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# Effect of Solanine on Arthritis Symptoms in Postmenopausal Female Albino Rats

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**ABSTRACT**

**Solanine is a toxic compound produced in nightshades family as potato,tomato and eggplant when exposed to light.The current study was carried out on 18 femal postmenopausal albino rats to investigate the effect of solanine on the symptoms of rheumatoid arthritis.Animals were classified into 3 groups feeding on balanced diet only (GI) or replaced by twothird with small pieces of diseased potatoes for 2 and 4 weeks (GII,GIII) respectively . Serum levels of arthritic biomarkers were investigated as the estimation of erythrocytes sedimentation rate ( ESR) , C-Reactive Protein (CRP), malondialdehyde (MDA),Tumor necrosis factor-α (TNF-α),Interleukin-6( IL-6) and Immunoglobuline G (IgG) were determined in all groups. There was a significant positive increase in the levels of ESR, CRP , MDA , TNF-α, IL-6 , and IgG among different groups depending on potatoes intake. There was positive correlation between the serum levels of CRP and TNF-α ,Il-6 and IgG.However, a non significantly positive correlation between serum level of CRP and the level of MDA was observed. The data of the present study showed that old age and postmenopausal suffering from arthritis and joint swollen must eliminat or avoid the nightshades plants to alleviate the joint pain and also decrease the destruction of the tissues.**

***Key Words: Solanine/ C-RP/ MDA/TNF-α/ Il-6/ IgG/Estradiol.***

## INTRODUCTION

Solanine is a natural toxic chemical compound that is a glycoalkaloid produced in some species of the nightshades family (solanaceae) such as potato, tomato, eggplant[(1)]. . It is produced in potatoes when exposed to light, turning to green and increase glycoalkaloid production. Solanine toxicity is primarily displayed by gastrointestinal and neurological disorders[(2)]. One of the major problems attributed to nightshades is rheumatoid arthritis.The toxicity of solanine is due to chemical interaction with mitochondrial membranes leading to open potassium channels of mitochondria and decreasing their membrane potential,this in turn leads to $ca^{2+}$ being transported from the mitochondria to the cytoplasm that triggers cell damage and apoptosis[(3)]. Some people seem to be sensitive to solanine because their digestive tract is unable to breakdown the solanine. There were correlation between joint pain and ingestion of solanine, so elimination diet could be used to discover wheather the nightshade family affects arthritis. Some people find improvement in their arthritis by avoiding diet producing solanine but other find that only one kind needs to be excluded. Solanaceae(nightshades) are an important causative factor in the etiology of arthritis in sensitive people particularly old age[(4)]. Osteoarthritis appear to be a result of long term consumption of the solanaceae. The nightshades are considered calcinogenic plant causing toxic calcification of soft tissues[(5)]. Solanine and related glycoalkaloids are poisonous because they are acetylcholinesterase inhibitors leading to increased levels of neurotransmitter causing prolonged muscle contractions, pain, tenderness, inflammation and

stiff body movement[6,7,8]. Sowllen joint are a clinical manifestation of synovitis and the acute-phase response act as biomarker of pro-inflammatory cytokine production[9]. Solanine may induce oxidative stress leading to generation of free radicals and alterations in antioxidant and scavengers of oxygen free radicals.These subsequently elevated serum malondialdehyde(MDA) as a marker of lipid peroxidation due to oxidative stress [10] . Erythrocyte sedimentation rate (ESR) doesn't diagnose a specific disease but it does indicate that there is a disease present . In postmenopausal stage there were vaginal atrophy associated with decline in the blood level of estrogen resulting in osteoporosis and cardiovascular disease[11]. The current study aimed to investigate the availability of solanine on the triggers of the rheumatoid arthritis symptomes and the elimination of it can reduce the pain,synovitis and reduction of tissue distruction .

## MATERIALS AND METHODS

Eighteen postmenopausal female Wistar albino rats obtained the from the Veterinary Rresearch Institute, weighting between 200-220g and age between14-16 monthes .Animals were classified to three groups (6 rats/group).
GrI: Postmenopausal group depending on normal balanced diet served as reference group.
GrII: Replaced twothrird of balanced diet by diseased potatos with green patches for 2 weeks.
GrIII: Replaced twothrird of balanced diet by diseased potatos with green patches for 4 weeks.
Blood samples were taken from all animals ,centrifuged for serum separation and kept at-20°C for estimation of arthritic biomarkers.

