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Influence of gold nanoparticles and domperidone on some hematological parameters in pregnant rabbits

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Abstract: The present study aims to investigate the effects of gold nanoparticles (AuNPs) alone or with the administration of the emetic drug (domperidone) on some hematological parameters of pregnant rabbits. In this study, twenty pregnant rabbits were collected and divided into four groups (n = 5 in each group) as follows: the control group was allowed to drink 1 ml/kg of distilled water orally, the G1 group received an injected dose (I.M.) of 150 µg/kg of AuNPs, while the G2 group was treated with 300 µg/kg of the domperidone. The combined group (G3) received both AuNPs injected and domperidone orally (1150 µg/kg and 300 µg/kg, respectively). Blood samples were taken from each animal at 0, 15, 30, and 40 days of experimental periods to test hematological parameters (White blood cell count, red blood cell count, hemoglobin level (HGB), and Hematocrit percentage (HCT), which were calculated by using a hematology analyzer. The results of the study demonstrated that there is no significant difference in WBC, RBC counts, hemoglobin, and hematocrit levels between the AuNPs and domperidone groups and the Control and G3 groups. As well as there is no effect between periods for each group in these parameters in the blood of pregnant rabbits. Thus, it is concluded that the injection of AuNPs had no toxic effect on blood, as well as, the domperidone had the same effect on blood.
Keywords: Golden nanoparticles, Domperidone, Hematological parameters.

1. Introduction

Gold nanorods (AuNRs) have sparked a lot of attention recently due to their promising optical and chemical properties, and they are currently used in applied research and industrial nanotechnology. The goal of this study was to investigate the effect of gold nanoparticle form (gold nanorods vs. gold nanospheres) on rabbit immune response [Mehanna, E. T., et al., 2022]. There are many studies that indicate the use of many drugs and chemical compounds that would affect human and animal health [Ahmed, M. N., et al., 2018]. The unique properties of gold nanoparticles, and their accurate ability to deliver medicines, make them suitable for chemotherapy, preventing and treating some diseases [Yang, Zhijing, et al.,2022].

Nanomaterials are used to detect biological molecules, image pathological tissues, and develop novel therapies. Nanoparticles are being used by scientists to target malignancies, in medication delivery systems, and to improve medical imaging, as well as, used an antibacterial activity. Some nanoparticle therapies are multifunctional: they can detect cancers as well as transport drugs for therapy [Damodharan, J., 2021]. The adverse consequences of these particles are mostly determined by their production of reactive oxygen species (ROS), instability of cellular compartments, and immunological responses. Nonetheless, as soon as healthy organs are safeguarded by selective targeting, the inherent hazardous capabilities of such nanoparticles might be used to ablate abnormal tissue [Shrivastava, R., et al. 2016]. The molecular structure of the nanoparticle, shape, size, aggregation, surface, and activity are the elements that influence the cytotoxic activity bio-kinetics of nanoparticles [Mocan, T., et al., 2010]. High quantities of gold nanoparticles were found to diminish body weight, red blood cells, and hematocrit. It was also demonstrated that consuming gold nanoparticles orally resulted in significant decreases in body weight, spleen index, and red blood cells [Zhang, X. D., et al., 2010; Kuznietsova, Halyna, et al., 2023].

Metals' therapeutic properties have been researched for millennia to cure illnesses and disorders, and they are still utilized today [Sibuyi, Nicole Remaliah Samantha, et al., 2021]. The most therapeutically relevant type of nanoparticle is gold nanoparticles (AuNPs). AuNPs are stable colloid particles with sizes ranging from one to one hundred nanometers. AuNPs, in particular, have outstanding physicochemical qualities as well as excellent chemical stability. Because of their affinity for thiolate compounds and diverse chemistries, they are easily stable with practically any sort of electron-donating molecule. [Thakor, A. S., et al., 2021, Sibuyi, Nicole Remaliah Samantha, et al., 2021]. Because of their biocompatibility, simple manufacturing, and easy surface modification, AuNRs, a precious metal nanomaterial (gold, silver, platinum), have been widely researched for various biological detection applications. AuNRs have two plasmatic peaks, one at 520 nm (transverse surface plasmon resonance) and one near 800 nm (longitudinal surface plasmon resonance). The latter may be tweaked by changing the synthesis conditions, and it has been widely used in biological detection and imaging [Weizhen Xu, et al., 2021].

