zingiberene, cineole, d-phellandrene, d-sabinene, borneol and other curcuminoids. The majority of the phytochemicals found in turmeric occur in the volatile oil that makes up 7 percent of its weight. Dry rhizomes yield 5.8% essential oil including sesquiterpene (e.g. Zingeberene), sesquiterpene alcohols and ketones, and monoterpenes. Fresh turmeric contains 0.24% oil containing zingiberene. The most Curcumin is a known bacteriostatic agent whereas the essential oil of turmeric is bactericidal and fungistatic. The active principle, curcumin is known for its inhibitory action on micro-organisms (Niamsa and Sittiwet 2009).

Chemical composition

Results in Table (3) indicated that the chemical composition of ginger was 9.25%, 4.64%, 70.71%, 9.1%, 6.3%, 5.89% and 67.60% for protein, fat, Carbohydrates, moistures, ash, crud fiber and TDN respectively. On the other hand, the values of protein, fat, Carbohydrates, moistures, ash, crud fiber and TDN in turmeric were 7.56%, 3.73%, 72.81%, 12%, 3.9%, 2.95% and 69.32% respectively. The mean values of calcium and phosphorous were in ginger (0.30% and 0.21) while calcium and phosphorous were in turmeric (0.29% and 0.24%). Many studies have proved that ginger is endowed with strong antioxidant (Nirmala et al., 2008; Nirmala et al., 2012). Antigenotoxic, antimutagenic and anticarcinogenic properties both in vitro and in vivo studies Powdered ginger rhizome contains 3.6% fatty oil, 9% protein, 60-70%
carbohydrates, 3.8% crude fiber, 8% ash, 9-12% water and other terpenes and terpenoids. Fresh ginger contains 80.9% moisture, 23% protein, 0.9% fat, 1.2% minerals, 2.4% fiber, and 12.3% carbohydrates. Ginger has been shown to be effective against the growth of both gram-positive and gram-negative bacteria including *Escherichia coli*, *Proteus vulgaris*, *Salmonella typhi*, *Staphylococcus aureus* and *Streptococcus viridians* (Mascolo et al., 1989).

**Table (3): The Chemical composition of Ginger and Turmeric**

| Chemical composition % | Ginger  | Turmeric |
|------------------------|---------|----------|
| Protein                | 9.25    | 7.56     |
| Fat                    | 4.64    | 3.73     |
| Carbohydrates          | 70.71   | 72.81    |
| Moisures               | 9.1     | 12       |
| Ash                    | 6.3     | 3.9      |
| Crude Fiber            | 5.89    | 2.95     |
| TDN                    | 67.60   | 69.32    |
| Calcium                | 0.30    | 0.29     |
| Phosphorous            | 0.21    | 0.24     |

**Phytochemicals**

Phytochemicals are component of plant foods play an important role in the treatment of diseases and as a major. The type and amount of various phytochemical in ginger and Turmeric presented in Table (4). The obtained data showed that ginger is a rich source of alkaloids 9.76% and Tannins 2.59% as well as Saponins 0.38% While Flavonoids 4.12 % and total phenolic 0.13% addition of ginger showed high significant in Alkaloids in all phytochemicals then Flavonoids. The date also showed that Turmeric is a rich source of alkaloids 4.26% and Tannins 2.03% as well as Saponins6.17% While Flavonoids 2.31% and total phenolic 3.05% addition of Turmeric showed high significant in Saponins in all phytochemicals then Alkaloids.

Phytochemicals are non-nutritive plant chemicals that have protective or disease preventive properties, they are found generally in plants. The Phytochemical screening in (Tijani et al., 2009) study were agree with our result, who showed that all leaves contain phenolics, Tannins, Alkaloids, Saponins, Flavonoids, Steroid and does not contain phylobatanin, and tripertenes (Deokar et al., 2016). The findings revealed that the knowledge of the antimicrobial activity of the extracts obtained from ginger can be very useful and can be applied in different areas of research such as the pharmaceutical and food industries Phytochemical constituents such as steroids, alkaloids, flavonoids, tannins, phenol and several other aromatic compounds are secondary metabolites of plants that serve a defense mechanism against prediction by many microorganisms, insects and herbivores. These secondary metabolites exert antimicrobial activity through different mechanisms. The alkaloids contain in plants are used in medicine as anesthetic agents. Ginger rhizome extract and their components can be used as alternative and effective novel therapeutic strategy.

