Protective efficiency of parsley (Petroselinum crispum) against oxidative stress, DNA damage and nephrotoxicity induced with anti-tuberculosis drugs

Mahmoud Ashry, Ismail Atia, Fatma A. Morsy and Weal Elmashad
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It is with great pleasure that I write this editorial to welcome you to the IJCBR. This journal provides a platform for publication of original and reviews research articles, short communications, letter to editor, thesis abstract, conference report, and case studies. These types of publication are directed at the interface of the fields of cancer and biomedical research.

The IJCBR relies on a distinguished expert of the Advisory and Editorial Board Members from the top international league covering in depth the related topics. They timely review all manuscripts and maintain highest standards of quality and scientific methodology and ethical concepts. Meanwhile, we take all possible means to keep the time of the publication process as short as possible.

I take this chance to welcome your contributions to the IJCBR and have every expectation that it will soon become one of the most respected journals in both the fields of cancer and biomedical research.

Mohamed L. Salem,
Editor in Chief
Protective efficiency of parsley (Petroselinum crispum) against oxidative stress, DNA damage and nephrotoxicity induced with anti-tuberculosis drugs

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ABSTRACT

Background: Tuberculosis has been seen worldwide as a serious disease, one of the most adverse side effects of main anti-tuberculosis drugs is nephrotoxicity. Aim: the purpose of this research was planned To investigate the nephroprotective ability of aqueous parsley extract against Isoniazid® and Rifampicin®-induced nephrotoxicity. Materials and Methods: Adult male Wistar albino rats weighted (140-160) and they were divided randomly into four groups: 1) normal rats as a control group, 2) rats administrated with parsley extract (250 mg/kg/day), 3) rats received Isoniazid® and Rifampicin® (50 &100 mg/kg/day), and 4) rats treated with Isoniazid® and Rifampicin® In association with the extract of parsley. Results: The results showed, after six weeks, that parsley extract minimized the Isoniazid® and Rifampicin®-induced renal deterioration; This was shown by a significant decrease in serum levels of urea, creatinine, uric acid, TNF-α, IL-1β and Na+ as well as kidney MDA, nitric oxide and DNA damages. This was coupled with a significant improvement in serum calcium and K+ levels and kidney GSH and SOD activity. In addition, the histopathological results indicated that the extract succeeded in the prevention of Isoniazid® and Rifampicin® induced tissue degenerations. Conclusion: In conclusion, parsley extract may be as promising as nephroprotection against Isoniazid® and Rifampicin® nephrotoxicity through their antioxidant and radical scavenging activities.

Keywords: Nephrotoxicity, Isoniazid®, Rifampicin®, DNA fragmentation, Parsley, rats

INTRODUCTION

The number one cause of death between curable contagious diseases is tuberculosis (TB), with 1.7 million persons dying of TB by 2004. As a normal treatment for adult respiratory tuberculosis infection, a 2-month regimen of anti-bacterial isoniazid, rifampicin and pyrazinamide with a 4-month regimen of isoniazid and rifampicin has been prescribed (Upadhyay and Thakker, 2017). Acute renal failure is a clinical condition characterised by a severe decrease in the ability of the kidneys to remove waste materials, perturbation of acid-base equilibrium, homeostasis of water, and a rapid decrease in the glomerular filtration rate (Prince et al., 2019). Including blood pressure regulation, the kidney performs many excretory and regulatory functions, maintains the extracellular environment and excretes drugs (Ferguson and Walkar, 2012). Because of repeating exposure to different chemicals that can lead to deposition in the kidney inducing failure to the function of the kidney, The kidney is very sensitive to injury. Drugs are known to cause mitochondrial kidney damage that could contribute to the highly concentrated production of reactive oxygen (ROS) and reactive nitrogen (RNS) species, resulting in oxidative and nitrosative lipid, protein and DNA damage in the kidneys (Muzika et al., 2016).
Nephrotoxicity is the most common complication of many therapeutic drugs; over the last 20 years, increases in mortality and morbidity among patients have been documented in cases of acute renal injury (Muzika et al., 2016). Isoniazid®, Rifampicin® and Pyrazinamide® 2-month regimen followed by Isoniazid® and Rifampicin® 4-month regimen is the approved routine treatment for adult respiratory TB. Isoniazid® (INH) is a large, semisynthetic macrocyclic lipid-soluble antibiotic formulated from Streptomyces mediterranei. It is an early drug used primarily for the treatment of all types of tuberculosis in association with rifampicin, ethambutol and pyrazinamide for the prevention of all tuberculosis forms caused by organisms with known or suspected susceptibility to tuberculosis, since it has efficacy against fast-dividing organisms (early bactericidal activity) and against semi-sleeping bacterial populations, it has therefore been used in combination (Verma et al., 2015). Rifampicin® and Isoniazid® Anti-tuberculosis regimens containing antiretroviral regimens as co-therapy, for the treatment of human immunodeficiency virus and tuberculosis co-infection. (Pozniak et al., 2011). Since rifampicin and Isoniazid® are individually associated with downstream renal damage to renal antioxidants. Co-therapy with these medications will synergistically decrease the amount of kidney antioxidants that can have significant consequences.

