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Assessment of Haematological Variation in Rat Bred Under Various Artificial Light Spectra at Night (ALAN)

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Abstract: Artificial light at night is considered as environmental stressor depending largely on the spectra. Haematological parameters have been used as bio-indicator of stress when animals are subjected to unfavourable environmental condition. Hence this study evaluated the effect of various spectra of light on the haematology of albino rats. Day old rats were exposed to blue (BL), green (GL), yellow (YL), red (RL) and white (WL) lights at night while darkness (DD) and ambient light (CL) served as control. Compact florescent bulbs were used and light intensity maintained at 300 lux. At days 35, 63, 91 and 126, six rats per treatment and per sex were euthanized. Blood was collected and analysed for haematocrit (Hct), haemoglobin (Hb) and red blood cells (RBC). At d35 and d63, Hct and Hb and RBC were significantly ($p < 0.05$) low in male and female rats exposed to coloured light. Hct and Hb recorded in the male rats exposed to green light and female rats exposed to blue and green lights were lower than the normal physiological range for rats at these ages bracket. Further exposure to light at d91 and d126 showed no negative effects on blood parameters. Linear regression showed significant increase in the blood parameter with time on exposure to coloured light which together signifies adaptation. Exposure to light of high energy (BL and GL) and WL during prepubertal could be detrimental. Normal day and night light cycle provided the optimum environmental lighting condition for adequate homeostatic of the blood in rats.

Keywords: Rat; ALAN, spectra; haematocrit; haemoglobin; Red Blood Cell

1. Introduction

Exposure to light at night has become one of the human life style and is becoming almost impossible to separate humans from it. Humans are exposed on daily basis to various light colours through cell phones, bill boards, television, street lights, and in restaurants, hotels, ports, boutiques, ware houses, hospitals, offices, car parks and eateries. Little is known about the health implication of exposure to light at night since not much empirical data is available to confirm or affirm some insinuations attributed to exposure to light at night.

Artificial light at night is of major concern to the epidemiologist and oncologist based on its implication in cancer of breast in females and prostate cancer in males (Haim and Portnov, 2014; Al-Naggar and Anil, 2016; Garcia-Saenz *et al.,* 2018 and Haim *et al.,* 2019).[1-4] The consequences and negative impact of exposure to light reported was directly linked to its ability to suppress melatonin (Falchi *et al.,* 2011; Haim and Zubidat, 2015),[5,6] an ubiquitous hormone known to play vital roles in the survival of animals due to its activity in combating oxygen radicals (Blask, 2009; Reiter *et al.,* 2011 and Guerrero *et al.*, 2013).[7-9] Melatonin is responsible for various physiological processes (Barrenetxe *et al.,* 2004; Golan *et al.,* 2018)[10-11] in the body and any alteration in its activity could be detrimental to the body.

Moreover, previous studies focus mostly on the effect of white light on the activity of melatonin (Haim and Portnov, 2014)[1] but recent studies have shown that all the light spectra have the potential to suppress melatonin, this time with respect to the light intensity (Zubidat *et al.*, 2011; Haim *et al.,* 2019).[12,4] Golan *et al.* (2018)[11] in their study establish the relationship between blood production, melatonin activity and light at night.

In evaluating environmental parameters that affect animal and human welfare, blood parameters have been in the front role due to its quick accessibility and functionality in knowing the internal status of animal. It is easier to evaluate the energy capacity of an animal when the blood parameter is known within a particular range of number. The energy available to animal is rudimental to determine its survival and resilience in combating severe condition of which gross haematological level play a vital role. The energy efficiency of animal is directly correlated with anaemia. Haematocrit, haemoglobin concentration and RBC are useful parameters to evaluate anaemia in animals (Dedeke *et al.,* 2017).[13]