Turmeric (*Curcuma longa*) is a dietary spice coloring and flavouring agent in foods and has been reported to possess
antioxidant properties both in vitro and animal studies. Aqueous extracts of turmeric showed antioxidant and antimicrobial activity due to the presence of curcumin (5%), a polyphenolic compound. It is known that the phenolic character of curcumin is responsible for its anti-oxidant properties (Varunraj et al., 2011). Fresh root contains good phytochemicals in turmeric include turmerone, zingiberene, cineole d-phellandrene, d-sabinene, borneol and other curcuminoids. The majority of the phytochemicals found in turmeric occur in the volatile oil that makes up 7 percent of its weight. Dry rhizomes yield 5.8% essential oil including. Fresh turmeric contains 0.24% oil containing zingiberene. The most significant curcuminoid is curcumin. It has been reported that turmeric has an antimutagenic effect on bacteria in vitro. Curcumin is a known bacteriostatic agent whereas the essential oil of turmeric is bactericidal and fungistatic. The active principle curcumin is known for its inhibitory action on micro-organisms (Virendra et al., 2013).

| Phytochemicals (%) | Ginger     | Turmeric   |
|-------------------|------------|------------|
| Alkaloids         | 9.76±0.32  | 4.26±0.28  |
| Tannins           | 2.59±0.08  | 2.03±0.19  |
| Saponins          | 0.38±0.04  | 6.17±0.25  |
| Flavonoids        | 4.12±0.17  | 2.31±0.16  |
| Phenols           | 0.13±0.05  | 3.05±0.29  |

Volatile compounds

The present data given in Tables (5 & 6) indicated the volatile compounds of ginger and turmeric essential oil. Volatile compounds of ginger essential oil (Concentration) as well as values are expressed as relative area percentage while (K1) Kovat index on DB5 were analyzed by compounds identified by GC-MS (MS) and (KI) of standard compounds run under similar GCMS conditions. Recorded the 29 volatiles were identified in Concentration the most abundant identified volatile compounds were Zingiberene which represent 41.05% then α-Cubebeche, which represent 21.31% respectively. But (KI) recorded the best result in β-Curcumene then β-Bisabolene which represent 1519, 1514 respectively. Also, Heptanol (0.03 %) was found in very low amounts. Volatile compounds of turmeric essential oil (Concentration) as well as values are expressed as relative area percentage while (K1) Kovat index on DB5 were analyzed by compounds identified by GC-MS because it was recorded the best result in sensory evaluation. A total of 17 volatiles were identified in Concentration the most abundant identified volatile compounds were Tumerone which represent 43.87% then Zingiberenol, which represent 14.69% respectively. While (KI) recorded the Xanthorhizol then Curcumenol which represent 1748, 1731 respectively. Also Eudesmol (0.43%) was found in very low amounts. Shagufanaz et al. (2010) indicated that these oils contain volatile substances which are terpenes and their oxygenated derivatives usually known as camphor. The chemical constituents of turmeric rhizomes include volatiles (ar-tumerone, zingiberene, turmerone and curlone) and non-volatiles which are colorings agents and rich source of phenolics. The aroma of the turmeric is curcumin and its analogues account for its bright yellow color. El-Baroty et al. (2010) indicated that ginger is a characterized oil (GEO) with high content of sesquiterpene hydrocarbons, including β-
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sesquiphellandrene (27.16%), caryophyllene (15.29) % zingiberene (13.97%), α-farnesene (10.52%) and α-curcumin (6.62%). Fijelu Frank et al. (2013) found that the major components of essential oil from Curcuma longa analysed by GC/MS were ar-turmerone (33.2%), α-turmerone (23.5%) and β-turmerone (22.7%). The antifungal activities of the oil were studied with regard to Aspergillus flavus growth inhibition.