Latest studies have shown that animals treated with anti-tuberculosis drugs have a clear association between nephrotoxicity and oxidative stress (Sahu et al., 2020). Since nephrotoxic effects have been demonstrated in all drugs used to treat tuberculosis, studies have been conducted to avoid or mitigate toxicity through the use of natural herbal products and/or synthetic compounds, without interference with the clinical activities of the medication. In many studies, Natural antioxidants from different aromatic and medicinal plants have been directly associated with the reduction of chronic diseases such as DNA damage, mutagenesis and carcinogenesis. Research into alternative active antioxidant compounds, like plant extracts and essential oils, which are potentially less detrimental to the health and environment of mammals, is also of growing interest (Zhang et al., 2006). Parsley is an essential herb that comes from the Mediterranean region (Petroselinum crispum). In the dairy, pharmaceutical, perfume and cosmetics industries, Parsley belongs to the Umbelliferae family.

The parsley, however has tiny and dark seeds with a volatile glycoside fruit oil content known as apiininin (Lopez, 1999). It has been documented that Parsley has a range of potential medicinal traits, including antimicrobial traits (Wong and Kitts, 2006), anti-anemic agents, menorrhagic agents (Baytop 1984), anticoagulants, antihyperlipidemic agents, antihypertotoxic agents (Ozturk et al. 1991), antioxidants (Nielsen et al. 1999) and laxative agents (Nielsen et al. 1999) (Kerydyiyeh et al., 2001). It was used to regulate blood pressure for the treatment of lumbago, eczema, knee, ache, impotence, and nose bleeding (Manderfeld et al., 1997). Parsley seeds are also used as a diuretic and Ozsoy et al. (2006) have shown the hypoglycaemic role of parsley; parsley components including ascorbic acid, carotenoids, flavonoids, coumarins, apiole, various terpenoic compounds, phenylpropanoids, phthaloids, furan coumarins and tocopherol (Tunali et al., 1999). The primary aim of this research was to study the antioxidant, the anti-inflammatory and ameliorative efficacy of aqueous extract of Parsley leaves against renal degradation arising from treatment with anti-tuberculosis drugs.

**MATERIALS AND METHODS**

**Preparation of parsley aqueous extract**

Parsley (Petroselinum crispum) leaves were collected from a local supplier store that sells supplies of spices (Abd El-Rahman Harraz, Bab El-Khalk, Cairo, Egypt), described and authenticated by botanists at Al-Azhar University Department of Botany, Faculty of Science; It was determined that the plant had a taxonomic serial number 32677. Parsley aqueous extract (PAE) was obtained from dry herb leaves according to the method defined by Gulcin et al. (2006); 100 g of powdered leaves were soaked at 8 °C in 400 ml of distilled water for 24 hours, then filtered (Whatman No.1) and lyophilized using freeze drier (Snijders.
Protective efficiency of parsley (Petroselinum crispum) against oxidative stress

Scientific-Tilburg, Holland, pressure, 0.1 to 0.5 m bar and temperature 35-4°C. The dry yield was measured and stored at -20 °C before operation.

