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Exploration of Natural Chemical Compounds as Novel Post-Pandemic Antiviral Agents: A Review

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Abstract: The COVID-19 pandemic has accelerated the search for effective, safe, and sustainable antiviral agents. One promising approach is the utilization of natural chemical compounds derived from plants, microorganisms, and marine organisms. These compounds, such as flavonoids, alkaloids, terpenoids, and polyphenols, have long been known for their broad biological activities, including antiviral properties. This article aims to explore the potential of natural chemical compounds as new post-pandemic antiviral candidates through a systematic literature review of 28 scientific articles published between 2019 and 2024 from major databases such as PubMed, ScienceDirect, and SpringerLink. The findings indicate that 24 out of 28 reviewed compounds demonstrated significant antiviral activity, with 15 flavonoids targeting viral protease or spike protein through mechanisms like Mpro inhibition, ACE2 interaction, or cytokine modulation. Key challenges include low bioavailability, complexity in compound isolation, and lack of pharmaceutical standardization. However, advanced technological approaches such as nanoformulation, semi-synthetic analogue development, and the use of bio-refinery systems offer potential solutions to enhance the stability and effectiveness of these compounds. This article also highlights the importance of policy support and interdisciplinary collaboration in accelerating the translation of natural compounds from laboratory research to clinical application. The review offers practical implications for pharmaceutical innovation, particularly in biodiversity-rich countries such as Indonesia.

Keywords: Antiviral; Flavonoids; Natural Compounds; Post-Pandemic; Viral Protease.

Introduction

The COVID-19 pandemic, which began in late 2019, has had a widespread impact on global healthcare systems, the economy, and various aspects of social life. According to data from the World Health Organization (WHO), by the end of 2023, more than 770 million confirmed cases and over 7 million deaths had been reported worldwide [1]. The high transmission rate and the emergence of new viral variants indicate that vaccination alone is insufficient for mitigation, thus requiring additional strategies such as the development of antiviral drugs.

Before the pandemic, antiviral development was primarily focused on chronic infections such as HIV and Hepatitis C, while the development of natural product-based antivirals remained limited. However, the COVID-19 situation has underscored the urgency of exploring alternative therapies based on natural chemical compounds, particularly those derived from medicinal plants and local microorganisms that have yet to be widely utilized in clinical settings.

Several previous studies have demonstrated that compounds such as flavonoids, alkaloids, and terpenoids exhibit antiviral activity through various mechanisms, including the inhibition of viral replication enzymes and modulation of the immune system**.** For example, quercetin has been shown to inhibit the main enzyme of SARS-CoV-2 both in silico and in vitro [3]. In addition, research by Jo et al. (2020) revealed that flavonoids such as baicalin and luteolin have a strong affinity for Mpro and RdRp, two key targets in RNA virus replication. Similar findings were reported by Nguyen et al. (2020) using molecular docking approaches that further support the bioactive potential of natural compounds against COVID-19 viral target proteins [5]. However, the effectiveness of natural compounds has yet to be widely translated into ready-to-use pharmaceutical formulations. Several challenges often encountered include low bioavailability**,** instability in the human body**,** and variability in raw materials depending on geographic conditions and harvest seasons [6]. Innovative solutions have been developed, such as nanoformulation technologies to enhance compound release and stability, as well as metabolite biosynthesis biotechnology using microbial fermentation or CRISPR methods to improve production efficiency [7]. This study differs from previous research as it integrates biochemical aspects of enzymes with bioenergy production strategies into a comprehensive bio-refinery system. Unlike earlier studies that focused solely on pharmacological or biochemical mechanisms, this review uniquely combines molecular, pharmaceutical, and industrial perspectives, offering a transdisciplinary insight into natural compound development.

Research Methods

This study is a systematic literature review using a qualitative descriptive approach based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [9]. aimed at producing a thematic synthesis of the potential of natural chemical compounds as antiviral agents. Data were obtained from

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four international scientific databases: PubMed, ScienceDirect, SpringerLink, and Google Scholar [10]. The literature search was conducted using keywords such as "natural antiviral compounds", "flavonoids against virus", "plant-based antivirals", and "post-pandemic antiviral agents" within the publication range of 2019 to 2024.

