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Research Paper

Topological Indices of Drug Molecular Structures: An Application with the Treatment and Prevention of COVID-19

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Abstract. This paper presents a comprehensive analysis of the role of topological indices and centrality measures in predicting the chemical properties of molecules, with a specific focus on six drugs known for their effectiveness in treating corona. The molecular structures of these drugs were carefully examined, and a range of topological indices were calculated. Utilizing regression analysis techniques, we reveal significant relationships between the chemical parameters of the drugs and two specific indices, namely ISI_5 and ISI_6, as well as various centrality measures.

Keywords: topological indices, chemical properties, centrality measures
Mathematics Subject Classification (2010): 05C09, 05C92.

1 Introduction

Human coronaviruses were discovered in the 1960s [9, 11]. The human coronavirus discovered in 2003, SARS-CoV, which causes severe acute respiratory syndrome (SARS), has a unique pathogenesis because it causes both upper and lower respiratory tract infections [3]. In December 2019, a pneumonia outbreak was reported in Wuhan, China [14] The coron-

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avirus soon spread throughout the world.

As of 4 May 2021, there have been at least 3,218,906 confirmed deaths and more than 153,819,254 [7] confirmed cases in the COVID-19 pandemic. So studies of the drugs are effective in treating the corona is of special importance. A type of molecular descriptor used to predict physicochemical properties is a topological index. using graph theory, the graph of a molecule is plotted and its topological indices are calculated.

The graph invariants or descriptors play significant roles in quantitative structure-activity relationship/quantitative structure-property relationship (QSAR/QSPR) models. Among them, the distance-based descriptors are the most famous such as Wiener index [18] and Balaban index [1]. The Wiener index was introduced in 1947 and it turned out to be applicable to several connections with physico-chemical properties such as boiling point, entropy or heat of vaporization.

Suppose G is a connected graph. For an arbitrary vertex $v \in V(G)$ and a subset $V \subseteq V(G)$, we define $w_G(v)$ and W(V) to be $w_G(v) = \sum_{v \neq u \in V(G)} d(v,u)$ and $W(V) = \sum_{v \in V} w_G(v)$, respectively.

Let $e = uv$ be an edge of graph G. The number of vertices of G lying closer to u than to v is denoted by $n_u(e)$. Analogously, $n_v(e)$ is the number of vertices of G lying closer to v than to u. The Szeged index [6] of G is defined with $Sz(G) = \sum_{uv \in E(G)} n_u(e) n_v(e)$.
For a vertex $u \in V(G)$, $d(u)$ denotes the degree of u. The eccentricity$\varepsilon(u)$of a vertex u is the maximum distance from u to any other vertex. The eccentric connectivity index [12] of G is defined with $\xi(G) = \sum d(u)\varepsilon(u)$.

Suppose $n(u)$ is the number of vertices of G whose distance to the vertex u is smaller than the distance to the vertex v [5], $m(u)$ is the number of edges of G whose distance to the vertex u is smaller than the distance to the vertex v [2], $s(u)$is the sum of the degrees of all neighbors of the vertex u in G [4], and $d_2(u)$is the 2-distance of the vertex u in G which is the number of 2-neighbors ($N_2(u) = \{v \in V : d(u,v) = 2\}$) [10]. Then the inverse sum indeg index [17] of a graph G is defined as:

$$ISI(G) = \sum \frac{d(u)d(v)}{d(u) + d(v)}.$$

By a similar way, the group of ISI_i indices (i=2,3,4,5,6) can be defined as follows:

$$ISI_2(G) = \sum \frac{n(u)n(v)}{n(u) + n(v)},$$

$$ISI_3(G) = \sum \frac{m(u)m(v)}{m(u) + m(v)},$$

$$ISI_4(G) = \sum \frac{s(u)s(v)}{s(u) + s(v)},$$

$$ISI_5(G) = \sum \frac{\varepsilon(u)\varepsilon(v)}{\varepsilon(u) + \varepsilon(v)},$$

$$ISI_6(G) = \sum \frac{d_2(u)d_2(v)}{d_2(u) + d_2(v)}.$$

The symmetric division deg index [15] is defined as:

$$SDD(G) = \sum \frac{d(u)}{d(v)} + \frac{d(v)}{d(u)}.$$

The geometric-arithmetic index [16] is defined as:

$$GA(G) = \sum \frac{2\sqrt{d(u)d(v)}}{d(u) + d(v)}.$$

Similar to the ISI_i indices the group of GA_i and SDD_i (i=2,3,4,5,6) indices were defined as:

$$GA_2(G) = \sum \frac{2\sqrt{n(u)n(v)}}{n(u) + n(v)},$$

$$GA_3(G) = \sum \frac{2\sqrt{m(u)m(v)}}{m(u) + m(v)},$$

$$GA_4(G) = \sum \frac{2\sqrt{s(u)s(v)}}{s(u) + s(v)},$$

$$GA_5(G) = \sum \frac{2\sqrt{\varepsilon(u)\varepsilon(v)}}{\varepsilon(u) + \varepsilon(v)},$$

$$GA_6(G) = \sum \frac{2\sqrt{d_2(u)d_2(v)}}{d_2(u) + d_2(v)},$$

$$SDD_2(G) = \sum \frac{n(u)}{n(v)} + \frac{n(v)}{n(u)},$$

$$SDD_3(G) = \sum \frac{m(u)}{m(v)} + \frac{m(v)}{m(u)},$$

$$SDD_4(G) = \sum \frac{s(u)}{s(v)} + \frac{s(v)}{s(u)},$$

$$SDD_5(G) = \sum \frac{\varepsilon(u)}{\varepsilon(v)} + \frac{\varepsilon(v)}{\varepsilon(u)},$$

$$SDD_6(G) = \sum \frac{d_2(u)}{d_2(v)} + \frac{d_2(v)}{d_2(u)}.$$

2 Results and discussion

The aim of this section is to compute the above indices for several molecular graphs of six drugs effective in the treatment of corona virus. We recall that the set of all permutations of a graph G preserving the adjacency between vertices compose the automorphism of graph G which is denoted by Aut(G). For a vertex $u \in V(G)$, an orbit containing the vertex u is the set

Figure 1. 2-D and 3-D graphs of Ethylene.

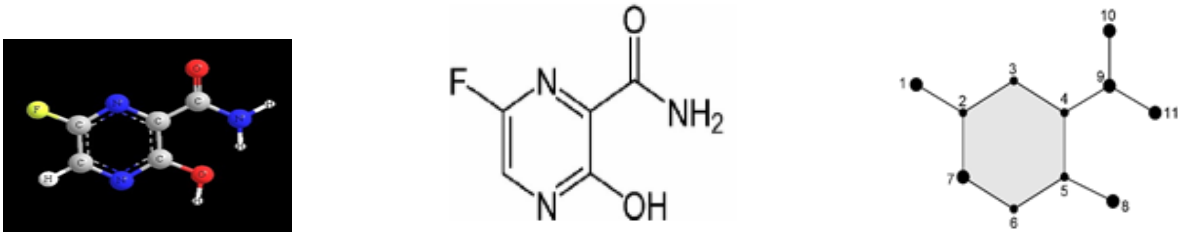


Figure 2. Favipiravir and its molecular graph.

