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EFFECTS OF SOME ANTIHISTAMINES ON RAT PLASMA ACID PHOSPHATASE AND LACTATE DEHYDROGENASE ACTIVITY.

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ABSTRACT

The antihistamines: Piriton, cypron, and Tavagyl are among the most common group of H1- antagonist used to manage cellular responses caused by histamine release in Nigeria and like any other drug, they have some side effects at therapeutic doses and toxic doses. The effects of the antihistamine piriton, Cypron, and Tavagyl on the activities of plasma Acid phosphatase (EC.3.1.3.2), and lactate dehydrogenase (EC.1.1.1.27) of rat were determined at an optimum Temperature of 37^{0c} pH 6.0, and 37^{0c} pH 8.0. Piriton, Cypron, and Tavagyl were found to increase Acid phosphatase activity. For instance, at maximum piriton, cypron, and Tavagyl dose of 0.04mg/ 300g body weight, and 30 days duration, ACP activity increased by 65.33±0.88% ($P>0.05$), 69.67±0.33% ($P<0.05$) and 79.67± 0.33% ($P<0.05$) respectively. In vitro, piriton, Cypron, and Tavagyl concentrations of 0.04mg/ml caused an increase of 49.00±0.38%, 52.60±0.43%, and 57.00±67% respectively in human plasma Acid phosphatase activity. However, piriton, cypron, and Tavagyl caused a decrease in lactate dehydrogenase ($P<0.05$). At an optimum piriton cypron, and Tavagyl dose of 0.04mg/ 300g body weight, the LDH activity decreased to 23.67±0.33%, 33.00±0.58%, and 38.67±0.33% within 30 days duration of the test repetitively. In vitro LDH decreased to 32.33± 0.33%, 32.00±0.58%, and 33.67±0.67% at piriton, cypron, and Tavagyl concentration of 0.04mg/ml respectively. These findings would be of relevance in clinical diagnosis involving these enzymes as well as metabolic processes mediated by the same.

KEYWORDS: Piriton, Cypron, Tavagyl, plasma Acid phosphatase, plasma Lactate dehydrogenase, Rat.

INTRODUCTION

Drugs elicit a number of pharmacologic effects at their sites of action; this may include toxic or side effects which may be unavoidable if they are to perform their desirable therapeutic function.

The antihistamines: Piriton, cypron, and Tavagyl are among the most common group of H1-antagonist used in Nigeria to manage cellular responses caused by histamine release. And like any other drug, they have some side effects at therapeutic doses and toxic doses. For instance, some antihistamines at toxic doses cause central nervous system depression, excitation, convulsion, and paralysis of vital centers [1]. At therapeutic doses they cause insomia, sedation, nervousness, nausea, frequent urination, diarrhea, and others [1]. Apart from the use of these antihistamines in the treatment of well defined non-allergic reactions, more often than not, the use of these drugs is abused through self medication.

Piriton, cypron, and Tavagyl exert their action on the body by binding competitively to the histamine receptor sites (H-1) on the cells inhibiting histamine from binding, thus, stopping the histamines from increasing vascular permeability which in turn causes fluid (mediators of inflammation) to escape from the capillaries into the tissues leading to allergic reactions [1].

Acid Phosphatase (EC. 3.1.3.2.) is a hydroxylase enzyme belonging to a group of phosphatase that catalyze the hydrolyses of organic phosphates with the liberation of phosphate ion. They require an acidic medium for optimum activity [2]. It is present in particularly all tissues of the body especially at or in the prostate gland, bone marrow, platelets, erythrocytes, milk, spleen, and liver [3]. It is used as a marker for prostate cancer and bone disease [3].

