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Research Article

QSPR Modeling with Topological Indices of Some Potential Drug Candidates against COVID-19

Özge Çolakoğlu

Mathematics Department, Mersin University, Mersin 33343, Turkey

Correspondence should be addressed to Özge Çolakoğlu; ozgeeclkgl@gmail.com

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COVID-19, which has spread all over the world and was declared as a pandemic, is a new disease caused by the coronavirus family. There is no medicine yet to prevent or end this pandemic. Even if existing drugs are used to alleviate the pandemic, this is not enough. Therefore, combinations of existing drugs and their analogs are being studied. Vaccines produced for COVID-19 may not be effective for new variants of this virus. Therefore, it is necessary to find the drugs for this disease as soon as possible. Topological indices are the numerical descriptors of a molecular structure obtained by the molecular graph. Topological indices can provide information about the physicochemical properties and biological properties of molecules in the quantitative structure-property relationship (QSPR) and quantitative structure-activity relationship (QSAR) studies. In this paper, some analogs of lopinavir, favipiravir, and ritonavir drugs that have the property of being potential drugs against COVID-19 are studied. QSPR models are studied using linear and quadratic regression analysis with topological indices for enthalpy of vaporization, flash point, molar refractivity, polarizability, surface tension, and molar volume properties of these analogs.

1. Introduction

COVID-19, which emerged in 2019, is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which is a new coronavirus. Coronavirus family refers to enveloped, positive-sense, and single-stranded RNA viruses [1]. SARS-CoV-2 is a positive single-stranded RNA virus containing proteins. COVID-19 is a respiratory disease transmitted from person to person. COVID-19 patients may present symptoms ranging from mild to severe diseases, such as fever, cough, sore throat, rhinorrhea, severe pneumonia, and septic shock [2]. With the rapid spread of this disease all over the world, the World Health Organization (WHO) declared COVID-19 as a pandemic in March 2020. The WHO reported that nearly 3 million people have died since the outbreak of the pandemic [3]. There is no medicine yet to alleviate or end this pandemic. Existing drugs are being used to alleviate the pandemic. These drugs are chloroquine, hydroxychloroquine, azithromycin, remdesivir, lopinavir, ritonavir, Arbidol, favipiravir, theaflavin, thalidomide, ribavirin, etc. [4]. Studies showed that some of these drugs are not suitable for the treatment of COVID-19 [5]. For example, FDA warns against the use of hydroxychloroquine or chloroquine for COVID-19 outside the hospital setting or a clinical trial due to the risk of heart rhythm problems [6]. Among these drugs, there are opinions that the use of remdesivir, favipiravir, and lopinavir is suitable for the treatment of COVID-19 disease [7]. Since the drugs used for HIV, SARS-CoV, and Mers-CoV do not have sufficient effect for SARS-CoV-2, many countries have focused on combinations of these drugs. In the United Kingdom, studies are being conducted on favipiravir and lopinavir/ritonavir or combination therapy [8]. In Egypt, studies are being conducted on favipiravir [9], lopinavir/ritonavir, and remdesivir combination [10], and in the United States, studies are being conducted on favipiravir, lopinavir/ritonavir [11, 12], and so on (see details in [4]).

New variants of the SARS-CoV-2 virus are emerging, and these variants are thought to be resistant to some vaccines produced for COVID-19. For this reason, it is

necessary to find a drug that will prevent and end this disease as soon as possible. Drug discovery takes effort and time and is a costly process. Recently, computer-aided drug design (CADD) has been used successfully to significantly alleviate this process. This includes the prediction of electronic, drug-like, pharmacokinetic, 3D-QSAR, and physicochemical properties of target candidates.

The graph theory, which was first introduced by Euler in 1736, is a branch of discrete mathematics. It has been studied in physics, biology, computer sciences, chemistry, and so forth [13]. Chemical graph theory combines mathematical modeling of chemical phenomena with graph theory. It is focused on topological indices that are well correlated with the properties of a molecule or molecular compounds. Topological indices are widely used to predict the physicochemical and bioactivity properties of a molecule or molecular compound in the quantitative structure-property/structure-activity relationship (QSPR/QSAR) modeling [14]. The topological index is a real descriptor of the topological structure of a molecule or molecular compounds [15]. The first known topological index was the Wiener index in 1947, which was used to determine the physical properties of paraffin [16].

