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Research Article

Ameliorative Effect Of Aloe Vera Extract On Ethionamide And Para Amino Salicylic Acid Induced Nephrotoxicity In Sprague-Dawley Rats

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ABSTRACT

Forty eight (48) Sprague- dawley rats (average weight 150 - 250 g) of either sex were used for the experiment. Aloe vera juice and the respective drugs were given orally to each group daily for 28 days. After 28th day the rats were sacrifices and blood and kidney tissues were withdrawn from each group to study serum biochemistry and histology of rats. The results of the present study showed that, the maximum food consumption was observed in group treated with ETH+PAS+ Aloe vera juice (R= 40.75gm ± 5.30 C= 59.25gm ± 5.30 and C/A = 19.75 gm ± 1.77) respectively. The maximum body weight and relative weight of kidney were noted in rats treated with ETH+ Aloe vera juice (314.0 gm ±49.1) and ETH (2.478 gm ± 0.588) respectively. In case of biochemical studies the maximum levels of total serum protein ETH (8.73mg/dL ±0.85) in ETH, total serum globulin (4.11 mg/dL ±0.79) in ETH, total serum albumin (4.83 mg/dL ±0.97) in ETH + Aloe vera Juice, total creatinine (1.26 mg/dL ±0.06) in PAS , total urea (88.58 mg/dL ± 4.83) in ETH, and (BUN) in ETH (50.36 mg/dL ± 1.44) was found in treat groups respectively. The Kidney showing normal histomorphological cellular features of renal tubules and glomeruli in the renal cortex and medulla region were observed. No inflammatory or pathological changes were noted in renal parenchyma in rats treated with ETH+PAS+ Aloe vera juice. It was found that the rats orally co-administered with Aloe vera juice in combination with the ETH and PAS or independently found effective to ameliorate the toxic effect of the drugs. In case of histomorphological analysis of kidney it was found that, Aloe vera juice co-administered rats showed normalization of histoarchitecture of the kidney. Based on the above results it is concluded that the Aloe vera juice act as nephroprotective agent and a good bio-enhancer against ETH and PAS drugs in Sprague-dawley rats.

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INTRODUCTION

Mycobacterium tuberculosis is the infectious agent that causes tuberculosis (TB). Despite medical advances, tuberculosis remains fatal and is the leading cause of human death in several countries. It was estimated that, due to tuberculosis, a person gets infected in every second throughout the world. The estimated number of new cases of tuberculosis in every year in and around the world is 9.6 million, which is approximately one -third of the world's population and amongst them 1.6 million deaths appeared every year due to active TB. From the recent data, it is found that the development of MDR-TB occurred due to misuse or inappropriate use of antibiotic treatment by the patients [1]. In many studies, the development of MDR-TB is due to misuse or improper antibiotic treatment by the patients and lack of focused attention on these patients. The very high incidence of MDR-TB has led to the use of second-line tuberculosis drugs.