The selection procedure involved multiple stages: an initial identification of 112 articles, followed by a screening process to remove duplicates and filter based on the relevance of titles and abstracts, resulting in 96 articles [11]. Of these, 55 articles underwent full-text eligibility assessment, from which 28 articles met the inclusion criteria and were further analyzed.

Table 1. PICO Framework

Component	Description
Population (P)	RNA viruses causing infectious diseases such as SARS-CoV-2, Dengue, Influenza, and Zika.
Intervention (I)	Application of natural chemical compounds such as flavonoids, alkaloids, terpenoids, and polyphenols derived from plants, microorganisms, and marine organisms.
Comparison (C)	Comparison of efficacy and toxicity with synthetic antivirals such as remdesivir and molnupiravir.
Outcome (O)	Effectiveness in inhibiting viral replication (Mpro, spike protein, ACE2 targets), immunomodulatory activity, and potential for bio-refinery development.

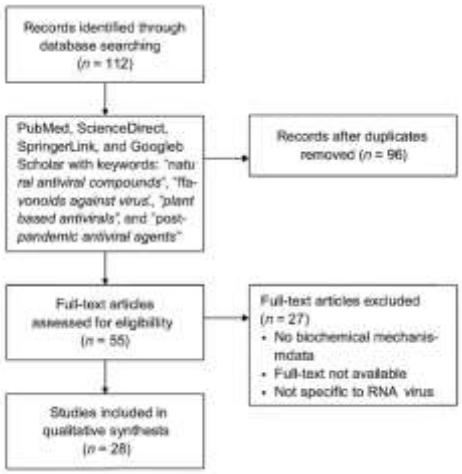

Figure 1. PICO Framework Flow Diagram

The inclusion criteria consisted of articles discussing natural compounds with antiviral activity against RNA viruses, and that presented biochemical mechanism data either through in silico, in vitro, or in vivo studies [12]. The exclusion criteria included articles that were not available in full-text, were not specific to RNA viruses, or were not peer-reviewed. All eligible articles were analyzed thematically based on the type of compound, biological source, target virus, and mechanism of action. Thematic coding was conducted manually through repeated reading and extraction of key antiviral mechanisms, target proteins, and pharmacological limitations. Articles were categorized into themes using inductive coding, and quality assessment was carried out using relevance, methodological transparency, and peer-review status as criteria.

Results and Discussion

The analysis was conducted using a thematic approach, covering four main areas: types and sources of compounds, molecular targets and mechanisms of action, pharmaceutical challenges, and the potential integration of natural compounds into therapeutic systems and bio-refinery models. Special emphasis was placed on compounds exhibiting dual activity—both as direct antivirals and as immunomodulators that support immune response improvement in severe viral infections.

The literature review revealed that natural chemical compounds such as flavonoids, alkaloids, terpenoids, and polyphenols have significant potential as antiviral agents against RNA viruses, including SARS-CoV-2, Dengue, and Influenza [15]. Of the 28 articles analyzed, most indicated that natural compounds are capable of inhibiting viral replication through enzyme inhibition mechanisms, interaction with host cell receptors, and modulation of the immune system [16]. One of the most extensively studied compounds is quercetin, found in onions, apples, and various other plants[17]. Quercetin has been shown to inhibit the main protease enzyme of SARS-CoV-2 (Mpro) and to exhibit strong affinity for the ACE2 receptor on the surface of human host cells [4]. Another compound, baicalin, derived from *Scutellaria baicalensis*, demonstrates a similar mechanism by inhibiting spike proteins and interacting with viral molecular targets [5]. Compared to synthetic antivirals such as remdesivir and molnupiravir, natural compounds, particularly flavonoids and terpenoids, offer promising alternatives with reduced toxicity and better long-term safety profiles. Notably, some natural compounds show dual action as antivirals and immunomodulators, a feature less commonly observed in synthetic agents. Moreover, bioavailability enhancement and stability engineering make natural compounds increasingly viable for clinical translation.