The molecular graph, G, is represented by unsaturated hydrocarbon skeletons of the molecule and molecular compounds. The vertices of the molecular graph correspond to non-hydrogen atoms and their set is defined by $V(G)$. The edges of molecular graph correspond to covalent bonds between the corresponding atoms and their set is defined by $E(G)$ [17]. The degree of a vertex v is defined by $d(v)$ (see [13] for basic definitions and notations on graph theory).

Omar et al. designed eight derivatives based on the core of hydroxychloroquine to use them in the treatment of COVID-19 and calculated the biological activity of designed molecules by QSAR [18]. Kirmani et al. established QSPR models with linear regression between physicochemical properties of potential antiviral drugs and some topological indices for various antiviral drugs used in the treatment of COVID-19 patients [19]. Havare obtained curvilinear regression models for boiling point of potential drugs against COVID-19 using various topological indices [20, 21]. Zhong et al. established QSPR between the ev-degree and ve-degree-based topological indices and measured the physicochemical parameters of the photochemical screened against SARS-CoV-2 [22]. Chaluvaraju and Shaikh established a multilinear regression model with the atom-bond connectivity (ABC) indices for the IC_{50} values of some drugs used in the treatment of COVID-19 [23]. Various topological indices were calculated to be used in QSPR and QSAR models of drugs used for the treatment of COVID-19 [24–27].

Rafi et al. studied analogs of lopinavir and favipiravir as potential drug candidates against COVID-19. They saw that all structurally modified analogs have been less toxic than the selected candidates and contain highly remediable properties [28].

In this paper, CID10009410, CID44271905, CID3010243, and CID271958 structures which are structural analogs of lopinavir, CID89869520 structure which is favipiravir analog, and lopinavir-d8 (CID71749833) which is ritonavir analog are considered. These structures have the property of being potential drugs against COVID-19. QSPR models are obtained by linear and quadratic regression analysis using topological indices for enthalpy of vaporization, flash point, molar refractivity, polarizability, surface tension, and molar volume properties of these structures.

2. Material and Method

Small molecules such as lopinavir and favipiravir significantly inhibit the activity of Mpro (main protease) and RdRp (viral RNA-dependent RNA polymerase) in vitro [4]. The structure of all selected compounds was downloaded from the PubChem database [29].

Lopinavir (see Figure 1) and ritonavir (see Figure 2) are inhibitors of human immunodeficiency virus-1 (HIV-1) aspartate protease. Since the previous SARS-CoV major protease has 96.1% similarity to the SARS-CoV-2 major protease, these two drugs can be used as a homologous target [30].

Favipiravir is a pyrazine carboxamide derivative with activity against RNA viruses (see Figure 2). It is an antiviral drug developed against influenza (flu virus). It was approved for the treatment of pandemic influenza emerging in Japan in 2014. It is used to treat moderate to mild COVID-19 patients. It is being studied for the treatment of COVID-19 [4, 31].

The structure of CID10009410 is a lopinavir analog and is generated by adding –F groups at the end of their two-dimensional (2D) structure [28]. CID44271905 structure which is lopinavir analog is generated by removing trimethyl-benzene fragment into the 2D structure of lopinavir [28]. CID44271958 structure is generated by adding 1,3,5-trimethyl-benzene and benzene fragments into the 2D structure of lopinavir [28]. The structure of CID3010243 is generated by removing tetrahydro-pyrimidionepropylene urea fragment and adding 2-imidazolinone fragments into lopinavir [28]. Figure 1 shows lopinavir and its analogs. CID89869520 structure which is the favipiravir analog is generated by adding –CH3 groups at the end of its 2D structure (see Figure 2) [28]. Lopinavir-d8 is a labeled selective HIV-1 protease inhibiting drug which is an analog of ritonavir, and this drug may act against COVID-19 (see Figure 2) [28].

In this study, the vertex-degree-based topological indices which are the first Zagreb index (M_1) [32], the second Zagreb index (M_2) [32], hyper-Zagreb index [33], max-min rodeg index [34], min-max rodeg index, Albertson index [35], sigma index [36], inverse symmetric deg index [37], atom-bond connectivity index [38], and inverse sum indeg index [34] are studied.

