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Effect of Cinnamaldehyde on Female Reproductive Hormones in 7, 12 Dimethyl Benzanthracene Induced Ovarian Cancer Rats

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Abstract: ***Ovarian cancer is the deadliest type of cancer in women. It is often presented at an advanced stage and has a poor prognosis. The current treatment methods for this tumor are not safe and have serious side effects. It has been suggested that the use of steroids for hormonal purposes is linked to the development of ovarian cancer. The current study aims to investigate the effects of cinnamaldehyde on these hormones. The objective of this study was to investigate the effects of cinnamaldehyde on the reproductive hormones of rats after being induced to develop ovarian cancer. Cinnamaldehyde is an active compound that has been used in Asia for over 4000 years. Cinnamaldehyde has different biological activities including antimicrobial, anti-inflammatory, antiviral, antioxidant, antitumor were reported by many investigators. In the present study, animals were randomly allocated into VI groups: Group -I served as a control with normal water and group-II was drug control (50 mg/kg b. w) rats received only cinnamaldehyde orally for 36 weeks. The rats in group III were given a single dose of 7,12 Dimethyl benzanthracene (100 µg/rat) dissolved in 10 µL of sesame oil to surgically exposed left ovary and maintained up to 36 weeks to initiate ovarian carcinogenesis. Group IV rats received DMBA + cinnamaldehyde 50 mg/kg b. w (before starting the experiment and continued up to 24 weeks). Group V rats received DMBA + cinnamaldehyde 50 mg/kg b. w (25-36 weeks). Group VI rats received DMBA + cinnamaldehyde 50 mg/kg b. w (1-36 weeks). Serum levels of Estrogen, progesterone, LH, FSH were estimated using ELISA. The results showed that significant increase in serum level of Estrogen, LH, FSH, and decreased progesterone in only DMBA treated group when compared with control groups. Also, there was a significant decrease in serum levels of Estrogen, LH, FSH, and increased progesterone in cinnamaldehyde treated groups (dose-dependent) when compared to only DMBA treated group. The results of the present study suggested that cinnamaldehyde has anticancer activity and further investigations are needed for evaluating the anticancer potential and mechanism of its action.***

Keywords: Cinnamaldehyde, DMBA, Ovarian cancer, Reproductive hormones.

I. INTRODUCTION

Ovarian cancer is regarded as the seventh most common type of cancer in women. It affects around twenty-four hundred thousand individuals each year globally. Ovarian cancer is a fatal disease that kills around 150,000 women globally each year [1]. Around 1 in 70 women is prone to developing this cancer. Due to the lack of symptoms during the early stages, this condition tends to get worse and eventually leads to higher mortality [2]. Various interventions are utilized to treat ovarian cancer cells. They include surgery, chemotherapy, radiation, and gene therapy. Although the scientific community widely praised the effectiveness of certain interventions, they often encountered certain limitations. This led to the development of drugs that can be used effectively and efficiently. Since ancient times, plants have been used to treat various human diseases. They have been known to exhibit various pharmacological actions related to their life functions. The importance of phytochemicals in drug discovery has been acknowledged. Their bio-chemicals have high value in the development of new drugs against cancer. There has been a significant increase in the number of plants that are used to prepare drugs [3]. Given the above, it may be rationalized that the anti-cancer potential of commonly used food ingredients and easily accessible herbs may be useful in controlling cancers. Cinnamaldehyde is an aromatic liquid that has a sweet, spicy, and warm smell. It is derived from cinnamon oil. [4][5]. Cinnamon is a spice obtained from the inner bark of several trees from the genus Cinnamomum belongs to the family Lauraceae and is widely used in either the East or West parts of the world as a spice for thousands of years. In Asia and Australia, more than 250 species are primarily cultivated and mainly is used in both sweet and savory foods. Cinnamaldehyde is one of the bioactive compounds of Cinnamon with medicinal properties such as antioxidant, anti-inflammatory, anti-ulcer, antiallergic and antiseptic properties this compound has previously been reported that cell cycle arrest in leukemia and melanoma cells and induction of apoptosis in cervical cancer, colon cancer, breast cancer, hepatoma [6]. Thus, the present study is aimed to investigate the serum biochemical parameters including estrogen, progesterone, FSH, and LH in DMBA induced ovarian cancer rats.