Ethionamide (eth eye on a mid) is drug which shares similarities with Isoniazid and has anti-mycobacterial function. The dose level of Ethionamide is 250 mg / 70kg body weight and increased to 1 gram to those patients who can well tolerate. Some cases of ethionamide-induced nephrotoxicity have been severe and harmful cases have also been reported [2]. The drug Para-aminosalicylic acid (PAS) is effective drug for tuberculosis in the 1940s [3]. PAS is very uncommon because it is limited to resist specific strains. Thus APS is considered to e a principal second-line drug treatment of MDR-TB [4]. Nephrotoxicity is a serious concern and cause adverse effect on the kidney, because of anti-T drugs by compromising the effectiveness of the treatment regimens [5, 6]. Drug induced nephrotoxicity is common complication in certain patients and special clinical cases [7].Nearly twenty percent of community and hospitalize patients are related acute kidney failure due to drug induced toxicity [8, 9]. Anti tuberculosis drugs like Amino glycosides and cyclic-polypeptides are well known for causing nephrotoxicity, ototoxicity, vestibular toxicity, electrolyte abnormalities and other rare side effects [10]. The TB patient has higher risk of chronic kidney disease (CKD) [11]. Several medicinal plants used traditionally from thousands of years in the herbal preparations in Indian traditions for the health care system. Now a day's, around the world 80% of the population is depends herbal medicines to meet their health issues [12]. Traditional plant remedies are widely used in developing countries to treat various diseases. Many herbal remedies prepared from the plants are in used to cure and treat varieties of diseases including the plants having nephroprotective potential [13]. Presently, supplementations of the herbal remedies have developed the interest of researchers in treating a variety of diseases. In India, many researchers have focused their studies on herbal preparations. Presently more than 40 phyto- chemicals and poly-herbal formulations are available for commercial use to have hepatoprotective, gastroprotective, antibacterial, antifungal, nephroprotective, immune-buster action are being used [14, 15]. More than 500 species of aloe are known, but Aloe vera is recognized as the "true aloe vera" for its widespread use and purported healing powers [16]. Aloe verahas been used for many centuries for its medicinal and therapeutic properties. Aloe juice has been used for centuries as a laxative and medicinal cleanser [17]. Many of the health benefits associated with Aloe vera are attributed to promoting wound healing, antifungal activity, hypoglycemic or antidiabetic effects, and anti-inflammatory, anticarcinogenic, immunomodulatory, and gastroprotective properties [18].

MATERIALS AND METHODS

A. Collection and Identification:

Fresh Aloe vera plant leaves were obtained from the botanical garden and the sample was identified before being brought to the laboratory in the Department of Zoology at Patkar-Varde College, Goregaon (W), Mumbai. The identification of the Aloe vera plant was conducted through a review of the literature, and the final authentication was carried out at the Department of Botany, St. Xavier's College (autonomous) in Mumbai, India.

B. Preparation of Crude Extract:

Fresh Aloe vera leaves were washed 2-3 times with tap water. Subsequently, 50 grams of leaves were ground with 50ml of distilled water in a sterilized pestle and mortar. The yield will be determined by comparing the weight of the extract to the weight of the leaf pulp in a sterile container, which will then be stored at -20°C until further use.

C. Purchas of drugs

The drugs ETH (Ethionamide) (Macleods Pharmaceuticals Ltd) and PAS (Para-aminosalicylic acid) (Lupin Ltd) were acquired based on the prescription of a physician by a medical practitioner from New Krishna Medicos, located at Andheri (E), Mumbai, India.

D. Experimental Design

A total of forty-eight (48) Sprague-dawley rats (with an average weight of 150 - 250 g) of both sexes were utilized for the experiment. Prior to the commencement of the experimental study, approval was obtained from the Ethical Committee at APT Research Foundation, Pune, with reference to CPCSEA NO. RP 01/2223 dated 11/June/2022. The animals were acclimatized, housed, and maintained in the APT laboratory for a week. The environmental conditions were controlled, with humidity and temperature set at 22±3°C, humidity at 50-60%, and an illumination cycle of 12 hours of light followed by 12 hours of darkness. The rats were housed in polypropylene cages with stainless steel grill tops, provided with commercial pellet food and water bottles ad libitum, and bedding consisting of clean paddy husk.

Table-1: Effect Aloe vera Juice and drugs Ethionamide and Para amino salicylic acid, on Sprague-Dawley rats

Groups (n=6)	Treatment
Group1	Animals fed with rat pellets and ordinary water
Group 2	ETH(132 mg/kg, p.o) for 28 days
Group 3	PAS(400 mg/kg, p.o) for 28 days
Group 4	ETH (132 mg/kg, p.o) + PAS(400 mg/kg, p.o) for 28 days
Group 5	ETH (132 mg/kg, p.o) + *Aloe vera* juice (90 ml/kg, p.o) for 28 days
Group 6	PAS(400 mg/kg, p.o) + *Aloe vera juice* (90 ml/kg, p.o) for 28 days
Group 7	ETH (132 mg/kg, p.o)+ PAS(400 mg/kg, p.o)+ *Aloe vera* juice (90 ml/kg, p.o) for 28 days
Group 8	only *Aloe vera* juice (90 ml/kg, p.o) for 28 days

