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Therapeutic Potential of Natural Pharmacological Agents: Flavonoids against Various Diseases

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ABSTRACT

Flavonoids, a naturally occurring substance that is extensively spread across the plant kingdom, are what give plants their diverse hues in the form of leaves, flowers, fruits, and seeds. These have strong antioxidant effects and are secondary metabolites of plants. Sedative, antioxidant, anticonvulsant, antidepressant, anti-inflammatory, anti-cancer, anti-microbial, antihypertensive, Vasorelaxant, cardiac protective, antidiuretic, antiulcerogenic, anti-fungal, antiviral, Antineoplastic, Neuroprotective, and Hepatoprotective properties are all possessed by flavonoids. Numerous studies have shown that its antioxidant property is primarily responsible for the pharmacological effects indicated above. As a result of their influence on mammalian enzymes such protein kinases, aldose reductase, and alpha-glucosidase flavonoids regulate a number of cellular signaling pathways that get disrupted under pathological situations. Due to their many health benefits, flavonoids are the subject of numerous ongoing studies. A variety of flavonoids are sold as pharmaceutical goods on the market due to their advantages in terms of cost-effective mass manufacture and health advantages. The classification, metabolic, pharmacological, and biological effects of flavonoid supplements sold on the market are the main topics of the current review.

INTRODUCTION

Flavonoids are a class of organic compounds with low molecular weight phenolic compounds that are found in fruit, nuts, vegetables, grains, seeds, stems, roots, flowers, and wine tea as secondary metabolites. [1] Numerous flavonoids, many of which are to the beautiful coloring of flowers, fruit, and vegetation, have been discovered. In nature, more than 4000 flavonoids can be discovered.

Classification and chemical structure

Both in their free state and as glycosides, flavonoids are found. A benzene ring (A) condensed with a six-membered ring (C), which at the 2-position bears a phenyl ring (B) as a substituent, makes up the aglycone portion of flavonoids. C6-C3-C6 is a characteristic of flavonoids. [2] Flavonoids can be categorized structurally based on the benzopyrone saturation and various ring substitutions. The primary classes' structures are displayed in Fig. 1.

Flavonoids can be classified into various classes. [3]

