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A Review on Medicinal Importance of Crucial Herbal Products

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Abstract: ***Most herbal products are the chief source of medicinal compounds that are known to exhibit various therapeutic properties. Many researchers have ensured the efficacy of traditional medicines at large. The evolving nature of the viruses cause major barriers in the fundamental blockage for illness, instead viruses show complexion which refers to genetic change which lead to accumulate during their lifespan. The immense works have been carried out for the probable best medications to deal with it. For decades, synthetic organic compounds have played a tremendous role in today's medications; however the possibilities for their adverse effects are scaring the human life. The perception to use herbal remedies as complementary vogue can reduce toxicities, has a minimum amount of side effects and can be easily available from nature. The identification of natural products as medicinal drugs is of critical importance and is an excellent source of protease inhibitor. In this review, we focused mainly on the herbal products that give a wide range of anti-viral, anti-cancer, antimicrobial and antioxidant properties which can be used in medications instead of synthetic once.***

Keywords: Natural products, Herbal medications, Anti-cancer properties, Anti-viral properties, Anti-microbial properties, Antioxidant properties.

I. INTRODUCTION

Ayurveda, Siddha and Unani had been evolved and used from last 2-3 millennia in the Indian subcontinent and traditional Chinese medicine, having unique understanding of physiology, pathogenesis, pharmacology and pharmaceuticals which are diverse from western biomedicines [1]. According to WHO, there is no sufficient data on efficacy and safety of traditional medicine due to which there is a wide range of research being carried out to make TM as commercial use [2, 3]. It was found that many natural products which are evaluated gives good anti-viral properties against Coronavirus, Coxsackievirus, Dengue virus, Enterovirus 71, Hepatitis B virus, Hepatitis virus, Herpes simplex virus, Human immunodeficiency virus, Influenza virus, Measles virus and Respiratory syncytial virus [4]. The evidence for the presence of antiretroviral activity, anti-malarial activity and broad spectrum of anti-cytoadhesion activity in azadirachta indica leaf extract lead to complete medication without adverse side effects [5]. Azadirachta indica seed oil and its active components have been displayed several pharmacological activities including anti-inflammatory, antiarthritic, antipyretic, hypoglycemic, diuretic, spermicidal, antifungal, antibacterial, anti gastric ulcer, antiviral and anti psoriasis activities [6,7]. Anti-viral and multipotent role of curcumin would be useful against new emerging viruses like bacteria and fungi as well as its synergistic effects like an antioxidant potential, anti-inflammatory and anti-tumoral activity had made it a wonder drug [8]. Curcuminoids are the promising natural compound with a large variety of therapeutic properties [9]. Zika (ZIKV) and Chikungunya (CHIKV) virus lost infectivity when incubated directly with curcumin or derivatives of curcumin which suggests that curcumin alters the ability of the virus to infect cells and hence shows the anti-viral properties [10].

Camphor based immines were synthesized and investigated for their antiviral activity against influenza viruses and found that derivatives with shorter chains possessed higher activity than the long aliphatic chain and thus camphor can also be used as a therapeutic application [11]. Camphor exhibits several biological activities or properties such as antimicrobial, antiviral, antitussive effects [12-16], used to relieve pain, anti-infective and anti-pruritic activities [17, 18]. Polysaccharides in aloe-vera gel have therapeutic properties such as immunostimulation, anti-inflammatory effects, wound healing, increases radiation damage repair, anti-bacterial, anti-viral, anti-fungal, anti-diabetic, antineoplastic activities, stimulation of hematopoiesis and antioxidant effects [19-22]. Aloe-vera can be used as an antiseptic, anti-inflammatory agent, curing agent for heart problems, helps in relieving the symptoms of severe illnesses like cancer and diabetes, as a beauty enhancer and improves health [23]. The most reliable book on traditional Chinese medicine, Bencao Gangmu, published in 1593 reported the use of scutellaria baicalensis in the treatment of diarrhea, dysentery, hypertension, hemorrhaging, insomnia, inflammation and respiratory infections [24].

An old tradition specifically goes that those who drink a large amount of green tea have less tooth decay and thus more scientfic studies are carried out about components of camellia sinensis [25]. The number of clinical trials in humans suggests that regular drinking tea may reduce the incidence and severity of decay or crumbling of teeth and bones [26].

It is estimated that by the end of year 2020, the number of cancer patients will reach up to 16 million per year [27]. In the prevention of cellular damage, aging and a variety of diseases [28], antioxidants compounds are also involved and many plants have been reported that produce various antioxidative compounds such as phenols, alkaloids and terpenoids which have various therapeutic potential [29]. Species of magnolia such as M. Obovata and M. Officinalis are especially important in traditional Chinese and Japanese herbal medicine for treatment of gastrointestinal disorders, anxiety and allergic disease. The applications include quantitative determination of chemical constituents of magnolia trees and therapeutic of its components [30]. Natural antioxidants can protect the body from free radicals which cause chronic diseases including cancer, cardiovascular diseases and cataract. Presence of bioactive compounds such as glycosides, flavonoids, proanthocyanidins, tannins, mono and sesquiterpenoids, phenylpropanoids, diterpenoids, resins, lignans, alkaloids, furocoumarins and naphthodianthrones in plants make them a safer choice as an antioxidant [31].

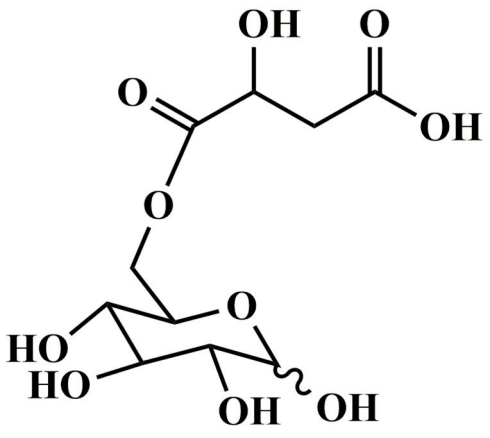
Kaempferol represents one of the most found flavonoids in the form of glycoside whose derivatives show cardio protective, neuroprotective, anti-inflammatory, antidiabetic, antioxidant, antimicrobial, antitumor and anticancer activities [32, 33]. Studies show that high amounts of kaempferol intake is associated with decreased amounts of cancer in organs like skin, liver, colon, ovary, pancreas, stomach and bladder [34-36]. The intake of fruit and vegetables also protects against various cancers. This is most marked for cancer in respiratory and digestive tracts [37, 38]. Increase in consumption of food and vegetables by 1-2 servings daily may reduce cardiovascular risk by 30% [39]. The importance of honey for human use is described in several classical texts of ancient Greece. Honey has been used in Ayurvedic medicine in India for at least 4000 years. The nutritional and medicinal qualities of honey have been documented in the Hindu, Greek, Roman, Jewish, Christian, Islamic & other faiths and cultures [40]. More than 20 alkaloids containing 15% amount, preferably as quinine, quinidine, cinchonidine and cinchonine are found in the bark of cinchona combined with principle active component such as tannins (3-10%) [41]. The main part of the cinchona tree is used for medicinal purposes and the bark can grow up to 30cm long and 2-6 cm thick. Alongside these, the bark also contains acids, essential oils and minerals, such as triterpene (quinovic acid), organic (quinic acid), phenolic (caffeic acid), flavonoids (proanthocyanidin) and phytosterols [42, 43].
The grape has been well recognized worldwide for over 2000 years as one among the edible sweet fruits and recognized for its wide spectrum of biological properties [44]. The production of antimicrobial textiles is expected to increase on daily basis which leads to greener planet following the use of sustainable natural resources [45]. The above-mentioned properties of natural products reveal that it can be used for many purposes which have good acceptability and least side effects which are desirable characteristics for therapeutic treatments.

