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A Systemic Review on the Pharmacological and Therapeutic Potential of Mentha Species

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Abstract: ***Menthol, a naturally occurring organic compound derived from mint, exhibits a wide range of pharmacological activities, including analgesic, anti-inflammatory, antibacterial, neuroprotective, and anticancer effects. Chemical modifications such as esterification and amination have been shown to enhance its biological activity and broaden its potential applications in drug discovery, agriculture, and food preservation. This review aims to explore both the traditional uses of Mentha longifolia and the pharmacological and therapeutic properties of its extracts and major constituents. The herb demonstrates significant effects on the nervous and gastrointestinal systems, contributing to its diverse medicinal profile. Furthermore, the review discusses the pharmacokinetics and safety aspects of menthol and its derivatives to better understand their clinical potential. Despite substantial progress in preclinical research, further studies are necessary to elucidate their mechanisms of action and optimize their therapeutic effectiveness in clinical practice. Continued development of novel menthol derivatives and advanced drug delivery approaches presents promising avenues for future therapeutic applications.***

I. INTRODUCTION

A. Botanical Description of Mentha

Mentha longifolia L., commonly known as wild mint and belonging to the family Lamiaceae. This perennial herb is characterized by a strong peppermint-like fragrance and exhibits considerable morphological variability. It possesses a creeping rhizome and erect to prostrate stems that typically range from 40 to 120 cm in height. The leaves are oblong-elliptic to lanceolate in shape, with a surface that varies from sparsely to densely hairy—green to greyish-green on the upper side and whitish underneath. The plant bears small flowers, about 3–5 mm long, which appear lilac, purple, or white and are arranged in dense clusters along tall, branched, tapering spikes.[1-3]

B. Geographical Description Of Mentha

With species found natively throughout Europe, Asia, Africa, Australia, and North America, the genus Mentha has a worldwide native distribution. Many species spread naturally and by human introduction from the Mediterranean region, which is sometimes regarded as its center of origin. Mentha species are found in temperate to subtropical regions, frequently in damp or semi-wet areas such as damp meadows, wetlands, riverbanks, and stream banks.

Figure : Mentha arvenis (Pudina)

Many species may establish in a variety of soil types as long as there is enough moisture present since they are perennials with rhizomes or stolons. The fragrant, culinary, medicinal, and industrial properties of Mentha species have led to their widespread introduction and cultivation outside of their natural ranges. Among other places, India, China, Brazil, Paraguay, Japan, Thailand, and Angola are major Mentha arvensis farming location.[4]

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Table no 1: Vernacular names of Mentha arvensis linn.

English	Field mint, Japanese mint, Pennyroyal, Spearmint, Garden mint
Hindi	Ban Pudina, Paudina, Podina, Pudina, pudinah
Sanskrit	Pudina, putiha, podinika, phudino, podina
Aarbic	Fodanaje, Fotanaje, Habaqulhind, Naanaaul-hind, Nana, Nana hindi, Nana yabani
Burmese	Bhudina
Canada	Chetni-muruga
Japan	Midorihakka
Nepal	Nawaghya
Kannada	Chetamargugu, chetni-marugu, chetnimaragu, chetnimaruga
Malyalam	Putina, putiina, puttityana
Marathi	Pudina

Table no 2: Taxonomical classification of Mentha arvensis linn.

Taxanomical Rank	Kingdom	Division	Class	Order	Family	Genus	Species
Taxon	Plantae	Magnoliophyta	Magnoliopsida	Lamiales	Lamiaceae	Mentha	Mentha arvensis

C. Phytochemical Constituents Of Mentha

Flavonoids, terpenoids, phenolic compounds, volatile oils, and tannins make up the majority of the various phytochemical elements found in the Mentha genus. The most important bioactive substances are the essential oils, which include menthol, menthone, menthyl acetate, menthofuran, pulegone, and 1,8-cineole. These compounds also give the plant its distinct scent and pharmacological properties. Rosmarinic acid, caffeic acid, ferulic acid, and chlorogenic acid are examples of non-volatile components that have potent anti-inflammatory and antioxidant qualities. Many different species of Mentha have also been discovered to contain flavonoids like luteolin, eriocitrin, apigenin, and hesperidin. The therapeutic potential of Mentha plants is further enhanced by the presence of triterpenes, coumarins, sterols (including β-sitosterol), and trace amounts of alkaloids. Species, place of origin, and environmental factors all affect the amount and presence of these components, which affects their industrial value and therapeutic effectiveness.[5-9]

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II. PHARMACOLOGICAL EFFECTS OF MENTHA SPECIES

Table no 3 : pharmacological effects of various Mentha species.

