

Full Length Research Paper

Effects of *Juniperus phoenicea* extract on uricemia and activity of antioxidant enzymes in liver, erythrocyte and testis of hyperuricemic (oxonate-treated) rats

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The aim of the present study was to determine whether administration of *Juniperus phoenicea* extract would have any advantage over allopurinol therapy on (1) lipids peroxidation level and (2) antioxidant activity in liver, erythrocyte and testis of hyperuricemic rats by oxonate administration. In hyperuricemic rats, levels of lipids peroxidation in liver, erythrocyte and testis were found to be significantly increased as compared to control rats ($p < 0.05$). Activities of glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (CAT) were also significantly increased as compared to the controls ($p < 0.05$). An ameliorative effect was obtained in hyperuricemic rats by oral treatment with either allopurinol (10 mg/kg body weight (bw)) or *J. phoenicea* extract (100 or 200 mg/kg bw). The 100 mg/kg dose revealed to be efficient in reducing uric acid level in blood and the 200 mg/kg dose strongly reduced the activities of SOD, CAT and GPX in liver and erythrocyte. Our results support that the consumption of *J. phoenicea* extract should be recommended in ethnomedicinal practice to reduce the risk of gout by decreasing the uric acid level in blood and to confer some protection against oxidative stresses at organs level.

Key words: Oxidative stress, oxonate, uric acid, allopurinol, *Juniperus phoenicea*, rat.

INTRODUCTION

Hyperuricemia, that is, high level of uric acid in blood, is present in 5 to 30% of the general population and seems to be increasing worldwide. Besides being considered the major risk factor for gout (Bieber and Terkeltaub, 2004), it is associated with the development of other disorders such as cardiovascular diseases, hyperglycemia/diabetes mellitus, inveterate alcoholism, renal failure, obesity, dyslipidemia and increased mortality (Vazquez-Mellado et al., 2004). Therefore, there is an obvious need for novel agents or therapeutic strategies that could act on

the physiological regulation of uric acid levels and prevention of uric acid-related diseases. *In vitro* and *in vivo* studies show that natural products have good anti-inflammatory effects (Sy et al., 2009; Bedi et al., 2010; Mwale and Masica, 2010). *Juniperus* L. (Cupressaceae) species have been used to cure various inflammatory and infectious diseases in Turkish folk medicine (Akkol et al., 2009). Inflammation is a physiopathological response of living tissues to injuries that lead to the local accumulation of plasmatic fluid and white blood cells. Although it is a defence mechanism, the complex events and mediators involved in the inflammatory reaction can induce, maintain or aggravate many diseases. Therefore, the use of anti-inflammatory agents is helpful in the therapeutic treatment of these pathologies.

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In the traditional medicines worldwide, several *Juniperus* species are used as remedies against common cold, urinary infections, nettle-rash (urticaria), dysentery, hemorrhages, leucorrhoea and rheumatic arthritis, to regulate menstruation and to relieve menstrual pain (Seca and Silva, 2007). For instance, *Juniperus drupacea* fruits are used to treat helminthes infections, stomach aches and hemorrhoids (Yesilada et al., 1993), decoction of fresh shoots is used for urinary inflammations, gout and to treat abdominal pain and the tar of this species is used against diarrhea (Yesilada et al., 1993). Fruits of another species, *Juniperus communis*, are swallowed like a pill against cough, to alleviate pain and to cure hemorrhoids, whereas tar of this species is used externally against scabies and heat rash (Fujita et al., 1995). The boiled fruit of *Juniperus oxycedrus* is widely used in the treatment of gastrointestinal disorders, common colds, as expectorant in cough, to treat calcinosis in joints, as diuretic to pass kidney stones, against urinary inflammations, hemorrhoids, and as antidiabetic (Yesilada et al., 1993; Abdou et al., 2011), while the resin was used for wound healing (Yesilada et al., 1993).

On the other hand, *Juniperus phoenicea* L. leaves were found to contain active components due to the anti-proliferative activity they show against a broad range of human tumors (Rizk et al., 2007) and antioxidant properties due to its content of flavonoid and phenolic compounds (Ibrahim and Risk, 2005). In spite of such a wide use of *Juniperus* species against pain and inflammatory conditions of various origins, it was discovered that only few studies have evaluated their anti-inflammatory and antinociceptive potentials in a reference survey (Moreno et al., 1998). Quite often, the real efficacy and/or the relevant active principles of many plants used in folk medicine remain unknown. Therefore, the aim of the present study was to find a scientific basis that could support the use of *J. phoenicea* in medicine. In this study, effects of *J. phoenicea* extract were compared to those of allopurinol, a standard non-steroidal anti-inflammatory drug, administered by oxonate in rats induced to be hyperuricemic.

MATERIALS AND METHODS

Leaves of *J. phoenicea* L. (Cupressaceae) were used in this study. Leaves were collected in Mars, 2009, in the region of Sfax, Tunisia. The plant was identified by (Chaieb and Boukhris, 1998) botanists in the University of Science (Sfax, Tunisia). The vouchers specimen were deposited at the herbarium of the department of botany in the cited institute.

Preparation of extracts

Plant material, either 1 or 2 g in order to test two concentrations (see below), was boiled for 10 min in 200 ml of distilled water in an Erlenmeyer flask. This procedure was repeated twice and aqueous extracts were mixed and kept frozen, after which they were orally administered in the drinking water, and were given with *J. phoenicea* extract (equivalent to 100 or 200 mg fresh leaves/kg

body weight (bw), respectively).

