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STUDY THE EFFECT OF SULFANILAMIE AND VITAMIN E ON SOME BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS IN ADULT MALE RABBITS

Hanadi A. Hafth Ahlam A. Al-Rekabi Wasfi A. Al- Masoudi

Department of Physiology, Pharmacology and Chemistry, College of Veterinary Medicine,
University of Basrah, Basrah, Iraq

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Corresponding author E-mail: hanadialhilfi@gmail.com

ABSTRACT

This study was designed to investigate the impact of sulfanilamide and sulfanilamide combined with vitamin E on - some biochemical and hematological parameters in adult male rabbits, this experiment was carried out on 18 male rabbits of (1000-1600 gm) were used in this study, these animal were adapted for one week before then were split into three groups (6 rabbits in each). First group as control group were given of dimethyl sulphoxide (DMSO 0.5 ml) I.P daily, second group were treated with sulfanilamide drug (195 mg/kg) I.P daily, however third group were given of sulfanilamide drug (195 mg/kg) I.P and were administered orally vitamin E (0.15 ml/kg) daily. The treatment continues for three weeks, the results showed in the treated with sulfanilamide significantly reduction in RBCs, Hb, PCV, this reduction was companied by a significant decrease in MCH, MCHC, as well as a significant decrease in total WBCs and Platelet count, while were observed a significant increase in total cholesterol, triglyceride, LDL, VLDL associated with the a significant decrease in HDL, also, significantly elevation in serum AST and ALT levels, the study produced significantly reduction in total protein and albumin and a significant elevation in globulin in male rabbits treated with sulfanilamide, from our results the group treated with sulfanilamide and vitamin E showed improvement in hematological and biochemical parameters, It was concluded that administration of sulfanilamide caused several

adverse effects while administration of vitamin E with sulfanilamide attenuation of this impact and get them close to its normal value.

INTRODUCTION

Sulfonamides are the first antimicrobial drugs. Sulfonamides' antimicrobial action comprise the competitive inhibition of synthesis of folic acid that impede the development and reproduction of microorganisms; sulfa drugs belongs to the bacteriostatic agents due to this mechanism of action. Sulfonamides are still the preferred medicines for the treatment of various diseases (1).

The first was discovered in 1932, between 1935 and 1937 when administrated to patients with puerperal fever; Leonard Colebrook showed that sulfonamides worked as an effective treatment for puerperal fever (2). Sulfonamide play a major role in pharmaceutical chemistry with several biological activities such as diuretic, anti-bacterial, anti-hyperglycemic, anti-thyroid, anti-inflammatory, anti-hypertensive, anti-carbonic anhydrase (CA), anti-cancer, anti-convulsant activities (3).

Negative impacts of sulfonamides in 4-6% of the treated cases from common population and fifty to sixty percent of cases with HIV infection ^[4]. The most prevalent negative response to sulfonamides is hypersensitivity and it is often referred to as an allergy to sulfa. The negative impacts of sulfonamides include anaphylactic shock, hemolytic anemia, neutropenia, thrombocytopenia, pancytopenia, serum sickness, pneumonia, hepatitis, myocarditis, interstitial nephritis and various skin responses, including serious responses such as Steven-Johnson syndrome and poisonous epidermal necrosis (5).

Vitamin E act a significant function in the protecting of inveterate illnesses. Various surveys with reduced incidence of heart disease in populations with high vitamin E consumption. The results have demonstrated a possible function for this vitamin in the chronic disease prohibition in humans. Moreover, wide-scale of clinical studies of vitamin E and other antioxidants in prevention of particular processes of illnesses (e.g., coronary artery disease) (6). Deficiency of vitamin E mostly causes neurologic dysfunctions, but the essential mechanisms are unclear. This

vitamin is thought to help prevent diseases correlated with oxidative stress such as chronic inflammation, cardiovascular disease, cancer and neurologic disorders. The aim of the study to evaluate the impacts of sulfanilamide with vitamin E on hematological and some biochemical parameters in male rabbits.