Haematological parameters are a useful tool for determining the health status of animals as it signals largely the state of the internal environment of animals. They are useful tools for the detection of some changes in the health and physiological status of the animal, which are not detected easily during physical examination (Jawed *et al.,* 2004).[14] Haematological parameters have been used extensively to determine stress induced by both internal and some environmental factors such as heat, photoperiod and pollution. For instance, environmental and physiological factors have been reported to elevate the haematocrits of Indian shad, *Tenualosa ilisha* (Pecinova *et al.,* 2015).[15] Also, apart from revealing the internal disorder in the animal, haematological parameters have great implication in the welfare, physical shape and performance of animals (Vecerek *et al.,* 2002).[16]

Furthermore, alteration in haematological parameters is frequently used to determine the impacts of some environmental, nutritional and pathological factors in animal models.[17] Etim *et al*. (2014)[17] remark that haematological studies represent a useful process in the investigation of the extent of damage to the blood cells. Since light at night is considered an environmental stressor, hence the need to evaluate its impact on the haematology of animals and probably to know how safe one is, when exposed to it. Therefore, this study aims at assessing the haematocrit, haemoglobin and erythrocytic variation in rat bred under various artificial lights at night.

2. Experimental Section

2.1. Breeding of experimental of rats

Albino rats, 90 females and 30 males were procured from the Institute for Medical Research and Training (IMRAT) and University College Hospital, Ibadan, Oyo State, Nigeria. The rats were acclimatized for two weeks after which they were grouped in ratio 3:1 (female/male) for the breeding of experimental rats. Day old rats obtained from the breeders were randomly distributed with their mothers into different cages for the light treatments.

2.2. Breeding of experimental of rats

The monochromatic lights used include Blue (BL), Green (GL), Yellow (YL) and Red (RL), while polychromatic White (WL) was also used. Ambient light (CL) (12L: 12D) and Darkness (DD) (0L: 24D) served as control while Compact Fluorescent bulb of 13 watts (ESTAR, China) was used as the source of light. The light intensity was regulated between 300 - 350 lux monitored by the light meter (LX-1010B model). Inverters were also used to ensure uninterrupted power supply throughout the study period.

2.3. Experimental design

Day-old rats (with their mothers) were randomly distributed into wooden cages for the light treatment. The pups fed on their mother's milk for the first 28 days after which the mothers were isolated; male and female were separated into different cages and the exposure continued. The rats were fed with standard rat pellet and tap water was given *ad libitum.* There were three replicates per treatment and per sex; each replicate had 10 rats. The rats were exposed to different light colours at night (6 pm – 6 am, 12 hours) for 126 days. By standard practise and procedure, the ethical guidelines of the National Institutes of Health guide for the care and use of Laboratory animals (NIH Publications No. 8023, revised 1978) was followed during this study.

2.4. Collection of Blood

At days 35, 63, 91 and 126, two rats from each replicate, given six per treatments were randomly selected and euthanized using diethyl ether (SIGMA ALDRICH, England). The rats were quickly opened up and the blood was collected by cardiac puncture into EDTA bottles for the analysis of haematological parameters.

2.5. Measurement of haematocrit, Red blood cell count and Haemoglobin

Haematocrit, Red blood cell count and haemoglobin were carried out according to the methods described by Das et al. (2011).[18]

2.6. Statistical analysis

Analysis of variance using ANOVA was carried out and the means separated by Duncan's multiple comparison and student T-test was used to compare between mean results of male and female rats. Linear regression analysis was also carried out to establish the relationship between the blood parameters and the period of exposure. The level of significant was considered at $p < 0.05$. Statistical package for the social sciences (SPSS) version 20 was used for the analysis.

