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ORIGINAL ARTICLE

Protective effects of fennel oil extract against sodium valproate-induced hepatorenal damage in albino rats

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Abstract *Foeniculum vulgare* (Apiaceae) is commonly known as fennel. This herb is well-known worldwide and traditionally used as curative herbal therapy for the treatment of epileptic disease, seizurescarminative, digestive, lactogogue, diuretic, treating respiratory and gastrointestinal disorders. The aim of present study is to investigate the possible effect of fennel oil against the toxicity of Sodium-Valproic (SVP) in albino rats. In order to assess the protection of fennel oil on SVP induced hepato- and nephro-toxicity, male albino rats were treated with 1 ml/kg b.w fennel oil 3 days/week for 6 weeks. The biochemical analyses of hepatic enzymes were evaluated by estimating blood biomarkers of liver and renal damage along with histological examination. The results obtained from this work showed that treating animals with SVP lead to many histopathological alterations in the liver and kidney tissues. The effect appeared in the liver tissue include leukocyte infiltrations, cytoplasmic vacuolization of the hepatocytes, fatty degeneration and congestion of blood vessels. This commonly used chemical (SVP) caused some unwanted effects on the kidney cortex which histologically observed as degeneration in renal tubules, atrophy of the glomeruli and edema. Biochemical results also revealed an abnormal increase in the enzyme level of AST, SAT, ALP, bilirubin, creatinine and urea-nitrogen, with a noticed decrease in total protein content. However, the results of treated rats with SVP plus fennel oil showed some positive histopathological changes in both the liver and kidney tissues. These results have confirmed that fennel oil has positive effects on the histological structure of the liver and kidney and the biochemical levels of AST, ALT, ALP, bilirubin, total proteins, creatinine and urea. It is concluded that fennel oil has various pharmacological properties including antioxidant, anti-cancer activity, anti-inflammatory. These valu-

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able effects might be due to the presence of aromatic compounds *trans*-anethole. This useful properties of fennel plant could be due to its antioxidant activity that prevents the toxicity of SVP.

1. Introduction

It is generally believed that prevention is better than treatment. Fennel plants (*Foeniculum vulgare*) have been widely used as a source of folk medicine since immortal time. Fennel is a medicinal plant belongs to the family Apiaceae (*Umbelliferae*) (Rather et al., 2012). This herb is traditionally used as treatment for colic, wind, irritable bowel, kidneys, spleen, liver, lungs, suppressing appetite, breast enlargement, promoting menstruation, improving digestive system, milk flow and increasing urine flow (Delaram et al., 2011).

This medicinal plant may be beneficial to humans as they have several phytoconstituents to cure diseases (Kooti et al., 2014). Essential oil of this herbal plant was found to have different medicinal and antioxidant properties against some diseases (Wesam et al., 2015; Mirabolghasemi and Alizadeh, 2014). It has been shown that the fennel oil with hexane extract of florence and antehole components illuminate the effect of probiotic bacteria and used as antimicrobial agent against other species (Ostad et al., 2001). Pai et al. (2010) has also reported that oil extracted from fennel plant has effect against Candida albicans and some other bacterial infections. Different pharmacological experiments in a number of *in vitro* and *in vivo* models have convincingly demonstrated the ability of Fennel to exhibit antifungal, antibacterial and as antioxidant agent. In addition, It has been suggested that fennel essential oil could inhibit contraction of an isolated uterus that was induced by oxytocin and prostaglandin E_2 (Ostad et al., 2001).