ACP is inhibited by dexrotatory tartarate ions, formaldehyde and cuppric ions. Lactate dehydrogenase (EC.1.1.1.27) is an oxidoreductase enzyme. It is involved in the last step of anaerobic glycolysis. LDH is soluble and localized in the cytosol. It is a marker enzyme for the intact cell, its activity providing information on cellular glycolytic capacity. LDH requires NADH and NAD^+ and has subunits LDH1 to LDH5. LDH1 higher than LDH2 is a marker for myocardial infarction [4]. Tissue break down elevates level of LDH. Other disorders indicated by elevated LDH include cancer, meningitis, encephalitis, acute pancreatitis, and HIV [4].

The random use of these drugs in our society especially in the treatment of allergy, demands for biochemical research to elucidate the possible effect this could have on the body via the enzyme system of the users. This is therefore the focus of this present study.

MATERIALS AND METHODS

Piriton, cypron, and Tavagyl drugs were bought from Evans pharmaceuticals plc Ogun State. Nigeria, PT Kabbe Ferma Jarkata- Indonesia, Schlering plough USA respectively. ACP and LDH enzyme kit was purchased from Randox Laboratories USA.Other chemicals used for the in vitro test were from BDH London.

For the in vivo test, a total of 53 Wistar albino rats Rattus rattus (Average weight of 280±22.03g) were used. All were obtained from the Vetenary Department University of Nigeria Nsukka. The rats were divided into three groups, each group with 16 rats comprising of male and female, while 5 rats served as control. Four doses of each drug (piriton: 0.005, 0.01, 0.02, and 0.04 mg / 300g body weight, Cypron: 0.005, 0.01, 0.02, and 0.04 mg / 300g body weight, and Tavagyl: 0.005, 0.01 0.02, and 0.04 mg / 300g body weight) were prepared. Each dose for 4 rats from each drug group. The drugs were administered orally according to their body weight. The rats were on their normal diets (standard commercial feed) before the administration of the drugs and were continued on the same diet after the administration.

The test was monitored for 30 days duration after which blood was collected by cardiac puncture into heparinized anticoagulant bottles and they were sacrificed and the liver organ weights taken, while the blood were used for analysis. In vitro test was conducted with human blood plasma collected by Vena-puncture from human health volunteers. The blood plasma from the rats (in vivo) was separated and used immediately for the assay. A UV spectrophotometer was used for the reading. The color assumed by the reaction product was measured kinetically at 405nm for ACP and 340nm for LDH using UV Spectrophotometer.

The technique used for the in vivo and in vitro assay is a continuous monitoring method according to Hillmann. □- naphthyl phosphate salt was used as substrate for ACP. For LDH, the technique used is a kinetic method according to [2]. Pyruvate solution was used as substrate.

For in vitro assay, four serial dilutions of each of the drugs were prepared (piriton, 0.005, 0.01, 0.02, and 0.04 mg/ ml, Cypron: 0.005, 0.01, 0.02, and 0.04mg/ ml, Tavagyl: 0.005,

0.01, 0.02, and 0.04mg/ml). Exactly 0.55ml of buffered substrate reagent PH 5.4 and 50µl of plasma was introduced in both labeled twelve test tubes placed in a water bath at 37^{0c} for 10 minutes. 0. 5ml each antihistamine drug preparation was introduced into the buffer substrate except the control tube which is added 0. 5ml of water. While incubating, a blank tube containing 1. 0ml of alkaline Reagent, 0.55ml buffered substrate, and 50µl of plasma reagent was prepared. After 30 minutes, 1.0ml of alkaline reagent was added to each test tube to stop the reaction and develop color. The absorbance was read at 595nm. Blank reading was subtracted from test reading to give the absorbance change ΔA in 30 minutes due to ACP activity. For in vitro assay of LDH, exactly 2ml of Tris-EDTA-NADH buffer pH10, and 50µl of plasma was introduced in both labeled twelve test tubes placed in a water bath at 37^{0c} for 15 minutes. 0.5ml of each drug preparation was introduced into the buffer except the control tube which is added 0.5ml of water. Alter 15 minutes, 2ml of pyruvate solution were added to each test tube. The absorbance was read at 340nm with UV- Spectrophotometer.

