iJRASET
International Journal For Research in Applied Science and Engineering Technology

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 13 **Issue:** V **Month of publication:** May 2025

DOI: https://doi.org/10.22214/ijraset.2025.70082

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International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.538
Volume 13 Issue V May 2025- Available at www.ijraset.com

Pharmacognostical and Pharmacological Evaluation of *Atropa belladonna*: An Overview

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Abstract: ***Medicinal plants are always having significant roles for preventing and treating different diseases. Solanaceae is among one of the family member for associating this one. Atropa belladonna is one of them. These plants were discovered centuries ago. Besides this plants are used for ethno-botanical purposes. These plants are rich sources of lots of chemical cum active constituents like tropane alkaloids such as hyoscyamine, atropine, and scopolamine. Tropane alkaloids are used as antimuscarinic or anticholinergic agents as they inhibit the production of acetyl choline. This review article provides detail knowledge of Belladonna including its history, chemical properties, pharmacological actions, etc.***
Keywords: Atropa belladonna, Atropine, Hyoscyamine, Scopolamine, Pharmacological action, Therapeutic uses.

I. INTRODUCTION

Atropa belladonna is one of the multipurpose botanical agents commonly known as deadly nightshade or belladonna. It is classified under the family *Solanaceae*. Among the people, it is also known by various names such as death bell, bear strawberry, wolfberry, yidin, bell paper, black grape, devil cherry. The name "*Atropa Belladonna*" originates from the Greek goddess "Atropos" refers to one of the three fates of life, while the Italian appellation of this plant translates to "beautiful lady". The plant is an extremely potent toxic agent owing to the presence of several tropane alkaloids such as Scopolamine and hyoscyamine; poisoning with manifested symptoms of delirium and hallucination. *Atropa belladonna* is having alkaloid atropine including dl-hyoscyamine. The plant is also very important in medical and cosmetic applications. Considering the importance of this overview, it attempts to gather the researcher in conscientious consideration of further creation and appropriate applications for human benefit in exploiting *Atropa belladonna*. [1, 2, 3, 4]

Figure no 1: Atropa belladonna

ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.538
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Table no 1: Botanical description of *Atropa belladonna*

Plants Parts	Description	Image	References
Roots	-The roots are fleshy. -the outside of root is brown or pale yellow and inside whitish in color. -they have coarse surface. -It extends horizontally when growth occurs.		1-6
Stem	-The stem of plant in upright is soft allows plant to grow. -The surface of stem is glabrous. -it has branched structure. -The color of stem change from green to dark purple.		
Leaves	The leaves are -brittle and stalked. -petiolate and lanceolate to broadly ovate. - have slight decurrently lamina. -The margins are entire transverly broken. -Colour dull green or yellowish green.		
Flowers	The flowers are campanulate shape. -Contain 5 small reflexed lobs of corolla with green tinges. -The corolla is 2.5-12 cm wide. -the colour of flower change to purple to yellowish-brown.		
Fruits	The fruit is looks like -fleshy berry. -It is green in colour ripening to shining black colour. -The fruit is bilocular and sub-globular in shape. -Each fruit contain many seeds.		

II. HISTORY

Atropa belladonna was discovered in Greece. In that time Atropa was mixed with different herbs and other ingredients for preparation of suitable pharmaceutical formulation called as elixir for showing their anticholinergic properties and activities. In later Andrew Duncan discovered and discussed different benefits of Atropa belladonna for the treatment of different disorders. [1, 2, 3, 7-10]

III. DISTRIBUTION

Atropa belladonna, commonly referred to as "deadly nightshade," is typically found in dry, uncultivated regions across Portugal, parts of West Asia and North Africa, and throughout much of Europe, excluding England and Scotland. The plant is believed to be Mediterranean, origin sparingly extending to its Southern Asia, including cultivation in the Himalaya and North America. The plant is found on rich soil with good drainage, preferably limestone or chalk, away from direct sunlight.