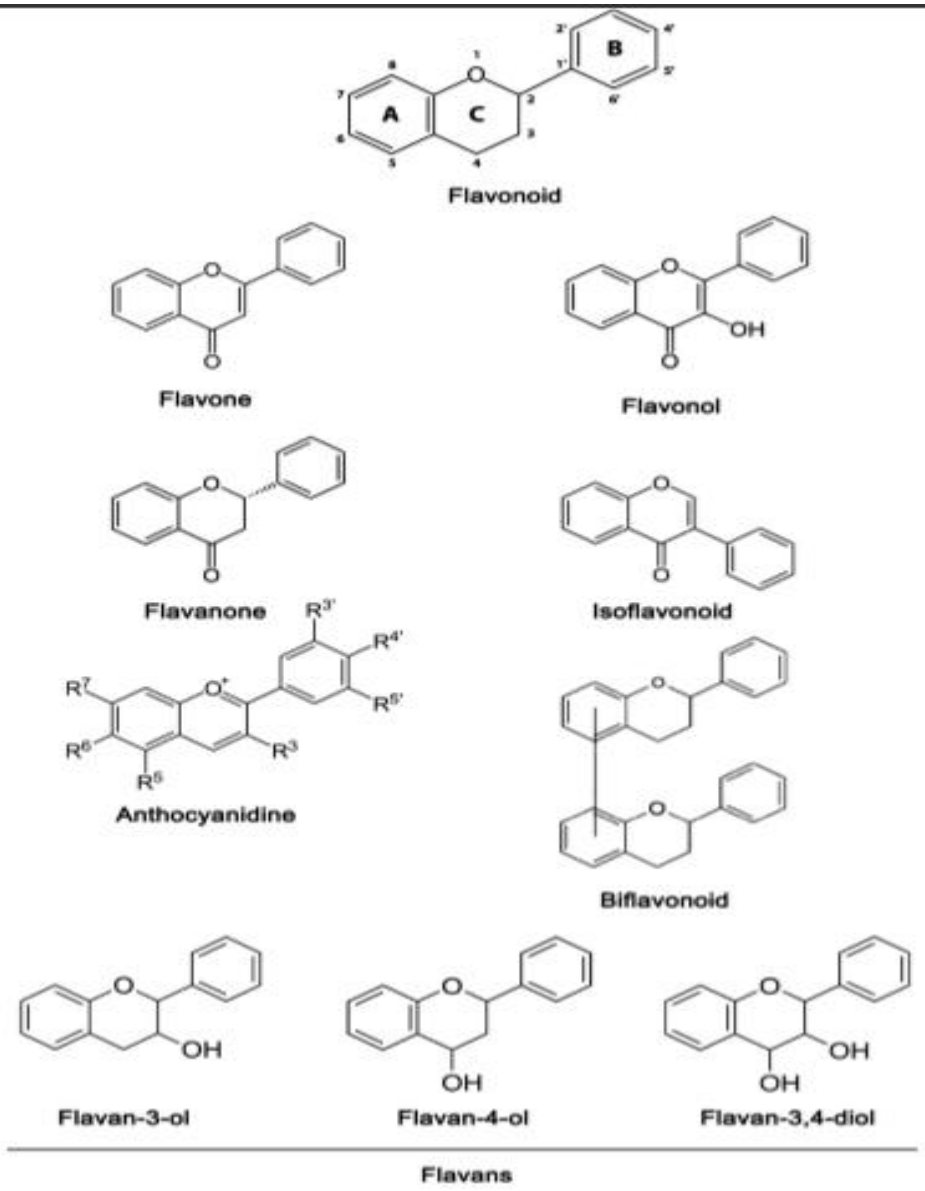

FIG. 1: BASIC STRUCTURE OF FLAVONOID

Hungarian physiologist Albert Szent Gyorgyi first demonstrated the biological activity of flavonoids in 1938. He claimed that the flavonoids in citrus peel had a protective effect against capillary bleeding and fragility. [4,5] There is a wide range of biological activity in flavonoids. Antibacterial, antiviral, anti-atherosclerotic, cardio protective, anti-ulcer genic, antineoplastic, anticancer, mutagenic, antidiabetic, antioxidant, anti-inflammatory, anti-hepatotoxic, anti-aging, hypolipidemic, anti-hypertensive and antiplatelet actions have all been demonstrated in them.

The breakdown of Flavanoids

O- glycosides, which include the common sugars glucose, galactose, arabinose, and rhamnose, are where many dietary flavonoids are found. The beta hydrolysis by pancreatic enzyme is resisted by the presence of sugar moieties. The small intestine's 2-endoglycosidase enzyme can hydrolyze flavonoid glycosides. It has been suggested that lactase phlorizin hydrolase and an unidentified cytosolic enzyme deglycosylate flavonoids and enable conjugation reactions. The position and structure of the sugar moiety in the flavonoid affect the flavonoid's bioavailability. The dosage, food, sex disparity, and the colon's bacteria community all affect absorption. The liver is crucial for the absorption of flavonoids, which are absorbed in the small intestine rather

than the colon. The gut flora affects how flavonoid metabolism is carried out. Microflora cleaves the pyrone ring of the flavonoid, which produces phenyl propionic acid, phenyl acetic acid and inert byproducts. The microflora will remove the sugar moiety from flavonoids during pyrone ring breakage, creating an aglycone moiety that can easily pass through the gut wall. The use of the HPLC technique to analyse flavonoids in urine and faeces reveals signs of methylation, hydroxylation, O-methylation, sulfation, and glucuronization, all of which are byproducts of microbial transformation that happens largely in the liver and intestine.

Flavonoid's pharmacological activity

Wide-ranging biological effects of flavonoids have been linked to them, including anti-cancer, anti-inflammatory anti-hepatocellular, anti-microbial, antiviral, anti-allergic, vasodilatory, and treatment of neurological diseases. Numerous enzymes, including hydrolases, hyaluronidase, alkaline phosphatase, lipase, -glucosidase, and kinase, cAMP phosphodiesterase were reported to be inhibited by them.

