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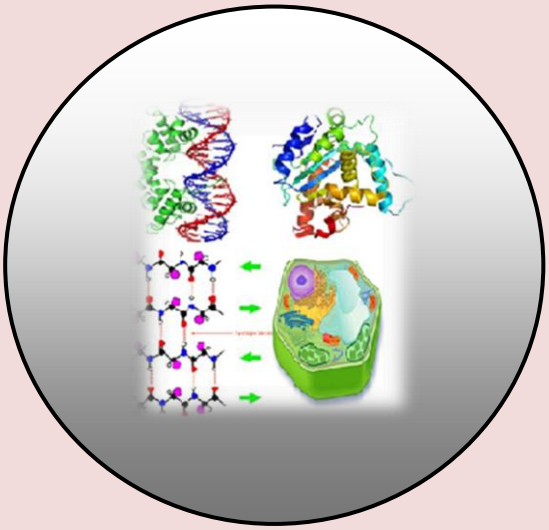

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Effect of Leaf Extract of *Ziziphus nummularia* on Liver and Kidney of Swiss Albino Mice exposed to Dimethoate

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ABSTRACT

Plant materials are a primary source of health care for the World's large population. Medicinal plants, both endemic and widespread, their resources and knowledge about their usage must be preserved since these plants could be renewable source for new drugs. It is known that chemicals and chemical reagents are typically non-renewable, and their use depletes our future resources. Today a need to focus on plant product to develop new generation drugs without harming the environment.

Dimethoate widely used pesticides, spray on vegetables, fruits through fruits and vegetables pesticides enter in living being and effect vital organ as like liver and kidney and damage these organs. The leaf extract of Ziziphus nummularia have antibacterial, antifungal, anti-cancer activity and also have healing activity of liver and kidney. There are ten groups' of swiss albino mice, five groups of 70 days (G A) and five groups of 105 days (GB). First group control, Group 2.Dimethoate treated (30 mg/kgbw) 3.Dimethoate 30 mg/kgbw +leaf extract of Ziziphus nummularia (250 ml/kgbw), 4. Dimethoate 15 mg/kgbw. 5. Dimethoate 15 mg/kg + leaf extract of Ziziphus nummularia (250 ml/kgbw). Dimethoate treated group shows the ALT, AST, ACP, ALP, urea and creatinine value significantly increased ($p<0.05$). There were differences in ZNLE treated groups shows decrease in ALT, AST, ALP, ACP, urea and creatinine values.

Key word: ACP, ALT, AST, Dimethoate, Liver and Kidney.

INTRODUCTION

Medicinal plants contain a wide variety of secondary metabolites or compounds such as tannins terpenoids, alkaloids, flavonoids, that have the therapeutic potency of the plants. [Evans 2002]. A wide range of physiological activity of saponins, steroids, phenols and tannins are found to be more predominant and therefore may be responsible for the antimicrobial action (Sule 2010).

Dimethoate is a compound called organophosphate and class II organic pollutants. Dimethoate is an insecticide used to kill mites and insects systemically and on contact. It is used against a wide range of insects, including aphids, thrips, plant hoppers and whiteflies, on ornamental plants, apples, corn, cotton, grapes, lemons, melons, oranges, pears, sorghum, soybeans, tangerines, tobacco, tomatoes, watermelons, wheat and other vegetables. Dimethoate has been administered to livestock for control of botflies. Dimethoate is available in aerosol spray dust, emulsifiable concentrate, and ULV concentrate formulations. Acute toxicity of Dimethoate is moderately toxic by ingestion, inhalation, dermal absorption. The organophosphate insecticides are cholinesterase inhibitors. The first effect usually respiratory, bloody runny nose, coughing. Eye contact will cause pain, bleeding, tears, pupil constriction, and blurred vision. *Ziziphus nummularia* is Indian medicinal plants are traditionally and carefully selected to curb against various ailments. Among the family Rhamnaceae is a very alternatives common tree in Rajasthan with a rich historical and religious background the roots, bark, and leaf of this plant are used in the treatment of a wide range of ailments, these include arthritis, chest pains, boils, liver diseases and gastrointestinal problems. *Ziziphus nummularia* leaves and fruits are used for cold, diarrhea, dysentery, indigestion, inflammation of gums and tonic. The leaves are antipyretic and reduce obesity. The of aim present study to find out the curing properties of leaf extracts of *Ziziphus nummularia* on target organs viz. liver and Kidney of swiss albino mice affected by Dimethoate.