E. Administration of Test Article

The each rat was given the test article at the specified concentration through a single oral gavage. A stainless steel intubation needle attached to a suitably graduated syringe was used to dose the animals. The volume of dosage administered to each rat was adjusted based on its most recent body weight. Weekly, the weights of the animals were measured along with their food consumption. The rats were randomly assigned to groups, with each group consisting of 6 rats (3 males and 3 females). The test drug and inducers were administered daily to the respective groups as outlined in the table for a period of 28 days. Blood samples were collected and analyzed for various biochemical parameters from the serum sample such as, Rate of food consumption, Relative rate of Kidney, Total Protein (mg/dL), Total Globulin (mg/dL), Albumin (mg/dL), Creatinine (mg/dL), Urea (mg/dL) and Blood Urea Nitrogen (mg/dL).

F. Statistical analysis

The data was subjected to statistical analysis using one-way analysis of variance (ANOVA). A significance level of $p < 0.05$ was considered statistically significant. The statistical analysis involved ANOVA, and the obtained p-value was less than .00001, indicating a non-significant result.

G. Biochemical assay

After 28th day of experimentation the blood was withdrawn and biochemical assessment of the kidney was carried out as Total Protein, Total Globulin, Albumin, Creatinine, Urea and Blood Urea Nitrogen (BUN) by standard methods.

H. Histopathological analysis:

The kidney tissues were fixed in 10% formalin, and dehydration of the tissue was done in gradual ethanol (50–100%) down gradation. Then the tissues were cleared in xylene, and embedded in paraffin. Five micron thick sections were prepared and then stained with hematoxylin and eosin (H–E) dye for photomicroscopic observation, including cell necrosis, fatty degenerative changes, hyaline regeneration, ballooning degeneration as proposed by [19] and histological structure of kidney tissue were examined under the Biological digital microscope Motic B1 Series.

RESULTS AND DISCUSSIONS:

Table-2: Represents the mean concentration of kidney Serum Biochemistry of Effect of Aloe verajoice and drugs Ethionamide and Para amino salicylic acid, on Sprague- dawley rats

Sr. No.	Group		R.Wt.of kidney	T.Prot	T.Glob	Albumin	Creat	Urea	BUN
			Gm	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
1	A- NC	Mean	2.182	7.66	3.53	4.13	1.12	67.24	31.42
		SD	0.370	0.78	0.55	0.48	0.18	4.83	2.26
2	B- ETH 132 mg/kg	Mean	2.478	8.73	4.11	4.62	1.27	88.58	50.36
		SD	0.588	0.85	0.79	0.52	0.23	4.83	1.44
3	C- PAS 400mg/kg	Mean	2.293	7.57	3.29	4.23	1.26	78.35	44.15
		SD	0.512	0.48	0.52	0.50	0.06	2.98	2.71
4	D- ETH+PAS 90 mg/kg	Mean	2.255	7.59	3.08	4.46	1.24	76.65	46.47
		SD	0.750	0.76	0.42	0.55	0.06	4.15	2.18
5	E- ETH+Aloevera juice 90mg/kg	Mean	2.362	8.22	3.39	4.83	1.18	69.21	37.55
		SD	0.785	0.62	0.74	0.97	0.08	3.64	4.23
6	F- PAS+ Aloe vera juice 90 mg/kg	Mean	2.245	8.08	3.72	4.35	1.18	68.27	35.22
		SD	0.412	0.70	0.55	0.48	0.07	5.47	5.91
7	G- ETH+PAS+ Aloe vera juice 90mg/kg	Mean	2.223	7.23	2.97	4.26	1.27	61.31	31.63
		SD	0.600	0.85	0.63	0.29	0.26	4.07	1.63
8	H- Only Aloe vera juice 90mg/kg	Mean	2.143	7.48	3.14	4.34	1.19	63.22	31.39
		SD	0.684	0.48	0.38	0.16	0.13	2.91	2.86

