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Prophylactic Effect of Silver Nanoparticles on Blood Indices Disturbances in Drug-Induced Photosensitivity

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***Abstract*—** *Understanding photosensitivity is one step in a comprehensive approach to skin health. This study aimed to illustrate the efficiency of silver nanoparticles (AgNPs) against an alteration of hematological indices in drug induced photosensitivity in male rats. A total of 24 male albino rats were randomly assigned into 4 groups (n=6). Control group received no treatment; whereas SJW group: rats treated with St. John's wort (SJW) to induced photosensitivity; SJW +Saff group: Co-administration of SJW along with saffron extract; and SJW +AgNPs group: Co-administration of SJW along with AgNPs. All studied rats were exposured to sunlight rays directly daily (30 minutes) for 15 days. As results, rats treated with SJW showed a significant decrease in red blood cells, hemoglobin, hematocrit, mean corpuscular volume, and platelets, cmbined with clear rduction in white blood cell counts.In constrat, co-administration of AgNPs along with SJW exerted a significant recovery effect in hematological disorders. As a result, these findings demonstrated that herbal AgNPs had a protective effect against photosensitivity-induced hematological changes in male rats.*

***Keywords*—** *Photosensitivity, hematological indices, silver nanoparticles.*

I. INTRODUCTION

Drug induced photosensitivity of the skin is drawing increasing attention[1]. In past few decades, photosensitivity has been reported with an array of drugs and is now recognized as a noteworthy medical problem by clinicians, regulatory authorities, and the pharmaceutical industry [2,3]. It results when certain chemicals or drugs are taken systemically or applied topically at same time with exposing to ultraviolet radiations or visible light, leading to generation of free radicals as phototoxic reaction, or changes drug structure into a form causing immune response as photoallergic reaction [4,5]. The list of drugs causing photosensitivity is long, with new photosensitizing agents added every year, including nonsteroidal anti-inflammatory drugs, cardiovascular drugs, central nervous system drugs, antibiotics, anticancer drugs, and retinoids [6,7]. St. John's wort (SJW) is a phototoxic to the skin [8,9] and generally represents an over-the-counter antidepressant that includes hypericin, a potent photosensitizer known to be effective when exposed to UV or visible light. It has also been demonstrated to cause apoptosis in human lens epithelial cells and retinal pigment epithelial cells [10] as well as to cross the blood-retinal barrier.

It was anticipated that the use of nanotechnology in medical fields would revolutionize healthcare [11–15]. It has potential to significantly improve medical diagnosis, treating and preventing many diseases [16-18]. It is bridging the gap between pharmaceutical limitations and the therapeutic potentials of natural phytochemicals by improving the compound's targeting and pharmacokinetics [19,20].

Among metallic nanoparticles, silver nanoparticles (AgNPs) have antimicrobial, antifungal, antiviral, catalytic, and other properties, which make it possible to apply in medicine and pharmaceutical industry [21-23]. It is worth noting that physical, chemical, and green biological methods are developed to produce silver nanoparticles [24]. The biological method is eco-friendly, low-cost, and does not require expensive instrumentations because the reducing and capping agents are derived from nature such as plants and microorganisms [25]. On the other hands using medicinal plants is advantageous as their medicinal properties are added to the nanoparticles during synthesis [26], they are considerably preferred for the biosynthesis of silver nanoparticles due to the diverse richness with potent antioxidant properties [27].

Saffron, the dried, dark red stigmas of Crocus sativus L. has been chosen for the current experimental study, it is a perennial stemless herb which belongs to the Iridaceae family [28]. In traditional medicine, as well as in modern pharmacology, saffron has been used in the treatment of numerous diseases [29]. It has multiple putative biological activities, such as antioxidant, anti-inflammatory, anti-tumor, anti-allergic, anti-genotoxic, anti-bacterial, anti-diabetic, neuro-protective, and cardioprotective [30,31]. This study is considered as the first one which included the designed to evaluate the efficiency of AgNPs synthesized by saffron on the hematopoietic system in induced photosensitized rats.

II. MATERIALS AND METHODS

A. Chemicals

Sigma Aldrich provided the silver nitrate, $AgNO_3$, which was used without any additional cleaning. All other reagents were of analytical grade with maximum purity. Saffron has been collected from the market. ST. John's Wort - Herb extract, manufactured by Solgar Inc., Leonia (USA).

B. Preparation of aqueous extract of C. Sativus L.

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Fifty g. of C.sativus L. flowers with stigmas were macerated for three days in one liter of deionized water at room temperature. The aqueous extract was refined using filter paper. The filtered solution was dried using an oven at the temperature of 45 C° [32].