II. METHODOLOGIES

The main herbal medications which showed positive results in multi-potent activities are listed below.

A. Aloe-Vera Gel

Figure A. The vital derivatives which are present in aloe vera gel; Veracylglucan A (I), Veracylglucan B (II) & Malic acid (III) [19] are shown below.



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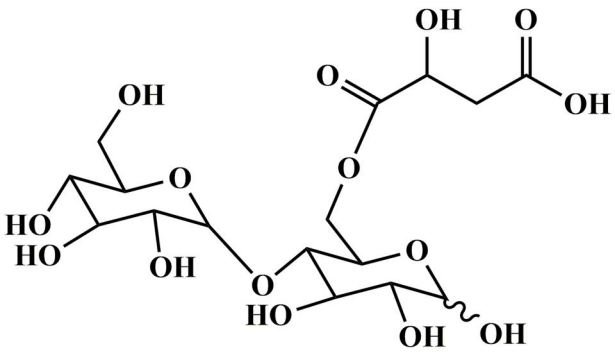

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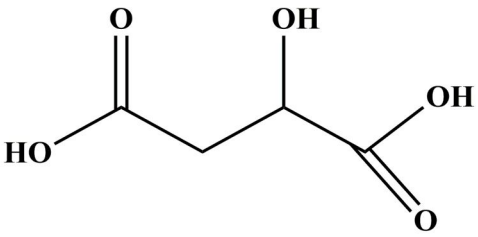


(III)

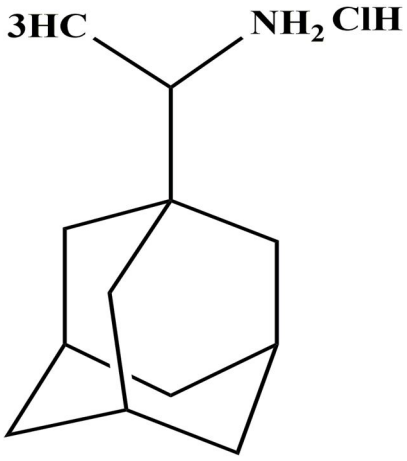
Active component in aloe-vera gel is polysaccharides which has therapeutic properties like immunostimulation, anti-inflammatory effects, wound healing, promotion of radiation damage repair, anti-bacterial, anti-viral, anti-fungi, anti-diabetic, anti-neoplastic activities, stimulation of hematopoiesis and anti-oxidant effects [19-22].

1) *Anti-diabetic Effects:* An oral administration of aloe-vera gel when given to streptozotocin-induced diabetic rats resulted in significantly reduce in the fasting blood glucose, hepatic transaminases, plasma & tissue cholesterol, triglycerides, free fatty acids & phospholipids and in addition also significantly increased plasma insulin levels [46]. Glucose lowering levels could be explained by an antioxidant mechanism because it attenuated oxidative damage in the brains of streptozotocin-induced mice and reduced peroxidation levels in the kidney of streptozotocin-induced diabetic rats [47].
2) *Immunomodulatory Effects:* Aloe-vera gel can prevent suppression of local and systematic immunity to haptens and delayed type hypersensitivity responses to candida albicans and alloantigen when applied after UV exposure while aloe-vera polysaccharides are effective even when applied up to 24 hours post UV exposure and thus immune protection therefore occurs to repair the damaged DNA [48]. On activation of macrophage cells to generate nitric oxide, secrete cytokines (e.g.; tumour necrosis factor-alpha or TNF-α, interleukin-1 or IL-1, interleukin-6 or IL-6 & interferon-γ or INF- γ) and present cell surface markers indicated immunomodulating activities of the polysaccharides present in aloe-vera gel [49-51]. The potential of macrophage stimulation accounted for the crude aloe-vera juice is present only in small amounts and is responsible for the macrophage activation [52].
3) *Anti-inflammatory Effects:* Aloe-vera gel reduces inflammation that is induced by agents via promotion of prostaglandin synthesis as well as increased infiltration of leucocytes, but it is less effective against inflammation caused by agents that produces allergic reactions [53]. Aqueous and chloroform extract of aloe-vera gel were found to inhibit the oedema formation because of well enough established anti-inflammatory agents while the ethanol extract of aloe-vera gel does not show any effect on oedema, but reduced the number of migrating neutrophils [54]. Aloe-vera gel shows potential in the treatment of inflammatory response of the gastric mucosa due to Helicobacter Pylori infection [55].
4) *Antioxidant, Wound healing & Anti-cancer Effects:* The fraction of aloe-vera gel has glutathione peroxidise activity, superoxide dismutase enzymes and a phenolic antioxidant which may be responsible for this antioxidant activity. On incubation of two cell-free in vitro systems with inflamed colorectal mucosal biopsies showed that aloe-vera gel has dose dependent antioxidant effect [56]. The isolation of 5.5 kDa glycoprotein from aloe-vera showed an increase in cell migration and accelerated wound healing in a human keratinocyte monolayer and confirmation of this glycoprotein fraction was enhanced further by wound healing effect and cell proliferation in hairless mice [57]. Glycoproteins and polysaccharides which are the fractions present in aloe-vera gel proved to have anti-cancer property [53].