$[x] = \{\alpha(x) | \ \alpha \in Aut(G)\}$. The set of all orbits of a graph partite the vertex set into non-empty sets with empty intersection. A graph with only one orbit is said to be vertex-transitive.

For example, consider the molecular graph of Ethylene depicted in Figure 1. The automorphisms of this molecular graph is a permutation group with the following elements:
{(),(1,2)(3,4)(5,6),(1,2)(3,4,5,6),(3,5),(3,5)(4,6), (1,2)(3,6,5,4), (1,2)(3,6)(4,5), (4,6)}.
Suppose τ = (4,6) and α = (1,2)(3,4,5,6), then $\tau\alpha\tau\alpha = 1 and so Aut(G) \cong D_8$. *This means that G has two vertex-orbits* $V_1 = \{1,2\}$ *and* $V_2 = \{3,4,5,6\}$.

In continuing this paper, we investigate six drugs effective in the treatment of corona.
The first considered molecule in this section is Favipiravir. The Favipiravir, also known as T-705, Avigan, or Favilavir, is an antiviral drug used to treat coronavirus 2019. Let G_1 *be the molecular graph of Favipiravir as depicted in Figure 1. This molecular graph has 11 vertices and 11 edges. The automorphism group elements of this graph are {(), (10,11)} and clearly the automorphism group is isomorphic with the cyclic group* Z_2. *In Table 1., the values of all above topological indices for this molecule are reported.*

Table 1. The values of selected topological indices of Favipiravir.

TI	1	2	3	4	5	6
IISI	11	8.09	8.02	4.54	5.62	8.43
GA	10.38	8.89	8.76	10.79	10.93	10.77
SDD	28	55.23	59.65	23.76	22.55	24.05
ISDD	4.55	3.1	3.03	5.12	5.37	5.1
W	148					
Sz	228					
ξ	80					

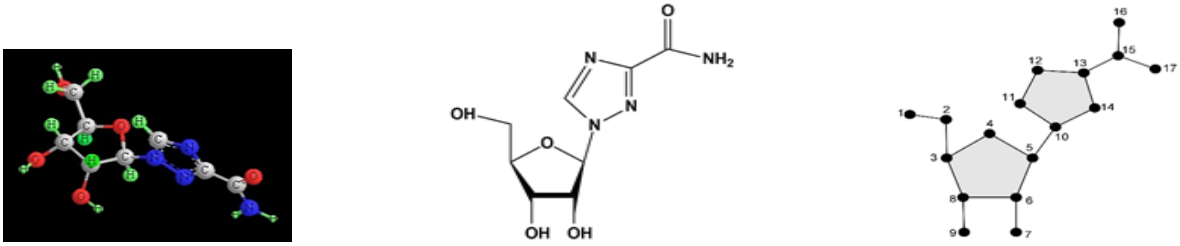


Figure 3. Ribavirin and its molecular graph.

The values of various physicochemical properties of this molecule were obtained from ChemSpider [8] and they are reported in the following table.

Table 2. The values of various physicochemical properties of Favipiravir.

Drugs	*MV*	*T*	*P*	*PSA*	*MR*	*FP*	*E*	*BP*
Favipiravir	97.2	81.5	13.2	89	33.2	288.0	86.4	552.6

In continuing, let G_2 be the molecular graph of Ribavirin which is depicted in Figure Ribavirin, also known as ribavirin, is an antiviral medication used to treat RSV infection, hepatitis C and some viral hemorrhagic fevers [13]. Ribavirin was patented in 1971 and approved for medical use in 1986. The number of vertices and the number of edges of this graph are respectively 17 and 18. Also, the automorphism group elements of this graph is are $\{(), (16,17)\}$. It is clear that $Aut(G_2) \cong Z_2$.
Also, a list of topological indices together with their values is given in Table 3..

Table 3. The values of topological indices of Ribavirin.

TI	1	2	3	4	5	6
IISI	17	13.06	11.04	6.92	5.81	12.18
GA	17.26	13.18	13.33	17.61	18.95	17.68
SDD	43	136.01	142.42	39.41	38.37	38.82
ISDD	7.83	4.15	4.41	8.31	9.41	8.422
W	515					
Sz	626					
ξ	243					

Besides, the values of physicochemical properties are given in the following table.

Table 4. The values of topological indices of Ribavirin.

Drugs	*MV*	*T*	*P*	*PSA*	*MR*	*FP*	*E*	*BP*
Ribavirin	117.1	106.8	20.3	144	51.1	340.7	99.3	639.8

The next molecular graph is Remdesivir where its molecular graph is depicted in Figure 3. It is an

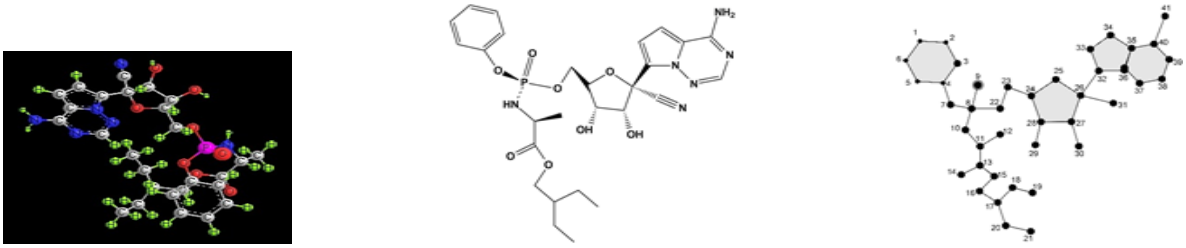


Figure 4. Remdesivir and its molecular graph.

adenine nucleotide drug that converts to its active form when it enters cells and acts as an adenosine triphosphate analogue. Let us denote this graph by G_3. Then $|V(G_3)| = 41$ and $|E(G_3)| = 43$. Also, the automorphisms of this graph are $\{(), (2,6)(3,5), (20,18)(19,21), (20,18)(2,6)(3,5)(19,21)\}$ and the whole automorphism group is isomorphic with Klein four-group $Z_2 \times Z_2$. The values of T-indices are reported in Table 6. and certain physicochemical properties are as follows:

Table 5. The values of topological indices of Remdesivir.

Drugs	*MV*	*T*	*P*	*PSA*	*MR*	*FP*	*E*	*BP*
Remdesivir	409.0	62.3	59.3	213	149.5	-	-	-

Table 6. The values of topological indices of Remdesivir.