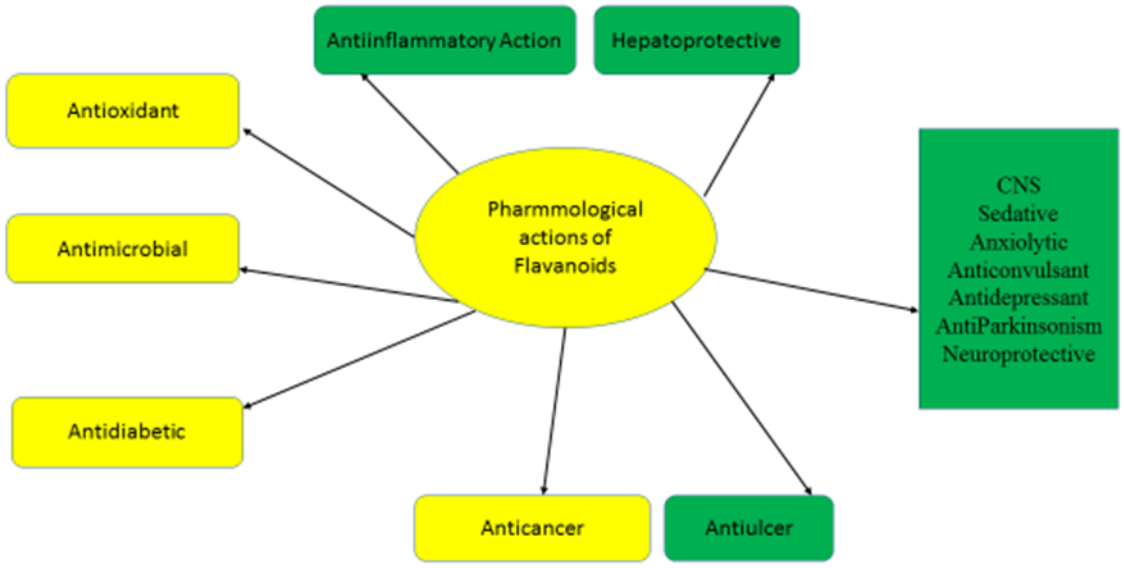

FIG. 3: BROAD SPECTRUM OF ACTIVITIES OF FLAVONOIDS

Flavonoids as antioxidants

Flavonoids' mechanism of action as antioxidants [6, 7] Free-radical scavengers is another name for flavonoids. Their capacity to donate hydrogen was the main cause of the antioxidant action. The high reactivities of the hydroxyl substituents involved in the reaction are principally responsible for the capacity of scavenging free radicals. Free radical levels are rising, which causes an imbalance in the antioxidant defense system and causes oxidative stress. Cells die as a result, resulting in tissue damage.

Central nervous system

Flavonoids are said to activate the Central nervous system through a number of different methods. They bind to the GABA (A) receptor's benzodiazepine site. GABA is an inhibitory neurotransmitter, therefore when a flavonoid bind to the GABA receptor, it has sedative, anxiolytic, and anticonvulsant effects [8]. By preventing monoamine oxidase, A or B from functioning, flavonoids are said to have antidepressant and anti-Parkinsonism effects [9]. By reducing oxidative stress, controlling the kinase signaling cascade, and controlling apoptotic

neuronal death, flavonoids have been shown to have neuroprotective effects in in vitro cells and animal models [10]. As a result of the flavonoids generated from Peltiphyllum pelatum's anticholinesterase action, Alzemiers

Disease can be treated [11]. By reducing NF-B signaling and MAPK phosphorylation, cudrania tricuspidata flavonoids have anti-inflammatory effects [12]. A flavonoid called baicalein, which was extracted from the scutellaria baicalensis plant, protects against neural tissue damage and improves cognitive and behavioural function. Baicalein has been linked by several studies to a reduction in brain infarction caused by focal brain ischemia, mostly as a result of its inhibition of MMP-9 [13].

