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Studies of *Salvia officinalis* leaf extract on some biochemical parameters in rats induced with overdosed-tramadol

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The aim of the study was to evaluate the effect of *Salvia officinalis* leaf extract in overdosed-tramadol induced rats. Standard methods of analysis were used for the study. Fifty rats were divided into Group A (Control) - feed and water only, Group B-induced with tramadol at 50 mg/kg body weight, Group C-induced with tramadol + 150 mg/kg of *S. officinalis* leaf extract, Group D-tramadol + 300 mg/kg *S. officinalis* leaf extract, and Group E-tramadol + 400 mg/kg *S. officinalis* leaf extract. The results showed high concentrations of phytochemical and trace elements at various concentrations. There were increases in aspartate amino transaminase, alanine aminotransferase, gamma gluamyltransferase, alkaline phosphatase and in total protein, albumin, total bilirubin, conjugated bilirubin, sodium, potassium, chloride, bicarbonate, urea, calcium, creatinine, total cholesterol, magnesium, hemoglobin, packed cell volume, and total white blood cell count at a significant difference ($p < 0.05$) in Group B when compared with Group A. However, in Groups C, D and E, there was statistically significant decrease ($p < 0.05$) in aspartate amino transaminase, alanine aminotransferase, gamma gluamyltransferase, alkaline phosphatase and total protein, albumin, total bilirubin, conjugated bilirubin, sodium, potassium, chloride, bicarbonate, urea, calcium, creatinine, total cholesterol and magnesium compared with the Group B. The study showed that *S. officinalis* leaf could be of an unalloyed health benefits in the management of tramadol-induced toxicity in rats.

Key words: Tramadol, *Sage*, phytochemicals/elements, markers, rats.

INTRODUCTION

Tramadol (TD) is a synthetic opioid analgesic agent, used parenterally and orally for the treatment of moderate to severe pain in humans (Miotto et al., 2017; Mohamed and Mahmoud, 2019). Tramadol is an ideal analgesic during and after day case surgery and in patients with acute ureteric spasm (Elkhateeb et al., 2015). Tramadol is responsible for life-threatening poisonings, resulting in consciousness impairment, seizures, agitation and respiratory depression (Hassanian-Moghaddam et al., 2013; Owoade et al., 2019). Scientists recommended that tramadol toxic effects should be kept in mind during long term therapy especially in large doses (DePries et al.,

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2015). There are about 35 million users of opioids globally and such opioids like tramadol are known to cause the greatest negative health impart (UNODC, 2017). Previous study observed that overdosed tramadol in man induces hypokalaemia, diarrhea, certain nervous disorder and maintenance of neuro-muscular irritability (Carroll et al., 2006).

Common sage (*Salvia officinalis*) plant, a perennial, evergreen subshrub, native to the Mediterranean region is one of the most commercially important species within the Lamiaceae family (Avato et al., 2005; Ghorbani and Esmaeilizadeh, 2017; Devin et al., 2021). It is found and cultivated world over (Raal et al., 2007; Ghorbani and Esmaeilizadeh, 2017). And it thrives well in Nigeria particularly within the semi urban areas of Vom-Jos, Plateau State (Figure 1). It has become a target for the search of the biologically active compounds and new drugs as it shows a broad range of medical activities (Padhye et al., 2008; Bommer et al., 2011; Keshavarz et al., 2011; Khalil and Li, 2011; Khan et al., 2011; Hamidpour et al., 2014). *S. officinalis* has enjoyed a reputation in Asia and Latin America for traditional medicine for treating all kinds of ailments (Garsia et al., 2016). Presently, the essential oils of it is known to have biological and antioxidant properties (Stagos et al., 2012; Kontogianni et al., 2013; Garsia et al., 2016; Alimpi et al., 2017). It also has anti-inflammatory and cytogenetic effects (Al-Barazanjy et al., 2012; Rodrigues et al., 2012; Alimpic et al., 2015). As tramadol is metabolized mainly in the liver, some researchers (Watson et al., 2004; Jensen-Ortho et al., 2005; Raffa et al., 2008) stated that its long-term therapy particularly in overdose is associated with hepatotoxicity with its corresponding kidneys toxicity especially as tramadol and its metabolites are released via the kidneys.