3. Results and Discussions

Environmental factors have been reported to have effects on the haematological parameters of animals (Mazzullo *et al.,* 2014*;* Kim *et al.,* 2013).[19,20] However, there is paucity of information on the effect of various light colours on the haematology of mammals. In this study, it was observed that sex, age and spectral power distribution of light altered the haematological profile of albino rats. The varying Haematocrit and haemoglobin levels in rats exposed to green and blue lights at d35 and d63 suggest probable induction of anaemia in both male and female rats (Table 1). At this said periods, all the monochromatic and polychromatic lights significantly reduced ($p < 0.05$) the level of Haematocrit as compared with the control. The least and significant ($p < 0.05$) values were recorded in the male and female rats exposed to green light (27.17 ± 2.40 and 27.50 ± 4.59 % respectively). Female rats exposed to blue and white light also recorded significantly ($p < 0.05$) lower values (28.67 ± 4.72 and 29.50 ± 5.05 % respectively).

Furthermore, Haemoglobin concentration was significantly ($p < 0.05$) low in the rats exposed to the monochromatic and polychromatic lights with the least in male rats exposed to green light (9.02 ± 0.80 g/dl) and female rats exposed to blue and green lights (9.10 ± 1.35 and 9.42 ± 0.86 g/dl respectively). At d63, Haemoglobin concentration was also significantly ($p < 0.05$) low in the rats exposed to the monochromatic and polychromatic lights

Table 1. Mean Haematocrit (Hct), Haemoglobin (Hb) concentration and Red Blood Cell (RBC) count of male and female rats exposed to ALAN spectra at Night at day 35 and 63.

		LIGHT TREATMETS						
Day	**Sex/Parameter**	**Ambient light**	**Blue Light**	**Green Light**	**Yellow Light**	**Red Light**	**White light**	**Darkness**
35	Male / Hct (%)	44.33±1.21^{d}	37.83±2.71^{c}	27.17±2.40^{a}	34.17±2.99^{b}	38.33±3.01^{c}	30.00±2.61^{a}	39.67±1.51^{c}
	Female/ Hct (%)	45.67±3.27^{c}	28.67±4.72^{a}	27.50±4.59^{a}	36.83±2.71^{b}	34.50±2.95^{b}	29.50±5.05^{a}	38.83±5.27^{b}
	P-value (dt = 10)	**0.371**	**0.002**	**0.878**	**0.137**	**0.050**	**0.834**	**0.717**
35	Male /Hb (g/dL)	14.48±0.29^{d}	12.48±1.03^{c}	9.02±0.80^{a}	11.90±0.53^{bc}	12.43±0.89^{c}	10.90±1.16^{b}	13.58±1.37^{d}
	Female /Hb (g/dL)	14.90±1.40^{d}	9.10±1.35^{a}	9.42±0.86^{a}	11.07±0.94^{b}	11.30±0.92^{b}	9.03±1.11^{a}	12.97±0.94^{c}
	P-value (dt = 10)	**0.492**	**0.001**	**0.422**	**0.086**	**0.055**	**0.017**	**0.384**
35	Male / RBC (1012 /L)	6.45±0.43^{de}	6.62±0.67^{e}	4.48±0.52^{a}	5.68±0.50^{bc}	6.37±0.56^{cd}	5.50±0.71^{b}	5.78±0.62^{bcd}
	Female / RBC (1012 /L)	7.53±0.68^{d}	5.02±0.49^{a}	4.77±0.37^{a}	5.85±0.60^{b}	5.37±0.43^{ab}	4.77±0.68^{a}	6.62±1.02^{c}
	P-value (dt = 10)	**0.008**	**0.001**	**0.301**	**0.614**	**0.006**	**0.098**	**0.119**
63	Male **/** Hct (%)	50.50±2.74^{c}	28.17±2.04^{a}	29.83±4.17^{a}	31.00±1.79^{a}	28.00±2.68^{a}	28.00±2.61^{a}	46.00±2.10^{b}
	Female / Hct (%)	42.33±4.59^{c}	24.67±3.14^{a}	28.83±4.26^{a}	48.00±5.97^{d}	41.17±4.79^{bc}	36.67±4.23b	49.00±3.03d
	P-value (dt = 10)	**0.004**	**0.045**	**0.69**	**0.000**	**0.000**	**0.002**	**0.074**
63	Male / Hb (g/dL)	15.92±1.4^{c}	9.58±0.45^{a}	9.83±1.45^{a}	10.18±0.58^{ab}	10.28±2.21^{ab}	9.42±0.91^{a}	12.03±2.47^{b}
	Female / Hb (g/dL)	14.03±1.63^{cd}	8.13±1.03^{a}	9.60±1.43^{a}	14.80±1.57^{d}	12.88±1.04^{bc}	12.17±1.41^{b}	14.47±1.17^{cd}
	P-value (dt = 10)	**0.059**	**0.010**	**0.785**	**0.000**	**0.026**	**0.002**	**0.054**
63	Male / RBC (1012 /L)	6.90±0.99^{b}	4.75±0.36^{a}	4.80±0.81^{a}	5.52±0.67^{a}	5.38±0.93^{a}	5.00±0.99^{a}	7.32±0.44^{b}
	Female / RBC (1012 /L)	6.77±0.40^{c}	4.30±0.35^{a}	4.88±0.68^{a}	8.17±0.67^{d}	6.68±0.56^{bc}	6.07±0.73^{bc}	7.98±0.26^{d}
	P-value (dt = 10)	**0.765**	**0.052**	**0.850**	**0.000**	**0.015**	**0.059**	**0.010**