5) *Effects on Gastric acid Secretion & Ulcers, Skin hydration, Hepatoprotective and Anti-microbial Activities:* Ethanol and water extract of aloe-vera gel exhibited concentration dependent inhibition of gastric acid secretion, which was explained by direct interaction with the acid producing cells or possible interaction between H_2-receptors on the parietal cells. Various studies have been made for the mechanism of cytoprotection, namely increased mucus synthesis, increased mucosal blood flow and increased phospholipid content of the mucosal coating [58]. The moisturising effects of aloe-vera gel after a single application were studied which showed formulations with higher concentration (0.25% w/w and 0.5% w/w) increased the water content of the stratum corneum while applying the formulation twice daily for a period of two weeks (concentration of 0.1% w/w, 0.25% w/w and 0.5% w/w) of aloe-vera gel powder had the same effect. The results showed that products containing aloe-vera gel improved skin hydration possibly by means of humectant mechanism [59]. Aqueous extract of dried aloe-vera significantly reduced hepatic damage induced by carbon tetrachloride in mice and reversed certain biochemical parameters. For preserving the metabolising enzymes of the liver through an antioxidant activity, hepatoprotective action was attributed [60]. Anthraquinones isolated from the exudated of aloe-vera gel have shown wide anti-microbial, anti-viral or anti-virucidal effects on enveloped viruses. Anti-bacterial activity of emodin against Escherichia coli (E. coli) was proposed to be mediated through inhibition of solute transport in membranes [61].

B. Camphor

Figure B. The structural formula of some anti-influenza drugs and anti-influenza A(H_1N_1) of camphor derivatives; Rimantadine (I) & Amantadine (II) [11] are given below.



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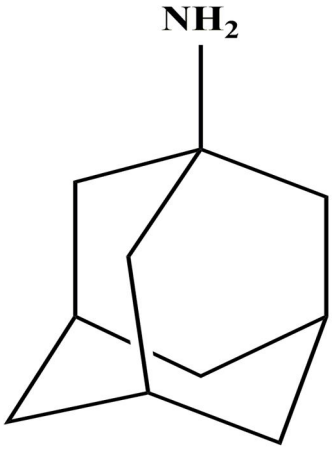

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It has three main active components which includes 1,8-cineole, α- & β-thujone and camphor which are used to treat viruses [17].

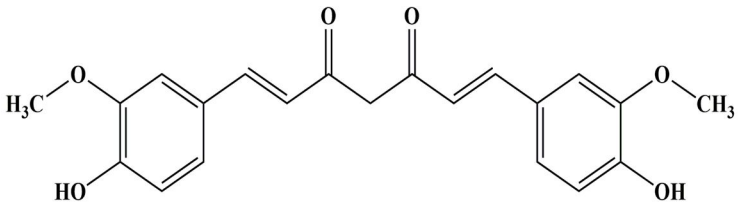
1) *Anti-microbial Activity:* Various species of essential oils and plants containing camphor has been found to have anti-microbial property [16, 62-65]. Through liquid diffusion method of essential oil containing camphor found to have weak anti-microbial activity against gram-positive bacteria, enterococcus hirae, fungi, candida albicans and saccharomyces cerevisiae while Greek sage (Salvia Fruticosa) essential oil which has camphor as the main component in it found to have poor activity against all bacteria's [66].On supercritical fluid extraction of camphor from rosemary essential oil found to have anti-microbial activity against S. aureus, B. subtilis, E. coli, P. aeruginosa, C.albicans and aspergillus niger and also rosemary oil found to have proficient anti-bacterial activity at 1/100 dilution on two gram-negative (Pseudomonas fluorescens and Serratia liquefaciens) and four gram-positive (Brochothrix thermosphacta, Carnobacterium piscicola, Lactobacillus curvatus, and Lactobacillus sake) bacteria. The effectiveness activity order wasborneol > camphor > verbenone against all the micro-organisms tested [67]. Camphor was found to be more active compound when 1, 8-cineole is fused with it against C. albicans and C. krusei. elemol, 1,8-cineole, camphor and p-cymene can be considered as the principal anti-microbial components of tea bush (Lippia chevalieri) oil [68]. The essential oils of salvia macrochlamys and decorative sage (S.recognita), rich in camphor (11% and 42% respectively) at 200µg/mL concentration found evince moderate antifungal activity against colletotrichum acutatum, C. fragariae, and C.gloeosporoides [69].
2) *Antiviral & Antitussive Activities:* Greek sage (Salvia Fruticosa) essential oil with its four main components (1, 8-cineole, α- and β-thujone, and camphor) exhibited high levels of virucidal activity against herpes simplex virus-1. Lavender cotton (santolina insularis) essential oil which has ample of camphor, revealed reduction assays with IC_{50} value of 0.88µg/mL for HSV1 and 0.7µg/mL for HSV2 and thus reduction of plague formation shows inhibition of cell to cell transmission of both HSV1 and HSV2 [70]. On inhalation of camphor had no effect on nasal resistance to airflow but a cold sensation in the nose with improved airflow was observed that indicated camphor stimulated cold receptors in the nose and was proven that 500 mg/L concentration of camphor significantly reduced (33%) cough frequency among the three concentrations (50 mg/L, 133 mg/L and 500 mg/L) of camphor vapour. Studies proved that camphor activated cold receptors are now identified as TRPM8 [71, 72]. Camphor was used to synthesise camphor lactam and was tested for its antitussive activity in guinea-pigs with citric-acid induced cough hence proving that on modification in chemical structure significantly increased cough latency by reducing cough frequency at concentrations of 125 µg/L, 250 µg/L and 500 µg/L which had higher inhibitory cough response compared to camphor [73].
3) *Anti-nociceptive Activity:* The camphor produces anti-nociceptive activity & reported that camphor activated and de-sensitised the capsaicin receptor (TRPV1) whilst inhibiting the garlic receptor (TRPA1) possibly suggesting that the analgesic effects of camphor may be due to de-sensitisation of TRPV1 and blocking of TRPA1 [74]. The pain-relieving effects of California sagebrush (Artemisia Californica) containing the two major compounds 1,8-cineole (24%) and camphor (18%) were reviewed and usage of anecdotal reported successful pain relief in all cases for patients suffering from lower back pain, arthritis, bruises, muscle & ligaments strains, broken bones and even cancer. Camphor against TRPV2, TRPA1 as well as TRPV1 quickly deactivates TRP channels resulting in long-term pain relief [75].
4) *Anti-mutagenic and Anti-cancer Activities:* Animal studies showed the potentials of camphor in treatment of cancer on cancerous cells that camphor had radio modifying effect [76-79]. Camphor showed anti-mutagenic effects at very low concentrations compared with other monoterpenes screened (about 40% reduction of UV-induced revertant at 0.5 and 1 µg/plate), although higher concentrations failed to increase anti-mutagenic effects [80]. Low doses of camphor were found as bio anti-mutagen on testing anti-genotoxic against 4NQO in mammalian cells and stimulate DNA repair. Camphor was found to have an inhibitory effect on thepentoxyresorufin-O-depenthylase (PROD) enzyme with an IC50 value of 7.89 µM and hence can be considered as antimutagenic [81].Cultivated sage (Salvia officinalis) rich in camphor reduced UV-induced mutagenesis when screened with the repair proficient strain, and had no effect on spontaneous mutation frequency in mismatch and showed anti-mutagenic activity at very low concentrations but at high concentrations it failed to increase anti-mutagenic effects [82, 83].
5) *Insecticidal Activity:* The insecticidal activity of camphor basil (O.kilimandscharicum) against rhyzopertha dominicaand S. zeamais was due to camphor and other components, but camphor had no effects on the rice weevil (Sitophilus oryzae) with an LC_{50} of greater than 100 µL/L. Camphor as a pure compound, showed contact and fumigant activity against S. oryzae and rhyzopertha dominica, but had no effect on tribolium castaneum after 24 hours exposure at a dose of 0.1 µL/720 mL volume [84]. Camphor exhibited the highest mortality (78.5%) just after 24 h at the highest tested dose (10.0µL/adult) for contact toxicity; for fumigant toxicity, camphor at its highest dose (120 µL/350 mL vol.) caused 93.5% mortality [85]. Qiantai and Yongcheng observed that camphor as a major isolate from essential oils of Chinese cinnamon, Chinese star anise and camphor laurel showed contact efficacy against the lesser grain borer and the maize weevil [86].