TI	1	2	3	4	5	6
IISI	41	22.62	20.91	16.79	6.59	30.3
GA	42.28	25.75	25.85	43.17	43.97	43.17
SDD	104.67	744.26	780.66	95.24	88.24	95.12
ISDD	19.29	6.6	6.8	20.55	21.94	20.49
W	6054					
Sz	7326					
ξ	1212					

Let G_4 be the molecular graph of Theaflavin as depicted in Figure 4. Theaflavins are polyphenolic compounds extracted from black tea and derivatives have inactivation activity against coronavirus. The number of vertices and the number of edges of this graph are respectively 42 and 48. Also, the automorphism of this graph is identity. Besides, a list of topological indices together with their values is given in Table 8. and certain physicochemical properties are as follows:

Table 7. The values of topological indices of Theaflavin.

Drugs	*MV*	*T*	*P*	*PSA*	*MR*	*FP*	*E*	*BP*
Theaflavin	301.0	138.6	54.4	218	137.3	336.5	153.5	1003.9

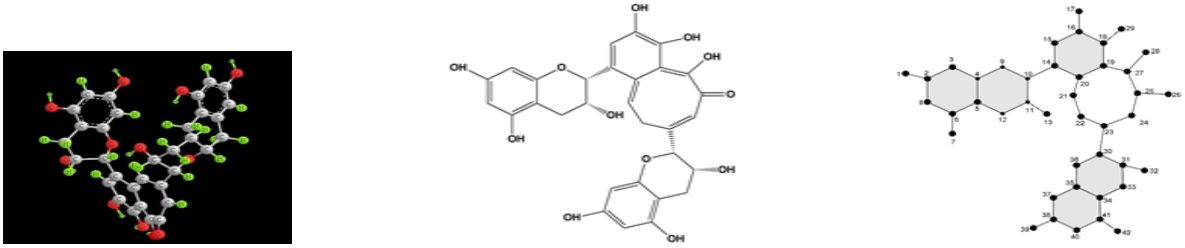


Figure 5. Theaflavin and its molecular graph.

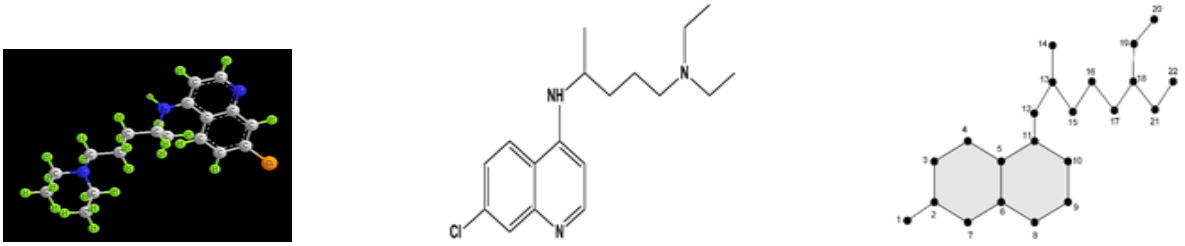


Figure 6. Chloroquine and its molecular graph.

Table 8. The values of topological indices of Theaflavin.

TI	1	2	3	4	5	6
IISI	41	17.84	17.18	15.93	7.84	27.35
GA	44.22	30.19	29.87	45.26	42.96	45.98
SDD	109	614.82	676.42	98.41	86.35	98.55
ISDD	20.15	8.49	8.47	21.68	21.41	21.58
W	5210					
Sz	9448					
ξ	1058					

The molecular graph of Chloroquine as depicted in Figure 5. Chloroquine was discovered in 1934 and it is on the World Health Organization's List of Essential Medicines. Chloroquine is anti-malarial medications also used against some auto-immune diseases. Chloroquine, along with hydroxychloroquine, was an early failed experimental treatment for COVID-19. Let us denote this graph by G_5. *The number of vertices and the number of edges of this graph are respectively 22 and 23. Also, the automorphism of this graph is* $\{(),(20,22)(19,21)\}$ *and clearly the automorphism group is isomorphic with the cyclic group* Z_2. *Besides, a list of topological indices together with their values is given in Table 10. and certain physicochemical properties are as follows:*

Table 9. The values of topological indices of Chloroquine.

Drugs	*MV*	*T*	*P*	*PSA*	*MR*	*FP*	*E*	*BP*
Chloroquine	287.9	44.0	38.6	28	97.4	232.3	72.1	460.6

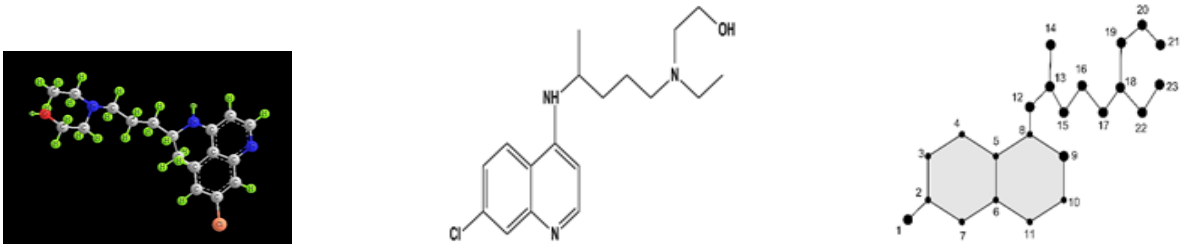


Figure 7. Hydroxychloroquine and its molecular graph.

Table 10. The values of topological indices of Chloroquine.

TI	1	2	3	4	5	6
IISI	22	11.66	11.54	9.66	4.77	17.93
GA	22.37	16.67	16.41	22.68	22.97	22.59
SDD	51.67	191.47	206.46	48.70	46.23	49.45
ISDD	10.44	5.248	5.09	10.90	11.44	10.75
W	156					
Sz	1717					
ξ	458					

The molecular graph of Hydroxychloroquine as depicted in Figure 6. Hydroxychloroquine is in a class of drugs called antimalarial. It works by killing the organisms that cause malaria. Hydroxychloroquine may work to treat rheumatoid arthritis and systemic lupus erythematosus by decreasing the activity of the immune system. Hydroxychloroquine has been studied for the treatment and prevention of coronavirus disease 2019 (COVID-19). Let us denote this graph by G_6. *The number of vertices and the number of edges of this graph are respectively 22 and 23. Also, the automorphism of this graph is identity. Besides, a list of topological indices together with their values is given in Table 12. and certain physicochemical properties are as follows:*

Table 11. The values of topological indices of Hydroxychloroquine.

Drugs	MV	T	P	PSA	MR	FP	E	BP
Hydroxychloroquine	285.4	49.8	39.2	48	99.0	266.3	83.0	516.7

Table 12. The values of topological indices of Hydroxychloroquine.

TI	1	2	3	4	5	6
IISI	23	12.07	11.88	10.23	4.66	19.77
GA	23.37	17.05	16.96	23.70	23.97	23.51
SDD	53.67	209.77	223.95	50.5	48.23	52.28
ISDD	10.94	5.17	5.28	11.44	11.94	11.15
W	1390					
Sz	1926					
ξ	502					

2.1. Numerical results: correlation between TI and chemical parameters

In order to investigate the relationship between the studied topological indices and some of their physicochemical properties, boiling point (BP), enthalpy of vaporization (E), flash point (FP), molar refraction (MR), pole surface (PSA), polarizability (P), surface tension (T) and molar volume (MV) of several drugs effective in the treatment of COVID-19, including favipiravir, ribavirin, remdesivir, theaflavin, and chloroquine and hydroxychloroquine have been investigated Values for different physicochemical properties, as shown in Table 13., were obtained from ChemSpider.