Mentha Species	Pharmacological Activity	Reported Effects / Applications
Mentha piperita	Antimicrobial,Antioxidant, Antispasmodic	Inhibits bacterial growth, scavenges free radicals, relieves gastrointestinal spasms.
Mentha arvensis	Analgesic, Anti-inflammatory, Antipyretic	Reduces pain and inflammation; used in topical formulations for muscle pain and fever relief.
Mentha spicata	Antioxidant,Antifungal, Antidiabetic	Protects against oxidative stress, inhibits fungal pathogens, and regulate blood glucose levels.
Mentha longifolia	Anthelmintic, Antibacterial, Antiviral	Effective against intestinal parasites, bacterial infections, and viral activity.
Mentha pulegium	Insecticidal, Antimicrobial, Antioxidant	Acts as a natural insect repellent and shows strong antimicrobial potential.
Mentha canadensis	Anti-inflammatory, Analgesic, Antitussive	Used in traditional medicine for cough, cold, and muscular pain relief.
Mentha aquatica	Hepatoprotective, Antioxidant, Antimicrobial	Protects liver cells from oxidative damage and shows antimicrobial action.

A. Effect on Nervous System

Studies have shown that the aqueous leaf extract of Mentha longifolia possesses significant antinociceptive and antipyretic effects. The high LD_{50} values observed for both oral and intraperitoneal administration indicate its safety and non-toxicity in mice. Additionally, methanolic extracts of M. longifolia demonstrated protective effects against hydrogen peroxide-induced toxicity in PC12 cells, along with strong antioxidant activity evaluated by ABTS and xanthine/xanthine oxidase assays.[10] The extract also showed inhibition of monoamine oxidase-A (MAO-A) and acetylcholinesterase, and exhibited affinity for GABA(A) receptors. Furthermore, M. longifolia essential oil produced a notable central nervous system (CNS) depressant effect, while fractions containing apigenin, luteolin glycosides, and phenolic acids exhibited spasmodic, choleretic, and CNS-stimulating properties.[11]

B. Effects on Gastrointestinal System

Mentha longifolia leaves are commonly used in herbal preparations to manage gastrointestinal ailments. Traditionally, the leaves are boiled in water with cardamom seeds, or their powder is mixed with green tea for children. The plant is valued as an antiemetic, particularly effective in chronic diarrhea. It also acts as a carminative, relieving gas, and is consumed as chutney with butter during summer to prevent diarrhea.[12-14] Additionally, it helps treat abdominal pain. The leaf extract exhibits relaxant effects on intestinal smooth muscles, supporting its traditional use for diarrhea and colic.[15] Its spasmolytic action occurs mainly through calcium channel blocking and partly by potassium channel activation.[16,17]

In a castor oil–induced diarrhea model, M. longifolia extract (100–1000 mg/kg) provided 31–80% protection, comparable to loperamide. Calcium channel blocking activity was confirmed as pretreatment with the extract caused a rightward shift in Ca^{2+} concentration–response curves, similar to verapamil. Fractionation studies showed the petroleum spirit fraction was more potent than the crude and aqueous extracts.[16] In isolated ruminal and abomasal tissues, M. longifolia essence (0.1–100 µg/mL) produced a mild spasmogenic effect, followed by relaxation and complete inhibition of spontaneous contraction at 1000 µg/mL ($P < 0.05$). Conversely, in rat ileum, it caused dose-dependent relaxation and reduced acetylcholine (ACh)-induced contractions after preincubation, indicating involvement of cholinergic receptors. The essence modulated gastrointestinal smooth muscle activity in a tissue-specific and dose-dependent manner.[18] Moreover, piperitenone oxide, a major compound in essential oils of Mentha species like M. longifolia, M. spicata, M. rotundifolia, M. suaveolens, and M. villosa, was found to relax guinea pig ileum basal tone (30–740 µg/mL) without affecting resting membrane potential.[19]