Table (5). Volatile compounds of ginger essential oil

| Volatile compounds          | KI  | Concentration | Identification method |
|-----------------------------|-----|---------------|-----------------------|
| Heptanol                    | 897 | 0.03          | MS, KI, SD            |
| α-Pinene                    | 936 | 0.88          | MS, KI                |
| Camphene                    | 941 | 3.28          | MS, KI                |
| 2-Methyl nonane             | 967 | 0.63          | MS, KI, SD            |
| Myrcene                     | 971 | 1.82          | MS, KI                |
| Pinene                      | 974 | 0.05          | MS, KI                |
| α-Phellandrene              | 982 | 0.05          | MS, KI                |
| Limonene                    | 1013| 0.04          | MS, KI, SD            |
| β-Phellandrene              | 1017| 4.43          | MS, KI                |
| 1,8-cineole                 | 1031| 2.16          | MS, KI                |
| α-Terpinolene               | 1062| 0.08          | MS, KI                |
| n-Nonenal                   | 1129| 0.58          | MS, KI, SD            |
| 2-Methyl undecane           | 1165| 0.16          | MS, KI                |
| 3-Methyl butanol            | 1198| 18.94         | MS, KI                |
| α-Cubebene                  | 1345| 21.31         | MS, KI, SD            |
| p-Menth-1-en-8-ol acetate   | 1349| 1.25          | MS, KI                |
| Geranyl acetate             | 1381| 0.07          | MS, KI                |
| Methyl eugenol              | 1402| 0.06          | MS, KI                |
| Geranyl propionate          | 1428| 0.27          | MS, KI                |
| α-Farnesene                 | 1432| 0.04          | MS, KI, SD            |
| γ-Elemene                   | 1439| 0.04          | MS, KI                |
| Neryl acetone               | 1442| 0.27          | MS, KI                |
| Germacrene D                | 1457| 1.90          | MS, KI                |
| Zingiberene                 | 1492| 41.05         | MS, KI                |
| Valencene                   | 1498| 0.05          | MS, KI                |
| Citronellyl n-butyrate       | 1503| 0.04          | MS, KI                |
| α-Bisabolene                | 1509| 0.09          | MS, KI                |
| β-Bisabolene                | 1514| 0.05          | MS, KI                |
| β-Curcumene                 | 1519| 0.17          | MS, KI                |

a: Kovat indices; b:Values are expressed as relative area percentage; c:compounds identified by GC-MS (MS) and / or Kovat index on DB5 (KI) and / or by comparison of MS and KI of standard compounds run under similar GCMS conditions.
Table (6). Volatile compounds of turmeric essential oil

| Volatile compounds | KI | Concentration a | Identification method b, c |
|--------------------|----|-----------------|--------------------------|
| Camphene           | 958 | 1.26            | MS, KI, SD               |
| -Fenchene          | 961 | 1.24            | MS, KI                   |
| Pinene             | 976 | 1.69            | MS, KI                   |
| α-phellanderene    | 983 | 1.82            | MS, KI, SD               |
| 3-Thujene          | 992 | 3.03            | MS, KI                   |
| Zingerenol         | 1612| 14.69           | MS, KI                   |
| Tumerone           | 1629| 8.00            | MS, KI                   |
| Tumerone           | 1651| 43.87           | MS, KI, SD               |
| Eudesmol           | 1658| 0.43            | MS, KI                   |
| Atlantone          | 1677| 1.12            | MS, KI                   |
| Eudesmol           | 1669| 0.79            | MS, KI                   |
| Curcumenone        | 1672| 3.55            | MS, KI, SD               |
| Germacrone         | 1688| 5.04            | MS, KI                   |
| ZZ-Farnesol        | 1691| 0.60            | MS, KI                   |
| ZE-Farnesol        | 1702| 2.90            | MS, KI, SD               |
| Curcumeneol        | 1731| 9.19            | MS, KI                   |
| Xanthorhizol       | 1748| 0.77            | MS, KI                   |

a: Kovat indices; b: Values are expressed as relative area percentage; c: compounds identified by GC-MS (MS) and / or Kovat index on DB5 (KI) and / or by comparison of MS and KI of standard compounds run under similar GCMS conditions.

Biological Determination

Data in Table (7) indicated that the two groups of rats fed on 10% and 15% turmeric and ginger, respectively showed increase in their body weight gain comparing with the positive control group. The body weight gain was higher in group (4) with level 15% ginger (57.26±8.733), while it was lower in group (5) that fed on basal diet of 10% turmeric (30.07±10.59) comparing with the positive control group. This result was in agreement with that obtained by Saber Sakr et al. (2011).

Many studies were carried out on ginger and its pungent constituents, fresh and dried rhizome. Among the pharmacological effects demonstrated is anti-platelet, antioxidant, anti-tumour, anti-rhinoviral, anti-hepatotoxicity and anti arthritic effect (Fisher-Rasmussen et al., 1991; Sharma et al., 1994; Kamchouing et al., 2002). Ginger was found to have hypocholesterolaemic effects and cause decrease in body weight, blood glucose, serum total cholesterol and serum alkaline phosphatase in adult male rats.

