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Exploring Nasal Anatomical Peculiarities: Illuminating Nasyakarma as a Paradigm Shift in Addressing Central Nervous System Disorders

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Abstract: ***The nasal route holds a special place in Ayurveda, particularly in the practice of Nasya karma. The nose, regarded as an opening to the "shiras" or head, possesses anatomical peculiarities that make it an ideal route for drug administration. The developmental origins of the nose lie in neural crest cells, which migrate during gestation, forming the nasal placodes and giving rise to the intricate nasal structure.***
Within the diverse approaches to drug delivery,nasya karma emerges as a promising carrier for brain-targeted therapeutics.
This comprehensive review bridges modern pharmaceutical advancements with ancient Ayurvedic wisdom, emphasizing the significance of the nose as a crucial route for drug delivery and its potential role in treating central nervous system disorders.
Keywords: Brain-targeted therapeutics, central nervous system disorders, nasal placodes, nasya karma

I. INTRODUCTION

Nasya, a therapeutic practice within *Ayurveda*, holds a unique place in addressing ailments localized above the neck. As the gateway to the head, the administration of medicinal substances via the nasal route has a profound impact, effectively extending its healing influence throughout the head and neck regions.

The nose comprises both an external and an internal component. The external aspect features a structural framework of bone and hyaline cartilage, enveloped by muscles and skin, and lined with a mucous membrane. The inner intricacies of the nasal structure serve three pivotal functions: first, they condition incoming air by warming, moistening, and filtering it; second, they serve as receptors for olfactory stimuli; and third, they function as resonating chambers that play a role in modifying speech sounds.

The goal of targeted drug delivery is to lower the relative concentration of medication in the remaining tissues while increasing the concentration of medication in the targeted tissues. enhancing the medication's effectiveness and minimizing adverse effects. For thousands of years, intranasal drug administration has been used, and it has now had a fresh impact on life.

II. METHODS

This review integrates information from Ayurvedic texts, modern anatomical studies, and pharmaceutical research to elucidate the nasal route's significance in drug delivery. Key concepts such as the nose's developmental origins, anatomical peculiarities, and the principles of *Nasyakarma* are analyzed to provide a comprehensive understanding of its therapeutic potential.

III. AIMS

1) To explore the unique anatomical features of the nose and their significance in the context of *Nasya* therapy within *Ayurveda*.
2) To investigate the pathways and mechanisms involved in nasal drug delivery for treating central nervous system (CNS) disorders.
3) To analyze the effectiveness of *Nasya Karma* in addressing specific CNS disorders and its potential as a complementary or alternative therapy.

IV. OBJECTIVES

1) Examine the anatomical peculiarities of the nose as described in *Ayurveda* and compare them with modern anatomical knowledge.
2) Investigate the mechanisms of drug delivery through the nasal route, including the olfactory, trigeminal, and blood circulation pathways.

3) Evaluate the therapeutic benefits of *Nasya Karma* in treating CNS disorders such as coma, migraine, motor neuron disease, epilepsy, and stroke.
4) Discuss the challenges and advancements in nasal drug administration, including nanotechnology applications and overcoming the blood-brain barrier.
5) Provide insights into the future prospects and potential research directions in utilizing *Nasya* therapy for neurological conditions.

V. ANATOMY OF NOSE

A. *Ayurveda*

The anatomy of the nose is not explained in great detail in *Ayurveda*, but the points that are mentioned are as follows: In the *Sushruta Samhita sutra sthana* and *sharir sthana*, the anatomy of the nose is mentioned. *Sushruta Acharya* mentions that the *nasaputa's praman* is given with two different measures, i.e., it is of 2 *angula pramana*, and its *vistara* is said to be of 1/3rd *angula*. This could be understood to mean that the circumference of the *nasaputa* is 2 *angula*, the diameter of the *nasaputa* is 1/3rd *angula*, and the length of the *nasika* is said to be 4 *angula*.

