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# Hematological dynamics following the co-administration of Resveratrol and Cisplatin in Sprague–Dawley rats

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**Abstract**

**Background:** Cisplatin, a platinum-based chemotherapy agent, is used in the effective treatment of a wide range of malignant cancers. Resveratrol, a polyphenolic plant-derived compound, has been shown to have several biological effects including protecting the body against several forms of damages.

**Objective:** This study assessed the effects of cisplatin and supplementation with resveratrol on some hematological parameters in Sprague-Dawley rats.

**Material and Methods:** Forty-five adult female Sprague–Dawley rats, grouped into 9, were used for this experimental study. Group 1 served as the control group and received distilled water only. Groups 2 and 9 received Cisplatin only while groups 3, 4, and 5 received different doses of Resveratrol after a single dose of Cisplatin. Groups 6, 7, and 8 received Resveratrol before Cisplatin.

**Results:** At the end of administration, blood samples were collected and different hematological parameters were accessed. Groups 2 and 5 showed a significantly higher Total WBC when compared to the control group ($p<0.05$). Group 7 showed a significantly higher ($p<0.05$) neutrophil count compared to both the control group and group 2, but a significant decrease in the lymphocyte count compared to the same groups ($p<0.05$). Groups 6 and 7 showed a significant reduction in monocyte when compared to the control group ($p<0.05$). There was no significant difference in the eosinophil count of all treatment groups when compared to the control group and cisplatin groups ($p<0.05$). Basophil increased significantly in group 7 when compared to the control group and group 2 ($p<0.05$). More so, a significant decrease in the Haemoglobin (Hb), Packed cell volume (PCV) and Mean corpuscular volume (MCV) level were observed when compared to group 9 ($p<0.05$).

**Conclusion:** This study showed that cisplatin-induced alteration in some hematological parameters is reversible by treatment with resveratrol. More so, resveratrol supplementation should be incorporated as part of dietary nutrients for patients on cisplatin during chemotherapy.

**Keywords:** cisplatin, hematology, resveratrol, Sprague-Dawley, supplementation

## РЕСВЕРАТРОЛ МЕН ЦИСПЛАТИНДІ ЕНГІЗГЕННЕН КЕЙІН СПРЕГ-ДОУЛИ ЕГЕУҚҰЙРЫҚТАРЫНЫҢ ГЕМАТОЛОГИЯЛЫҚ ПАРАМЕТРЛЕРІ

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**ТҰЖЫРЫМДАМА**

**Кіріспе:** Цисплатин – бұл түрлі қатерлі ісіктерді тиімді емдеуде пайдаланылатын химиотерапевтикалық препараты құрайтын платин. Ресвератрол, шығуы өсімдік түрінен болатын полифенольді байланысудың зақымдалудың кейбір формаларынан организмді қорғауды қосқанда, бірнеше биологиялық әсері бар екендігі дәлелденді.

**Мақсаты:** Осы зерттеуде Спрег-Доули егеуқұйрықтарындағы кейбір гематологиялық параметрлерге ресвератролдың қоспалары және цисплатиннің әсері бағаланды.

**Материалдар мен әдістер:** Осы зерттеуде 9 топқа бөлінген қырық бес ересек Спрег-Доули егеуқұйрықтары қолданылды. 1-топ бақылау тобы болды және дистилденген суды ғана қабылдады. 2-ші және 9-шы топтар тек қана цисплатин қабылдады, сол уақытта 3, 4-ші

және 5-ші топтар цисплатиннің бірінші дозасынан кейін ресвератролдың түрлі дозаларын қабылдады. 6, 7-ші және 8-ші топтар цисплатиннің алдынан ресвератролды қабылдады.