Animals and experimental design

Male Wistar rats (250 to 300 g) were used in this study. The animals were purchased from the Central Pharmacy of Tunisia (SIPHAT, Tunisia) and were housed in plastic cages and fed on standard chow pellets. They were given water *ad libitum*. All animals were maintained on a 12 h light/12 h dark cycle, at a constant temperature of 25°C. All procedures were in strict accordance with the sciences faculty legislation on the use and care of laboratory animals and with the guidelines established by Institute for Experimental Animals of Sfax University, being approved by the university committee for animal experiments. Experimental hyperuricemia was induced in rats by intraperitoneal (i.p.) injections of the uricase inhibitor potassium oxonate (300 mg/kg bw) as proposed by Liu et al. (2008) (oxonic acid = 1,4,5,6-tetrahydro-4,6-dioxo-1,3,5-triazine-2-carboxylic acid). Animals were divided in five groups. Group one, the controls, were sham-injected with saline solution. Group 2 (OxoT) and the remaining 3 groups were i.p. injected with potassium oxonate (300 mg/kg bw) one hour before administering either the *J. phoenicea* extract or allopurinol. Allopurinol, an analog of hypoxanthine, is a common remedy to treat hyperuricemia (Liu et al., 2008) which was used in this study for comparison with the effect of *Juniperus* extract. This procedure was carried out each day for 7 consecutive days. Orally administered in the drinking water, group 3 (OxoT + allopurinol) was given allopurinol (10 mg/kg/bw) and groups 4 and 5 (OxoT + J1 and OxoT + J2, respectively) were given *J. phoenicea* extract (equivalent to 100 or 200 mg fresh leaves/kg bw, respectively).

Sample preparation

Serum preparation

At the end of experiments, animals were rapidly sacrificed by decapitation and blood samples were collected. Blood samples collected in centrifuge tubes were centrifuged at 3000 rpm for 20 min. Serum was stored at -20°C until used for biochemical assays. Level of uric acid in serum was measured by the uricase colorimetric test (Biomaghreb kit, Tunisia, ref: 20091).

Tissue preparation

Liver and testis were excised, frozen and stored at -80°C until use. Tissue samples were homogenized in 50 mM sodium pyrophosphate buffer (pH 7.4). The homogenate was then centrifuged at 3000 ×g for 15 min at 4°C, and aliquots of supernatant were kept at -30°C until used for assays.

Assessment of oxidative stress markers

Level of lipids peroxidation in tissues was measured as the amount of thiobarbituric acid reactive substances (TBARS) according to Yagi (1976). 125 µl of supernatant were mixed with 125 µl of trichloroacetic acid (TCA) in order to discard proteins and after centrifugation (1000 ×g, 10 min, 4°C), 200 µl of the new supernatant were mixed with 40 µl HCl (0.6 M) and 160 µl of thiobarbituric acid (TBA) 20% in TBS. The mixture was heated at 80°C for 10 min and, after cooling, the absorbance was read at 530 nm. The amount of TBARS was calculated by using an extinction coefficient of $1.56 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$. Catalase (CAT) activity was measured according to Aebi (1984). 20 µl tissue homogenate (about 1.5 mg proteins) were added to 1 ml phosphate buffer (0.1

M, pH 7) containing 100 mM H₂O₂. Rate of H₂O₂ decomposition was followed by measuring the decrease in absorbance at 240 nm for 1 min. The enzyme activity was calculated using an extinction coefficient of 0.043 mM⁻¹ cm⁻¹ and expressed in international units (I.U.), that is, in μmoles H₂O₂ destroyed/min/mg protein, at 25°C. Superoxide-dismutase (SOD) activity was assayed by measuring its ability to inhibit the photoreduction of nitroblue tetrazolium (NBT) (Beyer and Fridovitch, 1987). In this assay, one unit of SOD is defined as the amount required to inhibiting the photoreduction of NBT by 50%. Riboflavin (0.26 mM final concentration) was added to start the reaction and absorbance was recorded at 560 nm for 20 min. The activity was expressed as units/mg protein, at 25°C. Glutathione peroxidase (GPX) activity was measured as previously described (Flohe and Gunzler, 1984). Change in absorbance at 340 nm was monitored for 5 min. A blank control with all the ingredients except the sample was also monitored. The specific activity was expressed as mmoles NADPH consumed per minute per mg protein (that is, U/mg protein).

Protein content was estimated by the method of Lowry et al. (1951) using bovine serum albumin as standard.

Histopathological studies

For histological studies, the Bouin-fixed tissue was dehydrated in graded alcohol and embedded in paraffin. Thin sections (6 μm) were stained with routine haematoxylin-eosin solution and examined classically with a photonic microscope to determine histopathological lesions.

Statistical analysis

Results are reported as mean ± SEM for at least 6 determinations throughout the study. Results were analysed by one-way analysis of variance (ANOVA) followed by the Duncan's multiple range test. The software SPSS 11.0 for Windows was used for statistical evaluation. P < 0.05 was accepted as significantly different.