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II. MATERIALS AND METHODS

1) *Procurement of Cinnamaldehyde and its Safety Data Sheet:* Cinnamaldehyde was purchased from Sigma-Aldrich Chemical Pvt Limited, India with CAS No- 104-55-2. Its molecular weight is 132.16 gm/mol, Density 1.0480 g/ cm3 and boiling point 2480 C, melting point -7.50 0 C with a light Skin irritant. Acute toxicity LD50 Oral-Rat 2,220 mg/kg body weight.
2) *Animal Model:* Female Wistar rats with ±200-230 g weights were used for this study. Rats were adapted to animal house conditions and fed with a standard pellet diet and provided water ad libitum.
3) *Induction of Ovarian Cancer:* The rats in group III-VI were anesthetized with 10% ketamine (60 mg/kg, b. w) and 2% xylazine (5 mg/kg, b.w) and given with a single dose of 7,12 Dimethyl benzanthracene (100 µg) dissolved in 10 µL of sesame oil to surgically exposed left ovary and returned intact to the body cavity [7]. The muscle and skin layers were closed using a 3-0 silk suture and an antibiotic was administrated for a week against the infection [8].Experimental animal handling and care followed according to CPCSEA guidelines (Reg. No. 1677/PO/Re/S/2012/CPCSEA/33/6.05.16).

A. Experimental Design

In the present study, rats were randomly divided into six experimental groups of six animals each, and the complete experimental period is 36 weeks as given below.

1) *Group 1*– Control rats with normal water.
2) *Group 2*- Drug control, rats were fed with (50 mg/k.g b.w) cinnamaldehyde during the experimental period(36 weeks).
3) *Group 3*- Carcinogen control, Rats were given with a single dose of 7,12 Dimethyl benzanthracene (100 µg) dissolved in 10 µL of sesame oil and maintained up to 36 weeks.
4) *Group IV*- (Initiation) rats received DMBA (same as group III) and meanwhile, Cinnamaldehyde (50 mg/k.g b.w) administration was started two weeks before the starting of the experiment and continued up to 24 weeks.
5) *Group-V* (Post-initiation) rats received DMBA (same as group III) and also the administration of Cinnamaldehyde (50 mg/k.g b.w) started after the termination of the cancer induction period and proceeds until the end of the experiment (25-36 weeks).
6) *Group -VI* (Entire period) rats received DMBA (same as group III) and also cinnamaldehyde was administrated from day one of the experiment and continued for the entire period of the experiment (1-36 weeks).

All animals were sacrificed after the end of the experimental period, blood and ovaries were taken out for further evaluation.

B. Biochemical Analysis

1) Estimation of Estrogen [9]
2) Estimation of Progesterone [10]
3) Estimation of Follicle-stimulating hormone [11]
4) Estimation of Luteinizing hormone [12]

III.DATA ANALYSIS

Result is expressed as mean ± S.D and compared to control group. statistical analysis was performed by one way ANOVA) followed by Dunnett's multiple comparison test. $P \leq 0.05$ was considered as statistically significant. All the data maintained as triplicates. GraphPad Prism program V.8 software system used for analysis.

IV.RESULTS

The results of Estrogen and progesterone, follicle-stimulating hormone (FSH), Luteinizing hormone (LH) are normal in control and drug control groups. The levels of Estrogen, FSH, LH were significantly increased and progesterone was significantly decreased in Group-III when compared to the control group.

After the treatment with cinnamaldehyde moderate changes were observed in group IV and V in hormones level when compared to Group-III. A significant decrease in Estrogen, FSH, LH, and a significant increase in progesterone was observed in Group-VI when compared to Group-III.