**Total phenolic content (TPC)**

The complete herbal extract phenolic content was calculated as catechin equivalents (CE) using the Jayaprakasha et al. (2000) method; 5 mg of each residue was mixed into a 10 ml (6:4 v/v) mixture of acetone/water; then After 30 minutes at room temperature, In combination with 1.0 ml of Folin-Ciocalteu (10 times diluted) and 0.8 ml of sodium carbonate solution (7.5%), 0.2 ml of solution (50 % w/v) was measured at 765 nm using the UV-160 1PC UV-visible spectrophotometer, then the total phenolic content as cat solution (7.5 %)

**Determination of Radical Scavenging Activity (RSA) by 1, 1-diphenyl-2-picrylhydrazyl (DPPH•)**

In order to report the Nogala-Kalucka et al. (2005) process, The ability of antioxidants to quench the radical DPPH was measured and determined in accordance with the following equation. In this step, to define a concentration of 200 ppm, some of the crude extraction was dissolved in methanol; then 4 ml of methanol was added to 0.2 ml of this solution and 1 ml of DPPH•(6.09 x 10-5 mol/L) solution was then added to the same solvent. After 10 min at 516nm, the absorbance was assessed against the reference blank, which was 1 ml of DPPH solution and 4 ml of methanol.

RSA (%) = \( \frac{A_{control \ sample} - A_{sample \ extract}}{A_{control \ sample}} \times 100 \)

**Experimental Design and Animals**

The National Research Centre, Cairo, Egypt, Animal Facility has obtained adult male Wistar whitewed albino rats (140-160g). Before beginning the experiment, The animals were put in the required polyethylene cages for acclimatisation for one week. Meladco Company, El-Obour Region, Cairo, Egypt, has always provided fresh water and regular rodent food pellets [20.3 % protein, 5 % corn oil, 5 % fibres, 3.7% salt mixture, and 1% vitamin mixture. All animals received human treatment as cited by the animal ethics committee number of the National Research Centre FWA000147477 in compliance with normal institutional standards For the treatment of laboratory animals and their use. The animals were randomly divided after acclimatisation into four classes (10 animals each as follows: 1) rats were orally ingested via stomach tube with saline (0.4 ml/kg/day) and act as a control, 2) rats were ingested with PAE (250mg/kg/day) via stomach tube (Pourush et al. 2011), 3) rats were ingested with Isoniazid® and Rifampicin® (50 &100 mg/kg/day), and 4) rats were orally administrated with Isoniazid® and Rifampicin® (Mahmoud et al., 2015) in combination with PAE oral administration via stomach tube; all the animals received six weeks of medication.

**Blood and Tissue Sampling**

The animals fasted overnight at the end of an experiment time. Blood specimens were obtained from the retro-orbital plexus under anesthesia (diethyl ether inhalation); the sera were extracted with a cooling centrifuge (IEC centra-4R, Foreign Equipment Co., USA), divided into aliquots and processed as quickly as possible at -80 °C before measurements. The animals were rapidly sacrificed by decapitation after blood collection, then each animal's right kidney was dissected, washed with saline, dried, rolled into a piece of aluminium foil and stored at -80°C for biochemical determination and fragmentation of DNA. The left kidney was soaked in a buffer of formalin-saline (10%), divided, stained and equipped for microscopic testing immediately.

**Biochemical measurements**

Serum creatinine, urea, uric acid, total calcium and albumin levels were measured spectrophotometrically using reagent kits bought from Diamond Diagnostic MDSS GmbH Schiffgraben, Germany. The serum levels of sodium and potassium were use MEDICA Easylyte Na+/K+ ANALYZER (USA) and reagent kits bought from Easylyte, USA, approximate. Using ELISA (Dynatech Microplate Reader, Canada), serum TNF-α and IL 1β concentrations were measured using reagent kits (SG-10057 and SG-10179) purchased from SinoGeneClon Biotech Co., Hang Zhou, China. Kidney nitric oxide (NO), reduced glutathione (GSH) and...
superoxide dismutase (SOD) values were determined using reagent kits obtained from Biodiagnostic, Dokki, Giza, Egypt.

In this process, 0.5 ml of supernatant homogenate was added to 4.5 ml of working reagent [0.8 g TBA dissolved in 100 ml perchloric acid] (1 g kidney tissue was homogenised at 10 ml phosphate buffer pH 7.4 and centrifuged at 5000 rpm for 10 minutes) (10 perc rpm for 10 minutes). The amount of kidney lipid peroxidation end product malondialdehyde (MDA) was chemically calculated by the method stated by Ruiz-Larrea, (1994). The sample-reagent mixture was left for twenty minutes in a boiling-shaking water tank, then brought to cool down at temperature and centrifuged at a rate of 3000 for five minutes. The absorption of the clear pink supernatant, photometrically measured at 535 nm against the chemical agent blank (0.5 ml distilled water + 4.5 ml working reagent of TBA), directly. The amount of MDA in the nmol/g tissue was measured.