**Нәтижелері:** Препараттарды енгізуді аяқтау бойынша қанның үлгілерін жинадық және түрлі гематологиялық параметрлерін бағаладық. 2-ші және 5-ші топтарда лейкоциттердің жалпы мөлшері бақылау тобымен ($p<0.05$) салыстырғанда айтарлықтай жоғары. 7-ші топта бақылау тобына және 2-ші топқа қарағанда, нейтрофилдердің мөлшері айтарлықтай жоғары ($p<0.05$), алайда сол топтармен салыстырғанда лимфоциттердің мөлшерінің айтарлықтай төмендеуі байқалды ($p<0.05$). 6-шы және 7-ші топтар бақылау тобымен салыстырғанда ($p<0.05$), моноциттер мөлшерінің айтарлықтай төмендігін көрсетті.

Барлық зерттелетін топтарда эозинофилдердің мөлшеріндегі айтарлықтай ерекшелігі бақылау топтармен және цисплатинді ($p<0.05$) қабылдаған топтармен салыстырғанда байқалмады. Базофилдердің мөлшері бақылау тобымен және 2-ші топпен салыстырғанда ($p<0.05$) 7-ші топтарда айтарлықтай артты. 9-шы топпен салыстырғанда, гемоглобин (Hb), гематокритті саны (PCV) мен эритроциттің орташа көлемі (MCV) деңгейінің айтарлықтай төмендеуі байқалды.

**Қорытынды:** Осы зерттеу цисплатинді енгізумен туындаған гематологиялық параметрлерінің өзгеруі – ресвератролмен терапиясының көмегімен қайтымды екендігін көрсетті. Ресвератролдың қоспасын химиотерапия кезінде цисплатинге диеталық құнарлы заттектердің бір бөлігі ретінде қосу қажет.

**Негізгі сөздер:** цисплатин, гематология, ресвератрол, Спрег-Доули, қоспа

## ГЕМАТОЛОГИЧЕСКИЕ ПАРАМЕТРЫ У КРЫС СПРЕГ-ДОУЛИ ПОСЛЕ ВВЕДЕНИЯ РЕСВЕРАТРОЛА И ЦИСПЛАТИНА

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**РЕЗЮМЕ**

**Введение:** Цисплатин это платин, содержащий химиотерапевтический препарат, используемый для эффективного лечения различных злокачественных опухолей. Было доказано, что ресвератрол, полифенольное соединение растительного происхождения, имеет несколько биологических эффектов, включая защиту организма от некоторых форм поражений.

**Цель:** В данном исследовании оценивались эффекты цисплатина и добавки ресвератрола на некоторые гематологические параметры у крыс Спрег-Доули.

Материалы и методы: В данном исследовании было использовано сорок пять взрослых крыс Спрег-Доули, разделенных на 9 групп. Группа 1 стала контрольной группой и получала только дистиллированную воду. Группы 2 и 9 получали только цисплатин, в то врем как группы 3, 4 и 5 получали различные дозы ресвератрола после одной дозы цисплатина. Группы 6, 7 и 8 получали ресвератрол перед цисплатином.

**Результаты:** По завершению введения препаратов, собрали образцы крови и оценили различные гематологические параметры. У групп 2 и 5 общее количество лейкоцитов было значительно выше, по сравнению с контрольной группой ($p<0.05$). В группе 7 количество нейтрофилов было значительно больше ($p<0.05$), чем в контрольной группе и группе 2, но отмечалось значительное снижение количества лимфоцитов, по сравнению с теми же группами ($p<0.05$). Группы 6 и 7 показали значительное снижение количества моноцитов, по сравнению с контрольной группой ($p<0.05$). Значительной разницы в количестве эозинофилов во всех исследуемых группах не отмечено, по сравнению с контрольной группой и группами, получавшими цисплатин ($p<0.05$). Количество базофилов значительно увеличилось в группе 7, по сравнению с контрольной группой и группой 2 ($p<0.05$). Более того, наблюдалось значительное снижение уровня гемоглобина (Hb), гематокритного числа (PCV) и среднего объема эритроцита (MCV), по сравнению с группой 9 ($p<0.05$).

**Заключение:** Данное исследование показало, что изменение гематологических параметров, вызванное введением цисплатина, обратимо с помощью терапии ресвератролом. Более того, добавку ресвератрола необходимо включать как часть диетических питательных веществ к цисплатину во время химиотерапии.

