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Roll of Spices in Controlling Microbial Infection and in Modulation of the Immune System

Sahana Ghosh[1]
[1]*Microbiology Department, Vijaygarh Jyotish Ray College affiliated to the Calcutta University*

Abstract: ***Nature provided us with different products like fruits, flowers, vegetables, spices, herbs and so on. People utilize them since ancient times. Among them spices play key role in the lives of people and are used in rituals and in traditional medicines, beside using as food additives, preservatives and flavoring agents. People use spices to cure various infectious diseases like cancer, diabetes, viral infection, bacterial infection, fungal infection. At present, entire world is combating the coronavirus disease by utilizing different means. Scientific communities are trying to develop vaccines. Numerous evidences suggested that some common spices have the ability to reduce the severity of SARS-CoV-2 (severe acute respiratory syndrome – coronavirus). One of the main factor to prevent the infection is to boost the immunity power, which is possible by using the spices in our diet chart. Spices also possess potent antioxidant and anti-inflammatory properties. This study discusses how the spices and their components act as anti-inflammatory agents and prevent infection. The review work is done to find out different beneficial activities of spices, identify the phytochemicals that are responsible for their activities. Aim of this review is to acquaint researchers and international communities with the functions of spices and their bioactive components which are responsible in minimizing the infectivity rate and how the spices are controlling the immune system in combating the diseases.***
Keywords: SARS-CoV-2, spices, antioxidant, anti-inflammatory properties, Nrf2

I. INTRODUCTION

Mother Nature has bestowed us with various medicinal plants and it's products. The word spice comes from Old French word "espice". Use of natural products such as plant parts (fruits, leaves, bark, root, twig, stem and sap) as medicines, not only reliable or cost effective but also show least side effects. They are widely used for treating several chronic diseases, including cough, fever, asthma, diarrhea, indigestion and skin diseases [1]. Among which SARS-CoV-2 is most important contagious disease. Millions of people throughout the world are affected by this virus. As per update given by WHO on January 2021, worldwide total number of cases was 88,387,352 with 1,919,204 deaths [2].

It has become worldwide concern and so WHO declared this as pandemic. SARS-CoV-2 belongs to the members of beta-coronavirus, family Coronaviridae [3]. They are enveloped viruses having non-segmented, positive-stranded RNA genome [3]. CoVs enter the host cells via interaction between S-protein expressed on the surface of the virus and angiotensin-converting enzyme 2 receptor (ACE -2) present on the host cell surface [4]. Main symptoms of coronavirus (CoVs) are fever, dry cough, respiratory distress, shortness of breath, malaise, diarrhea and sneezing. But as the viral strain is modifying itself to escape the human's immune system, its symptoms are also changing. Therefore scientists are facing a challenging situation in developing vaccines. Because of its variation in structure, they gain the ability to attack different aged people from elderly to children. Co-morbid patients such as diabetes, cerebral infarction, chronic bronchitis, hypertension, cardiovascular disease, cancer, Parkinson's disease have higher chance of getting infected [5], [6], [7].

Spices and its components have shown to possess antioxidant and anti-inflammatory properties, which are used to treat chronic diseases. These compounds possess their antioxidant activity via different mechanisms which includes activation of nuclear factor (erythroid-derived 2)-like 2 (Nrf2) directly or indirectly [8] and all of them are found to be TRP (transient receptor potential) protagonist [9]. Biochemical molecules known as phytochemicals includes flavonoids, phenolic compounds, tannins, alkaloids and many more are found in spices [1]. SARS-CoV-2 outbreak led to devastating situation as we don't know specific treatment of CoV till date.

Research work showed that increased immunity lessen the severity of the infection. So to boost up the immune system, spices play a key role. This review canvasses about some Indian spices like black pepper, cinnamon, clove, turmeric, coriander, cumin, tamarind and asafetida, which are known as immunity boosters [10]. More explorations need to be done to identify the spices which can inhibit microbes from causing infectious and contagious diseases by using various mechanisms.