-Erythrocyte sedimentation rate (ESR) was estimated in serum by Westergren method [12]
-C-Reactive Protein(CRP) level was estimated in serum by ELISA kit obtained from alpha-diagnostic Int-USA [13].
-Serum malondialdehyde(MDA) was determined by quantitative ELISA kit obtained from alpha-diagnostic Int USA[14].
-Serum TNF-α was estimated by ELISA kit [15].
-Serum IL-6 was measured by quantitative immunoassay ELISA kit[16].
-ELISA method for the quantitative determination of serum IgG [17].
-Serum estradiol RIA kit was purchased from Diagnotic systems laboratories(DSL) [18].
The data were subjected to one-way ANOVA and the differences between means at 0.05 probability were determined by Duncan's new multiple range test (Dytham,1999)[19].

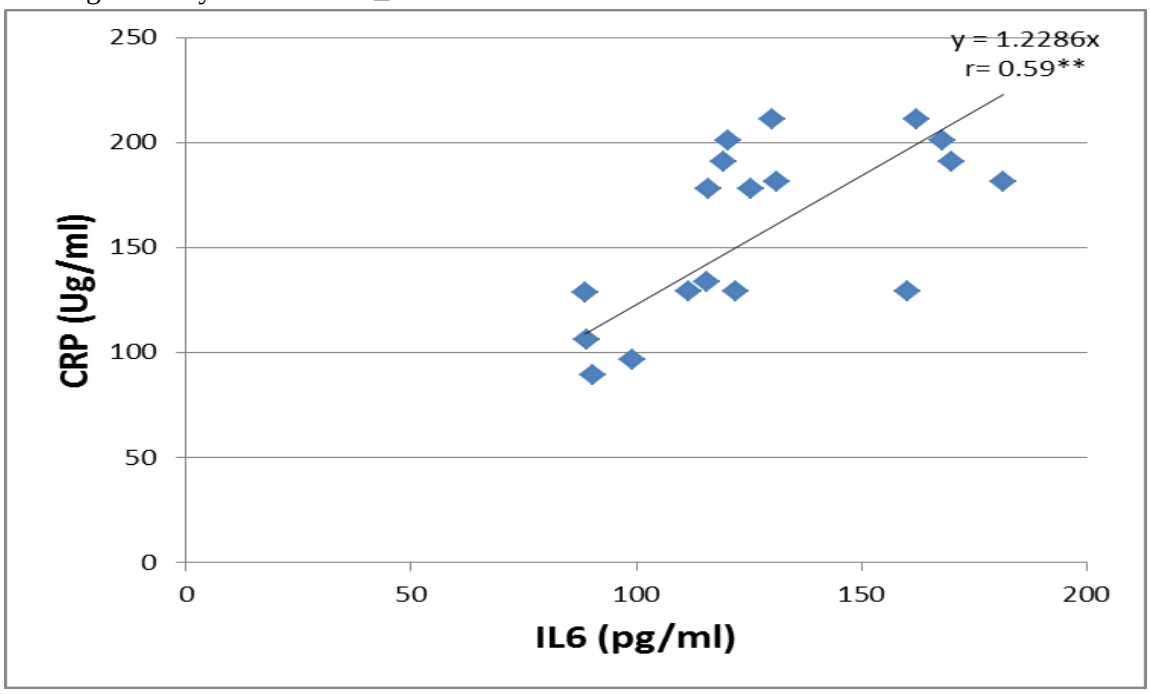
## RESULTS

Replacing two thirds of standard diet with nightshades family(Solanaceae) as green potatoes to postmenopausal albino rats for 2 and 4 weeks caused swollen joint(synovitis) with increase in arithritic biomarkers such as ESR and CRP. The activity of the pain was increased with the time of solanine ingestion. Elevation of CRP level was associated to significant elevation of procytokines TNF-α and IL6( table 1) . Consumption of toxic solanine in the present work caused increase in oxidative stress that detected by significant elevation in the level of oxidative stress marker (MDA) .Significant elevation in immune response leading to increase in the level of IgG as a consequence of solanine ingestion. Non significant difference was observed in the level of estradiol in the present work( table 1).There was positive correlation between the levels of IL6 and TNF-α against level of CRP among different groups (Fig 1,2). Non significant positive correlation was recorded between the level of MDA with the level of CRP in all groups( Fig 3). Significant positive correlation between the level of IgG and the level of CRP was observed (Fig 4).