Cardiovascular system

In diseases like hypertension and stroke, flavonoids have been shown to boost endothelial nitric oxide release and cause blood arteries to relax [14]. Flavonoids are a good source of antioxidants. Hespiridine and naringin are helpful in reducing blood pressure increases associated with ageing, according to studies [15]. Epicatechin, quercetin, and avicularin have been linked to cardioprotective effects [16].

Dyslipidemia

According to experimental models, flavonoids either increase decrease fatty acid synthesis or fatty acid oxidation preventing hepatic steatosis and dyslipidemia [17]. Experimental models have shown that quercetin [18] biochanin-A, isoquercitrin and formononetin are useful at lowering cholesterol. Total flavonoids found in Nelumbo nucifera leaves have been shown to exhibit hypolipidemic action in Wistar rats with hyperlipidemia brought on by a high-fat diet [19].

Diabetes

Numerous flavonoids are said to operate on biological targets implicated in type 2 diabetes such aldose reductase and -glucosidase to have antidiabetic effects [21, 22]. The development of activation of protein kinase C isomers, advanced glycation end products (AGEs) and an increase in hexosamine pathway flux all contribute to the development of diabetic sequelae such neuropathy, retinopathy, and nephropathy. Due to flavonoids' antioxidant properties, it has been demonstrated that they can lessen the harmful effects of hyperglycemia. Quercetin, a flavonoid, has been shown to improve pancreatic islet cell regeneration in people with insulin-dependent diabetes mellitus, increasing insulin release. [23]. Fiestin has been demonstrated to boost the islets' calcium uptake in non-insulin-dependent diabetic mellitus. [24, 25]

Action that reduces inflammation

[26, 27] According to reports, flavonoids have an anti-inflammatory effect, which explains many of their pharmacological effects. Many different mechanisms, such as antioxidant action, inhibition of eicosanoid producing enzymes, and inhibition of pro-inflammatory mediator generation, have been proposed to explain the anti-inflammatory action of flavonoids. Additionally, they control inflammatory cells such mast cells, neutrophils, macrophages, natural killer cells, lymphocytes, and monocytes.

Pain-relieving effect:

[28] Many flavonoids are said to have anti-inflammatory properties. According to studies [27, 28]. hesperidin, apigenin, luteolin, silymarin, and quercetin all have anti-inflammatory properties.

Anticancer

Numerous epidemiological research shown that flavonoids had protective effects against a

variety of cancer types, including pancreatic, lung, breast, and colon [29, 30]. Inactivation of carcinogens, cell cycle arrest, suppression of proliferation, induction of apoptosis, and inhibition of angiogenesis are a few of the mechanisms by which flavonoids are said to have anticancer activity [32, 33]. Multiple studies have shown that kinases such dual specificity tyrosine phosphorylation-regulated kinase 1A (DYRK-1A), glycogen synthase kinase 3 (GSK3), and cyclin-dependent kinases (CDKs) are involved in cancer [34, 35].

TABLE 3: FLAVONOIDS AND THEIR MODE OF ACTION AGAINST CANCER

Flavonoid	Mechanism	References
Quercetin, rutin,	Antiproliferative	[31]
Quercetin, rutin Hepiridin, Silymarin Curcumin, Naringenin, Quercetin Apigenin Luteolin	Action in different Cell Line Inhibit Angiogenesis Inhibit CYP3 A4 Cell Cycle arrest	[36] [37] [38]

Various research works was carried out to prove the anticancer properties of flavonoids. [39, 40]

Respiratory tract

The positive effect of flavonoids in respiratory tract diseases is due to their anti-inflammatory, antioxidant, anti-allergic, and antispasmodic properties [41]. Apigenin, silibinin, and wogonin are just a few of the flavonoids that are said to modulate airway mucus secretion [20].

Digestive tract

Flavonoids are said to be effective in addressing issues with the digestive tract. Numerous studies have shown that flavonoids have anti-ulcer, Hepatoprotective, and antidiarrheal properties. In an ethanol-induced animal model, naringenin and apigenin are said to have an antiulcer effect. The following mechanism underlies flavonoids' ability to prevent ulcers:

Protein kinase, c AMP, COX, and protein phosphorylation are all inhibited.