Values with the same superscript along the row are not significantly different p > 0.05; Note, n = 6

Table 2. Mean Haematocrit (Hct), Haemoglobin (Hb) concentration and Red Blood Cell (RBC) count of male and female rats exposed to ALAN spectra at Night at day 91 and 126.

		LIGHT TREATMETS						
Day	**Sex/Parameter**	**Ambient light**	**Blue Light**	**Green Light**	**Yellow Light**	**Red Light**	**White light**	**Darkness**
91	Male **/** Hct (%)	41.50±2.81^{b}	42.67±3.88^{b}	42.17±9.50^{b}	42.50±3.27^{b}	48.17±3.49^{a}	49.83±2.56^{c}	53.83±4.45^{c}
	Female / Hct (%)	41.17±3.82^{bc}	34.67±4.32^{a}	43.33±4.03^{c}	36.17±4.17^{ab}	40.33±2.66^{bc}	34.33±3.67^{a}	49.83±7.25^{d}
	P-value (dt = 10)	**0.867**	**0.007**	**0.787**	**0.015**	**0.024**	**0.000**	**0.276**
91	Male / Hb (g/dL)	14.95±1.37^{ab}	13.78±1.74^{ab}	18.02±1.92^{d}	14.27±1.23^{ab}	13.50±2.70^{a}	15.82±1.77^{bc}	17.38±1.03^{cd}
	Female / Hb (g/dL)	14.00±1.11^{abc}	11.83±1.84^{a}	14.58±1.86^{bc}	12.12±1.46^{a}	13.40±0.87^{ab}	12.28±2.25^{a}	16.03±1.87^{c}
	P-value (dt = 10)	**0.216**	**0.089**	**0.010**	**0.020**	**0.933**	**0.013**	**0.153**
91	Male / RBC (1012 /L)	7.70±0.44^{bcd}	6.67±0.24^{ab}	6.95±1.38^{abc}	6.88±0.35^{abc}	6.33±1.45^{a}	7.97±0.97^{cd}	8.68±0.83^{d}
	Female / RBC (1012/L)	7.68±1.10^{c}	5.70±0.60^{a}	7.20±0.71^{bc}	6.13±0.80^{a}	6.65±0.41^{ab}	6.13±1.10^{a}	7.85±0.63^{c}
	P-value (dt = 10)	**0.973**	**0.004**	**0.702**	**0.061**	**0.617**	**0.012**	**0.078**
126	Male / Hct (%)	49.00±3.52^{c}	44.17±2.79^{b}	36.67±4.59^{a}	47.33±2.88^{bc}	45.83±0.75^{bc}	37.33±1.51^{a}	53.00±2.10^{d}
	Female / Hct (%)	44.83±4.07^{b}	37.33±3.33^{a}	39.33±4.80^{a}	46.00±3.35^{b}	46.00±1.26^{b}	43.67±2.34^{b}	46.67±2.94^{b}
	P-value (dt = 10)	**0.087**	**0.003**	**0.349**	**0.476**	**0.787**	**0.000**	**0.002**
126	Male / Hb (g/dL)	13.57±1.00^{b}	12.92±1.09^{ab}	11.95±1.68^{a}	14.95±1.63^{c}	15.13±0.46^{c}	12.32±0.59^{ab}	16.52±0.82^{d}
	Female / Hb (g/dL)	14.03±1.71^{cd}	11.92±0.61^{a}	12.22±0.98^{ab}	15.27±1.11^{d}	14.92±0.79^{cd}	13.32±1.95^{ab}	13.77±1.29^{bc}
	P-value (dt = 10)	**0.577**	**0.080**	**0.744**	**0.702**	**0.575**	**0.257**	**0.001**
126	Male / RBC (1012 /L)	7.62±0.55^{c}	7.02±0.81^{bc}	6.25±0.86^{ab}	7.00±0.59^{bc}	7.37±0.59^{c}	6.08±0.33^{a}	7.72±0.51^{c}
	Female / RBC (1012/L)	7.00±0.72^{ab}	6.38±0.47^{a}	6.43±0.71^{a}	7.88±0.45^{c}	7.42±0.84^{bc}	6.90±0.77^{ab}	7.12±0.57^{ab}
	P-value (dt = 10)	**0.124**	**0.128**	**0.697**	**0.016**	**0.907**	**0.038**	**0.083**