6) *Cardiovascular Effects:* In cardiac failure and collapsed conditions characterised by cold skin, a feeble pulse & failing heart, the subcutaneous injection of camphor in sterile oil caused the surface of the skin to become flushed, dilated the peripheral blood vessels and improved the whole circulation. The results of controlled clinical studies on cardiovascular effects of (+)-camphor have been published [87]. Belz and Loew investigated the effects of (+)-camphor (extracted from fresh Crataegus berries) in orthostatic hypotension using independent, double-blind, randomised, placebo-controlled studies and was determined that (+)-camphor as well as the extract from fresh hawthorn (Crataegus) berries, contributed to the pressoric effects with (+)-camphor inducing the initial rapid effect and the extract is responsible for the long lasting effect [88].
7) *Camphor as a Potential Skin Penetration Enhancer:* Menthol in combination with camphor enhanced the skin penetration of methyl salicylate and inhibited both in vivo & in vitro hydrolysis of methyl salicylate to salicylic acid [89]. The flux of carvedilol obtained from solutions containing camphor, transcutol, d-limonene, carvone, labrasol and menthol were 7.81, 7.26, 6.52, 5.91, 4.21 and 2.28 times higher respectively than that observed with the control, using excised rat abdominal skin mounted in Franz diffusion cells. Camphor showed maximum permeation and basil oil (Ocimum basilicum) containing methyl chavicol, eugenol, linalool, camphor & methyl cinnamate showed potential in vitro penetration enhancement of labetolol hydrochloride [90].
8) *Allelopathic Activity:* The chemical release from leaf powder of the camphor laurel tree (C. camphora) was studied by monitoring soil and air concentrations of (+)-camphor when planted in soil which contained the leaf powder and (+)-Camphor was detected in this soil as well as the soil water & was therefore determined to be the main phytotoxic allelochemical responsible for the growth suppression [91]. The allelopathic activity of camphor and other monoterpenes were studied by determining the anti-germinative ability in radish (Raphanus sativus) & garden cress (Lepidium sativum) seeds 120 h after sowing and radish (R. sativus) seeds were found to be more sensitive than the garden cress (L. sativum) seeds at 10−3M, hence concluded that monoterpenes such as camphor, which exhibits phytotoxic activity are therefore potential bio-herbicides which could be developed into natural pesticides [92].
9) *Other Applications:* The effect of camphor on the sexual activity of male rats was investigated by Jamshidzadeh *et al.* and resultedin enhanced sexual desire and performance when camphor was administered at 50 mg/kg [93]. Camphor also have an effect on the reproductive function of the testes in mice, as it was revealed that administration of camphor to young male mice may result in vascularisation and proliferation of sexual cells which can affect maturation of seminiferous tubules [94]. Sweet wormwood (Artemisia annua) leaves and chemical constituents, including camphor, were investigated for its activity against coccidian parasites [95]. The essential oil of absinthe wormwood (Artemisia absinthium), containing 27.40% camphor, showed activity against promastigote (MIC 0.0097 µL/mL) and axenic amastigote forms (EC50 0.24 nL/mL) of both leishmania aethiopica and L. donovani. It also showed a weak haemolytic effect with a slightly decreased selectivity index (SI = 0.8) against the THP-1 cell line, this study showed the use of Artemisia absinthium oil as the source of innovative agent for the treatment of leishmaniasis [96].

C. Curcumin

Curcuminoids and their derivatives have been shown to possess wide range of biological activities which consist of neuroprotective activity, oxidative stress, memory acquisition ability, mitochondrial dysfunction in the brain, depressive disorder, premenstrual syndrome, transthyretin amyloidosis, alzheimer's diseases, antitumor activity, antioxidant activity, anticancer activity, cardioprotective activity, radioprotective effect, sexually transmitted infections, anti-esophageal adenocarcinoma activity, anti-nephrotoxicity, antiviral activity, antifungal activity, anti-angiogenic effects, anti-proliferative activities, anti-immunomodulatory activity, anti-inflammatory, anti-acidogenic activity, anti-arthritic activity, anti-acanthamoeba activity, mutagenicity, hepatoprotective activity, arsenic toxicity, chromium toxicity, various curcuminoids based metal complexes and there potential application like anti-cytotoxicity, neuroprotective activity, anti-oxidant activity, anti-cancer, anti-rheumatoid arthritis, antimicrobial activity & various curcuminoids based formulations and there prospective application like anti-cytotoxicity, anticancer activity, antioxidant activity, antibacterial activity, neuroprotective effect, anti-diabetic activity, anti-malarial activity, antifungal activity, anti-inflammation, anti-tumor activity, anti-diabetic activity, cardiovascular activity, radio protective effect, anti-tuberculosis activity, anticarcinogenic activity [9].

Figure C. The chemical structures of important constituents present in turmeric; Curcumin keto form (I), Curcumin enol form (II), Desmethoxycurcumin (III), Bisdemethoxycurcumin (IV), α-Turmeron (V), Ar-Turmeron (VI) & β-Turmeron (VII) [9] are given bellow.