As such, the perennial distribution of Atropa belladonna is throughout Central and Southern Europe, and many other ecologically forested areas of the earth. They thrive well in the shade of trees, attaining bush-like forms when grown in wooded hill slopes, whereas those exposed to more sunlight are dwarfed. India is home to this species in the western Himalayas range, more particularly from Shimla to Kashmir and the adjoining area of Himachal Pradesh, especially in Jammu and the forests of the Sindh and Chenab valleys. [1, 2, 3, 11, 12]

IV. CULTIVATION & COLLECTION

The influence of atmospheric conditions on the alkaloid content in Belladonna is considerable. The species cultivation prefers well-drained and lime soil and full sunlight or light shade will best work if it is light with enough calcium carbonate soil. The sowing of seeds in flats is currently the standard farming practice for Belladonna. Higher alkaloid yield occurs on the hill slopes cultivated for Belladonna while the plant can grow at sea level with some calcareous well-drained soil, and adequate shade. Fertilization with farmyard manure or a combination of nitrate of soda, basic slag, and kainite gives good effect in farming.

The plants normally grow to about 1.5 feet during their first year, with flowering around September. The flowering plants are cut back an inch above ground in June while the second-year flowering plants under good conditions will have a second harvest around September. Root harvest can begin in the autumn of the fourth year after planting. Collected drug is dried at 40^{o}-500^{o}C temperature. Undried leaves and root spread ammonia. Destroy infected Belladonna by the fungus Phytophthora belladonna to stop further infection. Occasionally, the insect as flea-beetle damages the leaves while the roots are attacked by fungi. Furthermore, it is imperative to dry them quickly under good sunshine; otherwise, wilted foliage and plant material may carry lower alkaloid levels. [1, 2, 3, 13-18]

V. PLANT TOXICITY

Belladonna is anticholinergic in nature and hence accounted to be one of the deadly poisonous plants due to three alkaloids involved, i.e., atropine, scopolamine, and hyoscyamine, which are distributed over the entire plant, mainly, the roots, leaves, and berries. The berries provide the greatest danger, Poisonous symptoms of belladonna produces effects on both the central and peripheral nervous systems. [19, 20]

VI. CHEMICAL CONSTITUENTS

Atropa belladonna contains l-hyoscyamine. Thirteen alkaloids are identified from the root and seven from the aerial parts of the plant. Major constituents include atropine, apoatropine, choline, belladonnine, hyoscyamine, 6-hydroxy apoatropine, Atropamine, cuscohygrine, 3-phenyl acetoxytropane, 6-hydroxy hyoscyamine, hygrine, chrysatropicacid, Octadecanoic acid, Oleic acid, N-methylpyrroline, pyridine, N-methyl pyridine, N-methyl-pyrrolidine are also present. Other constituents include homatropine, hyoscyamine N-oxide, rutin, scopoletin, and calcium oxalate which counted for 14% of acid-soluble ash and 4% of acid-insoluble ash. Additionally, belladonna has cumarins, such as umbelliferone, esculetin, scopoline, and kaempferol and quercetin-triglycosides compounds like kaempferol-3-rhamnogalactoside, quercetin-7-glucoside. [1, 2, 3, 4, 21-25]

A. Atropine

Atropine is fitted into the category of analgesics and antispasmodics. It plays within, and thus criticizes, the motor system that coordinates movement through its effect on various important areas of body activity like ophthalmology, cardiology, and gastrointestinal treatments. During embryonic and early age, it was shown that atropine well modulates the autonomic nervous system. It has ability in higher doses to cause tachycardia, raising the heart rate by as high as 30 beats per minute. In such emergencies, this becomes useful in cases where the heart rate dips below 60 beats per minute, with low blood pressure, especially during myocardial infarction, without affecting peripheral blood vessels and either blood pressure or respiration. As an antispasmodic, it tends to inhibit the secretions and prolonging the stay of antacids in the stomach in peptic ulcers: they diminish also the saliva secretion by 11-12 times in greater potencies. For dilation, atropine must be infused into the eyes before visual examination. [1, 2, 3, 4, 26-34]

B. Chemistry

Atropine is mainly obtained from *Atropa belladonna*, with content ranging between 0.8% and 1.2%. It forms crystals in a prismatic shape and melts at 118°C. It is inactive in nature. It is soluble in alcohol and chloroform. It is insoluble in water. Its chemical formula is $C_{17}H_{23}NO_3$.