C. Antioxidant Effect

Gulluce et al. [20] conducted a study to assess the antioxidant properties of the essential oil and methanol extract of M. longifolia. The methanol extract displayed greater antioxidant activity than the essential oil in assays such as DPPH and β-carotene/linoleic acid

systems. Other studies attributed this stronger antioxidant effect to the higher phenolic content in the methanol extract.[21] A positive correlation exists between antioxidant potential and phenolic compound levels.[22] The ABTS assay showed IC50 values of 476.3 ± 11.7 for M. longifolia.[23] Some studies identified apigenin derivatives as antioxidative molecules.Another investigation examined the DPPH radical-scavenging activity of nine Mentha species to explore new natural antioxidants. After 30 minutes of incubation, methanolic extracts of M. longifolia showed significant activity (79%).[24] Berselli et al. demonstrated that preincubation with M. longifolia extract (80 µg/mL) protected human keratinocytes (NCTC2544) from oxidative stress (500 µM H_2O_2 for 2–24 h), preserving cell viability, protein and DNA integrity, reducing lipid peroxidation, and maintaining glutathione and superoxide dismutase levels during early oxidative phases. Additionally, a mixture of Alchemilla vulgaris, Olea europaea, M. longifolia, and Cuminum cyminum, commonly used in traditional Arabic, Islamic, and European herbal medicine, exhibited strong antioxidant properties even at low concentrations (10 µg/mL) as per the lipid peroxidation assay.[25]

Furthermore, monoterpene ketones (menthone and isomenthone) were identified as potent scavenging agents in M. longifolia essential oils. Antioxidant effects varied depending on extraction methods. For example, the highest antioxidant activity determined by FRAP and DPPH assays was found in extracts from naturally dried herbs (2.76 ± 0.15 m/mol Fe^{2+}/mg extract; EC50 = 0.022 ± 0.001 mg/mL) due to higher phenolic (113.8 ± 2.0 mg gallic acid/g extract) and flavonoid contents. Conversely, the lowest activity occurred in oven-dried herb extracts (1.13 ± 0.11 m/mol Fe^{2+}/mg extract; EC50 = 0.033 ± 0.001 mg/mL). This emphasizes the importance of drying methods before extract preparation. Hydro-alcoholic extracts of M. longifolia exhibited strong antioxidant effects in several in vitro systems, including DPPH, nitric oxide-scavenging, Fe^{2+} chelation, linoleic acid, and hydrogen-peroxide scavenging assays.[26] Another study using DPPH, ABTS, reducing power, and FRAP methods showed M. longifolia had the strongest ABTS scavenging activity. High antioxidant activity in M. longifolia variants native to Israel was partly attributed to rosmarinic acid (RA).[27]

D. Cytotoxic Activity

Threef lavonoids—apigenin-7-O-glucoside, apigenin-7-O-rutinoside, and apigenin-7-O-glucuronide—were isolated from Mentha longifolia using E. coli WP2 genotoxicity assay-guided fractionation. Their mutagenic and antimutagenic effects were evaluated through the same assay. All three compounds demonstrated strong antimutagenic activity against 2-AF and N-methyl-N-nitro-N′-nitrosoguanidine-induced mutagenicity in a dose-dependent manner, with inhibition rates ranging from 25.3% (apigenin-7-O-glucoside with S9, 2.0 µM/plate) to 59.0% (apigenin-7-O-rutinoside without S9, 2.0 µM/plate). These apigenin derivatives were considered genetically safe, as no mutagenic effects were detected at tested doses.[56] The cytotoxic potential of M. longifolia essential oil across seasons was analyzed on MCF-7 (breast cancer) and LNCaP (prostate cancer) cell lines using the MTT assay. The essential oils exhibited IC_{50} values of 45.2 and 50.6 µg/mL for MCF-7, and 43.5 and 52.0 µg/mL for LNCaP, in summer and winter, respectively.[28]