Values with the same superscript along the row are not significantly different p > 0.05; Note, n = 6

with male rats had low values when exposed to blue, green and white lights (9.58 ± 0.45, 9.83 ± 1.45 and 9.42 ± 0.91 g/dl respectively) and female rats exposed to blue and green light (8.13 ± 1.03 and 9.60 ± 1.43 g/dl respectively). RBC count was also significantly low ($p < 0.05$) in the male rats exposed to green, yellow and white lights (4.48 ± 0.52, 5.68 ± 0.50 and 5.50 ± 0.71 x 1012 /L respectively) and female rats exposed to all the monochromatic and polychromatic lights and darkness as compared with the ambient light at d35. At d63, RBC was significantly low ($p < 0.05$) in male rats exposed to coloured lights and female rats exposed to blue and green light (4.30 ± 0.35 and 4.88 ± 0.68 x 1012 /L).

Consequently, the value of Haematocrit and haemoglobin recorded in the male rats exposed to green light at d35 and d63, and female rats exposed to blue and green lights at the same period were lower than the normal physiological range for rats at these ages bracket. However, the abnormality recorded could be as a result of alteration in the haematogenesis of the rats at early stages of development. It is imperative to state that normal homeostasis of bone marrow is essential to the analysis in order to prevent haematology failure (Golan *et al*., 2018).[11] The authors cited reported that light and darkness cycle play an active role in maintaining bone marrow homeostasis and that during the day due to light, the differentiation of haematopoietic stem and progenitor cells (HSPCs) occurred in order that mature blood cells and immature blood cell are mobilized into the circulation accordingly. And at night (darkness), the release of melatonin inhibits the differentiation of HSPCs in such a way which mediates the repopulation of the HSPCs in the bone marrow thus maintaining blood bank.

