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Central European Journal of Experimental Biology, 2013, 2 (1):27-32
(http://scholarsresearchlibrary.com/archive.html)

ISSN: 2278–7364

Pefloxacin and antioxidant interactions of vitamins C, E and garlic, on serum enzymes and histological tissues in Albino wistar rats

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ABSTRACT

The hepatic and some serum enzymes activity of garlic, antioxidant vitamins C and E on pefloxacin-induced toxicity in wistar rat were evaluated. Method: One hundred adult wistar rats (120-180), of either sex were randomly selected into five study groups. Each group comprised of 10 pairs (ten males and ten females) were not allowed to mate, with group 1 as control. Group 11 were pefloxacin treated only while group 111 to 1V were pefloxacin treated with either garlic, vitamins C and E. Pefloxacin, garlic vitamin C and E in doses 11.43mg/kg, 4.28mg/kg, 14.29mg/kg body weight in normal saline (vehicle) was administered orally by intubation to both male and female of groups 11 to V for 14 days. Control animals received 0.5ml of normal saline. In life observation measurements were taken and at the end of drug, garlic, antioxidant vitamins C and E combined administration animals were sacrificed and tissues obtained for biochemical assessment. The effect of pefloxacin only, pefloxacin in diet with antioxidant vitamins C, E and garlic supplements respectively on the activity of serum enzyme aspartate aminotransaminase, alanine aminotransaminase, alkaline phosphotase, acid phosphotase, prostatic acid phosphotase, Pefloxacin administration induced a significant ($P<0.05$) increase in the activities of AST and ALT in male and female rats relative to the control. There was a significant ($P<0.05$) decrease in AST and ALT of all the antioxidant supplemented groups.

Key words: Pefloxacin, garlic, vitamins C and E, serum enzymes and histological.

INTRODUCTION

Quinolones are very toxic antibiotics and they are not biological products but purely synthetic compounds that exact cidal or static effect on pathogens in the body system [1]. The whole problem with quinolones emerged from their narrow safety profile which is rarely respected. Although it is difficult to objectively establish the limits of what could be called safe or unsafe, it is crystal clear that clinical practice for prescribing quinolones is generally far beyond safety margins. The inadequate and risky practice of quinolones lies in prescribing doses longer than necessary [2].These drugs are distinctive in the sense that majority of the damages remain unnoticed for many weeks or months and do not inform the patient to top the treatment but only enhanced more clinical symptoms [3]. High

doses or prolonged administration causes a disproportionate percentage of adverse effect but most times public are denied of this clinical report [1].

Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are commonly used as indicators of hepatocellular damage. These enzymes are present in the liver in high concentrations and in conditions of hepatic intoxications, leak into circulation thus increasing the serum level of the enzymes [4]. The increase in concentration of these enzymes may be due to acute hepatocellular damage which may terminate into circulation. The extent of aminotransferase elevations depends on the severity of damage, which invariably cause an increase in cell permeability.

Garlic is reported to have diaphoretic, expectorant, antispasmodic, antiseptic, bacteriostatic, antiviral, hypotensive and antihelmintic properties, and to be a promoter of leukocytosis. Traditionally, it has been used as a potent therapeutic agent against chronic bronchitis, respiratory catarrh, recurrent colds, whooping cough [5]. Modern applications of garlic and its preparations is focused on their reputed antihypertensive, antiartherogenic, antithrombotic, antimicrobial, fibrinolytic, cancer-preventive and lipid-lowering effects [6] and [7]

MATERIALS AND METHODS

The drugs:
Pefloxacin injection (400mg/5ml), garlic supplement (300mg/5ml), vitamins C and E supplement (1000mg/ml) respectively were obtained Rabana Pharmacy, Calabar and used for the study.

***Experimental animals and treatment protocol*:**
One hundred mature albino wistar rats of both sexes, weighing between 120-180g obtained from the disease free stock of the animal facility of Biochemistry Department, University of Calabar, Calabar, Nigeria were used for the study. Prior to experimentation, permission for the use of animals and animal protocol was obtained from the facility of Basic Medical Science animal ethics Committee, University of Calabar.

The animals were randomly selected based on average body weight into five study groups of 20 animals (10 males and 10 females) per group.

Each male and female of the study group was housed differently in a stainless cages of dimension 15m x 15m, with plastic bottom and wire screen top and were housed 10 animals per cage.