RESULTS AND DISCUSSION

The effect of piriton, cypron, and Tavagyl on acid phosphatase activity and Lactate dehydrogenase activity is shown in tables 1.1, 1.2, and 1.3, figures 1.1, 1.2, and 1.3 (in vivo) and tables 2.1, 2.2, and 2.3, figures 2.1, 2.2, and 2.3 (in vitro).

Percentage increase in acid phosphatase activity and decrease in Lactate dehydrogenase activity was observed at varied concentrations of piriton. For instance a piriton dose of 0.005mg per 300g body weight caused percentage increase in acid phosphatase activity of 69.33±0.97%, and a percentage decrease in Lactate dehydrogenase activity of 32.67±0.33% while at 0.01mg per 300g body weight the increase in ACP was 76.00±0.00%, and decrease in LDH was 31.67±0.67% within 30 days duration of the test. Sirnilarly Cypron and Tavagyl showed an activator effect on acid phosphatase activity and inhibitory effect on lactate dehydrogenase activity, at varied concentrations. At cypron, and tavagyl dose of 0.02mg per 300g body weight, a percentage increase in ACP activity observed was 68.67± 0.33%, and 87.00±0.58% respectively, while at a dose of 0.04mg per 300g body weight, a percentage increase of 69.67± 0.33%, and 79.67± 0.33% was observed respectively and a percentage decrease of 33.00 ± 0.58% and 38.67 ± 0.33% in LDH activity was similarly observed at 30 days duration of the test.

The activatory effects of piriton, Cypron, and Tavagyl on acid phosphatase activity could possibly result from electrostatic and hydrogen binding interactions between the drugs and

amino acid residue at the active site. High values of acid phosphatase induced by the drugs could be a consequence of prostate carcinoma, leukemia, and hyperthyroidism. The increase in ACP activity in a non-dependent manner by piriton, Cypron, and tavagyl may possibly be due to clinical limitations, technical limitation, disorders in the drug absorption, bioavailability of the drugs, biotransformation of the drugs, and effects of the drug metabolizing enzymes in the liver microsomes [5]. It could also be due to low rate of ACP clearance from circulation caused by the drugs or due to high degree of induction of ACP synthesis caused by the drugs [5]. The reason could also be due to non promotion of the hydrolytic activity at the enzyme active site by the drugs. The activation of ACP could promote transport of phosphate ion across the cell membrane [6]. Acid phosphatase is used as a marker for prostate cancer, leukemia, and hyperthyroidism [3]. The enzyme is well appreciated as the most sensitive for prostate cancer [3]. By mechanism of enzyme induction, ACP is synthesized in response to any form of prostate cancer, leukemia and hyperthyroidism. Some of the newly formed enzyme enters into the blood circulation and raise the level in the plasma [7]. This could be the possible cause of the observed rise in the level of ACP activity. The inhibitory effects of piriton cypron, and Tavagyl on lactate dehydrogenase activity could possibly result from interactions between the drugs and the substrate at the active site. Low values of lactate dehydrogenase induced by the drugs may be the consequence of biotransformation, bioavailability, and excretion, thereby reducing the concentration of the drugs in the system and hence the effect on the enzyme. Low values of LDH could also be due to high rate of enzyme clearance from circulation or due to low degree of induction of enzyme synthesis caused by the drugs.

Table 1: In vivo effects of piriton on rat acid phosphatase and lactate dehydrogenase activity.