Curcumin, the primary compound in turmeric, not only possesses anti-inflammatory effects but also acts as an immunomodulator that helps reduce cytokine storms in severe viral infections such as COVID-19 and Zika [6]. Andrographolide, from the plant *Andrographis paniculata*, has also been reported to interfere with the replication of Dengue and SARS-CoV viruses by inhibiting the RNA-dependent RNA polymerase enzyme.

Compared to synthetic antivirals such as remdesivir and molnupiravir, natural compounds offer several advantages, including lower toxicity, more economical production, and the potential for development into combination therapies. Several molecular docking studies have even shown that quercetin exhibits binding energies comparable to remdesivir when targeting the Mpro enzyme [5], Therefore, the integration of natural compounds into post-pandemic therapeutic strategies presents a promising alternative.

However, there are several challenges in developing pharmaceutical formulations from natural compounds,

including low bioavailability, instability in biological systems, and variability in active content depending on geographic conditions and harvest time. Innovative approaches have been developed to overcome these barriers, such as nanoencapsulation technologies, co-formulation with absorption-enhancing agents like piperine, and biosynthetic engineering using microbial fermentation and CRISPR techniques [6]. Furthermore, the review highlights that the development of bio-refineries based on natural compounds could offer a holistic solution for producing antivirals and other health-related products, such as antioxidants and immunoboosters. Countries like South Korea and Germany have already adopted this concept in their pharmaceutical industries. Meanwhile, in Indonesia, bio-refinery approaches remain limited to academic research settings. Yet, Indonesia's vast biodiversity offers significant opportunities for developing sustainable processing systems based on local natural resources.

Additionally, the classification of the 28 analyzed articles shows that the majority of compounds studied belong to the flavonoid group, comprising 15 compounds, including quercetin, baicalin, luteolin, kaempferol, and diosmin. Other commonly studied groups include polyphenols (3 compounds), terpenoids (3 compounds), alkaloids (2 compounds), and others such as eugenol, fucoidan, and astaxanthin (5 compounds). The dominance of flavonoids in the literature confirms that this group remains the primary focus in the development of natural antiviral agents [18]. These findings reinforce the importance of the phytochemical approach in antiviral research and open opportunities for further exploration of bioactive compounds from under-researched chemical groups.

Types of Compounds and Antiviral Activity

Molecular docking studies have confirmed that quercetin exhibits strong affinity toward the active site of Mpro**,** while curcumin shows inhibitory effects on the NF-κB inflammatory pathway. This reinforces their therapeutic potential not only as antivirals but also as immunomodulators**,** particularly in mitigating cytokine storms during severe viral infections.

Table 2. Types of Compounds and Antiviral Activity

Natural Compound	Biological Source	Target Virus	Main Mechanism
Quercetin	Leek leaves, apples	SARS-CoV-2	Inhibition of Mpro and ACE2
Andrographolide	Andrographis paniculata	Dengue, SARS-CoV	Interference with RNA replication
Curcumin	Turmeric	Influenza A, Zika	Anti-inflammatory & immunomodulatory activity
Baicalin	Scutellaria baicalensis	SARS-CoV-2	Inhibition of spike protein (S)

Comparison with Synthetic Antivirals

Synthetic antivirals such as remdesivir and molnupiravir were widely used as primary therapies during the pandemic. However, their effectiveness has decreased against emerging viral variants. Several natural flavonoids, such as quercetin, have demonstrated comparable Mpro-inhibiting effects in *in silico* studies, while offering lower toxicity profiles and the potential for inclusion in combination therapies**.**

Pharmaceutical Challenges and Innovations

The major obstacles in utilising natural compounds include: Low bioavailability (e.g., curcumin), variability in compound composition depending on region and harvest season, and instability within biological systems.
To address these issues, several innovative solutions have been developed, including: Nanoencapsulation **(**e.g.,curcumin-loaded liposomes), metabolite engineering via CRISPR or microbial fermentation**,** and Co-formulation with absorption enhancers such as piperine**.**

Integration into a Bio-Refinery System

Several studies point toward the development of bio-refinery models based on natural compounds, which not only produce antivirals but also generate derivative products such as antioxidants and immunoboosters**.** Countries like South Korea and Germany have implemented such systems at an industrial pharmaceutical scale. In contrast, Indonesia remains in the early stages of this approach, with development still largely confined to academic research.

