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ORIGINAL ARTICLE

Protective effect of olive and juniper leaves extracts on nephrotoxicity induced by thioacetamide in male mice

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Abstract This study, for the first time, evaluates the effect of olive and juniper leaves extracts and their combination on thioacetamide (TAA)-induced nephrotoxicity in male mice. The experimental mice were divided into eight groups. Group 1 was served as control. Group 2 was exposed to TAA. Group 3 was treated with TAA and olive leaves extract. Group 4 was subjected to TAA and juniper leaves extract. Group 5 was exposed to TAA and olive and juniper leaves extracts. Groups 6, 7 and 8 were treated with olive, juniper, and olive and juniper leaves extracts respectively. In mice treated with only TAA, significant increases of blood urea nitrogen and uric acid were observed after six weeks. Moreover, levels of serum creatinine, blood urea nitrogen and uric acid were statistically increased in mice administrated with only TAA for twelve weeks. Insignificant alterations in levels of these haematobiochemical parameters were noted in other treated groups after six and twelve weeks. Histopathological evaluations of renal sections from mice treated with only TAA for twelve weeks showed severe damage of the renal corpuscles. Furthermore, the renal sections from mice treated with TAA and olive leaves extract, TAA and juniper leaves extract, TAA and olive and juniper leaves extracts, olive leaves extract, juniper leaves extract, and olive and juniper leaves extracts showed normal structures. In addition, it is conceivable therefore, that these extracts exhibit protective influences against TAA-induced nephrotoxicity, probably mediated through the antioxidative pathway roles.

1. Introduction

An exposure to environmental pollutants increased risks of kidney disease (Hendryx, 2009). Nephrotoxicity is one of the most common kidney problems and occurs when the body is exposed to a drug or toxin (Porter and Bennett, 1981). Toxic chemical-induced nephrotoxicity tends to be more common among certain patients and in specific clinical situations. Humans are exposed intentionally and unintentionally to a

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variety of diverse chemicals that harm the kidney. As drugs, natural products, industrial chemicals, and environmental pollutants that cause nephrotoxicity have increased (Prusty et al., 2012). Kidneys are highly vulnerable to damage caused by reactive oxygen species (ROSs), likely due to oxidative stress by polyunsaturated fatty acids in the composition of renal lipids (Ozbek, 2012). This damage can also be caused by a high volume of blood flowing through it, and filtering large amounts of toxins, which can concentrate in kidney lobules (Begum et al., 2011). The kidney's response to toxicants varies by multiple morphological patterns beginning with tubular or interstitial changes to nephropathy (Silva, 2004). Various useful drugs and some environmental and industrial toxicants can cause severe renal damage through activation of these drugs to highly reactive free radicals (Olagunju et al., 2009). Most drugs found to cause nephrotoxicity exert toxic effects by one or more common pathogenic mechanisms. These include altered intraglomerular hemodynamics, tubular cell toxicity, inflammation, crystal nephropathy, rhabdomyolysis, and thrombotic microangiopathy (Zager, 1997; Schetz et al., 2005). A number of physiologic factors have been implicated in the production of the nephrotoxic response caused by chemicals. Certainly it must be recognized that the large renal blood flow (25% of the cardiac output) is an important feature. Although we recognize that response is a function of concentration, it is nonetheless true that because of the high renal blood flow, the kidney is exposed to large quantities of whatever is in that blood, including nephrotoxicants. The ability of the kidney to concentrate the tubular fluid contents is a hallmark of renal function. Any nephrotoxic or potentially nephrotoxic compound present in the tubular fluid would be concentrated in a similar manner, which could contribute to direct damage to tubular epithelial cells or at least the creation of a concentration gradient that would facilitate the movement of the compound or compounds from the tubular fluid to the blood (Berndt, 1998).