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II. RELATION BETWEEN FOODS AND NRF2 AND TRPS

There are three different phases of COVID-19 infection – i. in this phase infection lasts for 1-2 weeks, ii. in next phase cytokine storm takes place along with oxidative stress storm and iii. then recovery phase which lasts for few months. Study proved that spices functions differently in different phases to combat the infection and to reduce this immune storm [9]. Further it is noted that biochemical compounds of spices have the ability to activate Nrf2 [11], [12]. Depending on the availability of spices, COVID-19 death rates varies among the countries. This is might be because of Nrf2 interaction with the spices which varies from place to place, and reduces the severity of infection [13], [14], [15]. Function of Nrf2 is to rebalance the oxidative stress [9]. Contrarily, as the balance between oxidant and antioxidant is difficult to obtain, many Nrf2 medicines were found to be toxic [9]. The TRP vanilloid 1 (TRPV1) and ankyrin 1 (TRPA1) belong to TRP superfamily. They are structurally correlated and nonselective cation channels [9]. To elicit symptoms of COVID-19 like vomiting, diarrhoea, cough, nasal obstruction, pain and sudden loss of smell and taste, TRPA1 and TRPV1 elevate sensory or vagal nerve discharges [16]. Reports confirmed that functions of TRPA1 and TRPV1 can be triggered by not all, Nrf2 interacting spices [16].

III.SPICES OF MEDICINAL VALUES

A. Black Pepper (Piper nigrum L.)

Black pepper is famous as the king of spices [1], [17]. It belongs to family Piperaceae [3]. It is found in India, Sumatra, Indonesia regions [18-20]. Studies showed that Black pepper has a dynamic activity like antimicrobial activity against *Escherichia coli, Pseudomonas aeurogenosa, Staphylococcus aureus, Aspergillus niger, Fusarium ox-ysporum, Aspergillus flavus* and *Mycobacterium tuberculosis* [21]. It also helps in stimulation of circulatory system. Piperine, alkaloid of black pepper has 1-peperoyl piperidine, which possess antihypertensive, anti-Alzheimer's, anti-inflammatory, antioxidant, antipyretic, antiasthmatic, antimicrobial, antitumor and many more properties [22]. Antioxidant capacity of pepper phenolic amides shown to be higher to the synthetic moieties Butylated hydroxytoluene (BHT) and Butylated hydroxyanisole (BHA) [23].

Experimental studies on evaluating the antiviral activity of chloroform and methanolic extracts of black pepper against human parainfluenza virus and vesicular stomatitis virus (an enteric virus) showed that antiviral activity in chloroform is higher because of having higher amount of alkaloids [24]. Another study showed that biochemical compound, piperine has the ability to inhibit methyltransferase of Dengue virus and VP35 of Ebola virus when compared to antiviral Ribavirin [25]. Another data depicts that consumption of black pepper in diet routinely may be helpful in preventing coronavirus [26]. Activity of black pepper as anti-inflammatory agent has been described in table 1.

B. Turmeric (Curcuma Longa)

Turmeric belongs to Zingiberaceae family. Since ancient times turmeric has been used in many rituals and in many traditional medicines as well. Turmeric is known as “Indian saffron” because of its brilliant yellow colour [36]. It is reported that for the treatment of various respiratory conditions, liver disorders, anorexia, rheumatism, diabetic wounds, runny nose, cough, and sinusitis, diseases associated with abdominal pain, turmeric is used [37], [38]. Sometimes, turmeric mixed with warm milk is consumed to treat intestinal disorders, colds and sore throats [36]. Many biochemical compounds present in turmeric act as antiviral, anti-cancer, anti-atherosclerotic, anti-depressant, anti-diabetic, anti-arthritic agents, among them most notable one is curcumin. Curcumin is signified as “Golden nutraceutical” because of its pharmacological activities like anti-cancer (breast, colorectal, ovarian, cervical, pancreatic, prostrate etc), anti-viral, illustrated in table 2, anti-fungal and many more [39], [40]. Hexane and methanol extracts of turmeric elicit antibacterial activities against *Vibrio harveyi, V. alginolyticus, V. vulnificus, Streptococcus agalactiae, Staph. aureus, Staph. intermedius, Staph. epidermidis, Edwardsiella tarda, V. parahaemolyticus, V. cholerae, Aeromonas hydrophila* and *Bacillus subtilis* [41]. Further the role of turmeric in anti-inflammation is de-scribed in the table 1.