RESULTS

Effect on serum level of uric acid

As shown in Table 1, oxonate treatment resulted in a hyperuricemia (329 versus 240 μmol/L in controls). Treatment with aqueous extract of *J. phoenicea* reduced the serum uric acid level of oxonate-treated animals to 122 μmol/L (group J1) and 267 μmol/L (group J2), whereas allopurinol treatment decreased the uric acid level to 185 μmol/L. Interestingly, the hypouricemic effect was more pronounced in J1 group than in J2 group. Somewhat similar results were observed about uric acid levels in hepatic tissue. Uric acid concentrations were 680 μmol/g in oxonate-treated rats versus 355 μmol/g in controls.

The values were reduced to 494 and 219 μmol/g in J1 and allopurinol groups, respectively. Surprisingly, no such lowering effect was obtained in the J2 group (710 μmol/g).

In order to analyze the relevance of uricemia reduction, level of lipids peroxidation and activities of main antioxidant enzymes were measured in liver, erythrocyte and testis. The results are reported in Figures 1, 2 and 3. In hyperuricemic (oxonate-treated) rats, the TBARS content in the liver was found to be significantly increased as compared to controls (p < 0.05). The SOD, CAT, and GPX activities in the liver of hyperuricemic rats were significantly increased as compared to normal rats (p < 0.05). In hyperuricemic rats treated with allopurinol or with the *J. phoenicea* extracts (100 or 200 mg/kg bw), an ameliorative effect was observed. *J. phoenicea* (200 mg/kg bw) extract induced a more pronounced decrease of TBARS level, and SOD, CAT, and GPX activities in liver as compared to control rats, hyperuricemic rats and allopurinol-treated rats (p < 0.05). In oxonate-treated rats, the TBARS content in erythrocyte is significantly increased, compared to controls (p < 0.05). Activities of SOD, CAT, and GPX are also increased in these cells as compared to controls (p < 0.05). Values of all these parameters were reduced toward normality by treatment with either allopurinol or *J. phoenicea* extracts, especially when administering the J2 dose. In testis of induced hyperuricemic rats, both TBARS content and SOD, CAT, and GPX activities were significantly increased compared to controls (p < 0.05). Treatment with allopurinol exerts some ameliorative effect. However, treatment with *J. phoenicea* extracts fails to produce any significant effect, suggesting that the active substances do not reach this organ.

Liver and testicular histopathology

Liver histology

Free radical formation during the metabolism of oxonate by hepatic microsome, cause lipid peroxidation of the cellular membrane leading to the necrosis of hepatocytes. Rats treated with oxonate developed significant hepatic damage as compared to controls (Figure 4a and b). An ameliorative effect was obtained in hyperuricemic rats by oral treatment with either allopurinol (Figure 4c) or *J. phoenicea* extract (Figure 4d and e).

Testis histology

Histopathology of testis of control group showed no marked changes. Micro thin sections from these three groups indicated the normal cycle of spermatogenesis. Seminiferous tubules had well preserved sertoli cells and well delineated tubular basement membrane (Figure 5a). The interstitium between tubules and Leydig cells were also intact in these groups. However, in the oxonate-treated groups (Figure 5b), differences were observed in the histology of the testis. Although the tubular basement

Table 1. Uric acid levels in serum and hepatic tissue after 1 week in oxonate-treated (OxoT) rats given allopurinol or *Juniperus* extracts.

Groups	Serum uric acid ($\mu\text{mol/l}$)	Liver uric acid ($\mu\text{mol/g}$)
Control	240.49 \pm 17.68	355.50 \pm 18.97
OxoT	329.16 \pm 36.35*	680.17 \pm 44.93*
OxoT+ allopurinol	185.40 \pm 17.25***	219.05 \pm 38.48***
OxoT+ J 1	122.64 \pm 15.83*****	494.36 \pm 19.90*****
OxoT+ J 2	267.94 \pm 27.28***	710.50 \pm 44.47***

J1 = 100 mg/kg bw; J2 = 200 mg/kg bw. Values are given as mean \pm SEM for group of 12 animals each; values are statistically *p < 0.05 for control rats, **p<0.05 for gouty rats, ***p < 0.05 for allopurinol-treated rats.