The selected bond additive and degree-based topological indices are the most studied indices and can well predict the physicochemical and bioactivity properties of chemical structures. The first and second Zagreb indices are topological indices that best predict the molar reaction and polarity of some new drugs used in cancer treatment [39]. The max-min rodeg index gives very good prediction in the linear model for enthalpy of vaporization and standard

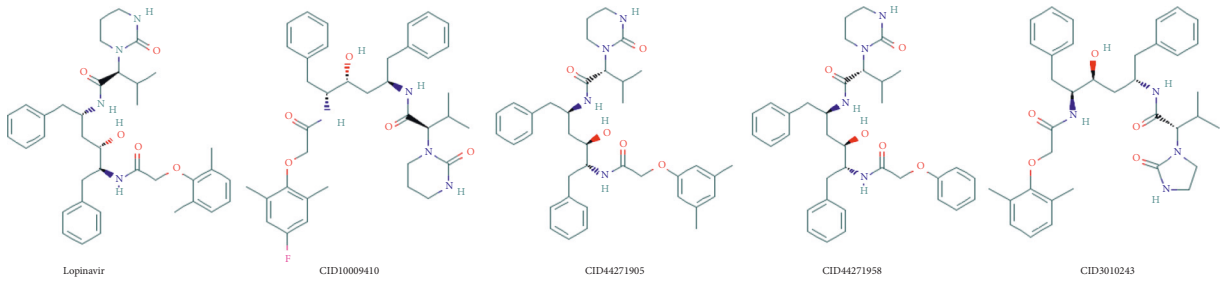

Figure 1: The chemical structures of lopinavir and lopinavir analogs [29].

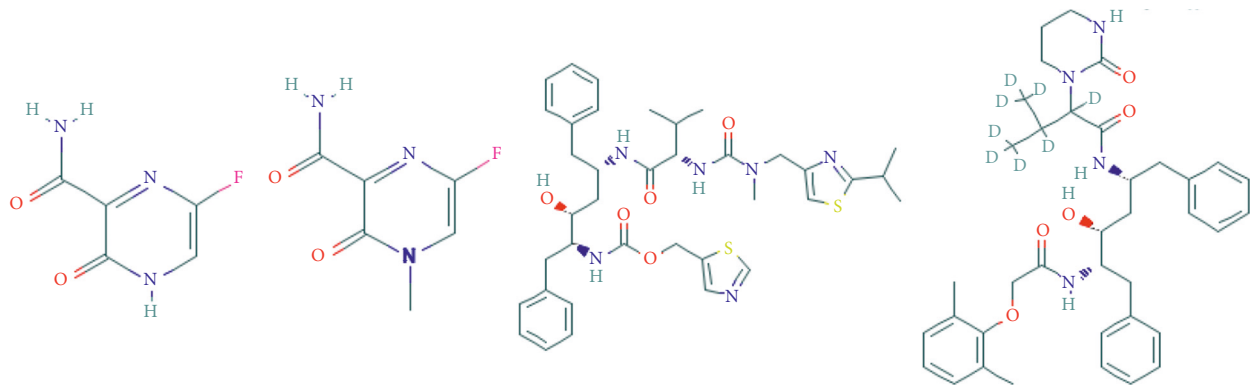

Figure 2: The chemical structures of favipiravir, ritonavir, and their analogs [29].

Table 1: Topological indices and their mathematical expressions.

Vertex-degree-based topological indices	Mathematical expressions
First Zagreb index	$M_1(G) = \sum_{uv\in E(G)} (d(u) + d(v))$
Second Zagreb index	$M_2(G) = \sum_{uv\in E(G)} (d(u)d(v))$
Hyper-Zagreb index	$HM(G) = \sum_{uv\in E(G)} (d(u) + d(v))^2$
Max-min rodeg index	$mM_{s\ de}(G) = \sum_{uv\in E(G)} \sqrt{\max\{d(u), d(v)\}/\min\{d(u), d(v)\}}$
Min-max rodeg index	$mM_{s\ de}(G) = \sum_{uv\in E(G)} \sqrt{\min\{d(u), d(v)\}/\max\{d(u), d(v)\}}$
Albertson index	$irr(G) = \sum_{uv\in E(G)} \lvert d(u) - d(v)\rvert$
Sigma index	$\sigma(G) = \sum_{uv\in E(G)} (d(u) - d(v))^2$
Inverse symmetric deg index	$IS\ DD(G) = \sum_{uv\in E(G)} d(u)d(v)/d(u)^2 + d(v)^2$
Atom-bond connectivity index	$ABC(G) = \sum_{uv\in E(G)} d(u) + d(v) - 2/d(u)d(v)$
Inverse sum indeg index	$ISI(G) = \sum_{uv\in E(G)} d(u)d(v)/d(u) + d(v)$