In *Sushruta Sharirsthana* Chapter 5, *Acharyas Sushruta* states, "*nasayam trini*," which implies that the *asthi* in the *nasika* are three in number. These bones in the nose are known as *tarunasthi*, which means they are predominantly cartilaginous. When we look at the current anatomy of the nose, we can observe that nearly two-thirds of the nose is cartilaginous, with only one-third being bony. While the *sandhi* or joints are supposed to be one and the same, as follows *"eka kaklake nasayasch"* According to *Acharya,* there are two *dhamani* that aid in the transmission of the fragrance or *gandha*, as well as 24 *siras*, four of which must be protected.

B. *Modern*

The detailed anatomy of the nose, as illustrated in Gray's Anatomy, includes several key components that are essential for understanding its structure and function. Here's a comprehensive overview:

1) *Bones*

- Ethmoid Bone: This bone forms the upper nasal septum and contributes to the lateral walls of the nasal cavity.
- Sphenoid Bone: Part of the base of the skull, it helps form the posterior wall of the nasal cavity.
- Vomer: A flat bone that forms the anterior part of the nasal septum.

2) *Cartilages*

- Nasal Septal Cartilage: Supports the nasal septum, dividing the nasal cavity into two halves.
- Alar Cartilages: Form the external shape of the nostrils.
- Lower Lateral Cartilages: Support the alar cartilages and contribute to the shape of the nostrils.

3) *Nasal Cavities*

- Nasal Cavity: The space within the nose where air is filtered and warmed before entering the lungs. It is divided into two by the nasal septum.
- Middle Nasal Concha: Located on the lateral wall of the nasal cavity, it helps filter and warm the air.
- Inferior Nasal Concha: Also on the lateral wall, it further filters and warms the air.
- Superior Nasal Concha: Found higher up on the lateral wall, it aids in the filtration and warming process.

4) *Other Structures*

- Nasal Septum: A partition made of bone and cartilage that separates the nasal cavity into two halves.
- Nasal Cartilages: Include the nasal septal cartilage and the alar and lower lateral cartilages, which contribute to the shape and support of the nose.

VI. THE ANATOMY OF THE CRANIAL FOSSA AND ITS IMPORTANCE IN NASYA TREATMENT

The anatomy of the cranial fossa and its importance in *Nasya* treatment in *Ayurveda* are interconnected through the nasal cavity's direct communication with the cranial structures.

This relationship is foundational to understanding how *Nasya* therapy, which involves the administration of medicated oils or powders into the nostrils, can have profound effects on the brain and the entire nervous system.

A. *Cranial Fossa Anatomy*

The cranial fossa, comprising the anterior, middle, and posterior sections of the skull, houses the brain and provides essential protection. Each of these fossae has distinct features and contents, playing crucial roles in the structure and function of the human head.

B. *Anterior Cranial Fossa*

Boundaries: The anterior cranial fossa is bounded by the frontal bone above, the ethmoid bone below, and the sphenoid bone laterally. It extends from the frontal bone to the cribriform plate of the ethmoid bone .

Contents: It contains the frontal lobes of the brain, the olfactory bulbs, and the frontal sinuses. The anterior cranial fossa is also home to the anterior communicating artery and the anterior cerebral arteries .

C. *Middle Cranial Fossa*

Boundaries: The middle cranial fossa is bordered by the temporal bones and the sphenoid bone. It is situated between the anterior and posterior cranial fossae .

Contents: This fossa accommodates the temporal lobes of the brain, the middle meningeal artery, and the cavernous sinus. It also houses the internal auditory canal, which transmits the vestibulocochlear nerve (CN VIII) and the facial nerve (CN VII) .

D. *Posterior Cranial Fossa*

Boundaries: The posterior cranial fossa is defined by the occipital bone and the temporal bones. It is located at the back of the skull .

Contents: It houses the cerebellum, the pons, and the medulla oblongata. The posterior cranial fossa also contains the fourth ventricle of the brain and the openings for the hypoglossal canal and the jugular foramen .

E. *Importance in Nasya Therapy*

The anatomy of the cranial fossae is crucial in *Nasya* therapy because of the close proximity of the nasal cavity to these structures. The nasal cavity communicates directly with the cranial fossae, allowing for the easy absorption and distribution of substances administered through *Nasya*. This direct route facilitates the treatment of various conditions affecting the head, including those related to the brain and nervous system. The rich vascular supply to the nasal cavity enhances the absorption of medicated oils or powders, ensuring they reach their intended targets within the cranial cavity efficiently.