Table (7): Effect of ginger and turmeric on weight gains of rats suffering from osteoporosis.

| Groups | Parameters | Final weight (g) | Initial weight (g) | body weight gain % |
|--------|------------|------------------|--------------------|--------------------|
| Group (1): negative control | 221.83±110.241 | 177.67±13.571 | 24.86±7.391 |
| Group (2): positive control | 246.53±17.833 | 177.33±12.711 | 39.01±7.192 |
| Group (3): 10% ginger | 262.83±18.311 | 177.33±12.471 | 48.21±9.211 |
| Group (4): 15% ginger | 277.83±22.162 | 176.67±11.691 | 57.26±8.733 |
| Group (5): 10% turmeric | 230±11.429 | 176.83±9.831 | 30.07±10.59 |
| Group (6): 15% turmeric | 246±12.652 | 176.83±10.311 | 39.11±11.377 |
| Group (7): 10% ginger and turmeric | 238±11.7281 | 177±8.292 | 34.46±11.611 |
| Group (8): 15% ginger and turmeric | 272.17±14.591 | 176.83±8.492 | 53.91±12.477 |

ANOVA (F) 0.305 0.119 0.297

- Values are expressed as mean ± SD. 
- Significant at p<0.05 using one way ANOVA test.
- Values which have different letters in each column differ significantly, while those with have similar or partially are not significant.
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The results in Table (8) indicated the effect of ginger and turmeric on relative organs weight of rats suffering from osteoporosis. The mean values of relative weights of liver and kidney in positive control group was lower than the all experimental groups. But the mean values of liver and kidney for rats in group (6) were higher than those of the positive control group (8.491±1.552g, 5.342±0.591g and 1.728±0.165g, 0.957±0.746g, respectively). On the other hand, the mean values of relative weights of femoral bones in positive control group was similar to group (6) (3.917±0.493g and 3.962±1.162g) while the positive control group in relative weights of femoral bones was lower than group (8) (3.917±0.493g and 6.72±1.101g) the results agreed with that obtained by (Stanley Iheanacho et al., 2017).

Table (8): Effect of ginger and turmeric on relative organs weight of rats suffering from osteoporosis.

| Groups                  | Relative weights of liver (g) | OW/BWG  | Relative weights of kidney (g) | OW/BWG  | Relative weights of femoral bones (g) | OW/BWG  |
|-------------------------|-------------------------------|---------|-------------------------------|---------|--------------------------------------|---------|
| Group (1): negative control | 5.88±0.551                   | 2.648±0.837 | 1.255±0.16                | 0.565±0.115 | 3.57±0.828                         | 1.609±0.641 |
| Group (2): positive control | 5.342±0.591                   | 2.164±0.668 | 0.957±0.746                | 0.388±0.558 | 3.917±0.493                         | 1.589±0.737 |
| Group (3): 10% ginger     | 5.766±1.011                   | 2.192±0.798 | 1.392±0.235                | 0.529±0.347 | 4.462±0.981                         | 1.699±0.819 |
| Group (4): 15% ginger     | 6.811±0.462                   | 2.449±0.848 | 1.397±0.181                | 0.303±0.047 | 4.875±0.666                         | 1.755±0.704 |
| Group (5): 10% turmeric   | 6.471±0.952                   | 2.814±0.61 | 1.664±0.233                | 0.723±0.324 | 6.718±0.582                         | 2.921±0.777 |
| Group (6): 15% turmeric   | 8.491±1.552                   | 3.450±0.497 | 1.728±0.165                | 0.702±0.928 | 3.962±1.162                         | 1.611±0.223 |
| Group (7): 10% ginger and turmeric | 6.681±0.441            | 2.808±0.789 | 1.396±0.216                | 0.587±0.057 | 6.628±0.227                         | 2.785±0.049 |
| Group (8): 15% ginger and turmeric | 6.592±0.391            | 2.424±0.854 | 1.635±0.173                | 0.601±0.700 | 6.72±1.101                          | 2.469±0.044 |
| ANOVA (F)                | 0.049                         | 0.436    | 0.169                       | 0.354    | 0.017                               | 0.053    |
| Sig.                     | **                            | *        | *                           | **       | **                                  | **       |

Values are expressed as mean ± SD. - Significant at p<0.05 using one way ANOVA test. Values which have different letters in each column differ significantly, while those with have similar or partially are not significant.