enthalpy of vaporization in the set of octane isomers and also for log water activity coefficient in the set of polychlorobiphenyles [40]. Atom-bond connectivity index has a good prediction ability when it comes to the enthalpy of formation of alkanes [38]. The first hyper-Zagreb index gives the best predictor model in the linear model for the boiling point of benzenoid hydrocarbons [41]. The inverse sum indeg index is the best predictor for the total surface area of octane isomers [34]. In addition, the ISI index is very good at predicting the vaporization enthalpy and sublimation enthalpy of monocarboxylic acids [42]. Various degree-based irregularity indices such as Albertson index and sigma index give a good prediction for physicochemical properties of octane isomers [43]. Table 1 shows the mathematical expressions of these indices.

The values of enthalpy of vaporization (E), flash point (FP), molar refractivity (MR), polarizability (P), surface tension (T), and molar volume (MV) of these potential drugs against COVID-19 are taken from ChemSpider [44]. Table 2 shows some of the physicochemical properties of potential drugs that can be used in the treatment of COVID-19.

Curvilinear regression analysis can be used to fit curves instead of straight lines. In this study, the following equations are tested:

$$\begin{aligned} &Y = a + b_1 X; n, R^2, F\,(\text{linear equation}),\\ &Y = a + b_1 X + b_2 X^2; n, R^2, F\,(\text{quadratic equation}), \end{aligned} \tag{1}$$

where Y is the response or dependent variable, a is the regression model constant, b_i $(i = 1, 2)$ are the coefficients for

Table 2: The physicochemical properties of potential drugs to be used in the treatment of COVID-19.

PubChem ID	Formula	E	FP	MR	P	T	MV
CID71749833	$C_{37}H_{40}D_8N_4O_5$	140.8	512.7	179,2	71	49,5	540,5
CID10009410	$C_{37}H_{47}FN_4O_5$	141,1	513,7	179,2	71	49	544,7
CID44271905	$C_{37}H_{48}N_4O_5$	140,8	512,7	179,2	71	49,5	540,5
CID3010243	$C_{36}H_{46}N_4O_5$	140	509,5	174,6	69,2	50,5	522,7
CID44271958	$C_{35}H_{44}N_4O_5$	138,9	505,1	169,5	67,2	50,9	507,9
CID89869520	$C_6H_6FN_3O_2$	63,2	185,5	41,3	16,4	72,9	110

Table 3: The values of topological indices of the molecular structures of potential drugs to be used in the treatment of COVID-19.

PubChem ID	$\mathbf{M_1}$	$\mathbf{M_2}$	**HM**	$\mathbf{Mm_{sde}}$	$\mathbf{mM_{sde}}$	**irr**	σ	**ISDD**	**ABC**	**ISI**
71749833	282	328	1432	74,646	46,159	60	120	24,296	24,916	63,72
10009410	236	270	1138	61,532	42,159	40	58	22,353	36,056	55,65
44271905	230	261	1100	60,250	41,214	40	56	21,976	35,321	54,3
3010243	226	259	1088	58,351	40,948	36	52	15,130	34,533	58,75
44271958	218	247	1032	55,887	40,794	32	44	19,030	33,688	52
89869520	58	66	288	16,559	9,152	14	24	4,846	8,910	13,05

the individual descriptor, X, X are independent variables, n is the number of samples used for building the regression equation, R^2 is the square of the correlation coefficient, R is the correlation coefficient, and F is the calculated value of the F-ration test. For more detailed information, see [45]. Note that when the experimental and theoretical results are close to each other, the correlation coefficient is close to 1. The observed values and model predictions must be compared to measure the predictive quality of the model (see details in [46, 47]). Therefore, it is necessary to consider the RMSE (root mean square error) metric for the predictive power of the model. It is clear that the best predictive model is the minimum error, i.e., the minimum RMSE is defined as

$$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^{n}\left(y_i - \hat{y}_i\right)^2}{n}}, \tag{2}$$

where y_i is the observed value of the independent variable in the test set, $\hat{y}_i$ is the predicted value of the independent variables in the test set, and n is the number of samples in the test [47]. R^2, R, F, and RMSE are considered for the goodness of fit of the model, i.e., $\max(R^2)$, max (R), $\max(F)$, and min(RMSE). The curvilinear regression analyses are obtained by using the SPSS statistical software. The independent variables in the curvilinear regression models are the values of the topological indices, which are described above, of various drugs used in the treatment of COVID-19.