MATERIALS AND METHODS

Collection of plant and preparation of extract

Fresh samples of sage (*S. officinalis*) were obtained from farmlands in Vom-Jos, Plateau State, Nigeria. The plant was identified, authenticated, and a voucher number (20/21/00121) was given it and stored for future reference (Figure 1). The leaves were removed from the stalk and air dried in the laboratory for 21 days. The dried plant-leaves samples were well ground and sieved into a fine powder from which an extract was made for the experiment. 30 g of the ground leaves was kept in an air-tight container for phytochemical and analytical studies while another 50 g was weighed and added to 400 ml of absolute methanol for 3 days. The mixture was then filtered using muslin cloth and later concentrated using Soxhlet apparatus. Then the extract obtained were kept in airtight sample bottles, labeled and stored in the refrigerator for animal experiments.

Phytochemical analysis

Quantitative phytochemical analysis

Tests for tannins, terpenoids, cardiac glycosides, flavonoids, alkaloids, phenolics, and saponins were carried out using standard methods (Marcono and Hasenaira, 1991).

Test for Tannins

One gram of sample was extracted with 25 ml 80:20 acetone: 10% glacial acetic acid for 4 h. It was then filtered and measured at 500 nm absorbance. The absorbance of the reagent blank was also measured. A standard graph with 10, 20, 30, 40, and 50 mg/100 g of tannic acid was made (Marcono and Hasenaira, 1991).

The concentration of tannins was read taking into consideration the dilution factor.

Test for terpenoids

One gram of sample was weighed into 250 ml beaker and 10 ml petroleum ether was added. It was allowed to extract for 15 min and filtered. The absorbance was then read at 420 nm (Marcono and Hasenaira, 1991).

Test for cardiac glycosides

One gram of sample with 40 ml of water was extracted and placed in an oven at 100°C for 15 min. Then, to 1 ml of the extract dissolved in 5 ml of water was added 2 ml of glacial acetic acid followed by one drop of iron chloride ($FeCl_3$) and 1 ml of H_2SO_4. The absorbance was then measured at 410 nm (Marcono and Hasenaira, 1991).

Tests or flavonoids

One gram of the sample was extracted with 10 ml of 80% methanol and left to stand for 2 h. It was filtered through Whatman filter paper into a Petri-dish, evaporated to dryness in an oven at 40°C and weighed (Marcono and Hasenaira, 1991).

Test for alkaloids

One gram of each sample (W) was extracted with 20 ml of 10% acetic acid in ethanol, mixed and allowed to stand for 4 h. The extract was filtered through Whatman filter paper. The filtrate was evaporated to about a quarter of its original volume and one drop of concentrated ammonia was added. The extract was filtered through weighed (W1) Whatman filter paper.

The filter paper was dried in the oven at 60°C. The dried filter paper was weighed to a constant weight (W_2) (Marcono and Hasenaira, 1991).

$$\% \text{ Alkaloids} = (W_2 - W_1)/W \times 100/1$$

Test for phenolics

Two grams of each sample were extracted with 20 ml of acetone, 0.5% formic acid for 2 min and was filtered. 2 ml of the extract was mixed with 0.5 ml Folin-Ciocalteau reagent, mixed for 15 s and allowed to stand at 40°C for 30min to develop a colour. The absorbance was measured at 765 nm and expressed as mg/g Gallic Acid Equivalent (GAE) (Marcono and Hasenaira, 1991).

Test for Saponnins

One gram of each sample was dispersed in 15 ml of 20%

Figure 1. *S. officinalis* leaves.
Source: Photograph of *Salvia officinalis* leaves taken before drying the leaves

ethanol. The suspension was put inside the water bath at 55°C for 4 h. The mixture was filtered and the residue re-extracted with another 15 ml of 20% ethanol twice. The extract was reduced to about 5 ml in the oven. The concentrate was transferred into a 250 ml separating funnel and 5 ml of petroleum ether was added and mixed vigorously. The petroleum ether layer was discarded and 3 ml of butanol was added to the aqueous layer. The extract was washed twice with 5 ml of 5% sodium chloride. The remaining solution was poured into a weighed Petri-dish, evaporated to dryness in the oven and the residue weighed (Marcono and Hasenaira, 1991).