It is white crystalline powder or colorless crystals. It is the tropine ester of racemic tropic acid and is not optically active. Atropine in potency at some molar quantities must block several moles of acetylcholine. One kind of antagonist activity may directly or electrostatically prevent it from binding to the receptor on adjacent cells, rendering the receptor unavailable for the binding of acetylcholine or other similar agents. [1, 2, 3, 4, 34-38]

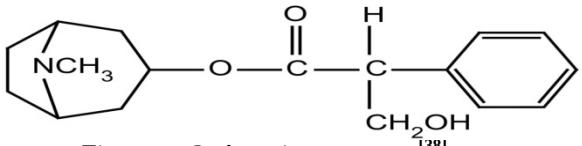

Figure no 2: Atropine structure [38]

C. Hyoscyamine

Hyoscyamine is a tropane-based alkaloid mainly present in Solanaceae family plants, including henbane (*Hyoscyamus niger*) and belladonna (*Atropa belladonna*). Its chemical structure constitutes a bicyclic tropane skeleton coupled with a hydroxyl group, both of which contribute enormously to its pharmacological interactions. Its appearance is as thin, crystal needles, resembling silk threads, melting at temperature 109 °C. It is insoluble in water. Hyoscyamine work through inhibition of the action of acetylcholine- a neuro transmitting agent involved in muscle contraction and secretion-reduces abdominal cramps, diarrhea, excessive salivation, and a potential side effect is dry mouth, blurred vision, constipation, and dizziness. [1, 2, 3, 38-41]

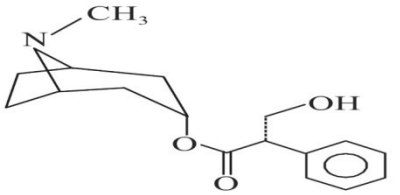

Figure no 3: Hyoscyamine structure [38]

D. Scopolamine

Hysocine, also referred to as scopolamine, is a tropane alkaloid mainly derived from the plants in the genus of Datura and the family of belladonna. The drug form is either a kind of syrupy liquid or a crystalline compound with a colorless form, yet melting at 59 °C and easily dissolving in a polar organic solvents. Its chemical formula is $C_{17}H_{21}O_4N$. This alkaloid is mostly known for its autonomic inhibition. While it shares anticonvulsant properties with atropine, but it acts with more potency upon specific secretory glands such as the sweat gland, salivary gland and tracheal glands. Hysocine is sometimes used to treat acute abdominal pain associated with functional disorders of the digestive, urinary, and reproductive systems, as well as lessen spasms associated with childbirth. It also induces drowsiness, which makes it useful in treating motion sickness in travelers and postoperative dizziness. [1, 2, 3, 38, 42-44]

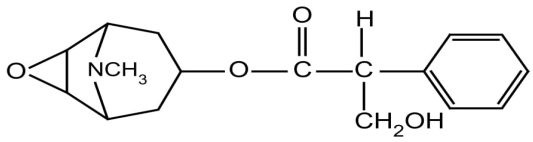

Figure no 4: Hysocine structure [38]

VII. ADULTERANTS OF BELLADONNA

Leaves of *Phytolacca decandra* (Phytolaccaceae), *Phytolacca acinosa* (Phytolaccaceae) and *Ailanthus glandulosa* (Simaroubaceae) have played a significant part as pollutants of belladonna leaves. The leaves of Ailanthus are triangular ovate and have straight-walled epidermal cells showing an explosively striated cuticle cluster chargers of calcium oxalate. Others plants *Scopolia japonica* (family-Solanaceae) *Scopolia carniolica (*family- Solanaceae), *Medicago sativa* (family-Fabaceae) *various parts* among the most common shops that are considered backups for A. belladonna. [1, 2, 3, 45-48]