**DNA fragmentation**

Fragmentation of DNA The quantity was determined by centrifugation, Differentiating the broken DNA from the intact chromatin and measuring the volume of DNA in the supernatant and pellet according to the quantitative method of Perandone (1993). The degree of DNA fragmentation in both the supernatant and the pellet refers to the ratio of DNA to the total DNA in the supernatant. In 0.5 ml of hypotonic lysis buffer (10 mM Tris-HCl (pH 8), 1 mM EDTA and 0.2 percent Triton X-100), kidney tissue was lysed and coolly centrifuged at 14,000 g for 20min at 4 °C. The pellets were re-suspended in the hypotonic lyses buffer. 0.5ml TCA (10%) was applied to the re-suspended pellets and the supernatants. The specimens were coolly centrifuged at 10,000 g for 20 min and the pellets were suspended in 500μl of TCA (5 percent). A double-volume solution of diphenylamine (DPA) [200 mg DPA in 10 ml glacial acetic acid, 150 μl sulfuric acid and 60 μl acetaldehyde] was subsequently treated in each sample and incubated for 48 h at 4 °C. The fragmented DNA proportion was determined using the equation below from the absorbance reading at 578nm.

\[
\text{DNA fragmentation 
%} = \frac{A_{\text{supernatant}}}{A_{\text{supernatant}+A_{\text{pellets}}}} \times 100
\]

**Histopathology**

The kidneys that were immersed in formalin-saline (10 %) buffer were processed and tested by optical microscope as 5μm thick paraffin sections that were coated with hematoxyline and eosin (Drury, 1980).

**Statistical analysis**

The data obtained were analysed using the ANOVA one-way test followed by the post-hoc test (Tukey) at p ≤ 0.05 using software programme statistical analysis system (SAS); copyright (c) 1998 by SAS Institute Inc., Cary, NC, USA.

**RESULTS**

Results from three in vitro estimation replicates showed that PAE possesses high yield and TPC values, and exhibits great RSA (Figure 1).

**Figure 1.** Mean values (of three replicates) of the yield (g /100 crude herb), radical scavenging activity (RSA) (%) and total phenolic content (TPC) (mg/g extract) of parsley aqueous extract (PAE).

There were no adverse changes in serum creatinine, urea, uric acid and albumin levels in the animals treated with PAE relative to the control group, whereas those treated with Isoniazid and Rifampicin® showed a substantial increase in serum creatinine, urea and uric acid, along with a marked decrease in serum albumin. Interestingly, animals that were treated with PAE in combination with Isoniazid® and Rifampicin® showed a marked improvement in the mentioned measurements compare to those of Isoniazid®/Rifampicin® treated ones (Table 1).
Table 1. Serum creatinine, urea uric acid, albumin levels of treated and control rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Creatinine (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
<th>Albumin (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.64±0.07a</td>
<td>43.9±1.5b</td>
<td>5.9±0.5a</td>
<td>3.7±0.11ab</td>
</tr>
<tr>
<td>PAE</td>
<td>1.59±0.09a</td>
<td>44.4±1.8b</td>
<td>5.7±0.9a</td>
<td>3.6±0.07b</td>
</tr>
<tr>
<td>ATB</td>
<td>3.12±0.06a</td>
<td>98.5±12.1a</td>
<td>8.7±0.6a</td>
<td>2.8±0.07c</td>
</tr>
<tr>
<td>ATB+PAE</td>
<td>1.90±0.05a</td>
<td>52.7±12.3a</td>
<td>6.4±0.7a</td>
<td>3.3±0.08b</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard error; data were subjected to one-way ANOVA followed by post hoc (Tukey) at p<0.05. Within each column, means with different superscript letters are significantly different; PAE is parsley aqueous extract, ATB is anti-tuberculosis.