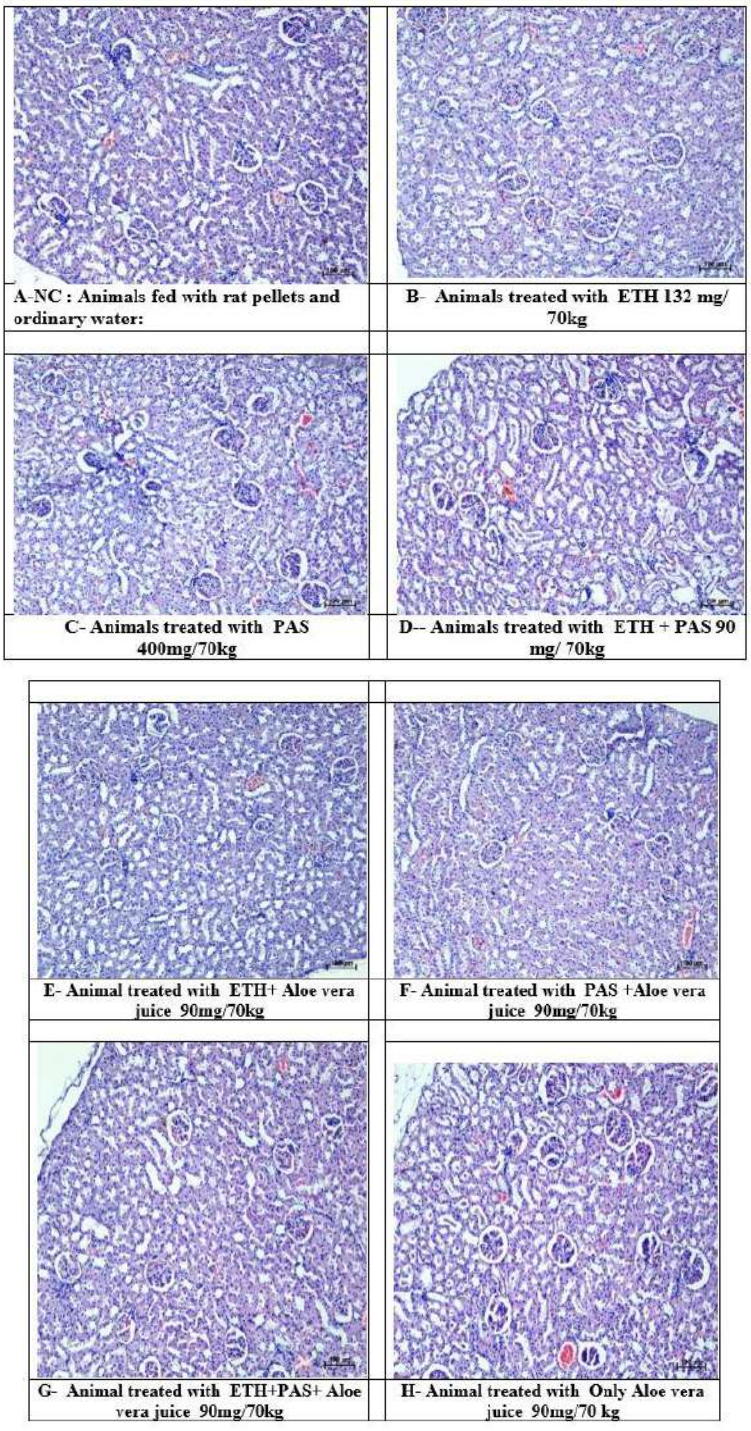
*Each value is the mean of 8 determinations.
R.Wt.of kidney: Relative rate og Kidney (Gm)
T.Prot : Total Protein (mg/dL)
T.Glob: Total Globulin (mg/dL)
Albumin: Albumin(mg/dL)
Creat: creatinine (mg/dL)
Urea: Urea (mg/dL)
BUN: Blood Urea Nitrogen (mg/dL)

