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Nigella oriental seeds as a model for examining the impact of silver nanoparticles and cabergoline on female rats with hyperprolactinemia: a comparative study

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ABSTRACT

Plant extracts from *Nigella sativa* seeds were employed to synthesize silver nanoparticles (AgNPs) from silver nitrate solution. The AgNPs were characterized by spectroscopy, UV spectrophotometry, scanning electron microscopy (SEM), and F-TIR. Thirty female Albino Wistar rats were divided mainly into (3) groups (Group 1, Group 2: Group 2a and Group 2b) where (10) rats have been distributed for each. The animal experiment was undergone through three stages; in the first stage, group 2 was given chlorpromazine orally (30 mg/BW) by gavage needle for a period of 28 days. After three days from the treatment, serum prolactin levels were estimated. During the subsequent phase, G2a received intraperitoneal (IP) injections of AgNPs (25 mg/BW) whereas G2b received IP injections of cabergoline (30 mg/BW). In the third stage, all animals were put out two months after the experiment began, and an Elisa Kit was used to measure the prolactin levels in the serum. This study investigated the effects of cabergoline and AgNPs on prolactin levels in female rats and utilized AgNPs to treat hyperprolactinemia. The study's extracted AgNPs has shown a strong inhibitory effect on hyperprolactinemia, which may bolster the role of AgNPs in the field of nanomedicine.

KEYWORDS

silver nanoparticles, *nigella sativa* seeds, cabergoline, hyperprolactinemia, plant extracts

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1. INTRODUCTION

Hypothalamic-pituitary hyperprolactinemia, mostly in females owing to increased prolactin production, is one of the most prevalent endocrine dysfunctions. Pathological, physiological, or pharmacological factors are the major causes of this condition. Approximately 25% of female infertility linked to secondary amenorrhea is caused by the neuroendocrine Hyperprolactinemia condition. Treatment options include the use of cabergoline, a dopamine agonist [1]. Pituitary lactotroph cells release prolactin, which is increased in blood levels in prolactinomas, thereby can be treated with the cabergoline trade names Dostinex and Cabase, which were authorized by the FDA in 1996. Although hyperprolactinemia is effectively treated with cabergoline, however it can cause significant side effects in non-breastfeeding women or men such as sexual problems, infertility, genetic defects and bone loss [2]. Numerous new applications for nanomaterials have been found in industries as diverse as energy generation, electronics, aerospace, and medicine as a result of a rise in interest in nanoscale research worldwide [3]. Known as the "Black Seed", *Nigella sativa* is a member of the ranunculus plant family and is frequently used in Middle Eastern and certain Asian traditional medicine to boost health and treat a variety of ailments [4]. Beyond its anti-parasitic properties, *Nigella sativa* seeds are also used in traditional medicine as a natural cure for increasing the female menstrual cycle and acting as a *carminative, galactagogue, laxative, etc*. Recent research on animals has demonstrated the several therapeutic benefits of N. sativa seed extracts, including antioxidant, antibacterial, anti-inflammatory, anti-anxiety, and digestive protection [5]. In his 2018 study, Senaa Malik Hussein elucidated the inhibitory impact of *Nigella sativa* seeds on serum prolactin levels in female rabbits following parturition. The investigation was done on the effect of liquid solution of *Nigella sativa* seeds on prolactin levels in rabbits [6]. Nevertheless, the lack of comparable studies utilizing silver nanoparticle drug delivery is what first motivated us to carry out this investigation. In order to cure hyperprolactinemia, the study's objectives include synthesizing silver nanoparticles from *Nigella sativa* seeds and comparing their effects on female rats' prolactin concentrations with those of cabergoline extract.

2. METHODOLOGY

2.1. Plant materials and extraction procedure

The following methods were employed to create and characterize small silver particles in an eco-friendly manner by using a water-soluble component of the sativa type found in sprouts.

2.1.1. Materials

The inorganic substance silver nitrate ($AgNO_3$) is prepared by dissolving 0.1 Molar of $AgNO_3$ in 100 millilitres of deionized water.

2.1.2. Plant extraction

A gram of *Nigella sativa* was ground up and mixed with 100 millilitres of deionized water. The mixture was then incubated for 10 minutes at room temperature in an ultrasonic cell inactivator. After that, the mixture was centrifuged for 15 minutes at (4000 rpm) and filtered through filter paper.

2.1.3. The use of *Nigella sativa* to synthesize Ag|AgO

The process of converting Nigella Sativa extract into Ag|AgO. First, place the Nigella sativa extract in the magnetic stirrer that has been adjusted to 80°C. Next, add the silver nitrate solution gradually as the temperature is steadily raised—not to exceed 160°C—and let it for an hour [7].