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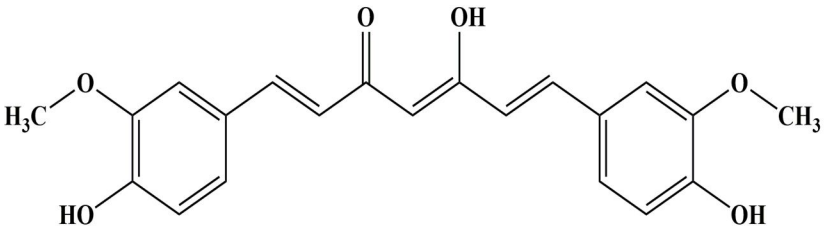

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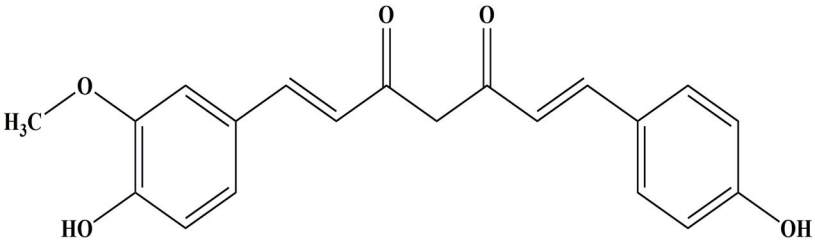

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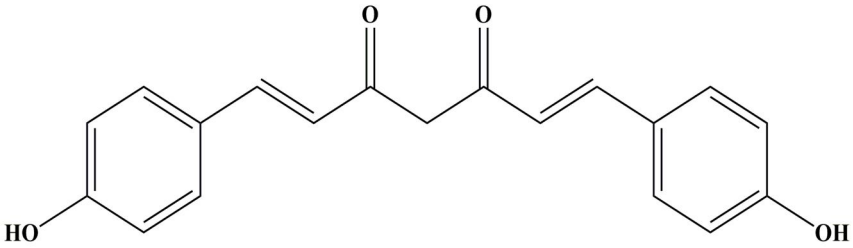

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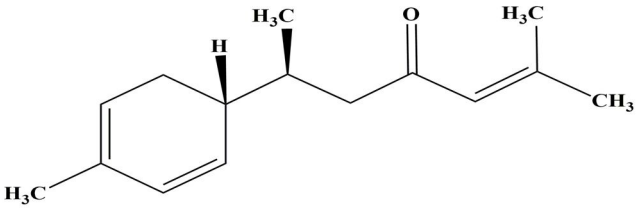

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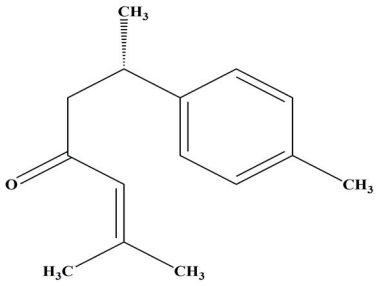

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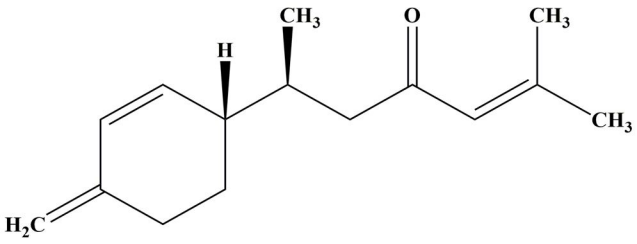


(VII)

Turmeric is an Indian rhizomatous herbal plant of the ginger family (Zingiberaceae) of well-known medicinal benefits [97].

1) *Anti-Viral Property:* Various studies have proved that curcumin as a plant derivative has a wide range of antiviral activity against different viruses such as: Papillomavirus Virus (HPV), Influenza Virus, Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Adenovirus, Coxsackie Virus, Human Norovirus (HuNoV), Respiratory Syncytial Virus (RSV) and Herpes Simplex 1 (HSV-1) [98-102]. Curcumin functioned as a graphene oxide, shown antiviral effect against respiratory syncytial virus infection which is implicated as severe lung disease. A Beta-cyclodextrin (CD) was developed and functionalized which displayed excellent antiviral activity and efficiently showed that the composite could prevent the RSV from infecting the host cells by inhibiting the viral attachment which possessed prophylactic and therapeutic effects toward virus [103]. Curcumin inhibits activity of Inosine-mono phosphate dehydrogenase (IMPDH) enzyme in competitive manner or non-competitive manner thus by inhibition of IMPDH Curcumin have potential anti-proliferative, antiviral and anti-parasitic effects [104].
2) *Anti-Inflammatory Activity:* Curcumin has been demonstrated to be safe in six human trials and has been proved anti-inflammatory by showing inhibition of number of different molecules that play a role in inflammation which shows many transcription factors, cytokines, protein kinases, adhesion molecules, redox status and enzymes [105-107]. Tumour necrosis factor α (TNF-α) is a major mediator of inflammation in most of diseases. The agents that downregulate NF-kB and NF-kB regulated gene products have potential efficacy against various diseases (like environmental pollutants, chemical, physical, psychological stress, ultraviolet radiation, cigrate smoke). Curcumin has been shown to block NF-kB activation increased by several different inflammatory stimuli which also suppresses inflammation through many different mechanisms [108].
3) *Antioxidant & Anti-cancer Properties:* Curcumin has improved systemic markers of oxidative stress, module the activity of GSH, catalase, and SOD enzymes active in the neutralization of free radicles [109-111]. Curcumin is known to scavenge different forms of free radical, such as reactive oxygen and nitrogen species (ROS and RNS) and like vitamin E, curcumin is also considered as a chain-breaking antioxidant [112-114]. The study of curcumin as an anti-cancer has been extensively investigated recently and improvements in gastrointestinal, melanoma, genito-urinary, breast and lung cancer has been seen [115-118]. Curcumin also prevents carcinogenesis by affecting two primary processes: Angiogenesis and Tumour growth [119] while analogues S1 - S3 containing sulfone stopped the growth of human prostate, colon, lung and pancreatic cancer cells [120, 121].
4) *Anti-Bacterial Property:* Curcumin inhibits the growth of a variety of periodontopathic bacteria and porphyromonas gingivitis Arg- and Lys- specific proteinase (RGP and KGP) activities. Bacterial growth was put an end to almost completely at very less concentration of 20 µg/mL inhibited these P. Gingivitis biofilm formations by more than 80% and moreover at high concentration than above mentioned, curcumin targets bacterial membranes (Escherichia coli) [122, 123]. Curcumin – polymyxin B is used for topical therapy to treat and put a stop to traumatic wound and infections of the skin [124]. Also, curcumin loaded in zein (zein-CUR) fibers show antibacterial activity towards S.aureus & E.coli and the efficiency to inhibit the growth increased with the increase of curcumin contents. The study has showed that zein-CUR fibres are potential material for antimicrobial applications to stop the bacterial growth and also use for food packaging [125]. The zone inhibition method also showed the antibacterial activity of curcumin-chitosan film against staphylococcus aureus and rhizoctania solani class of bacteria [126]. The small size of curcumin nanoparticles plays a key role in enhancing antimicrobial activities and the blend films of curcumin & chitosan can be used as a promising anti-microbial packaging for food & agriculture products. The fabricated curcumin nanoparticles showed best anti-microbial activity against listeria monocytogenes [127, 128].
5) *Anti-Allergy & Anti-Asthma Effects:* Curcumin decreased the nasal airflow by alleviating sneezing, rhinorrhea and nasal congestion. It also stops the IL-4, IL-8, and tumour necrosis factor alpha as well as also enhanced the levels of IL-10 & soluble intercellular adhesion molecule. Curcumin stopped the ERK 42/44, p38 MAPK and JNK 54/56 activation in asthma progression in rats. The different concentration (2.5 and 5.0mg/kg) in ovalbumin (OVA) of Balb/c mice markedly regulates airway inflammation and airway obstruction mainly by changing cytokine levels [129].