Golan *et al*. (2018)[11] remarked that the inhibition of melatonin by light at night prevents repopulation of HSPCs in the bone marrow and thus reduced the level of progenitor cells and invariably reduced the quantity of blood cell released into the circulation during the day. Since ALAN suppresses melatonin (West *et al*., 2011; Wright and Shelford, 2013; Haim and Portnov, 2014),[22,23,1] therefore the result

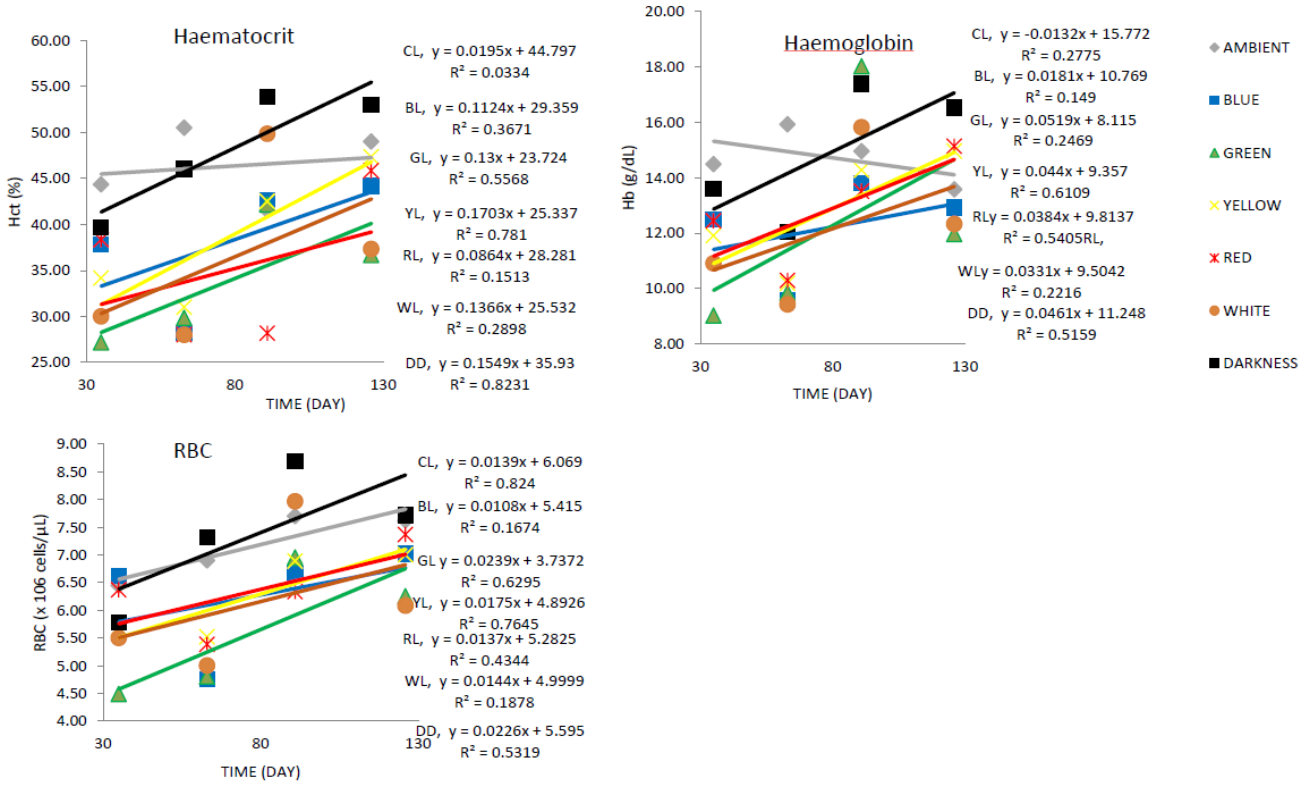

Fig. 1. Trend in the Hct, Hb and RBC of male albino rats exposed to the light of varying wavelength for 126 days.