2.1.4. Identification of tiny nanostructures particles (NSSSNPs) in N. species seeds

The characterisation of NSSSNPs was conducted using the Perkin Elmer Lambda (PEL) 35 ultraviolet spectrometer (U.S.A.), Fourier transform infrared (FTIR) spectrometry (Shimadzu-8400S Japan), and a Czech-made scanning electron microscope (SEM-Tescan Vega 3) [8].

2.2. Animals

2.2.1. Animals housing

Thirty mature female albino Wistar rats weighing between 180 and 200 grams are used in this experimental investigation. These adoptable animals were split into two groups at random and kept in the College of Veterinary Medicine's animal housing at the University of Baghdad. The animals were housed under tight supervision, in sanitary conditions, with a light-dark 12:12 cycle and a standard temperature of 24±26ºC. The animals' entire body weight was measured three times during the experiment, and at the conclusion, the animals were put to death.

2.2.2. The three stages of the experiment

Twenty of the thirty female Albino Wistar rats in the first stage were assigned to the test group (group 2), while the remaining ten acted as the control group (group 1). Using a gavage needle, the test group was given oral chlorpromazine (CPZ) at a dose of 30 mg/kg|day for 28 days. Three days following the conclusion of the drug's treatment, four animals were put to death in order to estimate the levels of prolactin in the serum. In the second stage, the group was split into two sets and reared under standard conditions. For eight weeks in a row, AgNPs (25 mg/BW) were given intraperitoneally to G2a, whereas G2b received cabergoline (30 mg/BW) via the same route. In stage three, blood samples were taken via heart puncture after all animals were killed by CO_2 gas inhalation, two months after the animal experiment began. The Elisa Kit was then used to centrifuge blood for 10 minutes at room temperature and 3000xg in order to measure the prolactin levels in the serum.

2.3. Statistical analysis

For data expression, the mean ± SD was employed. Significance is defined as *P*-value ≤0.05, and non-significance as *P*-value > 0.05. The mean difference between the groups was compared using the *t*-test. For the statistical analysis of this study, SPSS Statistics 21 was utilized.

3. RESULTS

The combination of $AgNO_3$ and the Nigella sativa strain produced precipitated material that sank to the bottom of the barrel and stiff pieces. To test the ocular sensitivity of the produced AgNPs, an ultraviolet spectrometer was used, with an accuracy of around 1 nanometer over 200 and 1100 nanometer ranges. An intake maximum that appears at about 428.5 nanometers indicates the presence of NSSSNPs.

The range of reactive units present in the structure formed by reacting $AgNO_3$ with the *Nigella sativa* strain is shown in Figure 1. The FTIR spectra of AgNPs reveal several significant peaks at 3275.13, 2877.79, 2121.7, 1631.78, 594.08, and 570.93 cm^{-1}. These peaks correspond to various functional groups, including aromatic C=N and C=C stretching vibrations, phenol and alkane functional groups, C=O and C=C stretching vibrations, N-H and O-H stretching vibrations, and CH aromatic bending, respectively. The bioactive effective components were demonstrated to be efficient anchoring and cutting regulators when silver nanoparticles were produced. In Figure 2, the SEM picture illustrates the AgNPs round shape.

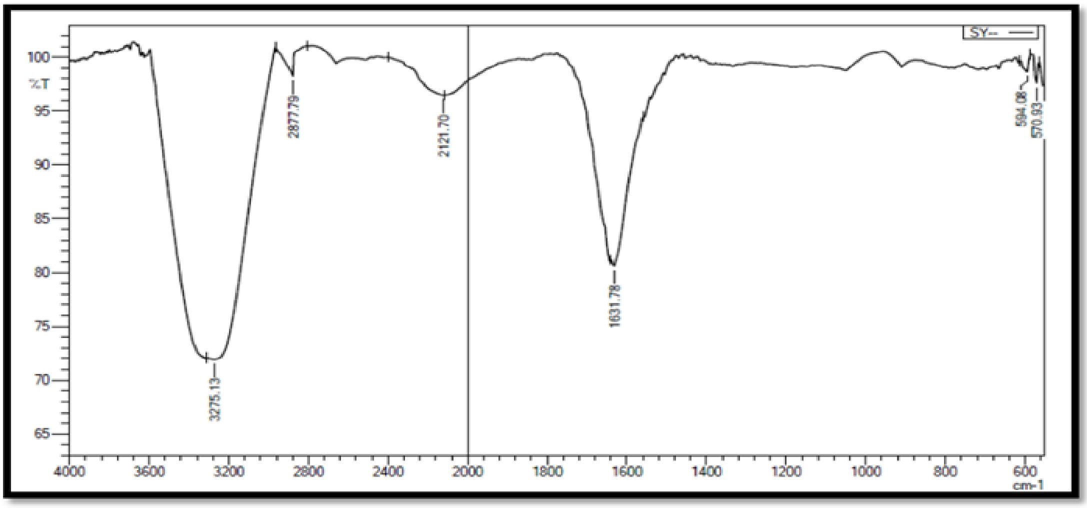

Figure 1. N.S. seed silver ions F-TIR spectra.