MATERIAL AND METHOD

Experimental animal

Thirty adult male rabbits aged 6 months and weights 1000-1600 grams were used and were brought from Basrah city's local market. The animals were first acclimatized for seven days at the experiment site, animals located in normal cages maintained under laboratory controlled at temperature $25 \pm 2^{\circ}\text{C}$ also, light /dark cycle of 12 hours, food and water *ad libitum* provided every day.

Experimental design: The rabbits were distributed into 3 groups that consisted 6 rabbits as follows:-

Control group: 6 male adult rabbits were administered 0.5ml dimethyl sulphoxide (DMSO) intraperitoneally daily for three weeks.

Treated 1 (T1) group: 6 male adult rabbits were given 1/20 of LD_{50} (195 mg/kg) of sulfanilamide drug dissolved by 0.5ml (DMSO) Intraperitoneally daily for three weeks.

Treated 2 (T2) group: 6 male adult rabbits were received 1/20 of LD_{50} (195 mg/kg) of sulfanilamide drug dissolved by 0.5ml (DMSO) Intraperitoneally and 0.15 ml/kg of vitamin E were given orally daily for three weeks.

At the end of the experiment, the samples of blood was gathered from the puncture of the heart, 2 ml of blood was placed in EDTA tube containing as an anticoagulant for hematological examinations and 3-5 ml of blood was placed into an anticoagulant-test tube to separate blood serum for biochemical analysis.

Biochemical analysis:

Serum total cholesterol (TC) was determined according to the method of (7) by Chemical kit used (Biocon/ CHOP – PAP, Germany). The triglycerides (TG) in the serum was measured enzymatically by a special chemical kit used (Spread, S.A. /S.A.U. Spina), (8), HDL –

cholesterol serum was determined by a special kit used (Biocon/FLUTES HDL – cholesterol, Germany)(9). Serum LDL – cholesterol was calculated by the formula (9).

$$\text{LDL cholesterol} = \text{TC} - \text{HDL} + (\text{TG}/5).$$

The concentration of VLDL in the serum was measured by dividing serum TG by five (10), whereas serum total Protein and albumin level were determined by a colorimetric method (11). The serum globulin was calculated by the formula:

$$\text{Serum globulin} = \text{Serum total protein} - \text{Serum albumin}$$

Serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) were enzymatically determined via a special chemical kit used (Redox Laboratories Limited, United Kingdom) (12).

Hematological Parameters:

Auto Hematology Analyzer BC-5300 was used to measure the parameters of blood which comprised Red blood cells count (RBC), Hemoglobin concentration (Hb), packed cell volume percentage (PCV), Hb rate in the red blood corpuscle (MCH), rate of Hb concentration in red blood corpuscle (MCHC), total WBC count and platelets count.

Statistical analysis:

In this study, ANOVA analysis one way (IBM SPSS, version 20) the program has been used to analyze the outcomes of this research. The information was given as mean \pm standard deviation (mean \pm SD). Least significant difference test (LSD) was used to test the difference between means (groups); $P \leq 0.05$ was regarded significant (SPSS, 2001).

RESULTS

Table (1) showed a significant ($p \leq 0.05$) decrease in the number of RBCs count, hemoglobin concentration, packed cell volume and platelet count in male rabbits treated group with sulfanilamide when compared with control, while in group treated with sulfanilamide and vitamin E showed a significant ($p \leq 0.05$) elevation in the RBCs count, Hb, PCV and platelet count compared with the treated group with sulfanilamide.

Table (1): Red blood cell count, hemoglobin concentration (Hb), packed cell volume (PCV) and platelets count in control group and treated groups.