TABLE 2: Antiviral properties of curcumin and its mechanism of action

SL. NO.	VIRUS	MECHANISM of ACTION	REFERENCES
1	SARS coronavirus	Inhibits replication and protease activity	50
2	Herpes virus	Inhibits gene expression	51
3	Hepatitis B virus	Inhibits replication and cccDNA	52
4	Hepatitis C virus	Entry inhibitor	53
5	Human immunodeficiency virus	Impedes protease, integrase and Tat protein function	54

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6	Human papilloma virus	Suppress gene expression	55
7	Respiratory syncytial virus	Entry inhibitor replication and budding inhibition	56
8	Chickun gunya virus	Blocks entry of the virus	57
9	Dengue virus	Entry inhibitor, Particle production, Inhibition	58
10	Zikavirus	Blocks entry of the virus	57
11	Influenza A virus	Prevents virus uptake, replication and particle production	59

C. Clove (Syzygium aromaticum)

Clove belongs to the family Mirtaceae, is known for its action against oral bacteria [3]. Native of Indonesia, but it is cultivated across the world. Cloves act as larvicidal agent to resist dengue, acts as an analgesic for joint pains, toothache and other serious health problem in tropical countries [60], [61]. One of the important bioactive com-pound of clove is eugenol which exhibits broad antimicrobial activities ranging from *Escherichia coli, Bacillus subtilis, Candida albicans, Salmonella typhimurium, Staphylococcus aureus to Rhizopus nigricans* and *Aspergillus niger* [3], [62]. According to World Health Organization (WHO), humans can uptake clove daily 2.5mg/kg body weight [63]. Ethanolic and aqueous extracts of clove have antioxidant activity, hydrogen donating ability, metal chelating ability and scavenging of free radicals, hydrogen peroxide and superoxide [64]. Reports suggested that eugeniin, extract of *Syzygium aromaticum* possess inhibitory action against the HSV-1 DNA polymerase [3].

D. Coriander (Coriandrum Sativum)

Coriander belongs to Apiaceae/Umbelliferae family [65]. Geographical distribution of coriander is from Turkey, Italy, Russia, India, Morocco, Bulgaria, Central and Eastern Europe, China to Western Asia and Mediterranean regions [66]. Different parts of coriander exhibit antioxidant activity, sedative, anti-microbial activity, anti-convulsantactivity, diuretic, hypnotic activity, hepatoprotective, anti-diabetic, anti-helmintic activity and anti-mutagenic activity [67], [68]. Seed oil of coriander exhibits antimicrobial activity against *Staphylococcus aureus and Gram negative bacterial strains including Escherichia coli, Klebsiella pneumoniae, Salmonella typhimurium* and *Pseudomonas aeruginosa* and two clinical multidrug-resistant *Acinetobacter baumannii* [69]. Reports suggested that coriander extracts inhibit Human Immuno-deficiency Virus (HIV) by interfering it's replication cycle, dengue viruses and Middle East Respiratory Syndrome (MERS) coronaviruses [66]. Extracts of ethanol, methanol, acetone, chloroform, hexane and petroleum ether showed activity against infectious diseases such as *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and *Klebsiella pneumonia* fungus like *Aspergillus niger, Candida albicans, Candida kefyr* and *Candida tropicalis* [70]. Extracts of *Coriandrum sativum* are used to induce potent anti-inflammatory effects both in vitro and in vivo as well, illustrated in table 1.