Thioacetamide (TAA) is a potent experimental hepatotoxin and hepato-carcinogenic compound; therefore, it is used often to induce fulminant hepatic failure in experimental animal models (Sarkar and Sil, 2007). Additionally, the influences of TAA are not limited to the liver as profound structural and functional changes have been described in the kidney, spleen, lung, intestine, stomach and brain (Al-Bader et al., 2000; Liu et al., 2000; Caballero et al., 2001; Avraham et al., 2009; Latha et al., 2003; Kadir et al., 2013; Gao et al., 2014). Moreover, the toxic influences of TAA depend on several factors such as its concentration, number of doses, administration period, administration methods, animal's gender, strain, age, weight and physiological case.

Medicinal plants play an important role in pharmacology and medicine for many years. Today, it is estimated that about 80% of the world population relies on botanical preparations as medicine to meet their health needs (Ogbera et al., 2010). Apart from currently available therapeutic options, many herbal medicines have been recommended for the treatment of many diseases. Medicinal plants and herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost (Venkatesh et al., 2003; Tohidi et al., 2011). Therefore investigation on some active principles from traditional medicinal plants has become more important (Suba et al., 2004). Furthermore, in different countries many herbs are used in folk medicine to treat drug or toxin induced renal damage (Palani et al., 2009). The olive tree and in particular its leaves have been used for the treatment of wounds, fever, diabetes, gout, atherosclerosis and hypertension since ancient times (Jänicke et al., 2003). Olive leaves are considered a cheap raw material and a useful source of high-added value products (Briante et al., 2002; Jemai et al., 2008). Different studies have shown that olive leaves extracts and their constituents possess a wide range of pharmacologic and health promoting properties including antiarrhythmic, spasmolytic, immune-stimulant, and liver, kidney and heart protective effects. Moreover, antiatherosclerotic, hypotensive, anti-inflammatory, antioxidant, anti-thrombic and hypoglycemic effects were reported (Visioli et al., 1998; Andrikopoulos et al., 2002; Wang et al., 2008; Wainstein et al., 2012; Kumral et al., 2015). The natural forests of Saudi Arabia spread along the Western mountainous area from North to South. Juniper trees represent more than 90% of these forests (Abo-Hassan et al., 1984). Juniperus is a unique genus from the family Cupressaceae. The genus *Juniperus* consists of approximately 68 species (Seca and Silva, 2006; Adams, 2011). In traditional medicine, *Juniperus* species are used as remedies against the common cold, urinary infections, urticaria, dysentery, hemorrhage, and rheumatic arthritis and to relieve menstrual pain worldwide (Seca and Silva, 2006). Therefore, the objective of the present study was to evaluate the possible protective influences of olive (*Olea oleaster*) and juniper (*Juniperus procera*) leaves extract against TAA-induced nephrotoxicity in male mice.

2. Materials and methods

2.1. Animals

A total of one hundred sixty male albino mice of the SWR strain, weighing 15.0–25.0 g were taken for the present study. The principles of laboratory animal care were followed throughout the duration of experiment and instruction given by King Abdulaziz University ethics committee was followed regarding experimental treatments. The mice were distributed into eight groups (twenty mice per group) and were housed in standard cages at an ambient temperature of 20 ± 1 °C with 12-h light:12-h dark cycle and humidity of 65%. The mice were fed *ad libitum* on normal commercial chow and had free access to water.

2.2. Preparation of olive and juniper leaves extract

The fresh leaves of olive and juniper were directly collected from the outskirts of the Albaha region of Saudi Arabia. The collected leaves were completely washed, air dried at room temperature and stored in a dry plastic container until use for extraction processes. The extract of these leaves was prepared according to the method of Al-Attar and Abu Zeid (2013). The dried leaves of olive (50 g) were powdered, added to 2 liters of cold water and mixed using an electric mixer for 20 min. Furthermore, the dried leaves of juniper (50 g) were powdered, added to 2 liters of cold water and mixed using an electric mixer for 20 min. Thereafter, the solutions of olive and juniper leaves were gently filtered. Finally, the filtrates were evaporated in an oven at 40 °C to produce dried residues (active principles). With references to the powdered samples, the yield means of olive and juniper extracts were 19.3% and 17.8% respectively.