**Ключевые слова:** цисплатин, гематология, ресвератрол, Спрег-Доули, добавка

## Introduction

Cisplatin is an effective chemotherapeutic agent, which belongs in the platinum-based anti-neoplastic family of medications [1]. It is used in the treatment of a wide range of malignant diseases including testicular cancer, ovarian cancer, cervical cancer, breast cancer, bladder cancer, head and neck cancer, esophageal cancer, lung cancer, mesothelioma, brain tumors and neuroblastoma. However, it exhibits certain toxic effects on several organs such as the kidneys and liver, which interfere with its therapeutic efficiency [2]. Previous works by Wood and Hrusheeky in 1995 [3] showed, that cisplatin causes significant effects on various hematological parameters only during chronic treatment in humans and rats. Cisplatin-induced anemia is also a well-known side-effect [4], which occurs in 9-40% of patients [5]. However, some previous results showed that high, acute doses of cisplatin did not affect the RBC maturation in rats [1].

Resveratrol (3, 4’ 5-trihydroxystilbene) is a polyphenol synthesized by a wide variety of plant species, including aliments such as grapes, peanuts and mulberries, in response to injury, UV irradiation and fungal attack. Resveratrol belongs to a group of compounds called polyphenols; it is the most extensively studied and has long been considered a therapeutic agent for various diseases, including inflammatory diseases [7]. Studies by Loehrer et al., 1998 [8] also showed resveratrol to have cytotoxic effects against human cancer cell lines derived from various tumor types. Preclinical studies have revealed this compound to have several biological effects including antioxidant effects thus protect the body against damages.

Thus, this study investigated the effects of cisplatin and supplementation with resveratrol on various hematological parameters in Sprague-Dawley rats.

## Material and methods

### Animal Care and Handling

This experimental animal study was carried out in the research laboratory of the Department of Anatomy, College of Medicine of the University of Lagos, Nigeria. Forty-five adult female Sprague–Dawley rats with average weight of 160 g were procured from the Animal House, College of Medicine of the University of Lagos. They were acclimatized for two weeks to exclude any intercurrent infection under standard housing of 24 ± 2°C and 12 hr light/dark cycle. The rats were fed with standard rat chow and water ad-libitum.

### Experimental Drugs

Resveratrol with brand name ‘Restorlyf’, manufactured by Nature’s Way U.S.A., was procured from Alliance in Motion Global Ltd., Ikeja, Lagos, Nigeria. 325 mg of Resveratrol were diluted immediately before each use in 20 ml of distilled water

and doses of 5, 10 and 20 mg/kg/b.wt were administered orally using the oral cannula. The remaining formulation was discarded after each use. The drug dosages and formulations were chosen on the basis of previously published studies on Resveratrol [7, 8]. Cisplatin (Zuplatin, 50 mg/ 50 ml) injection manufactured by Taj pharmaceuticals Ltd. India was procured from Bayston Pharmacy, Mushin, Lagos, Nigeria. The injection was given intraperitoneally according to body weight in a single dose of 5 mg/kg. The drug dosages were chosen on the basis of previously published studies on Cisplatin [9, 10].

## Experimental Design

Forty-five adult female Sprague–Dawley rats with average weight of 160 g were divided into 9 groups (n=5) and used for this experimental study. Group 1 served as the normal control group and received distilled water only. Group 2 was given only a single dose intra-peritoneal injection of 5 mg/kg b.wt Cisplatin and allowed to stay for 7 days before sacrifice. Groups 3, 4 and 5 were given 5, 10 and 20 mg/kg/b.wt. Resveratrol respectively for 7 days, starting 24 hours after a single dose intra-peritoneal injection of 5 mg/kg/b.wt. Groups 6, 7 and 8 were treated with 5, 10 and 20 mg/kg/b.wt. Resveratrol respectively for 14 days before a single dose intra-peritoneal injection of 5 mg/kg b.wt. Cisplatin; the respective doses of Resveratrol treatment was repeated for another 7 days. Group 9 was given only a single dose intra-peritoneal injection of 5 mg/kg b.wt. Cisplatin and allowed to stay for 21 days before sacrifice. At the end of the study, body weight and hematological indices were taken.