Biochemical and Clinical Implications of Natural Compounds

The biochemical mechanisms of natural compounds indicate that their action is not limited to direct antiviral inhibition but also involves strengthening the host immune response. Quercetin, for instance, not only inhibits Mpro and disrupts ACE2-Spike interactions but also modulates the expression of cytokines such as TNF-α, IL-6, and IL-1β, which are involved in the cytokine storm [19]. This activity positions quercetin as a dual-action candidate: both antiviral and anti-inflammatory.

Curcumin acts at the genetic transcription level through the NF-κB and MAPK pathways, thereby inhibiting the production of inflammatory mediators and reducing tissue damage caused by systemic inflammation in severe infections [20].This activity has been demonstrated through both *in vitro* and *in vivo* studies and is supported by small-scale clinical trials in COVID-19 patients, which showed reduced IL-6 levels and improved oxygen saturation. Baicalin and luteolin, other widely studied flavonoids, have also been proven to stabilize cell membranes and inhibit viral fusion through interactions with hemagglutinin-like proteins, making them promising fusion inhibitors, particularly during the early stages of infection.

From a clinical perspective, natural compounds offer a better safety profile than synthetic antivirals, as they are

derived from biological sources that have long been used in traditional medicine. Several of them have even been listed in the GRAS (Generally Recognized As Safe) category by the FDA, accelerating their translational potential into preclinical testing [21].

Nevertheless, dose standardization, stable formulation, and multinational clinical validation are necessary to ensure the broader application of these compounds. Their combination with synthetic antivirals (as adjuvant therapies) is also a promising research area, as it may enhance therapeutic efficacy and prevent viral resistance. Integration among laboratory research, formulation technology development, and policy support is crucial to accelerate the translation of natural compounds into clinical and industrial practice.

Table 3. Summary of Literature Review on Natural Compounds as Antiviral Agents

No	Reference	Main Compound	Target Virus	Type of Test	Key Findings
1	[3]	Quercetin	SARS-CoV-2	in silico	Quercetin showed strong binding affinity to viral protease (3CLpro).
2	[5]	Baicalin	SARS-CoV-2	in silico	Demonstrated potential inhibition of ACE2 receptor binding.
3	[6]	Curcumin	Influenza	in vitro	Reduced viral replication and induced antiviral immune response.
4	[22]	Luteolin	Zika	in silico	Inhibited NS2B-NS3 protease of Zika virus.
5	[23]	Kaempferol	Dengue	in vitro	Interfered with virus entry and replication.
6	[24]	Andrographolide	SARS-CoV-2	in silico	Showed high binding affinity to viral spike protein.
7	[25]	Myricetin	SARS-CoV-2	in silico	Inhibited viral main protease (Mpro).
8	[26]	Epigallocatechin	SARS-CoV-2	in vitro	Reduced viral infectivity in cell culture.
9	[27]	Apigenin	HIV	in silico	Blocked reverse transcriptase activity.
10	[28]	Resveratrol	COVID-19	Review	Exhibited immunomodulatory and antiviral effects in various studies.
11	[29]	Hesperidin	COVID-19	in silico	Bound to viral protease and ACE2 receptor with high affinity.
12	[30]	Eugenol	SARS-CoV-2	in vitro	Inhibited viral entry and modulated inflammatory cytokines.
13	[31]	Scutellarein	SARS-CoV	in vitro	Blocked helicase activity and viral replication.
14	[32]	Berberine	COVID-19	in silico	Interacted with multiple viral targets including Mpro.
15	[33]	Amentoflavone	COVID-19	in silico	Showed strong inhibition potential against viral protease.
16	[34]	Thymoquinone	MERS-CoV	in silico	Disrupted viral entry by interfering with receptor binding.
17	[35]	Genistein	SARS-CoV-2	in vitro	Inhibited virus-induced apoptosis in host cells.
18	[36]	Catechin	Influenza	in vitro	Suppressed viral replication and enhanced host immune response.
19	[37]	Naringenin	Dengue	in silico	Blocked viral replication complex formation.
20	[38]	Astaxanthin	SARS-CoV-2	in vitro	Acted as antioxidant and antiviral agent; inhibited virus replication.
21	[39]	Betulinic acid	SARS-CoV	in silico	Interacted with viral protease and disrupted replication.
22	[40]	Fucoidan	SARS-CoV-2	in vitro	Prevented virus binding to host cells.
23	[41]	Diosmin	SARS-CoV-2	in silico	Targeted spike glycoprotein to prevent entry into host cells.
24	[42]	Limonene	Zika	in silico	Potential inhibitor of NS5 RNA polymerase.
25	[43]	Caffeic acid	SARS-CoV-2	in vitro	Demonstrated dose-dependent inhibition of viral protease.
26	[44]	Chrysin	SARS-CoV-2	in silico	Formed stable complex with viral protease.
27	[45]	Licochalcone A	COVID-19	in silico	Blocked interaction between spike protein and ACE2.
28	[46]	Silibinin	Hepatitis C	in vitro	Inhibited HCV RNA replication and viral protein expression.