Analysis of elements

The major trace elements comprising iron, manganese, copper, fluorine, chromium, iodine, selenium, molybdenum, cobalt and zinc were determined according to the method of Shahidi et al. (1999). The ground samples were sieved with a 2 mm rubber sieve and 2 g of each of the samples subjected to dry ash in a well cleaned porcelain crucible at 55°C in a muffle furnace. The resultant ash was dissolved in 5 ml of HNO_3/H_2O_2 (1:1) and heated gently on hot plate until brown fumes disappeared. To the remaining material in the crucible, 5 ml of deionized water was added and heated until a colourless solution was obtained. The mineral solution in each crucible was transferred into a 100 ml volumetric flask by filtration through a Whatman filter paper and the volume made to mark with de-ionized water. This solution was used for elemental analysis by atomic absorption spectrophotometer (AAS) and the concentration of each element was calculated on percentage of dry matter.

Experimental animals

A total of 50 Wistar albino rats of either sex weighing between 150 and 250 g were used for the study. The animals were fed with standard growers' marsh diet and water *ad libitum*, in a standard wire meshed plastic cages for 14 days prior to commencement of the experiment. The animals were handled according to the guidelines of Institutional Animal Ethics Committee (IAEC) (Rowlands, 2013). The protocol was approved by Faculty of Science Research Ethics Committee, Delta State University.

Tramadol-induced toxicity

Wistar albino rats were divided into five groups comprising ten animals in each group: Group A: control was fed with feed and water daily, Group B: Tramadol (50 mg/kg bwt) with feed and water, Group C: Tramadol + 150 mg/kg of sage plant with feed and water, Group D: Tramadol + 300 mg/kg of sage plant with feed and water, Group E: Tramadol + 450 mg/kg of sage plant with feed and water.

Tramadol hydrochloride, bought from a registered pharmaceutical store, made into saline solution was given to the animal through oral route using oral gauge for 14 days after acclimatization (Rowlands, 2013).

Sample collection

At the end of the treatment period the animals were sacrificed 48 h following the last given dose. And at the time of sacrifice, their weights were taken and then cervical decapitation was conducted before laparotomy section was carried out. Blood samples were collected from vena cava and heart into EDTA bottles for full blood count and plane tubes for clotted samples for biochemical analysis. Each plane tube was properly labeled, centrifuged at 4000 rpm for 10 min for serum separated and stored at −8°C pending biochemical analysis using spectrophotometric methods with reagents. The liver, brain, kidney and heart were taken for observations.

Determination of body weight

Body weight of experimental animals was determined at day 0 (before administration) and subsequent days and on the last day of experiment. Dose of Silymarin and extract was given to each rat according to their body weight, respectively (Lipscombe et al., 2021). Percentage weight gain was later calculated as follow:

$$Percentage\ weight\ gain\ (\%) = \frac{Final - Initial\ body\ weight\ (g)}{Initial\ body\ weight\ (g)} \times 100$$

Biochemical assays

The serum of each rat was analyzed for the following biochemical

Table 1. The mean Phytochemicals concentration in mg/100g of *Sage officinalis* leaf extract.

Phytochemical	Tannins (mg/100 g)	Terpenoids (mg/100 g)	Cardiac Glycosides (mg/100 g)	Flavonoids (mg/100 g)	Alkaloids (mg/100 g)	Phenolics (GAE/g)	Saponins (mg/100 g)
Mean value	518.21	321.00	145.00	4288.00	3863.00	60.81	2450.00

Source: Author

Table 2. The mean values of elemental concentration (mg/100g) of *S. officinalis* leaf.

Fe^{++}	Mn^{++}	Cu^{++}	F^{-}	Cl^{-}	I^{-}	Se^{++}	Mo^{++}	Co^{++}	Zn^{++}
9.77	0.05	0.71	0.02	56.45	0.42	0.04	0.04	0.03	0.52

Source: Author

parameters (assays): AST (E.C. 2.6.1.1) and ALT (E.C. 2.6.1.2) were determined by Reitman and Frankel (1957), GGT{E.C. 2.3.2.2} was determined by Gjerde and Marland (1985), ALP (E.C. 31.3.1) by Kind and King (1954), TP and ALB by Reinhold (1953), TB and CB by method of Malloy and Evelyn (1937), UR by March et al. (1965), CR by Reinhold (1953), TCHOL by Robinson & Pugh (1958), sodium level by Buzanovskii (2018), potassium level by Wong et al. (1985), bicarbonate by Sobel and Eichen (1952), chloride by Henry (1964), while HB, PCV and TWBC were determined by the method as documented by Dacie and Lewis (2001).