VIII. MECHANISM OF ACTION

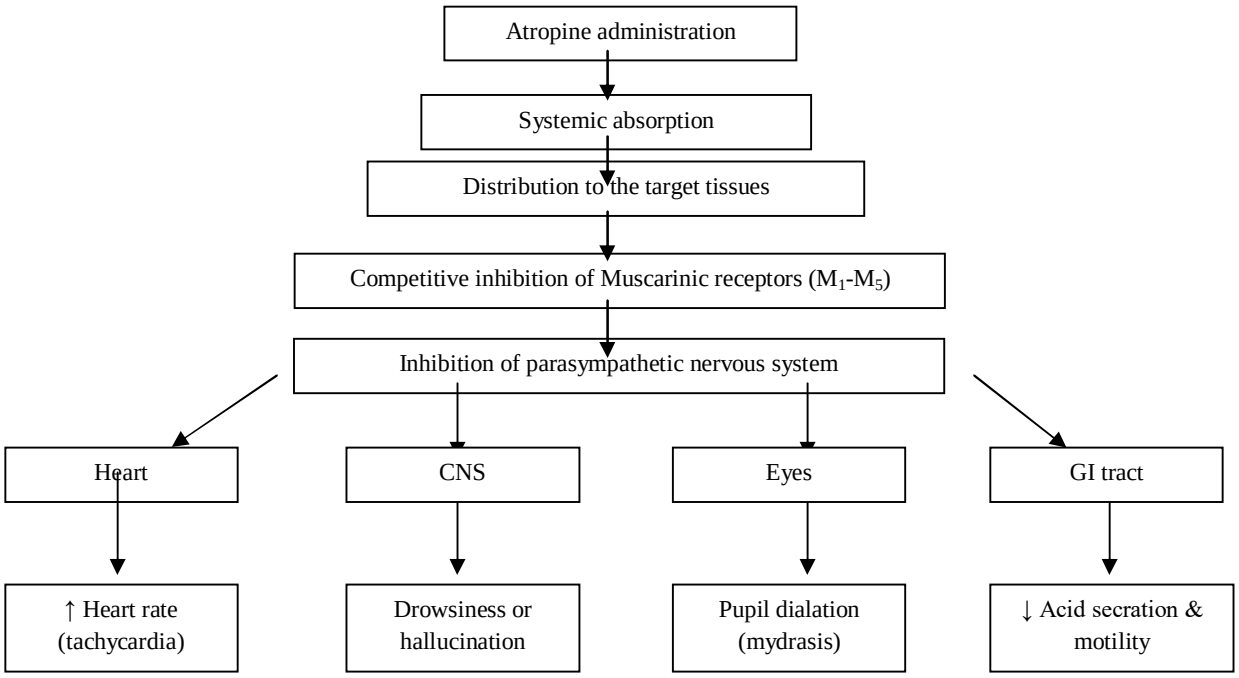

Figure no 5: Mechanism of action [49-51]

IX. PHARMACOLOGICAL ACTIONS

The Pharmacological effects of drugs can be predicted from parasympathetic responses. Prominent effects are seen in organ which normally receive strong parasympathetic tone and provide a good background for understanding the therapeutic uses of the various muscarinic antagonists. All the muscarinic antagonists produce similar peripheral effects, although some show a degree of selectivity, for example, for the heart or bladder reflecting the heterogeneity among muscarinic acetylcholine receptors (mAChRs).[49-53]

Table no 2: The main effects of Atropine

Sl. No.	System	Effect	References
1.	Cardiovascular System	Effect on Heart: When it given in large doses, produces an increase in heart rate due to the blockade of M_2 receptors on the Sino atrial node and thus reduction of vagal tone.	49, 50,51,54-58
		Effect on Circulation: The impact of atropine on blood pressure by itself is small.	49, 50,51,59-61
2.	Eye	Effect on Eye: Muscarinic antagonists are substances that counteract the cholinergic activity of the sphincter muscle of the iris and the ciliary muscle responsible for the convexity of the lens.	49, 50,51,62-64
3.	GI tract	Effect on Gastric acid secretion: Atropine like substance inhibits gastric acid secretion by vagal stimulation partially due to secretion of gastrin-releasing peptide (GRP) by peptidergic neurons in the vagus nerve.	49,50,51,65,66
		Effect on Motility: Atropine increase parasympathetic nerves tone and motility of the gastrointestinal system while relaxing sphincters, and by doing so, facilitate the movement of the GI contents.	49,50,51,67,68

		Effect on Salivary secretion: Muscarinic receptor antagonists greatly inhibit plentiful, water-like saliva secretion with parasympathetic stimulation, preventing dry mouth with possible swallowing and speaking problems.	49,50,51,69,70
4	Pulmonary System	Effect on Pulmonary System: Atropine may provoke a certain degree of bronchial dilation and a reduction of tracheobronchial secretion by inhibiting parasympathetic (vagal) activities of the lungs however, the effect is greater in patients with respiratory illnesses.	49,50,51,71-74
5.	Smooth muscles	Effect on Smooth muscles: It inhibits parasympathetic innervation of all visceral smooth muscle by M3 receptor blockage, decreasing tone and contraction amplitude in the stomach and intestines. This leads to decreased transport of chyme through the digestive system.	49,50,51,75-78
6.	Sweat Glands	Effect on sweat glands: Administration of atropine blocks M3 receptor and depresses the secretion from the sweat, salivary, tracheobronchial, and lacrimal glands. This causes dryness in the skin .	49,50,51,79-81