Genitourinary tract

For conditions involving prostatitis and urinary tract infections that affect the genitourinary tract, many herbal products that contain flavonoids are recommended. In the preparations for the bladder and uterus, flavonoids are said to have antispasmodic effects.

Skin conditions

Numerous studies have shown that flavonoids have positive effects on skin conditions, primarily because of their anti-inflammatory, antioxidant and soothing properties.

Antimicrobial effects most flavonoids have been shown to have antimicrobial properties and are utilized as therapeutic agents in a variety of preparations.

Antiulcer Activity

Recent research suggests that flavonoids have antiulcerogenic properties. Ocimum basilicum (Labiatae) flavonoid glycosides reduced the ulcer index and prevented pepsin and stomach acid output in rats with aspirin-induced ulcers. Rats exposed to intraperitoneal doses of quercetin, rutin, and kaempferol (25–100 mg/kg) showed reduced stomach damage brought on by acidified ethanol. [42]

Antineoplastic Activity

There are enough flavonoids that have shown anti-cancer action. Recent reviews have emphasized this behaviour several times. Additionally, cell proliferation was inhibited by the flavonoids kaempferol, catechin, toxifolin, and fisetin. Genistein, an isoflavone, was found to have a significant impact on the antileukemic efficacy of 28 naturally occurring and synthetic flavonoids on human promyelocytic leukemic HL-60 cells. [43,44].

Antiviral Activity

Since the 1940s, it has been known that naturally occurring flavonoids have antiviral properties, but it has only lately been attempted to synthetically alter natural molecules to increase their antiviral properties. There have been reports of the antiviral properties of quercetin, morin, rutin, dihydroquercetin (taxifolin), apigenin, catechin, and hesperidine against some of the 11 different types of viruses. The non-glycosidic molecules seem to have the antiviral action, and it seems that hydroxylation at the 3-position is necessary for antiviral activity [45].

Antimicrobial Activity

Researchers have also looked at the antibacterial, antifungal, and antiviral properties of flavonoids and phenolic acid esters. According to some reports, quercetin totally prevents Staphylococcus aureus from growing. None of the examined flavonols or flavonolignans exhibited inhibitory effect on microbes, although the majority of flavonones with no sugar moiety did. [45].

Antifungal Activity

When evaluated for fungistatic action against Deuterophoma tracheiphila, several flavonoids extracted from tangerine orange peelings were shown to be effective; langeritin and nobiletin showed weak activities and strong activities, respectively, whereas hesperidin could modestly increase fungal growth. Aspergillus candidus strains initially developed chlorflavonin, the first antifungal antibiotic of the flavonoid type to contain chlorine. [46]

Hepatoprotective Activity

Phalloidin (the poisonous component of the mushroom Amanita phalloides), CCl4, galactosamine, ethanol, and other chemicals can all cause severe and potentially fatal liver damage. Additionally, discovered to have Hepatoprotective properties are flavonoids. The flavonoid derivatives silymarin, apigenin, quercetin, and Naringenin were examined as potential therapeutic agents against microcrystal LR-induced hepatotoxicity, and it was discovered that silymarin was the most successful one [47]. In experimental cirrhosis, the flavonoids rutin and venoruton demonstrated regenerative and Hepatoprotective properties. [48].

Vasorelaxant Agent

By improving the vasorelaxant process and lowering arterial pressure, flavonoids may prevent endothelial dysfunction [49,50]. A significant factor in the onset of cardiovascular diseases, as well as the main contributor to atherosclerosis and arterial thrombus formation, is endothelial dysfunction [51]. 1. Consuming flavonoids can help prevent atherosclerosis and hypertension, two common cardiovascular diseases. [52,53].

Green Tea Extract Flavonoids against influenza A, B virus

The Ortho-myxoviridae family of viruses, which includes influenza A and B viruses, are members of the viral genus alpha- and beta-influenza virus. They are RNA viruses, and the envelope that contains their genetic material.