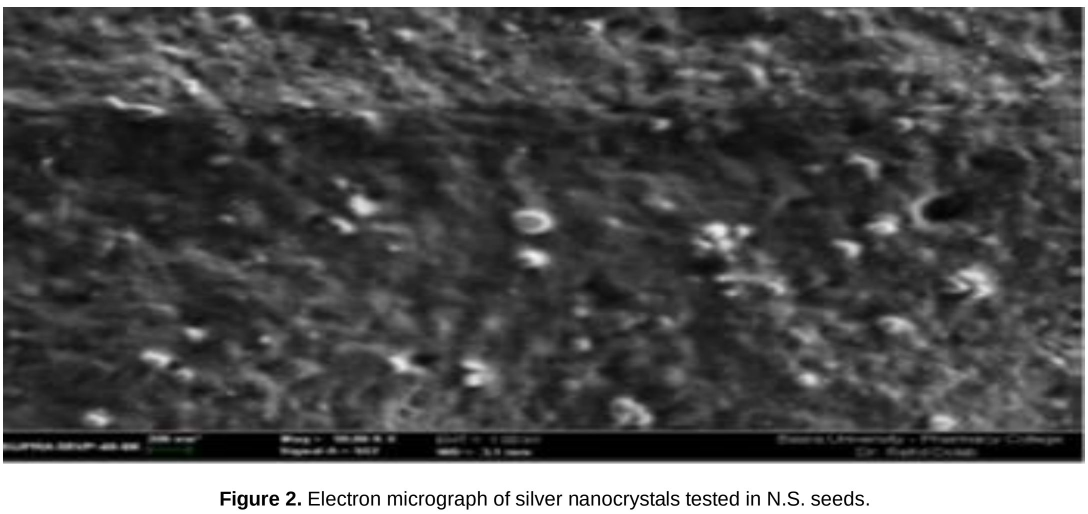

Figure 2. Electron micrograph of silver nanocrystals tested in N.S. seeds.

4. DISCUSSION

In this study, silver oxide nanoparticles were produced using Nigella sativa extract. Its effect on prolactin levels was evaluated.

Since one of the most well-known antipsychotic medications, chlorpromazine (CPZ), selectively inhibits post-synaptic dopaminergic neurons, it raises prolactin levels [9]. Because of its impact on dopamine D2 receptors, chlorpromazine is frequently utilized in the treatment of schizophrenia [10]. Postural hypotension, sexual dysfunction, arrhythmia, and cardiac mortality are just a few of the negative effects that have been linked to antipsychotic drug usage [11]. Nonetheless, research indicates that the use of antipsychotic drugs is typically associated with hyperprolactinemia, or elevated blood prolactin levels [12]. This study employed chlorpromazine to cause hyperprolactinemia in female rats; Table 1 displays the hyperprolactinemia that resulted from the drug's treatment.

Table 1. Serum prolactin levels in G1 and G2 (mean±SD).

Parameters	G1 (Baseline)	G2 (After using CPZ)
Serum prolactin (ng/ml)	14.85 ±2.3	51.85 ±7.3

Two drugs were employed to treat the elevated prolactin levels: AgNPs (25 mg/BW) was administered intraperitoneally (i.p.) into G2a, and cabergoline (30 mg/kg body weight) was given intraperitoneally (i.p.) into G2b. Table 2 displays the outcome following therapy.

Table 2 demonstrates that the cabergoline group (G2b) significantly decreased the serum prolactin levels (*P* ≥0.05) in both G2b and G2a, whereas the AgNPs IP Infusion subgroup (G2a) performed better than the other groups. AgNPs can therefore be used as a medication to treat hyperprolactinemia.

Table 2. Serum prolactin levels in G1, G2a and G2b.

Parameters	G1	G2a	G2b	*T*-Test G1 vs G2a (*P*-value)	*T*-Test G1 vs G2b (*P*-value)
S.prolactin (ng/ml)	14.85 ±2.3	18.85 ±2.3	14.85 ±2.3	≤0.05	≤0.05

5. CONCLUSION

Similar to the effects of the medication cabergoline, nigella sativa seeds-based silver nanoparticles can effectively cure hyperprolactinemia.

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CONFLICT OF INTEREST STATEMENT
The authors declare no conflicts of interest.

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