Table 13. The values for the various physicochemical properties were obtained from ChemSpider.

Drugs	*MV*	*T*	*P*	*PSA*	*MR*	*FP*	*E*	*BP*
Favipiravir	97.2	81.5	13.2	89	33.2	288.0	86.4	552.6
Ribavirin	117.1	106.8	20.3	144	51.1	340.7	99.3	639.8
Remdesivir	409.0	62.3	59.3	213	149.5	-	-	-
Theaflavin	301.0	138.6	54.4	218	137.3	336.5	153.5	1003.9
Chloroquine	287.9	44.0	38.6	28	97.4	232.3	72.1	460.6
Hydroxychloroquine	285.4	49.8	39.2	48	99.0	266.3	83.0	516.7

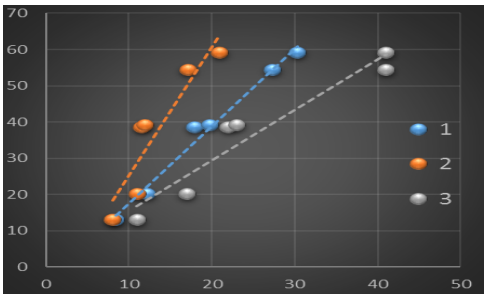
Table 14. The correlation between topological indices and physicochemical properties of various COVID-19 drugs.

	MV	T	P	PSA	MR	FP	E	BP
$IISI_1$	0.764	0.515	0.939	0.598	0.939	0.296	0.804	0.800
$IISI_2$	0.586	0.654	0.812	0.726	0.811	0.528	0.837	0.834
$IISI_3$	0.721	0.560	0.913	0.641	0.912	0.376	0.817	0.813
$IISI_4$	0.839	0.403	0.975	0.494	0.974	0.191	0.722	0.716
$IISI_5$	0.081	0.949	0.410	0.960	0.409	0.771	0.972	0.978
$IISI_6$	0.891	0.299	0.991	0.396	0.991	0.098	0.644	0.636
GA_1	0.749	0.534	0.931	0.616	0.931	0.316	0.816	0.812
GA_2	0.755	0.526	0.934	0.608	0.934	0.305	0.810	0.807
GA_3	0.750	0.533	0.932	0.615	0.931	0.317	0.814	0.810
GA_4	0.742	0.542	0.927	0.623	0.927	0.323	0.822	0.819
GA_5	0.750	0.532	0.932	0.615	0.931	0.326	0.810	0.806
GA_6	0.733	0.554	0.921	0.634	0.921	0.334	0.830	0.827
SDD_1	0.693	0.599	0.897	0.675	0.897	0.378	0.861	0.858
SDD_2	0.664	0.626	0.878	0.698	0.878	0.398	0.880	0.878
SDD_3	0.661	0.628	0.875	0.700	0.875	0.397	0.882	0.880
SDD_4	0.724	0.565	0.917	0.644	0.916	0.348	0.836	0.833
SDD_5	0.747	0.537	0.930	0.619	0.929	0.330	0.813	0.809
SDD_6	0.742	0.542	0.927	0.624	0.927	0.325	0.823	0.819
$ISDD_1$	0.769	0.508	0.942	0.592	0.942	0.292	0.797	0.793
$ISDD_2$	0.774	0.500	0.944	0.582	0.943	0.270	0.790	0.787
$ISDD_3$	0.753	0.528	0.933	0.611	0.933	0.323	0.806	0.802
$ISDD_4$	0.750	0.532	0.931	0.614	0.931	0.312	0.816	0.812
$ISDD_5$	0.752	0.530	0.933	0.613	0.932	0.324	0.808	0.804
$ISDD_6$	0.736	0.550	0.924	0.630	0.923	0.331	0.827	0.823
W	0.540	0.710	0.784	0.776	0.783	0.518	0.935	0.928
Sz	0.616	0.654	0.840	0.720	0.839	0.409	0.900	0.898
ξ	0.799	0.464	0.956	0.551	0.956	0.241	0.772	0.767

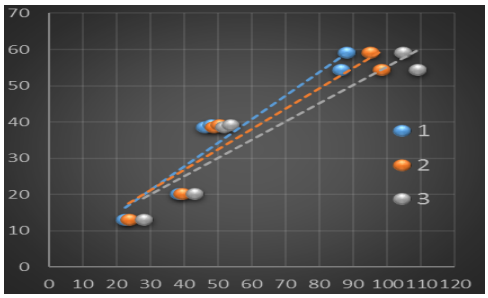
The Table 14. presents the correlation coefficients between various topological indices and physicochemical properties of different drugs for COVID-19. From the table, it can be observed that most of the topological indices have moderate to strong positive correlations with the physicochemical properties. For example, the topological indices $IISI_1$, $IISI_2$, $IISI_3$, GA_1, and GA_2 have correlation coefficients above 0.8 with the physicochemical properties. On the other hand, the topological indices $IISI_5$, SDD_6, $ISDD_3$, and Sz have relatively weaker correlations with the physicochemical properties. Overall, the table suggests that there are associations between these topological indices and the physicochemical properties of the COVID-19 drugs. However, further analysis is required to determine the nature and significance of these associations.

2.2 Multi-linear regression models

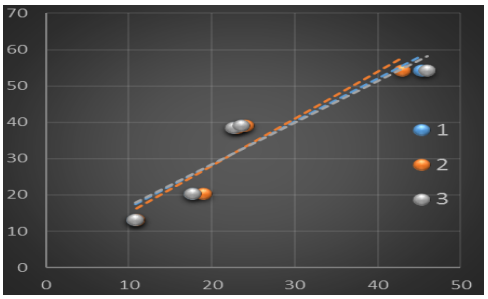
Multiple linear regression method was used to construct a model that shows the structural relationship between the studied compounds and topological indices. The names of the variables, regression



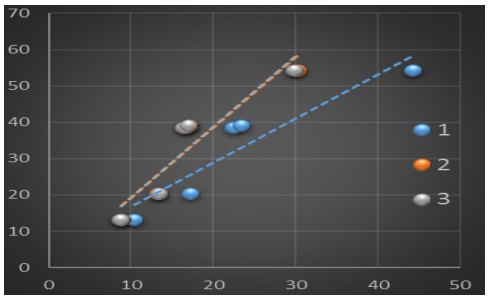
Corr($IISI_6$, P) = 0.991,
Corr($IISI_3$, P) = 0.913,
Corr($IISI_1$, P) = 0.939.



