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Protective Effects of Amla (*Emblica officinalis*) Fruit Pulp Extract and Selenium Against Dimethoate Induced Nephrotoxicity in Wistar Rats

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Abstract: The aim of the present study was to investigate histological changes in the kidney of Wistar rats induced by dimethoate and to evaluate the protective role of amla (*Emblica officinalis*) fruit pulp extract and selenium on dimethoate induced nephrotoxicity. Wistar rats were divided into 6 numerically equal groups and treated as -- Group A: Control; Group B: dimethoate (20 mg/kg b wt.); Group C: dimethoate (20 mg/kg b wt.) and selenium (0.5 mg/kg b wt.); Group D: dimethoate (20 mg/kg b wt.) and amla fruit pulp extract (200 mg/kg b wt.); Group E: selenium (0.5 mg/kg b wt.) and Group F: amla fruit pulp extract (200 mg/kg b wt.). For light microscopic studies, kidney were fixed on 7 and 14 day following the treatments. In 7 day dimethoate (Group B) treated rats kidney exhibited shrinkage of glomeruli. In dimethoate and selenium (Group C) and dimethoate and amla fruit pulp extract (Group D) treated rats for 7 day, kidney exhibited similar changes as noticed in dimethoate (Group B) treated rats. Kidney of rats treated for 7 day with selenium (Group E) and amla fruit pulp extract (Group F) have not shown any histological changes. Vacuolization and degeneration of tubules and glomerulus was noticed in 14 day dimethoate (Group B) treated rats. In dimethoate treated group, hypertrophied glomerulus was noticed. In dimethoate and selenium (Group C) and dimethoate and amla fruit pulp extract (Group D) treated rats there was no shrinkage in glomerulus. Also, tubular degeneration was not noticeable in group C and group D. However, hypertrophied glomerulus and glomerular degeneration was noticed in kidney of group C and group D. In selenium (Group E) and amla fruit pulp extract (Group F) treated rats for 14 day no histological changes were noticed. From present study it can be concluded that dimethoate caused histological changes in kidney of rats. These histological changes can be protected by providing selenium and amla fruit pulp extract.

Keywords: Dimethoate, Amla fruit pulp extract, Selenium, Glomerulus, Kidney, Hypertrophy, Degeneration, Renal tubules, *Emblica officinalis*

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Introduction

Pesticide is a combination of substances used to prevent, eradicate, repel, or decrease the harm caused by any pest. Pesticides are divided into four main classes according to their chemical composition: organochlorines, organophosphates, carbamates, and pyrethroids (Yadav *et al*., 2017; Kaur *et al*., 2019). Dimethoate is an organophosphate insecticide that is used worldwide in agriculture and urban areas due to its high efficacy and rapid environmental degradation (Van Scoy *et al*., 2016). Dimethoate is widely used, but because it persists in soil and crops, it is unhealthy for both humans and animals. The serum of agricultural workers who are chronically and occupationally exposed to dimethoate has been found to contain dimethoate residues, according to a prior discovery. In both animals and humans, dimethoate poisoning is typically accompanied by a block in neuromuscular transmission. This short-term exposure to dimethoate predominantly results in the inhibition of acetylcholinesterase in the target tissues, which leads to the accumulation of acetylcholine and the activation of muscarinic and nicotinic receptors on the cholinergic system (Saafi-Ben Salah *et al.*, 2012). Dimethoate intoxication results in cellular damage and oxidative stress, which causes lipid peroxidation and the generation of free radicals (Ben Amara *et al*., 2013).

The most significant therapeutic plant in the Indian traditional medical system, Ayurveda, is probably *Emblica officinalis or Phyllanthus emblica* also known as Indian gooseberry or amla. The fruit is the most significant portion of the plant and is used to treat a variety of ailments (Baliga and Dsouza, 2011). According to reports, the fruit possess expectorant, purgative, spasmolytic, hypoglycemic, hepatoprotective, and hypolipidemic activity (Mirunalini and Krishnaveni, 2010). According to earlier research, amla extract is helpful in avoiding both age-related renal failure (Yokozawa *et al*., 2007) and acute kidney dysfunction (Tasanarong *et al.*, 2014).