C. Preparation of green silver nanoparticles

Different concentration of colloidal AgNPs solution was synthesized according to a method previously described using a green biosynthesis method for aqueous extract of Crocus sativus L act as a reducing and capping agents [33]. The form of the AgNPs was spherical and varied in size, as determined by scanning electron microscopy (SEM). The size of AgNPs ranged between 15 and 28 nm.

D. Rats and experimental design

Twenty four healthy adult male rats aged between 16-24 weeks, weighing 175-225 gm, were used in this study. They were kept in polypropylene cages under typical laboratory conditions. The animals had unrestricted access to regular pellet food and water. Prior to the start of the experiment, they spent a week getting acclimated to the lab environment. In the time between 10 a.m. and 12 p.m., every rat was subjected to direct sunlight for 30 minutes at a time. September has a 15-day period. They were split into four groups, each with six animals. The experimental design was as follows:

- Control group: Healthy rats without any treatment.
- SJW treated group: Rats induced with photosensitivity by giving St. John's wort SJW (3mg /kg/ day) orally for 15 days.
- SJW+SAFF treated group: Rats were received SJW (3 mg/kg/day) orally along with co-administration of Crocus sativus L. extract (150 mg / kg /day) for 15 days.
- SJW+AgNPs treated group: Rats were of SJW at a dose of 3mg orally along with co-administration of green synthesized AgNPs (150 mg/kg/day) orally for 15 days.

After the experimental regimen, the animals were sacrificed by cervical dislocation under mild chloroform anesthesia. Blood samples were collected by heart puncher and placed in tubes with EDTA for hematology procedures.

E. Hematological Analysis

Blood assessment was performed by automatic hematology analyzer (HORIBA - Medical / France) to determine hematological parameters including: red blood cells (RBCs), hemoglobin (HB), mean corpuscular volume (MCV), hematocrit (HCT)%, platelets (PLTs), and white blood cells (WBCs).

F. Statistical analysis

Data were expressed by mean ± SD, and differences between groups were assessed by one-way analysis of variance (ANOVA), using SPSS software package for Windows. Post hoc testing was performed for intergroup comparisons by Duncan's multiple comparisons, significance at p-value <0.05.

III. Results

About two weeks after induced photosensitivity in SJW treated group, results showed lower values of all red blood cell indices including; red blood cells count, hemoglobin, mean corpuscular volume, hematocrit value , and platelets count, and also lymphocytes. On the other hand, the white blood cell count showed the opposite pattern of changes to that observed with the red cell indices, platelets, and lymphocytes. There was no effective alteration in all hematological parameters with co-administration of green synthesized AgNPs, compared to SJW -intoxicated rats ($p<0.05$), as shown in Figure (1).

IV. Discussion

In principle, solar radiation represents the most important environmental stress, and UV radiation can penetrate skin and blood [34]. Biological targets for photosensitivity are cell membranes, cytoplasm organelles, and the nucleus, originating minor effects such as cutaneous reactions or severe effects such as genetic mutations, melanoma, which not always concern the light-exposed areas but may reach internal organs as well [35,36]. Erythrocytes count showed significantly decreased as compared to a normal control group, indicating an occurrence of anemia and hypoxia. It means destruction of red blood cells and a reduction in rate of erythropoiesis [37]. Normally RBCs are produced from hemopoietic stem cells in bone marrow and undergo maturation directed by erythropoietin. Thus, alteration in RBCs count might be due to the hematopoietic system [38]. A decrease in the HB level and HCT % in photosensitive induced rats, in contrast to the control rats, might be related to the destruction and decrease in the production of RBCs [39]. Hematocrit is a major determinant of blood viscosity, and a lower than normal hematocrit is representative of anemia [40]. Mean corpuscular volume is a red blood cell parameter, and tells about the red blood cell size. This parameter is important when interpreted along with Hb, hematocrit, and red blood cell count [41]. Platelets are produced from megakaryocytes and have prominent roles in hemostasis [42]. Thrombocytopenia, which represents a drop in platelet count caused by either decreased platelet production or increased platelet destruction [43]. A high white blood cells count may indicate acute infection, inflammation, or tissue damage. Also, an increased count of WBC is supposed to help boost the immune system [44].

Nanomedicines are applied in many therapeutic areas, including inflammatory diseases, infections, and anemia [45,46]. Moreover, AgNPs have been used in solar fuel cell efficiency improvement [47]. The changes in white and red blood cells reported hereafter the administrated nanoparticles had been described before and are possibly due to an increased immunogenic response or disturbances in signaling pathways and maturation of cells, which can affect RBC as well as division and development of other cells. The smaller diameter of nanoparticles is more its influence on cells and its molecular effects on intracellular mechanisms were increase [48,49]. Due to higher contact surface and more influence on cell membrane in high doses, silver nanoparticles lead to influence in WBC mitochondria and changes in their enzyme activity [50]. However, AgNPs manifested effective protection of all hematological factors during exposure to inducing

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photosensitivity in rats.