From the data shown in Table (9), it could be observed that the level of ALT in group (7) fed on 10% ginger and turmeric was lower than the positive control group (7.4±5.639 U/L, 13.667±4.589U/L) The results agreed with that obtained by Uma Bhandari et al. (2003). While the mean level of AST in group (8) fed on 15% ginger and turmeric was lower than the positive control group (14.2±3.421 U/L, 18.5±1.225 U/L). The results agreed with that obtained by (Stanley et al., 2017). On the contrary, the mean value of P was similar in the experimental group except group (7) fed on 10% ginger and turmeric was higher than the positive control group (5.367±0.907, 5.2±0.1). Treating animals with water extract of ginger and adriamycin led to an improvement in the histological changes induced by adriamycin together with significant decrease in ALT and AST activity. Moreover, ginger reduced the level of malondialdehyde and increased the activity of superoxide dismutase. The results of the present work indicated that ginger had protective effect against liver damage induced by adriamycin and this is due to its antioxidant activities. (Saber et al., 2011).
Table (9): Effect of ginger and turmeric on liver function and phosphorus of rats suffering from osteoporosis.

| Groups                        | ALT U/L    | AST U/L    | P          |
|-------------------------------|------------|------------|------------|
| Group (1): negative control   | 9.2±7.120  | 21.4±2.191 | 4.8±0.5    |
| Group (2): positive control   | 13.66±4.589| 18.5±1.225 | 5.2±0.1    |
| Group (3): 10% ginger         | 10.83±3.601| 18±1.549   | 4.73±0.153 |
| Group (4): 15% ginger         | 13.83±3.764| 17±1.549   | 4.76±0.115 |
| Group (5): 10% turmeric       | 8.83±4.997 | 14.5±5.282 | 4.86±0.289 |
| Group (6): 15% turmeric       | 14.2±4.087 | 16±3.0     | 4.63±0.153 |
| Group (7): 10% ginger and turmeric | 7.4±5.639    | 14.4±4.979 | 5.37±0.907 |
| Group (8): 15% ginger and turmeric | 9.8±4.919    | 14.2±3.421 | 4.66±0.115 |
| ANOVA (F)                     | 0.834      | 0.163      | 0.566      |
| Sig.                          | *          | *          |            |

- Values are expressed as mean ± SD.
- Significant at p<0.05 using one way ANOVA test.
- Values which have different letters in each column differ significantly, while those with have similar or partially are not significant.

The results in Table (10) indicated that the mean values of the total Ca in positive control group was higher than that in group (4) fed on 15% ginger (8±1.082 and 6.967±0.462, respectively), and Ca++ in positive control group was higher than that in group (3) fed on 10% ginger (1.288±0.081 and 1.236±0.021, respectively). On the other hand, total Ca and Ca++ levels in all experimental groups fed on ginger and turmeric were significantly less than that in positive control group. On the contrary, the mean value of Ca/Ca++ in the positive control group was significantly less than the all experimental groups fed on ginger and turmeric. In healthy rats, both simvastatin and fenofibrate treatment showed a negative effect on the trabecular bone located at the level of femoral diaphysis. These results are consistent with other studies which concluded that to a certain extent, statins inhibit bone resorption and promote bone formation, but have no significant effect on bone mineral density in healthy rats (Chang et al., 2011; Gradosova et al., 2011).

Effects of extra-skeletal estrogen deficiency are mainly based upon increased renal calcium excretion and decreased intestinal calcium absorption (Khosla et al., 1997). Estrogen plays an important role in calcium absorption in the gut (Gennari et al., 1990) and its reabsorption in the kidney (McKane et al., 1995). The presence of estrogen receptors in the intestine has been reported and has been shown to increase intestinal calcium absorption in both rats and humans. Curcumin (Diferuloylmethane, 1, 7- bis (4-Hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5 - dione) is the active polyphenolic compound extracted from the rhizomes of turmeric (Curcuma longa L., Zingiberaceae), grown in tropical Southeast Asia (Jagetia and Aggarwal 2007; Padhye et al., 2010). Some studies demonstrated the efficacy of turmeric extracts in the prevention of bone loss in animal models of rheumatoid arthritis and postmenopausal osteoporosis (Wright et al., 2010). It was found in vitro investigations that the anti-inflammatory effects of curcumin prevent osteoclast differentiation (Bharti et al., 2004; von Metzler et al., 2009). Thus, curcumin produces beneficial changes in bone turnover and increase in bone strength using the ovary ectomized mature rat model of postmenopausal osteoporosis (Houet et al., 2016).
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Table (10): Effect of ginger and turmeric on total and ionized calcium of rats suffering from osteoporosis.