6) *Anti-Fungal, Anti-arthritis, Anti-venom & Anti-obesity Activities:* The curcumin powder in plant tissue at the 0.8 and 1.0 g/L had good inhibition against fungal contamination [130]. Reduction in proteinase secretion and alteration of membrane-associated properties of ATPase activity are other major and important factors for anti-fungal activities of curcumin [131]. Another effective method of using curcumin with light showed noteworthy improvement in the anti-fungal activity against planktonic form in the yeast [132]. The result of the curcumin treatment showed the greater number of improvements in overall rheumatoid arthritis and also the results were far better than the patients in the diclofenac sodium group [133]. The properties of antioxidant, anti-proliferative, anti-inflammatory and immunesuppressive showed improvement in the symptoms to patients suffering from rheumatoid arthritis [134]. Curcumin as a plant metabolite is effective against snake venom PLA2, as studies revealed that curcumin has a favourable interaction with the amino acid residues at the active site of the venom PLA2 and this could result into inhibition [135, 136]. Curcumin improved the results as fat content on treated individuals for studies on obese patients. Significant changes only in TG levels were observed, while other parameters remained unchanged after 30 days-curcumin administration [137].

7) *Anti-Diabetic:* The anti-diabetic effect of curcumin can also be linked to antioxidant property [138]. Recent studies have shown the ability of curcumin to have the capacity to directly quench reactive oxygen species (ROS) which can contribute to oxidative damage, this property contributes to the overall effective property of curcumin. Curcumin can make the cell death caused by oxidative stress less effective and weaker, indirectly by induction and/or activation of antioxidant/cytoprotective enzymes such as heme oxygenase-1 (HO^{-1}) [139]. Curcumin was tested for the prevention of type-2 diabetes in pre-diabetic human population. The curcumin treated group results showed a better overall function of β-cells, with higher HOMA-β and lower C-peptide while the group of people treated with curcumin showed a lower level of HOMA-IR (Insulin Resistance Index) and higher adiponectin, thus curcumin intervention may have a positive effect to a pre-diabetic population [140].

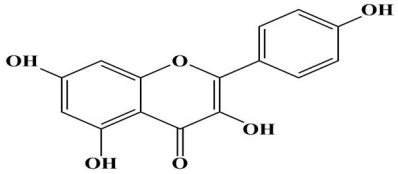
8) *Wound-Healing, Anti-alzheimer, Depression & Anxiety Activities:* The main aspects of wound repair including re-epithelization, neovascularisation, collagen synthesis; granulation tissue formation is significantly recovered by curcumin. The presence of curcumin also inhibits the growth of the burn bacterial flora including Pseudomonas aeruginosa as predominant bacteria among isolations for 14 days as a part of treatment. Curcumin fights against wound infections and promotes wound repair in burn injuries in rats and also stimulates the growth factors which participate in wound healing process [141, 142]. Novel curcumin formulations were optimized to ensure a higher bio-availability in lower dose (80-180 mg/day), showed good results in both acute and chronic as improved sustained attention & working memory tasks immediately after a single dose, while after 4 weeks administration the results showed enhanced memory, mood, alertness and contentedness [143, 144]. Curcumin (500-1000 mg daily) with standard anti-depressive agent's escitalopram, venlafaxine or fluoxetine was given orally in several clinical trials and the results showed a marked improvement in depression-related symptoms [145-150]. In other tests it was found that curcumin decreased IL-1β and TNFα levels, increased plasma BDNF and decreased salivary cortisol levels in curcumin-treated groups, & also stated a significant increase in urinary thromboxane B2, substance P, baseline plasma endothelin-1 and leptin, thus it can be related to the antidepressant mechanism of curcumin [151].

9) *Curcumin Used In Eye Disease:* Clinical trials of the curcumin effect on various opthalmological disorders showed high activity of this compound, by oral intake it has reported that 15 days eye-drop application containing turmeric can improve symptoms of various infections of conjunctivitis, conjunctival xerosis (dry eye), acute dacryocystitis, and degenerative conditions of postoperative cataract patients [152]. Oral curcumin intake for 12 weeks and 18 months also demonstrated a marked symptom of improvement in all patients & reduced eye discomforts [153, 154]. Patients with central serous chorioetinopathy also showed significant improvement after oral curcumin administration [155].

D. Kaempferol

Kaempferol which is present in various plant sources including tea, broccoli, grapefruit and apple shows anti-viral property on JEV & plethora of anti-cancer properties [34].