Statistical analysis

All the data obtained were expressed as mean ± standard error of mean (SEM) and was subjected to ANOVA analysis using Dunnett's *t*-test. A p-value of less than 0.05 was considered significant.

RESULTS

The results in (Table) 1 show the concentrations of phytochemicals in common sage plant leaf with flavonoids having the highest concentration of 4288 mg/100 g, followed by alkaloids 3863 mg/100 g, saponins 2450 mg/100 g, tanins 518.21 mg/100 g, terpenoids 321.00 mg/100 g, cardiac glycosides 145 mg/100 g and phenolics 60.81 GAE/g. (Table) 2 shows the elemental composition of *S. officinalis* leaf with Cl^{-} having the highest concentration of 56.45 mg/g, followed by Fe^{2+} 9.77 mg/g, Cu^{2+} 0.71 mg/g, Zn^{2+} 0.52 mg/g, I^{-} 0.42 mg/g, Mn^{2+} 0.05 mg/g, Se 0.04 mg/g, Co^{2+} 0.03 mg/g, Mo^{2+} 0.04 mg/g and F 0.02 mg/g in that order.

The results in (Table) 3 show the mean concentration of body weights of the experimental rats before and after induction with tramadol and tramadol plus *S. officinalis* leaf extract at various concentrations. The group A-103.63 ± 16.25^{b} shows significant increase in the body weight ($p< 0.05$) when compared with group B (Tramadol) induced rats-97.93 ± 4.65^{b}. The group A control (103.63 ± 16.25^{b}) also shows significant decrease ($p< 0.05$) across the Groups C (115.43 ± 12.47^{b}) and Group D (117.43 ± 13.28^{b}) rats while the Group A (103.63 ± 16.25^{b}) is not significantly different ($p > 0.05$) when compared with Group E (104.83 ± 17.18^{a}). However, there are statistical differences ($p< 0.05$) in the body weight before and after tramadol induction plus *S. officinalis* extract in addition at different levels in comparison with the group B and this is particularly visible at the tramadol plus 300 ml *S. officinalis* leaf extract addition.

Table 4 shows the effect of *S. officinalis* leaf extract on various biochemical parameters on tramadol induced rats. From the table, there are statistical significant increases in activity/increase ($p < 0.05$) in the liver function tests parameters: AST, ALT, Alk. Phis, GGT, TP, ALB, TB, and CB in group B compared with normal control group. There was also significant increase ($p < 0.05$) in Serum Electrolytes levels: Na^{2+}, k^{2+}, Cl, HCO_3^{-} in group B compared with the group A. Equally, statistical comparison between group A and group B with regards to the kidney function tests: Serum UR, Serum CR as well as Ca^{2+}, UA, TChol biochemical parameters levels revealed significant difference ($p < 0.05$). Also, the mean concentration of TWBC in rats induced with Tramadol showed significant difference ($p < 0.05$) compared with the group A rats. While the level of the biochemical parameters: HB and PCV in the group B showed significant decrease ($p < 0.05$) in comparison with the group A. Equally, there is no significant difference ($p > 0.05$) in the level of Mg^{2+} in the group A compared with group B. However, significant statistical reduction ($p < 0.05$) exist in the various biochemical parameters except in the levels of HB and PVC where there are significant increase ($p < 0.05$) analyzed in the groups with tramadol plus *S. officinalis* leaf extract at different levels of administration compared with the group B that was induced with tramadol alone.

DISCUSSION

Enormous interest abounds in the use of herbal remedies

Table 3. Effect of Sage plant leaf on body weight of Rats before and after induction of Tramadol.

Biochemical parameter	Group A Normal Feed & Water	Group B Tramadol	Group C Tramadol +150 mg Sage L	Group D Tramadol +300 mg Sage L	Group E Tramadol +450 mg Sage L
Before	94.00±5.45[a]	91.33±6.11[a]	95.67±20.50[a]	93.00±16.64[a]	93.33±4.16[a]
After	103.63±16.25[a]	97.93±4.65[b]	115.43±12.47[c]	117.43±13.28[c]	104.83±17.18[a]

Values are expressed in Mean ± S.E.M., n=10. Values sharing the same superscript in the row did not differ significantly ($p > 0.05$). Values sharing different superscript in the same column are statistically significant ($p < 0.05$).
Source: Author

Table 4. Effect of Sage plant leaf on the various biochemical parameters on Tramadol induced rats.