A trace element selenium is necessary for healthy physiological functions. The amino acid selenocysteine (Sec), a component of the trace element selenium (Se), is co-translationally integrated into the polypeptide chain (Zoidis, 2018). Due to its beneficial antioxidant characteristics, the trace element selenium (Se) has been used as a dietary supplement to enhance health. Because it plays a role in enhancing antioxidant defence, immunological functions, and metabolic homeostasis, it may reconstruct progressive and spontaneous biochemical and physiological changes that could result in disease prevention and healthy ageing (Burk, 2002). The amino acid selenocysteine is essential for the manufacture of a variety of selenoenzymes, including glutathione peroxidase, iodothyronine deiodinases (regulating thyroid hormone activity), and thioredoxin reductases, which regenerate antioxidant systems (Barciela *et al*., 2008). Se prevents the apoptosis and mitochondrial malfunction brought on by ROS. Se is found in high concentrations in renal tissue, which can shield the kidney against lipid peroxidation (Gunes *et al*., 2018). The present study was aimed to investigate the protective effects of amla fruit pulp extract and selenium against dimethoate induced nephrotoxicity in Wistar rats.

Materials and Methods

Male Wistar rats were purchased from Asia Scientific Emporium, Varanasi, India. The animals were housed in polypropylene cages and were acclimatized for two weeks prior to different treatments. During acclimation and experimental period, rats were provided food and tap water *ad libitum.* Experimental design was approved by Research Degree Committee, D.D.U. Gorakhpur University, Gorakhpur, India.

Dimethoate (30 EC) was purchased from local fertilizer shop and dissolved in distilled water for use in experiment. Sodium selenite was purchased from Eastern Scientific Emporium (Gorakhpur, India) and dissolved in distilled water for experimental use. The Amla fruit, *Emblica*

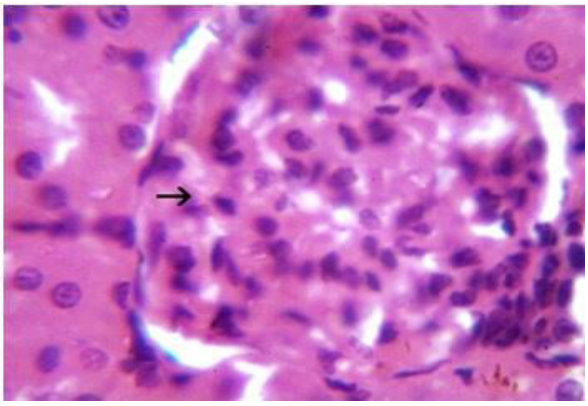

Fig. 1: Kidney of control rat depicting glomerulus (arrow). HE x 500

officinalis were purchased locally. The amla fruits pulp were washed thoroughly with water and dried in hot air oven at 40 °C. After drying, these were cut into small pieces, dried and powdered. Powdered amla fruits pulp were mixed with 90% ethanol in 1:20 ratio (w/v) and kept at orbital shaker for 48 h. Then the samples were filtered with Whatman grade No. 1 filter paper. The filtrates were dried in oven at 40 °C. For use, the dried residues of amla fruits pulp extract were dissolved with ethanol to provide desired dose to be given to rats.

Experimental design:

The acclimatized rats were divided into 6 groups (A-F), each group containing 20 rats. The rats were treated (at 10:00 am throughout experiment) as follow:

Group A (Control): No treatment was given

Group B (Dimethoate treated rats): These rats were given daily dose of dimethoate (20 mg/kg b wt.)

Group C (Dimethoate + Selenium): These rats were given daily dimethoate (20 mg/kg b wt.) and Selenium (0.5 mg/kg b wt.)

Group D (Dimethoate + Amla fruit pulp extract): These rats were given daily dimethoate (20 mg/kg b wt.) and amla pulp extract (200 mg/kg b wt.)

Group E (Selenium): These rats were given daily selenium (0.5 mg/kg b wt.)

Group F (Amla fruit pulp extract): These rats were given only amla fruit pulp extract (200 mg/kg b wt.)