Parameters Groups	Red blood corpuscle $\times 10^6$ cell/mm ³	Hb concentration g/100ml	PCV %	Platelet Count $\times 10^6$ cell/mm ³
Control group 0.5 ml DMSO	5.84 \pm 0.47a	12.41 \pm 0.88a	41.13 \pm 1.10a	638.27 \pm 8.64 a
Sulfanilamide drug(195 mg/kg)	2.89 \pm 0.11c	7.16 \pm 0.47c	23.79 \pm 1.39c	372.90 \pm 13.83c
Sulfanilamide (195 mg/kg) and 0.15ml/kg of vitamin E	3.56 \pm 0.50b	8.04 \pm 0.23b	30.39 \pm 1.16b	432.73 \pm 13.15b

The small letters indicate to the difference is significant

According to Table (2) the results showed in the treated group with sulfanilamide had a significant ($p \leq 0.05$) decrease in MCH and MCHC concentrations and total WBC count when compared with control group, while in the treated group with sulfanilamide and vitamin E had a significant ($p \leq 0.05$) elevation in MCH, MCHC concentration and WBC count than the treated group with sulfanilamide.

Table (2): Mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and total white blood cells (WBC) count in control group and treated groups.

parameters Groups	MCH(pg)	MCHC%	WBC × 10³ cell/mm
Control group 0.5 ml DMSO	41.49 ±4.90a	38.28 ±1.40a	6.49 ±0.44 a
Sulfanilamide drug(195 mg/kg)	26.30 ±1.83 c	20.99 ±1.82c	4.04 ±0.18 c
Sulfanilamide (195 mg/kg) and (0.15ml/kg)of vitamin E	31.27 ±1.47 b	23.46 ±1.51b	4.76 ±0.46 b

The small letters indicate to the difference is significant

The datum to *Table (3)* showed significantly ($p \leq 0.05$) elevation in total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein concentrations associated with significantly ($p \leq 0.05$) reduction in HDL concentration in the group were administrated sulfanilamide compared to the control. The findings in *Table(3)* indicated that significantly ($p \leq 0.05$) reduction in total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein concentrations and this reduction proportion with significantly ($p \leq 0.05$) elevation in HDL concentration in the group treated with sulfanilamide and vitamin E compared with the treated group with sulfanilamide.

Table (3): Serum total cholesterol (TC), Triglyceride (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and high density lipoprotein (HDL) in control group and treated groups.

Parameters Groups	Total cholesterol concentration n mg/dl	Triglyceride s mg/dl	HDL concentration mg/dl	LDL concentration n mg/dl	VLDL concentration mg/dl
Control group 0.5 ml DMSO	88.99 ±1.69c	90.59 ±1.79c	36.32 ±2.04a	20.12 ±1.38c	14.99 ±1.21c
Sulfanilamide drug (195 mg/kg)	137.89±1.68a	140.57±2.6a	18.77 ±0.88c	40.46 ±1.24a	28.24 ±1.35a
Sulfanilamide (195mg/kg) and (0.15ml/kg) of vitamin E	114.25±1.35b	121.51±2.4b	22.74 ±1.15b	31.59 ±2.51b	23.39 ±1.44b

The small letters indicate to the difference is significant

According to datum in results clarified in Table (4) it appears that the level of AST and ALT in the group treated with sulfanilamide in comparison with control group elevation significantly ($p \leq 0.05$) elevation. While in the group treated with sulfanilamide and vitamin E reveled a significant ($p \leq 0.05$) reduction in AST and ALT concentrations from the effect of sulfanilamide only.

Table (4): Serum alanine transaminase (ALT) and aspartate transaminase (AST) in control group and treated groups.

Parameters Groups	AST unit/L	ALT unit /L
Control group 0.5 ml DMSO	32.34 \pm 2.24c	60.50 \pm 3.49c
Sulfanilamide drug (195 mg/kg)	48.73 \pm 2.02 a	87.78 \pm 1.20a
Sulfanilamide (195mg/kg) and (0.15ml/kg) of vitamin E	40.01 b \pm 1.93b	78.54 \pm 1.59b

The small letters indicate to the difference is significant

The findings in *Table (5)* there was a significant ($p \leq 0.05$) reduction in total protein and albumin concentrations and a significant ($p \leq 0.05$) elevation in globulin concentration in the treated group with sulfanilamide in compared with control. While in the treated group with sulfanilamide and vitamin E the results showed that there was a significant ($p \leq 0.05$) elevation in total protein and albumin concentrations and a significant ($p \leq 0.05$) reduction in globulin concentration in the comparison with the group treated with sulfanilamide.