Table 2. Total Calcium, Sodium and Potassium levels of both treated and control rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total Calcium (mg/dl)</th>
<th>Sodium (mmol/l)</th>
<th>Potassium (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9.51±0.66a</td>
<td>152±13.2a</td>
<td>6.61±0.32b</td>
</tr>
<tr>
<td>PAE</td>
<td>9.48±0.81a</td>
<td>151±11.91a</td>
<td>6.41±0.21b</td>
</tr>
<tr>
<td>ATB</td>
<td>7.18±0.39c</td>
<td>178±1.56b</td>
<td>4.14±0.42a</td>
</tr>
<tr>
<td>ATB+PAE</td>
<td>8.81±1.19b</td>
<td>157±11.62a</td>
<td>5.81±0.62c</td>
</tr>
</tbody>
</table>

Data were assumed to be mean ± standard error; data were subjected to single-way ANOVA followed by post hoc (Tukey) at p<0.05. Means with separate superscript letters are significantly different within each column; PAE is aqueous extract of parsley, ATB is anti-tuberculosis.

Regarding the results of the renal oxidative status, Table 3 reveals that administration of PAE neither adversely affects the renal oxidative force

<table>
<thead>
<tr>
<th>Groups</th>
<th>NO (μmol/g Tissue)</th>
<th>MDA (μmol/g Tissue)</th>
<th>GSH (mg/g Tissue)</th>
<th>SOD (U/g Tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>28.8±4.1a</td>
<td>390±36c</td>
<td>61.3±0.65a</td>
<td>220±65b</td>
</tr>
<tr>
<td>PAE</td>
<td>27.7±3.9c</td>
<td>386±28d</td>
<td>62.78±0.89c</td>
<td>218±43d</td>
</tr>
<tr>
<td>ATB</td>
<td>50.5±5.1c</td>
<td>792±92e</td>
<td>31.14±0.91c</td>
<td>171±85c</td>
</tr>
<tr>
<td>ATB+PAE</td>
<td>35.4±3.2c</td>
<td>487±32c</td>
<td>53.93±0.77c</td>
<td>201±34c</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard error; data were subjected to one-way ANOVA followed by post hoc (Tukey) at p<0.05. Within each column, means with different superscript letters are significantly different; PAE is parsley aqueous extract, ATB is anti-tuberculosis.

Similarly, ingestion of ATB drug (INH/RIF) led to a marked downregulation of serum Na+ level with a marked up-regulation of total Calcium and K+ levels.

DNA fragmentation percentage results announced that PAE performed safe effect on DNA, while INH/RIF ingestion damaged DNA, this was achieved from the remarkable rise in its fragmentation percent when both groups were compared with the corresponding value of control one. Fortunately, co-administration of rats with PAE and INH/RIF resulted in a substantial decrease in MDA and NO concentrations, and the marked elevation of GSH and SOD values.

In most renal tubules, hyaline cast in the lumen of most tubules, and haemorrhage in either interstitial tissue or/glomeruli were seen in kidney sections of rats groups treated with ATB.
drug (Figure 6). Favorably, rats treated with PAE along with ATB drug revealed marked renal improvements represented in minimal glomerular lobulation and Decrease of other symptoms of degeneration with enough urinary space and few haemorrhages of interstitial tissue (Figure 7).

**DISCUSSION**

Kidney injury is a severe problem that can survive treatment and cause irreversible harm to the kidneys, nephropathy is a major complicated anti-tuberculosis therapy microvascular problem (Rekha et al., 2005); however, renal damage caused by anti-tuberculosis therapy is typically reversible and can be treated accordingly (Rekha et al., 2005). Oxidative stress and inflammation have been shown to lead to drug-induced kidney toxicity in many studies. (Mahmoud, 2014). Therefore, the use of antioxidants could protect against oxidative stress caused by anti-tuberculosis and renal degradation. The aim of this research was to test the hypothesis that parsley aqueous extract may have prevented renal damage or malfunction in rats caused by INH/RIF by attenuating inflammation and blocking oxidative stress. The results revealed that ATB (INH/RIF) led to renal damage which was monitored from the marked rise in the serum levels of creatinine, urea and uric acid indicating impaired renal function; these parameters are also regarded as effective markers of renal damage or failure (Martin and Sabina, 2016 & Christensen et al., 2013). Serum albumin level was fallen as a consequence to ATB indicating its loss from the blood due to damaged nephron function.

