

# MOLECULAR DRUG DISCOVERY OF POTENTIAL INHIBITOR OF COVID-19 USING SEVERAL MEDICINAL PLANT INGREDIENTS: A PROMISING THERAPY FOR VIRAL DISEASE<sup>a</sup>

## DESCUBRIMIENTO MOLECULAR DE UN INHIBIDOR POTENCIAL DE COVID-19 UTILIZANDO VARIOS INGREDIENTES DE PLANTAS MEDICINALES: UNA TERAPIA PROMETEDORA PARA LAS ENFERMEDADES VIRALES

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Research paper

**ABSTRACT:** This research article aims to investigate the compounds of apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin extracted from *Goji berries*, *Green tea*, *Turmeric*, *Chinese cabbage*, *Citrus fruit*, *Olive* and *Chili pepper*, respectively, as a probable anti pandemic Covid19 receptor derived from medicinal plants. The physicochemical properties including heat of formation, Gibbs free energy, electronic energy, charge distribution have been evaluated for the active sites of natural drugs which can be proposed for Covid19 treatment. These phytochemicals can be attached to the active site of the database amino acids fragment of Tyr160–Met161–His162 as the selective zone of the Covid19 due to formation of hydrogen bonding. The theoretical calculations were done at various levels of theory to gain more accurate equilibrium geometrical results, and IR spectral data for each of the complex proposed drugs of N–terminal or O–terminal auto–cleavage substrate were individually determined to elucidate the structural flexibility and substrate binding of seven medicinal plants jointed to active site of Covid19 molecule. A comparison of these structures with two configurations provides new insights for the design of substrate–based anti–targeting Covid19. This indicates a feasible model for designing wide–spectrum of anti–Covid19 drugs. The structure–based optimization of these structures has yielded two more efficacious lead compounds, N and O atoms through forming the hydrogen bonding with potent anti–Covid19.

**KEYWORDS:** Covid19; medicinal plant; apigenine–7–glucoside; catechin; demethoxycurcumine; kaempferol; naringenin; oleuropein; quercetin

**RESUMEN:** Este artículo de investigación pretende investigar los compuestos de apigenina–7–glucósido, catequina, demetoxicurcumina, kaempferol, naringenina, oleuropeína y quercetina extraídos de *bayas de Goji*, *té verde*, *cúrcuma*, *col china*, *cítricos*, *olivo* y *chile*, respectivamente, como probable receptor antipandémico Covid19 derivado de plantas medicinales. Se han evaluado las propiedades fisicoquímicas, incluido el calor de formación, la energía libre de Gibbs,

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la energía electrónica y la distribución de la carga, de los sitios activos de los fármacos naturales que pueden proponerse para el tratamiento de Covid19. Estos fitoquímicos pueden unirse al sitio activo del fragmento de aminoácidos de la base de datos de Tyr160–Met161–His162 como zona selectiva del Covid19 debido a la formación de enlaces de hidrógeno. Los cálculos teóricos se realizaron en varios niveles de la teoría para ganar era más precisa de equilibrio resultados geométricos, y los datos espectrales IR para cada uno de los complejos propuestos drogas de N–terminal o O–terminal auto-cleavage sustrato se determinaron individualmente para dilucidar la flexibilidad estructural y sustrato de unión de siete plantas medicinales se unió al sitio activo de Covid19 molécula. La comparación de estas estructuras con dos configuraciones proporciona nuevos conocimientos para el diseño de Covid19 basado en el sustrato anti–objetivo. La optimización basada en la estructura de estos compuestos ha producido dos líderes más eficaces: los átomos N y O, a través de la formación de enlaces de hidrógeno, con el potente anti–COVID-19

**PALABRAS CLAVE:** Covid19; planta medicinal; apigenina–7–glucósido; catequina; demetoxicurcumina; kaempferol; naringenina; oleuropeína; quercetina

## 1. INTRODUCTION

The SARS–CoV–2 variant: B.1.1.529 was monitored and evaluated by experts of the technical advisory group on SARS–CoV–2 Virus Evolution in 2021 (González–Vázquez & Arenas, 2023; Pan *et al.*, 2021). The epidemiological situation in South Africa has been identified by three different peaks in announced cases, the latest of which was predominantly the Delta variant. Then, infections increased sharply, simultaneously with finding B.1.1.529 variant. This variant has a grand number of mutations, some of which are worrying. There is an increased risk of reinfection with this variant compared to other VOCs. So, current SARS–CoV–2 PCR diagnostics can find this variant. Some experiments have shown that for one large PCR test, one of the three target genes is not found, and this test can be applied as a sign for this variant, waiting sequencing approval. By this method, this variant has been found at more rapid amounts than previous waves in infection, recommending that this variant might have a growth privilege. It has been approved that a detrimental change in COVID19 epidemiology should be determined as a VOC, and the WHO has determined Covid19. People are reminded to take measures to decrease their risk of COVID19 consisting of public health and social measures such as wearing masks, hand hygiene, physical distancing, increasing ventilation of inside spaces, preventing crowded spaces, and getting vaccinated (Zhang *et al.*, 2020; Pandey *et al.*, 2020; Mollaamin *et al.*, 2023). As a matter of fact, CoV closely corresponds to intense breathing syndrome CoV (SARS–CoV) which is an epidemic with short period at its living time. SARS–CoV and MERS–CoV relate to the family Coronaviridae’s family as enveloped, positive stranded RNA viruses with around 30,000 nucleotides. It has been reported that the global outbreak of a life-threatening typical pneumonia caused about 800 deaths which was world identified as the harsh syndrome CoV (SARS–CoV) (Yan *et al.*, 2019; Tahan *et al.*, 2009; Sarasia *et al.*, 2011; Shi *et al.*, 2019; Mollaamin *et al.*, 2023). Moreover, developed investigations have indicated that the origin of SARS–CoV based on the phylogenetic analysis is mostly likely from bats which are transferred to human aerosols due to intermediate hosts like infectious palm civets by the virus (Mitton *et al.*, 2021; Khalili *et al.*, 2011; Yen *et al.*, 2020).