Most patients suffering diarrheal illness are now sent to the hospital not because of acute dehydration, but because of severe vomiting that interferes with fluid and food intake. The use of anti-vomiting medications is not advised due to the potential for negative effects. Domperidone is a benzimidazole derivative that acts as a dopamine antagonist and has pro-kinetic and antiemetic benefits with relatively minor extrapyramidal side effects [Irene, A. O., et al. 2007]. Domperidone works as a peripheral dopamine D2-receptor antagonist, increasing blood pressure and heart rate while stimulating stomach motility [Sigurðardóttir, G. R., et al., 2007]. Domperidone will also have endocrine effects via increasing prolactin production. According to preliminary evidence, domperidone may reduce vasoconstriction and decrease laminar blood flow in horses with laminitis by inhibiting alpha-adrenergic and serotonergic receptors [Papich, M. G., 2016].

AuNPs' influence on blood components is not entirely understood. When AuNPs were first utilized as drug delivery vehicles, they reacted with blood. As a result, it is vital to investigate the impact of AuNPs on blood, specifically its components. We investigated the potential role of AuNPs in avoiding the negative effects of domperidone medication on hematological parameters in pregnant rabbits in this study. However, investigating these events is critical to learn more about the mechanism of interaction between biological tissue and gold nanoparticles in vivo [Sumit Kumar, et al., 2020].

2. Materials and Methods

The present study was conducted on twenty pregnant oryctolagus cuniculus rabbit 35 weeks old and weighing from 2 to 4 kilograms. The animals were left for two weeks for acclimatization to the experimental conditions. The animals received treatment every day for 40 days. The blood was collected from pregnant rabbits in tubes containing anticoagulant EDTA to test hematological parameters (WBC count, RBC count, hemoglobin level (HGB) and Hematocrit percentage (HCT). These were calculated by using a Hematology analyzer which is specific for veterinary blood tests using the cardiac puncture procedure at 0, 15, 30, and 40 days of experimental periods. In this investigation, the twenty pregnant rabbits were randomly divided into four groups (n = 5) as follows:

- Group control: rabbits were allowed to drink 1 ml/kg of distilled water orally.
- Group one (G1): rabbits received an injected dose (intra musc IM) of 150 µg / kg of AuNPs, AuNPs purchased from Sigma-Aldrich (USA).
- Group two (G2): rabbits were treated orally with 300 µg /kg of the domperidone.
- Group Three (G3): rabbits were treated with both AuNPs injected and domperidone orally 150 µg / kg and 300 µg / kg, respectively).

The results were subjected to statistical analysis using Two-way ANOVA (SPSS program version 24) to express differences between the groups and times. The values were represented as means ± SE at P≤0.05 [Keeney, W. L., et al., 1976].

3. Results and Discussion

Gold nanoparticles can cause an inflammatory response, enhance or decrease immune function, and affect relevant hematologic parameters such as blood cell counts. However, to better understand the process of interaction between biological tissue and gold nanoparticles in vivo, it is crucial to look at these occurrences [Gjetting, T., et al., 2010]. The recorded results after 40 days are illustrated in Table 1.

Parameters	Groups	Periods				LSD
		zero	20	30	40	
WBC Thousands/ mm3	Control	9.28±1.49 Aa	6.7±0.37 ABb	6.5±0.75 A ab	8.9±0.62 A ab	2.8
	G1 AuNPs	6.62±0.68 A	5.4±0.5 B	5.9±0.68 A	6.2±0.31 A	
	G2 Domperidone	6.7±1.28 A	7.9±0.25 AB	8±0.9 A	7.6±0.62 A	
	G3 AuN+Dyp	6.64±1.9 A ab	9.4±0.7 A a	6.4±0.85 A b	6.26±0.61 A b	
RBC million cells/ mm3	Control	5.9±0.37 A a	5.4±0.48 A a	5.4±0.30 A a	5.38±0.16 A a	1.41
	G1 AuNPs	5.5±0.46 A a	5.3±0.24 A a	5.2±0.24 A a	5.15±0.19 A a	
	G2 Domperidone	5.8±0.30 A a	5±0.31 A a	6.1±0.17 A a	5.8±0.18 A a	
	G3 AuN+Dyp	4.5±0.33 A a	5.1±0.18 A a	4.8±0.58 A a	4.9±0.65 A a	
HGB (gm/dl)	Control	14±0.87 A b	12.8±1.0 A b	12.7±0.67 A b	37±0.46 A a	2.25
	G1 AuNPs	13.4±0.83 A	12.8±0.41 A	12.9±0.53 A	12.4±0.49 B	