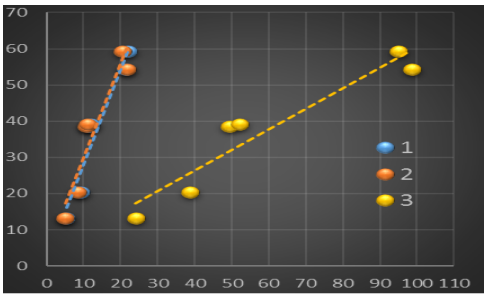
Corr(SDD_5, P) = 0.930,
Corr(SDD_4, P) = 0.917,
Corr(SDD_1, P) = 0.897.



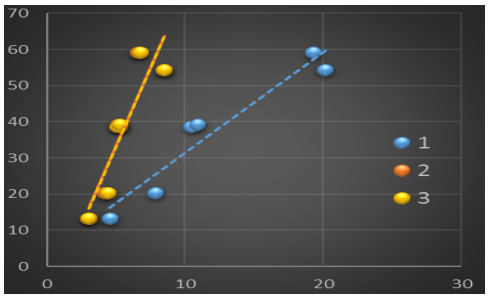
Corr(GA_4, P) = 0.927,
Corr(GA_5, P) = 0.932,
Corr(GA_6, P) = 0.921.



Corr(GA_1, P) = 0.931,
Corr(GA_2, P) = 0.934,
Corr(GA_3, P) = 0.932.

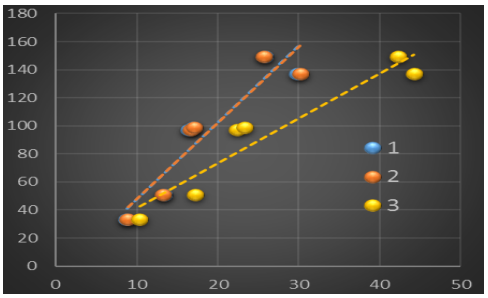


Corr($ISDD_5$, P) = 0.993,
Corr($ISDD_6$, P) = 0.924,
Corr(SDD_6, P) = 0.927.

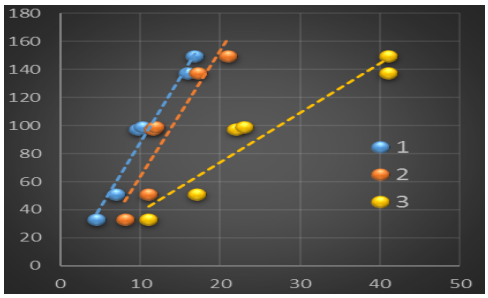


Corr($ISDD_1$,P) = 0.942,
Corr($ISDD_2$, P) = 0.944,
Corr($ISDD_3$, P) = 0.933.

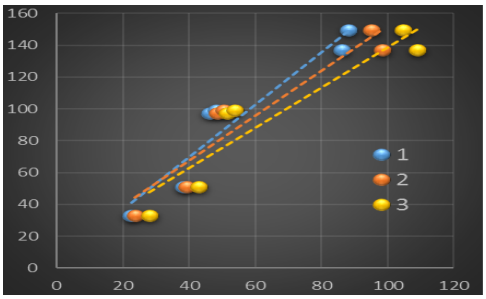
Figure 8. The correlation between topological indices and physicochemical properties of various COVID-19 drugs.



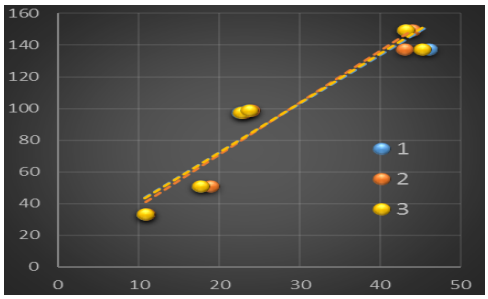
Corr(GA_1, MR) = 0.931,
Corr(GA_2, MR) = 0.934,
Corr(GA_3, MR) = 0.931.



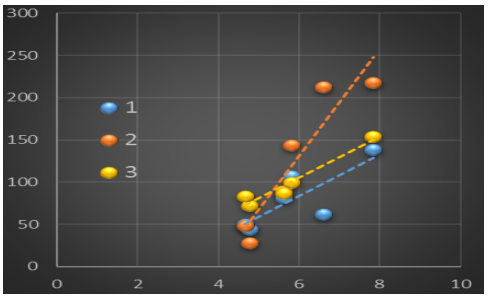
Corr($IISI_4$, MR) = 0.974,
Corr($IISI_3$, MR) = 0.912,
Corr($IISI_1$, MR) = 0.939.



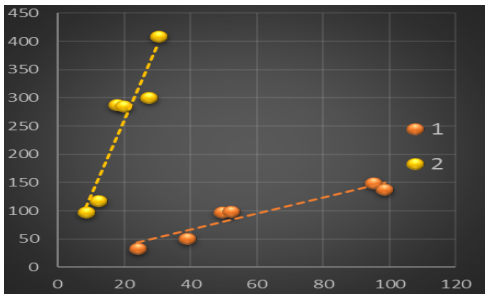
Corr(SDD_5, MR) = 0.929,
Corr(SDD_4, MR) = 0.916,
Corr(SDD_1, MR) = 0.897.



Corr(GA_6, MR) = 0.921,
Corr(GA_5, MR) = 0.931,
Corr(GA_4, MR) = 0.927.

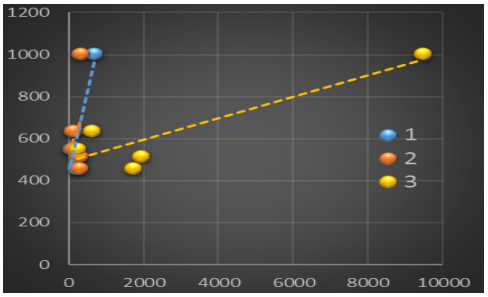


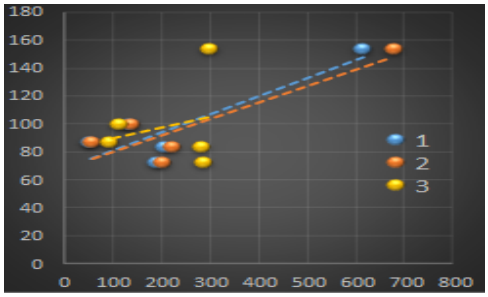
Corr($IISI_5$, T) = 0.949,
Corr($IISI_5$, PSA) = 0.960,
Corr($IISI_5$, E) = 0.972.



Corr(SDD_6, MR) = 0.927,
Corr($IISI_6$, MV) = 0.891.

Figure 9. The correlation between topological indices and physicochemical properties of various COVID-19 drugs.





Corr(SDD_3, BP) = 0.880,
Corr(W, BP) = 0.928,
Corr(Sz, BP) = 0.898.

Corr(SDD_2, E) = 0.880,
Corr(SDD_3, E) = 0.882,
Corr(W, E) = 0.935.