The animal room was adequately ventilated and kept at room temperature and relative humidity of 29 ± 2^0 C and 40-70% respectively with 12 hours natural light/dark cycle. Rat chow (Pfizer feeds Nigeria Ltd, Calabar, Nigeria), and water were given to the animals *ad-libutum*. Good hygiene maintained by constant cleansing and removal of waste products of metabolism and spilled from cages daily.

Group 1 served as the control and groups 11 to V were pefloxacin, garlic, vitamin C and E supplemented groups.

Pefloxacin, garlic, vitamins C and E supplements in dose 11.43mg/kg, 4.28kg/ml and 14.29mg/kg body weight in normal saline were co-administered via oral route by intubation to animals of the test groups 11-V while control received 0.5ml of normal saline for 14 days. Dose administration was done between the hours of 0.90am and 10am daily and the doses calculated corresponds with therapeutic dosage in humans of 800/70kg, 300/70kg and1000kg body weight respectively.

In test group 11, male and female animal were treated with pefloxacin but not allowed to mate. In test group 111 to V, pefloxacin, garlic, vitamins C and E supplements were co-administered to male and female animals but not allowed to mate.

The animals were checked daily to ascertain for number of dead animals. Clinical signs of over poisoning such as hair coat, motor activity and state of feces were observed. Urine colour was also monitor daily. The animals were weighed at the commencement of the experiment and thereafter weekly to assess body weigh gains and growth rate.

Estimation of Serum Aspartate and Alanine Transaminase enzyme

Serum aspartate and alanine aminotransaminases were determined by catalytic activity from the rate of decrease in NADH measured at 340nm by malate dehydrogenase (MDH) in AST and lactate dehydrogenase (LD) coupled reaction for ALT (Reitmann and Frankel method, 1957).

Histological Analysis:

The method of Drunny and Wellington (1980) was used for the histological analysis.

Statistical analysis

Data generated were analyzed for statistical significance by one way ANOVA and t-test of the SPSS (Statistical Package for Social Science) statistical programme using the Microsoft (MS) excel programme. All data were expressed as Mean ± SEM and the probability tested at 95% level of confidence so as to established research hypothesis.

RESULTS

Table 1 Effect of pefloxacin in diet supplemented with garlic and antioxidant vitamins C and E on male rat serum aminotransaminase

Group	Treatment	Aspartate aminotransaminase ()	Alanine aminotransaminase ()
1	Normal Control (water)	45.4 ± 0.17	29.3 ± 0.27
2	Pefloxacin Control	57.2 ± 0.36^{f}	39.4 ± 0.28^{f}
3	Pefloxacin +vitamin C	48.1 ± 1.28^{g}	29.4 ± 0.62^{g}
4	Pefloxacin + vitamin E	51.2 ± 2.84^{g}	32.5 ± 1.55^{g}
5	Pefloxacin + garlic	46.1 ± 1.24^{g}	30.7 + 1.33^{g}

Value are expressed as Mean ±SEM, n =10,

f = *Indicates significant difference in the effect of pefloxacin (only) in diet compared with the control at (P < 0.05) level of confidence.*

g = *Indicates significant difference in the effect of diet with pefloxacin supplemented with antioxidant vitamins when compared with diet with pefloxacin only at (p<0.05) level of confidence.*

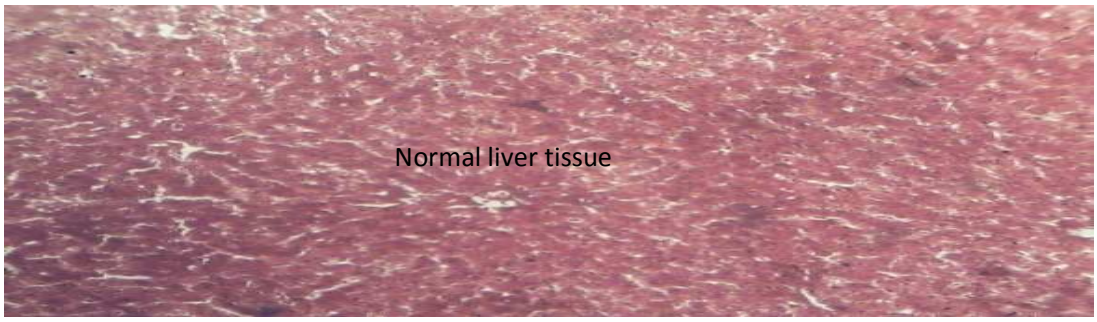
Table: 2 Effect of pefloxacin in diet supplemented with garlic and antioxidant vitamins C and E on female rat serum aminotransaminase