## Animal Sacrifice and Sample Collection

At the end of the study, the animals were fasted overnight and sacrificed by cervical dislocation. Blood samples were collected by cardiac. The serum was separated by allowing blood sample to stand for 15 minutes at 25 oC and then centrifuged at 4000 rpm for 20 minutes. Serum was kept in plastic vials at -40oC until further biochemical analysis.

## Determination of Hematological Parameters

Full blood count was done using BC-5300 Mindray Autohematology analyzer and all examinations were done using the CDC laboratory manual guide 2016. The blood parameters analysed include red blood cell count (RBC), white blood cell (WBC) and differentials' count, haemoglobin (Hb) concentration, packed cell volume (PCV). Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were also computed according to Jain (1986).

## Ethical consideration

Ethical approval was gotten from the College of Medicine of the University of Lagos Health Research Ethics Committee (CMULHREC) with ID number CMULHREC/09/16/025. All procedures were carried out in accordance with the National Academy of Science's Guide for Care and Use of Laboratory Animals [11].

## Statistical analysis

The results were analyzed using the Statistical Package for the Social Sciences version 21.0 (SPSS, Chicago, IL, USA). Data was reported as mean ± SD Differences between mean and the main effects of treatment group were determined by the one way analysis of variance (ANOVA) and multiple comparisons was done using the LSD post-hoc tests. The mean difference is significant at the 0.05 level (P<0.05).

## Results

### White blood cell counts and Differentials (Table I)

Groups 2 and 5 showed a significantly higher Total WBC when compared to the control group (p<0.05). The control group and groups 6 - 9 showed a significant reduction in Total WBC when compared to the group 2 (p<0.05). All treatment groups showed no significant difference in their Neutrophil differential when compared to the control group, groups 2 and 9 (p > 0.05) except for group 7 that have a significantly higher neutrophil count compared to both the control group and group 2 (p<0.05). Group 7 showed a significant decrease in the lymphocyte count compared to the control group (p<0.05). The control group and groups 2, 4, 6 and 8 showed a significant increase in lymphocyte count when compared to the group 9 (p<0.05). Only group 7 showed a significant decrease in lymphocyte when compared to the control group and group 2. Groups 6 and 7 showed a significant reduction in monocyte when compared to the control group (p<0.05).

There is no significant difference in the eosinophil count of all treatment groups when compared to the control group and groups 2 and 9 (p>0.05). Basophil increased significantly in group 7 when compared to the control group and the group 2 (p<0.05).

**Table 1** The Effect of Cisplatin and Supplementation with Resveratrol on the White blood cells and Differentials.

| GROUPS | TOTAL WBC (/103cm3) | NEUTROPHIL (%) | LYMPHOCYTE (%) | MONOCYTE (%) | EOSINOPHIL (%) | BASOPHIL (%) |
|---|---|---|---|---|---|---|
| GROUP 1 | 6.57 ± 1.50 b | 31.67 ± 1.67 | 64.67 ± 1.33 c | 2.67 ± 0.33 | 0.67 ± 0.33 | 0.33 ± 0.33 |
| GROUP 2 | 11.70 ± 2.34a,c | 31.33 ± 2.33 | 65.67 ± 2.73 c | 2.00 ± 0.00 | 0.67 ± 0.33 | 0.33 ± 0.33 |
| GROUP 3 | 8.00 ± 1.04 | 33.67 ± 2.73 | 63.67± 3.33 | 2.00 ± 0.58 | 0.67 ± 0.33 | 0.00 ± 0.00 |
| GROUP 4 | 8.90 ± 1.25 c | 31.00 ± 4.62 | 65.67 ± 4.63 c | 1.67 ± 0.67 | 1.33 ± 0.67 | 0.33 ± 0.33 |
| GROUP 5 | 11.67 ± 1.66a,c | 33.67 ± 0.97 | 63.00 ± 2.89 | 2.00 ± 0.58 | 1.33 ± 0.33 | 0.00 ± 0 .00 |
| GROUP 6 | 4.63 ± 0.15 b | 32.67 ± 2.03 | 65.33 ± 2.03 c | 1.00 ± 0.00 a | 0.67 ± 0.33 | 0.33 ± 0.33 |
| GROUP 7 | 5.9667 ± 1.72 b | 46.00 ± 5.69a,b | 50.33 ± 6.36a,b | 1.00 ± 0.58 a | 1.67 ± 1.20 | 1.33 ± 0.33a,b |
| GROUP 8 | 5.03 ± 1.28 b | 32.33 ± 4.18 | 64.67 ± 4.18 c | 1.67 ± 0.33 | 0.67 ± 0.33 | 0.67 ± 0.33 |
| GROUP 9 | 4.27 ± .769 b | 40.67 ± 0.89 | 53.67 ± 2.85 | 2.00 ± 0.58 | 3.00 ± 2.00 | 0.67 ± 0.33 |

