Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 1, 2021, Pages. 597 - 602
Received 15 December 2020; Accepted 05 January 2021.

Clinicohematological Study of Gold Nanoparticles Toxicity and Ameliorative Effect of *Allium Sativum*

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Abstract

Administration of chemical substances at toxic doses usually lead to blood parameter alterations, which indicates occurrence of hematological disorders like anaemia. In addition to the positive effects of nanoparticles, they are considered as potential hazardous agents to human's health. In the present study, (24) healthy albino rats were divided into 4 groups, 6 rats for each. The control animals included rats without treatment, while the GNPs group rats received gold nanoparticles. GNPs +AS group rats were co-administrated with a combination of GNPs with *Allium sativum*. The AS group animals were treated with *A. sativum* only. Blood parameters were measured to find the negative effects of gold nanoparticles. Results in the GNPs group showed that the hematological parameters were significantly decreased ($p<0.05$) including the red blood cell count (RBCs), hemoglobin (Hb) concentration, hematocrit value (Hct) and platelet count (PLTs), while the white blood cell count (WBCs) showed a significant increase in comparison to the control group. The co-administration of *A. sativum* along with GNPs exerted a significant modulation in all hematological disorders. Therefore, these results demonstrated that *A. sativum* has shown a defensive impact against GNPs induced hematological alterations in male rats.

Keywords: *Gold nanoparticles, blood parameters, Allium sativum.*

Introduction

Gold nanoparticles (GNPs) have various applications in the medical field[1]. Several reports revealed the presence of toxic impacts of nanoparticles in vivo, although nanoparticles are known to be safe materials[2]. At the (1–100 nm)[3] Nano scale, materials are different from their bigger counterparts as they are more reactive owing to the relatively high surface to diameter ratio[4]. The evaluation of hematologic parameters is essential to determine gold nanoparticle toxicity[5]. Under certain conditions, it is difficult to translate the adverse impacts from animal to human, but the detection of animal's blood parameters is of great predictive value for human toxicity [6].

Till now, herbs are used mainly in the treatment in several developing country for primary health care due to their excellent culturing compatibility and acceptance in the human body as well as their lesser side effects[7]. *Allium sativum* L., Family: Amaryllidacae is the scientific name of garlic, which is the aromatic annual spice herb and the oldest authenticated and most essential herbal plant which was used from ancient times in traditional medical treatments[8,9].The existence of sulfur containing chemicals in garlic provides substantial anti-inflammatory, immunomodulatory, antitumor, anticancer, antidiabetic, anti-atherosclerotic as well as cardio protective features[10,11].

The present study has been designed for investigation of the impacts of repeated intraperitoneally injections of 14 nm size GNP on some haematologic parameters and Co-administrated gold nanoparticles with *Allium sativum*.

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Materials and Methods

Chemicals

Gold (Au) Nanopowder Water Dispersion was purchased from US Research Nanomaterials, Inc. Company (Houston, TX, USA). Particle Average Size: 14 nm, PH= 7±0.5, Purity: 99.99 %., went through a rigorous scientific preparation process of Nano gold productions in aqueous solutions. A 50 µL (0.25 mL/kg/day) dose was administered intraperitoneally to the rats[12]. *Allium sativum* was obtained in the form of Odorless Garlic powder from pure, healthy and odorless garlic plant USA.

In vivo experimental design

In this study, (24) adult male albino rats with weighing (200-215 gm) were used. Animals were housed in humidity and temperature-controlled ventilated cages on 12 hour light–12 hour dark cycles, with free access to the standard laboratory rats' water & diet. The animals have been divided randomly into 4 groups (6 animals in each group): The control animals included normal healthy rats; the (GNPs) group included rats received GNPs; the (GNPs+AS) group included GNPs intoxicated rats treated with *A. sativum* at 300 mg/kg bw [13]; (AS) group included animals which were given *A. sativum* at 300 mg/kg dose alone, for 14 consecutive days. The animals received their daily doses for 14 consecutive days. At the end of the experiment, animals were sacrificed. Blood was collected by cardiac puncture in (EDTA) containing tubes for performing complete blood count.