3. Main Results

From Figures 1 and 2, the edge and vertex numbers of molecular graphs of chemical structures are seen. Let $E_{i,j} = \{i = d_u, j = d_v | uv \in E(G)\}$. The molecular graph of CID71749833 has 54 vertices and 57 edges. Its edges can be partitioned as $|E_{1,3}| = 6$, $|E_{1,4}| = 8$, $|E_{2,2}| = 14$, $|E_{2,3}| = 22$, $|E_{3,3}| = 2$, $|E_{3,4}| = 2$, $|E_{4,4}| = 3$. The molecular graph of CID10009410 has 47 vertices and 50 edges. Its edges can be partitioned as $|E_{1,3}| = 9$, $|E_{2,2}| = 12$, $|E_{2,3}| = 22$, $|E_{3,3}| = 7$. The molecular graph of CID44271905 has 46 vertices and 49 edges. Its edges can be partitioned as $|E_{1,3}| = 8$, $|E_{2,2}| = 12$, $|E_{2,3}| = 24$, $|E_{3,3}| = 5$. The molecular graph of CID3010243 has 45 vertices and 48 edges. Its edges can be partitioned as $|E_{1,3}| = 8$, $|E_{2,2}| = 13$, $|E_{2,3}| = 20$, $|E_{3,3}| = 7$. The molecular graph of CID44271958 has 44 vertices and 47 edges. Its edges can be partitioned as $|E_{1,3}| = 6$ $|E_{2,2}| = 16$, $|E_{2,3}| = 20$, $|E_{3,3}| = 5$. The molecular graph of CID89869520 has 12 vertices and 12 edges. Its edges can be partitioned as $|E_{1,3}| = 5$, $|E_{2,3}| = 4$, $|E_{3,3}| = 3$. The values in Table 3 are obtained from Table 1 and the above values using combinatorial computation and edge partition technique. The values of these indices were also obtained [21].

The linear and quadratic models are obtained by using the data in Table 2 and 3 with the SPSS program. Table 4 shows the correlation coefficient (R) obtained by the linear regression model between various topological indices and physicochemical properties of potential drugs against COVID-19. These physicochemical properties are the enthalpy of vaporization (E), the flash point (FP), the molar refractivity (MR), the polarizability (P), the surface tension (T), and the molar volume (MV). Among the correlation coefficients obtained for a physicochemical property, the model with $\max(R)$ is the best predictor of the regression model for that physicochemical property. Therefore, $\max(R)$ for each physicochemical property is marked in bold in Table 4.

From Table 4, the mM_{sde} index is the best estimator index for molar refraction, polarity, surface tension, and molar volume in linear regression models. The linear models obtained with these topological indices are as follows. Table 5 shows linear regression models that give the best estimate for physicochemical properties.

Table 6 shows the correlation coefficient (R) obtained by the quadratic regression model between various topological indices and physicochemical properties of potential drugs against COVID-19. max (R) for each physicochemical property is marked in bold in Table 6.

Table 4: The correlation coefficient (R) obtained by linear regression model between topological indices and physicochemical properties of various drugs used in treatment of COVID-19.

	E	FB	MR	P	T	MV
$\mathbf{M_1}$	0.960	0.960	0.965	0.966	0.964	0.966
$\mathbf{M_2}$	0.952	0.951	0.958	0.958	0.957	0.959
HM	0.934	0.934	0.941	0.942	0.940	0.942
$\mathbf{Mm_{sde}}$	0.948	0.948	0.955	0.955	0.955	0.956
$\mathbf{mM_{sde}}$	**0.991**	**0.991**	**0.992**	**0.992**	**0.991**	**0.992**
irr	0.768	0.768	0.785	0.789	0.783	0.788
σ	0.540	0.540	0.559	0.560	0.555	0.562
ISDD	0.902	0.901	0.913	0.913	0.918	0.917
ABC	0.922	0.922	0.917	0.916	0.919	0.916
ISI	0.977	0.977	0.980	0.980	0.978	0.980

Table 5: Linear regression models that give the best estimate for physicochemical properties.