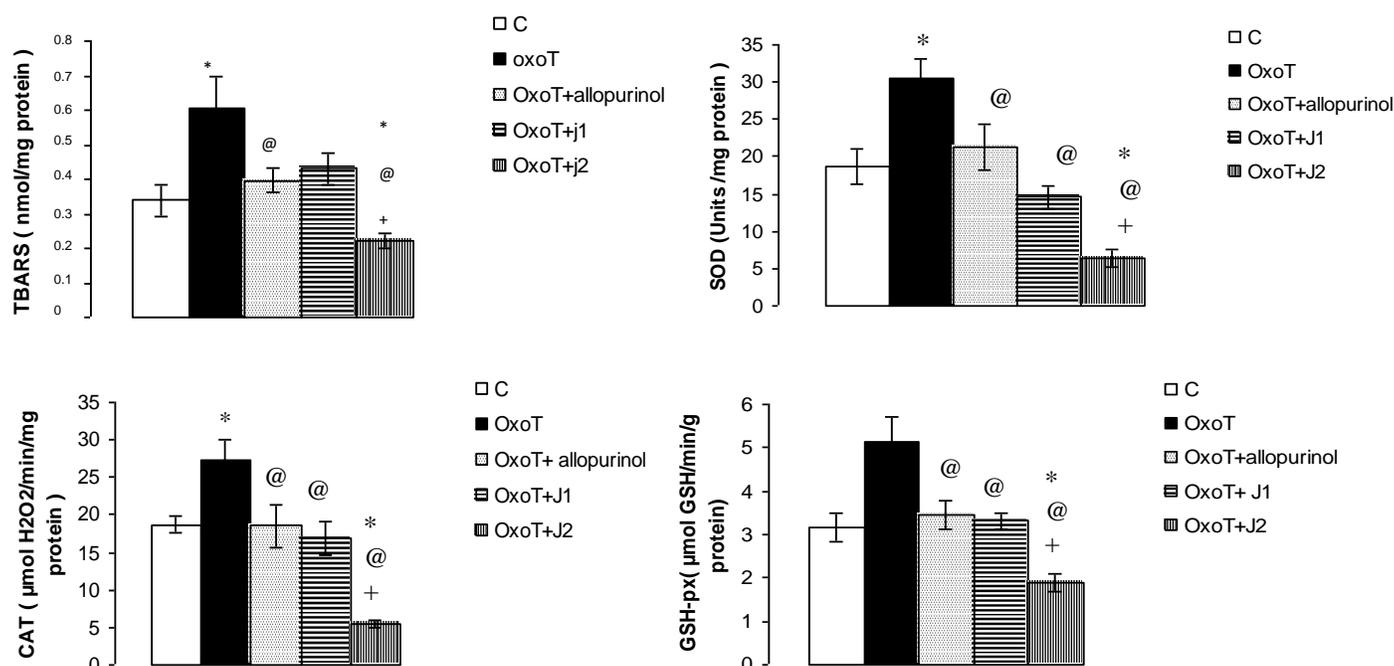


Figure 1. Effect of *Juniperus phoenicea* extract (100 or 200 mg/kg bw) and allopurinol (10 mg/kg bw) on TBARS level and activities of SOD, CAT and GPX in liver of oxonate-treated (hyperuricemic) rats after 1 week treatment. Values are the mean \pm SEM for group of 6 animals each. Statistically significant: *p < 0.05 as compared to controls; @p < 0.05 as compared to hyperuricemic rats; +p < 0.05 as compared to allopurinol-treated rats.

membranes of seminiferous tubules were identified in some areas, tubules could exhibit focal or diffuse intermediate necrosis. Treatment of *J. phoenicea* extracts ameliorated the toxic effects of the oxonate, in a dose dependent manner (Figure 5d and e), in particular, in the group treated with low dose of *J. phoenicea* (100 mg/kg bw) (Figure 5d).

DISCUSSION

Today, millions of people around the world use medicinal plants as part of traditional medicine for a large range of medical disorders (Namukobe et al., 2011). The use of traditional medicine in developing countries contributes

directly to the socio-economic status and benefit of the rural communities (Chiranjibi et al., 2006). People, especially herbalists and traditional healers, generate income from medicinal plants. Uganda is one of the developing countries where about 80% of the population depends on herbal medicine for treating various diseases (Tabuti et al., 2003). It is reasonable to consider that a survey of ethnomedical uses of a plant may provide useful clues for drug discovery. In such ethnomedical research, one must identify a clear preferential use of a particular plant and its objective effect upon a specific disease or symptom (Lansky et al., 2008). The disorder of uric acid metabolism in gouty patients is in part attributed to an oxidative stress due to several factors. An over-production of free radicals may exert deleterious effects