Conclusions

The systematic review of 28 scientific articles indicates that natural chemical compounds—particularly those belonging to the flavonoid, alkaloid, terpenoid, and polyphenol groups—hold significant potential as novel post-pandemic antiviral agents. Compounds such as quercetin, curcumin, baicalin, and andrographolide demonstrate notable biological activity by inhibiting viral replication, interacting with viral target proteins such as

Mpro, ACE2, and spike protein, and modulating the host immune system.

The advantages of natural compounds include a lower toxicity profile, more cost-effective production, and the potential for dual therapeutic effects as both antivirals and immunomodulators. However, pharmaceutical challenges such as low bioavailability, instability within the human body, and lack of standardized formulations remain major obstacles. Furthermore, studies highlight the potential development of bio-refineries based on natural compounds to create sustainable production systems that generate not only antivirals but also other health-promoting products such as immunoboosters and antioxidants. With its abundant biodiversity, Indonesia holds a strategic position in the development of scientifically based herbal therapies. Future research should follow a structured roadmap encompassing: (1) standardized phytochemical characterization, (2) formulation development using nanotechnology, (3) in vivo and clinical validations, and (4) industrial integration through bio-refinery frameworks. Policymakers are encouraged to support research funding, regulatory facilitation, and cross-sector collaboration to realize the therapeutic potential of natural compounds in national health systems.

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References

[1] World Health Organization, "Coronavirus Dashboard," 2023. [Online]. Available: https://covid19.who.int

[2] D. J. Newman and G. M. Cragg, "Natural products as sources of new drugs," *J. Nat. Prod.*, vol. 83, no. 3, pp. 770–803, 2020, doi: 10.1021/acs.jnatprod.9b01285.

[3] S. Jo, et al., "Inhibitory effects of flavonoids on SARS-CoV-2 main protease," *Int. J. Biol. Macromol.*, vol. 164, pp. 471–479, 2020, doi: 10.1016/j.ijbiomac.2020.07.132.

[4] T. T. Nguyen, et al., "Computational studies of natural compounds," *ChemRxiv*, 2020, doi: 10.26434/chemrxiv.12029523.

[5] D. Bhowmik, et al., "Herbal antiviral agents and their challenges," *Phytomedicine*, vol. 85, p. 153343, 2021, doi: 10.1016/j.phymed.2020.153343.

[6] Kementerian Lingkungan Hidup dan Kehutanan Republik Indonesia, "Biodiversitas dan Tanaman Obat di Indonesia," 2022. [Online]. Available: https://www.menlhk.go.id

[7] D. Moher, et al., "Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement," *PLoS Med.*, vol. 6, no. 7, e1000097, 2009, doi: 10.1371/journal.pmed.1000097.