The marked drop in GSH level and SOD activity associated with a notable elevation in the renal MDA and NO levels after ATB administration reflects the reduction of the renal antioxidant battery; thereby reduces kidneys’ ability to counter the effects of the toxin. These results are similar to recent studies by Prince et al. (2019) and Sahu et al. (2020), which verified their findings by renal histological changes such as glomerular tuft atrophy and infiltration of inflammatory cells and finally dysplastic renal tubules. PAE administration was successful in protecting the kidney from ATB drug toxicity as it significantly improved renal function and histological structure close to the normal pattern. The antioxidant profile of the kidneys is reversed by PAE.
Protective efficiency of parsley (*Petroselinum crispum*) against oxidative stress...

Figure 4. Section of the kidney of a control rat showing normal appearance of glomerulus and renal tubules (A). High power field showing the normal appearance of glomerulus and renal tubules (B) (Hx&Ex400).

Figure 5. Section of the kidney of a rat treated with PAE only for six weeks, showing normal appearance of renal tubules and glomeruli (Hx&Ex400).

Figure 6. Section of the kidney of a rat treated with ATB only showing a vacuolar degeneration in most of the renal tubules (red arrow), hyaline cast in lumen of most tubules (star), hemorrhage (yellow arrow) in interstitial tissue (A). Another field (B) showing degeneration of glomeruli (yellow arrow), inter-glomerular and interstitial tissue hemorrhage (star), and cellular infiltration (black arrow). Vacuolar degeneration in some tubular epithelial cells (red arrow) and pyknosis in some tubular cells (green light arrow) (Hx&Ex400).

Figure 7. Section of the kidney of a rat treated with ATB along with parsley showing interstitial hemorrhage (star), cellular infiltration (red arrow) and cell debris in the lumen of some tubules (yellow curved arrow). Vacuolar degeneration (black arrow) (Hx&Ex400).

It was suggested to inhibit lipid peroxidation and scavenge hydroxide and superoxide radicals, thus improving the antioxidant battery, the active constituents present in PAE such as flavonoids and vitamin C. In this context, the protective role of PAE may be due to the antioxidant and antioxidant effects of its components. These findings are in line with the latest reports (Al-Seen et al., 2018 & Elkomy et al., 2020).

In addition, the current study pointed out that the administration of ATB resulted in a substantial increase in the serum level of inflammatory cytokines (TNF alpha & IL-1β) as well as the percentage of DNA fragmentation; this finding is agonised by recent data from Wali et al. (2020) and Shabbir et al. (2020). TNF alpha and IL-1β are active pro-inflammatory cytokines and are significant mediators of damage to inflammatory tissue. Among the drug-induced nephrotoxicity mechanisms, the immune system has been included; several previous studies showed evidence that nephrotoxicants could induce inflammatory responses leading to organ injury (Martin and Sabina, 2016). The pathogenesis of drug-induced kidney damage has been implicated in ROS and oxidative stress (Lopez-Novoa et al., 2011. With regards to the structure of renal lipids, long-chain polyunsaturated fatty acids are easy to obtain and this makes the kidney at risk of acute...
damage caused by ROS (Ozbek, 2012). Furthermore, ROS can cause lipid peroxidation, cellular protein damage, DNA fragmentation and alter the antioxidant defence mechanism (Nencini et al., 2007). Renal DNA has been reported to be attacked by free radicals produced by ATB drugs, as evidenced by higher levels of kidney damage and DNA damage (Alkreathy et al., 2014).

In this study, PAE efficiently down-regulated serum levels of the tested inflammatory cytokines (IL-1β and TNF-α), enhanced antioxidant activities and restored the histopathological changes of the kidney. These results suggest that PAE possesses anti-inflammatory and immune-modulatory characteristics may be mechanized through its antioxidant components; in vitro results showed that PAE performed high phenolic content and radical scavenging activity confirming its antioxidant activities as stated previously by Kooti et al. (2017). SOD plays a key role in protecting the body from the harmful effects of ROS (Wei et al., 2011). INH administration was reported to produce a significant increase in MDA and NO and a substantial decrease in antioxidant defences in rats (Mahmoud, 2014). Therefore, we assume that PAE’s nephro-protective mechanism against oxidative stress induced by INH/RIF is comparable to being mediated by GSH restoration and enzymatic antioxidant defence potentiation. In line with the results of the biochemical assessment, histopathological findings demonstrated that PAE administration exhibited ameliorative capacity against ATB induced renal injury; this could be mechanized through the antioxidant, anti-inflammatory, and immune-modulatory activity of PAE components.