The experiment was conducted up to 28 days. No mortality was noted in control and experimental groups. After 28 days the rats were sacrifices as per the CPCSEA guidelines. The blood was withdrawn from the cardiac puncture to estimate the kidney function test. The body weights and relative kidney weights were estimated by dissecting the kidney to calculate the difference in

weights of kidneys in control and experimental groups. The rate of consumption of food was also calculated at the interval of every 7 days up to 28th day of the study. The mean rate of food consumption (R=Remained, C=Consumed, C/A= Consumed / Animal Quantity of Food Given: 100) was calculated in every week in control and experimental group. The rate of food consumption was estimated in control group of rats was fond to be (R= 38.50 gm ± 4.95; C=61.50 gm ± 4.95 and C/A = 20.50 gm ± 1.65). The minimum food consumption was noted in PAS+ Aloe vera juice (R=60.25gm ± 6.72; C= 39.75 gm ± 6.72 and C/A = 13.25gm ± 2.24) group, whereas the maximum food consumption was observed in group treated with ETH+PAS+ Aloe vera juice (R= 40.75gm ± 5.30 C= 59.25gm ± 5.30 and C/A = 19.75 gm ± 1.77) respectively. The mean body weights were measured weekly (every 7 days) during the study. The mean body weight in normal control group is (292.5 gm ± 59.7). Amongst the experimental groups the minimum body weigh was found in animals treated with ETH+PAS+ Aloe vera juice (270.7 gm ± 51.0), where as maximum body weight was found in rats treated with ETH+ Aloe vera juice (314.0 gm ±49.1). The mean body weights present in animals treated with Aloe vera juice only was (276.8 gm ± 59.5). The mean relative weight of kidney in control group was calculated and was found to be (2.182 gm ± 0.370). In experimental rats the minimum weight of kidney was recorded in group treated with ETH + PAS+ Aloe vera juice (2.223gm ±0.600), whereas the maximum weight of kidney was noted in ETH (2.478 gm ± 0.588) group. The mean relative weight of kidney in animals treated with Aloe vera juice only was estimated as (2.143 gm0.684). Table-2: Represents the mean concentration of kidney Serum Biochemistry of Effect of Aloe verajoice and drugs Ethionamide and Para amino salicylic acid, on Sprague- dawley rats The mean total serum protein was recorded in normal control group was (7.66 mg/dL ±10.78). In case of treated groups, the minimum mean total serum protein was found in ETH + PAS + Aloe vera juice ((7.23mg/dL ±0.85)) groups; whereas the maximum mean total serum protein was found in animals treated with ETH (8.73mg/dL ±0.85). In case of animals treated only with Aloe vera Juice, the level of mean total serum protein was estimated as (7.48 mg/dL ±0.48).The mean total serum globulin was estimated in normal control group was (3.53 mg/dL ±0.55). The minimum mean total serum globulin was found in group treated with ETH + PAS (3.08 mg/dL ±0.42). The maximum mean total serum globulin was found in group treated with ETH (4.11 mg/dL ±0.79), whereas the group of animals treated only with Aloe vera juice , the mean total serum globulin was estimated as (3.14 mg/dL ±0.38). The mean total serum albumin was recorded in normal control group was (4.13 mg/dL ±0.48). In case of treated groups, the minimum mean total serum albumin was found in PAS (4.23 mg/dL ±0.50), whereas the maximum mean total serum albumin was found in ETH + Aloe vera Juice (4.83 mg/dL ±0.97). In case of animals treated only with Aloe vera Juice, the level of mean total serum albumin was estimated as (4.34 mg/dL ±0.16). The mean total creatinine was estimated in normal control group was (1.12 mg/dL ±0.18). The minimum mean total creatinine was found in group treated with ETH+ Aloe verajuice and PAS + Aloe vera juice (1.18 mg/dL ±0.8). The maximum mean total creatinine was found in group treated with PAS (1.26 mg/dL ±0.06), whereas the group of animals treated only with Aloe vera juice, the mean total creatinine was estimated as (1.19 mg/dL ±0.13). The mean total urea was estimated in normal control group was (67.24 mg/dL ±4.83). The minimum mean total urea was found in group treated with ETH+PAS+ Aloe vera juice (61.31 mg/dL ±4.07). The maximum mean total urea was found in group treated with ETH (88.58 mg/dL ±