Figure D. Structure of Kaempferol (I) [156]



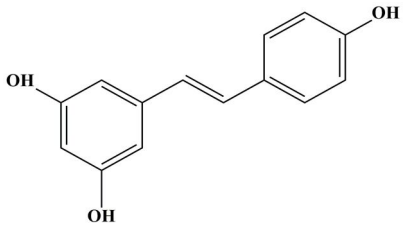
(I)

1) *Antioxidant Activity of Kaempferol:* The antioxidant activity of kaempferol is highlighted due to presence of hydroxyl groups at C3, C5 and C4, an oxo group at C4, and a double bond at C2-C3 [157]. Moreover, kaempferol activates antioxidant enzymes such as superoxide dismutase, catalase and heme-oxygenase-1 [158, 159]. Conclusive evidence has shown that kaempferol can control cancer through its anti-oxidative/antinitrosative and anti-inflammatory activity by restoring the cell redox haemostasis by inhibiting the NF-kB pathway and to up-regulate the Nrf2 transcriptional pathway [34].
2) *Anti-Cancerous Activities:* Kaempferol significantly activates mitogen-activated protein kinase (MAPK) cascades, which are important signalling pathways involved in the regulation of normal cell proliferation, survival and differentiation. On activating MAPK pathway leads to the transcription factor of activator protein-1 (AP-1), cathepsin B and D, MMP-2 and -9 activation, this reduces cell adhesion, migration and invasion [160-163]. Gliboblastoma is one of the most invasive and aggressive brain tumours, with a very poor prognosis, among other reasons, secondary to the development of resistance against current therapies and reports have shown that kaempferol has stopped both growth & migration of glioma cells, even when kaempferol was loaded to mucoadhesive nanoemulsion (KPF-MNE) [164-166]. Hepatocellular carcinoma (HCC) is the most found primary liver cancer among adults [167]. Kaempferol can significantly inhibit human hepatic cancer cell proliferation when taken in a dose-dependent manner which induces cell apoptosis and causes cell cycle arrest on preventing cell migration & invasion, in addition diethyl nitrosamine and 2-acetylaminofluorene persuaded HCC from rats when treated with kaempferol combined to lute Olin stopped cell growth and induced cell depth [168, 169]. Experimental studies show that kaempferol and 5-Fluorouracil in LS174-R cells report effective anti-proliferative effects; also, kaempferol together with tumour necrosis factor ligand superfamily member (TRIAL) led to death of colon cancer cells by up-regulation of TRIAL receptor and death receptor 5 that improved TRIAL activity. Kaempferol was found to possess cytotoxic effect on different human colorectal cancer cell lines which included HCT116, HT-29, HCT-15, LS174-R colon and SW480 cells [170-172]. The transcriptome of prostate cancers cells is also greatly affected by the treatment with kaempferol as proved by the downregulation of androgen receptor genes expression. Kaempferol-3-O-rhamnoside when taken in dose dependent manner inhibits prostate cancer cells proliferation, by upregulating expression of caspase-8, -9,-3 and poly (ADP-ribose) polymerase proteins [173, 174]. The dose of kaempferol stops the growth of pancreatic cancer cells through inducing apoptosis and effectively stopping cell migration, epidermal growth factor receptor (EGFR)-related & AKT pathways [175]. It also improves suppressive activity of regulatory T cells by increasing the expression level of FOXP3 [176, 177]. Kaempferol dose dependently decreased cell viability in human leukaemia cells, also it promoted apoptosis and DNA damages, down-regulated the expression of AKT, ABCB1, BCL2 and ABCC1 genes and also protein associated with DNA repair system as well as DNA dependent proteins [178-185]. Kaempferol dependently prevented the growth of lung adenocarcinoma, decreased colony formation and triggered apoptosis. Kaempferol showed a significant effect in killing cancer cells by radiation in a BALB/c nude mouse xenograft model of A-549 cells [186]. Kaempferol significantly stops cell growth and triggers apoptosis in RCC [187, 188]. Kaempferol prevents cell migration and invasion thus showing anticancer property by increasing focal adhesion kinase property [189]. Kaempferol can stop bladder cancer cells by increasing cell cycle arrest and apoptosis. Also, it downgrades the PTEN/PI3K/AKT pathway, and upregulates p53, p38, p21, p-ATM, p-BRCA1, DNA methylation and Bid and Bax expression [190-192]. It effectively suppresses tumor growth, cancer metastasis and invasion in xenografted mice with regards to the untreated control compared to the control group mice & yet upgraded apoptosis markers [193]. Kaempferol showed anti-proliferative effect on pharynx and oral cavity carcinoma, human oesophagus squamous carcinoma & human tongue squamous carcinoma, prevented clone formation & cell migration and invasion which induced substantial apoptosis [194-196]. Kaempferol downgrades the AP-1 DNA binding activity, MMP-2, -9 and urokinase plasminogen activator (uPA) that, in turn, reduces phosphorylated p38, ERK and JNK [197]. Kaempferol significantly reduced the number of viable cells and decreased the tumour size [198]. Kaempferol was found to be preventing the growth of human cervical cancer cells, such as HeLa, multidrug-resistant human cervical carcinoma, KB-V1 and SiHa cells with regards to the normal cells and HFF cells. It causes cell cycle arrest at the G2/M phase and apoptosis coreleated with downregulation of PI3K/AKT and human telomerase reverse transcriptase (hTERT) pathways, Pgp, Rh123, cyclin B1, NF-kB nuclear trans location, CDK1, Bcl-2 and upregulation of p53 with mitochondrial membrane potential disruption [199-202]. Experimental studies related to stomach cancer revealed the anti-proliferative activity of kaempferol on human gastric cancer cells by increasing autophagy, cell cycle arrest at G2/M phase and cell death [203, 204]. Kaempferol inhibits tumour growth, proliferation and angiogenesis by reducing the amount of vascular endothelial growth factor (VEGF) expression [205].

E. Essential Oils

Resveratrol, which is a component present in peanut oil, is responsible for anti-viral property against ZIKV [156].

Figure E. Structure of Resveratrol (I) [156]



(I)