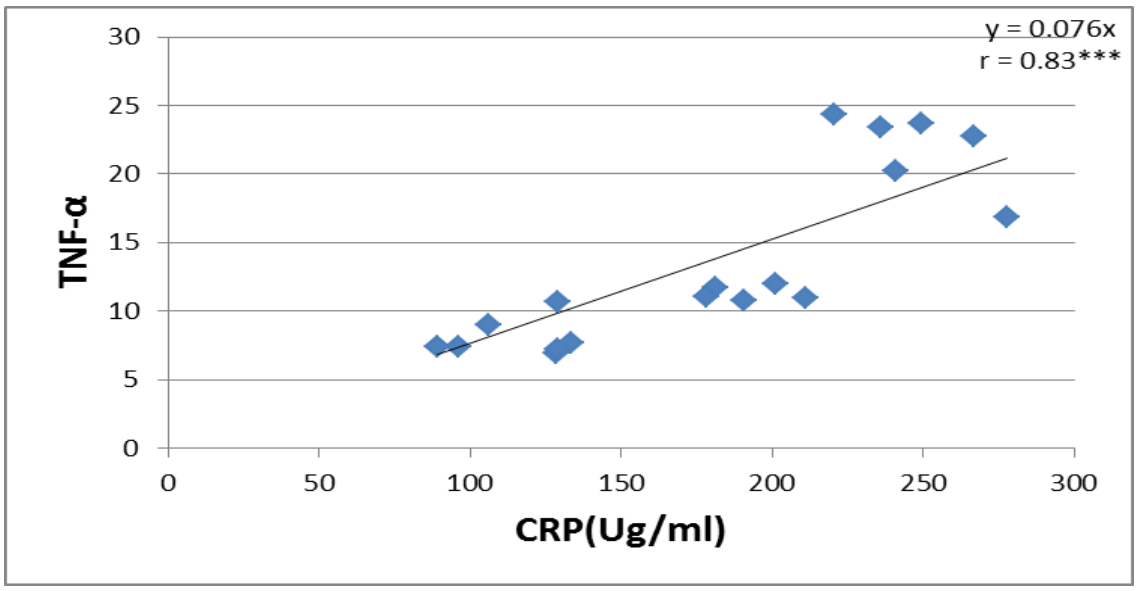
**Table(1):- Serum level of different arthritic biomarkers and estradiol level in different groups.**

| Groups/Parameters | GI | GII | GIII |
|---|---|---|---|
| ESR(mml/hr) Mean±SE | 3.2±0.2 **C** | 4.4±0.2 **b** | 5.8±0.3 **a** |
| CRP(Ug/ml) Mean±SE | 113.8±7.7 **C** | 181.9±11.7 **b** | 248.7±8.5 **a** |
| MDA(mmol/ml) Mean±(SE) | 2.9±0.04 **C** | 3.5±0.13 **b** | 4.5±0.1 **a** |
| TNF-α(pg/ml) Mean±SE | 7.6±0.3 **C** | 11.2±0.2 **b** | 21.9±1.2 **a** |
| IL-6(pg/ml) Mean±SE | 99.1±4.9 **C** | 123.2±2.5 **b** | 161.3+7.8 **a** |
| IgG(ng/ml) Mean±SE | 1112.6±35.6 **C** | 1309±14.9 **b** | 1484.9±15.1**a** |
| Estradiol(pg/ml) Mean±SE | 4.5±0.2 **a** | 4.7±0.34 **a** | 4.8±0.3 **a** |