$E = 44.913 + 1.514\mathrm{mM_{sde}}$	$R^2 = 0.898$	$F = 35{,}387$	SE = 11.221	RMSE = 9.161
$FB = 108.463 + 6.382\mathrm{mM_{sde}}$	$R^2 = 0.898$	$F = 35{,}242$	SE = 47.409	RMSE = 38.709
$MR = 7.814 + 2.677\mathrm{mM_{sde}}$	$R^2 = 0.913$	$F = 41.906$	SE = 18.239	RMSE = 14.891
$P = 3.148 + 1.060\mathrm{mM_{sde}}$	$R^2 = 0.913$	$F = 41.798$	SE = 7.231	RMSE = 5.904
$T = 78.578 - 0.456\mathrm{mM_{sde}}$	$R^2 = 0.910$	$F = 40.444$	SE = 3.161	RMSE = 2.580
$\mathrm{MV} = 4.834 + 8.365\mathrm{mM_{sde}}$	$R^2 = 0.914$	$F = 42.607$	SE = 56.514	RMSE = 46.143

Table 6: The correlation coefficient (R) obtained by quadratic regression model between topological indices and physicochemical properties of various drugs used in treatment of COVID-19.

	E	FB	MR	P	T	MV
$\mathbf{M_1}$	**1**	**1**	0.999	0.999	**0.999**	**0.999**
$\mathbf{M_2}$	**1**	**1**	0.999	0.999	**0.999**	**0.999**
HM	**1**	**1**	0.999	0.999	**0.999**	**0.999**
$\mathbf{Mm_{sde}}$	**1**	**1**	**1**	**1**	**0.999**	**0.999**
$\mathbf{mM_{sde}}$	**1**	**1**	0.998	0.998	0.998	0.998
irr	0.990	0.989	0.994	0.994	0.994	0.995
σ	0.962	0.962	0.973	0.972	0.973	0.975
ISDD	0.994	0.994	0.992	0.992	0.994	0.992
ABC	0.998	0.998	0.994	0.994	0.993	0.992
ISI	**1**	**1**	0.998	0.998	0.998	0.998

Table 7: The quadratic regression models that give the best estimate for the enthalpy of vaporization (E).

Regression models	R^2	F	SE	RMSE
$\mathbf{E} = 10.610 + 1.022\mathbf{M_1} - 0.002\mathbf{M_1^2}$	**1**	**100473.208**	**0.157**	**0.111**
$E = 11.244 + 0.886M_2 - 0.001M_2^2$	1	30536.699	0.285	0.201
$E = 9.401 + 0.211\mathrm{HM} - (8.320E + 5)\mathrm{HM}^2$	1	11702.730	0.460	0.325
$E = 18.477 + 5.438\mathrm{mM_{sde}} - 0.060\mathrm{mM_{sde}}^2$	1	3994.438	0.788	0.557
$E = 2.903 + 4.154\mathrm{Mm_{sde}} - 0.031\mathrm{Mm_{sde}}^2$	1	23347.231	0.326	0.230
$E = 13.056 + 4.318\mathrm{ISI} - 0.036\mathrm{ISI}^2$	1	3667.709	0.822	0.581

Table 8: The quadratic regression models that give the best estimate for the flashpoint.

Regression models	R^2	F	SE	RMSE
$\mathbf{FB} = -36.499 + 4.314\mathbf{M_1} - 0.008\mathbf{M_1^2}$,	**1**	**109749.28**	**0.634**	**0.448**
$\mathrm{FB} = -33.789 + 3.741M_2 - 0.006M_2^2$,	1	25599.895	1.312	0.928
$\mathrm{FB} = -41.520 + 0.890\mathrm{HM} - 0.000\mathrm{HM}^2$	1	9442.841	2.161	1.527
$\mathrm{FB} = -3.511 + 22.989\mathrm{mM_{sde}} - 0.255\mathrm{mM_{sde}}^2$	1	4653.265	3.078	2.176
$\mathrm{FB} = -69.004 + 17.537\mathrm{Mm_{sde}} - 0.131\mathrm{Mm_{sde}}^2$	1	16434.89	1.638	1.158
$\mathrm{FB} = -26.202 + 18.231\mathrm{ISI} - 0.154\mathrm{ISI}^2$,	1	4051.916	3.298	2.332

Table 9: The quadratic regression models that give the best estimation for the molar refractivity (MR), the polarizability (P), and the surface tension (T).