Drug dose (mg/300g body weight)	% increase in ACP activity	% decrease in LDH activity
Control	64.07 ± 0.33	45.67 ± 1.20
0.04	65.33 ± 0.88	23.67 ± 0.33
0.02	65.33 ± 0.33	27.67 ± 0.33
0.01	76.00 ± 0.00	31.67 ± 0.67
0.005	69.33 ± 0.97	32.67 ± 0.33

*All the values are mean ±SD of triplicate determinations

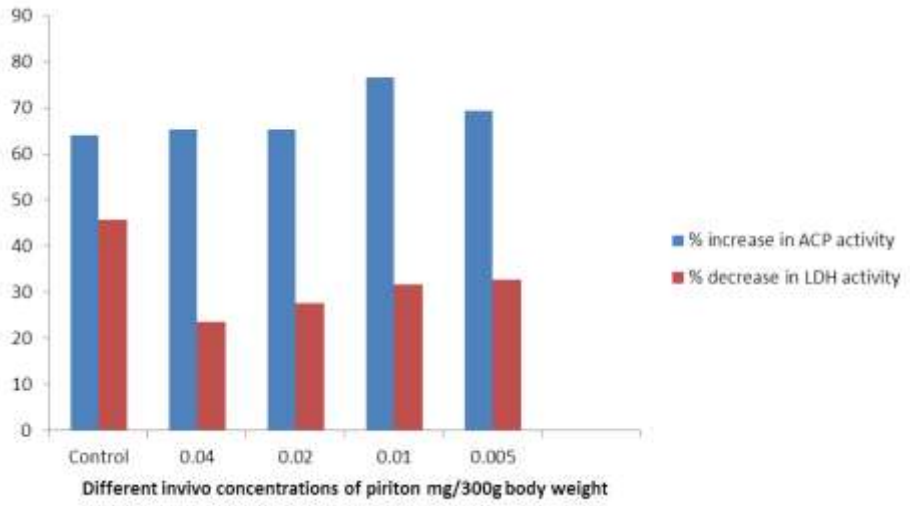

Figure 1: In vivo effects of piriton on rat acid phosphatase and lactate dehydrogenase activity

Table 2: In vivo effects of cypron on rat acid phosphatase and lactate dehydrogenase activity

Drug dose (mg/300g body weight)	% increase in ACP activity	% decrease in LDH activity
Control	64.07 ± 0.33	45.67 ± 1.20
0.04	65.67 ± 0.33	33.00 ± 0.58
0.02	68.67 ± 0.33	25.67 ± 0.33
0.01	76.33 ± 0.88	32.67 ± 0.33
0.005	79.33 ± 0.67	33.33 ± 0.33

*All the values are mean ±SD of triplicate determinations

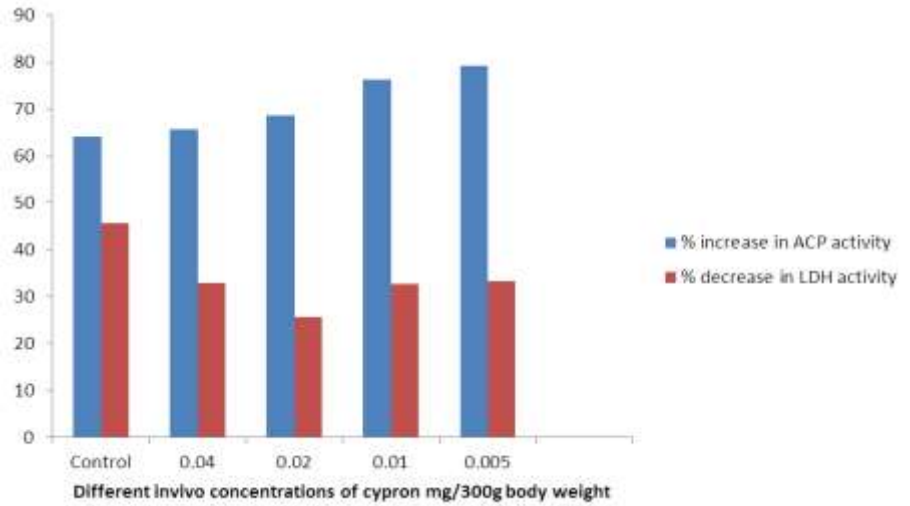

Figure 2: In vivo effects of cypron on rat acid phosphatase and lactate dehydrogenase activity