1) Middle Cephalic Fossa: This region, in connection with the Ethmoid and Sphenoid sinuses, contains meningeal vessels, primarily the internal carotid artery. It also houses the cranial nerves (3rd, 4th, 5th, and 6th) and the optic nerve. The pituitary gland can be accessed through the Sphenoidal sinus, highlighting the cranial fossa's complex network of vessels and nerves .
2) Connection with Nasopharynx and Brain Stem: The sphenoidal sinus is inferiorly connected with the nasopharynx and posteriorly with the brainstem, further emphasizing the cranial fossa's role in bridging the nasal cavity with deeper brain structures.

F. *Importance in Nasya*

1) Direct Pathway to the Cranium: According to *Acharya Charaka*, the nasal cavity serves as the only entrance to the cranium. This means that substances administered through the nose can rapidly spread to the head and be absorbed, making *Nasya* a highly effective method for delivering treatments directly to the brain.
2) Stimulation of Olfactory Nerves: *Nasya* treatment stimulates the olfactory nerves, which are directly connected to the brain. This stimulation can promote mental clarity, improve memory, and enhance overall cognitive function, underscoring the therapy's impact on brain health.
3) Role of *Shringataka Marma*: The concept of *Shringataka Marma*, situated on the inner side of the middle part of the head, is crucial in *Nasya* Karma. It acts as a conduit for the assimilation and transportation of *Nasya* drugs, enabling them to reach both local and general circulation. This mechanism supports the rapid absorption of *Nasya* drugs into the bloodstream and their subsequent distribution throughout the body.

4) Increased Blood Circulation: The primary principle behind *Nasya* is that any irritation in the body leads to increased local blood circulation. When *Doshas* are provoked in the head, the irritating effect of the administered drug results in enhanced blood circulation to the brain, aiding in the expulsion of morbid *Doshas* as nasal discharge, tears, and saliva.
5) Holistic Approach to Health: *Nasya* treatment is a cornerstone of *Ayurvedic* panchakarma therapy, focusing on cleansing and rejuvenating the nasal passages and upper respiratory tract. It offers a holistic approach to treating a wide range of diseases, from those affecting the head, throat, and eyes to conditions related to the respiratory system, ears, and speech disorders.

VII. NASAL ANATOMICAL PECULARITIES IN THE CONTEXT OF NASAL DRUG ADMINISTRATION

The anatomy of the nose plays a crucial role in the administration of drugs through the nasal route, offering a non-invasive method for delivering medications directly to the bloodstream. This method bypasses the gastrointestinal tract, potentially reducing side effects and improving bioavailability. The nasal cavity's unique structure facilitates this process, but it also presents challenges in terms of drug deposition and absorption efficiency. Here's a detailed look at the anatomy of the nose in the context of nasal drug administration:

1) Nasal Cavity: The nasal cavity is divided into two passages by the nasal septum, with each passage leading to one nostril. The nasal cavity's size and shape can vary significantly between individuals, affecting drug deposition patterns.
2) Nasal Turbinates: These are three pairs of small, scroll-like structures within the nasal cavity that help warm, filter, and humidify inhaled air. They also play a role in drug deposition and clearance from the nasal cavity.
3) Mucosal Surface: The lining of the nasal cavity is rich in blood vessels and glands that produce mucus. This mucosal surface is crucial for drug absorption, as it allows for direct contact between the drug and the bloodstream.
4) Blood Supply: The extensive blood supply to the nasal mucosa facilitates rapid absorption of drugs into the systemic circulation, making the nasal route an efficient method for drug delivery.
5) Nasal Membrane Thickness: The thickness of the nasal membrane can influence drug absorption. Thinner membranes may allow for more efficient drug absorption, while thicker membranes may require larger doses or different formulations to achieve therapeutic levels.

VIII. NOSE-TO-BRAIN DELIVERY PATHWAYS

Physiological possibilities for NDDS are provided by the physiological anatomy of the nasal cavity and brain. Drug molecules are delivered to the cranial compartment's entry close to the pial brain surface by nasal administration. This occurs after the molecules traverse the nasal passages' olfactory or respiratory epithelium barrier in various methods (MAIGLER et al., 2021). Following their initial entry into the brain, they are then transferred to other CNS tissues.