Rats were sacrificed 24 h after last dose on 7th and 14th day after initiation of the experiment under light ether anesthesia. Rats were fasted overnight before sacrifice. Kidneys were fixed in Bouin's fluid. These fixed tissues were dehydrated in an ethanol gradient, treated with clearing agent xylene, infiltrated and embedded in paraffin wax, sectioned at 6 µm, and mounted on glass slides. The slides were stained with hematoxylin and eosin (HE) for light microscopic examination.

Results

There are numerous nephrons in kidney of control rats. These nephrons consist of a dilated portion having renal corpuscle; the proximal tubule; loop of Henle and the distal tubule. The renal corpuscles contain the glomerulus which is a tuft of capillaries. Each glomerulus is surrounded by the Bowman's capsule (Fig. 1). An urinary space is present between the glomerulus and Bowman's capsule. The epithelium of proximal tubule is lined by simple cuboidal or columnar cells whereas the epithelium of distal tubule is lined by simple cuboidal cells.

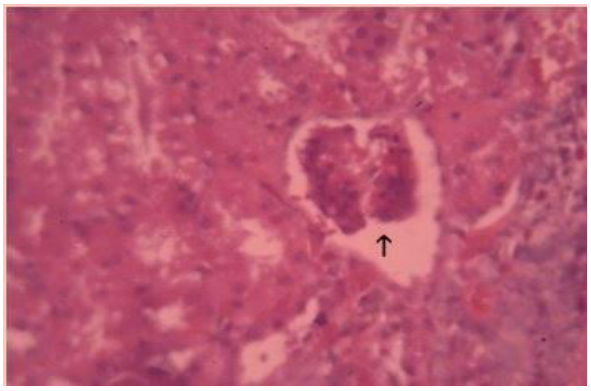

Fig. 2: Kidney of 7 day dimethoate exposed rat showing shrunken glomerulus (arrow). HE x 100

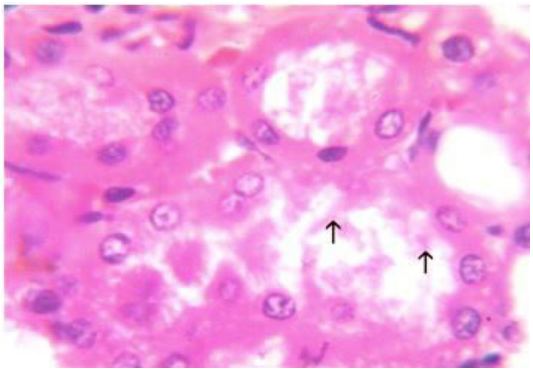

Fig. 3: Kidney of 14 day dimethoate exposed rat showing tubular degeneration (arrows). HE X 500

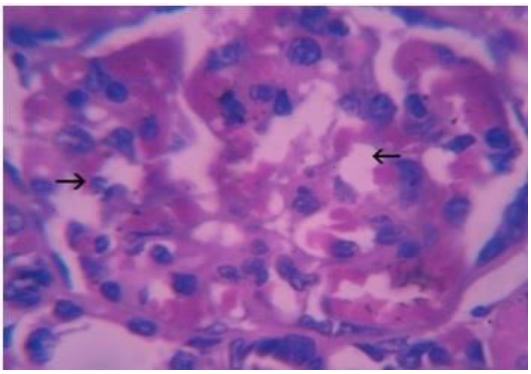

Fig. 4: Kidney of 14 day dimethoate exposed rat showing glomerular degeneration (arrows). HE X 500

In 7 day dimethoate (Group B) treated rats the glomeruli are noticed to be shrunken which resulted into more space between the Bowman's capsule and glomerulus (Fig. 2). In dimethoate and selenium (Group C) and Dimethoate and Amla fruit pulp extract (Group D) treated rats for 7 day, kidney exhibited similar structural changes as seen in dimethoate (Group B) treated rats. In Selenium (Group E) and Amla fruit pulp extract (Group F) treated rats there was no histological changes.