Table (5): Serum total protein, albumin and globulin in control group and treated groups.

Parameters Groups	Total protein Concentration mg/dl	Albumin concentration mg/dl	Globulin concentration mg/dl
Control group 0.5 ml DMSO	5.93 \pm 0.86 a	4.36 \pm 0.24 a	2.21 \pm 0.08 c
Sulfanilamide drug(195 mg/kg)	4.17 \pm 0.12 c	3.03 \pm 0.07 c	3.83 \pm 0.30 a
Sulfanilamide (195 mg/kg) and (0.15ml/kg) of vitamin E	5.08 \pm 0.15 b	3.36 \pm 0.08 b	3.30 b \pm 0.34 b

The small letters indicate to the difference is significant

DISCUSSION

From our results in Table (1) showed changes in the parameters of blood of the male rabbits handled with sulfanilamide in which a significant decrease in number of RBC count, HB, PCV. The results compatible with (13) who showed the adverse effects of sulfonamides for example; interstitial nephritis, hemolytic anemia, neutropenia, thrombocytopenia and pancytopenia. The datum also, showed a significant decrease in the platelet count in comparison to control that due to initiate the production of platelet- specific autoantibodies, this result agreed with(14) that showed drug-induced thrombocytopenia which identify in many cases; platelet react with antibodies in the presence in the sensitizing medications. However, the sulfanilamide and vitamin E administration lead to rise in blood parameters above than the treated group with sulfanilamide, this agreed with (15) which indicates that the first line of protection against the peroxidation of lipid and free radical attack of the cell membrane is the vitamin E. This vitamin has a greater lipid peroxidation inhibitory influence because of its antioxidant effect which lead to protect blood cells from damage.

The result in Table (2) showed a significant decrease in MCH, MCHC and total WBC count in the treated group with sulfanilamide this result agreed with(16) who showed aplastic anemia-induced drugs recognized by pancytopenia like sulfonamide. These drugs more commonly cause mild suppression of the bone marrow which cause preliminary damage that proceed to more serious damage. The data in the same Table indicates a significant increase in MCH, MCHC and total WBC count this result due to protective impact of this vitamin on blood cells.

The results shown in Table (3) indicated the impact of sulfanilamide on lipid profile that there was a significant elevation in total cholesterol, triglyceride, low density lipoprotein, very low density lipoprotein concentrations and a significant reduction in high density lipoprotein concentration due to the effect of sulfanilamide on liver which lead to disturbance liver functions agreed with (17) that reported liver is the primary site for regulating internal chemical environment and for many years liver injury caused by hepatotoxicity substances has been recognized as a problem. The specific metabolic functions of the liver and its gastrointestinal tract relationship: liver is a significant target against oxidative stress, and toxic chemicals (antibiotics, chemotherapeutics, carbon tetrachloride, etc.). The data in the results showed in the

treated group with sulfanilamide and vitamin E had a significant decrease in lipid profile except HDL concentrations due the powerful antioxidant effect of this vitamin, which prevent the peroxidation of lipid by the free radicals agreed with (18) who indicated that the pathogenesis of various diseases includes lipid peroxidation mediated by free radicals, this vitamin is a powerful antioxidant, and it suppresses the peroxidation of lipid both *in vivo* and *in vitro*. This effect of vitamin E reduce the harmful impact of sulfanilamide on the hepatic tissues.

The data in Table (4) showed a significant elevation in AST and ALT concentrations in the group treated with sulfanilamide in comparison to control this results agreed with (19) who showed liver is the specified metabolic organ of sulfanilamide, AST and ALT enzymes are released in the extracellular fluid by liver damage caused by the sulfa drugs which lead to elevation their plasma level. While in the treated group with sulfanilamide and vitamin E had a significant decrease in ALT and AST concentrations than treated group with sulfanilamide due to effect of vitamin E agreed with (20) that showed vitamin E's protective effect against malathion caused oxidative stress which lead to degenerative and necrotic modifications in the liver's hepatocyte cells.