Table no 3: Therapeutic uses

Specific site of action	Plant part used	Uses	References
Central nervous system	Roots, leaves and berries	The first medication introduced for preventing motion sickness. They also used to treat the extra pyramidal symptoms that commonly occur as side effects of conventional antipsychotic drug therapy.	49,50,51,82,83
Respiratory system	Aerial parts of plant	These agents are important in the treatment of chronic obstructive pulmonary disease. It have used in nasal inhalers for the treatment of the rhinorrhea.	49,50,51,84,85
Cardiovascular system	Aerial parts of plant	Atropine may be employ in the initial treatment of patients with acute myocardial infarction in whom excessive vagal tone causes sinus bradycardia or AV nodal block. Atropine occasionally is useful in reducing the severe hyperactive carotid sinus reflex.	49,50,51,86,87
Eye	berries, leaves	It induces the dilated pupil called mydriasis. Used in ophthalmological practice. These agents are used only in coronary care units for short-term interventions or in surgical settings.	49,50,51,88,89
Salivary secretions	Aerial parts of plant	They are effective in reducing excessive salivation, such as drug-induced salivation	49,50,51,90,91

		and that associated with heavy-metal poisoning.	
Gastrointestinal tract	Roots, leaves and berries.	They are widely used for the management of peptic ulcer. They can reduce gastric acid secretion. Reduced spasm in case of intestinal gripping.	49,50,51,92,93
Urinary tract	leaves and roots	It relaxes smooth muscles of urinary bladder and prolongs the period urination and can provide development of urine retention. Used in urinary infections.	49,50,51,94,95

Table no 4: Adverse effects

Disorder	Effects	References
Photophobia	Abnormal sensitivity or intolerance to light, often causing discomfort or pain in bright environments.	49,50,51,95-100
Insomnia	It is a condition characterized by difficulty falling asleep lead to poor sleep quality, daytime fatigue, and affect mood.	
Dizziness	It is feelings of lightheadedness, vertigo, unsteadiness, or a sensation of floating or spinning.	
Mydriasis	It refers to dilation of the pupils, an abnormal enlargement or widening of the pupils beyond their normal size, occur in one or both eyes.	
Leukocytosis	A condition characterized by an abnormally high number of white blood cells in the bloodstream, exceeding the normal range.	
Anaphylaxis	A rapid-onset, severe allergic reaction that can be life-threatening and typically involves multiple organ systems throughout the body.	
Hyperpyrexia	Hyperpyrexia is the term for exceptionally high fever greater than 41^0 C body temperature, which can occur in patients with severe infections.	
Fibrillation	An irregular heartbeat that occurs when electrical signals in the atria fire rapidly than the ventricles that can cause blood clot in heart.	
Hyperthermia	Fever or body temperature is increased above the normal range.	
Ataxia	A lack of coordination or uncontrolled movements due to dysfunction of the nervous system.	

X. CONCLUSION

Atropa belladonna is considered profoundly important in our modern pharmacological history as well as the ancient one because of its powerful anti-cholinergic effects. The key bioactive compounds in this plant-atropine, scopolamine, and hyoscyamine block acetylcholine at the muscarinic receptor, and thus elicit a wide range of physiological impacts, for instance, pupil dilation, tachycardia, decreased secretions, and smooth muscle relaxation. Such properties have been exploited extensively in medicine for treating bradycardia, motion sickness, and gastrointestinal conditions, among others, where muscarinic blockade is reasonably therapeutically favorable. However, despite being significantly vital, the use of the plant is always erratic in therapeutically endeavors. The narrow therapeutic window of alkaloids found in *Atropa belladonna* demands extremely meticulous dosing to avoid administration that may provoke severe toxicity, variable from simple confusion and hallucinations to seizures or even death. Such is the toxic risk that, for some time now, a shift has been made toward synthetic analogs and more precisely controlled breeding variants of these compounds, such as atropine sulfate and scopolamine patches that offer all the branched benefits of anti-cholinergic activity and reliability in safety profiles.