Table 3: In vivo effects of Tavagyl on rat acid phosphatase and lactate dehydrogenase activity

Drug dose (mg/300g body weight)	% increase in ACP activity	% decrease in LDH activity
Control	64.07 ± 0.33	45.67 ± 1.20
0.04	79.67 ± 0.33	38.67 ± 0.33
0.02	87.00 ± 0.58	39.33 ± 0.33
0.01	75.67 ± 2.19	31.33 ± 0.33
0.005	78.33 ± 0.33	30.33 ± 0.33

*All the values are mean ±SD of triplicate determinations

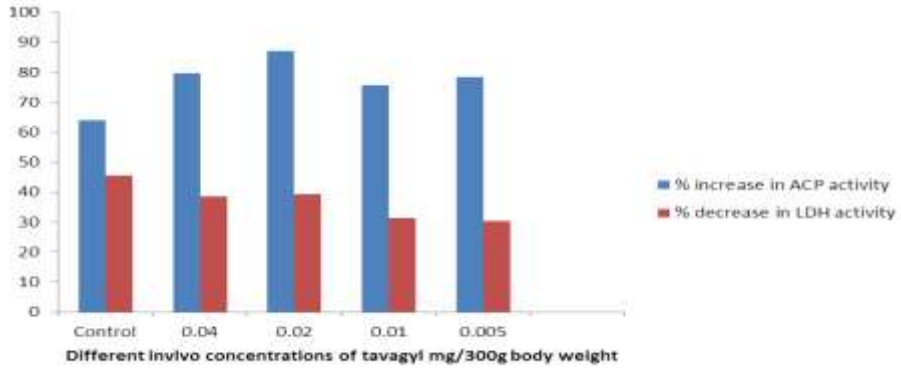

Figure 3: In vivo effects of Tavagyl on rat acid phosphatase and lactate dehydrogenase activity

Table 4: In vitro effects of piriton on human acid phosphatase and lactate dehydrogenase activity.

Drug dose (mg/300g body weight)	% increase in ACP activity	% decrease in LDH activity
Control	29.00 ± 0.47	37.00 ± 0.58
0.04	49.00 ± 0.38	32.33 ± 0.33
0.02	37.10 ± 0.08	30.33 ± 0.33
0.01	32.10 ± 0.68	27.67 ± 0.67
0.005	29.70 ± 0.39	27.00 ± 0.01

*All the values are mean ±SD of triplicate determinations

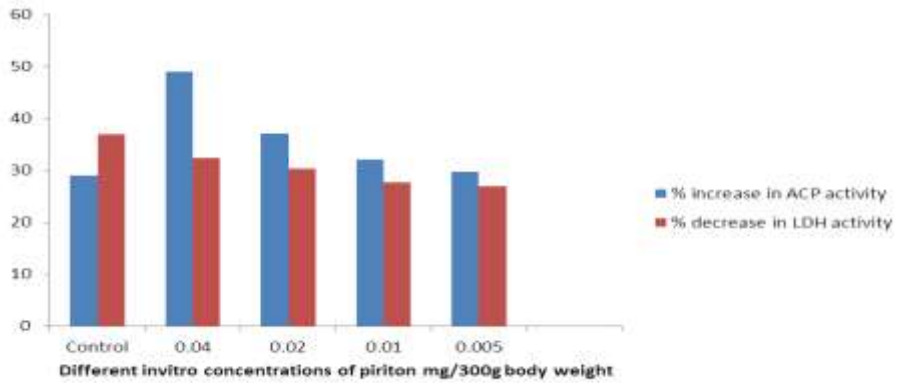

Figure 4: In vitro effects of piriton on human acid phosphatase and lactate dehydrogenase activity.