Green tea extracts and their constituent flavonoid epigallocatechin

The influenza virus strains employed by Imanishi et al. [54] in their test of GTE's inhibitory impact in the Madin-Darby canine kidney (MDCK) were, H3N2 Aichi strain, PR8 (H1N1 subtype) and Sing influenza virus-strain. These influenza virus strains were multiplied in MDCK cell culture at a rate of 5 PFU per cell. MTT assay used to assess GTE's cytotoxicity [55] There are several flavonoids in GTE, and about 44% of them are flavonoids called epigallocatechin (-) EGC. EGC was then examined for its anti-influenza-A, B action as a key component of GTE. For MDCK cells, the determined CC50 value of (-) EGC was 400 g/ml. This finding demonstrates that the primary antiviral agent inhibiting the early viral infection phase of the influenza-A, B virus numerous strains is the flavonoid epigallocatechin (-) EGC. [54].

Baicalein flavonoid mitigate the Japanese encephalitis virus

Japanese encephalitis virus is a positive-sense single-stranded RNA virus that is enclosed. Its genome is 11 kb in size. Japanese encephalitis virus is a flaviviridae (arthropod-borne) virus [56]. Japanese encephalitis virus is the agent responsible for viral encephalitis in people and can produce symptoms ranging from fever to fatal infections, with 30,000–50,000 cases of it occurring each year in children around the world. Japanese encephalitis virus infection is widespread in countries throughout East and South Asia. According to estimates, Japanese encephalitis virus infections have a fatality rate of about 30% and leave half of those who survive with lifelong neurological damage. These results show that baicalein has potent antiviral action mitigate the different Japanese encephalitis virus replication stages when used in vitro. [57].

Quercetin, Baicalin Flavonoids mitigate dengue virus type-2

The Flavivirus class of the Flaviviridae family includes the Dengue virus (DENV). Its single positive-stranded RNA genome is the source of a number of human diseases, including dengue and dengue hemorrhagic fever (DHF) (DF). Its four genotypes are DENV-2, DENV-1and DENV-4. DENV-3. These viruses are passed from people to mosquitoes of the Aedes agypti and Aedes albopictus species [58]. These findings demonstrate that quercetin significantly inhibits intracellular DENV virus replication and possesses anti-DENV-2 replication capabilities, but not DENV entry or attachment into the host cell [59]. Further research revealed that baicalin, with an IC50 of 13.50 g/ml, also significantly inhibited DENV-2 replication at a concentration of 50 g/ml [60].

Baicalein, fisetin and quercetagetin Flavonoids mitigate the Chikungunya virus

Chikungunya virus is a member of the Togaviridae family of viral genera. It is an enclosed virus with a positive sense single stranded RNA genome that is approximately 11.8 kb in size. Aedes aegypti and Aedes albopictus are two types of mosquitoes that carry this virus from them to their human hosts. Over two million people have been impacted by various CHIKV epidemics, which have also contributed to hundreds of fatalities globally [61]. These findings suggest that the studied flavonoid compounds had greater intracellular anti- Chikungunya virus activity when compared to the IC50 value of ribavirin, a positive control with defined anti-Chkungunya virus activity (11.07 g/ml). [62].

Ladanein, Naringenin, Quercetin, Silymarin, Apigenin, Sorbifolin and pedalitin Flavonoids mitigate hepatitis C virus (HCV)

More than 3% of the world's population is infected with the hepatitis C virus which can also cause acute and chronic hepatitis with symptoms ranging from a minor illness that lasts a few weeks to a devastating, lifelong illness [65]. It is the primary contributor of liver cancers. Since HCV is a blood-borne virus, exposure to small amounts of infected blood is one of the most frequent ways it is spread. This can happen as a result of injecting drugs, hazardous injection techniques, unscreened blood transfusions, and risky sexual activities, which can expose one to

blood that is infectious [63]. Many researches have shown that HCV secretion is connected to lipid metabolism and that it spreads throughout the host by attaching to different lipoproteins like (VLDL),(LDL), and apolipoprotein AII (ApoAII). While acyl-coenzyme A: cholesterol acyltransferase (ACAT2) transcription was reduced by 55%, hepatic gene transcription was altered by Naringenin and decreased by 57%. This suggests that Naringenin can prevent the release of hepatitis C virus by preventing the release of apoB and VLDL lipoproteins. [64].