E. Tamarind (Tamarindus Indica L.)

It belongs to group of the Fabaceae, sub-family Caesalpinioideae [74]. The major tamarind producing countries are in the Asian countries India and Thailand, but also in Bangladesh, Sri Lanka, Thailand and Indonesia [75]. Different parts of tamarind can be used for treatment of several chronic diseases [76]. The seed kernels or tamarind seed coat extract (TSCE) possess high antioxidant activity. It prevents anemia, regulates glutathione levels and reduces lipid peroxidation [77]. Extracts of tamarind leaves showed antioxidant activity in the liver. Hypolipemic activity was noticed from tamarind fruit extract for the treatment of hypercholesterolemic hamsters, besides anti-oxidant properties [78]. Extracts from tamarind flowers showed antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* [79], [80]; against fungal cultures of *Aspergillus niger* and *Candida albicans* [75], [81]; anti-viral activities against watermelon mosaic viruses, cow pea mosaic viruses and tobacco mosaic virus [81]; exhibit anti-nematodal activity, moluscicidal activity, anti-diabetic activity [82], cytotoxic activity [80]. Tamarind also known as Imli known for its mutagenic, antihepatotoxic, cholesterolemic, anti-inflammatory properties [83]. Tamarind acting as an anti-inflammatory agents against diseases shown in table 1.

F. Cumin (Cuminum Cyminum)

Cumin belongs to Apiaceae family. Geographical distribution of cumin is from East Meditaranian to South Asia, Central Asia to Northern India, mountainous regions of North India, Syria, Turkey, Iran, and Saudi Arabia [87]. There is another type of cumin – Black cumin (Nigella sativa). Black cumin is widely used as anti-inflammatory, hepatoprotective, anti-diabetic, hypotensive agents and so on [88]. Pharmacological properties of it includes hypotensive, antinociceptive, uricosuric, choleretic, antifertility, antidiabetic, antihistaminic, anti-oxidant, anti-inflammatory, anti-microbial, anti-tumor and immunomodulatory effects [89].

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It's aqueous and oil extracts possess antioxidant, anti-inflammatory, anticancer, analgesic, antimicrobial activities, table 1 [90], [91]. Extracts of cumin possess antimicrobial effects against *Aspergillus spp., Penicillium spp., Saccharomyces, Candida spp., Escherichia coli* [92] and antiviral activity against HSV-1[93]. Apart from these, used in the treatment of bronchial asthma and eczema [94], antihelminthic [95], antinematodal [96], antischistosomal [97], antimicrobial [98], [99], [100] and antiviral [101]. Cuminaldehyde inhibit the fibrillation of alpha-synuclein (α-SN), Parkinson's disease [102].

G. Cinnamon (Cinnamomum sp.)

Cinnamon belongs to the family Lauraceae. Geographically it is distributed in the tropical countries like India, Sri Lanka, Malabar, Caribbean, Sumatra, Myanmar, China, Caribbean, Central and South America and Africa [111]. Cinnamon bark oil, cinnamaldehyde and eugenol exhibit potent antibacterial effects against *Bacillus cereus, Campylobacter jejuni, Enterococcus faecalis, Escherichia coli, Penicillium roqueforti, Staphylococcus aureus, Listeria monocytogenes, Streptococcus pneumoniae, Haemophilus influenzae, Pseudomonas aeruginosa, Pediococcus halophilus, Salmonella choleraesuis, S. enterica, Mucor plumbeus, Aspergillus flavus, Eurotium sp., S. pyogenes* and *Yersinia enterocolitica* [112], [113], [114], [115]. Study showed that cinnamon has anti-inflammatory, antifungal, antiviral, antioxidant, antitumor, cardiovascular, cholesterol lowering, and immunomodulatory effects, illustrated in table 1. Reports suggested that cinnamon may act as an insulin mimetic, to potentiate insulin activity or to stimulate cellular glucose metabolism [116].