Figure 10. The correlation between topological indices and physicochemical properties of various COVID-19 drugs.

coefficients and standardized coefficients are listed in Table 9. The results show that $IISI_5$ index can predict the pole surface (PSA), enthalpy of vaporization (E), boiling point (BP), and surface tension (T) parameters.

Table 15. Multiple linear regression results.

Dependent Variable	Independent Variable	R	R Square	Adjusted R Square	Std. Error of the Estimate
PSA	ISI_5	0.93	0.87	0.83	33.54
MR	ISI_6	0.99	0.99	0.98	6.34
E	ISI_5	0.97	0.95	0.92	8.64
BP	ISI_5	0.98	0.96	0.94	52.46
P	ISI_6	0.99	0.99	0.98	2.49
T	ISI_5	0.81	0.66	0.57	23.94
MV	ISI_6	0.93	0.88	0.85	46.98

The table 21. presents the results of multiple linear regression models for different dependent variables (PSA, MR, E, BP, P, T, and MV) in relation to the independent variables ISI_5 and ISI_6. From the table, we can see that for most of the dependent variables, there is a strong positive correlation ($R \geq 0.8$) with the independent variables. The R Square values are also high (above 0.8), indicating that the independent variables explain a significant portion of the variance in the dependent variables. The Adjusted R Square values are slightly lower than the R Square values, which suggests that including more independent variables in the models does not improve the fit significantly. This may indicate that the independent variables included are already capturing most of the variance in the dependent variables. The Std. Error of the Estimate values vary across the models, with some being relatively low (e.g., for MR and P) and others being relatively higher (e.g., for MV and BP). Lower values indicate higher accuracy in predicting the dependent variable. Overall, the table suggests that the independent variable (ISI) has a strong positive relationship with all of the dependent variables. The regression models have high R-Square values, indicating a good fit of the data.

3. Centrality measures

In this section, we analyze various centrality measures for the six drugs that have proven effective in treating corona. Centrality measures are mathematical metrics that help assess the importance or prominence of individual molecules within a larger network or system. By calculating these measures for each drug, we gain insights into the structural and functional properties of the molecules. The first centrality measure we consider is the "Degree" centrality. This measure quantifies the number of connections or neighbors that a molecule has to other molecules in the network. A higher degree centrality indicates a molecule with more interactions, suggesting its potential significance in the chemical network. Next, we look at the "Betweenness" centrality measure. This metric assesses the extent to which a molecule acts as a bridge or mediator between other molecules in the network. A higher betweenness centrality value suggests that the molecule plays a critical role in the flow of information or substances within the chemical system. We also examine the "Eigenvector" centrality measure. This measure assigns importance to a molecule based not only on its direct connections but also the connections of its neighboring molecules. Molecules with a higher eigenvector centrality are considered influential if they are connected to other well-connected molecules in the network. The "Katz" centrality measure takes into account both direct and indirect connections of a molecule, assigning higher importance to molecules that are connected to other important molecules in the network. This measure helps us identify molecules that have significant influence within the chemical system. Another centrality measure we explore is the "Closeness" centrality. This metric evaluates how close a molecule is to all other molecules in the network, considering the lengths of the shortest paths between them. A higher closeness centrality suggests that a molecule can efficiently transmit information or substances to other molecules in the system. The "Harmonic" centrality measure is similar to closeness centrality but considers the sum of the reciprocals of the distances rather than the distances themselves. It captures the inverse of the average distance from a molecule to all others, highlighting molecules that are well-connected and central within the network. Lastly, we compute the "Subgraph" centrality measure. This metric calculates the number of walks of different lengths passing through each molecule in the network. It identifies molecules that participate in numerous paths or cycles in the chemical system, implying their potential importance in various chemical processes. By calculating and analyzing these centrality measures for the six drugs, we gain valuable insights into their roles and significance within the chemical network, which can aid in predicting their chemical properties and effectiveness in treating corona.

Table 16. The centrality measures of G_1.

Vertices	Degree	Between ness	Eigen vector	Katz	Close ness	Harmonic	Subgraph	
1	0.1	0	0.145	0.27	0.294	3.767	1.641	
2	0.3	0.28	0.334	0.326	0.4	5.412	3.028	
3	0.2	0.27	0.351	0.304	0.455	5.333	2.393	
4	0.3	0.57	0.475	0.334	0.526	6.167	3.192	
5	0.3	0.34	0.413	0.329	0.455	5.750	3.085	
6	0.2	0.13	0.298	0.301	0.4	5.0	2.339	
7	0.2	0.1	0.275	0.301	0.357	4.817	2.337	
8	0.1	0	0.179	0.271	0.323	3.95	1.643	
9	0.3	0.38	0.331	0.326	0.417	5.5	3.028	
10	0.1	0	0.143	0.271	0.303	3.817	1.641	
11	0.1	0	0.143	0.271	0.303	3.817	1.641	
sum	2.2	2.07	3.087	3.304	4.233	53.33	25.968	**94.192**

Cumulative centrality index

Table 17. The centrality measures of G_2.

Vertices	Degree	Between ness	Eigen vector	Katz	Close ness	Harmonic	Subgraph	
1	0.0625	0.0	0.064	0.212	0.193	4.283	1.592	
2	0.125	0.125	0.156	0.236	0.235	5.626	2.285	
3	0.1875	0.25	0.321	0.263	0.291	7.019	3.156	
4	0.125	0.225	0.298	0.242	0.32	6.700	2.414	
5	0.1875	0.55	0.411	0.266	0.372	7.733	3.216	
6	0.1875	0.275	0.363	0.263	0.326	7.283	3.161	
7	0.0625	0.0	0.148	0.215	0.25	5.136	1.645	
8	0.1875	0.175	0.334	0.263	0.291	7.019	3.160	
9	0.0625	0.0	0.136	0.215	0.228	4.960	1.645	
10	0.1875	0.533	0.349	0.263	0.364	7.533	3.159	
11	0.125	0.083	0.214	0.239	0.302	6.317	2.358	
12	0.125	0.033	0.178	0.239	0.271	6.076	2.358	
13	0.1875	0.333	0.222	0.263	0.286	6.910	3.153	
14	0.125	0.333	0.232	0.241	0.32	6.650	2.412	
15	0.1875	0.242	0.135	0.258	0.239	6.227	3.026	
16	0.0625	0.0	0.055	0.215	0.196	4.490	1.641	
17	0.0625	0.0	0.055	0.215	0.195	4.490	1.641	
Sum	2.25	3.157	3.671	4.108	4.679	104.452	42.022	**164.339**

Cumulative centrality index

Table 18. The centrality measures of G_3.