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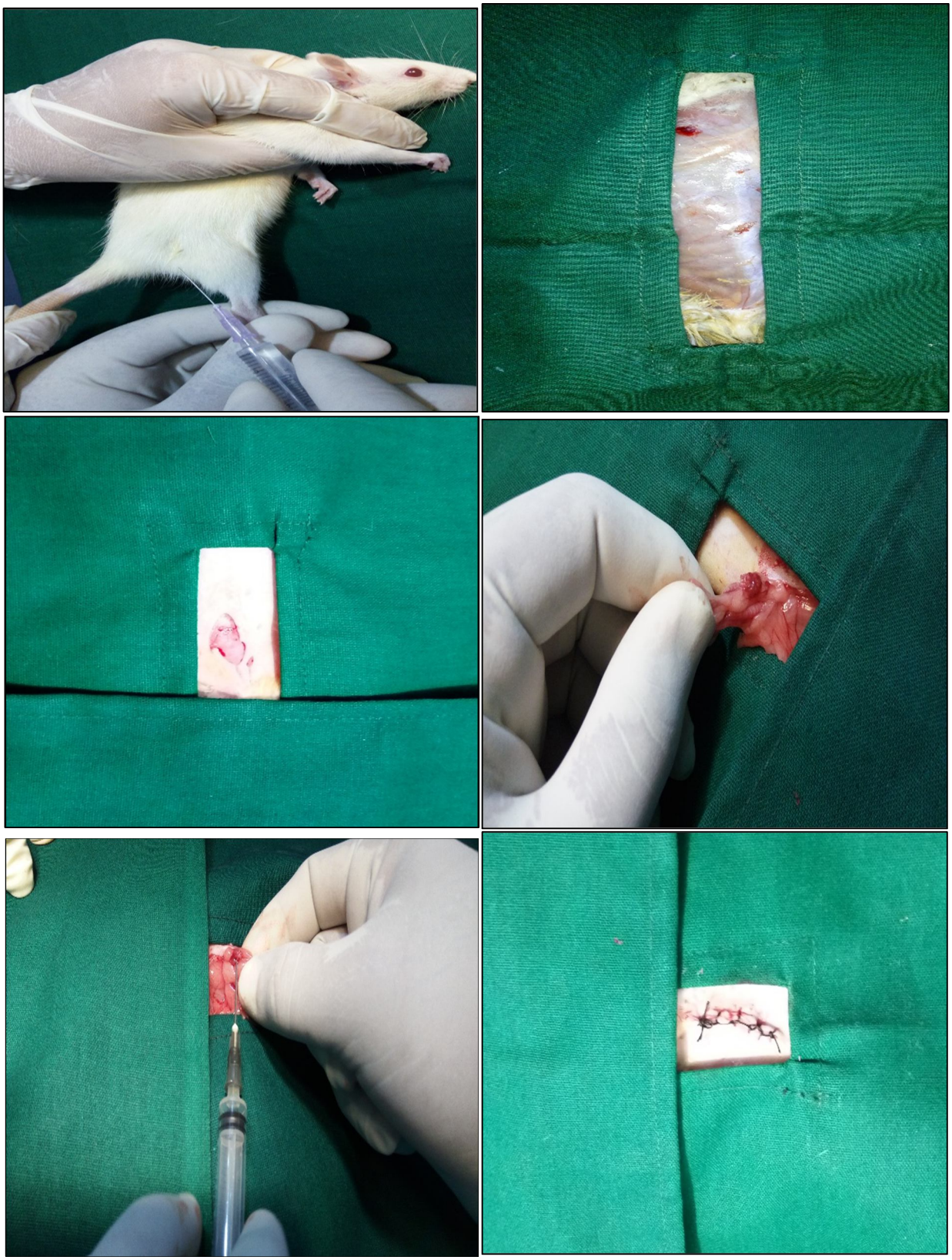