Values are expressed as mean ± Standard Error of Mean (SEM). ap<0.05 significant compared to control group; bp<0.05 significant compared to group 2; cp<0.05 significant compared to group 9. WBC means white blood cells. CIS = cisplatin; RES = Resveratrol; MED = Medium. Group 1 = control; Group 2 = Cisplatin only; Group 3 = CIS + RES LOW; Group 4 = CIS + RES MED; Group 5 = CIS + RES HIGH; Group 6 = RES LOW + CIS + RES LOW; Group 7 = RES MED + CIS + RES MED; Group 8 = RES HIGH + CIS + RES HIGH; Group 9 = Cisplatin only

## Anaemia Blood markers (Table II)

The Red Blood Count (RBC) count was not significantly different in all the treatment groups when compared to the control group and cisplatin groups ($p>0.05$). All the experimental groups showed no significant difference in the Hemoglobin (Hb) levels and packed cell volume (PCV) when compared to groups 1, 2 and 9 except group 4 which showed a significant decrease when compared to group 9 ($p<0.05$). There was no difference in the Mean Corpuscular Volume MCV of all treatment groups when compared with the control group and cisplatin groups ($p>0.05$) except for groups 4 and 5 which showed a significant decrease when compared with group 9 ($p<0.05$). There was no significant difference in the Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) between all experimental groups ($p>0.05$).

**Table 2** The Effect of Cisplatin and Supplementation with Resveratrol on RBC, Hb, PCV and their derivatives in female Sprague-Dawley rats.

Values are expressed as mean ± Standard Error of Mean (SEM). ap<0.05 significant compared to control group; bp<0.05 significant compared to group 2; cp<0.05 significant compared to group 9. CIS = cisplatin; RES = Resveratrol; MED = Medium. Group 1 = control; Group 2 = Cisplatin only; Group 3 = CIS + RES LOW; Group 4 = CIS + RES MED; Group 5 = CIS + RES HIGH; Group 6 = RES LOW + CIS + RES LOW; Group 7 = RES MED + CIS + RES MED; Group 8 = RES HIGH + CIS + RES HIGH; Group 9 = Cisplatin only. MCV means mean corpuscular volume; MCH means mean corpuscular hemoglobin; MCHC means mean corpuscular hemoglobin concentration.