Currently, there are three different types of transport pathways :

1) Blood circulation pathway
2) Trigeminal nerve pathway
3) Olfactory nerve pathway

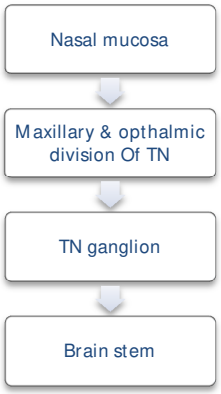
Once absorbed into the nasal cavity, the medications can then travel via the trigeminal nerve or the olfactory bulb to the cerebrospinal fluid, from which they can be further absorbed into the brain for therapeutic effects. On the other hand, it could enter the bloodstream through the gastrointestinal or respiratory systems and then cross the blood-brain barrier to reach the brain.

1) *Olfactory Pathway*

The olfactory system is divided into two parts: the intracellular pathway and the extracellular pathway. The intracellular pathway, also known as the olfactory nerve pathway, begins when an olfactory receptor neuron internalizes a nanoparticle, after which an endocytic vesicle traffics within the neuron's cells such as OEC, and finally the molecule is released through exocytosis by mitral cells (SINGH et al., 2020). The extracellular pathway is divided into two sections: the paracellular pathway and the transcellular pathway. The olfactory epithelium can be traversed by a paracellular pathway that entails going through a gap in the sustentacular cells (SUS) and basement membrane.

The paracellular pathway, in contrast to the transcellular pathway, which depends on receptor-mediated endocytosis or passive diffusion, does not require receptor binding and is best suited for tiny, hydrophilic compounds. The transcellular pathway, on the other hand, is appropriate for hydrophobic nanoparticles and proceeds via receptor-mediated endocytosis or passive diffusion of nanoparticles over the SUS membrane (LEE D. and MINKO T., 2021).

2) Trigeminal Pathway



The trigeminal nerve is the fifth cranial nerve and the thickest nerve on the face, with three big branches composed of peripheral processes from the trigeminal node anteriorly, followed by the ophthalmic nerve, maxillary nerve, and mandibular nerve inside-out (TERRIER et al., 2022). Among them, ophthalmic nerve branches and maxillary nerve branches enter the epithelial cells of the olfactory and respiratory regions of the nasal cavity, and the other end enters the CNS at the pontine site and terminates in the spinal nucleus of the trigeminal nerve in the brain cadre (SCHAEFER et al., 2002).
Once the drug reaches the trigeminal branch of the olfactory and respiratory regions, it can be transferred into the brain via the intra-axonal pathway of neurons (TUCKER, 1971; ANTON and PEPPEL, 1991; THORNE et al., 2004). Although the trigeminal route is a less important drug delivery system than the olfactory pathway, it does provide a novel perspective on how to introduce medicine directly into the brain (COSTA et al., 2019).

3) Blood Circulation Pathway

The blood circulation pathway is a complex network of blood arteries and organs that work together to transport blood, oxygen, and nutrients throughout the body. Because there are abundant blood vessels and lymphatic vessels distributed in the lamina propria of the nasal mucosa, where blood flow is abundant, the substance can be transported into the circulatory system and later reach the brain through the BBB for low molecular weight lipophilic molecules and medications (BOURGANIS et al., 2018). Furthermore, the blood circulation pathway provided by NDDS has various advantages over intravenous injection, including quicker absorption, non-invasive delivery, avoidance of first-pass metabolism, and lower systemic exposure.
Although the nasal route is a non-invasive means of administration that efficiently overcomes BBB, only a limited number of medications can be absorbed directly into the brain via this route. For medications with a high hydrophilic or molecular weight that makes BBB penetration challenging. To address this issue, scientists have merged nanotechnology with nasal medicine delivery. Polymers, lipids, and inorganic nanoparticles are examples of common nanocarriers. Drugs can be encapsulated in nanocarriers, which shield them from degradation and clearance by the body's immune system, extending their circulation time and improving their chances of crossing the BBB. Another advantage is that surface changes can be used to improve the ability of nanoparticles to traverse the BBB.