Thus, the animal disease of CoV due to its power of intermediate transition into persons is a threat which has been summarized with the novel MERS–CoV suggesting bats and dromedary camels as the storage for this virus (Mollaamin *et al.*, 2022; Caméléna *et al.*, 2021; Dien & McElvania, 2020; Vanet *et al.*, 2020; Tansarli & Chapin, 2020; Nabower *et al.*, 2019). Besides, MERS–CoV declares SARS–like symptoms due to human infections including malaise, rigors, fatigues and high fevers, signs like influenza, but it has been seen later development to a typical pneumonia in most cases Caille *et al.* (2020).

In some researches, it has been discovered that a prototype of the Coronaviridae family is an infectious bronchitis virus (IBV) which relates to the genetic group III of CoV, and causes severe economic defeat for the poultry industry in the world (Mollaamin *et al.*, 2020; Juttukonda *et al.*, 2020; Bakhshi *et al.*, 2011; Blauwkamp *et al.*, 2019). Actually, the scientists have not discovered any vaccine or specific antiviral treatment, by management concerning care of symptoms, supportive treatment, and experimental data (Hagen *et al.*, 2020; Mollaamin, 2023; Lee *et al.*, 2019).

Environmental elements can greatly affect the secretion of secondary metabolites from tropical plants. Therefore, great attention has been paid to the secondary metabolites secreted by plants in tropical regions that may be developed as medicines (Monajjemi *et al.*, 2020; Yang *et al.*, 2018; Zadeh *et al.*, 2015). Several compounds, such as flavonoids, from medicinal plants, have been reported to have antiviral bioactivities (Khaleghian *et al.*, 2011; Mollaamin *et al.*, 2023; Jo *et al.*, 2020; Akbulut, 2021). In the present study, we investigated apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin extracted from *Goji berries*, *Green tea*, *Turmeric*, *Chinese cabbage*, *Citrus fruit*, *Olive* and *Chili pepper*, respectively, as the probable anti–Covid19 receptor derived from medicinal plants (Table 1).

The findings of the present study will provide other researchers with opportunities to identify the right drug to combat Covid19 using theoretical methods to estimate the impact of hydrogen bonding in different linkage through seven medicinal plants of apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin jointed to the active site of Covid19 protein (Figure 1).

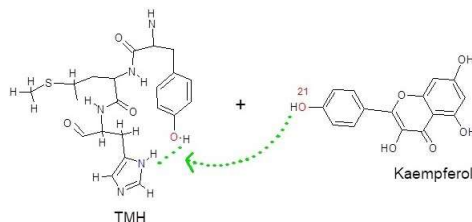
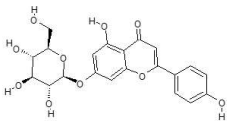
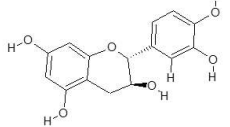
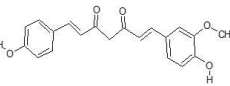
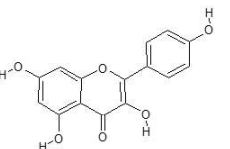
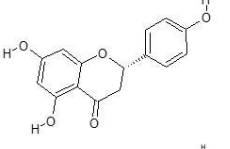
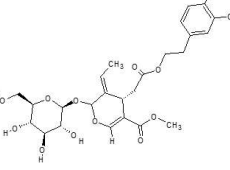
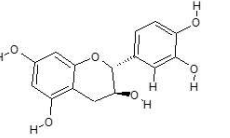


Figure 1: The junction of kaempferol as an anti–Covid19 drug through O21 atom to TMH (Tyr160–Met161–His162) by hydrogen bonding.

Table 1: Medicinal ingredients of apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin as the probable anti-Covid19 receptor derived from medicinal plants.