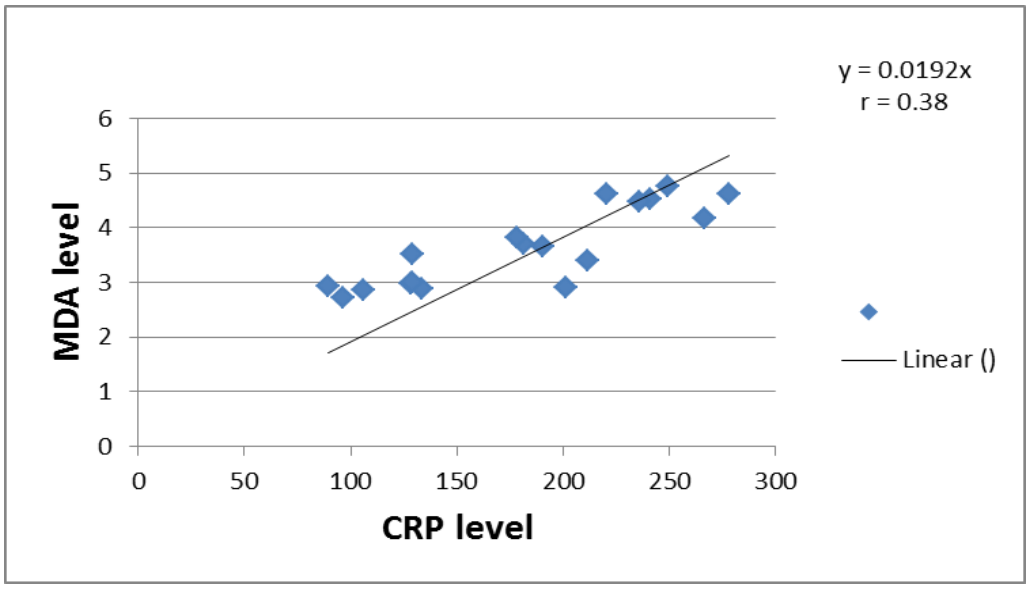
Data are means ± standard error. Means in the same raw have the same letter are not significantly different at P≤ 0.05.