Azadirachta indica leaf extracts provides evidence of the presence of anti-retroviral activity which tends to show antimalarial activity, anti-cytoadhesion activity and prevents the invasion of human lymphocytes by the HIV with minimum side effects. Quercetin, β-sitosterol and polyphenolic flavonoids were purified from azadirachta indica fresh leaves & were shown to have antibacterial and antifungal properties, anti-inflammatory, hepatoprotective effects, wound healing effects, anti-diabetic effects, anti-microbial effects, methanolic extracts of azadirachta indica leaves against cisplatin induced nephrotoxicity and oxidative stress in rats confirmed that it effectively rescues the kidney from CP-mediated oxidative damage [5]. Plethora methodologies of cocos nucifera showed to possess anti-oxidant, anti-hyperlipidemic, anti-viral, anti-microbial, healing activities, immunomodultor & moisturizing activity, anti-diabetic activity, anti-cancer & anti-thrombotic activities and anti-obesity effects [206, 207]. Prunus dulcis oil has multi-properties including anti-inflammatory, immunity boosting, anti-hepatotoxicity effects and also showed reduction in colon cancer [208]. Neem seed oil was significantly effective as an analgesic in the dose of 1 & 2 ml/kg and also concluded that animals treated with the dose of 100 mg/kg of Carbon Tetrachloride Extract (CTCE) of azadirachta indica fruit skin and isolated ingredient azadiradione showed anti-nociceptive and anti-inflammatory activities [209, 210]. It was found that on introducing carbon tetrachloride in rat's liver, the nimbolide present in azadirachta indica possesses heptoprotective effect against it and also the leaf extract of azadirachta indica have protection against paracetamol-induced liver necrosis in rats [211, 212]. The wound healing activity of the extracts of azadirachta indica and T. cordifolia using excision and incision wound models in sprague dawley rats, revealed promotion of wound healing activity [213, 214]. Aqueous extract of neem cake inhibited spore germination against three sporulating fungi such as C. lunata, H. pennisetti and C. gloeosporioides F. sp. Mangiferae showed antimicrobial role [215] and revealed that methanol & ethanol extract of azadirachta indica showed growth inhibition against Aspergillus flavus, Alternaria solani and Cladosporium [216]. Cocos nucifera oil as a diet of Sri Lankan males found decrease in cholesterol level by 18.7 % from 179.6 mg/dl to 146.0 mg/dl, LDL cholesterol decreased by 23.8 % from 131.6 mg/dl to 100.3 mg/dl, HDL cholesterol decreased by 41.4 % from 43.4 mg/dl to 25.4 mg/dl and the LDL/HDL ratio increased 30 % from 3.0 to 3.9. Adding cocos nucifera oil to the diet of hypercholesterolemics lowers serum cholesterol from 450 mg/dl to 367 mg/dl [217]. Virgin cocos nucifera treated wounds that healed much faster due to higher collagen and antioxidant enzyme activities, also observed the increase in fibroblast proliferation and nevovascularization in wounds [218]. On consumption of 73 g prunus dulcis in the diet reduces 9.4% low density lipoproteins cholesterol [219].

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IV. CONCLUSION

Throughout history, the use of natural products remedies delineated the basis of synthetic products treatment. Azadirachta indica provides the evidence of the presence of anti-retroviral activity in leaf extract which also have anti-malarial activity with no side effects. Poly saccharide is an active component in aloe Vera gel which has so many therapeutic properties and is effective when tested for a specific biological activity. 1, 8-cineole, α– & β-thyone and camphor are used to treat viruses. Camphor is used both as an aphrodisiac and antiaphrodisiac agent. Curcumin studies have proved that curcumin as a plant derivative has a wide range of antiviral activity. The study shows that cocos nucifera oil was more protective than unsaturated oils. Prunus dulcis oil has many multi-properties including anti-inflammatory, immunity boosting and anti-hepatotoxicity effects. The use of kaempferol as cancer-fighting properties highlights its full potential. Many citrus fruits are also known for its multi-potent activities. Indispensable herbal

components may have great applications in future of textiles because of its strong activities against viruses & diseases. More applications are been discovered as research from different point of view to provide a better understanding of its composition and effects. Further ongoing vivo and vitro studies can give stronger results for the usage of herbal medications and may show superior effects against new emerging diseases like COVID-19.

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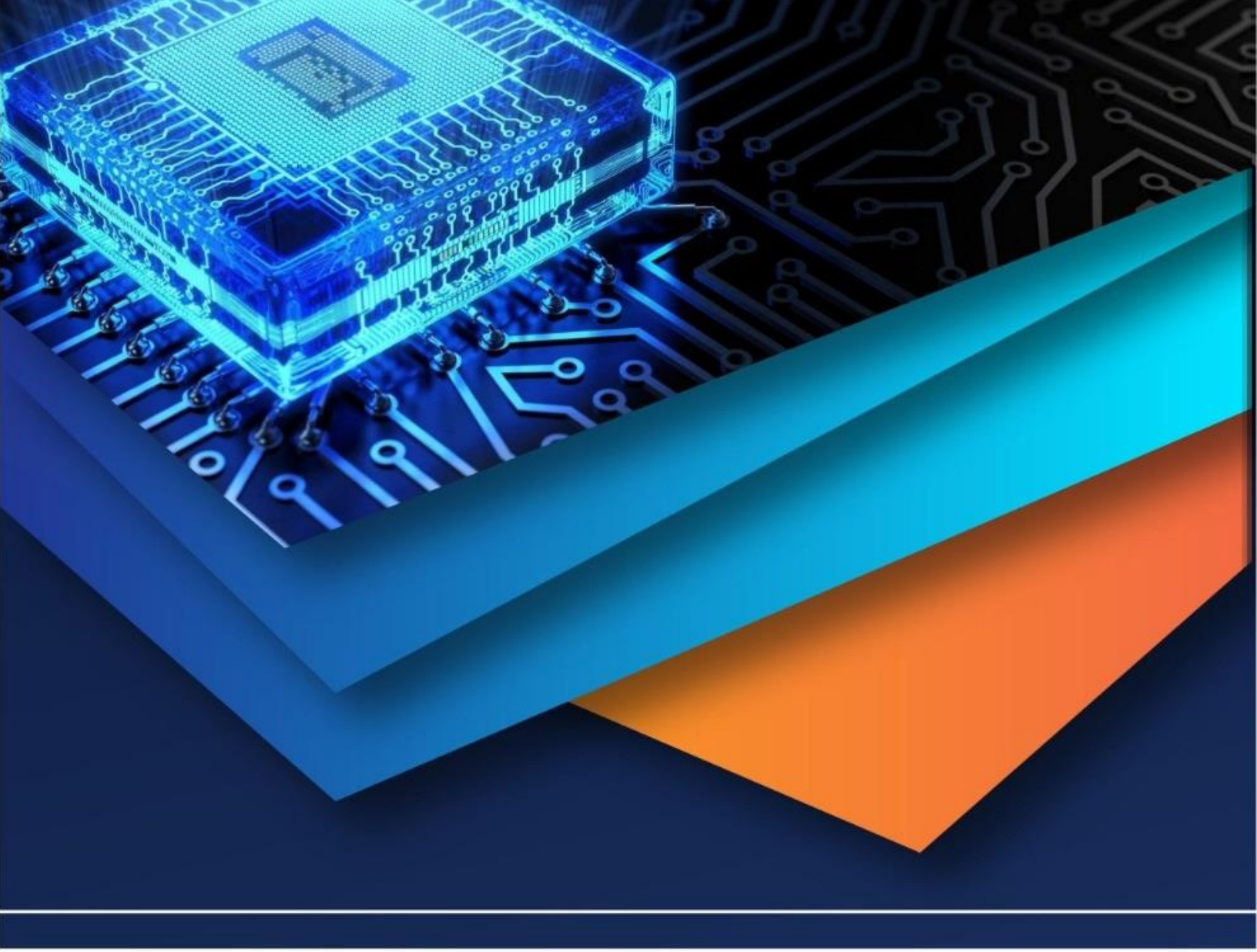

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