In accordance with, the phagocytic index, serum immunoglobulin levels increased due to higher dose (100 mg/kg) of cinnamon. Whereas low dose (10mg/kg) leads to increase in serum immunoglobulin levels only. Hence, higher dose increases both the humoral and cell-mediated immunity and low dose increases humoral immunity only [3]. Reports revealed that hydroalcoholic extracts of cinnamon was effective in reducing the viral load of HSV-1 by preventing the attachment of viral particles onto the cells [3].

H. Asafoetida (Ferula asafetida)

It belongs to kingdom Plantae, class Magnoliopsida, family Umbelliferae [124]. Geographically asafoetida is ex-tended from central Asia, eastern Iran to Afghanistan [125]. Pharmacological studies showed that it possesses anti-fungal, antioxidant, antidiabetic, antispasmodic, anticancer, hypotensive etc in oleo-gum-resin part [126]. It's secondary metabolite sesquiterpene coumarin acts as an important compound in synthesizing new drug against Influ-enza A (H1N1) viral infection. It manifests antimicrobial activities against *Escherichia coli, Shigella flexneri, Bacillus megaterium, Staphylococcus epidermidis, Vibrio cholera, Micrococcus leuteus* [1] and antiviral activities against type 1 or 2 herpes virus, strains of influenza virus and rhinoviruses [127]. Asafoetida controls liver and breast cancer by regulating inflammatory responses which is illustrated in the table 1.

TABLE 1: Role of spices in anti-inflammation

SPICES	COMPOUND USE/FORM OF USE	DISEASE	MECHANISM	REFERENCES
Black Pepper	Extract	Asthma	↓ IL-1β, ↓ TNF-α, ↓ IL-4, ↓ RORγt, ↓IgE, ↓ IL-17A	27
		AR	↓ E-cadherin, ↑ HO-1, ↑ Nrf2	28
			↓ p-STAT3, ↓ IL-6, ↓ TNF-α, ↓ NF-κB p65, ↓ IL-1β	29
	Pipernigramides	Edema	↓ TNF-α, ↓ IL-1β, ↓ IL-6, ↓ PGE2, ↓ p-IKKβ	30
			↓ NO, ↓ neutrophils infiltration	
	Piperine	Lung metastasis	↓ tumor nodule formation, ↑ survival rate, ↓ SA, ↓ GGT	31
		Bacterial sepsis	↓ IL-1β, ↓ HMGB1, ↓ p-AMPK	32
			↓ IL-1β release	
		AP	↓ MPO, ↓ TNF-α, ↓ IL-1β, ↓ IL-6, ↓ p-ERK1/2, ↓ p-p38, ↓ p-JNK	33