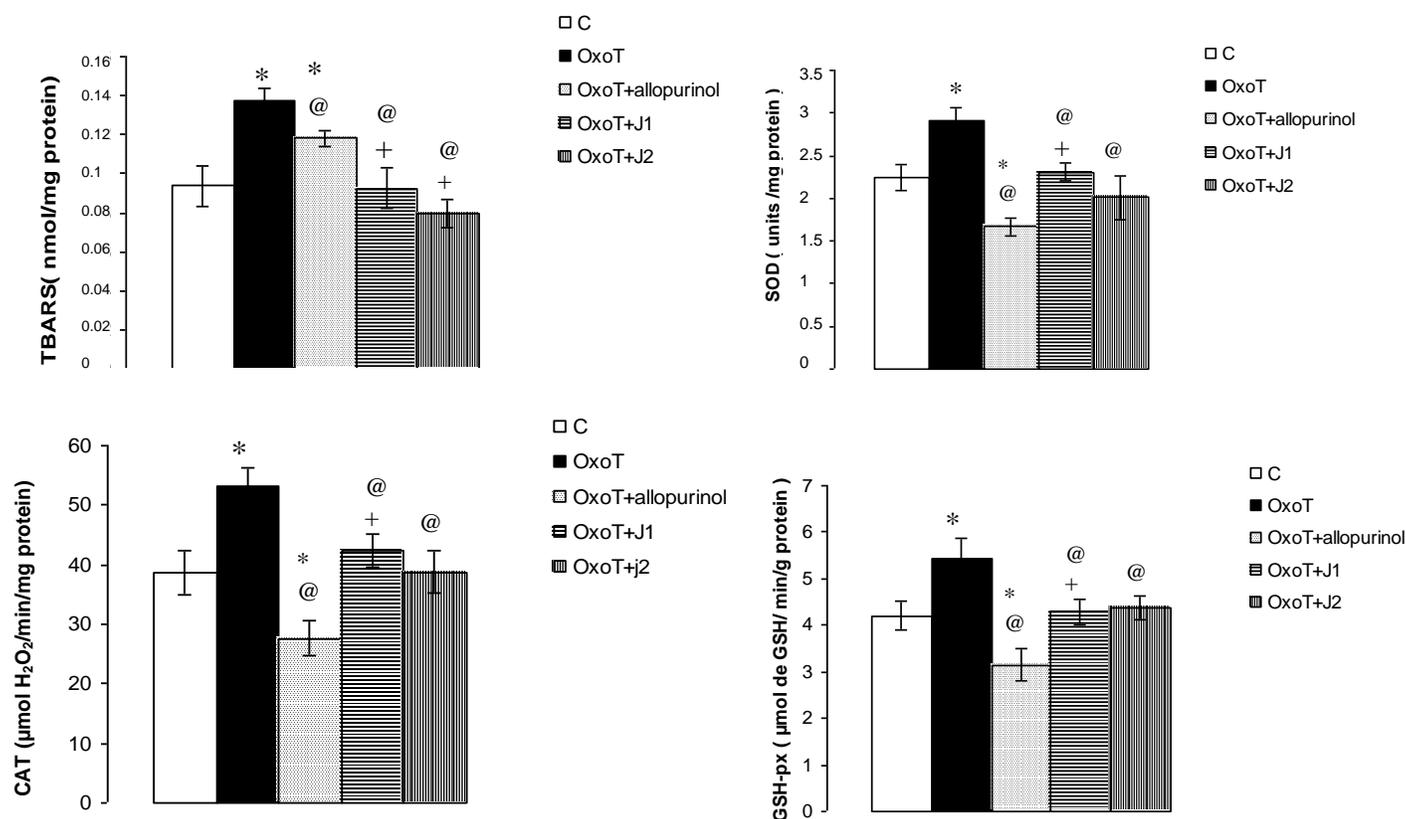


Figure 2. Effect of *Juniperus phoenicea* extract (100 or 200 mg/kg bw) and allopurinol (10 mg/kg bw) on TBARS level and activities of SOD, CAT and GPX in erythrocyte of oxonate-treated (hyperuricemic) rats after 1 week treatment. Values are the mean \pm SEM for group of 6 animals each. Statistically significant: *p < 0.05 as compared to controls; @p < 0.05 as compared to hyperuricemic rats; +p < 0.05 as compared to allopurinol-treated rats.

on liver, leading to different purines metabolism in this organ. Under our experimental conditions, the oxonate-induced hyperuricemia is accompanied by an oxidative aggression as evidenced by the significant increase in hepatic lipids peroxidation levels and a significant increase of SOD, CAT, and GPX activities in liver.

In order to better evaluate the effects of *Juniperus* extract, allopurinol, a classical drug for treatment of gout exerting a well documented hypouricemic activity, was used for comparison. Administration of *J. phoenicea* in hyperuricemic rats appears to be very efficient in reducing uricemia. This action could be consequence of an increased expression and/or activity of antioxidant enzymes; or inactivation of the circulating free radicals and reactive oxygen species. The reactive oxygen species produced by mitochondria and during inflammation process are considered as responsible for many pathological aspects in gouty patients. These reactive oxygen species are present in cells under physiological conditions, producing toxic effects when their production rate increases and exceeds the antioxidant defence capacity of the cells (Glantzounis et al., 2005). Thus, oxidative stress generally means a disturbance in the prooxidant-antioxidant balance in favour of the former. The protection system

to prevent and repair the oxidative damage includes enzymes such as superoxide dismutase and glutathione peroxidase, as well as antioxidants and radical scavengers such as vitamin E and the β -carotenes in the lipid portion of the cells, and glutathione, ascorbic acid and uric acid in the aqueous phase (Watanabe et al., 2002). Globally, the beneficial effect of *Juniperus* extracts could be in large part attributed to the presence of flavonoids and other anti-oxidative molecules.

It is also interesting to underscore the dual property of uric acid. Being a powerful radical scavenger as well as being able to act as chelator of metal ions, such as iron and copper, by converting them to poorly reactive forms unable to catalyse free-radical reactions, uric acid is one of the most important endogenous antioxidants in human biological fluids (Glantzounis et al., 2005). Although plasma uric acid is not as effective as plasma ascorbate in preventing the initiation of lipid peroxidation, it does lower the rate at which lipid peroxidation occurs (Frei et al., 1989). Roughly, it is thought that uric acid contributes to more than 50% of the antioxidant capacity of blood (Glantzounis et al., 2005; Parmar, 2009). The increase in blood uric acid concentration could have enabled the hominids to maintain blood osmotic pressure in times of