Regression models	R^2	F	SE	RMSE
MR = −60.153 + 6.950**Mm$_{sde}$** − 0.050**Mm$_{sde}^2$**	**0.999**	**1743.03**	**2.092**	**1.479**
P = −23.805 + 2.754**Mm$_{sde}$** − 0.020**Mm$_{sde}^2$**	**0.999**	**1819.3**	***0.811***	**0.573**
T = 88.026 − 0.292M_1 + 0.001M_1^2	0.998	637.521	0.589	0.416
T = 87.825 − 0.255M_2 + 0.000M_2^2	0.998	667.918	0.576	0.407
T = 88.573 − 0.061HM + (2.360E − 5)HM^2	0.998	862.918	0.518	0.366
T = 90.313 − 1.193**Mm$_{sde}$** + 0.009**Mm$_{sde}^2$**	**0.998**	**956.122**	**0.482**	**0.340**

Table 10: The quadratic regression models that give the best estimate for the molar volume.

Regression models	R^2	F	SE	RMSE
MV = −163.089 + 5.271M_1 − 0.010M_1^2	0.997	592.767	11.191	7.913
MV = −161.643 + 4.605M_2 − 0.007M_2^2	0.998	633.566	10.826	7.654
MV − 173.989 + 1.107HM + 0.000HM^2	0.998	808.010	9.589	6.780
MV = −204.851 + 21.546**Mm$_{sde}$** − 0.154**Mm$_{sde}^2$**	**0.998**	**946.143**	**8.862**	**6.266**