Compound	Molecular structure
Apigenine-7-glucoside	
Catechin	
Demethoxycurcumine	
Kaempferol	
Naringenin	
Oleuropein	
Quercetin	

## 2. MATERIALS AND METHODS

The junction of apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin jointed to the active site of Covid19 protein has been accomplished in this work by forming relatively stable complexes through the hydrogen bonding Mollaamin *et al.* (2023). Thus, a series of quantum theoretical methods of m062x/cc-pvdz pseudo = CEP for complexes of seven inhibitors for Covid19 has been done due to finding the optimized coordination of the best structures of medicinal plant-Tyr160-Met161-His162 drug design model with infrared computations using the Gaussian 16 revision C.01 program Frisch *et al.* (2016).

In this study, the geometries were optimized at the framework of DFT using the three-parameter Becke's exchange (Becke, 1988; Becke, 1993) and Lee-Yang-París correlation non-local functional (Lee *et al.*, 1988), usually known as B3LYP method and basis sets of LANL2DZ. The density functional theory (DFT) is one of the most employed approximations of Hohenberg, Kohn and Sham which permit the theoretical study of material properties (Monajjemi *et al.*, 2020; Mollaamin, 2014; Mollaamin *et al.*, 2024; Mollaamin & Monajjemi, 2023; Mollaamin, 2023). It has been indicated that polarization functions into the applied basis set in the computation always introduce us an important achievement on the modeling and simulation theoretical levels (Shahriari *et al.*, 2022; Shahriari *et al.*, 2018; Monajjemi *et al.*, 2009; Mollaamin, 2022; Mollaamin *et al.*, 2011). Normal mode accomplishment is the verdict of harmonic potential wells by analytic methods which maintain the motion of all atoms at the same time in the vibration time scale leading to a natural explanation of molecular vibrations. Therefore, the optimized geometry coordination of medicinal ingredients-TMH complexes toward the drug design has been run through the active site of indicated oxygen, nitrogen, and hydrogen atoms in the junction of bond and torsion angles (Figure 1).

Therefore, for accomplishing a stable structure of medicinal plant linkage of Covid19 active site, geometry optimization plus the NMR estimation, the frequency and intensity of the vibrational modes were calculated with the quantum mechanical method, and the principal vibrational modes were analyzed by their changes of Gibbs free energy at 300K (Monajjemi *et al.*, 2010; Mollaamin, 2015; Mollaamin & Monajjemi, 2021).

Besides, the data has been achieved from thermodynamic parameters of  $\Delta G$ ,  $\Delta H$  and  $\Delta S$  for medicinal plant-Covid19 drug design. Thermochemistry analysis follows the frequency and normal mode data. The zero-point energy output in Gaussian 16 revision C.01 program (Frisch *et al.*, 2016) has been expanded and corrected as: Thermal correction to energy, thermal correction to enthalpy and thermal correction to the Gibbs free. In addition, the total energies can be calculated as sum of electronic and zero-point energies, sum of electronic and thermal energies, sum of electronic and thermal enthalpies and sum of electronic and thermal Gibbs free energies.

The theoretical calculations were done at various levels of theory to gain the more accurate equilibrium

geometrical results, NMR, IR, UV spectral data and HOMO–LUMO of frontier orbitals parameters for each of the identified compounds. It is supposed that an additional diffuse and polarization functions into the basis set applied in the computation conduct us to the magnificent progress on the results of theoretical methods.

### 3. RESULTS AND DISCUSSION

#### 3.1. Thermodynamic properties analysis & infrared spectroscopy

Thermodynamic parameters for apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin extracted from *Goji berries*, *Green tea*, *Turmeric*, *Chinese cabbage*, *Citrus fruit*, *Olive* and *Chili pepper*, respectively, have been calculated using density functional theory method and m062x/cc–pvdz pseudo = CEP level by Gaussian 16 revision C.01 program (Frisch *et al.*, 2016) and been reported in Table 2 and Figure 2.

Table 2: Thermodynamic parameters for apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein, and quercetin using density functional theory method and m062x/cc–pvdz pseudo=CEP level.

Phytochemicals	Dipole moment (Debye)	$\Delta E^o \times 10^{-3}$ (kcal.mol <sup>-1</sup> )	$\Delta H^o \times 10^{-3}$ (kcal.mol <sup>-1</sup> )	$\Delta G^o \times 10^{-3}$ (kcal.mol <sup>-1</sup> )	$S^o \times 10^{-3}$ (cal.K <sup>-1</sup> mol <sup>-1</sup> )
Apigenine–7–glucoside	5.4672	-968.078	-968.077	-968.117	134.625
Catechin	4.2660	-638.496	-638.495	-638.530	116.702
Demethoxycurcumine	4.4508	-711.496	-711.495	-711.531	119.571
Kaempferol	3.1205	-637.052	-637.051	-637.084	109.232
Naringenin	2.6658	-591.276	-591.275	-591.307	106.656
Oleuropein	6.1962	-1206.850	-1206.849	-1206.893	147.632
Quercetin	4.4357	-683.579	-683.578	-683.612	112.611

