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Effects of oral aspirin and aspirin nanoparticles on hematological parameters in rats

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Abstract
Aspirin (ASA) is the antiplatelet drug that is given to patients the majority of the time. Although there is a considerable body of evidence that supports the efficacy of aspirin in the secondary prevention of ischemic events in persons who already have cardiovascular disease, the function that aspirin plays in primary prevention has been a subject of debate for decades. There has only been a slight reduction in the number of ischemic events, notably myocardial infarction and, to a lesser extent, stroke, which is associated by an increased risk of hemorrhage. This is the only thing that has been determined by historical studies. It is because of these discoveries that professional organizations have come up with a variety of recommendations for the utilization of ASA for the primary prevention of symptoms associated with cardiovascular disease. Recent findings from three primary prevention trials indicate that there are either no benefits or only slight benefits on combined ischemic endpoints. Furthermore, there is no effect on serious cardiovascular events such as myocardial infarction or stroke, and there is an increased risk of bleeding. Over the course of the study, it was determined that the use of aspirin in people who did not have any obvious signs of cardiovascular disease was either associated with a net benefit that was neutral or even a net disadvantage. As a direct result of these findings, the recommendations that are currently in place regarding the utilization of ASA in primary prevention have been subjected to a reevaluation. The purpose of this article is to provide a comprehensive assessment of the existing body of evidence about the utilization of aspirin as a major preventative therapy for cardiovascular disease. With each and every dosage of aspirin, there is a possibility of experiencing bleeding. When compared to people who do not use the substance, those who use 75 milligrams per day have a risk of upper gastrointestinal bleeding that is twice as high. Nano emulsions, also known as NEs, are a type of emulsion system that is defined by the careful distribution of oil or water droplets in the opposing phase, which is stabilized by an appropriate surfactant. The droplet sizes of the individual droplets are in the nanoscale range.
This investigation investigates the impact of oral aspirin and aspirin nanoparticles on the parameters of the complete blood count (CBC) in the rodent. The results indicate that rodents that were administered aspirin experienced significant hematological changes, with the nanoparticle-treated cohort exhibiting partial normalization.

Keywords: Aspirin, aspirin NP, blood picture, rats

Introduction
Aspirin is extensively utilized for its antiplatelet and anti-inflammatory properties; however, its influence on hematological markers remains inadequately comprehended. Nanoparticles present a potential delivery mechanism that could alter the bioavailability and adverse effects of aspirin [1]. This study evaluates the hematological profiles of control rats, rats administered oral aspirin, and those treated with aspirin nanoparticles. Acetylsalicylic acid, which is commonly known as aspirin (ASA), is the most widely used antiplatelet medication. It has traditionally been the cornerstone of pharmacological therapy for the prevention of atherothrombotic disorders that are associated with cardiovascular disease (CVD). Despite the fact that the benefits of aspirin in secondary prevention have been well-established, the question of whether or not it is useful in primary prevention is still open. Despite the fact that ASA had no effect on mortality and a higher risk of bleeding, it was able to reduce the incidence of myocardial infarction (MI) and stroke, according to clinical trials that were carried out more than twenty years ago. These trials were undertaken during a time when other major preventative strategies, such as lipid-lowering drugs, were not widely used. (four) The widespread use of aspirin for primary prevention was a direct result of these findings. According to the most recent findings from contemporary clinical trials, there is either no net clinical benefit or the possibility of damage. Three less eight As a result of these discoveries,

a reassessment of the effectiveness of ASA for primary prevention has been suggested, as has the requirement that practice guidelines publish new recommendations. The purpose of this book is to give a thorough analysis of the application of ASA in the primary prevention of cardiovascular disease (CVD) [5].

Nanoparticles (NPs) are microscopic molecules of an immiscible liquid that are dispersed in another. A traditional emulsion consisting of infinitesimal particles can be imagined as NPs [6]. Drug solubility, absorption rate, and targeted drug delivery can be improved by nanoparticles. In terms of medication solubility, the extremely small particle size of oil-in-water or water-in-oil nano emulsions can solubilize both hydrophilic and lipophilic medicines, thereby improving dissolution. Additionally, these minute particulates can easily penetrate the epithelial layer, thereby enabling the medicine to be absorbed at a high rate. Scientists are able to prevent dose-related toxicities by determining and regulating optimal concentrations, which is facilitated by the minuscule particle size. As a result, NP has created a unique opportunity for scientists to precisely create medications that are less accessible and inadequately soluble, which are not able to be produced using conventional methods [7].