Another study investigated the mutagenic and antimutagenic effects of luteolin derivatives—luteolin 7-O-glucoside, luteolin 7-O-rutinoside, and luteolin 7-O-glucuronide—isolated from M. longifolia using the Ames Salmonella test (TA1535 and TA1537 strains). Maximum inhibition rates on TA1537 were 84.03%, 87.63%, and 67.77% for the respective compounds, while on TA1535 the rates were 23.86% and 23.76% for luteolin 7-O-glucoside and luteolin 7-O-rutinoside.[68] The antimutagenic capacity of apigenin-7-O-rutinoside (A7R) was also assessed against ethyl methane sulfonate (EMS) and acridine (AC) in Saccharomyces cerevisiae RS112. A7R showed variable inhibition levels against EMS- and AC-induced mutations, suggesting significant pharmacological potential in preventing reactive oxygen species-related disorders.[29]

Similarly, rosmarinic acid (RA), a phenolic compound from M. longifolia, was evaluated for its antimutagenic effects against EMS and AC in S. cerevisiae RS112. At high concentrations, RA exhibited slight mutagenicity, whereas lower concentrations effectively reduced EMS- and AC-induced mutations. The highest inhibition rates in the yeast DEL assay ranged from 10% (4 µM/mL with EMS) to 63.3% (2 µM/mL with AC).[30]

E. Nutritional Usage

Van Herby Cheese, a traditional dairy product from eastern Turkey, incorporates local herbs, among which Mentha longifolia showed the highest lead content at 1.69 mg/kg.[31] One study evaluated the effects of M. longifolia essential oil at 0, 50, 150, and 300 ppm, alone or combined with Lactobacillus casei (10^8–10^9 CFU/mL), on the growth of Staphylococcus aureus and Listeria monocytogenes during production, ripening, and storage of Iranian white-brined cheese. Both essential oil concentrations ≥50 ppm and the probiotic, individually or combined, significantly inhibited pathogen growth ($P < 0.01$). The combination of 150 ppm essential oil with the probiotic showed the strongest inhibitory effect and was rated most favorable in sensory evaluations.[32]

Additionally, M. longifolia essential oil influenced the viability and cellular structure of L. casei in probiotic Feta cheese. Treatments with 0.0% to 0.03% essential oil demonstrated that 0.03% provided the highest L. casei viability and the lowest pH ($P < 0.05$), with electron microscopy confirming no damage to the probiotic cells, indicating beneficial effects for maintaining L. casei during cheese storage.[33]

F. Anti-Inflammatory Effects

Menthol and its derivatives have attracted interest due to their anti-inflammatory properties, positioning them as potential therapeutic agents for treating inflammatory conditions. Their anti-inflammatory effects arise from interactions with critical signaling pathways and inflammatory mediators. This section examines how menthol and its derivatives mediate these effects and their potential use in managing various inflammatory diseases. Ghori et al. developed an oily menthol formulation (OFCMT) and applied it to inflamed rat paws.[34] The study found that OFCMT significantly reduced inflammation compared to controls. The researchers proposed that menthol's anti-inflammatory action involves inhibition of cyclooxygenase (COX) activity and a subsequent decrease in prostaglandin E2 (PGE2) production, a key mediator of inflammation, mirroring the mechanism of the COX inhibitor indomethacin.[34]

Menthol and its derivatives have shown notable anti-inflammatory effects in a variety of models, including atopic dermatitis, schistosomiasis, and inflammatory bowel disease. Both topical and oral administration of menthol has been effective in lowering inflammatory markers, enhancing oxidative stress responses, and alleviating symptoms in animal studies.[35, 36].As research continues to clarify menthol's mechanisms of action, its potential role in treating inflammatory diseases may broaden, providing new, effective, and well-tolerated therapeutic options. Preclinical studies have highlighted several mechanisms underlying these effects, such as cytokine suppression, immune modulation, TRP channel activation, and antioxidant activity. [37, 38] However, clinical validation remains limited, with most evidence coming from in vitro and animal experiments, and well-structured, large-scale human trials are still needed. [37, 38]

G. Analgesic Effects

Menthol and its derivatives are widely recognized for their analgesic properties and are commonly employed in both traditional and modern medicine for pain management. Beyond their effects on transient receptor potential (TRP) channels, particularly TRPM8 [39,40], other inflammatory mediators and ion channels involved in pain perception also contribute to their analgesic actions. Menthol's pain-relieving mechanisms are multi-targeted, involving TRP channel activation, opioid receptor agonism, enhancement of the GABAergic system, and ion channel blockade, collectively suppressing nociceptive signaling at peripheral and central levels.