	G2 Domperidone	13.9±0.52 A	11.9±0.76 A	13.7±0.37 A	12.7±0.25 B	
	G3 AuN+Dyp	10.8±0.93 B	11.5±0.37 A	11.4±0.77 A	11.2±1.5 B	
HCT (%)	Control	38.8±2.3 A	32.5±2.1 A	37.5±1.6 A	37.5±0.9 A	7.2
	G1 AuNPs	36.9±2.2 AB	36±2.7 A	37±1.3 A	36±1.4 A	
	G2 Domperidone	38.8±1.20 A	34.7±1.2 A	39.6±1.0 A	37.9±0.79 A	
	G3 AuN+Dyp	30.6±0.65 B	32.7±1.0 A	35±3.2 A	35±1.7 A	

Table 1- The effect of AuNPs, domperidone, and both on the WBC, RBC counts Hemoglobin (HGB), and Hematocrits (HCT) during 0, 20, 30, and 40 days of experimental periods in pregnant rabbits.

Values = mean ± SE. The significant differences are represented by different capital letters between groups within one column at ($P \leq 0.05$). The significant differences are represented by different capital letters between times within one row.

The result strongly suggested that there was no significant variation in WBC, RBC counts, hemoglobin, and hematocrit levels in the G1 and G2 groups as compared to the Control groups. Also, there was no significant effect between periods for each group in these parameters in the blood of pregnant rabbits (Figure 1).

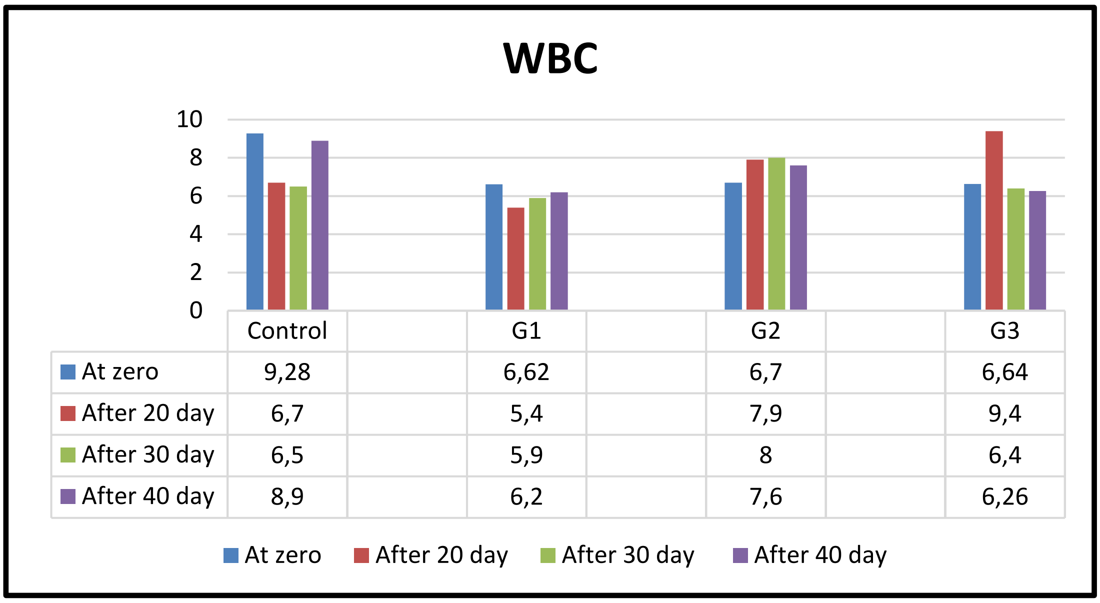

Figure 1 – White blood cells in pregnant rabbits at the periods zero, 20, 30, and 40 days of pregnancy.