Methodology

Chemicals agent

Sigma Aldrich Co. (USA) procured aspirin (acetylsalicylic acid). The nanoparticles were analyzed for size and shape utilizing transmission electron microscopy (TEM) (Figure 1). Formulation of aspirin nanoemulsion. The ideal physicochemical properties were attained by integrating Aspirin (250 mg), 9% w/w Lauroglycol 80, 10% w/w Transcutol, 4.5% w/w Cremophor EL, and 75.4% w/v deionized water. The combination underwent 15 minutes of premixing, 20% ultrasonic amplitude, and 80 seconds of irradiation. This approach produces aspirin nan emulsions with an average droplet diameter of about 200 nm. Lauroglycol 90 served as the dispersed phase, while deionized water functioned as the continuous phase in the formulation of Aspirin NE. Transcutol served as the primary solvent for the solubilization of aspirin. The emulsion was subsequently generated by integrating the resultant solution into the aqueous phase, which included Cremophor EL as the emulsifier. The premixed emulsion underwent further ultrasound treatment via an ultrasonic horn processor [8, 9].

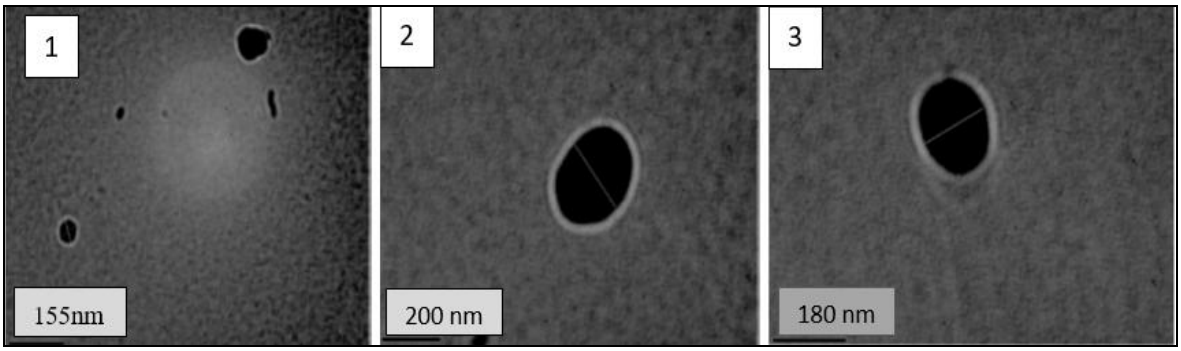

Fig 1: Transmission electron microscopy was utilized to examine aspirin-containing nanoparticles in the current work. Observation: 1. The size of one of the synthesized nanoparticles is 155 nm. 2. A synthesized nanoparticle having a spherical form and a diameter of 200 nm. 3. A nanoparticle measuring 180 nm.

Characterization of salicylate nanoparticles.

Particle size analysis

Using photon correlation spectroscopy (UK), the average particle size diameter and polydispersity index were measured in solution just after synthesis. Two milliliters of Aspirin NEs were placed in the quartz cell of the spectrometer. The incoming light source was angled at 90 degrees, and three separate readings were made.

Detection of nanoparticles

Before being investigated using high-resolution TEM, a droplet of aspirin NE was placed onto metal grids and left to dry in room temperature air. Droplet size evaluation using transmission electron microscopy (TEM) supported the findings of the particle-size study. The two measurements-with a range of 150-200 nm-indicate that the nanoparticles had an average size of 200 nm. The TEM investigation revealed that the aspirin NE particles had a nearly spherical shape and a homogeneous distribution of nanometric sizes [10].

Animals study

This experiment was sanctioned by the College of Health and Medical Technique's Committee of Scientific Ethics at Middle Technical University in Baghdad, Iraq. It was conducted in conformity with their standards for animal exploitation. In this study, 30 male Wistar rats had an average weight of 190±10 g. The specimens were collected at the Baghdad Cancer Research Center's animal facility. They were kept in an ideal environment for 10 days so they could acclimate. The animals were housed in stainless steel cages in a properly ventilated animal facility and kept at a constant temperature of 22 °C±5 °C. A 12:12 light-dark cycle was imposed on them. In addition to a standard fare diet, they were also given free access to water. Each of the three groups of ten rats was chosen at random. Oral saline (0.2 ml) was given to the rodents in Group 1, which served as the control. The second group took 30 milligrams of aspirin per kilogram of body weight orally. The third group of rats received one injection of aspirinNP at a dosage of 30 mg/kg. Participants in Group 3 received a single oral dose of aspirin 30 mg/kg body weight. The rats were given 0.3 ml of ketamine (75 mg/kg) and 5 mg/kg of xylazine (0.3 ml each) 24 hours after their last treatment to put them to sleep over the 30-day trial. Blood samples were collected through cardiac puncture using a 5 ml syringe and then analyzed by automated hematology analyzers for standard CBC values.