In studies using hotplate and abdominal constriction tests in mice, (−)-menthol demonstrated analgesic effects through κ-opioid receptor (KOR) activation, which could be blocked by opioid receptor antagonists. This indicates that (−)-menthol binds KOR, promoting the release of endogenous opioid peptides like dynorphin and inhibiting cAMP-dependent pain pathways [44]. In contrast, the (+)-menthol isomer showed no effect on pain thresholds, highlighting the stereospecificity of menthol's interaction with opioid receptors. [41] The menthol derivative WS-12 has been investigated for its analgesic mechanism, with Liu et al. confirming it as a selective TRPM8 agonist whose effects can be blocked by naloxone, indicating engagement of endogenous opioid-dependent pathways.[42] Compared to menthol, WS-12 shows higher selectivity and fewer side effects. Additionally, Pan et al. demonstrated that menthol can induce inward and outward currents in dorsal horn neurons, producing central analgesic effects [43].

H. Antibacterial and Insecticidal Effects

Menthol and its derivatives have attracted considerable interest for their combined antibacterial and insecticidal properties, positioning them as promising natural alternatives to synthetic chemicals. These properties make menthol useful in food preservation, where it inhibits harmful bacteria, and in pest control, where it disrupts insect nervous systems. Its antibacterial activity mainly arises from disruption of bacterial cell membranes [45], while its insecticidal effects are linked to interference with pest nervous systems [46].

Menthol-containing essential oil (EO) derivatives 1–8 exhibited varying antibacterial effects against Clostridium perfringens, Salmonella typhimurium, Salmonella enteritidis, and Escherichia coli. Compounds 1 and 2 showed particularly strong activity, with good water solubility and minimal odor, making them suitable for feed additives or packaging coatings. These derivatives likely enhance menthol's activity by improving its penetration into bacterial membranes and interaction with membrane proteins [44].

The EO of Japanese mint (Mentha arvensis L.) achieved 100% mortality against 15 fungal species, including Helminthosporium oryzae, and 99% mortality against Candida and Staphylococcus within 1 hour, likely through disruption of fungal cell walls and

membranes. Menthol-modified nanodiamond (ND-menthol) particles also significantly inhibited biofilm formation in Gram-positive (S. aureus) and Gram-negative (E. coli) bacteria by altering membrane structure and fluidity, causing morphological damage. [48] Repellency tests of L-menthol against Callosobruchus maculatus, Rhyzopertha dominica, Sitophilus oryzae, and Tribolium castaneum revealed repellency rates of 82%–100% at 0.353 µg/cm², attributed to activation of TRP channels in insect sensory neurons, causing discomfort and deterring feedings.[45]]

Additionally, menthyl propionate displayed high contact toxicity, and menthyl acetate showed strong ovicidal effects against T. castaneum eggs. Nikitin et al. reported that (–)-(1R,2S,5R)-menthol is non-toxic to nematodes, but its dithiophosphoric derivatives, such as O,O-di-(–)-menthyldithiophosphoric acid, induce dose-dependent nematode death by interacting with neuronal receptors, causing paralysis, with maximum effect after 24 hours at 191.5 µg/mL.[49] Jankowska et al. reviewed that menthol-containing EOs exert neurotoxic effects on insects via the octopaminergic system, increasing cAMP and calcium in nerve cells, blocking octopamine receptors, and ultimately causing insect death. [46]

III. CONCLUSIONS

Mentha species, particularly Mentha longifolia and Mentha arvensis, exhibit a wide spectrum of pharmacological, nutritional, and therapeutic benefits supported by numerous experimental and ethnobotanical studies. Their rich phytochemical profile—including menthol, menthone, rosmarinic acid, and apigenin derivatives—plays a crucial role in mediating antioxidant, anti-inflammatory, analgesic, antibacterial, and neuroprotective effects. The reviewed literature demonstrates that extracts and essential oils of Mentha species possess significant bioactivities, validating their traditional medicinal applications and revealing potential for future drug development. Additionally, their use in food preservation and probiotic enhancement highlights their industrial relevance. Despite promising preclinical results, gaps remain regarding precise mechanisms of action, standardized dosages, and long-term safety profiles. Therefore, future research should focus on well-designed clinical trials and advanced formulation strategies to optimize bioavailability and therapeutic efficacy. Menthol and its derivatives continue to serve as valuable models for the design of novel natural and semi-synthetic compounds for managing inflammation, infection, pain, and oxidative stress-related disorders.