Trans-Anethole, [1-methoxy-4-(1-propenyl) benzene], is a chief constituent of fennel plant, anise, clove, cinnamon, thyme and camphor. Anethole containing oils are widely used in the food and liquor industries (Castro et al., 2010). It has been suggested that the antehole may play a major role in blocking both inflammation and carcinogenesis (Bharat et al., 2008). This compound and related ones have been reported to strike metabolic effects (Singh and Kale, 2008). Stohs et al. (1986) and Mohamad et al. (2011) have demonstrated that fennel oil acts like antioxidants due to its ability to inhibit lipid peroxidation. Moreover, it has been revealed that oil extracted from this fennel herb has a protective affect against the toxicity induced by carbon tetrachloride in rat liver (Ozbek et al., 2003). In other study, it has been reported that fennel extract caused a significant improvement against hepatic fibrosis patients with fibrosis, liver tissue inflammation and excessive fat degradation (Wang et al., 2012). Although, this medicinal herb has few side effects than synthetic drugs, it is still widely and medicinally used due to its antioxidant properties (Asadi-Samani et al., 2013). Also, it has been illustrated that the components of the fennel plant have a positive effects to reduce drugs toxicity in some biological system (Asadi-Samani et al., 2013; Kooti et al., 2014).

Valproic acid (VPA) is a medicine widely prescribed as an anticonvulsant and mood stabilizer. It has been commonly used in the treatment of epilepsy and bipolar disorder (Henry, 2003 and Johannessen, 2000). VPA has been prescribed as anti-epileptic drugs (AEDs) over the past 40 years (Chang et al., 2016). It has been reported by Jessberger et al. (2007) that SVP treatment could cause a neuronal abnormality and contributes to the aberrant neurogenesis associated with epileptic activity in adult rodents. In other study, a wide range of side effects have been reported in patients exposed to SVP treatment such as; gastrointestinal disturbances, tremor and weight gain (Brandt et al., 2006).

Sodium valproate (SVP) has been associated with a number of serious unwanted effects affecting the blood, pancreas, liver and kidney (Chang et al., 2016). Ornoy (2006) has revealed that SVP is a teratogen agent causing an induction of neural tube defects, heart abnormalities, craniosynostosis, and cause abnormalities to the skeletal malformations, such as ectrodactyly and syndactyly. Moreover, rare serious complications may occur in some patients receiving SVP chronically, including fatal haemorrhagic, pancreatitis, bone marrow suppression and *Hyperammonemic encephalopathy* (Sztajnkrycer, 2002). Also, it has been documented that patients undergoing VPA therapy for a period of time often show changes and instability in mood reaction, cognition and behavior (Senturk et al., 2007). Nadebaum et al. (2011) has reported that VPA can noticeably develop cognitive dysfunction in epileptic patients. Furthermore, VPA could alter hepatic triacylglycerol (TAG) and cholesterol biosynthesis, fatty acid catabolism, and lipid transport-related gene expression patterns (Lee et al., 2007). Stephens and Levy (1992) have reported that SVP may cause liver damage and led to pancreatitis, which occasionally progress to bleeding and death. It has been also suggested that liver dysfunction is one of the common negative side effect of SVP treatment. Morán-Salvador et al. (2011) has demonstrated that liver biopsy revealed portal inflammation, severe bile duct loss, and cholestasis as result of SVP effect. Clinical record have reported that more than 40% of patients who received VPA also developed unexpected obesity and fatty liver disease (Saleh et al., 2012). However, how VPA affects hepatic lipid metabolism to induce fatty liver remains unclear.

Coyle et al. (2005) has reported that in three cases, the valproic acid was found to be associated with leukemia. Moreover, Janneke et al. (2010) has also demonstrated that there was a significant association between exposure of the unborn child to valproic acid monotherapy and Spina bifida, arterial septa defects, cleft palate, hypospadias, polydactyl and craniosynostosis. In addition, VPA was also documented to be a major cause leading to degenerative changes in kidney of pregnant rats (Aktas et al., 2010). Gokee et al. (2010) has noticed that valproic acid-associated vanishing bile duct syndrome in an 8-year old girl treated with valproic acid. These results have of the above mentioned authors stimulated us to study the possible preventive effect of According to these scientific knowledge found and reported about the fennel plant and its effective components, The aim of this study was to investigate the positive antioxidant properties of fennel oil against valporic acid (SVP) exposed to liver and kidney organs