Results

The control group exhibited normal hematological values in the total blood count, as illustrated in Table 1. Oral aspirin administration markedly diminished white blood cell counts, mostly through a reduction in granulocytes, and produced anemia, as demonstrated by decreased hemoglobin and hematocrit levels. Aspirin nanoparticles slightly mitigated these effects, enhancing WBC, HGB, and HCT levels, but led to a notable reduction in platelet counts. All treated groups demonstrated microcytic hypochromic anemia, as evidenced by diminished MCV and MCH levels.

Table 1: Showed complete blood count of rats showed control, aspirin group, and aspirin nanoparticles group

Parameter	Control (Mean ±SD)	Aspirin (Mean ±SD)	Aspirin Nanoparticle (Mean ±SD)	Statistical Significance*
WBC (10^9/L)	2.52 ±0.4	1.32±0.25	3.09±0.5	a, b
Lymphocytes %	92.3±2.5	86.6±3	80.8±3.5	a, b
Granulocytes %	3.2±1	9.3±1.5	14.0±2	a, b
RBC (10^{12}/L)	6.96±0.45	5.97±0.5	8.42±0.6	a, b
HGB (g/dL)	12.8±0.6	10.7±0.5	12.5±0.5	a, b
HCT (%)	33.4±2	29.0±1.8	41.2±2.5	a, b
MCV (fL)	50.9±1.2	48.7±1.1	48.9±1	-
MCH (pg)	20.4±0.9	18.0±0.8	14.9±0.7	a, b
MCHC (g/dL)	38.4±1.3	36.9±1.4	30.4±1.6	a, b
Platelets (10^9/L)	392±35	275±30	97±15	a, b
PCT (mL/L)	3.30±0.25	2.12±0.18	0.73±0.1	a, b

Discussion

Aspirin tablets and capsules are the most effective anti-inflammatory medications now available. Nonetheless, numerous issues and adverse effects are linked to the prolonged use of these dosage forms [11]. The current investigation involved the administration of aspirin in nanoparticle form to boost medication efficacy, Consequently, the severity of drug-related adverse effects is reduced and the necessary dosage levels are reduced. The current study demonstrates that the aspirin emulsion and aspirin nano emulsion both exhibit significant anti-inflammatory effects. however, the nano emulsion presents notably reduced toxicity and greater benefits.

Oral aspirin induces significant immunosuppression and anemia, presumably due to its systemic effects. The nanoparticle formulation seems to alleviate certain hematological toxicities but may negatively impact platelet homeostasis [12, 13]. The anti-inflammatory efficacy of aspirin nano emulsion was assessed in rats using a previously established method. The lymphocytosis noted among groups may indicate immunological activity or a response to treatment [14]. Additional research is required to clarify the processes underlying these findings and the clinical significance of aspirin nanoparticle treatment.

Hematological tests revealed changes to the blood parameters. It is possible that these changes in RBCs reflect the effect of nanoparticles on hemoglobin production while RBCs are still developing in the bone marrow [15, 16]. Immune responses rely on white blood cells, which serve as the body's first line of defense. Different types of neutrophils can show up when there's an infection, an allergic reaction, or a toxic reaction to drugs or chemicals.

The RBC count was lower in the treated animals than in the control group. Hypoxia is the cause of anemia, and a drop in red blood cell (RBC) counts indicates that RBC breakdown is more severe. Deficits in iron, cobalamin, or folic acid, as well as several chronic illnesses and poisonous chemicals that reduce the number of red blood cells the bone marrow produces, can all contribute to this destruction. The toxic effect of aspirin nanoparticles on red blood cells is induced by their oral administration and intraperitoneal injection [19].

The hematopoietic system was influenced by ASPIRIN nanoparticles, resulting in a reduction in red blood cell count. Furthermore, nanoparticles that disrupt the functionality of the immune system [20]. The slight reduction in hemoglobin and red blood cell count may have resulted from the suppression of the circulating hormone erythropoietin, a glycoprotein that promotes erythropoiesis. Normochromic, normocytic anemia can occur due to a reduction in erythropoietin levels in the bloodstream [22]. Iron deficiency represents the predominant etiology of hypochromic anemia, a term that broadly includes all forms of anemia [23]. Aberrant microcytic red blood cells are the consequence of numerous diseases. Certain varieties of anemia are accompanied by abnormal red blood cells [24]. Platelets (thrombocytes) are essential for blood coagulation; consequently, an elevated platelet count may induce thrombus formation within blood vessels, thereby exacerbating the progression of atherosclerosis, which is a consequence of nanoparticle administration [25, 26].

Conclusion

In comparison to oral aspirin, aspirin nanoparticles may provide a safer hematological profile; however, monitoring the effects on platelets is necessary. These findings substantiate the potential for nanoparticle-based drug delivery to improve therapeutic outcomes.

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(Conflict of interest): The author affirms that there is no conflict of interest.

Contributions by the author: the author certifies that all experimental work was completed by him, but the statistical analysis was conducted by another specialist.

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