Vacuolization and degeneration of tubules (Fig. 3) and glomerulus (Fig. 4) was noticed in 14 day Dimethoate (Group B) treated rats. In Dimethoate treated group, hypertrophied glomerulus was noticed (Fig. 5). In Dimethoate and Selenium (Group C) and Dimethoate and Amla fruit pulp extract (Group D) treated rats there was

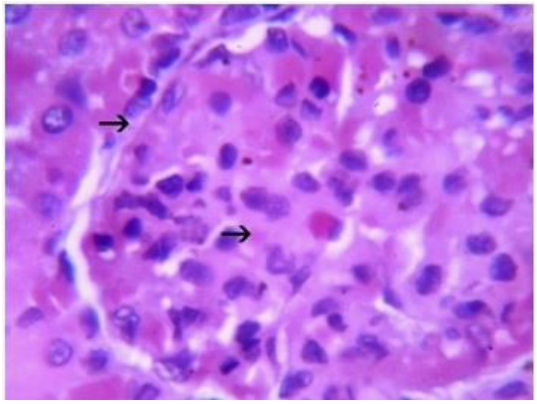

Fig. 5: Kidney of 14 day dimethoate exposed rat showing glomerular hypertrophy (arrows). HE X 500

no shrinkage in glomerulus. Also, tubular degeneration was not noticeable in group C and group D. However, hypertrophied glomerulus and glomerular degeneration was noticed in kidney of group C and group D. In selenium (Group E) and (Group F) treated rats the histological structure of kidney was almost similar to control rats.

Discussion

Dimethoate exposure to rats caused kidney alterations which is evident by occurrence of shrunken glomeruli after 7 day treatment and glomerular degeneration, hypertrophy of glomeruli and tubular degeneration after 14 day exposure. Glomerular shrinkage (as observed in 7 day dimethoate treated rats) has also been noticed by few workers after exposure to various toxicants/chemicals - *paraquat* (Abdel-Mageid, 1994), *Lithium* (Sharma and Iqbal, 2005), *chlorpyrifos* (Tripathi and Srivastav, 2010, Raina and Hamid, 2013), *cadmium* (Tripathi and Srivastav, 2011), *2, 3, 7, 8-tetrachlorodibenzo-p-dioxin* (Ciftci *et al.*, 2012), *Triazophos* (Sharma and Sangha, 2014), *Endosulfan* (Khan, 2014), *Silver* (Roda *et al.*, 2017), *Malathion* (Mamun *et al.*, 2015), *Abmactin* (Moqbel *et al.*, 2017), *Mercuric chloride* (Langeswaran *et al.*, 2018), *MCLR* (Srivastava *et al*., 2020), *Aluminium chloride* (Okail *et al.*, 2020), *Cypermethrin* (Srivastava *et al.*, 2021), *Bisphenol-A* (Ishtiaq *et al.*, 2022), and *Chromium* (Baiomy *et al.,* 2023).

In the present study degeneration of glomeruli has been noticed after dimethoate exposure. This is in agreement with the studies of other investigators who have also reported glomerular degeneration in vertebrates such as fish --- after treatment with chlorpyrifos (Srivastava *et al.*, 1990), deltamethrin (Cengiz, 2006), cadmium (Wangsongsak *et al.*, 2007), microcystin (Atencio *et al.*, 2008), and cypermethrin (Korkmaz *et al.*, 2009); chick -- after treatment with cypermethrin (Aslam *et al.*, 2009); and rat -- after treatment with paraquat (Lamfon and Al-Rawi, 2007), chlorpyrifos (Tripathi and Srivastav, 2010; Raina and Hamid, 2013), cadmium (Tripathi and Srivastav, 2011), lead (EI-Newesy and EI-Sayed, 2011), gentamicin (Alrifi *et al.*, 2012), deltamethrin (EI- Gerbed, 2014), triazophos (Sharma and Sangha, 2014), abmactin (Moqbel *et al.*, 2017), MCLR (Srivastava *et al.,* 2020), cypermethrin (Srivastava *et al*., 2021), and Chromium (Baiomy *et al.,*2023). Dimethoate provoked glomerular degeneration which may decrease glomerular filtration rate as suggested by Barrouillet *et al.* (1999) who have also noticed decrease in GFR in their *in vitro* studies of cadmium exposure.