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		Lupus nephritis	↓p-AMPK, ↓ IL-1β, ↓ HMGB1, ↓ pro-caspase-1	34
			↓ NLRP3 inflammasome activitation	34
	Chabamide	Inflammation	↑ HO-1, ↑ Nrf2, ↓ iNOS	35
Turmeric	Curcumin	PIVP	↓ IL6, ↓ TNF-α, ↓ MCP-1, ↓ NF-κB, ↑ IκBα, ↑ HO-1	42
		Cystic fibrosis	↑ CFTR, ↓ cox-2, ↓ PGE2, ↓ IL-8	43
		Diabetes	↓ NF-κB, ↓ TNF-α, ↓ IL-1β, ↓ IL-6 ↓ NO, ↓ PGE2, ↓ cox-2	44
		ALI	↓ TNF-α, ↓ IL-8, ↓ MIF	45
		Asthma	↓ NICD1, ↓ Notch 1/2 receptors	46
		Cerebral I/R injury	↓ IL-1β, ↓ IL-8, ↑ p-JAK2, ↑ p-STAT3	47
	ATM	Psoriasis	↓ NF-κB, ↓ cox-2, ↓ p-p38 MAPK, ↓ TNF-α, ↓ IL-6, ↓ mRNA synthesis of IL-17, -22, and -23	48
	MTrPP	Ulcer	↓ TNF-α, ↓ IL-8, ↓ NF-κB, ↓ p-p38, ↓ MMP-9, ↓ cox-1 and -2	49
Coriander	Extract	Inflammation	↓ pro-IL-1β, ↓ PGE2, ↓ p-MAPK, ↓ NF-κB p65, ↓ cox-2, ↓ NO, ↓ iNOS	71
		CD	↓ IL-1, ↓ IL-4, ↓ IL-13, ↓ TNF-α, ↓ IFN-γ, ↓ IgE, ↑ GSH, ↑ HO-1	72
		Arthritis	↓ IL-1β, ↓ IL-6, ↓ TNF-R1	73
Tamarind	Extract	Pulmonary inflammation and fibrosis	↓ ROS, ↓ LPO, ↓ PCC, ↓ NF-κB, ↓ p38α MAPK, ↓ NOX4, ↓ cox-2, ↑ HO-1, ↑ SOD2, ↑ catalase, ↑ GST, ↑ GSH, ↑ GPx	84
		Arthritis	↓ IL-1β, ↓ IL-6, ↓ IL-23, ↓ TNF-α, ↓ cox-2, ↓ MMP	85
	Xyloglucan	Ulcerative colitis	↓ IL-1β , ↓ IL-6, ↓ TLR4, ↓ NF-κB	86
Cumin	Seed	Hypertension	↓ mRNA expression of IL-6, Bax, and TNF-α, ↑ mRNA of expression TRX1, TRXR1, eNOS, and Bcl-2	103
		Gastric ulcer	↓ TNF-α, ↓ MDA, ↑ GSH, ↑ catalase, ↑ ATPase activity	104
Black cumin	Extract	Lung inflammation	↓ TGF-β1, ↓ IFN-γ, ↓ PGE2, ↑ IL-4, ↑ catalase, ↑ SOD, ↓ MDA, ↑ thiol	105
		Diabetes	↓ mRNA expression of VCAM-1 and LOX-1, ↑ mRNA expression of eNOS,	106
		-	↓ MDA, ↓ NO, ↓ IL-6, ↑ thiol, ↑ SOD, ↑ catalase, ↓ AST, ↓ ALT, ↓ ALP, ↑ serum protein, ↑ albumin	107
	Oil	Low-grade inflammation	↓ IL-1β, ↓ MCP-1, ↓ gene expression of DNMT3A and HDAC1	108
		Allergic asthma	↓ IL-4, ↓ NO	109
	TQ	AD	↓ TLR-2, ↓ TLR-4, ↓ TNF-α, ↓ MyD88, ↓ IL-1β, ↓ IRF-3, ↓ NF-κB	110
Cinnamon	TCA	OA	↓ mRNA expression of MMP-1, -3 and -13, ↓ mRNA expression of ADAMTS-4 and -5, ↑ p-	117

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			IκBα, ↓ NF-κB, ↓ IκBα, ↓ p-JNK 1/2, ↓ p-p38	
	TCA	-	↓ NO, ↓ iNOS	118
	TCA	Neuroinflam-mation	↓ NO, ↓ iNOS, ↓ cox-2, ↓ IL-1β, ↓ IκBα, ↓ NF-κB	119
	Oil	Skin disease	↓ MCP-1, ↓ MIG, ↓ IP- 10, ↓ IL-8, ↓ VCAM-1, ↓ M-CSF, ↓ PAI-1, ↓ ICAM-1, ↓ EFGR, ↓ MMP-1, ↓ TIMP-1, ↓ TIMP-2	120
	Extract	Inflammation	↓ mRNA expression of TNF-α, ↓ p-p38, ↓ IκBα degradation, ↓ p-ERK 1/2, ↓ p-JNK, ↓ TNF-α, ↓ IL-6	121
			↑ IL-2, ↓ IL-4, ↓ IFN-γ, ↓ p-ERK1/2, ↓ p-p38, ↓ p-STAT4, ↓ p-JNK	122
	BCA, HCA	-	↓ IFN-γ, ↓ IL-2Rα, ↓ IgM, ↓ AFC response	123
Asafoetida	Oil	Liver cancer	↓ NF-κB, ↓ TGF-β1, ↑ caspase-3, ↑ TNF-α	128
	Resin	Breast cancer	↓ LOX	129
			↓ cyt-P450, ↓ cyt b5, ↑ catalase, ↑ GSH, ↑ GST, ↑ SOD, ↓ TBARS, ↑ DT-diaphorase	130