Group	Treatment	Aspartate aminotransaminase	Alanine aminotransaminase
1	Normal Control (water)	48.0 ± 0.22	31.5 ± 0.53
2	Pefloxacin Control	61.1 ± 0.11^{f}	43.5 ± 0.18^{f}
3	Pefloxacin +vitamin C	50.0 ± 0.95^{g}	32.3 ± 0.00^{g}
4	Pefloxacin + vitamin E	54.2 ± 2.97^{g}	35.2 ± 1.66^{g}
5	Pefloxacin + garlic	52.8 ± 2.55^{g}	34.5 ± 2.10 ^{g}

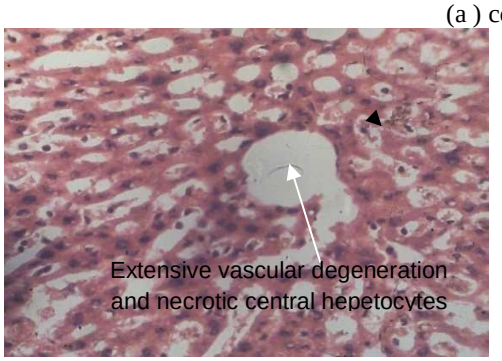
Value are expressed as Mean ±SEM, n =10,

f = *Indicates significant difference in the effect of pefloxacin (only) in dietcompared with the control at (P < 0.05) level of confidence.*

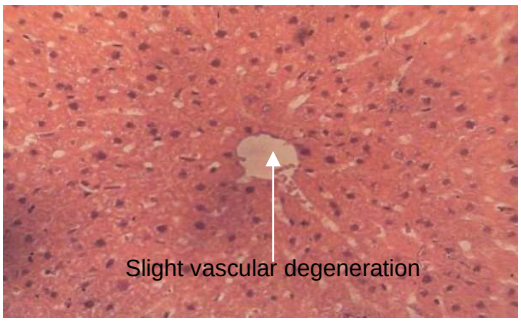
g = *Indicates significant difference in the effect of diet with pefloxacin supplemented with antioxidant vitamins when compared with diet with pefloxacin only at (p<0.05) level of confidence.*