Biochemical parameter	Control Group A	Group B Tramadol induced	Group C Tramadol +150 mg Sage L	Group D Tramadol +300 mg Sage L	Group E Tramadol +450 mg Sage L
AST	12.50±2.28[a]	23.60±2.90[b]	13.15±2.18[a]	14.98±3.18[c]	15.67±2.19[c]
ALT	10.35±2.28[a]	18.56±3.10[b]	11.00±2.16[a]	13.10±2.16[c]	13.87±3.12[c]
GGT	29.01±2.18[a]	41.14±3.19[b]	31.28±2.19[a]	30.17±3.12[c]	30.10±3.18[c]
ALP	15.0±3.08[b]	48.0±5.34[a]	17.3±3.89[b]	22.3±1.10[c]	23.67±3.63[c]
TP	6.00±0.53[a]	4.33±0.12[b]	5.90±0.30[a]	7.57±0.40[c]	7.53±0.40[c]
ALB	3.37±0.39[a]	3.93±0.29[c]	3.23±0.11[b]	3.23±0.04[b]	3.2±0.14[b]
TB	0.28±0.01[b]	2.83±1.56[a]	0.26±0.01[b]	0.21±0.3[b]	0.20±0.05[b]
CB	0.52±0.29[b]	2.4±0.14[a]	0.76±0.01[b]	0.43±0.19[b]	0.29±0.00[b]
Na^{2+}	135.00±3.51[a]	145.00±0.500[b]	131.67±2.89[a]	140.67±1.15[a]	146.67±7.64[a]
K^{2+}	3.30±0.61[a]	3.70±0.40[a]	3.77±3.38[a]	3.93±±0.53[a]	3.63±0.25[a]
Cl^{-}	105.00±2.18[a]	132.45±3.12[b]	108.06±2.18[a]	120.95±3.14[c]	119.81±3.21[c]
HCO_3	26.67±3.51[a]	26.00±3.00[a]	25.67±1.15[a]	26.00±1.00[a]	25.00±3.61[a]
UR	30.00±10.00[a]	58.57±3.21[b]	25.43±2.18[c]	27.70±1.18[c]	29.85±3.71[a]
Ca^{2+}	7.67±0.40[a]	9.27±1.66[b]	8.27±1.69[b]	7.73±0.32[a]	10.30±1.17[c]
UA	7.00±0.00	12.70±2.61b	4.43±0.86a	4.90±1.10a	4.90±2.78a
TChol	4.44±0.38[a]	8.34±0.36[b]	4.87±2.14[a]	5.90±3.18[c]	5.91±3.18[c]
Mg^{2+}	1.88±0.06[a]	1.95±0.14[a]	1.85±0.40[a]	2.04±0.10[b]	2.01±0.08[b]
HB	13.86±0.89[a]	8.34±0.36[b]	14.47±0.19[a]	14.14±0.18[a]	13.90±0.38[a]
PCV	0.46±0.01[a]	0.31±0.01[b]	0.47±0.19[a]	0.45±0.01[a]	0.45±0.18[a]
TWBC	8.52±0.41[a]	16.62±0.75[b]	8.98±0.58[c]	8.75±0.61[b]	8.65±0.31[b]

AST = Aspartate amino transaminase, ALT = Alanine aminotransferase, GGT= Gamma gluamyltransferase, ALP = Alkaline phosphatase, TP = Total protein, ALB = Albumin, TB = Total bilirubin, CB = Conjugated bilirubin, Na^{2+} = Sodium, K^{2+} = Potassium, CL^{-} = Chloride, HCO_3 =Bicarbonate, UR = Urea, Ca^{2+}= Calcium, CR =Creatinine, TCHOL = Total cholesterol, Mg^{2+}= Magnesium, HB = Hemoglobin, PCV = Packed cell volume, TWBC = Total white blood cell count.
Source: Author