1) *Abbreviations:* AD: Alzheimer‟s disease, ADAMTS: a disintegrin and metalloproteinase with thrombospondin motifs, ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, AMPK: Adenosine monophosphate-activated protein kinase, AST: Aspartate aminotransferase, ATM: Aromatic-turmerone, Bax: B-cell lymphoma 2 (Bcl-2)-associated X protein, BCA : 2´-benzoxycinnamaldehyde, Bcl-2: B-cell lymphoma 2, CFTR: Cystic fibrosis transmembrane conductance regulator, DNMT3A: DNA methyltransferase 3A, EFGR: Epidermal growth factor receptor, eNOS: endothelial nitric oxide, ERK: Extracellular signal-regulated kinase, GGT: Gamma glutamyl transpeptidase, GM-CSF: Granulocyte macrophage colony-stimulating factor, GPx: glutathione peroxidase, GSH: Glutathione, GST: Glutathione S-transferase, HCA : 2´-hydroxycinnamaldehyde, HDAC1: Histone Deacetylase 1, HO-1: Heme oxygenase-1, HMGB1: High mobility group box-1 protein, ICAM-1- intercellular cell adhesion molecule-1, IFN: Interferon, iNOS: Inducible nitric oxide synthase, IP-10: Interferon-inducible protein 10, JAK: Janus kinase 2, JNK: c-Jun N-terminal kinase, LOX: Lipoxygenase, LPO: Lipid peroxidation, MAPK: Mitogen-activated protein kinase, MDA: Malondialdehyde, MCP: Monocyte chemoattractant protein, M-CSF: Macrophage colony-stimulating factor, MIG: Monokine induced by gamma, MIP: Macrophage inflammatory protein, MMP: matrix metalloproteinases, MPO: Myeloperoxidase, MTrPP: Modified pectin polysaccharide from turmeric, NICD: Notch intracellular domain, NLRP3: Nucleotide oligomerization domain (NOD)-like receptor protein 3, NO: Nitric oxide, NOX4: Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase 4, Nrf2: Nuclear factor erythroid 2-related factor 2, OA: Osteoarthritis, PAI-1: Plasminogen activator inhibitor-1, PCC: Protein carbonyl content, PIVP: Primary influenza viral pneumonia, PGE2: prostaglandin E2, ROS: Reactive oxygen species, RORγt: Retinoic acid-related orphan receptor-γt, SA: serum sialic acid, SOD: Superoxide dismutase, STAT: Signal transducer and activator of transcription, TBARS: Thiobarbituric acid reactive substances, TCA: Trans cinnamaldehyde, TGF-β : Transforming growth factor-β, TIMP-1: Tissue inhibitor of metalloproteinase, TLRs: Toll-like receptors, TQ : Thymoquinone, TRX1: Thioredoxin 1, TRXR1: Thioredoxin reductase 1, VCAM-1: Vascular cell adhesion protein 1

IV. CONCLUSIONS

The modulation by Nrf2 of TRPA1/V1 is still not clear, so more investigation need to be done on this area. In pre-sent pandemic situation more immune boosting is required to beat the COVID-19 infection. From the above study it can be concluded that spices like black pepper, turmeric, clove etc possess antioxidant, immunity boosting proper-ties, anti-inflammatory activities and play vital role against many bacteria, fungus, yeast and also viruses including SARS-COV-2. More data need to be explored about the biochemical compounds present in the Indian spices and their affectivity and mode of action against diseases.