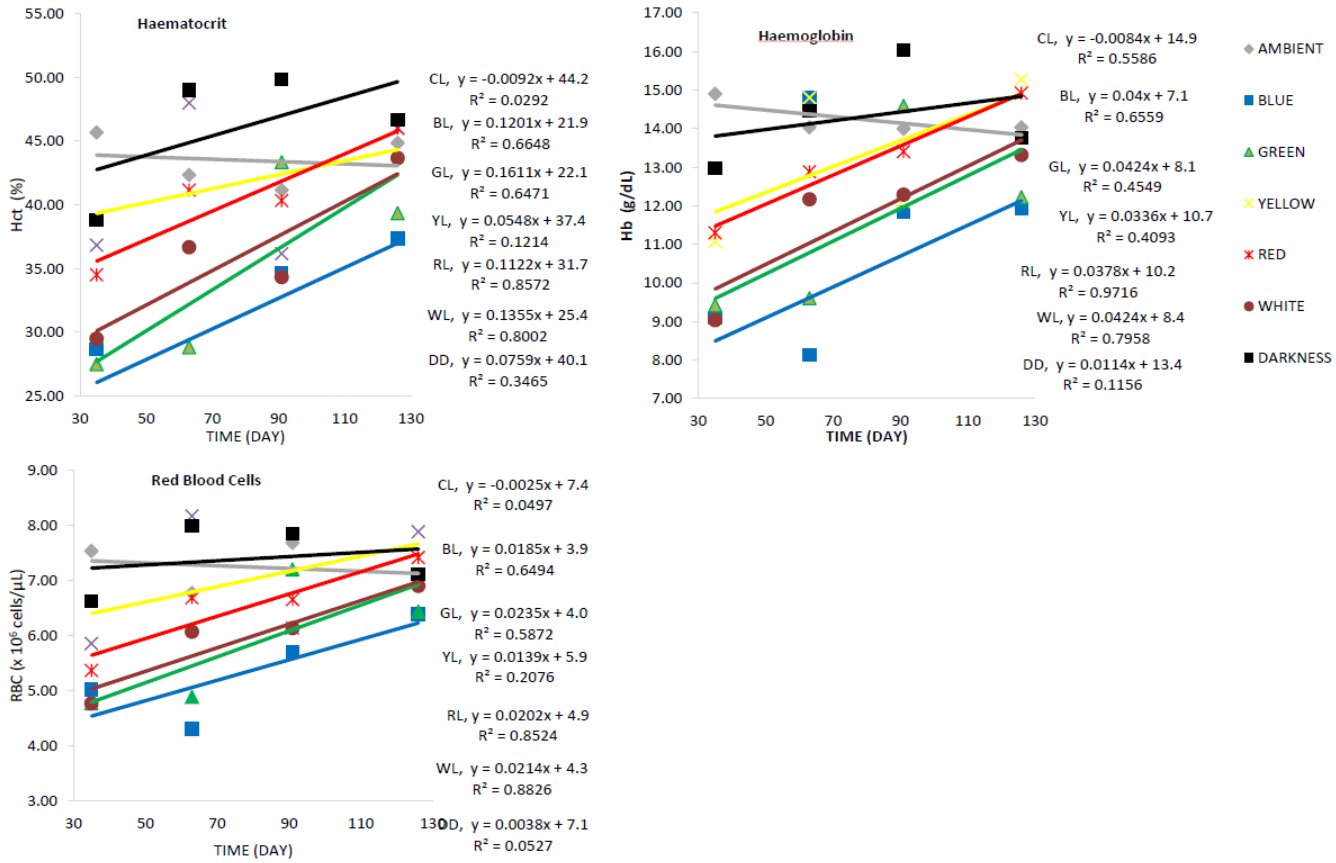

Fig. 2. Trend in the Hct, Hb and RBC of female albino rats exposed to the light of varying wavelength for 126 days.

obtained from this study clearly demonstrated that the suppression of melatonin by blue, green and white lights at night was responsible for the low level of the blood cells hence the induction of anaemia at the early stage of development.