MATERIAL AND METHODS

Healthy albino mice of age group (70 days and 105 days of 52.65+_2.41 and 61.09+_2.89 grams respectively) were taken for experimental study. They were acclimatized to laboratory condition (room temp 25 +_5C RH 50+_10%) for two week before starting the experiment. Swiss albino mice were divided in to Group A and Group B according their age as 70days (Group A) and 105 days (Group B), and each group again divided in to five subgroup as –

G1A - control group, age of 70 days. G2A- Dimethoate treated group (30 mg /kgbw day^{-1}) age of 70 days. G3A. Dimethoate + ZNLE treated group (30 mg/kg.bw) day^{-1} and after 60 min *Ziziphus nummularia* leaf extract (250 mg/kg.bw day−1) age of 70 days. G4A. Dimethoate treated group (15mg/kg.bw.) $day^{-1]}$ of age 70days. G5A. Dimethoate +ZNLE treated group (15 mg/kg.bw) day^{-1} and after 60 min *Ziziphus nummularia* leaf extract(250mg/kg.bw) day^{-1} of age 70 days.

G1B. Control group age of 105 days, G2B. Dimethoate treated group (30 mg/kg.bw) day^{-1} age of 105 days, G3B. Dimethoate +ZNLE treated group (30 mg/kg.bw) day^{-1} and after 60 min *Ziziphus nummularia* leaf extract (250 mg/kg.bw day^{-1}) age of 105 days, G4B. Dimethoate treated group (15 mg/kg.bw.) day^{-1}age of 105 days, and G5B. Dimethoate + ZNLE treated group (15 mg/kg.bw) day^{-1} and 60 min after *Ziziphus nummularia* leaf extract (250 mg/kg.bw) day^{-1} age of 105 days.

After the experimental period the animals sacrificed, the blood was collected and centrifuged to obtain serum and kept at 21 ^{0}C for biochemical test.

Biochemical Assay- ALT measured according to IFCC (1972) method. AST evaluation based on IFCC (1980).

AST is a pyridoxal phosphate (PLP) dependent enzyme that catalyzes the conversion of Aspartate and alpha- ketoglutarate to oxaloacetate and glutamate. ACP determines by UV kinetics method (2008).ALP determines by UV kinetics method (2008).Urea determines by Thomas 1998 b method. Serum creatinine by kinetic test (Newman and price, 1999) method.

Statistical Analysis

Observed values were expressed as Mean+-SD. Total variations present in the data were estimated by unpaired t test by using R software[R version 3.4.1. (2017-6-30)] – "Single candle". Differences at p <0.05 were considered as statistically significant.

Table 1

Group A value are given in Table 1.- Effect of ZN leaf extract on hepatic enzyme and kidney of Dimethoate treated mice(70days). Value are expressed as mean ± SEM, n=5 for each treatment group P>0.5 consider highly significant compare to control. GA 1- control group age of 70 days.GA2- Dimethoate treated group (30 mg /kgbw day^{-1}) age of 70 days. G3A.

Groups	ALT(U/L)	AST(U/L)	ACP(U/L)	ALP(U/L)	UREA (mg/dl)	CREATININE mμol/l
G1A	52.12± ±2.12	56.42 ± ±3.45	90.4± ±1.14	107 ± ±0.548	23.06± 1.7	46.15± 1.75
G2A	102.86± ±2.15	92.15 ± ±2.46	110± ±1.14	164 ± ±.707	32.90± 4.23	82.15± 4.4
G3A	70.82± ±1.24	69.26 ± ±.02	93.6± ±0.894	110 ± ±.894	23.60± 2.05	62.80± 7.66
G4A	82.14± ±1.48	79.12 ± ±1.44	94.2± ±0.447	129 ± ±0.548	28.94± 2.02	52.72± 1.7
G5A	68.92± ±1.44	62 ± ±1.81	91.4± ±0.84	105 ± ±0.894	21.92± 2.51	53.79± .42