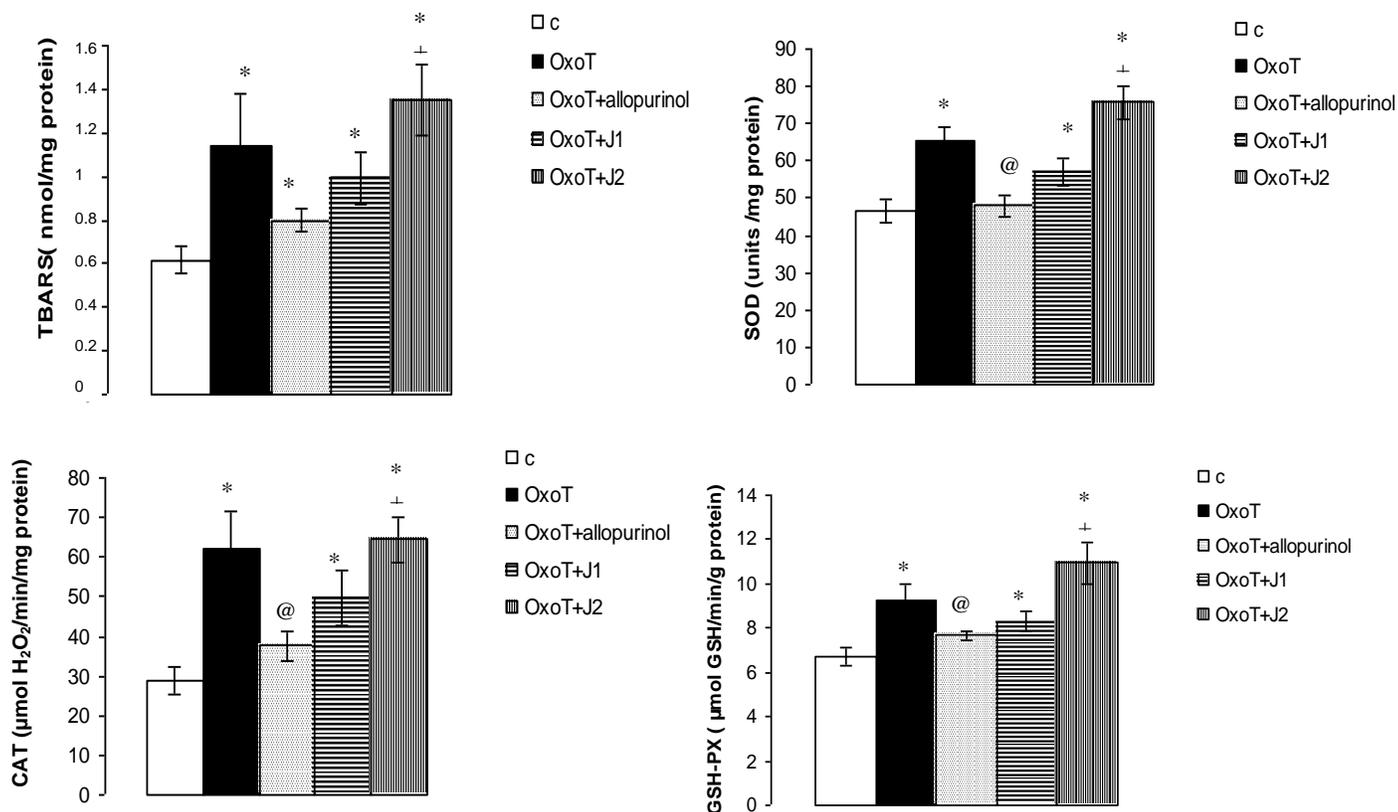


Figure 3. Effect of *Juniperus phoenicea* extract (100 or 200 mg/kg bw) and allopurinol (10 mg/kg bw) on TBARS level and activities of SOD, CAT and GPX in testis of oxonate-treated (hyperuricemic) rats after 1 week treatment. Values are the mean \pm SEM for group of 6 animals each. Statistically significant: * $p < 0.05$ as compared to controls; @ $p < 0.05$ as compared to hyperuricemic rats; † $p < 0.05$ as compared to allopurinol-treated rats.

low salt ingestion and it has been suggested that this increase in blood pressure from the increase in uric acid could be essential for hominids to maintain their vertical position (Parmar, 2009).

Increased uric acid may be a compensatory mechanism trying to counteract oxidative stress (Ames et al., 1981). After showing that uric acid is an effective antioxidant, Ames et al. (1981) hypothesized that uric acid may be an evolutionary antioxidant substitute for the loss of ability to synthesize ascorbic acid in higher primates. In humans, uric acid exists in blood at concentration close to maximum solubility. Same authors explained that these high levels of uric acid may be the result of the evolution of effective protective mechanisms against oxygen radicals and that this may partly explain the marked increase in life-span and the decrease in cancer rates in the evolution from prosimians to modern humans.

However, uric acid is one of the potential uremic toxins. It is a potent stimulator of the pathological apoptosis in mononuclear cells. It activates the two most important apoptotic pathways while its pro-inflammatory action might represent a further mechanism (Bordoni et al., 2005). Questioning the multifaceted relationship between uric acid and oxidative stress generates a series of directly

testable hypotheses with significant implications. One hypothesis is that purines catabolism can be modulated to augment mitochondrial defence in times of oxidative stress, such as in gouty patients. A related hypothesis is that impairing purines catabolism would compromise mitochondria functions when exposed to oxidative stress. Testing these hypotheses will require further investigations. Our study demonstrated a potential and beneficial effect of *Juniperus phoenicea* in attenuating oxidative stress and enhancing the body's own antioxidant defences in oxonate-treated rats. As afore presented, most of the measured parameters were restored to values comparable to those of controls. Previous studies have shown that different types of chemical constituents were found in the various parts of *Juniperus* species. These were mainly flavonoids, coumarins, lignans, sterols (Seca and Silva, 2007), terpenoids (Seca et al., 2008), polysaccharides (Schepetkin et al., 2005) and other aliphatic or aromatic compounds (Seca and Silva, 2007). Among these compounds, diterpenoids such as honokiol isolated from *J. polycarpus* was shown to exert anti-inflammatory activity (El-Sayed, 1998).