Baicalin (BA) flavonoid mitigate HIV-1 virus

Two forms of Lentiviruses (a subclass of retroviruses) that cause infections in humans are the human-immunodeficiency (HIV) viruses. They eventually lead to immunodeficiency syndrome (AIDS), a condition in which the immune system steadily deteriorates and makes it easier for malignancies and deadly opportunistic infections to spread and worsen the situation. It is an enclosed RNA virus with a single-stranded, positive-sense genome. An enzyme known as reverse transcriptase transforms the viral RNA genome into dsDNA in the host cell upon entry. [66].

3-methyl quercetin, 6-chloro-3-hydroxyflavone-4′- carboxylic acid Flavonoids, 6-chloro-4′-oxazolinyl and mitigate Poliovirus

The primary cause of polio (poliomyelitis) is the poliovirus (PV), which is a serotype of enterovirus C. It belongs to the family Picornaviridae. The RNA genome of the poliovirus is single-stranded positive-sense. Its genome is around 7.5 kb long and has a protein-based capsid. Humans become infected by PV when it binds to the cell's outer CD155 receptor. [67].

Kaempferol and juglanin flavonoids mitigate SARS-CoV-1

The SARS-CoV-1 virus was the root of the 2002–2004 SARS outbreak. Lung epithelial cells are infected by a single-stranded, enclosed, positive-sense RNA virus. The virus enters the host cell by tying up with the ACE-2 receptor. Mostly people and bats are affected by it [46]. Researchers have demonstrated that the SARS-1 coronavirus's ORF-3a-coded viral protein generates a cation-selective ion channel. The virus uses these channels, which are subsequently produced in the infected host cells, to release its offspring from the host cell and infect more host cells. Drugs that block the viral coded channels prevent the virus from being released from infected cells, which prevents the virus from spreading to other host cells. [68].

Genistein flavonoid mitigate HIV virus vpu-ion channel

Ion-selective channels are created by viruses' genes and subsequently incorporated into the host cells' membranes. The process by which viruses are released from infected cells includes the activation of such channels. The discharge of viruses can be stopped by inhibiting these viral ion channels. Viral-protein-U (Vpu), a viral ion channel that plays a variety of tasks including releasing viruses, is encoded for by HIV-1. The flavonoid Genistein was utilized by Sauter et al. to block this ion-channel. In order to express the HIV-associated Vpu of the virus, Xenopus oocyte cells from female Xenopus laevis clawed toads were treated with 5–40 ng of cRNA one–three days prior to the addition of Genistein. Then, using voltage-clamp techniques, its effects on HIV-1 viral protein U (Vpu) were examined. Other flavonoids, such as quercetin, kaempferol, and (-) EGC, were initially tried to block this ion channel in addition to Genistein, but at concentrations of 20 M, they could only decrease the Vpu-Mediated current by 10%. Genistein started to work as a treatment when it started to suppress the Vpu-mediated current. The ion-channel was observed to be 50% inhibited at a concentration of 80 M. These findings suggest that creating Genistein derivatives could result in compounds that are more active and bioavailable than Genistein itself. For instance, the glucoside Genistein derivative exhibited the same inhibitory properties as Genistein. HIV-1 must be released, and if VPU-channel activity is inhibited, the virus cannot be released and infect further host cells. [69].

Quercetin mitigate cardio virus infection in mice model

The Picornaviridae family includes the several varieties of cardio viruses, each of which has a single-stranded RNA genome and is not enclosed. Its many forms can infect mice and induce neurological disorders, including encephalomyelitis and acute gastroenteritis in people [50]. When in vitro tests were conducted on L-929 cells infected with a cardio virus, it was discovered that quercetin had no effect on the cardio virus in the lab and only shown a protective effect in vivo. [70].