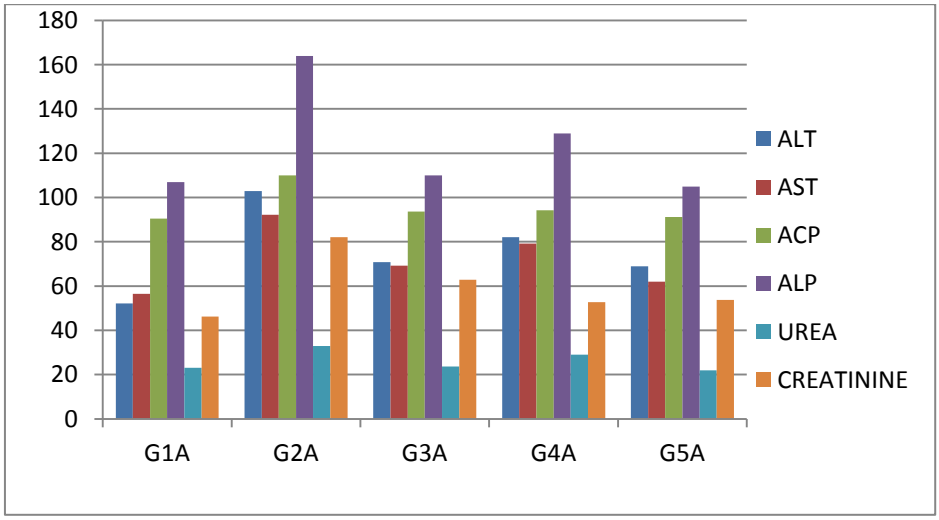

Figure 1. Graphical representation of data table 1.

Dimethoate +ZNLE treated group (30 mg/kg.bw) day^{-1} and after 60 min *Ziziphus nummularia* leaf extract (250 mg/kg.bw day−1 age of 70 days. G4A. Dimethoate treated group (15mg/kg.bw.) day^{-1}] of age 70days, G5A. Dimethoate+ ZNLE treated group (15 mg/kg.bw) day-^{1} and after 60 min *Ziziphus nummularia* leaf extract(250mg/kg.bw)day-^{1} of age 70 days. ZNLE-*Ziziphus nummularia* leaf extract.

Table 2

Group B values are given in Table 2- Effect of ZN leaf extract on hepatic enzyme and kidney of Dimethoate treated mice (105days). Value are expressed as mean ± SEM, n=5 for each treatment group P>0.5 consider highly significant compare to control. G1B. Control group age of 105 days, G2B. Dimethoate treated group (30 mg/kg.bw) day^{-1} age of 105 days, G3B. Dimethoate+ZNLE treated group (30 mg/kg.bw) day^{-1} and after 60 min *Ziziphus nummularia* leaf extract (250 mg/kg.bw day^{-1}) age of 105 days, G4B. Dimethoate treated group (15 mg/kg.bw.) day^{-1}age of 105days, and G5B. Dimethoate + ZNLE treated group (15 mg/kg.bw) day-^{1} and 60 min after *Ziziphus nummularia* leaf extract (250 mg/kg.bw)day-1] age of 105 days.

Groups	ALT (U/L)	AST(U/L)	ACP(U/L)	ALP(U/L)	UREA (mg/dl)	CREATININE µmol/l
G1B	45.18± ±1.48	48.16± ±1.24	120± ±0.548	120± ±0.548	24.08± 2.86	44.96± 1.7
G2B	98.98± ±2.48	104.14± ±2.54	190± ±0.894	190± ±0.894	34.48± 1.55	102.34± 3.26
G3B	68.18± ±1.68	69.23± ±2.14	101± ±0.447	124.80± ±0.837	23.73± 2.40	63.11± 1.57
G4B	101.12± ±3.46	85.16± ±3.21	110± ±1.22	140± ±1.79	30.16± 1.49	57.54± 1.72
G5B	65.12± ±3.32	56.12± ±2.26	102± ±0.837	120± ±0.894	19.76± 1.23	52.12± .41