Furthermore, we found no significant variation in hematological parameters during the administration of AuNPs. This indicates that these particles have no toxicity to the animals. Therefore, these nanoparticles may be used as drug carriers to reduce the toxicity of the incorporated drug, but it can be difficult to distinguish the toxicity of the drug from that of the nanoparticle. Despite an increase in the number of studies in this field, more research is needed to understand the mechanisms of toxicity following diverse modalities of AgNP exposure [Ferdous, Z., & Nemmar, A., 2020]. In addition, the toxicity of gold nanoparticles is demonstrated at high concentrations, whereas, our results showed no harm at a dose of 150 µg/kg (Figure 2). As a consequence, the toxic effect of nanoparticles may lead to the liver impairing function such as silver nanoparticles, which cause oxidative stress, membrane damage, and hemolysis through direct impacts on red blood cells (RBCs) [AL-Baker A. A, et al., 2020].

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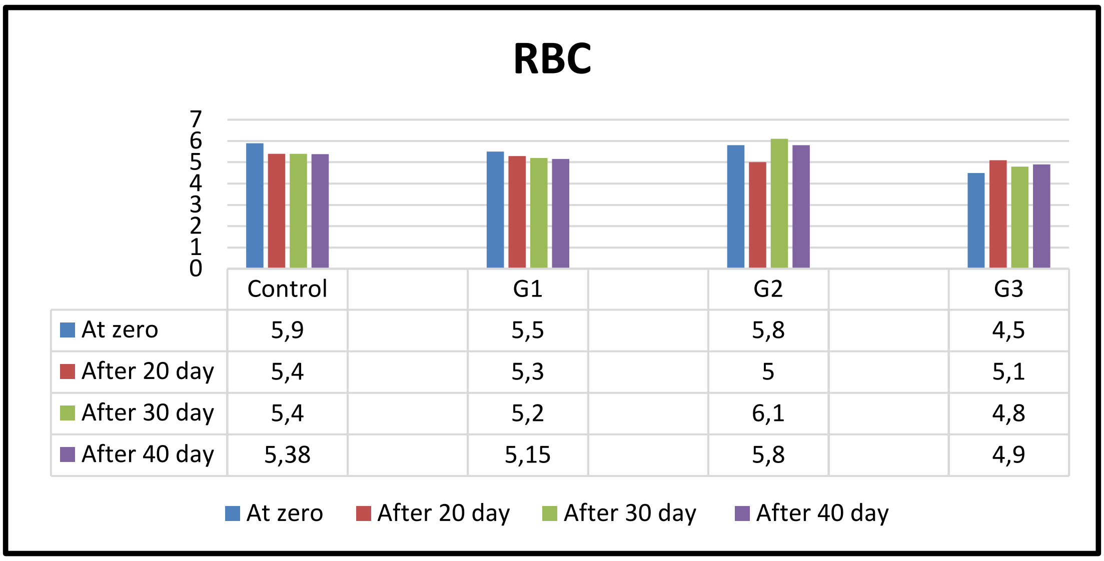
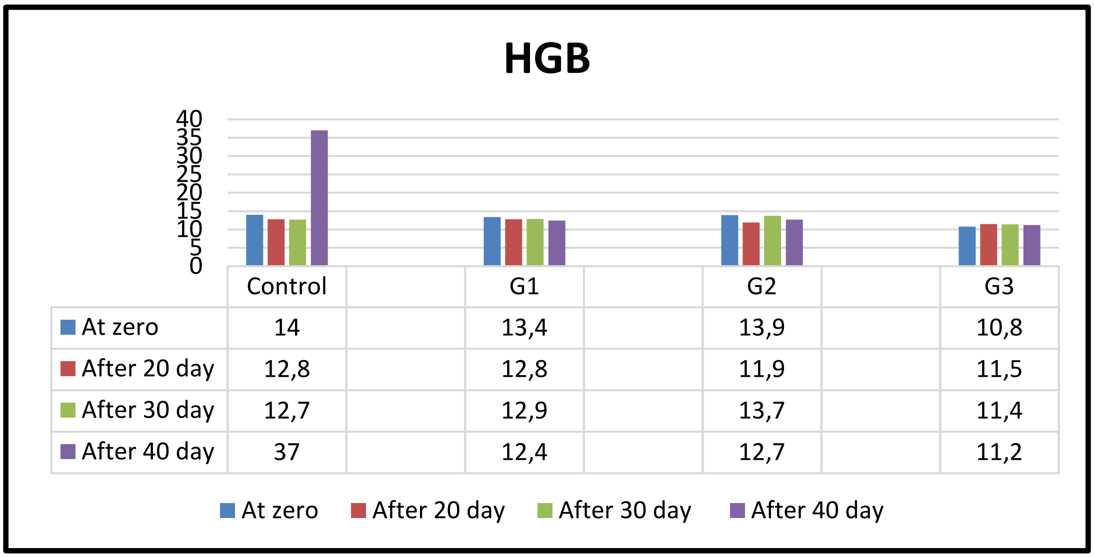