| Groups                        | Parameters | Total Ca | Ca** | Ca/Ca** |
|-------------------------------|------------|---------|------|---------|
| Group (1):negative control    |            | 8.567±2.369 | 1.323±0.049 | 6.436±1.519 |
| Group (2):positive control    |            | 8±1.082  | 1.288±0.081 | 2.999±3.295  |
| Group (3):10% ginger          |            | 7.8±0.781 | 1.236±0.021 | 6.313±0.709  |
| Group (4):15% ginger          |            | 6.967±0.462 | 1.27±0.017 | 5.488±0.407  |
| Group (5):10% turmeric        |            | 7.8±0.693 | 1.263±0.046 | 6.187±0.691  |
| Group (6):15% turmeric        |            | 7.133±1.012 | 1.25±0.026 | 5.716±0.902  |
| Group (7):10% ginger and turmeric |        | 7.733±1.168 | 1.253±0.0321 | 6.173±0.957 |
| Group (8):15% ginger and turmeric |        | 7.667±1.026 | 1.24±0.0458 | 6.205±1.044  |
| ANOVA (F)                     | 0.168      | 0.176   | 0.588 |

- Values are expressed as mean ± SD. - Significant at p<0.05 using one way ANOVA test.
- Values which have different letters in each column differ significantly, while those with have similar or partially are not significant.

**X-ray and Histopathology**

In the present study; radiographic imaging of the negative control group radiographic view showed normal radiographic finding of tibia and distal extremity of femur, and showing normal histological structure of the periosteum, compact shaft of long bone and bone trabeculae with bone marrow in between (Figs. 1, 2, 3).

![Radiographic findings of group (1).](image)

**Fig. (1): Radiographic findings of group (1).**

a- Lateral radiographic view showed Normal radiographic finding of femur.

b- Lateral radiographic view showed Normal radiographic finding of tibia and distal extremity of femur.

![Histological structure of femur bone in group (1).](image)

**Fig. (2): L.S. of Femur bone of rat in group (1) showing normal histological structure of the periosteum, compact shaft of long bone and bone trabeculae with bone marrow in between. Stained Hx.E, X40.**
In the present study; radiographic imaging of the positive control group after glucocorticoids (GC) administration for three weeks revealed bone loss of different part such as fibula, tibia and femur in addition to bone demineralization and thinning of femoral cortex in rats, disappear of cortex of tibia in others and fibula and these agree with the observations of Hallberg et al. (2009), Weinstein (2001) and Sipos et al. (2015). Osteoporosis is characterized as a reduction in bone mass and an impairment of bone architecture resulting a bone thinning with direct effects on increased cortical porosity, bone fragility and fracture risk. GC therapy is the most common cause of osteoporosis, leading to osteonecrosis of the femoral head and fractures, which may also be associated with fracture-related morbidity and a decreased quality of life.

Radiographic findings of group (2) show demineralization of tibia and bone loss of proximal part of fibula (Fig 4). Histopathologically, there were bone trabeculae osteoporosis and resorption associated with dystrophy of the articular cartilaginous surface and congestion of the blood vessels, these findings were confirmed the radiological findings (Figs. 5, 6).
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Fig.(5): L.S. of Femur bone of rat in group (2) showing osteoporosis and resorption or the bone trabeculae. Stained H&E, X16.

Fig.(6): L.S. of Femur bone of rat in group (2) showing cartilaginous dystrophy of the articular surface with congestion of the blood vessels. H&E, X16.

Radiologically in treated group by ginger 10% in group (3) after two months revealed mineralization improvement of bony loss and demineralized area as following remineralization at proximal extremity of femur and normal architecture without disruption at distal extremity of femur, rebuilding of fibula with mineralization in compare to untreated group and Remineralization Bridge at tibia with different degree of callus formation but still there was thinning in fibula (Fig. 7). Histopathologically, there was no histopathological alteration (Figs.,8, 9).