IX. CONCEPT OF NASYA KARMA IN AYURVEDA

The Ayurvedic classics do not provide a detailed description of the *Nasya Karma's* manner of action.

1) In accordance with *Acharya Charaka* The doorway to *Shira* is *Nasa*. *Nasya*, the medication delivered through the nose, reaches the brain and destroys the morbid *Dosha* that causes the sickness.
2) Nasa is also referred to as *Shirah's* entrance in *Ashtang Sangraha*. As a result, the medication is delivered through the nostrils. The substance penetrates the *Shringataka (Sira marma)* and spreads through the *Murdha* (brain), reaching the *marmas* of *Netra, Shrotra, Kantha*, and *Shiramukha*. It then scratches the morbid *Dosha* in the supraclavicular region and expels it from *Uttamanga* due to its power.
3) *Sushruta* defines *shringataka marma* as a *Sira Marma*, which is formed by the union of *siras* (blood vessels) supplying the nose, ear, and tongue. He goes on to say that any injury to this *marma* will be fatal.

4) Among the *Nasya Karma* problems, *Sushruta* reported that excessive eliminative errhine may cause *Mastulunga* (CSF) to run out of the nose.
5) Detailed descriptions of *Nasya Karma's* mechanism of action are not found in *Sushruta, A.H., B.P.,* and others.
6) According to all prominent *Acharyas, Nasya* is *Shira's* gateway. It does not imply that any channel connects directly to the brain, but they may be linked via blood vessels or the neurological system (olfactory nerve, for example).

X. CNS DISORDERS THAT CAN BE TREATED WITH NASYAKARMA

Nasya Karma, a form of nasal therapy in *Ayurveda*, has been utilized in treating various central nervous system (CNS) disorders, including conditions like coma, migraine, motor neuron disease (MND), epilepsy, and stroke. Here are examples of specific CNS disorders that can be treated with *Nasyakarma*:

1) Coma: *Ayurvedic* treatment for coma involves the application of nasal drops, fumigation, and powders, as indicated by *Charaka.* A case study reported the successful management of a patient with hypoxic coma using *Ayurvedic* treatment, including nasal medication, leading to a remarkable recovery .
2) Migraine: *Nasya Karma* with *Vrihatjivakadya* oil, specifically with medium viscosity oil (MVO), has shown significant improvement in migraine management. This treatment is advocated for both episodic and chronic migraines, with MVO providing better results .
3) Motor Neuron Disease (MND): *Ayurvedic* treatments for MND, such as *Sodhana Chikitsa*, involve purificatory therapies like *Panchkarma,* including *Nasya*. These treatments aim to pacify aggravated *Vata dosha*, nourish nerve cells, and rejuvenate them
4) Epilepsy: *Ayurvedic* treatment for epilepsy focuses on addressing the underlying causes, such as *dosha* imbalances, through *Panchkarma* therapies like *Vamana, Virechana, Vasti,* and *Nasya*. Specific practices like *Shirodhara* and *Sirolepam* are advised to strengthen and rejuvenate the nervous system .
5) Stroke: *Ayurvedic* treatment for stroke involves addressing the root causes, such as hypertension, diabetes, and heart disease, alongside strengthening the nervous system. *Nasya*, which is nourishing in nature, is given alongside *Shirovasti* and *Shirodhara* to support recovery .

These examples illustrate the versatility of *Nasya Karma* in treating a range of CNS disorders, emphasizing its potential as a complementary or alternative therapy in the management of these conditions.

XI. CONCLUSION

Nasya therapy in *Ayurveda* harnesses the intricate anatomy of the nose to deliver therapeutic agents directly to the central nervous system, offering a unique and effective approach to treating a variety of CNS disorders. The olfactory and trigeminal pathways, along with the abundant blood supply in the nasal mucosa, facilitate rapid drug absorption and delivery to targeted brain regions. While challenges such as the blood-brain barrier exist, advancements in nanotechnology hold promise for enhancing drug efficacy and overcoming these barriers.