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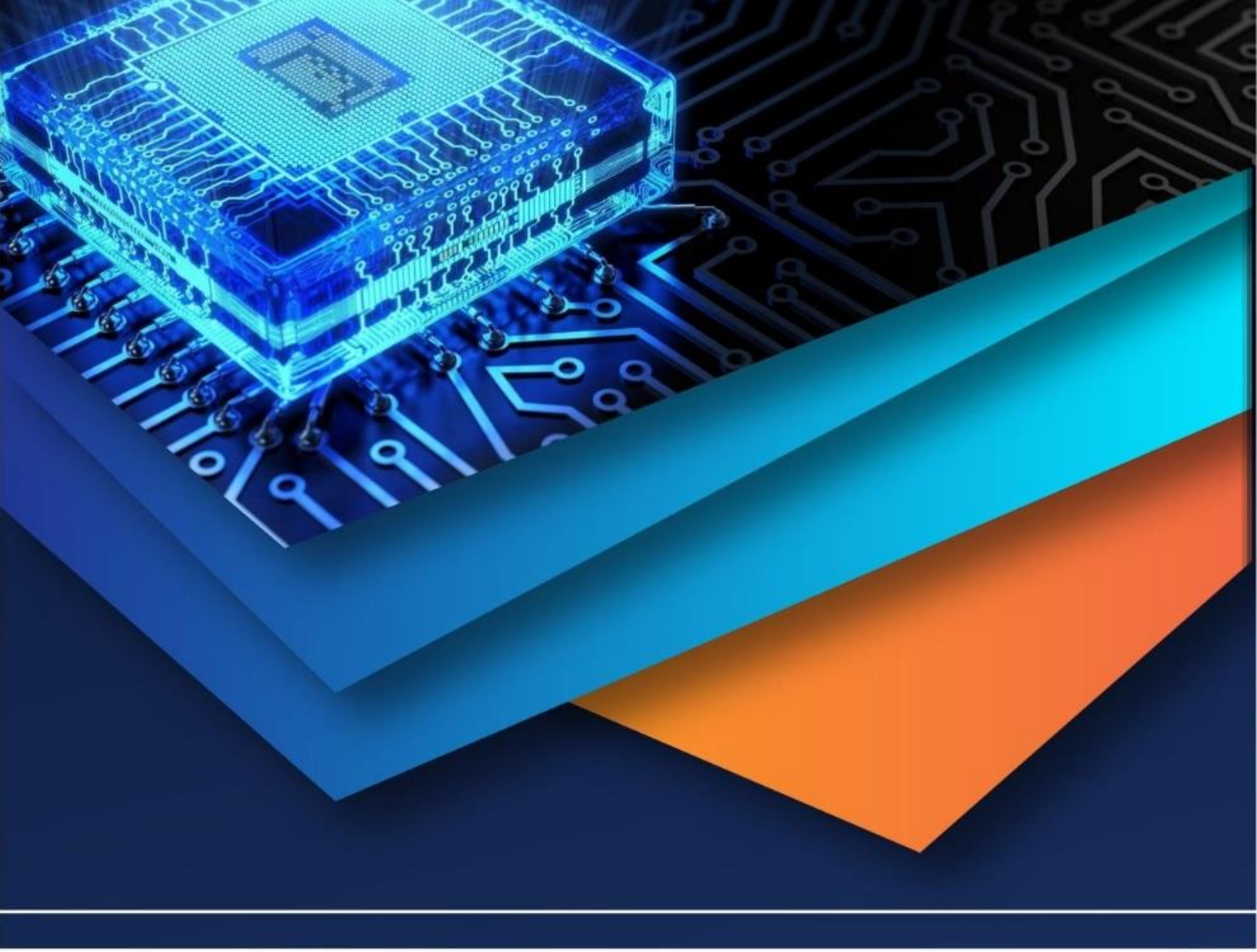

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