The results of the this study in Table(5) showed that there was a significant reduction in total protein and albumin concentrations while a significant elevation in globulin concentration in the group treated with sulfanilamide due to adverse effect of this drug on kidney (21). Medications cause inflammatory modifications in renal tissues that lead to fibrosis and scarring in the tissues and these drugs which cause acute inflammations are believed to connect to antigens in the kidney or it has function as antigens then are deposited into the renal tissues, to induce an immune response(22). The acute interstitial nephritis, due to an allergic reaction to a specific drug, this inflammation develops on dose- dependent like sulfonamide (22) and (23). Also, the results of showed elevation in total protein and albumin and reduction in globulin concentrations in the group was administrated sulfanilamide and vitamin E than the treated group with sulfanilamide due to protective effect of vitamin E which decrease the deleterious effect of sulfanilamide on kidney this results agreed with (24) indicated this vitamin was shown to be effective against cisplatin- induced damage in renal tissues and minimize its toxic effect by the antioxidant activity of vitamin E against free radicals. Depending on the results it seems that vitamin E has protective effect on kidney function tests, it is the significant antioxidant lipophilic

chain breaking in the membranes of the cells which has the probable role against ROS that cause tissue damage(25).

CONCLUSION

Administration of sulfanilamide cause several adverse effects on hematological and biochemical parameters while the administration of vitamin E with sulfanilamide attenuation of this adverse effect.

دراسة تأثير عقار السلفانيلامايد و فيتامين ه على المعايير الدموية و الكيموحيوية في ذكور الارانب

هنداءى عبد الجبار حافظ احلام على الركابى وصفى عبود المسعودى

جامعة البصرة، كلية الطب البيطرى، فرع الفلسفة والأدوية والكيمياء، البصرة ، العراق

الخلاصة

تهدف هذه الدراسة الى تقييم تأثير السلفانيلامايد والسلفانيلامايد مع فيتامين هاء(E) على المعايير الدموية والكيموحيوية في ذكور الارانب.

المجموعة الاولى(مجموعة السيطرة) اعطيت ٠.٥ مل من ثنائى مثيل سلفوكسايد حقنا بالجدار البطنى البريتونى يوميا والمجموعة الثانية (معاملة) اعطيت السلفانيلامايد بجرعة (195ملغم/كغم) حقنا بالجدار البطنى البريتونى يوميا والمجموعة الثالثة (معاملة) اعطيت السلفانيلامايد بجرعة (195ملغم/كغم) حقنا بالجدار البطنى البريتونى وفيتامين E بجرعة (٠.١٥ مل/كغم) عن طريق الفم يوميا واستمرت المعاملة لمدة ثلاثة اسابيع. أظهرت النتائج في المجموعة الثانية وجود انخفاضاً معنوياً في العدد الكلى لخلايا الدم الحمر وتركيز هيموغلوبين وحجم خلايا الدم المرصوصة ويقترن هذا بانخفاضاً معنوياً في معدل هيموغلوبين الكرية وتركيز معدل هيموغلوبين الكرية (MCH,MCHC) والصفائح الدموية بالإضافة الى وجود انخفاضاً معنوياً في العدد الكلى لخلايا الدم البيضاء ، بينما بينت النتائج زيادة معنوية في مستوى الكلوسيترو ل الكلى والدهون الثلاثية والبروتينات الدهنية واطئة الكثافة والبروتينات الدهنية واطئة الكثافة جداً مقترنة بانخفاض معنوي في مستوى البروتينات الدهنية العالية الكثافة وكذلك لوحظ وجود زيادة معنوية في مستوى انزيمات الكبد (AST,ALT) وانخفاضاً معنوياً في مستوى البروتين الكلى والالبومين وارتفاعاً معنوياً في مستوى الكلوبيولين في مجموعة المعاملة بالسلفانيلامايد مقارنة مع مجموعة

السيطرة. بينما اظهرت النتائج في المجموعة المعاملة بالسالفانيلامايد وفيتامين(E) تحسين في المعايير المدروسة (الدموية والكيموحيوية) وهذا يعود الى الدور الايجابي لفيتامين E في تقليل الاثار الجانبية لعقار السلفانيلامايد.

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