for the treatment of various diseases in humans worldwide. In this study, the phytochemicals found are similar to the observation of Khiya et al. (2019) who detected polyphenols, gallic tannins, flavonoids, saponins and terpenoids at various levels in the leaves of Moroccan *S. officinalis.* Also, the finding of phenols in the present work is in agreement with the work of Abdulkader et al. (2014) and that of Sarhan et al. (2013) who both documented that *S. officinalis* is rich in polyphenolic compounds. Our findings are in line with the work and observation of El-Feky and Aboulthana (2016) that the biologically active phenolic constituent characterized by aromatic ring with hydroxyl group, is responsible for the various medicinal properties of *S. officinalis*. Equally, the findings are similar to the observation of Khiya et al. (2019) and Kadhim et al. (2016) that *S. officinalis* leaf contains phytochemicals at various levels which confer antioxidant activity to it. From our findings, the mean concentrations of phytochemicals in mg/100 g obtained are far higher than the values reported in *Vernonia amygdaline* leaf (Mokogwu et al., 2014). Also, the mean concentration of the elements in mg/100 g obtained are higher than the values reported in *Vernonia amygdalina* leaf extract (Mokogwu et al., 2014) though from an entirely different species and family. Equally, the detection of phytochemicals: flavonoids, alkaloids, saponins,

phynolic acids, etc., is in line with other works (Dogan, 2004; Slamenova, 2004; Lima et al., 2005; Baranauskiene et al., 2011) that reported that the leaves, roots and water soluble extractions of *S. offisinalis* contain volatile fatty acids, saponins, diterpenes, flavonoids, ohenolic acids, salviatamins, resin and oestrogenic substances.

Trace elements are inorganic substances that act as co-factors and are required in the body in minute amount (Darwish, 2014). The values of trace elements found in our work are similar to the observations of Darwish (2014) and Abu-Darwish et al. (2010) who noted high contents of trace elements: Cu^{2+}, $^{Fe2+}$, Mn^{2+}, and Zn^{2+} at various concentrations in different areas of Jordan. The findings of the current study are also in agreement with earlier work that reported tangible quantities of trace elements in ginger and *Sage* plants in Algeria (Lamari et al., 2011). The level of Zn^{2+} observed by us is equally in line with that of Stef et al. (2010) who noted very high level of Zn^{2+} in Romania.

In this study, the increase in the body weight of rats after tramadol induction in the presence of *S. officinalis* leaf extract does not agree with the work of Ninomiya et al. (2004) that reported reduction of body weight and accumulation of epididymal fat weight in high-fat diet fed mice after 14 days.

Functions of the liver and the kidneys are impaired in overdosed tramadol metabolism and excretion (Matthiesen et al., 1998). In this study, there is toxicity of the liver in the group B which is a reflection as shown in the increased activity of the aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT), alkaline phosphatase (ALP) and increase in the levels of total proteins (TP), albumin (ALB), total bilirubin (TB), and conjugated bilirubin (CB). This is similar to the results obtained by other workers (Wu et al., 2002; Atici et al., 2005; Jensen-Ortho, 2005) who reported statistical increase in the activities of AST, ALT and lactose dehydrogenase (LDH) in rats after induction with tramadol. Some researchers stated that AST though a mitochondrial enzyme, its increased serum activity is not specific of hepatic disorder but rather denote persistent cellular injury with other enzyme like ALT (Vazarova et al, 2002). Other works noted that serum ALT, as a cytoplasmic enzyme is relatively specific of hepatic disorder and connotes early hepatotoxicity (Moss and Henderson, 1999). However, GGT is highly specific of hepatotoxicity. Also, sosme researchers opined that the increase activity of these hepatic enzymes could be secondary events following tramadol-induced lipid peroxidation of hepatocytes with the subsequent increase in the leakage of these biochemical markers from the liver (Nehu and Anand, 2005). Equally, the impairment of the kidney functions in the group B as indicated by increased in serum urea, creatinine and variations in the electrolytes levels compared to the group A levels portrays kidney toxicity. This result is in tandem with the reports of other studies (Atici et al., 2005; El-Gaafarawi, 2006). A study suggested that renal insufficiency associated with tramadol may be due to the decreased glomerular filtration rate or secondary to the increase in reactive oxygen species (Noori and Mahboobe, 2010).

In this study, the fact that the administration of *S. officinalis* leaf extract along with tramadol-induced toxicity in rats led to increased HB and PCV levels, is an indication that *S. officinalis* leaf extract could poses immunogenic properties. In the same vain its reduction in total cholesterol level also shows that the extract might have anti-hypertensive properties.

Conclusion

The study shows that the administration of *S. officinalis* leaf extract at proper concentration during tramadol-induced toxicity would be of good benefit to the subjects. Also, the fairly high concentration of phytochemicals along with the valuable trace elements observed in this study portends *S. officinalis* leaf as an unalloyed health benefits in the management of liver and kidney related disorders in humans.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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