Fig. (7): Radiographic findings of group (3)

a-Lateral radiographic view of tibia, fibula and distal extremity of femur showing normal radiographic findings and architecture (thinning in fibula) Remineralization Bridge at tibia
b-Lateral radiographic view of femur showing remineralization at proximal extremity (black arrow) and normal architecture without disruption at distal extremity
c-Lateral radiographic view of tibia showing remineralization and small callus formation at lost bony part (white arrow).
In parallel to it the treated group by ginger 15% in group (4) after two months revealed continuation of rebuilding of different demineralized parts such as difficult notification of remineralization and callus formation over epiphyseal fracture, traces of callus formation at tibial lost bony part, normal radiographic findings of fibula and femoral discontinuation of proximal cortical surface, and disital part but there was small callus formation at femoral lost bony part at distal epiphysis which confirmed histopathologically resorption of the bone trabeculae was detected. These findings revealed that ginger has important role in remineralization and improvement of osteoproctic changes of tibia, fibula and femur especially at extremities of femur and tibia (articular surface) due to ginger has anti inflammatory effect in osteoarthritis cases in agree with Baer et al. (2005) and Amorndoljai et al. (2017) who indicated that ginger has been used for time immemorial for treatment of rheumatic disorder due to its anti-inflammatory properties and ability to inhibit arachidonic acid metabolism. It relieve joint pain and improve problematic symptoms and the quality of life in knee patients, it is effective as 1% Diclofenac gel and it can be considered as complementary therapy in patients with osteoarthritis of knee, in addition to it reduce the risk of systemic toxic (Figs. 10, 11).
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Fig.(10): Radiographic findings of group (4)

a-Lateral radiographic view of tibia showing remineralization and bridge formation over epiphyseal fracture (black arrow) and normal radiographic findings of fibula

b-Lateral radiographic view of femur showing discontinuation with small callus formation at lost bony part at distal epiphysis (white arrow) and discontinuation of proximal cortical surface (white arrow).

Fig.(11): L.S. of Femur bone of rat in group (4) showing bone resorption of the trabeculae.

Radiologically in treated group by curcumina 10% in group(5) after two months revealed good mineralization improvement of bony loss and rebuilding bone process as following no radiographic findings of tibia, fibula, proximal femur and still there were moderate remineralization of tibial epiphysis and bridged callus formation at oblique epiphyseal fracture of tibia (Fig. 12), Histopathologically the bone trabeculae showed dystrophy and resorption. these findings revealed that curcumin treatment attenuated and treated degrees to osteoporosis induced by GC in compare to untreated group in agree with (Yang et al., 2011; Chen et al., 2015) who demonstrated that curcumin improved bone microarchitecture and enhanced mineral density in APP/PS1 transgenic mice, and it attenuated GIOP by inhibiting osteocytic apoptosis (Fig.13).
Fig.(12): Radiographic findings of group (5)
a. Lateral radiographic view of tibia and fibula showing moderate remineralization of epiphysis and normal radiographic finding of fibula  
b. Lateral radiographic view of femur showing discontinuation of femoral cortex  
c. Lateral radiographic view of femur, tibia and fibula showing normal radiographic findings of femur, fibula and bridged callus formation at oblique epiphyseal fracture of tibia (white arrow).

Fig.(13): Femur bone of rat in group (5) showing dystrophy and resorption of the bone trabeculae. Stained H&E, X 16.

While in the treated group by curcumina 15% in group (6) after two months revealed some repairs to damaged bony parts as normal radiographic findings of femur (Fig. 14). There was no histopathological alteration in the articular cartilaginous surface and bone trabeculae and thick radiopaque tibial cortex but there were also bony loss of proximal part of fibula, in complete remineralization of fibula and discontinuation of femoral cortex, these findings in compare to untreated group revealed that the curcumina 15% stimulate rebuilding process (Yang et al., 2011; Chen et al., 2015) but not as curcumina 10%, the curcumina 10% was more effective (Figs. 15,16).
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Fig. (14): Radiographic findings of group (6)
a. Lateral radiographic view of femur, tibia and fibula showing normal radiographic findings of femur and incomplete remineralization of fibula (white arrow).
b. Lateral radiographic view of tibia and fibula showing bony loss of proximal part of fibula (still incomplete remineralization).