Vertices	Degree	Betweenness	Eigenvector	Katz	Closeness	Harmonic	Subgraph	Cumulative centrality index
1	0.05	0.003	0.004	0.152	0.110	7.146	2.283	
2	0.05	0.025	0.006	0.152	0.121	7.700	2.285	
3	0.05	0.070	0.010	0.153	0.135	8.507	2.337	
4	0.075	0.227	0.021	0.167	0.154	9.964	3.083	
5	0.05	0.070	0.010	0.153	0.135	8.507	2.337	
6	0.05	0.025	0.006	0.152	0.121	7.700	2.285	
7	0.05	0.261	0.033	0.156	0.173	10.308	2.444	
8	0.1	0.645	0.064	0.182	0.196	11.952	3.938	
9	0.025	0.0	0.025	0.139	0.165	8.792	1.696	
10	0.05	0.409	0.033	0.156	0.181	10.513	2.444	
11	0.075	0.396	0.020	0.167	0.167	10.400	3.082	
12	0.025	0.0	0.008	0.138	0.143	7.917	1.643	
13	0.075	0.337	0.012	0.167	0.152	9.915	3.078	
14	0.025	0.0	0.005	0.138	0.132	7.568	1.643	
15	0.05	0.261	0.006	0.153	0.138	8.918	2.335	
16	0.05	0.224	0.003	0.153	0.125	8.485	2.335	
17	0.075	0.190	0.002	0.167	0.114	8.552	3.073	
18	0.05	0.05	0.001	0.152	0.103	7.203	2.283	
19	0.025	0.0	0.0	0.136	0.094	5.822	1.592	
20	0.05	0.05	0.001	0.152	0.103	7.203	2.283	
21	0.025	0.0	0.0	0.136	0.094	5.822	1.592	
22	0.05	0.511	0.075	0.155	0.195	10.666	2.391	
23	0.05	0.508	0.128	0.154	0.192	10.485	2.339	
24	0.075	0.504	0.255	0.169	0.188	11.183	3.160	
25	0.05	0.369	0.267	0.157	0.177	10.575	2.471	
26	0.1	0.424	0.433	0.185	0.169	11.858	4.084	
27	0.075	0.081	0.317	0.170	0.163	10.775	3.221	
28	0.075	0.111	0.262	0.169	0.171	10.644	3.162	
29	0.025	0.0	0.102	0.138	0.147	8.061	1.645	
30	0.025	0.0	0.123	0.138	0.140	8.087	1.647	
31	0.025	0.0	0.168	0.140	0.145	8.601	1.700	
32	0.075	0.361	0.364	0.172	0.155	11.118	3.276	
33	0.05	0.041	0.209	0.154	0.137	9.257	2.362	
34	0.05	0.005	0.175	0.154	0.125	8.748	2.360	
35	0.075	0.119	0.243	0.170	0.127	9.832	3.217	
36	0.075	0.254	0.294	0.171	0.141	10.507	3.222	
37	0.05	0.066	0.152	0.153	0.125	8.748	2.341	
38	0.05	0.024	0.097	0.152	0.114	7.947	2.286	
39	0.05	0.005	0.098	0.153	0.105	7.714	2.337	
40	0.075	0.076	0.156	0.167	0.115	8.947	3.086	
41	0.025	0.0	0.060	0.138	0.104	6.797	1.643	
Sum	2.2	6.702	4.248	6.38	5.791	369.444	102.021	**496.786**

Table 19. The centrality measures of G_4.

Vertices	Degree	Between ness	Eigen vector	Katz	Close ness	Harmonic	Subgraph	Cumulative centrality index
1	0.024	0.000	0.037	0.135	0.111	6.932	1.642	
2	0.073	0.065	0.094	0.162	0.125	9.002	3.029	
3	0.049	0.097	0.113	0.151	0.139	9.262	2.391	
4	0.073	0.210	0.192	0.165	0.156	10.731	3.146	
5	0.073	0.127	0.187	0.166	0.141	10.312	3.199	
6	0.073	0.083	0.129	0.164	0.127	9.468	3.087	
7	0.024	0.000	0.051	0.135	0.113	7.206	1.643	
8	0.049	0.010	0.088	0.151	0.115	8.372	2.390	
9	0.073	0.230	0.185	0.152	0.172	10.610	2.396	
10	0.073	0.432	0.278	0.167	0.192	11.922	3.197	
11	0.073	0.153	0.202	0.164	0.169	10.810	3.087	
12	0.049	0.083	0.154	0.151	0.154	9.931	2.395	
13	0.024	0.000	0.080	0.135	0.145	8.224	1.643	
14	0.073	0.484	0.316	0.167	0.207	12.367	3.201	
15	0.049	0.066	0.208	0.151	0.178	10.534	2.395	
16	0.073	0.072	0.210	0.164	0.163	10.469	3.085	
17	0.024	0.000	0.083	0.135	0.140	7.988	1.643	
18	0.073	0.093	0.241	0.165	0.168	10.825	3.143	
19	0.073	0.000	0.095	0.135	0.144	12.078	1.645	
20	0.073	0.202	0.306	0.168	0.193	12.514	3.255	
21	0.049	0.482	0.315	0.167	0.216	11.088	3.201	
22	0.049	0.358	0.176	0.150	0.207	10.864	2.339	
23	0.073	0.351	0.130	0.150	0.201	11.760	2.337	
24	0.049	0.461	0.153	0.165	0.197	10.534	3.138	
25	0.073	0.110	0.124	0.151	0.178	11.062	2.390	
26	0.024	0.140	0.160	0.164	0.185	8.425	3.082	
27	0.073	0.000	0.063	0.135	0.156	11.455	1.643	
28	0.024	0.154	0.218	0.165	0.190	8.652	3.140	
29	0.024	0.000	0.086	0.135	0.160	8.192	1.645	
30	0.073	0.432	0.135	0.166	0.183	11.550	3.195	
31	0.073	0.153	0.098	0.164	0.163	10.555	3.087	
32	0.024	0.000	0.039	0.135	0.140	8.037	1.643	
33	0.049	0.083	0.075	0.151	0.149	9.744	2.395	
34	0.073	0.127	0.091	0.166	0.137	10.169	3.199	
35	0.073	0.210	0.093	0.165	0.151	10.544	3.146	
36	0.049	0.230	0.090	0.152	0.165	10.355	2.396	
37	0.049	0.097	0.055	0.151	0.134	9.119	2.391	
38	0.073	0.065	0.046	0.162	0.121	8.888	3.029	
39	0.024	0.000	0.018	0.135	0.108	6.839	1.642	
40	0.049	0.010	0.043	0.151	0.112	8.280	2.390	
41	0.073	0.083	0.063	0.164	0.123	9.354	3.087	
42	0.024	0.000	0.025	0.135	0.110	7.113	1.643	
Sum	2.312	5.953	5.545	6.462	6.538	412.136	107.77	**546.716**

Table 20. The centrality measures of G_5.