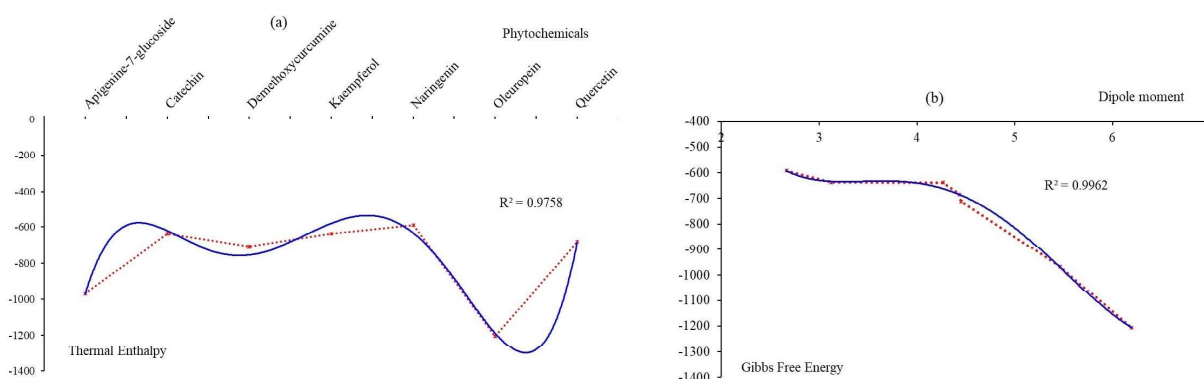


Figure 2: The values of a) gibbs free energy (kcal.mol<sup>-1</sup>) versus dipole moment (debye) and b) thermal enthalpy (kcal.mol<sup>-1</sup>) for apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin (Source: Author's Own Work).

Figure 2a, with relation coefficient ( $R^2$ ) of 0.9758 has indicated an appropriate accordance of thermal enthalpy for phytochemical of apigenine-7-glucoside, catechin, dimethoxy curcumine, kaempferol, naringenin, oleuropein and quercetin. In fact, many solutes dissolve in water with a decrease in temperature. Moreover, Figure 2b has shown the minimum Gibbs free energy consisting of La energía libre de Gibbs consiste en  $-1206.893 \times 10^3$  (kcal.mol<sup>-1</sup>) for oleuropein versus dipole moment which can indicate the most stability of these structures of the antiviral natural medications. The  $R^2 = 0.9962$  has demonstrated that with increasing the dipole moment, the stability of principal compounds of apigenine-7-glucoside, catechin, dimethoxy curcumine, kaempferol, naringenin, oleuropein and quercetin are enhanced based on the existence of H-bonding and dipole-dipole interactions in the solvent.

Furthermore, the spectroscopy of infrared for major sesquiterpenes of apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin has been achieved due to density functional theory method and m062x/cc-pvdz pseudo = CEP keyword (Figure 3a-g).