Complete blood count

The estimation of red blood cell counts (RBCs), hemoglobin (Hb) concentrations, hematocrit values (Hct), platelet counts (PLTs) and white blood cell counts (WBCs) were performed by the automatic hematology analyzer.

Statistical analysis

The obtained results were performed as mean (±) standard deviation (n=6). The statistical significance between the different groups was analyzed using the one way analysis of variance (ANOVA) followed by Duncan multiple range analysis.

Results

Results of the experimental groups showed significantly lower red blood cell counts (RBCs), hemoglobin (Hb) concentration, hematocrit value (Hct) and platelet count (PLTs) in the GNPs group ($p<0.05$). Leukocytosis was evident in GNPs intoxicated rats, as shown in figure (2). This finding indicates that the blood is slightly altered with the administration of GNPs. Co-administration of *A. sativum* to GNPs rats significantly improved all these hematological parameters ($p<0.05$) when compared with the GNPs intoxicated rats.

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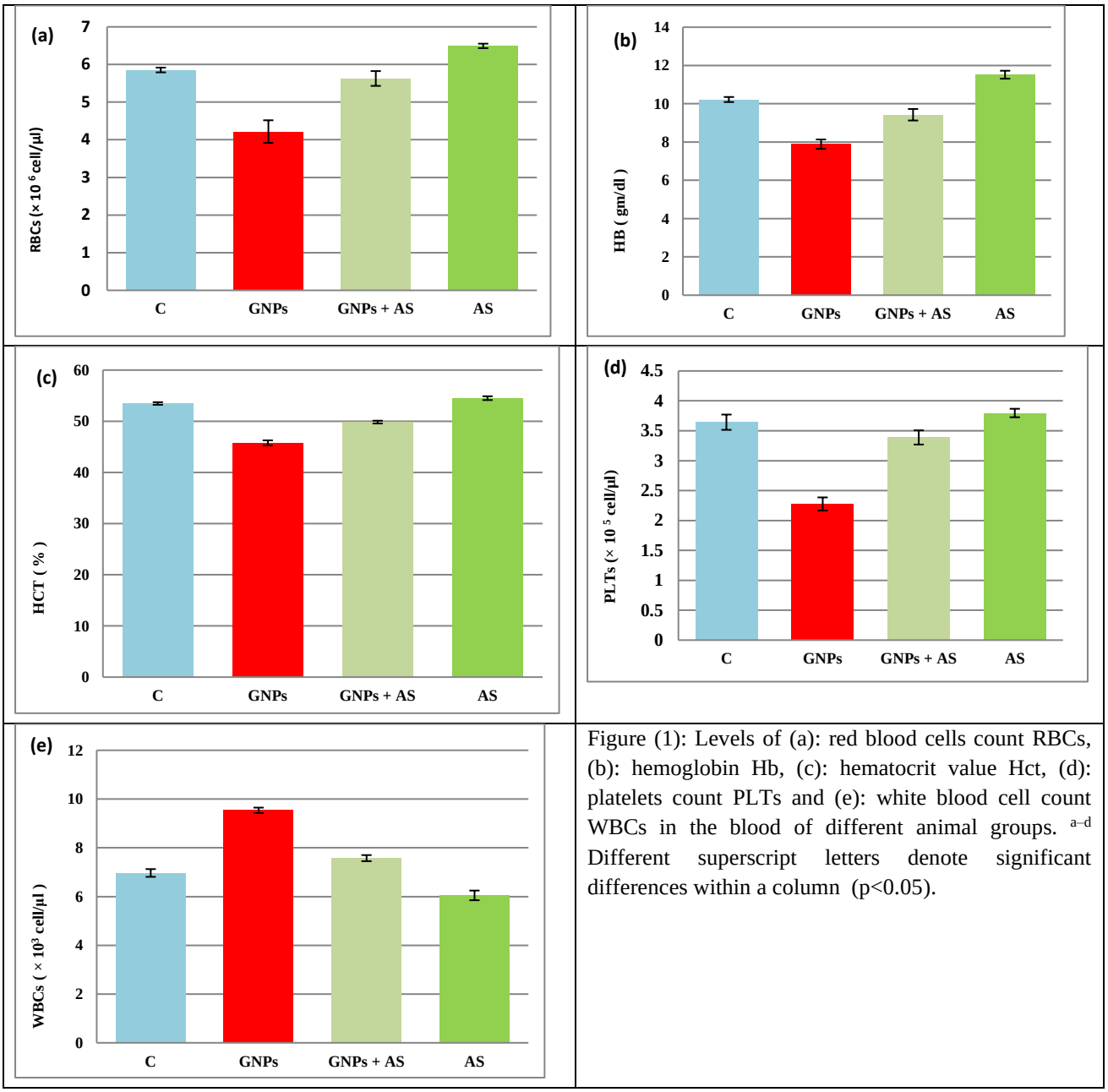