Vertices	**Degree**	**Between ness**	**Eigen vector**	**Katz**	**Close ness**	**Harmonic**	**Subgraph**	
1	0.048	0.000	0.102	0.190	0.146	4.915	1.641	**Cumulative centrality index**
2	0.143	0.109	0.244	0.229	0.169	6.704	3.028	
3	0.095	0.077	0.215	0.211	0.184	6.411	2.337	
4	0.095	0.140	0.271	0.212	0.210	6.923	2.342	
5	0.143	0.417	0.435	0.235	0.244	8.232	3.199	
6	0.143	0.217	0.398	0.233	0.219	7.840	3.144	
7	0.095	0.103	0.268	0.214	0.191	6.794	2.391	
8	0.143	0.556	0.374	0.233	0.263	6.544	3.141	
9	0.095	0.092	0.242	0.212	0.219	6.407	2.339	
10	0.095	0.041	0.206	0.210	0.198	6.848	2.286	
11	0.095	0.035	0.252	0.212	0.188	8.269	2.339	
12	0.095	0.524	0.220	0.214	0.263	7.519	2.388	
13	0.143	0.552	0.153	0.229	0.256	7.643	3.024	
14	0.048	0.000	0.064	0.190	0.206	5.604	1.641	
15	0.095	0.467	0.083	0.211	0.239	6.935	2.332	
16	0.095	0.429	0.046	0.210	0.219	6.648	2.283	
17	0.095	0.381	0.027	0.211	0.198	6.548	2.334	
18	0.143	0.343	0.020	0.230	0.178	6.835	3.073	
19	0.095	0.095	0.010	0.209	0.154	5.650	2.283	
20	0.048	0.000	0.004	0.188	0.135	4.399	1.592	
21	0.095	0.095	0.010	0.209	0.154	5.650	2.283	
22	0.048	0.000	0.004	0.188	0.135	4.399	1.592	
Sum	2.19	4.673	3.648	4.68	4.368	143.717	53.012	**216.288**

Table 21. The centrality measures of G_6.

Vertices	Degree	Between ness	Eigen vector	Katz	Close ness	Harmonic	Subgraph	Cumulative centrality index
1	0.045	0.000	0.102	0.186	0.139	4.987	1.641	
2	0.136	0.103	0.244	0.224	0.161	6.781	3.028	
3	0.091	0.074	0.215	0.207	0.175	6.494	2.337	
4	0.091	0.136	0.271	0.207	0.198	7.014	2.342	
5	0.136	0.407	0.435	0.230	0.229	8.332	3.199	
6	0.136	0.208	0.398	0.228	0.206	7.931	3.144	
7	0.091	0.098	0.268	0.209	0.180	6.877	2.391	
8	0.136	0.548	0.374	0.228	0.247	8.380	3.141	
9	0.091	0.090	0.242	0.207	0.208	6.948	2.339	
10	0.091	0.040	0.206	0.205	0.188	6.498	2.286	
11	0.091	0.032	0.252	0.207	0.177	6.627	2.339	
12	0.091	0.524	0.220	0.209	0.250	7.644	2.388	
13	0.136	0.558	0.153	0.224	0.247	7.786	3.024	
14	0.045	0.000	0.064	0.186	0.200	5.729	1.641	
15	0.091	0.485	0.083	0.207	0.234	7.101	2.332	
16	0.091	0.455	0.046	0.205	0.218	6.848	2.283	
17	0.091	0.416	0.028	0.207	0.200	6.798	2.334	
18	0.136	0.394	0.020	0.226	0.182	7.168	3.075	
19	0.091	0.173	0.011	0.207	0.159	6.150	2.332	
20	0.091	0.091	0.005	0.203	0.140	5.399	2.231	
21	0.045	0.000	0.002	0.184	0.124	4.275	1.591	
22	0.091	0.091	0.010	0.205	0.157	5.900	2.283	
23	0.045	0.000	0.004	0.184	0.137	4.599	1.592	
Sum	2.179	4.923	3.653	4.785	4.356	152.266	55.293	**227.455**

Table 22. The correlation between centrality measures and physicochemical properties of various COVID-19 drugs.

	MV	T	P	PSA	MR	FP	E	BP
Degree	-0.066	0.958	0.215	0.688	0.215	0.828	0.954	0.960
Betweenness	0.966	-0.040	0.994	0.486	0.994	-0.038	0.496	0.488
Eigenvector	0.541	0.637	0.754	0.726	0.754	0.497	0.917	0.916
Katz	0.870	0.231	0.972	0.681	0.971	0.252	0.755	0.751
Closeness	0.559	0.627	0.761	0.891	0.761	0.618	0.973	0.975
Harmonic	0.780	0.373	0.918	0.782	0.917	0.390	0.876	0.874
Subgraph	0.822	0.314	0.945	0.747	0.945	0.340	0.834	0.831
Cumulative cetrality index	0.790	0.362	0.924	0.775	0.924	0.379	0.868	0.865

The Table 22. provides the correlation between centrality measures and physicochemical properties of various COVID-19 drugs. The correlation coefficients for each combination of centrality measures and physicochemical properties are listed in the table. The coefficients range from -0.066 to 0.994, indicating the strength and direction of the relationship between the centrality measures and physico-

chemical properties. For example, the Degree centrality measure has a negative correlation with MV (-0.066), a strong positive correlation with T (0.958) and BP (0.960), a moderate positive correlation with PSA (0.688), MR (0.215), FP (0.828), E (0.954), and a weak positive correlation with P (0.215). Similarly, other centrality measures also show varying degrees of correlation with the physicochemical properties. The Betweenness centrality measure has a very strong positive correlation with P (0.994) and MR (0.994), a moderate positive correlation with PSA (0.486), FP (-0.038), and a weak positive correlation with T (-0.040), E (0.496), and BP (0.488). The table provides a comprehensive analysis of the correlation between centrality measures and physicochemical properties, which can be used to understand the relationship between network centrality and the physicochemical characteristics of COVID-19 drugs.

3. Conclusion

In this paper, some of the topological indices of the six drugs used in the treatment of Covid 19 were calculated and the relationship between the indices and the physicochemical parameters of the drugs has investigated. The results of multiple linear regression analysis showed that among the topological indices studied in this paper, $IISI_5$ index had the best discriminate power for prediction of pole surface (PSA), enthalpy of vaporization (E), boiling point (BP), and surface tension (T) parameters. Also, the $IISI_6$ index had the discriminate power for anticipating the molar volume (MV), polarizability (P), and the molar refraction (MR) parameters. Additionally, centrality measures were computed for each molecule, and the results are presented in Table 22.. Notably, significant correlations were found between the centrality indices and specific physical-chemical properties. The observed relationships between the chemical parameters of the drugs and topological indices as well as centrality measures highlight the potential of these computational tools in drug discovery and design. The identified correlations provide a deeper understanding of how specific structural features influence the chemical behavior of anti-corona drugs. Leveraging this knowledge can aid researchers in rapidly screening and identifying novel molecules with desirable chemical properties. This study underscores the significance of topological indices and centrality measures in predicting the chemical properties of anti-corona drugs. The demonstrated correlations between the chemical parameters of the drugs and selected indices and centrality measures offer valuable insights for the design and optimization of new drug candidates. By employing advanced computational techniques, researchers can accelerate the drug discovery process and contribute to combating the corona virus more efficiently and effectively.

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