Fig. (15): L.S. of Femur bone of rat in group (6) showing normal histopathological structure of articular cartilaginous surface and treabeculae. Stained H&E, X 16.

Fig. (16): L.S. of Femur bone of rat in group(6) showing the magnification of (T.G.65). Stained H&E, X40.

In the present study, the radiological findings of treated group by curcumina 10% and ginger 10% in group (7) indicated normal radiographic findings of femur, tibia and fibula (Fig. 17). Also, there was no histopathological alteration (Figs. 18, 19). Along with moderate remineralization of tibial and femoral epiphysis. These findings revealed that the mixture of both curcumina 10% and ginger 10% has more compelling effect against osteoperotic changes than each one alone, in
contrast curcumina 10% acts on improved bone microarchitecture and enhanced mineral density while ginger strengths it by acting on osteoarthritis changes (Chen et al., 2015; Amorndoljai et al., 2017).

Fig.(17): Radiographic findings of group(7)
Lateral radiographic view of femur (a), tibia and fibula (b) showing normal radiographic findings. c-Lateral radiographic view of femur showing moderate remineralization of epiphysis (low radiodensity area) (white arrow) and normal radiographic finding of diaphysis and proximal epiphysis

Fig.(18): Femur bone of rat in group (7) showing normal histopathological structure of articular cartilaginous surface and bone trabeculae. Stained H&E, X16

Fig.(19): L.S. of Femur bone of rat in group (7) showing the magnification of (T.G.71 ). Stained H&E, X 40

On the other hand, mixture of curcumina 10% and ginger 10% was less qualified in 15% percentage in group (8) due to the radiographic findings revealed that the most obvious radiographic finding, small radiolucent area at epiphysis of femur and tibial (Fig. 20).
There was no histopathological alteration in the articular cartilaginous surface, compact bone and trabeculae (Figs.21, 22, 23).
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Fig. (20): Radiographic findings of group (8). a and b: Lateral radiographic view of femur, tibia and fibula showing normal radiographic findings.

Fig. (21): L.S. Femur bone of rat in group (8) showing the magnification of (T.G.74) to identify the bone trabeculae. Stained H&E, X40

Fig. (22): L.S of Femur bone of rat in group (8) showing the magnification of (T.G.74) to identify the in fact compact bone. Stained H&E, X80

Fig. (23): L.S. Femur bone of rat in group (8) showing the magnification of (T.G.74) to identify the in fact bone cartilaginous structure. Stained H&E, X40.
On the other hand, the radiological and histological findings of the group (9) bone loss of different part such as fibula, tibia and femur in addition to bone demineralization and femoral fracture and fibula bone trabeculae showed dystrophy and resorption and osteoporosis (Figs. 24, 25, 26). This agrees with the findings of Henneicke et al. (2011) and Sipos, et al.(2015) who found that using of oral corticosteroids is associated with serious side effects, including osteoporosis and consequently an increase in fractures.

Fig.(24): Radiographic findings of group (9).

a. Lateral radiographic view of femur and tibia showing fractured distal extremities of femur (white arrow) and demineralization and loss of proximal part of fibula (white arrow).

b. Lateral radiographic view of tibia and fibula showing bony loss of fibula (white arrow).

Fig.(25): L.S. of Femur bone of rat in group (9) showing zesorption, dystrophy and osteoporosis of the bone trabeuclae. Stained H&E, X16

Fig.(26): L.S. of Femur bone of rat in group (9) showing resorption, dystrophy and osteoporosis of the bone trabeuclae. Stained H&E,X16
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Conclusion
In the present study; Osteoporosis is characterized as a reduction in bone mass and an impairment of bone architecture resulting a bone thinning with direct effects on increased cortical porosity, bone fragility and fracture risk. GC therapy is the most common cause of osteoporosis, leading to osteonecrosis of the femoral head and fractures, which may also be associated with fracture-related morbidity and a decreased quality of life, ginger has important role in remineralization and improvement of osteoprotic changes of tibia, fibula and femur especially at extremities of femur and tibia (articular surface) due to ginger has anti-inflammatory effect in osteoarthritis cases. And also these findings revealed that curcumin treatment attenuated and treated degrees to osteoporosis induced by GC in compare to untreated group. Also findings revealed that the mixture of both curcumins and ginger has more compelling effect against osteoprotic changes than each one alone.

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