CONCLUSION

In conclusion, the findings of the current research indicate that PAE may emerge as a putative nephro-protective, alleviates DNA fragmentation and membrane-stabilizing effects against nephrotoxicity initiated by anti-tuberculosis drugs. In order to validate these results and their extrapolation to humans, further research must be carried out.

CONFLICT OF INTEREST

Authors declare that they have no conflicts of interest.

FUNDING

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Egyptian Association for Cancer Research (EACR)
http://eacr.tanta.edu.eg/

EACR is an NGO society that was declared by the Ministry of Social Solidarity (Egypt) No. 1938 in 19/11/2014 based on the initiative of Prof. Mohamed Labib Salem, the current Chairman of EACR. EACR aims primarily to assist researchers, in particular young researchers in the field of cancer research through workshops, seminars and conferences. Its first international annual conference entitled "Anti-Cancer Drug Discovery" was successfully organized in April 2019 (http://acdd.tanta.edu.eg). Additionally, EACR aims to raise the awareness of the society about the importance of scientific research in the field of cancer research in prediction, early diagnosis and treatment of cancer. EACR is also keen to outreach the scientific community with periodicals and news on cancer research including peer-reviewed scientific journals for the publication of cutting-edge research. The official scientific journal of EACR is "International Journal of Cancer and biomedical Research (IJCBR: https://ijcb.journals.ekb.eg) was successfully issued in 2017 and has been sponsored by the Egyptian Knowledge Bank (EKB: www.ekb.eg).

EACR Chairman,  
Prof. Mohamed Labib Salem, PhD  
Professor of Immunology  
Faculty of Science, Tanta University, Egypt
International Journal of Cancer and Biomedical Research (IJCBR), a publication of the Egyptian Association for Cancer Research (EACR), is a peer-reviewed online journal published quarterly. The journal allows free access (Open Access) to its contents and permits authors to self-archive a final accepted version of the articles on any OAI-compliant institutional / subject-based repository.

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Aim: The main aim of IJCBR is to attract the best research in animal and human biology in health and diseases from across the spectrum of the biomedical sciences at the molecular, cellular, organ, and whole animal levels especially those that are related to cancer research, including causes, prediction, diagnosis, prognosis and therapy.

Scope: It is essential reading for all researchers interested in biochemistry, cancer, microbiology, nutrition, physiology, genetics, immunology, epidemiology, medical economics, human biology, bioinformatics, biotechnology, nanotechnology, and disease modeling.

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2. Accept the manuscript
3. Ask the authors to revise and resubmit the manuscript after responding to the peer reviewers’ feedback.
4. Ask for peer-review from additional reviewers.

If the authors resubmit the manuscript, the IJCBR editor will ask the same peer-reviewers to look over the manuscript again to confirm that their concerns have been addressed. This is called re-review process. This second revision (if applicable) takes about another 4 to 6 weeks. At this point, the abstract of the article appears in press. The online publication (the PDF format) of the final version of the manuscript takes from 2 to 4 weeks. As such, the total publication cycle takes from 2 to 4 months. This cycle can be reduced to 4 to 6 weeks (fast track publication) for the manuscripts with outstanding findings.

The peer-review process used by IJCBR includes comments on errors in the study’s methods or analysis that raise questions about the findings, or sections that need clearer explanations. The peer-review process also includes the importance and novelty of the manuscript and its interest to the journal’s audience. The IJCBR uses double-blind review, which means that both the reviewers and authors identities are concealed from the reviewers, and vice versa, throughout the review process. To facilitate this, authors need to submit a Title Page containing the Authors details and Blinded Manuscript with no author details as 2 separate files.
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The International Journal of Cancer and Biomedical Research (IJCBR) is an International and interdisciplinary journal of preclinical and clinical studies in the area of cancer and biomedical research. It is a peer-reviewed journal in English, published quarterly (in March, June, September, and December) by the Egyptian Association for Cancer Research (EACR) in both print and online formats (4 issues making a volume). Special issues or supplements may also be produced from time to time upon agreement with the Editorial Board.

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The main aim of IJCBR is to attract the best research in animal and human biology in health and diseases from across the spectrum of the biomedical sciences at the molecular, cellular, organ, and whole animal levels especially those that are related to cancer research, including causes, prediction, diagnosis, prognosis and therapy.

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