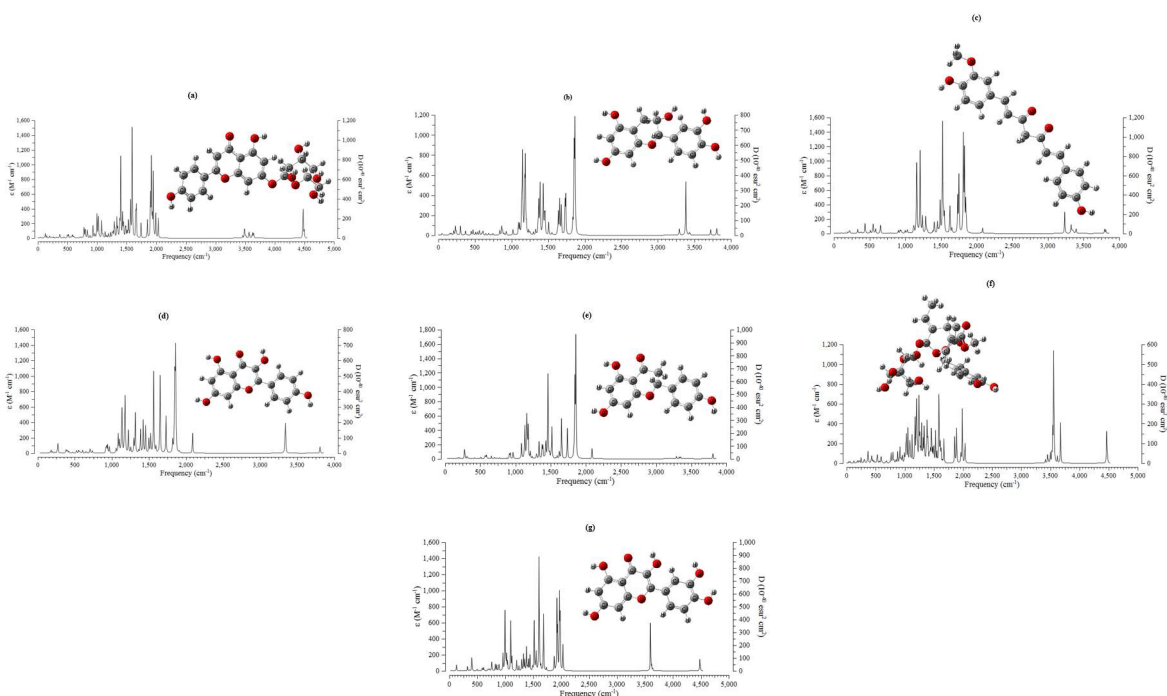


Figure 3: Infrared spectra of a) apigenine-7-glucoside, b) catechin, c) demethoxycurcumine, d) kaempferol, e) naringenin, f) oleuropein, and g) quercetin to TMH (Tyr160-Met161-His162) through the drug design method calculated by m062x/cc-pvdz pseudo=CEP. [Note:  $\epsilon$  ( $M^{-1}cm^{-1}$ ) is the absorbance unit and D ( $10^{-4}esu^2cm^2$ ) is the dipole strength via the esu or electrostatic unit, which is a unit of charge in the cgs (centimeter-gram-second system)] (Source: Author's Own Work)

The most fluctuation of frequency of infrared spectra for apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin has been approximately seen between 500–2000  $\text{cm}^{-1}$  (Figure 3a–g).

### 3.2. Chemical shielding insight through nuclear magnetic resonance spectrum

The heterocyclic antiviral phytochemicals of apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin have approximately exhibited the equal manner from 20 to 300 ppm for different atoms of these phytochemicals (Figure 4a–g).

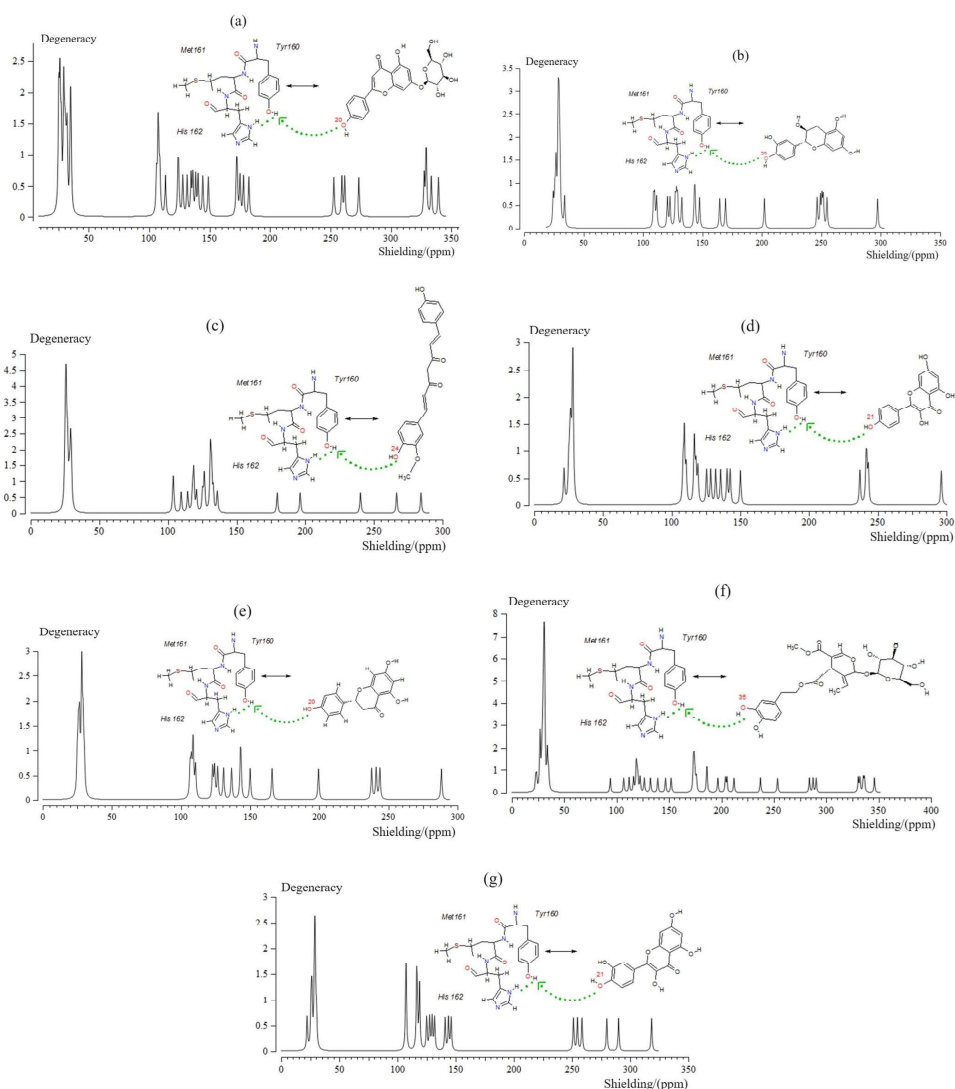


Figure 4: NMR spectra of a) apigenine-7-glucoside, b) catechin, c) demethoxycurcumine, d) kaempferol, e) naringenin, f) oleuropein and g) quercetin bonded to TMH (Tyr160-Met161-His162) COVID19 active site through the drug design method by showing the active region of TMH in the drug design process (Source: Author's Own Work).