Figure 1; Induction of Ovarian cancer with DMBA though surgical procedure

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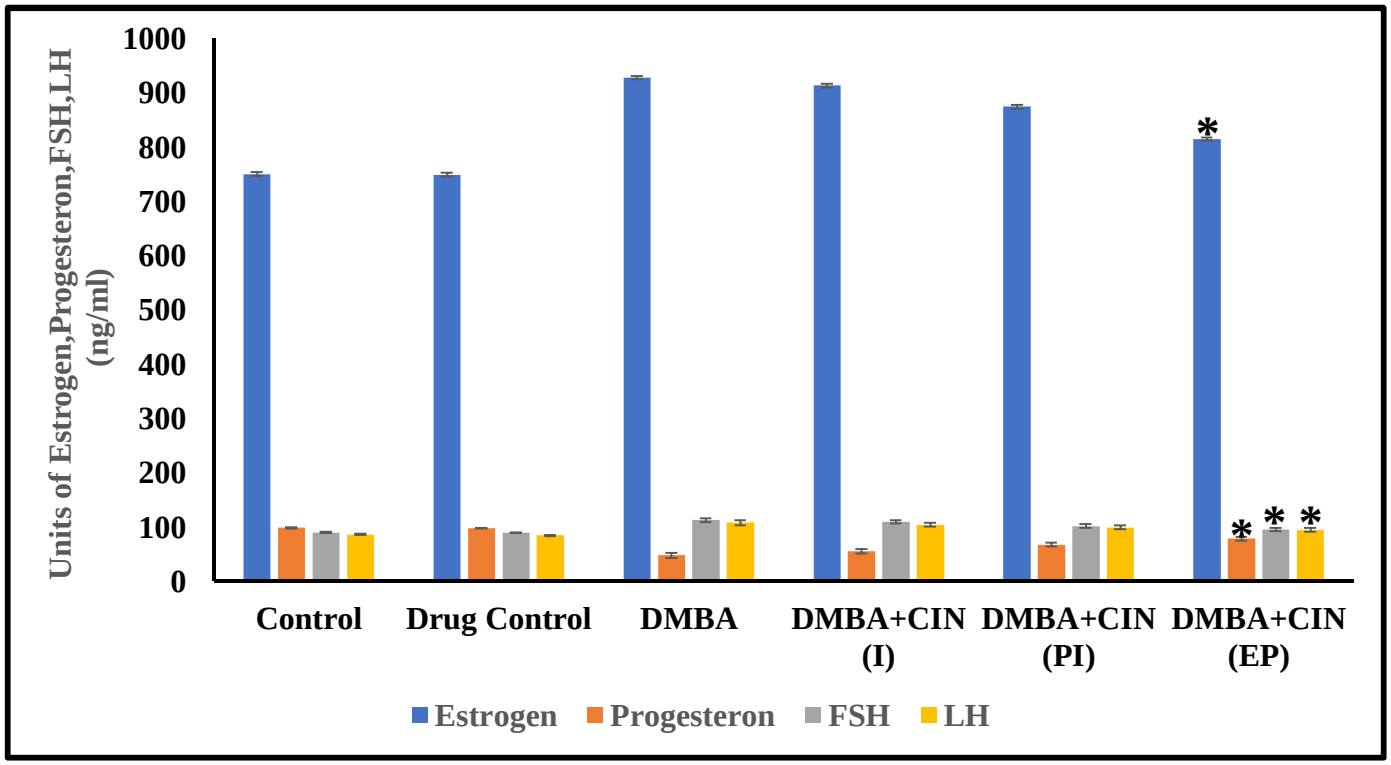


Fig2. Effect of cinnamaldehyde on hormones levels: Estrogen (ng/ml), Progesterone (ng/ml), FSH (ng/ml), and LH (ng/ml) levels in the serum of cinnamaldehyde treated and control groups. All experimented values are expressed as mean ± SD with percent change over control of six individual observations and *indicates significant difference in comparison to positive control ($p<0.05$).

V. DISCUSSION

The etiology of ovarian cancer has not yet been fully elucidated. One of the factors for ovarian carcinogenesis is changes in reproductive hormones [13]. The hormonal milieu is known to modulate the growth of tumor cells and the progression of cancer. It is also known to promote cellular proliferation and tissue invasion. Several reports suggest that estrogens, FSH, and LH present in the ovulatory follicles contribute to the initiation and/or promotion of ovarian carcinogenesis and progesterone present found during pregnancy, and protects against ovarian cancer development [14]. The results in the present study also revealed decreased levels of estrogens, FSH and LH and increased level progesterone in cinnamaldehyde treated group as normal group. These results from the experiments support cinnamaldehyde have anticancer activity and further investigation is planned.