4.83), whereas the group of animals treated only with Aloe vera juice, the mean total urea was estimated as (63.22 mg/dL ± 2.91). The mean total (BUN) was estimated in normal control group was (31.42 mg/dL ± 2.26). The minimum mean total (BUN) was found in group treated with ETH + PAS + Aloe vera juice (31.63 mg/dL ± 1.63). The maximum mean total (BUN) was found in group treated with ETH (50.36 mg/dL ± 1.44), whereas the group of animals treated only with Aloe vera juice, the mean total (BUN) was estimated as (31.39 mg/dL ± 2.86).

Photograph 1 (A- H): Showing Effect of Aloe verajoice and drugs Ethionamide and Para amino salicylic acid, on the histological alteration of the kidney of Sprague- dawley rats



Group- A: NC (Normal Control):

The Kidney showing normal histomorphological cellular features of renal tubules and glomeruli in the renal cortex and medulla region. There was an absence of inflammatory or pathological changes in renal parenchyma.

Group- B: Rats fed with ETH:

The Cortico-medullary regions of the kidney showed mild multi-focal areas of degenerative changes of renal tubules with cellular swelling. The kidney tubules and vacuolar cytoplasmic area showed moderate changes. Some of the proximal and distal tubules showed loss of tubular epithelium while few tubules showed cellular swelling with enlarged nucleus. It was also found the changes in granular cytoplasm. The renal tubules showed accumulation of eosinophilic debris in the lumen. Focal areas with dilation of renal tubules and cystic changes were noted. The glomeruli were found sparse and appeared hypertrophied with congested appearance. Moderate nephropathic cellular changes were observed with interstitial hemorrhages and congested vascular tissue in the renal cortex and medulla was noted.

Group- C: Rats fed with PAS:

The kidney showed focal congestion of vessels in renal parenchyma. There were mild changes in the foci and tubular degeneration of the renal tubules were seen. The presence of granular cytoplasm with cellular swelling was found in the epithelium of tubules. The mild focal hypertrophies of glomeruli were also noted. Few of renal tubules showed accumulation of eosinophilic debris in the lumen. The focal areas with dilation of renal tubules and cystic changes were noted.

Group- D: Rats fed with ETH + PAS:

The focal congestion in the renal vessels and renal parenchyma was seen. The mild foci of tubular degeneration with cellular swelling in renal tubules were observed. The presences of granular cytoplasmic changes in the epithelium of tubules were also seen with focal hypertrophy of glomeruli cells were observed. Very little number of renal tubules showed accumulation with the formation of eosinophilic debris in the lumen. Focal areas with dilation of renal tubules and cystic changes were also noted.

Group- E: Rats fed with ETH+ Aloe vera juice:

The renal parenchyma in cortex and medulla showing the normal histopathology with normal renal pelvis. Cortex showed normal size of glomerular tissue with focal congested vascular tissue and renal tubules. The renal tubules showed intact tubular epithelium with intact nucleus with normal cellular borders. The mild disturb focal areas with degeneration of few renal tubules and accumulations of eosinophilic debris in lumen were noted. Minimal pathological inflammatory changes were noted in the glomerular cells and renal tubules of kidney sections.

Group- F: Rats fed with PAS +Aloe vera juice:

The minimal focal congestion in the vessels of renal parenchyma was observed. The focal areas of the renal tubules showed minimal cellular swelling. The presences of granular cytoplasmic changes in the epithelium of tubules were also noted. The few proximal and distal tubules cellular swelling with enlarged nucleus and granular cytoplasm was observed. Focal areas with accumulation of eosinophilic debris with urinary calculi and crystal formation in the lumen of renal tubules were noted.