The nuclear magnetic resonance spectrum displayed the steepest peak in 40 ppm and the fragile peaks of nuclear magnetic resonance have approximately in 100–200 ppm for all antiviral phytochemicals including apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin, respectively (Figure 4a–g).

The computation of hydrogen nuclear magnetic resonance on the foundation of amino acids in the beta-sheet conformation Tyrosine–Methionine–Histidine and the main ingredients of medicinal plants including apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin have been evaluated to explorer the certain atoms of hydrogen, nitrogen and oxygen in the critical areas of these antivirus medicines through the generating of H–bonding by identifying the attack point of Tyrosine–Methionine–Histidine (Figure 4a–g).

The nuclear magnetic resonance analysis shows the critical points of the principal components of medicinal plants for binding to the Tyr160–Met161–His162 (TMH) due to producing the antivirus drugs, while each active atom of O and N as the electronegative atoms for binding to the H remarks the maximal shift in all steps in the NMR spectrum (Figure 4a–g).

### 3.3. In silico analysis of nuclear quadrupole resonance (NQR)

In this research, the calculated nuclear quadrupole resonance/NQR specifications extracted from electrostatic properties have been calculated for apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin which is accord to the results of the nuclear quadrupole moment, a trait of the nucleus, and the electric field gradient/EFG about the nucleus. As the EFG at the citation of the nucleus in apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin is allocated by the valence electrons twisted in the attachment with close nuclei of TMH (Tyr160–Met161–His162) COVID19 active site, the NQR frequencies at which transitions occur is particular for inhibitor–TMH complexes. NQR is a straight frame of the interaction of the quadrupole moment with the EFG which is produced by the electronic structure of its ambiance. Therefore, the NQR transition frequencies are symmetric to the electric quadrupole moment of the nucleus and a measurement of the strength of the local EFG (Kawczak *et al.*, 2018; Trontelj *et al.*, 2020; Begus *et al.*, 2017; Seliger *et al.*, 2012).

In this research work, the electric potential as the quantity of work energy through carrying over the electric charge from one position to another position in the essence of electric field has been evaluated for apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin bonded to TMH (Tyr160–Met161–His162) COVID–19 active site 5a–g).

In Figure 5(a–g), it has been sketched the electric potential of nuclear quadrupole resonance for some atoms of aluminum, magnesium, nickel, palladium, platinum, copper, silver, and gold in the linkage bond between apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin and TMH (Tyr160–Met161–His162) COVID19 active site which has been calculated by m062x/cc-pvdz