Figure (1): Levels of (a): red blood cells count RBCs, (b): hemoglobin Hb, (c): hematocrit value Hct, (d): platelets count PLTs and (e): white blood cell count WBCs in the blood of different animal groups. [a–d] Different superscript letters denote significant differences within a column ($p<0.05$).

Discussion

Haematopathology is a laboratory medical practice and science which is concerned with the study, investigation and diagnosis of blood disorders. The functional characteristics of hematological parameters are altered because of adding altered tissue and biochemical product to blood and their interaction with the blood component[15]. The first physiologic system that gold nanoparticles interact with after administration is blood & blood components. The gold nanoparticles are able to stimulate inflammatory responses and decrease or increase the immune system's activities and change related hematological parameters e.g blood cell count. The alterations in the physicochemical characteristics including form, length, combination, chemical make-up, high specific surface area & solubility were because of the toxicity induced by GNPs[16,17]. In our study, the low red cell number was related to development of anemia[18], which represented a pathologic condition characterized hemoglobin concentration under the normal value. This could be resulted from blood loss (hemorrhage), inadequate red cell and Hb production, or accelerated red blood cell

destruction [19-22] . Hemoglobin is the main intracellular protein in the red cell, which is synthesized in bone marrow. Low hemoglobin concentration may result from blood loss or immature reticulocytes or accelerated red blood cell destruction, leading to anaemia[23-25]. Bone marrow is the site of platelet production and therefore, their counts may be reduced in diseases of bone marrow as well as anaemia. Circulating platelets may be decreased (thrombocytopenia) by either decreased production or increased platelet destructions[26-28]. Hematocrit, the volume of red blood cells in a column of whole blood and is clinically used for detection of suspected or known anemia. Factors affecting red cells will have effect on the haematocrit since red cells constitute 99% of the whole blood cells. Hematocrit is the main measure of blood viscosity[29,30]. A hematocrit value below the normal represents anemia .This may be resulted from a reduction in the erythrocyte count, a decrease in the hemoglobin concentration in each red cell, or both. It often occurs due to myeloid tissue damage by chemicals like toxins, which inhibit enzymes required for haemopoiesis[31,32]. The white cells (WBCs) are responsible for body's immunity against antigenic invasions. These white cells are synthesized in the bone marrow from a pluripotent hematopoietic stem cell (myeloid) [33, 34]. The usual inflammatory response includes white cell accumulation, in the site of foreign particle position to remove cells selectively and restore homeostasis[35,36]. The hematological parameters were shown to be significantly improved in the GNPs + *A. sativum* group when compared with the GNPs group. This might be attributed to the organosulfur compound (OSC) in the garlic. This compound plays an essential role in preventing different pathological progressions[37]. Several experiments demonstrated the anti-inflammatory characteristics of (OSC) and highlighted their indirect mechanisms as well as providing chemoprotections [38,39]. Thus, this study revealed that *A. sativum* acts as a protective agent against blood disorders caused by hematotoxicity of GNPs.

Conclusions

It can be concluded from the current study that gold nanoparticles have toxic effects on blood components. Here, we have discussed the probability of blood toxicity reduction by using *A. sativum* as herbal plant. Our findings showed that garlic may have an important role in ameliorating heamatotoxicity.

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