Methodical preparation of medicinal remedies involving precise dosage would determine activity and effectiveness

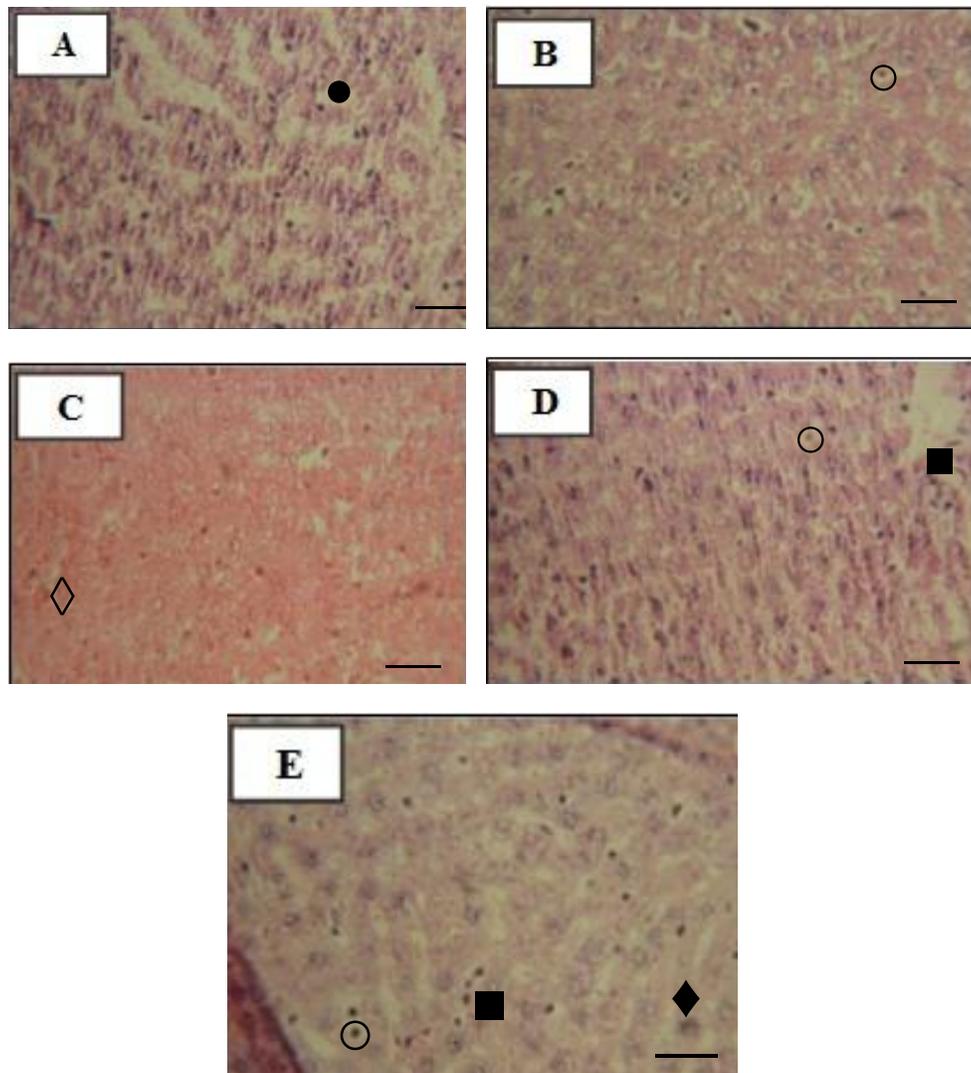


Figure 4. Microscopic observation of rat liver; (A) Representative section from control depicting the normal structure of lobule and hepatocytes; (B) section from the oxonate showing the centrilobular degeneration and fatty infiltration in hepatocytes; (C) section from the allopurinol (10 mg/kg bw) group showing the near normal architecture of the lobule and hepatocytes; (D and E) Section from the *Juniperus phoenicea* extract (100 or 200 mg/kg bw) group showing the architecture of the lobule and hepatocytes. Filled circle: normal hepatocyte, open circle: hyper vacuolation of hepatocytes; filled diamond: infiltration of mononuclear cells, open diamond: Inflammation; filled box: kupfer cell, H&E stain ($\times 400$); scale bar, 50 μm .

of main compounds. However, most of the medicinal plants used to treat gout are administered as decoctions and infusions, so, the biologically active compounds are most likely water-soluble. In the search for anti-inflammatory agents, alternative strategies such as natural products are becoming more popular and are being practiced extensively by a large number of people. These natural products are increasingly being investigated for their biological activity to confirm their role in the prevention and treatment of inflammatory diseases (Ghavimi et al., 2012). Our findings regarding the *in vivo* hypouricemic actions of *J. phoenicea* indicate that, besides anti-

inflammatory agents, xanthine-dehydrogenase and xanthine-oxidase inhibitors can be a viable natural drug included in a cocktail therapeutic approach. Although the mechanism of action of the hypouricemic effect of *Juniperus* extract is not fully understood, it has the potential to be a viable substitute for allopurinol, regarding the many reported side-effects of allopurinol.

Some species of *Juniperus* are reported to contain toxic substances or to provide toxic secondary metabolites when ingested. It has been reported that all parts of the plant contain poisonous taxine alkaloids, whose toxic effects are maintained during the year (Alden et al., 1977).