| GROUPS | Red Blood Cell (/cm3) | Hemoglobin (g/dl) | Packed Cell Volume (%) | MCV (Fl) | MCH (Pg) | MCHC (g/dl) |
|---|---|---|---|---|---|---|
| GROUP 1 | 6.73 ± 0.35 | 12.63 ± 0 .44 | 40.67 ± 2.03 | 60.33 ± 0.33 | 18.67 ± 0.33 | 31.33±0.33 |
| GROUP 2 | 6.87 ± 0.19 | 12.90 ± 0.21 | 40.67 ± 0 .88 | 58.67 ± 0.33 | 18.67 ± 0.33 | 32.33±0.33 |
| GROUP 3 | 7.03 ± 0.09 | 13.47 ± 0.12 | 42.00 ± 1.15 | 59.00 ± 0.58 | 19.33 ± 0.33 | 32.33±0.67 |
| GROUP 4 | 6.17 ± 0 .46 | 11.80 ± 0.91 c | 35.67 ± 2 .91 c | 57.67 ±0.88c | 19.00 ±0.00 | 33.00±0.58 |
| GROUP 5 | 6.83 ± 0.09 | 12.50 ± 0.25 | 38.33 ± 1.33 | 56.67 ±1.67c | 18.33 ± 0.33 | 32.33±0.67 |
| GROUP 6 | 6.37 ± 0.20 | 12.50 ± 0.40 | 39.00 ± 2.00 | 61.67 ± 2.03 | 19.67 ± 0.33 | 32.00±0.58 |
| GROUP 7 | 6.77 ± 0.27 | 12.87 ± 0.38 | 42.00 ± 2.51 | 62.00 ± 3.06 | 18.67 ± 0.33 | 31.00±1.15 |
| GROUP 8 | 6.63 ± 0.33 | 12.70 ± 0.50 | 39.67 ± 1.86 | 60.00 ± 0.00 | 19.00 ± 0.00 | 31.67±0.33 |
| GROUP 9 | 6.90 ± 0.10 | 13.20± 0 .21 | 43.33 ± 1.20 | 62.33 ± 0.33 | 19.00 ± 0.00 | 30.67±0.33 |

## Platelet count (Table III)

There is no significant difference in the platelet count of all experimental groups when compared with group 1 except for group 2 which showed a significant increase ($p<0.05$). All experimental groups showed significant decrease in platelet count when compared with group 2 ($p<0.05$) except for group 8 which showed no significant difference ($p>0.05$). Only group 4 showed a significant decrease in platelet count when compared with group 9 ($p<0.05$).

**Table 3** The Effect of Cisplatin and Supplementation with Resveratrol on the Platelet count of female Sprague-Dawley rats.

| GROUPS | PLATELET (/103cm3) |
|---|---|
| GROUP 1 | 0.73± 0.03 b |
| GROUP 2 | 1.03 ± 0.11 a,c |
| GROUP 3 | 0.68 ± 0.05 b |
| GROUP 4 | 0.37 ± 0.05b,c |
| GROUP 5 | 0.65 ± 0.09b |
| GROUP 6 | 0.63 ± 0.05 b |
| GROUP 7 | 0.68 ± 0.10 b |
| GROUP 8 | 0.83 ± 0.13 |
| GROUP 9 | 0.74 ± 0.10 b |

Values are expressed as mean ± Standard Error of Mean (SEM). ap<0.05 significant compared to control group; bp<0.05 significant compared to group 2; cp<0.05 significant compared to group 9. CIS = cisplatin; RES = Resveratrol; MED = Medium. Group 1 = normal control; Group 2 = Cisplatin only; Group 3 = CIS + RES LOW; Group 4 = CIS + RES MED; Group 5 = CIS + RES HIGH; Group 6 = RES LOW + CIS + RES LOW; Group 7 = RES MED + CIS + RES MED; Group 8 = RES HIGH + CIS + RES HIGH; Group 9 = Cisplatin only.

## Discussion

This present study assessed the effect of cisplatin and supplementation with resveratrol on some hematological parameters including white blood cell counts, differentials, anaemia blood markers and platelet counts in Sprague- Dawley rats. The significant differences observed in the various Parameters were compared with the normal control and the cisplatin control groups.

Research findings have established that haemolytic anaemia can be developed after several courses of cisplatin which was suggested to be due to the reaction of an antibody with a cisplatin-red-cell membrane [12]. Thus, anaemia has been stated as a common side effect of cisplatin, especially after repeated infusions; the primary mechanism is a myelosuppression caused by cisplatin's interference with iron metabolism, resulting in a lower count of red cell precursors [13]. Some authors report that haemolysis is caused by an antiglobulin antibody directed against red cell membrane-bound cisplatin. Cisplatin- based therapy has been discovered

to result in a cumulative anaemia that is disproportionate to the effects on other blood cells. On examination of the hematological parameters in this present study, we found no significant change between groups in the red blood cell, eosinophils and mean corpuscular haemoglobin concentration (MCHC) ($p>0.05$).