Moreover, previous studies reported that exposure to white light altered some blood parameters. For instance, Dedeke *et al.* (2017)[13] reported that albino rats exposed to White light for 63 days had low Haematocrit. The study of Pecinova *et al*. (2015)[15] which was also experimented revealed a reduction in the haematocrit of Brown rats after 5 weeks of exposure to white light at 400 lux. The same with the study of Kim *et al*. (2013)[20] showed that broiler birds exposed to white light for 5 weeks recorded lower numerical haematocrit value when compared with other light treatments. But on the contrary, Hassan *et al*. (2017)[21] reported that monochromatic lights have no effect on the haematocrit of duck although the intensity of light used for their study was lower and could attribute to the differences recorded. The decreased haematocrit value induced by green and blue lights during an early stage could therefore be that these high energy lights altered the physiological pathways that lead to the production of blood.

It is very important to state however that the level of Haematocrit, haemoglobin and RBC of the rats in this study became normalized, attaining normal physiological ranges as the rats grew older based on the values recorded at d91 and d126 (Table 2). Zakari *et al*. (2016)[24] submitted that haematological parameters can be used to know the adaptability of animal to adverse environmental condition. Ashkenazi and Haim (2013)[25] in their study also concluded that as animals are being continually exposed to light, acclimatization and adaptation set in such animals' body systems respond in an anticipatory manner. Invariably, at d91, haemoglobin concentration was significantly higher in the male rats exposed to green light and darkness (18.02 ± 1.92 and 17.38 ± 1.03 g/dl respectively) and female under darkness (16.03 ± 1.87 g/dl). This study as analysed and experimented showed that the rats got adapted with time as they were exposed to the light.

This also explains the significant increase in the levels of Haematocrit, haemoglobin and RBC with time in rats exposed to the monochromatic and polychromatic lights (Fig. 1). In the male rats, the regression analysis showed that haematocrit increased significantly with time in the rats under DD, YL and GL (R2 = 0.82, 0,781 and 0.56 respectively). Hb concentration increased significantly with time in the rats exposed to YL and RL (R2 = 0.61 and 0.54 respectively) and DD (R2 = 0.52). RBC increased significantly with time in the rats exposed to YL and GL (R2 = 0.78 and 0.63) and DD (R2 = 0.53). In the female rats, haematocrit increased significantly with time in the rats exposed to RL, WL, BL and GL (R2 = 0.85, 0.80, 0.66 and 0.65 respectively). The concentration of Hb increased significantly with time in the rats exposed to RL, WL and BL (R2 = 0.97, 0.80 and 0.66 respectively). RBC increased significantly with time in the rats exposed to RL, WL, BL (R2 = 0.85, 0.88 and 0.65 respectively) (Fig. 2). This study clearly pointed to the fact that female rats exposed to blue and white lights recover faster than their male counterpart and thus demonstrated the resilience of female over male to adverse condition. This study clearly demonstrates that normal day and night cycle as well as continuous darkness provided the optimum environmental lighting condition for adequate homeostatic of the blood in the rats.

4. Conclusions

In conclusion, this study clearly demonstrated that light as an environmental parameter has significant effect on animal haematology and this time with respect to the spectra quality of the light and age. It is important to know that exposing children to light of high energy or short wavelength could be detrimental to their health. This understanding probably explains why the eyes of premature babies in incubators are usually wrapped so as to prevent blue light from entering the eyes. Exposure to blue and green lights at an early stage of development seemed harmful and can possibly be avoided. Normal day and night light cycle can be termed best for as long as the ideal environmental lighting condition for passable homeostatic of the blood is provided in rats during early age of development.

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Author's contributions

The research concept and design were done by F. O. Kehinde, G. A. Dedeke, M. A. Olude and K. O. Ademolu. The main experiment was conducted by F. O. Kehinde. Data Analysis was done by A. A. Aladesida. The manuscript was prepared, read and approved by all authors.

Conflicts of Interest

The authors declare no conflict of interest.

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