Quercetin Flavonoids mitigate rhinovirus

(RV) is a member of the Picornaviridae family of viruses, which are non-enveloped and have a single-stranded RNA genome. Its positive-sense single-stranded RNA genome is around 7.1–7.2 kb in size. Humans who are infected with this virus will get upper respiratory tract infections. Researchers found that it worsens the condition in people with asthma and chronic obstructive pulmonary disease (COPD). [71]

Epigallocatechin gallate. Isoquercitrin. Myricetin and quercetin Flavonoids mitigate Zika virus

The Flaviviridaee viral family and the Flavivirus class include the Zika virus (ZIKV). Its genome is 10.7 kb in size. It is an enclosed virus with a single-stranded, positive-sense RNA genome [72–74]. Two kinds of Aedes mosquitoes— Aedes albopictus and Aedes aegypti —transmit this virus. It results in microcephaly and other brain abnormalities in newborn children. [75].

Pectolinarin, herbacetin and rhoifolin. Amentoflavone Flavonoids mitigate coronavirus 3CLprotease

(CoVs) are positive-sense, single-stranded RNA viruses that are enclosed. Its genome ranges from 27 to 30 kbp in size. By adhering to angiotensin-converting enzyme 2, these viruses mostly infect lung epithelial cells (ACE-2). It infects a variety of species, including pigs, birds, bats, and people. Many viral diseases, pandemics, and epidemics including MERS, SARS-1, and SARS-CoV-2 have CoVs as their primary etiological agents. [76,77].

Quercetin 7-rhamnoside mitigate porcine epidemic diarrhea virus (PEDV)

The Alphacoronavirus class and Coronaviridae family of viruses are the home to the Porcine Outbreak Diarrhea Virus (PEDV). It has a single-stranded, positive-sense RNA genome that is 30 kb in size and is an enclosed virus. The PEDV virus causes acute diarrhea and/or vomiting, dehydration, and significant mortality in pigs [78]. Choi et al. [79] examined the antiviral activity of quercetin 7-rhamnoside using PEDV, which was propagated in Vero cells. The PEDV replication mechanism was severely hindered by quercetin 7-rhamnoside. It prevented PEDV proliferation in its initial stages. Quercetin 7-rhamnoside has an IC50 of 0.014 g/ml. It had a CC50 of 100 g/ml when tested against Vero cells. [79].

Silymarin (flavonolignan complex) mitigate influenza-A virus

The Orthomyxoviridae family of viruses, which includes influenza A and B viruses, are classified as alpha- and beta-influenzaviruses. They are RNA viruses, and the envelope that contains their genetic material. As respiratory pathogens, influenza-A viruses can cause acute respiratory illnesses in humans, such as fever, cough, and so forth. Since 1918, this virus has been the root of numerous outbreaks and pandemics. According to the World Health Organization, these yearly epidemics are predicted to cause between 3-5 million cases of acute disease and 290,000–650,000 cases of respiratory deaths globally. These findings demonstrate that silymarin was more effective at preventing virus infection than the commercially available drug oseltamivir. [80].

Flavonoids mitigate coronavirus 3CLprotease

Coronaviruses (CoVs) are positive-sense, single-stranded RNA viruses that are enclosed. Its genome ranges from 27 to 30 kbp in size. By adhering to angiotensin-converting enzyme 2, these viruses mostly infect lung epithelial cells (ACE-2). It infects a variety of species, including pigs, birds, bats, and people. Many viral diseases, and epidemics and pandemics including MERS, SARS-1, and SARS-CoV-2 have CoVs as their primary etiological agents. [76,77].

CONCLUSION

This review demonstrates that flavonoids are effective against cancer, diabetes, dyslipids, skin, viruses, liver respiratory, cardiovascular, Vasorelaxant and digestive disorders as well as neurological diseases. It has also been demonstrated to have antiviral, antifungal, antimicrobial and antibacterial properties. The majority of flavonoids' pharmacological effects are primarily brought about by their antioxidant activity. Worldwide, several flavonoids are used as dietary supplements.

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