The total white blood cell count showed the cisplatin control group to have significantly increased when compared to the normal control group ($p<0.05$). The other treatment groups were observed to be the same with the normal group except for rats post-treated with high dose of Resveratrol which showed a significant decrease in total white blood cell count.

Unlike Juan and co-workers in 2002 who found out that high-dose resveratrol administration did not change hematological parameters in rats, this present study found WBC count to be significantly lower in the group that received high dose of resveratrol, as compared to the control group. This decrease could be as a result of the anti-inflammatory effect of resveratrol, which is in consonance with the observation of Donnelly et al., 2004 [14]. This is equally in line with the observation of Hişmioğulları et al., 2013 [6] who reported that WBC count was decreased in rats given resveratrol.

An assessment of the white blood cell (WBC) differentials showed that there was no significant change in the neutrophil of all groups except for rats treated with prophylactic medium dose of Resveratrol which showed a significant increase. An increase in leucocyte number could be consequence of infection and inflammation during cisplatin treatment and cisplatin metabolism in experimental rats [15]. This same group equally showed a significant decrease in the lymphocyte compared to the normal group as opposed to the no significant change seen across the other groups. These other groups also showed a significant increase in lymphocytes when compared to the cisplatin control group. Thus, lymphopenia which is often found in patients undergoing chemotherapy and radiotherapy was seen to be prevented across the resveratrol -treated groups.

The low and medium dose prophylactic groups showed a decrease in their number of monocyte while only the medium dose group showed a significant increase in basophil when compared to the normal control groups ($p<0.05$). This increase in basophils could have been as a result of an inflammation, as basophils take part in inflammatory response [16].

Our study, on assessment of the anemia blood markers showed that haemoglobin (Hb) and packed cell volume (PCV) of all treatment groups is the same with the normal control group ($p>0.05$). However, a decrease was observed in the haemoglobin level and packed cell volume of the group post-treated with medium dose Resveratrol when compared with the cisplatin control group. Mean cell volume (MCV) was seen to be significantly decreased in the medium and high dose post-treated with resveratrol when compared to the cisplatin control group, but other treatment groups showed no significant difference in MCV. There was no significant change observed in all groups when compared to the normal control in the mean cell haemoglobin (MCH) of the treated rats. However, only the medium dose post-treatment with Resveratrol showed a significant increase in MCH when compared to the normal control ($p<0.05$). There were no significant differences in the RBC count and MCHC in all treatment groups when compared to the control group and cisplatin groups.

Thus, the anemia blood markers were seen to be normal and unaffected in the cisplatin control groups, indicating that the cisplatin-treated groups did not suffer anaemia. This could have been because there were no chronic or repeated infusions of cisplatin on the rats. This finding is in agreement with previous research results by Markovic et al., 2010 [1] which showed that high, acute doses of cisplatin did not affect the RBC maturation in rats. More so, another study, in 1995 [3], showed that cisplatin causes significant effects on hematological parameters only during chronic treatment in humans and rats [4].

Previous studies by Olas and his colleagues in 2005 [15] have shown that cisplatin causes oxidative stress in human platelets and lymphocytes, which might reflect on their life expectancy, the induction of apoptosis, and thereby ultimately reduce the number of these cells in the blood. However, the platelet assessment in this study rather showed a significant increase in platelet count of cisplatin control group when compared to the normal group ($p<0.05$). This change seen may be unconnected to the cisplatin-triggered platelet activation as discovered in research by Calvert et al., 1989 [17]. Also, there was no significant difference in the platelet count across all the experimental groups when compared to the control group ($p<0.05$).

## Conclusion

Cisplatin used in the treatment of a wide range of malignant diseases has been associated with notable toxic effects on several organs. In this study, we have been able to show that cisplatin-induced alteration in some hematological parameters is reversible by resveratrol supplementation.

## Recommendation

Resveratrol supplementation should be incorporated as part of dietary nutrients for patients on cisplatin during chemotherapy. It is recommended, that further studies be conducted to fully ascertain the mechanisms of action of resveratrol and its anti-cisplatin properties.

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