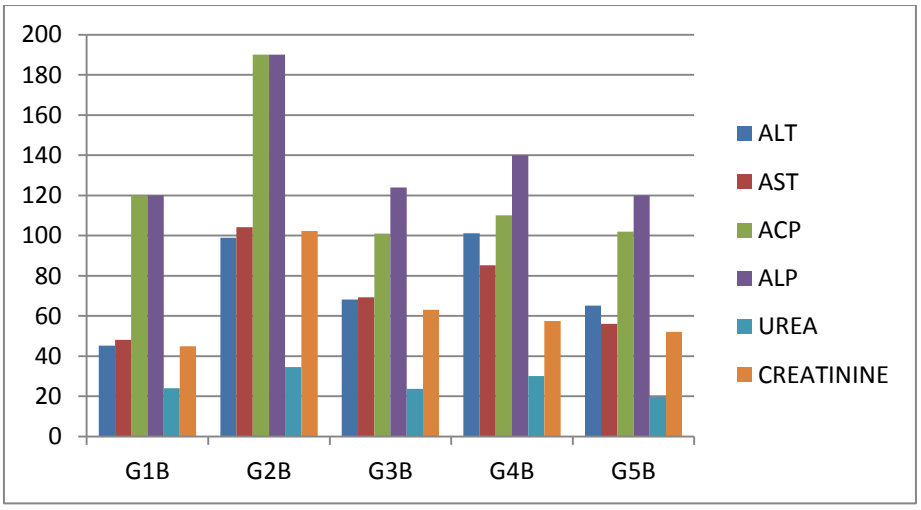

Figure 2. Graphical representation of data table 2.

RESULTS

Oral administration of Dimethoate with 30 mg/kgbw of 70 day aged Mice (G1A-G2A) caused highly significant increase in ALT (97%), AST (63%), ACP (21%), and ALP (53%).

In the group of 105 days aged mice (G1B-G2B) treatment with 30 mg/kgbw Dimethoate a significant increase occurred in ALT (119%) AST (116%) ALP (58%) ACP (58%). Administration of dimethoate 15 mg /kgbw to the 70 days aged mice (G1A-G4A) a significant increase occurred in AST, ALT, ACP, and ALP. The result of present study showed that highly significant increase in ALT, AST, ALP, and ACP, in Dimethoate treated groups. ALT significantly increases about 97 % in G2A group in compare to control. (t value 6. 23). Treatment of ZZLN leaf extract in G3A group decrease ALT value 31% compare to G2A. (t value 3.26).

The comparison in G4A and G5A, ALT value decrease 16 % in G5A group. AST value significantly increase in G2A group 63 % (t=5.25) compare to control.AST value significantly decrease 24 % (t value 4.25) in G3A group (G3A-G2A) .compare in G4A and G5A group AST value decrease 21 % (6.26).ACP value significantly increase in G2A group about 17%.(t value 26.62)in compare to control. Comparison in G2A and G3A group ACP value significantly decrease 21.68 % (t value 24.68). ZNLE treatment in G5A group decrease ACP value significantly 2.9 %. (t value 6.26). ALP value significantly increases about 53 % (t value 143.5) in G2A group (G2A-G1A). Comparison in G2A and G3A group ALP value decrease about 32 % (t value 16.69). In G5A group ALP value decrease 18% (t value 51.16) significantly (G5A-G4A).

In G2B group ALT value increase about 119.07 % (t=45.3) in compare to control. Comparison in G2B and G3B group ALT value decrease about 31.11 % (t=21.23). ALT value decrease about 35.60 % (t=6.56) in G5B group compare to G4B group. AST value increase in G2B about 116.23 % (t=53.23) compare to control. Compare to G2B and G3B the AST value decrease about 33.52 % (t=6.34). In G5B group AST value decrease about 34.10 % (t=5.96) compare to G4B. ALP value increase about 58.33 %(t=149.24) in G2B group compare to control. ALP value decrease about 34.315 % (t=119.77) in G3B compare to G2B .In G5B group the ALP value decrease about 22.58 % compare to G4B (t=22.58). ACP value increase in G2B group 58% (t=149.24) compare to control .healing properties of ZZLN leaf extract in G3B group decrease value of ACP 46% (t=48.58).Comparison in G5B and G4B ACP value decrease about 7.2%(t=12.36).