In the present study the observed tubular degeneration after dimethoate treatment is in conformity with similar observation made by other investigators from vertebrates after toxicant/chemicals exposure --- fish (*chlorpyrifos*-–Srivastava *et al.*, 1990; *cadmium*-– Wangsongsak *et al.*, 2007; *microcystin*-- Atencio *et al.*, 2008; Rabergh *et al.*, 1991; Kotak *et al.*, 1996

cypermethrin-- Ayoola and Ajani, 2008); chick (*cypermethrin*-- Aslam *et al.*, 2009); quail (*lead*– Almansour *et al.*, 2008); wood mouse and whitetoothed shrew (*landfill leachates containing toxic metals* -- Sanchez-Chardi *et al.*, 2009); monkey (*lead*-- Colle *et al.*, 1980); mice -- (*chlorpyrifos*-- Thijssen *et al.*, 2007, *microcystin*-- Rangel *et al.*, 2014; Al-Sultan *et al.*, 2015; Al-Majeed *et al.*, 2016); rabbit (*fluoride* – Shashi *et al.*, 2002); rat (*chlorpyrifos* -- Aughey *et al.*, 1984; Karmakar *et al.*, 1986; Gatta *et al.*, 1989; Brzoska *et al.*, 2003; Abdel-Moneim and Said, 2007; Kukner *et al.*, 2007; Jihen *et al.*, 2008; Tripathi and Srivastav, 2010; Raina and Hamid, 2013; Tanvir *et al.*, 2016; *microcystin*-- Hooser *et al.*, 1989; Srivastava *et al*., 2020**;** *metal mixture* – Jadhav *et al.*, 2007; *paraquat* – Damain *et al.*, 1992; Abdel Mageid, 1994; Lamfon and Al-Rawi, 2007; *cypermethrin* – Muthuviveganandavel *et al.*, 2008; Srivastava *et al.,* 2021; *fenthion* – Kerem *et al.*, 2007; *cigarette smoke* – Kuru *et al.*, 2009; *cadmium*-- Tripathi and Srivastav, 2010; Brozska *et al.,* 2003; *Lead* --EI-Newesy and EI-Sayed, 2011; Gentamicin --Abdel-Raheem *et al.*, 2009, Alrifi *et al.*, 2012; 2,4-D-- Tayeb *et al.*, 2012; *zinc*-- Faddah *et al.*, 2012; *streptozotocin*-- Omara *et al.*, 2012; *Monosodium glutamate*-- Dixit *et al.*, 2014; *Deltamethrin*-- EI-Gerbed, 2014; *Endosulfan*-- Khan, 2014; *Lead acetate*-- Aksu *et al.*, 2017; Abmactin--Moqbel *et al.*, 2017; *Cymoxanil* -- Ahmed *et al.*, 2020; *Polystyrene nanoparticle*--- Ahmed *et al.,* 2022; *Chromium*---Baiomy *et al.,* 2023; *Arsenic*--- Irak *et al.,*2024). In contrast there is no change in kidney morphology after bifenthrin exposure to fish (Velisek *et al.*, 2009).

In dimethoate treated rats the observed glomerular hypertrophy is strengthened by similar findings in rats after exposure to toxicants/chemicals-- Abdel-Raheem *et al.* (2009); Tayeb *et al.* (2012); Mansour and Mossa (2010); Raina and Hamid (2013); Omara *et al.* (2012); Morya and Vachhrajani (2014); Tripathi and Srivastav (2010); Srivastava *et al.* (2020); Srivastava *et al.* (2021).

Hydrolic changes occurred in kidney tubule after toxicant exposure may be the plausible reason for the vacuolization and degeneration of tubules which have been noticed in dimethoate treated rats. The changes after pump transport of tubular cells caused by toxicant and provoke physiological disturbances in kidney. Sanchez-Chardi *et al*. (2009) have suggested that tubular dilation may be a compensatory mechanism for failure of excretory function.

Conclusion

It can be concluded from the present study that exposure of dimethoate adversely affect the kidney structure of rats. The histological changes caused by dimethoate in kidney could be protected by supplementation of selenium and amla fruit pulp extract. Giving dietary supplements including amla fruit pulp extract and selenium to organisms exposed to dimethoate is advised in order to reduce their toxic symptoms.

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