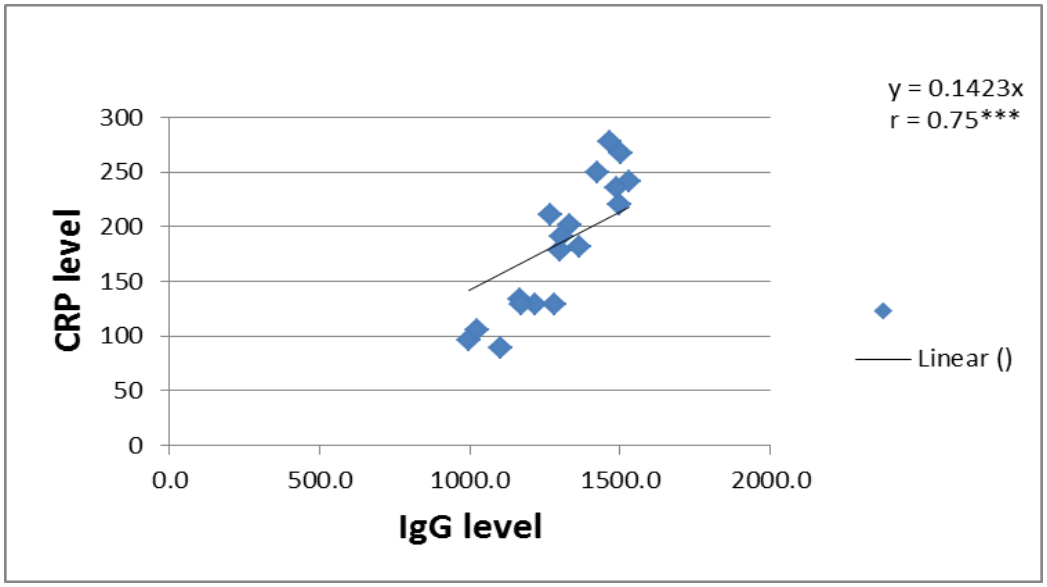

**Fig(1):- Correlation between serum level of IL6 and CRP in different groups.**




**Fig(2):- Correlation between serum level of TNF-α and CRP in different groups.**




**Fig(3 ):- Correlation between levels of CRP and MDA in different groups.**




**Fig(4):- Correlation between levels of CRP and IgG in different groups.**

## DISCUSSION

Solanine is a poisonous substance that occurs naturally in potatoes and other members of the nightshade family,such as tomatoes and eggplants. A very small amount of solanine can be toxic and in very large doses it can be fatal. Solanine occurs in all parts of the potatoes but the largest amounts are in the sprout and in green potato particularly in the skin, also it is found in tomatoes , eggplants and peppers[1,2]. Elimination of the diet could be used to investigate wheather the nightshade family affect arthritis[20]. Solanine appear to be an important factor in the etiology of arthritis[21]. Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder characterized by the chronic inflammation of synovial joint and subsequent progressive and errosive destruction of the articular tissues[22]. RA can also produce diffuse inflammation in the lung, membrane around the heart (pericardium), the membrane of the lung(pleura) and white of the eye (sclera) [23]. Cytokines production in joints and/or hepatic kupffer cells leads to increased activity of hepatocytes with increased production of acute-phase proteins as C-Reactive Protein[24]. Age is a critical factor that play an important role in causing rheumatoid arthritis , so old age are more susceptible to bone turnover due to sex hormonal deficiency [25]particularly postmenopausal female[26,27],beside age, consumption of solanine may induce oxidative stress leading to generation of free radicals and alteration in antioxidant and scavengers of oxygen free radicals. These lead to elevation in lipid peroxidation that are manifested by elevation of serum malondialdehyde [28,10]. Oxidative stress and/or defective antioxidant status contribute to the pathology of arthritis[29]. The inflammatory process develops in the tissue of the synovium where leukocytes are recruited, accumulate and become primary sources of reactive oxygen species[29,30]. Solanine consumption lead to alteration in arthritic biomarkers[31]. Inflammatory processes play an important role in the level of C-reactive protein which is a marker of inflammation . C-reactive protein is an acute phase protein produced by hepatocytes in respose to acute and chronic inflammation. These inflammatory conditions causes release of IL-6 and TNF-α that triggers the synthesis of C-reactive protein and fibrinogen by the liver [32, 33]. Elevated C-reactive protein are associated with many pathological states including rheumatoid arthritis, trauma , viral or bacterial infection and hepatitis,[34].

There is a relationship between oxidative stress and C-reactive protein So,C-reactive protein is a marker of inflammation and tissue damage [35,36]. ESR doesn, t diagnose a specific disease.When an inflammatory processes is present,there were high proportion of fibrinogen cause RBCs to stick to each other.The ESR is governed by balance between fibrinogen and those factor resisting sedimentation[37]. ESR is called an acute-phase reactant. The level of ESR was increased in adjuvant model that coincided with the result of the present study when compared with the level of base line[38]. A marked increase of proinflammatory cytokines TNF-α and IL-6 in the current study were agreed with [39,40,41,42] who declared that IL-1 and TNF-α initiated IL-6 pathway in mediating inflammatory cytokines in inflammatory arthritis. Malondialdehyde (MDA) is a stress marker and act as a measure of lipid peroxidation[43]. High level of IL-6 is a critical determinant of increase bone resorption in postmenopausal rheumatoid arthritis with high activity[44]. The up-regulated cytokines represented the adaptive immune system. High prevelance of IgG were found in patients with RA that were evaluated by ELISA and there was positive correlation between the level of IgG on one hand and disease activity on the other [28,45]. High serum level of IgG were also reported in postmenopausal mice with osteoporosis as a result of estrogen deficiency[46]. RA is a common inflammatory joint disease which is common in female than male due to deficiency of estrogen that coincided with the time of menopause [47].

## CONCLUSION

Female postmenopausl albino rats with estrogen defifiency depending on standard diet mixed with diseased potatoes containing solanine causing increase in rheumatoid arthritis markers. It can be suggested that old age people suffering from rheumatoid arthritis must avoid nightshaded plants to reduce the pain , swollen joints ,inflammation and destruction of cartilage.

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