Dimethoate toxicity elevates the urea value in G2A group 32.90 mg/dl about 42 % in compare to G1A. In ZNLE treated group (G3A-G2A) urea value decrease and value near to control 23.60mg/dl .In G4A its uremia condition value is 28.94 mg/dl. The treatment of ZNLE in G5A urea value decrease to 21.92 mg/dl. Treatment of ZNLE (G3A-G2A) and (G5A-G4A) group decrease urea value 28% and 24% respectively. In 105 days aged mice dimethoate treated group (G2B) urea value elevated 24.08 mg/dl in comparison of control about 43% increase. Comparison in G3B and G2B urea value decrease 31% in G3B urea value 23.73mg/dl. In G5B urea value 19.76 and G4B urea value 30.16mg/dl decrease about 54%. creatinine value increase in G2A 82.15 µmol/l in compare to G1A 46.15 µmol/l approx 78%. (t=12.32).Comparison in G3A 62.80 µmol/l and G2A creatinine value decrease 25.37% (t=8.24). In G5A creatinine value 53.79 µmol/l in G4A creatinine value 52.72 µmol/l increase in G5A 2.02 %.

In 105 day aged mice in G2B group creatinine value elevated 102.34 µmol/l in compare to G1B 44.96 µmol/l approx 113 % increase(t=6.64). In G3B creatinine value 63.11 mol/l. In G3B the creatinine value 38% significantly decrease(t value 9.4) compare to G2B .In G4B creatinine value 57.54 µmol/l and decrease in G5B 52.12mol/l about 9.2% .(t=2.73).

CONCLUSION

The need of the present time is to use the isolated phytochemical, which can replace synthetic and costly medicine and attract the interest from large pharmaceutical companies. This paper provides review of information regarding ethnomedicinal uses of *Ziziphus numularia*, with the purpose to drawing scientific focus toward this medicinal plant. Zizynummin, a new dammarane saponin isolated from dried leaves of *Ziziphus nummularia*, has been assigned the structure β-D glucopyranosyl-(1→2)-6-deoxy-α-L-talopyranosyl-(1→3)-α-Larabinopyranosyl-(1→3)-jujubogenin.(Khan S 2017). The leaves are antipyretic and reduce obesity. The fruit is cooling, tonic, digestible, laxative aphrodisiac and removes biliousness, thirst, vomiting and burning

Organophosphorous a pesticide induces lipid peroxidation. Lipid peroxidation has been extensively used marker of oxidative stress. According to Ahmed.et.al (2000) large numbers of xenobiotics have been identified to have a potential to generate free radicals in biological system. In our study we have investigated the lipid peroxidation increased due to dimethoate. In the present study oral administration of Dimethoate to mice, caused a significant hepatic damage, as observed from the elevation of hepatic enzymes ALT, AST, ALP, ACP in serum. A significant elevation of AST, ALT, ACP, ALP is an indicator of liver damage. The result of present study showed that the treatment with dimethoate significantly (P<0.05) increased the activities of AST, ALT, ALP, ACP, Urea, creatinine in serum compared to control mice. The present study strengthens the hypothesis and suggests that the induction of oxidative stress is perhaps the central mechanism by which OP pesticides exert their cellular action. Oxidative damage primarily occurs through production of reactive oxygen species, including hydroxyl radicals and hydrogen peroxide that subsequently react with biological molecules as well as causing damage to membranes and other tissues (Banerjee *et al.*, 1999).

Dimethoate-intoxicated mice showed disorders in renal function witnessed by increased urine output and changes in creatinine, urea and uric acid levels. Compared to controls, creatinine levels in treated mice were three-fold higher in serum of dimethoate-intoxicated mice. Dimethoate treatment led to a reduction in creatinine clearance, an indicator of Glomerular dysfunction in adult mice. Treatment of mice with ZNLE significantly (P<0.05) reduced creatinine concentration compared to dimethoate-treated mice .The ameliorative properties of ZNLE treated groups showed the highly significant decrease in AST, ALT, ACP ALP, urea, creatinine. Pesticide causes liver damage and leakage of cytosolic enzymes from hepatocytes and other body organs into the blood.

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