	Control	G1	G2	G3
At zero	5,9	5,5	5,8	4,5
After 20 day	5,4	5,3	5	5,1
After 30 day	5,4	5,2	6,1	4,8
After 40 day	5,38	5,15	5,8	4,9

Figure 2 – Red blood cell in pregnant rabbit at the periods zero, 20, 30, and 40 days.

The administration of nanoparticles on the 26th week of pregnancy, popielno white rabbits experienced a statistically significant decline in RBC and Hb values when compared to the pre-mating blood sample (Figure 3). There was also a significant reduction in MCH in sampling III compared to sampling II, as well as a significant reduction in WBC in sampling III compared to both pre-mating sampling and blood collection on the 15th day of pregnancy [Chmurska-Gąsowska, M., et al., 2021].



	Control	G1	G2	G3
At zero	14	13,4	13,9	10,8
After 20 day	12,8	12,8	11,9	11,5
After 30 day	12,7	12,9	13,7	11,4
After 40 day	37	12,4	12,7	11,2

Figure 3- Hemoglobin in the pregnant rabbit at the periods zero, 20, 30, and 40 days of pregnancy.

Domperidone, on the other hand, had no influence on hematological markers white blood cell count (WBC), red blood cell count (RBC), hemoglobin level (HGB), and Hematocrit percentage (HCT) in pregnant rabbits. Because of this investigation, no detrimental effects on the blood were discovered, implying that these medications can be administered during any stage of pregnancy. In contrast, there is a significant effect of the combination of AuNPs and domperidone of the G3 group in all periods of hematological parameters that showed no toxic effect of these drug on the blood (Figure 4).

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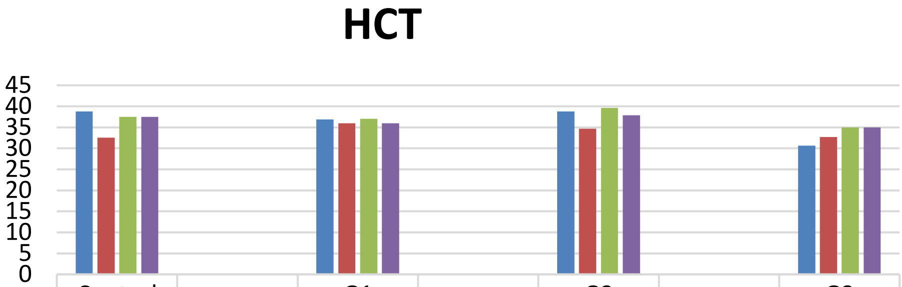

	Control	G1	G2	G3
At zero	38,8	36,9	38,8	30,6
After 20 day	32,5	36	34,7	32,7
After 30 day	37,5	37	39,6	35
After 40 day	37,5	36	37,9	35

Figure 4 - Hematocrit in pregnant rabbits at the periods zero, 20, 30, and 40 days of pregnancy.

4. Conclusions

The results of our research have come in conformity with the literature. We concluded that intramuscular injection of AuNPs at a dose of 150 µg/kg alone or in combination with an emetic medication (domperidone) had no effect on hematological markers.

Conflict/ of interests : The author(s) declared no potential conflicts of interest regarding the research, authorship, and publication of this article.

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Declarations and Ethics: All the procedures performed in the study involving human participants were in accordance with the Declaration of Helsinki and ethical standards. Our study was done based on the ethical board approval of Fallujah University and approved by the Scientific Committee of the College of Applied Science Faculty.

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