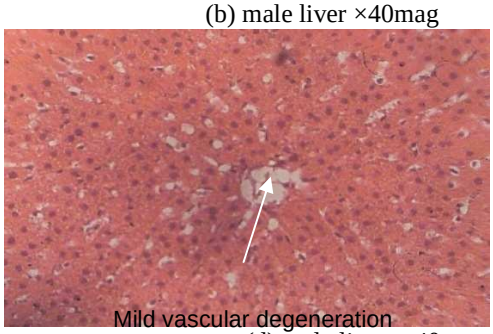
(a) control male liver X40mag



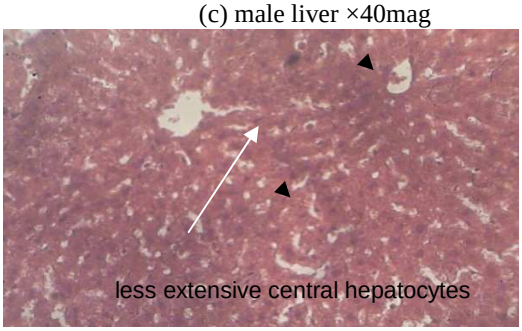
(b) male liver ×40mag



(c) male liver ×40mag

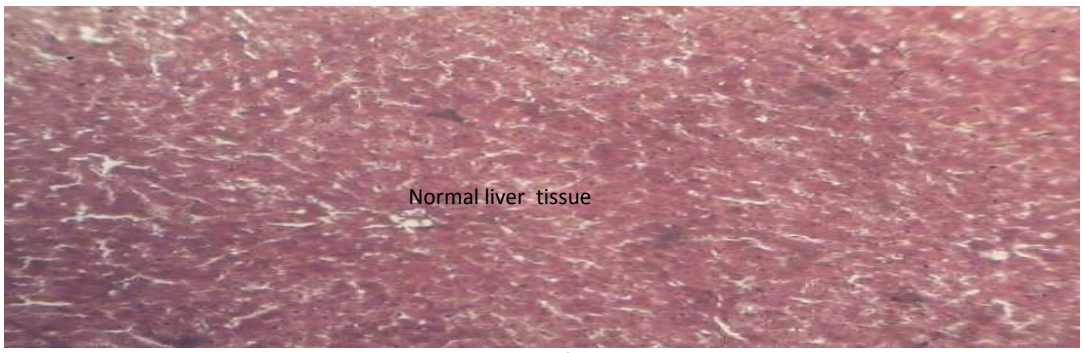


(d) male liver × 40mag

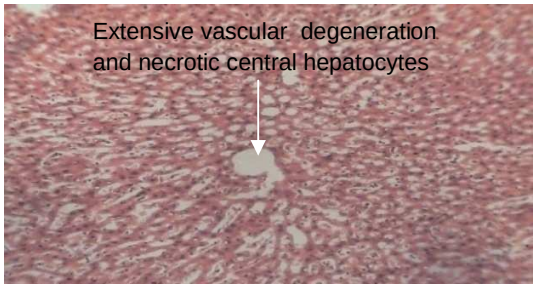


(e) male liver × 40mag

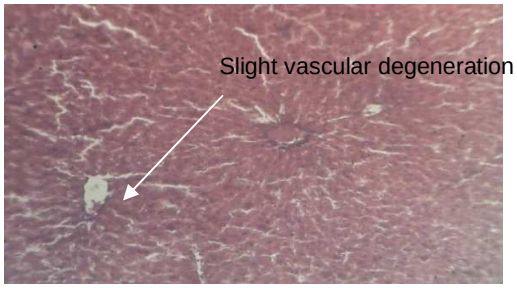
PLATE 3: Photomicrographs of male rat liver showing effect of pefloxacin at 11.43mg/kg body weight as compared with control group.



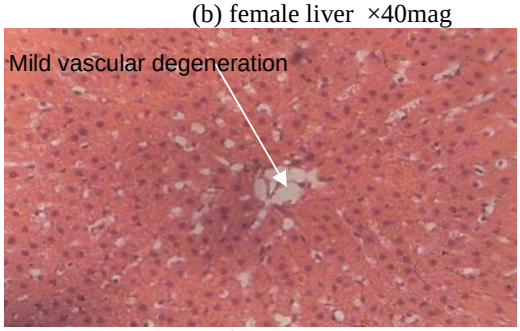
(a) control female liver x40mag



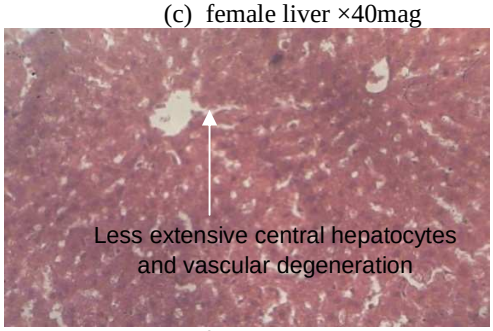
(b) female liver ×40mag



(c) female liver ×40mag



(d) female liver × 40mag



(e) female liver ×40mag

PLATE 4:Photomicrographs of female rat liver showing effect of pefloxacinat 11.43mg/kg body weight as compared with control group

DISCUSSION

In this research, pefloxacin treatment caused a significant increase in serum levels of AST and ALT. This increase is in agreement with the histological changes of the liver observed in rats administered pefloxacin. Similar increase in serum levels of AST and ALT has been reported for quinolone to cause damage to tissues, releasing and increasing the level of free radical species [8]. Administration of pefloxacin and antioxidant vitamins caused a significant decrease in AST and ALT which may due to the detoxifying effects of the antioxidant vitamins on the liver, thereby ameliorating the damage effect of pefloxacin. These further reduce the cellular inflammatory reactions of the hepatocytes which may have initiated leakage of enzyme into circulation. Our findings were in the agreement with the report of [9] that administration of *P. amarus* in acute and chronic hepatitis caused a significant decrease in the concentration of AST and ALT enzymes level in circulation.

The liver showed extensive vascular degeneration with hypertotropic peripheral and periportal hepatocytes, prominent germinal centers with white pulp hyperplasia and massive enteritis on pefloxacin treated rats. Administration of antioxidant vitamins mitigated the toxic effect initiated in the liver poison. A similar observation was reported by Naaz *et al*, [10] for administration of *C. odorata* extract in experimentally induced liver damage in rats.

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