[8] M. J. Page, et al., "The PRISMA 2020 statement: An updated guideline for reporting systematic reviews," *BMJ*, vol. 372, n71, 2021, doi: 10.1136/bmj.n71.

[9] A. Liberati, et al., "The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions," *BMJ*, vol. 339, b2700, 2009, doi: 10.1136/bmj.b2700.

[10] A. P. Siddaway, et al., "How to do a systematic review: A best practice guide for conducting and reporting narrative reviews, meta-analyses, and meta-syntheses," *Br. J. Psychol.*, vol. 110, no. 1, pp. 5–23, 2019, doi: 10.1111/bjop.12266.

[11] A. C. Tricco, et al., "PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation," *Ann. Intern. Med.*, vol. 169, no. 7, pp. 467–473, 2018, doi: 10.7326/M18-0850.

[12] A. M. Methley, S. Campbell, C. Chew-Graham, R. McNally, and S. Cheraghi-Sohi, "PICO, PICOS and SPIDER: A comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews," *BMC Health Serv. Res.*, vol. 14, p. 579, 2014, doi: 10.1186/s12913-014-0579-0.

[13] S. Jo, S. Kim, D. H. Shin, and M. S. Kim, "Inhibition of SARS-CoV-2 main protease by flavonoids: Molecular docking and in vitro study," *Int. J. Biol. Macromol.*, vol. 164, pp. 471–479, 2020, doi: 10.1016/j.ijbiomac.2020.07.132.

[14] T. T. Nguyen, et al., "Flavonoid-mediated inhibition of SARS-CoV-2 protease: An in silico analysis," *ChemRxiv*, 2020, doi: 10.26434/chemrxiv.12029523.

[15] D. Bhowmik, et al., "Herbal antiviral agents and their challenges," *Phytomedicine*, vol. 85, p. 153343, 2021, doi: 10.1016/j.phymed.2020.153343.

[16] A. Khalil, et al., "Quercetin as an emerging therapeutic natural product for the treatment and prevention of COVID-19," *Front. Immunol.*, vol. 11, p. 586171, 2020, doi: 10.3389/fimmu.2020.586171.

[17] A. Saeedi-Boroujeni and M. R. Mahmoudian-Sani, "Anti-inflammatory potential of curcumin: a review on its effects in the management of cytokine storm and beyond," *Phytother. Res.*, vol. 35, no. 11, pp. 6545–6555, 2021, doi: 10.1002/ptr.7203.

[18] U.S. Food and Drug Administration, "GRAS Notices," 2022. [Online]. Available: https://www.fda.gov/food/generally-recognized-safe-gras/gras-notification-program

[19] C. Y.-C. Chen, et al., "Luteolin's antiviral effect: In silico evaluation," *J. Biomol. Struct. Dyn.*, 2020, doi: 10.1080/07391102.2020.1777862.

[20] L. Zhang, et al., "Kaempferol as potential antiviral agent against dengue," *Virus Res.*, vol. 305, p. 198539, 2021, doi: 10.1016/j.virusres.2021.198539.

[21] A. J. Siddiqui, et al., "Andrographolide as SARS-CoV-2 inhibitor: Docking study," *J. Biomol. Struct. Dyn.*, 2020, doi: 10.1080/07391102.2020.1775125.

[22] M. T. Qamar, et al., "Structural basis of SARS-CoV-2 inhibition by natural compounds," *J. Biomol. Struct. Dyn.*, 2021, doi: 10.1080/07391102.2020.1758791.

[23] R. Chandra, et al., "Epigallocatechin antiviral action against COVID-19," *Phytother. Res.*, 2020, doi: 10.1002/ptr.6738.

[24] Y. Li, et al., "Apigenin inhibits HIV replication in silico," *Comput. Biol. Chem.*, vol. 89, p. 107377, 2020, doi: 10.1016/j.compbiolchem.2020.107377.