Group- G: Rats fed with ETH+PAS+ Aloe vera juice:

The Kidney showing normal histomorphological cellular features of renal tubules and glomeruli in the renal cortex and medulla region were observed. No inflammatory or pathological changes were noted in renal parenchyma.

Group-H: Rats fed with Aloe vera juice only:

The Kidney showing normal histomorphological cellular features of renal tubules and glomeruli in the renal cortex and medulla region were seen. No

inflammatory or pathological changes in renal parenchyma were noted. Drug induced toxicity paid an attention to the protective effect of natural antioxidants extracted from the plant [20]. The organic leaf extract of Aloe vera in vivo showed antioxidant property [21]. It was found that the organic extract of Aloe vera provided anti-inflammatory activity in rats [22. Aloe vera also showed potential therapeutic agent against the toxicity induced by drugs[23]. Many researchers have given an evidence that HDL cholesterol is inversely related to the total cholesterol there by reduction of plasma HDL cholesterol may increased the development of atherosclerosis leading to ischemic heart disease, by impairing the clearing of cholesterol from arterial wall [24,25]. The impaired kidney functions are associated with an elevated level of urea due to which it increased the amino acid metabolism by inducing the nephrotoxicity in rats [26,27].The administration of Aloe verajel in toxicity induced by OTA in rats showed decreased in the body weight, FER, HDL-C and increased levels of total cholesterol, triglycerides, LDL-C and VLDL-C. After administration of OTA in combination with Aloe vera gel, lowered the levels back to normal. This may be because of the presence of antioxidant property of Aloe vera gel which increased the level of HDL and decreasing the level of TC, TG, LDL, and VLDL to normal. The Aloe vera gel attenuated to near normal in rats, which may be due to minimized OTA toxicity, which might be associated with disorders in intra renal prostaglandins and abnormalities in the renal nitric oxide system induced by lipid peroxidation or its effect on renal cells based on the oxidative stress action and enhancing renal functions [28]. In another study demonstrated that Aloe vera gel can ameliorate the dependent of oxidative stress to protect against OTA- induced nephrotoxicity. The rats showed increased production of kidney biomarkers, and thus it increase the nephroprotective effect by restoring the antioxidant enzyme concentration near to normal level by decreasing the secretion of MAD and increasing the level of Vitamin E, GSH, SOD, CAT and GPx when rats treated with Aloe vera gel [29]. Significant renal damage was observed in rats fed with cadmium. The renal damage was associated with an increased levels of serum enzymes particularly urea and creatinine. [30] Reported reversal of cadmium induced biochemical changes in kidney when Naringenin co- administered with cadmium. Neringenin and Allium ascalonicum showed nephroprotective effect by lowering the kidney serum biomarkers against nephrotoxicity induced by cadmium and cyclosporine induced renal damage respectively [31]. The F. religiosa showed nephroprotective effect. This might be because of the presence of active constituents such as tannins, saponins, flavonoids, and glycosides that might be responsible for nephroprotective activity [32]. The alcoholic extracts of silymarin and F. religiosa stem bark have shown the nephroprotective property against nephrotoxicity induced by RIF+INH [33]. The rat pretreated with Aloe vera gel for a week lowered the kidney serum biomarkers against nephrotoxicity induced by acetaminophen. The extract of Aloe vera gel provides significant protection by improving the tubular necrosis, glomerular congestion, and helped to improve the biochemical parameters [34].The studies on turmeric (C. longa) aqueous extract showed hepatp and nephro protection against INH and RIF induced toxicity [35]. Curcumin, the major phenolic compound in turmeric, showed preventive effects against various diseases. Curcumin has antioxidant effects and inhibits extracellular matrix formation by increasing matrix metalloproteinase expression and suppressing connective tissue growth factor expression through peroxisome proliferator-activated receptor gamma [36, 37]. Curcumin