Table 5: In vitro effects of cypron on human acid phosphatase and lactate dehydrogenase activity

Drug dose (mg/300g body weight)	% increase in ACP activity	% decrease in LDH activity
Control	29.00 ± 0.47	37.00 ± 0.58
0.04	52.60 ± 0.43	32.00 ± 0. 58
0.02	43.30 ± 0.37	25.67 ± 0. 67
0.01	37.10 ± 0.44	23.67 ± 0.58
0.005	34.70 ± 0.80	23.33 ± 0.58

*All the values are mean ±SD of triplicate determinations

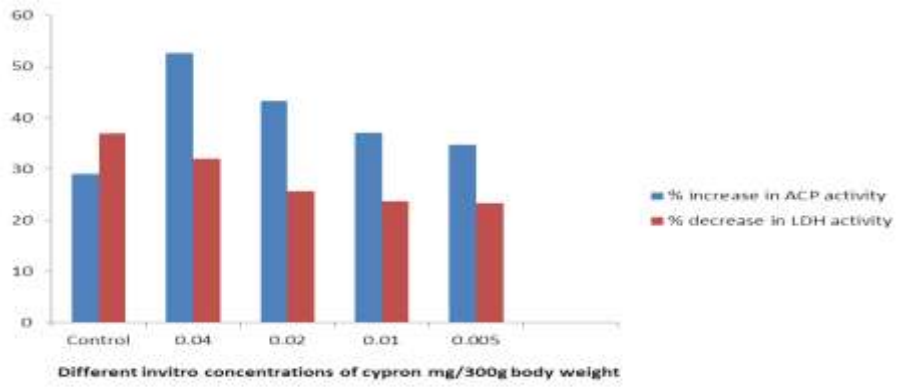

Figure 5: In vitro effects of cypron on human acid phosphatase and lactate dehydrogenase activity.

Table 6: In vitro effects of Tavagyl on human acid phosphatase and lactate dehydrogenase activity

Drug dose (mg/300g body weight)	% increase in ACP activity	% decrease in LDH activity
Control	29.00 ± 0.47	37.00 ± 0.58
0.04	57. 00 ±0.67	33.67 ± 0.67
0.02	42. 00 ±0.62	31.00 ± 2.52
0.01	36.00 ± 0.68	26.67 ± 0.67
0.005	33.10 ± 0.85	26.00 ± 0.61

*All the values are mean ±SD of triplicate determinations

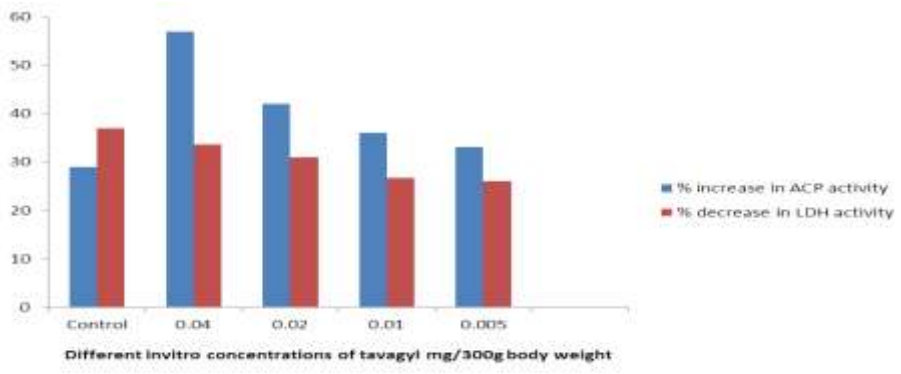

Figure 6: In vitro effects of Tavagyl on human acid phosphatase and lactate dehydrogenase activity

CONCLUSION

In conclusion, it is advisable that caution should be the watch word while using antihistamines, especially in treating non-allergic reactions. Abuse of these drugs could elicit some biochemical reactions deleterious to the body.

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