The historical and contemporary use of *Atropa belladonna* exemplifies a dual problem of many plant-based medicines in that they provide a strong potential with equally significant dangers on the other side when not managed properly. Further research in more selective muscarinic receptor antagonists is ongoing as is the development of safer formulations, highlighting the need for careful balance in maximizing effectiveness versus minimizing the adverse effects. Ultimately, while Atropa belladonna remains a tool of great utility in medicine, its application must always be dealt with sober caution and precision.

Conflicts of Interest: Nil

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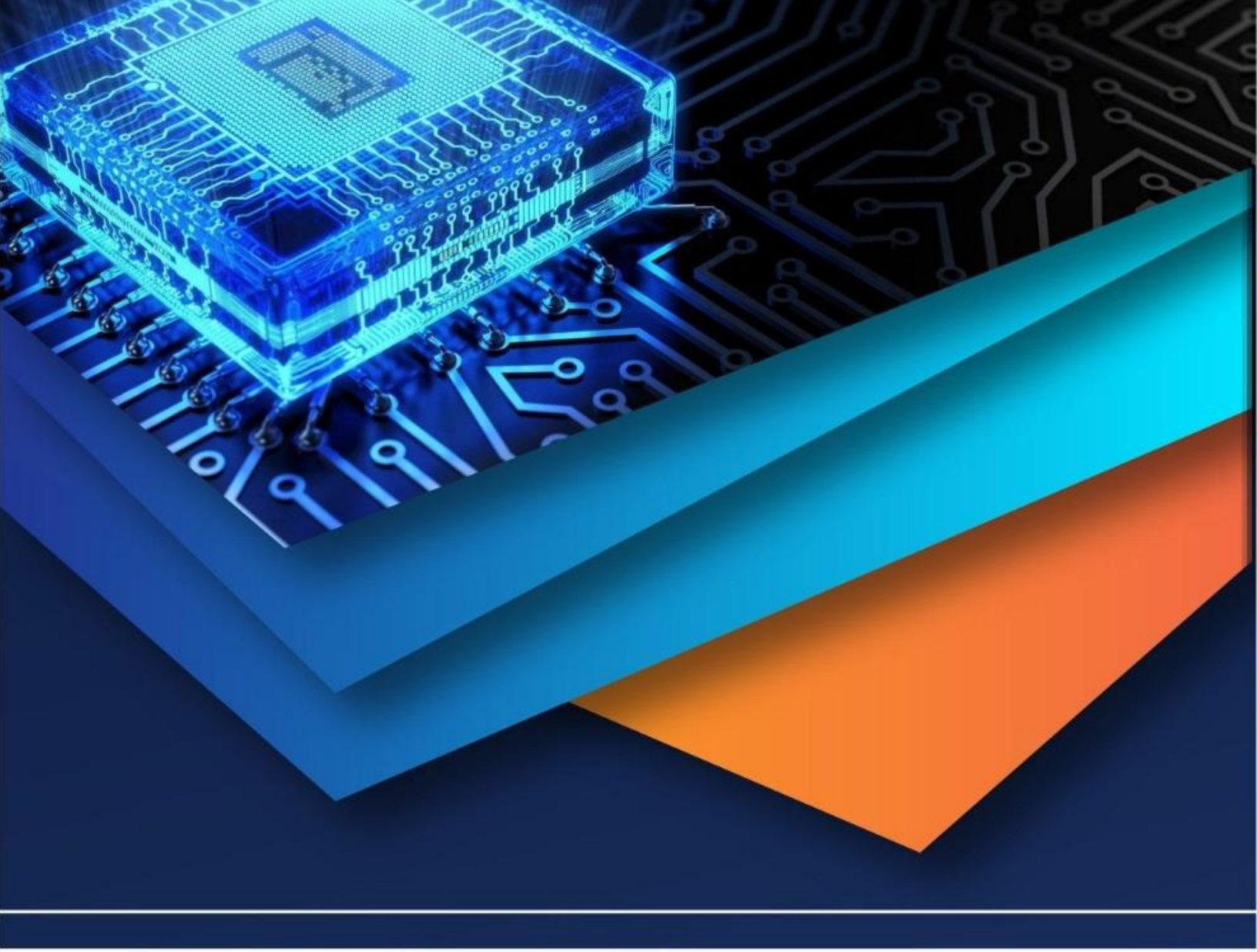

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