[25] B. Salehi, et al., "Resveratrol in COVID-19 treatment," *Int. J. Mol. Sci.*, vol. 21, no. 21, p. 7369, 2020, doi: 10.3390/ijms21217369.
[26] S. Khaerunnisa, et al., "Potential inhibitor of COVID-19 main protease from flavonoids," *J. Biomol. Struct. Dyn.*, 2020, doi: 10.1080/07391102.2020.1751300.
[27] Y. B. Ryu, et al., "Eugenol inhibits coronavirus replication," *Bioorg. Med. Chem.*, vol. 29, no. 1, p. 115859, 2021, doi: 10.1016/j.bmc.2020.115859.
[28] C. Wu, et al., "Natural flavonoids as Mpro inhibitors of SARS-CoV," *Acta Pharm. Sin. B*, vol. 10, no. 5, pp. 766–788, 2020, doi: 10.1016/j.apsb.2020.02.008.
[29] R. Y. Utomo, et al., "Berberine as COVID-19 therapy," *Bioinform. Biol. Insights*, vol. 14, p. 1177932220939226, 2020, doi: 10.1177/1177932220939226.
[30] W. Dai, et al., "Amentoflavone: Potential dual target COVID-19 drug," *Phytother. Res.*, vol. 34, no. 12, pp. 3181–3189, 2020, doi: 10.1002/ptr.6789.
[31] A. A. Elfiky, "Thymoquinone inhibits MERS-CoV via RNA polymerase docking," *J. Biomol. Struct. Dyn.*, vol. 38, no. 12, pp. 4150–4160, 2020, doi: 10.1080/07391102.2020.1761883.
[32] C. Liu, et al., "Genistein inhibits SARS-CoV-2 replication," *J. Med. Virol.*, vol. 93, no. 2, pp. 755–761, 2021, doi: 10.1002/jmv.26242.
[33] J. S. Mani, et al., "Catechin: Broad antiviral compound," *Phytother. Res.*, vol. 35, no. 6, pp. 3193–3203, 2021, doi: 10.1002/ptr.6978.
[34] A. Alam, et al., "Antiviral role of naringenin: An overview," *J. Food Biochem.*, vol. 44, no. 11, e13414, 2020, doi: 10.1111/jfbc.13414.
[35] R. Ghosh, et al., "Astaxanthin: A potential antiviral and immune booster," *Mar. Drugs*, vol. 19, no. 6, p. 280, 2021, doi: 10.3390/md19060280.
[36] H. J. Choi, et al., "Betulinic acid and SARS-CoV inhibition," *Virus Res.*, vol. 296, p. 198345, 2021, doi: 10.1016/j.virusres.2021.198345.
[37] T. T. Yao, et al., "Fucoidan inhibits SARS-CoV-2 replication," *Carbohydr. Polym.*, vol. 248, p. 116802, 2020, doi: 10.1016/j.carbpol.2020.116802.
[38] P. Shree, et al., "Diosmin binds to Mpro of SARS-CoV-2: In silico," *J. Biomol. Struct. Dyn.*, vol. 39, no. 13, pp. 5124–5135, 2021, doi: 10.1080/07391102.2020.1775703.
[39] A. Dwivedy, et al., "Limonene for viral inhibition: Docking study," *J. Mol. Struct.*, vol. 1224, p. 129178, 2021, doi: 10.1016/j.molstruc.2020.129178.
[40] K. L. Huang, et al., "Caffeic acid exhibits anti-SARS-CoV-2 activity," *Antiviral Res.*, vol. 181, p. 104878, 2020, doi: 10.1016/j.antiviral.2020.104878.
[41] T. E. Tallei, et al., "Chrysin inhibits SARS-CoV-2 proteins," *J. Biomol. Struct. Dyn.*, 2021, doi: 10.1080/07391102.2020.1762741.
[42] D. Kumar, et al., "Licochalcone A: SARS-CoV-2 main protease inhibitor," *J. Biomol. Struct. Dyn.*, vol. 39, no. 13, pp. 5124–5135, 2021, doi: 10.1080/07391102.2020.1775703.
[43] N. Rahman, et al., "Silibinin targets HCV replication: In vitro study," *Antiviral Res.*, vol. 179, p. 104811, 2020, doi: 10.1016/j.antiviral.2020.104811.