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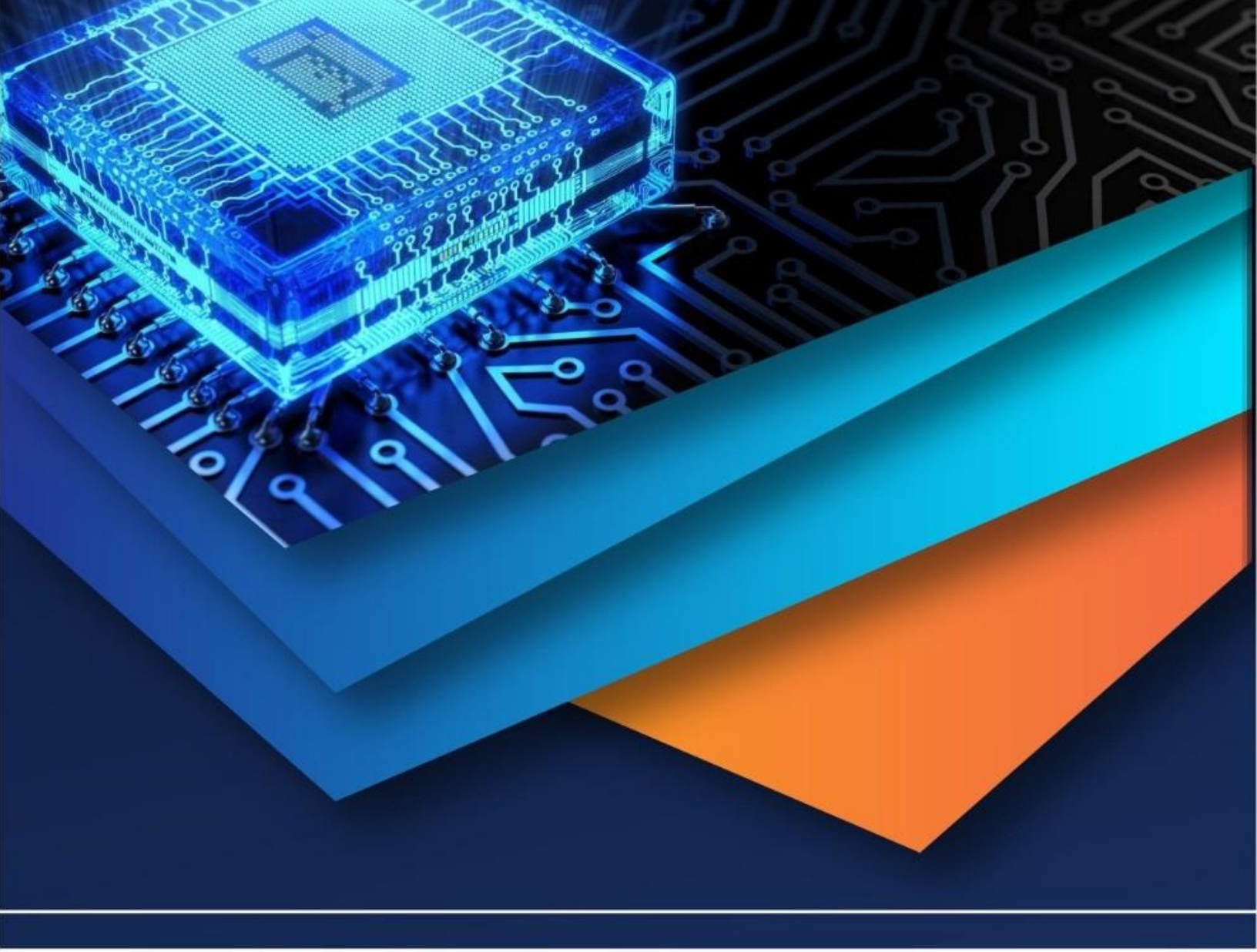

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