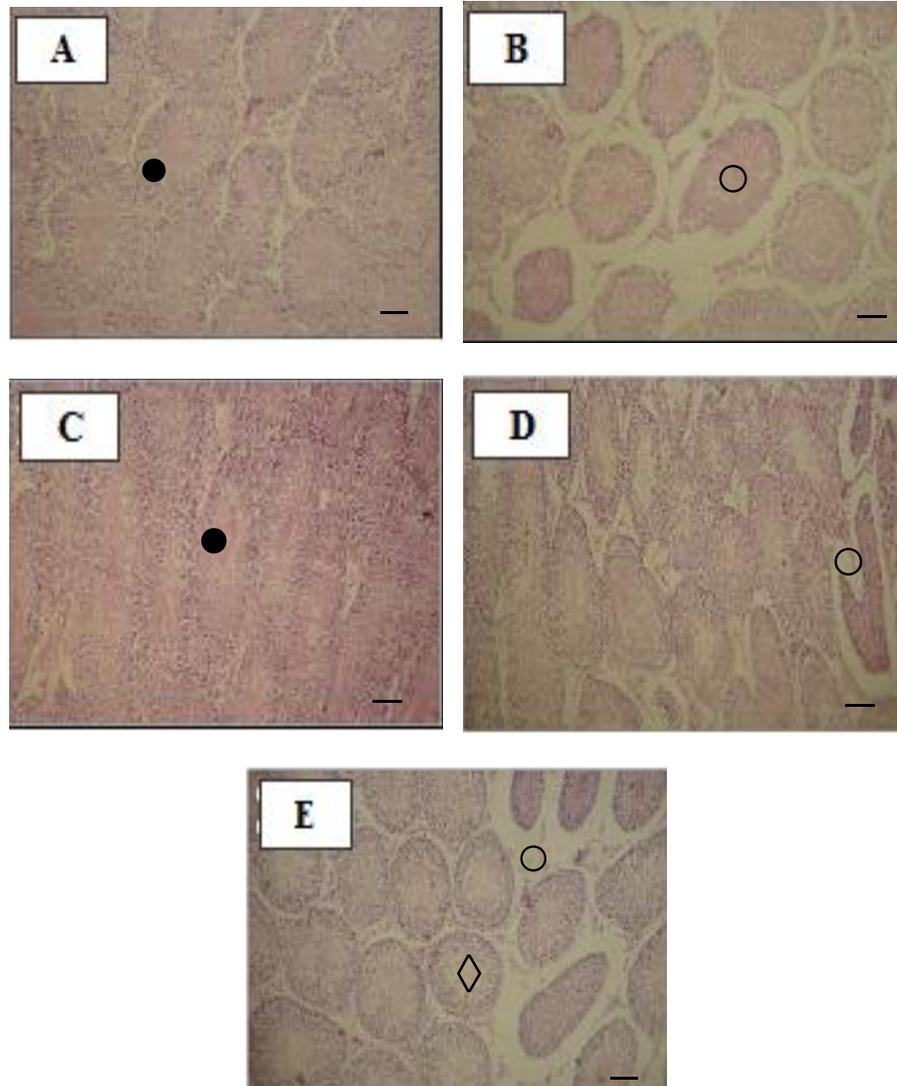


Figure 5. Microscopic observation of rat testis; (A) representative section of control group showing normal architecture of the seminiferous tubules; (B) section from the oxonate group showing deterioration of seminiferous tubules; germinal layers, basement membrane is absent and seminiferous tubule is infiltrated with the inflammatory cells; (C) section from the allopurinol (10 mg/kg bw) group showing the near normal structure of seminiferous cells; basement membrane and germinal layers are well developed; (D and E) section from the *Juniperus phoenicea* extract (100 or 200 mg/kg bw) group showing the architecture of seminiferous cells. Filled circle: Germ cells show normal maturation and spermatogenesis is normal, open circle: atrophy of seminiferous tubules, open diamond: anormal spermatogenesis. H&E stain ($\times 100$); scale bar, 50 μm .

However, previous investigations revealed that different parts of some species of *Juniperus* present cytotoxic effects on some human cancer cell lines (Jafarian et al., 2003). Therefore, an excessive or prolonged use of this plant should be avoided, even if its content in toxic principles is low. Our study demonstrated a potential and beneficial effect of *J. phoenicea* in attenuating oxidative stress and enhancing the body's own anti-oxidant defences in oxonate-treated rats. The increase in uric acid concentration in blood favouring role of in the development

of metabolic syndrome (Sanchez-Lozada et al., 2008), acting synergistically, are probably responsible for the strong damages appearing in the liver and genital tract. Our histopathological data substantiate liver dysfunction. There are inflammatory leucocytic infiltrations considered, according to Abdel-Rahman and Zaki (1992), as a prominent response of the body tissue facing injurious impacts. The intrahepatic blood vessels, central and portal veins are congested and their lining epithelia are eroded. Nevertheless, rats treated with oxonate developed

significant hepatic damage as compared to controls. An ameliorative effect was obtained in hyperuricemic rats by oral treatment with either *J. phoenicea* extract.

Conclusion

In conclusion, this study is the first to demonstrate that *J. phoenicea* (100 or 200 mg/kg bw) possess significant antioxidant and anti-uricemic activities in oxonate-treated rats. This corroborates the fact that there are many traditional uses of *Juniperus* extracts in folk medicine. Further studies on this species may yield fruitful results and isolation of some active constituents may lead to the provision of new drugs for treatment of hyperuricemia and gout.

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