XII. DISCUSSION

The discussion delves into the historical perspectives and contemporary understanding of *Nasya Karma*, highlighting its relevance in modern healthcare. It explores the potential synergy between traditional *Ayurvedic* practices and modern pharmacology, emphasizing the need for further research and clinical trials to validate the efficacy and safety of *Nasya* therapy for CNS disorders. Additionally, considerations such as patient-specific variations in *nasal* anatomy and personalized drug delivery approaches are addressed, paving the way for personalized medicine strategies in neurological care.

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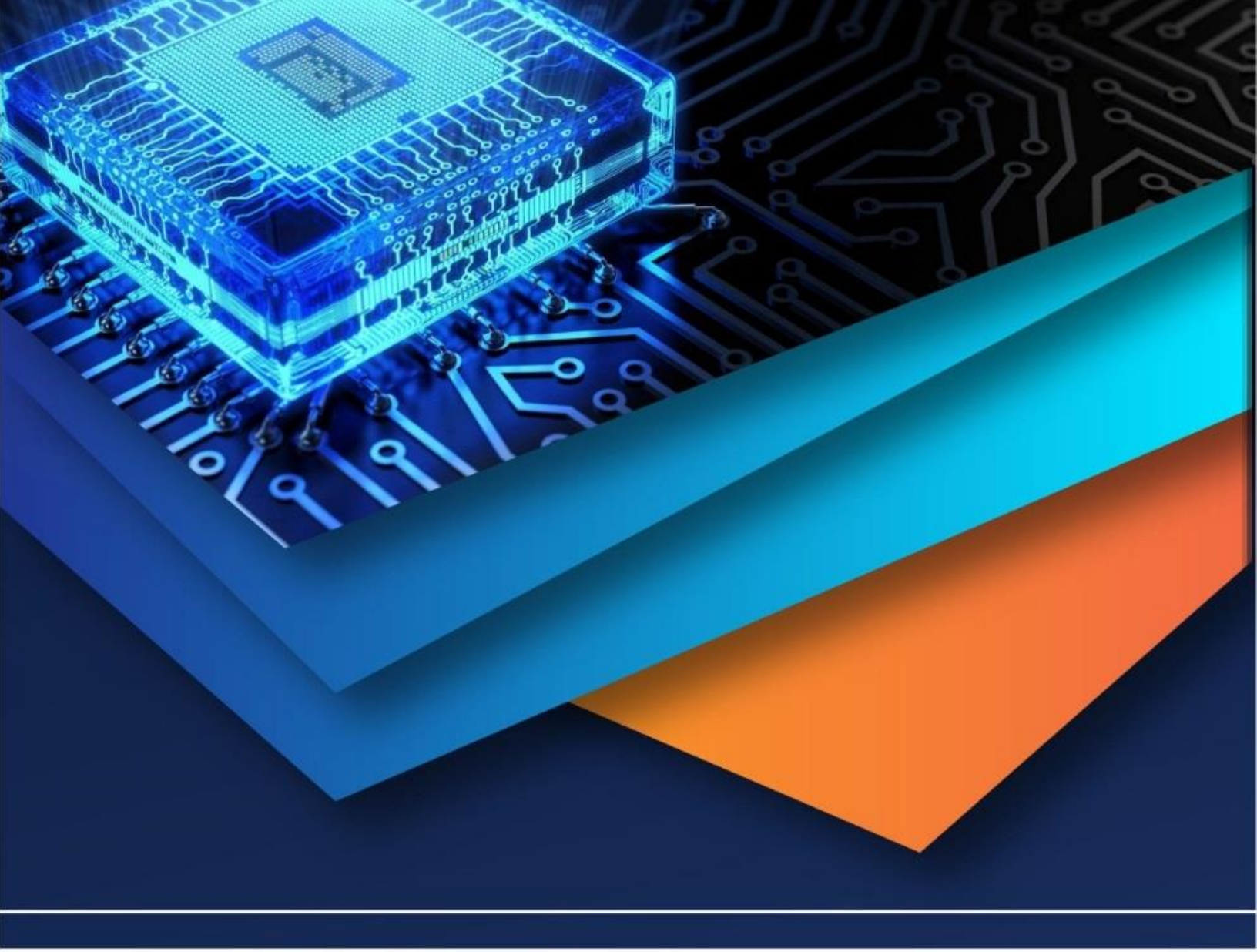

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