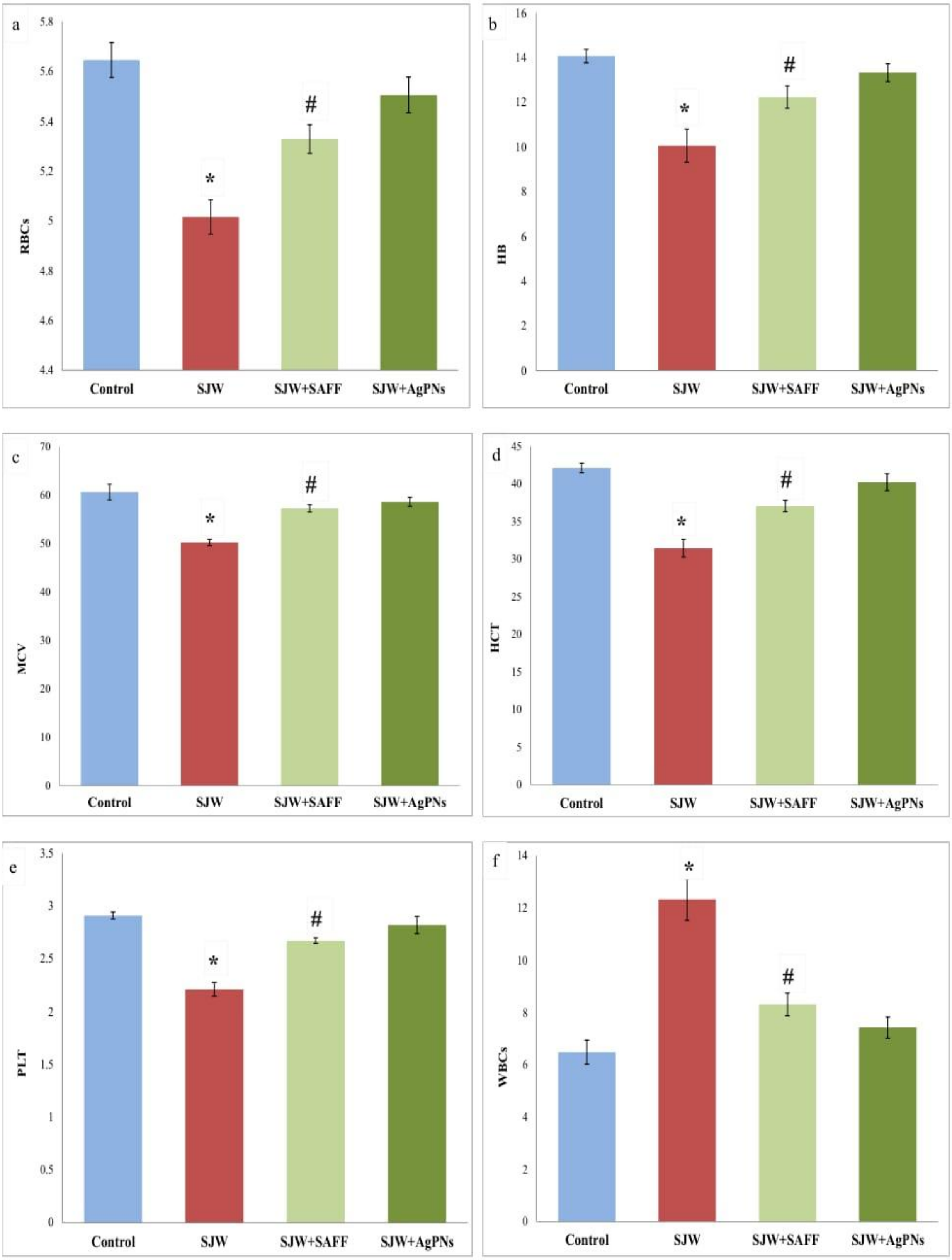

Fig. 1. Levels of hematological incidences: (a) RBCs (×106 cell/µl), (b) HB (gm/dl),(c) MCV(fL), (d) HCT(%),(e) PLT (×105 cell/µl), and (f) WBCs (× 103 cell/µl) in studied groups. Data are expressed as Mean± SD. * Indicates a significant difference compared to control, and # indicates a significant difference compared to SJW group.

V. Conclusion

In conclusion, the result of this study suggests that green AgNPs have a positive, beneficial effect against the drug-induced photosensitivity in rats, and might be a useful agent to restore hematological alterations. Moreover, results suggest that Saffron-AgNPs might serve as a harmless therapeutic approach for protection against diseases.

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