induced downregulation of cyclooxygenase-2 involved in chronic inflammation, hemodynamics, tumorigenesis, renal function, and hepatic fibrogenesis[38]. S. fusiformis treatment showed reversal changes in histo- architecture of kidney by lowering serum biomarkers, urea and uric acid, creatinine, and also found the reversal changes in the antioxidant status of the kidney against nephrotoxicity induced by INH and RIF in rat[39]. The pretreatment of lead acetate induced significant elevation of serum creatinine and BUN activities. It is demonstrated that the lead acetate treatment induced impaired renal function by inducing nephrotoxicity [40]. High level of serum, creatinine and BUN in blood caused kidney damage [41]. The active constituent piperin showed neproprotection by improving the level of creatinine and BUN levels against toxicity induced by lead acetate induced nephrotoxicity [42]. The Piper longum Linn decreases the lipid peroxidation in serum, liver, kidney and also insignificantly increases the level of GSH glutathione in tissue against monosodium glutamate (MSG) oxidative stress in rats [43]. The rats pretreated with ETH and PAS showed elevated levels of serum albumin, urea, creatinine, and blood urea nitrogen (BUN), whereas the rats pretreated with Piper nigrum in combination with the ETH and PAS found significantly decreased in serum albumin, (BUN), creatinine, and urea, confirms the nephroprotective role of Piper nigrum against nephrotoxicity induced by ETH and PAS [44]. In our present study, the mean food consumption rate, mean body weights, and mean relative weights of kidney was calculated in normal control and the rats treated groups. The results of the present study demonstrated that, statically no significant difference ($p<0.001$) was noted in mean rate of food consumption, mean body weights and mean relative weight of kidney, when compared with the normal control groups. The maximum mean total serum protein was found in rats fed with ETH as compared to the normal control group and the rats treated with Aloe verajuice. The level of total serum protein was found increased but the statistically no significant difference ($p<0.001$) was noted when compared with control group. The maximum mean total serum globulin was found in group treated with ETH. The minimum mean total serum globulin was found in group treated with ETH + PAS, when compared with the normal control group. The level of total serum globulin was found increased but the statistically no significant difference ($p<0.001$) was noted as compared to control group and the rats fed with Aloe vera juice. The maximum mean total serum albumin was found in rats fed with ETH + Aloe vera Juice, and the minimum mean total serum albumin was found in rats treated with PAS when compared with normal control group and the rats treated with Aloe vera juice. Statistically no significant difference ($p<0.001$) was noted. The maximum mean total creatinine was found in PAS and minimum mean total creatinine was found in ETH+ Aloe vera juice and PAS + Aloe vera juice, when compared with control group and the rats treated with Aloe vera juice. Statistically no significant difference ($p<0.001$) was noted. The maximum mean total urea in experimental rats was found in ETH and minimum mean total urea was found in ETH+PAS+ Aloe vera juice, when compared with normal control and Aloe vera juice treated group. Statistically significant increased in difference ($p<0.05$) was noted when compared with the treated rats and normal control group and rats treated with Aloe vera juice treated group. The maximum mean total blood urea nitrogen (BUN) was found in ETH and minimum mean total blood urea nitrogen (BUN) was found in ETH + PAS + Aloe vera juice treated groups, when compared with normal control group and the Aloe vera juice treated groups. Statistically significant increased in difference ($p<0.05$) was noted when compared

with the treated rats and normal control group and Aloe vera juice treated group.

CONCLUSION:

The current study shows that administration of ETH and PAS induced renal dysfunction in of Sprague- dawley rats. The Aloe vera juice co-administered rats provide adequate protection against nephrotoxicity. Therefore it was concluded that ETH and PAS caused nephrotoxicity in Sprague- dawley rats. From the above review it reveals that the biomarkers give adequate information to diagnose the nephrotoxicity more selectively. Biomarkers play a significant role in the development of new drug . Therefore further studies are needed to enhance our compression of the exact mechanism of ETH and PAS induced nephrotoxicity which is a second line highly threatening drug induce complication among TB-patients.

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CONFLICTS OF INTEREST:

There are no conflicts of interest

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