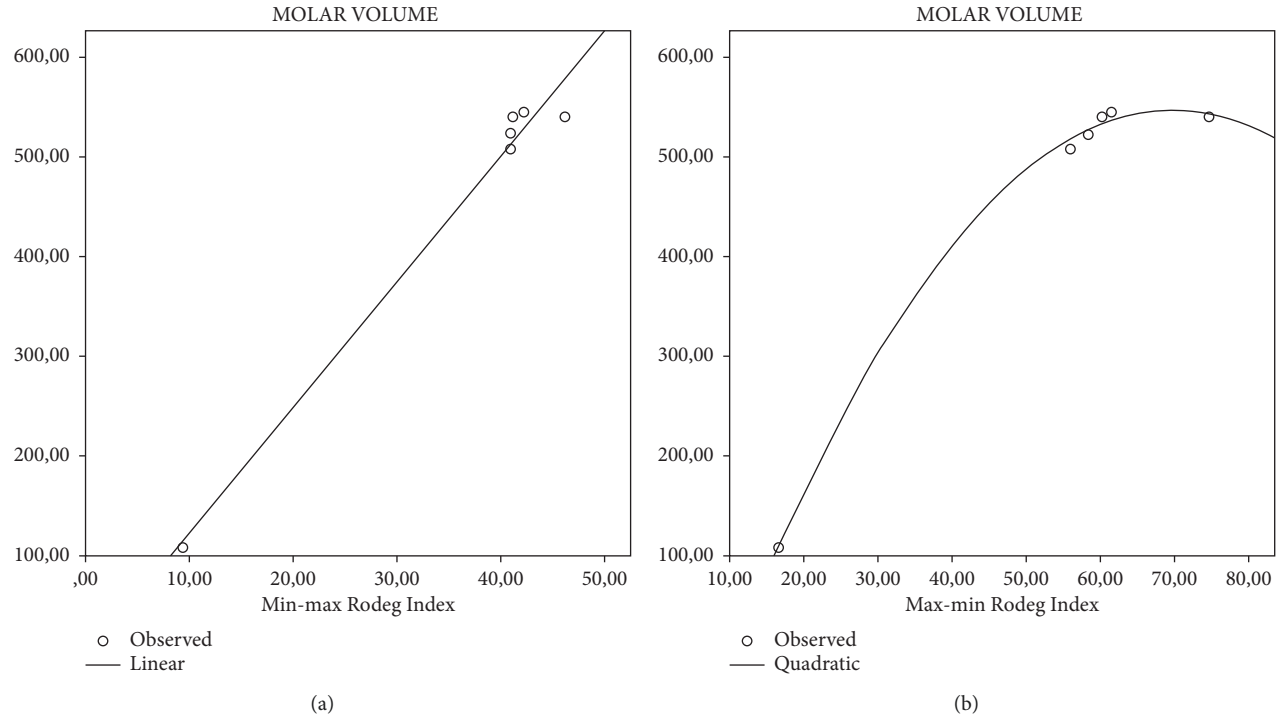

Figure 3: The plots of the linear and quadratic regression equations of the molar volume with the min-max rodeg index and the max-min rodeg index, respectively.

The regression models of the best predictive indices are given below for molar refraction, polarity, surface tension, and molar volume in quadratic regression models from Table 6. Table 7 shows quadratic regression models that give the best estimate for the enthalpy of vaporization.

From the above equations, M_1 is the best predictor index for the enthalpy of vaporization in quadratic regression models from min(RMSE), max(R^2), and max(F). Table 8 shows quadratic regression models that give the best estimate for the flash point (FP). The model that predicts the best is marked in bold (Table 8).

From the above equations, M_1 is the best predictor index for the flash point in quadratic regression models from min(RMSE), max(R^2), and max(F) (Table 8). Table 9 shows quadratic regression models that give the best estimate for the molar refractivity (MR), the polarizability (P), and the surface tension (T).

From the above equations, Mm_{sde} is the best predictor index for the polarizability, the surface tension, and the molar refractivity (MR) in quadratic regression models from min(RMSE), max(R^2), and max(F) (Table 9). Table 10 shows quadratic regression models that give the best estimate for the molar volume.

From the above equations, Mm_{sde} is the best predictor index for the molar volume in quadratic regression models from min(RMSE), max(R^2), and max(F) (Table 10).

Figure 3 shows plots of the linear and quadratic regression equations of the molar volume with the min-max rodeg index and the max-min rodeg index, respectively.

4. Conclusions

New variants may be emerging that are resistant to some vaccines produced for COVID-19. Therefore, it is necessary to produce medicine as soon as possible against COVID-19. There is no medicine yet to alleviate or end this pandemic. Existing drugs are being used to alleviate the pandemic. This study's aim is to obtain information about the topology of some chemical structures with minimum cost and minimum time with topological indices.

Four structural analogs of lopinavir, one structural analog of favipiravir, and one structural analog of ritonavir are studied. Rafi et al. [28] conducted a QSAR study for some properties of these analogs and found that their drug properties were higher and stressed that there could be potential drugs against COVID-19. In this study, QSPR modeling for some physicochemical properties of these structures is performed using the topological indices of the molecular graphs of these structures. These types of modeling are done by linear and quadratic regression analysis. Models were studied with 6 descriptors and 10 topological indices.

QSPR modeling shows that the best predictive topological index is the min-max rodeg index for enthalpy of vaporization, flash point, molar refractivity, polarizability, surface tension, and molar volume in linear regression. Also, in quadratic regression models, the best predictive topological indices are the first Zagreb index for enthalpy of vaporization and flash point and the max-min rodeg index for molar refractivity, polarizability, surface tension, and molar volume. Correlation coefficients obtained in QSPR modeling are very close to 1 and 1 in some models. The experimental and theoretical results of the models obtained are very close to each other. The predictive strength is tested for these degree-based topological indices by using some physicochemical properties of these structures. Moreover, models that are the best predictive among linear and quadratic regression models are quadratic models. The results of this study will shed light on new drug discoveries, most importantly in the treatment of COVID-19, chemistry, and pharmacy science.

The physicochemical properties of a drug are important for its use. The study is based on the idea that these drugs, which are tried and thought for the treatment of COVID-19, are used together and/or their analogs are used. By using the results of the study, if a single drug is obtained from these drugs, information about that drug can be obtained without experimenting. Thus, it can provide information about the properties of drugs that are similar to these structures or that will be obtained from the combination of these structures, saving time and money without experimenting.

Data Availability

No data were used to support this study.

Conflicts of Interest

The author declares that there are no conflicts of interest.

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