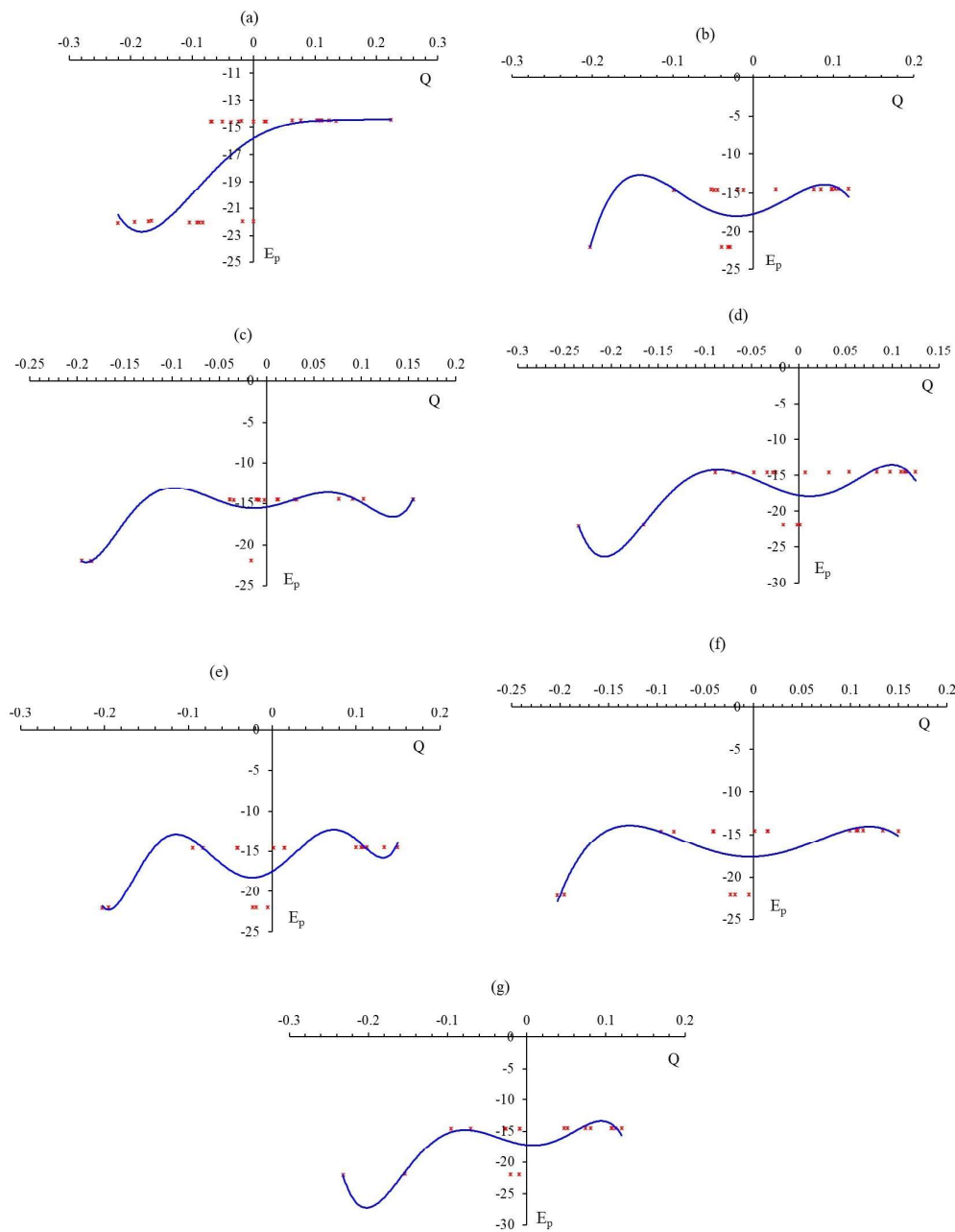


Figure 5: Electric potential/(a.u.) versus Bader charge/(e) through NQR calculation for a) apigenine-7-glucoside, b) catechin, c) demethoxycurcumine, d) kaempferol, e) naringenin, f) oleuropein and g) quercetin bonded to TMH (Tyr160?Met161?His162) COVID-19 active site by m062x/cc-pvdz pseudo=CEP.

Table 3: The Frontier orbitals' parameters (eV) of antiviral phytochemicals including apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin.

Molecule	$E_{LUMO}$	$E_{HOMO}$	$\Delta E = E_{LUMO} - E_{HOMO}$
Apigenine-7-glucoside	-1.6751	-2.8819	1.2068
Catechin	3.1633	-2.6612	5.8245
Demethoxycurcumine	1.1276	-2.4406	3.5682
Kaempferol	1.6245	-2.7195	4.344
Naringenin	1.9946	-3.0422	5.0368
Oleuropein	2.3676	-0.9254	3.293
Quercetin	1.3570	-2.5780	3.935

Molecule	$\mu = \frac{E_{HOMO} + E_{LUMO}}{2}$	$\chi = -\frac{E_{HOMO} + E_{LUMO}}{2}$	$\eta = \frac{E_{LUMO} - E_{HOMO}}{2}$	$\xi = 1/(2\mu)$	$\psi = \frac{\mu^2}{2\eta}$
Apigenine-7-glucoside	-2.2785	2.2785	0.6034	0.8286	4.3019
Catechin	0.25105	-0.25105	2.91225	0.17169	0.0108
Demethoxycurcumine	-0.6565	0.6565	1.7841	0.2802	0.1208
Kaempferol	-0.5475	0.5475	2.172	0.2302	0.0690
Naringenin	-0.5238	0.5238	2.5184	0.1985	0.0544
Oleuropein	0.7211	-0.7211	1.6465	0.3036	0.1579
Quercetin	-0.6105	0.6105	1.9675	0.25412	0.0947

pseudo=CEP. In Figure5(a-g), it has been described the influence of each active atom of O and N as the electronegative atoms for binding to the H atom.

### 3.4. Frontier orbitals

The Frontier orbitals have been estimated for some effective phytochemicals of apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin extracted from *Goji berries*, *Green tea*, *Turmeric*, *Chinese cabbage*, *Citrus fruit*, *Olive* and *Chili pepper*, respectively (Table 3).

The highest occupied molecular orbital energy (HOMO/eV), the lowest unoccupied molecular orbital energy (LUMO/eV) and band energy gap  $\Delta E$  (eV) indicated the pictorial description of positive and negative areas that are a crucial agent for recognizing the molecular specifications of antiviral phytochemicals consisting of apigenine-7-glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin (Table 3).