VI. CONCLUSION

Menstrual and reproductive factors, as well as female hormones, have long been related to ovarian carcinogenesis. A significant difference in serum level of total Luteinizing hormone (LH), follicle stimulating hormone (FSH) and Estrogen and progesterone were observed in Group-III rats. The results of this study demonstrated that cinnamaldehyde (50mg/k.g b.w) had the ability to restore the estrous cyclicity and down-regulate serum levels of hormones like control rats. These preliminary data suggest that cinnamaldehyde supplementation improves estrous cycle. Further experiments are planned to study the anticancer properties of cinnamaldehyde in ovarian cancer model.

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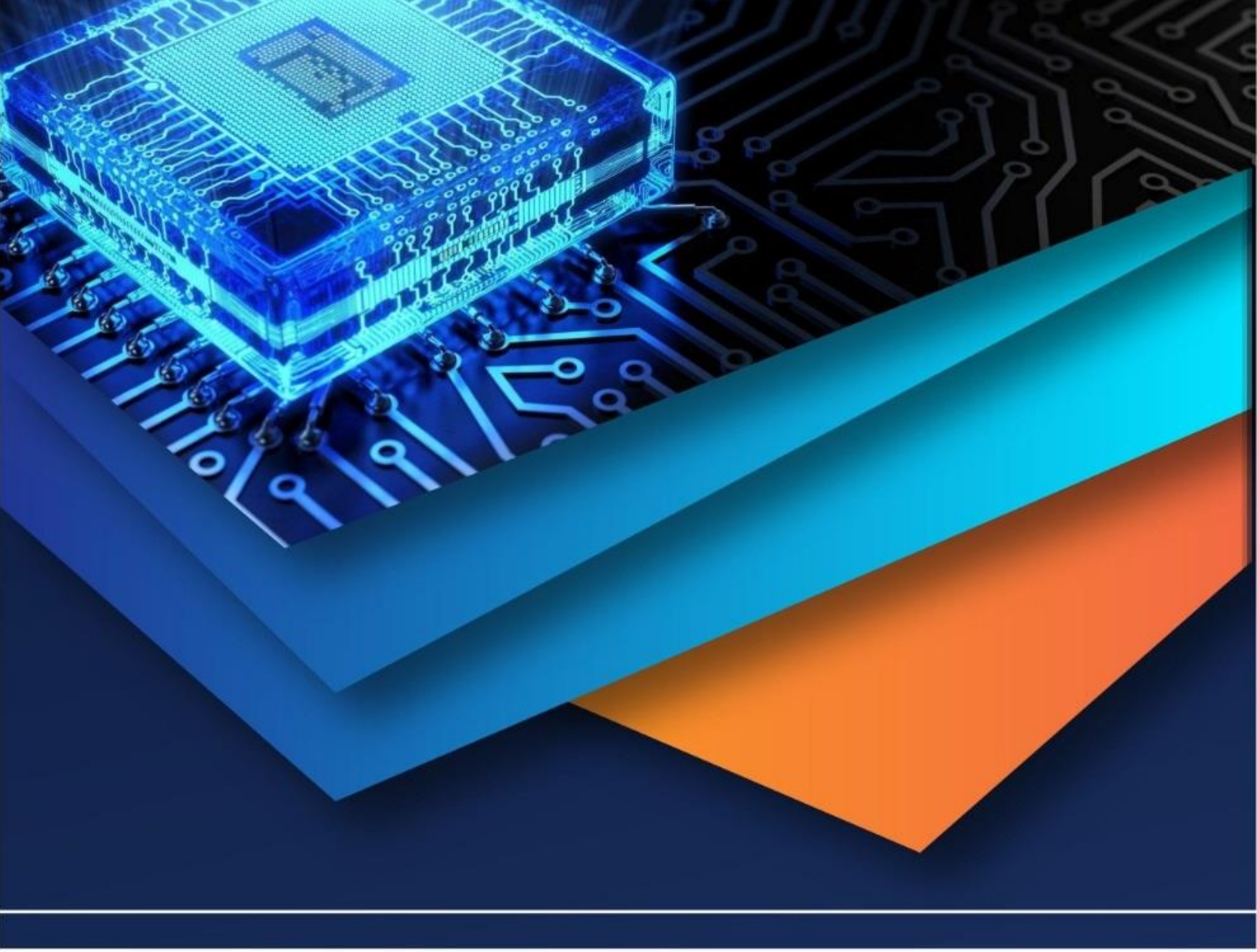
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