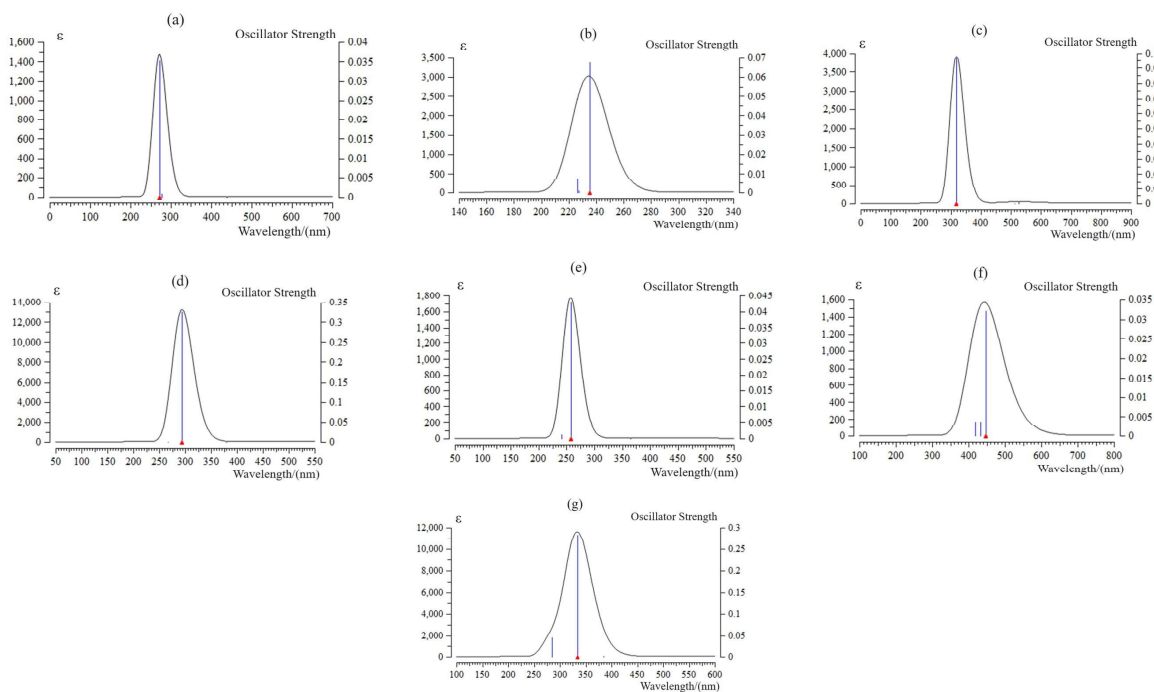


Figure 6: Ultraviolet–Visible spectrums of a) apigenine–7–glucoside, b) catechin, c) demethoxycurcumine, d) kaempferol, e) naringenin, f) oleuropein and g) quercetin.

### 3.5. Analysis of Ultraviolet–Visible spectroscopy

Generally, organic materials are clear to the large energy radiation which forms the ultraviolet (200–400 nm) and visible (400–700 nm) section of the electromagnetic spectrum.

In the measured amounts of Ultraviolet–Visible spectrums for principal phytochemicals of apigenine–7–glucoside, catechin, demethoxycurcumine, kaempferol, naringenin, oleuropein and quercetin, there are maximum absorption bands between 250–350 nm for apigenine–7–glucoside with a sharpest peak in 270 nm (Figure 6a), around 200–260 nm for catechin with a keen peak in 234 nm (Figure 6b), about 250–400 nm for demethoxycurcumine with a pointed peak in 320 nm (Figure 6c), around 250–350 nm for kaempferol with a strong peak in 290 nm (Figure 6d), around 225–300 nm for naringenin with a strong peak in 260 nm (Figure 6e), around 350–600 nm for oleuropein with a strong peak in 450 nm (Figure 6f), and near 250–400 nm for quercetin with a steepest peak in 330 nm (Figure 6g). Notwithstanding vaccine progress, Coronavirus disease therapy still stays dramatically supportive with a prompt demand to recognize impressive anti-coronavirals. A noteworthy method is reusing medications already released for other maladies. In this regard, several investigations have been carried out to inquire whether antimalarial medications could cure Coronavirus disease. Quality control and standardization of natural drug–based products also require to be confirmed. However, given the unique challenges faced, pharmacological research should be given a just value of regard for contribution in COVID–19 pandemic.

## 4. CONCLUSIONS

The results in this article have remarked that natural drugs due to potential active phytochemicals might grow a further effective species in the remedy of the new coronavirus of severe acute respiratory syndrome coronavirus 2 accountable for Coronavirus malady. Some physical and physicochemical attributes from optimized structure of alliin, curcumin, epicatechin-gallate, luteolin-7-glucoside, and zingerol extracted from *Goji berries*, *Green tea*, *Turmeric*, *Chinese cabbage*, *Citrus fruit*, *Olive* and *Chili pepper*, respectively, disclosed to be potent in displaying antiviral activities by interrupting the viral life. Thus, these natural drugs may be either a new or safe treatment or even is employed as antiviral nutraceuticals in elevating immunity and producing endurance to virus infections.

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### Authors contributions

Fatemeh Mollaamin: Conceptualization and idea, Methodology, Software, Validation, Formal analysis, Investigation, Data Curation, Writing-original draft preparation, Visualization, Supervision, Project administration.

Majid Monajjemi: Methodology, Software, Formal analysis, Investigation, Data Curation, Writing-review and editing, Visualization, Resources.

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