Publication Date: 30 June 2024
Archs Sci. (2024) Volume 74, Issue 3 Pages 51-55, Paper ID 2024309.
https://doi.org/10.62227/as/74309

Numerical Descriptors of Top Ranked Zinc Databased Inhibitors of Sars Cov-2

M.C. Shanmukha[1], A. Usha[2], Mohammad Reza Farahani[3,*], Mehdi Alaeiyan[4] and Murat Cancan[5]
[1]Department of Mathematics, P.E.S. Institute of Technology and Management, Shivamogga-577204, India.
[2]Department of Mathematics, Alliance School of Applied Mathematics, Alliance University, Bangalore-562106, India.
[3]Department of Mathematics, Iran University of Science and Technology, Tehran 16844, Iran.
[4]School of Mathematics and Computer Science, Iran University of Science and Technology, Tehran 16844, Iran.
[5]Faculty of Education, Van Yuzuncu Yil University, Zeve Campus 6500, Van, Turkey.

Corresponding authors: Mohammad Reza Farahani (e-mail: mrfarahani88@gmail.com).

Abstract From the year 2019, the pandemic has been a threat to the mankind and the entire world is behind the making of the SARS-COV-2 vaccine. This work attempts to find various topological indices such as $ABC(G)$, $\chi(G)$, $S(G)$, $GA(G)$, $M_1(G)$, $M_2(G)$, $H(G)$, $ZG_3(G)$, $SSD(G)$, $I(G)$, $A(G)$, ${}^mM_2(G)$ for top ranked Zinc databased molecules of SARS-COV-2 inhibitors as per ChemAI. ChemAI is a network where chemistry uses artificial intelligence to test various chemicals using Turing test. A conclusion is drawn for the Zinc databased molecules with respect to physical property, logP to understand Lipophilicity since, if any of the variant like Covid comes Zinc databased molecules alone and also in combination are the main supplements required as a preliminary for all human beings.

Index Terms topological indices, zinc databased molecules, partition coefficient

I. Introduction

The main threat of current situation globally is the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2) is caused by novel coronavirus which needs immediate therapies and novel drugs to fight against the virus and its infections. Although the study of SARS-COV-2 is in progress, SARS-COV-2 affected persons are experiencing symptoms of the novel coronavirus- fever, sore throat, loss of smell and taste, fatigue, lower respiratory infection. These symptoms may be mild in few people and may continue to deteriorate which can result in fatality in the cases where the patient has other complications such as diabetes, cancer, high blood pressure and heart ailments. Also, in few cases, the virus becomes dangerous for senior citizens aged above 65 years because of lack of immunity caused from the long term ailments such as diabetes and heart related issues.

The treatment of the patients includes supportive treatment like treating the specific problem, antiviral treatment and oxygen therapy by oxygen support. Apart from this, there are other traditional therapies using Ayurveda where natural ingredients like spices and herbs are used. The other treatments is plasma therapy where the antibodies of Covid-19 recovered person will be injected in to the virus affected patient. A few cases have been successful so far but many cases drastically failed where the patient has succumbed to death after the plasma therapy. As the exact drug is yet to be invented, the above are the therapies available at the moment. The whole world is struggling to find a vaccine/drug to fight against the dangerous virus, which was initially spotted in humans in Wuhan city, China in December, 2019.

As it spreads rapidly, the people are educated about the virus symptoms and the consequences of infections so that the people take enough precautions such as wearing face masks and frequent usage of sanitizer to avoid the spread of the dreadful virus.

"ChemAI" is a neural network, in other words, where chemistry uses artificial intelligence to predict a large number of biological effects of the chemical compounds. In detail, the network is tested on a data set available on ZINC [1], pubchem [2] and many such databases. Here, ZINC database is used as it has large data of molecules. In this study, a set of top ranked molecules are considered for which topological indices are determined. Also, the physical property, logP of these molecules are correlated with the degree based topological indices. Conclusions are drawn with regard to the correlation coefficient.

In theoretical chemistry, chemical compounds are represented as molecular graphs with vertex and edge, such that vertex depicts an atom and edge depicts link between the two atoms. Let $G(V, E)$ be a molecular graph with vertices and edges respectively. Here degree of a vertex is d_s of vertices s in G. In this work the graphs considered are simple graphs with no cycles and multiple edges [3]–[5].

In this paper, a large number of molecules were considered

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for inference with ChemAI [6] to obtain predictions against the SARS-COV-2 (COVID-19) virus. In the cited paper, the construction of screening library of potential inhibitors of SARS-COV-2 molecules were considered. The same strong inhibitors of SARS-COV-2 are studied here for QSPR analysis [7]–[12] . Degree-based topological indices are determined and tabulated. The degree of correlation coefficient is determined with each of the degree-based topological indices with respect to physical property, logP of these inhibitors.

logP is extensively used in drug discovery/drug design as logP gives the clear picture of the biological activities of the drug molecules in the body. Lipophilicity is the critical parameter of a drug which defines the biological and metabolic activities. It is a significant parameter to define toxicity of a drug.

logP being the partition coefficient, not only predicts how the compound acts inside the body but also gives the information about formulation, dosing and toxicity of the drug.

In the literature various topological indices are discussed for various drugs used in the treatment of Covid-19 [13]–[16].

II. Materials and Methods

The materials used for this work are [17], [18] and the molecules, which are considered for this study are the top ranked SARS-COV-2 inhibitors with reference to ChemAI using Zinc database provided by Sterling and Irwin in 2015 [1]. In ordered to find the topological indices of 17 top ranked SARS-COV-2 inhibitors, each molecule is considered as a graph. The links between the atoms are regarded as edges and the atoms of each link are considered as vertices of that molecule [19]–[22]. The degree of every vertex and the types of edges are studied for each molecule.

This data is clearly explained in the Theorem III for the molecule $ZINC000254565785$. Topological index is a numerical measure which flows a specific rule. The complete information of the types of edges are used in the definitions of 12 degree-based topological indices to obtain the results. Similarly, for the other 16 molecules also, the above procedure is repeated. Every molecule has the set of bivariate data namely topological indices and partition coefficient logP. Karl Pearson's coefficient of correlation is determined for this bivariate data using any one of the following tools, Microsoft Excel, Origin and SPSS.

Definition 1. Degree-based topological index ABC was introduced by Estrada et al., [23] as

$$ABC(G) = \sum_{e=st\in E(G)} \sqrt{\frac{d_s + d_t - 2}{d_s d_t}}. \tag{1}$$

Definition 2. Milan Randic defined Randic index [24] as

$$\chi(G) = \sum_{e=st\in E(G)} \frac{1}{\sqrt{d_s d_t}} \tag{2}$$

Definition 3. Zhou et al., [25] proposed the sum-connectivity index and is defined as

$$S(G) = \sum_{e=st\in E(G)} \frac{1}{\sqrt{d_s + d_t}}. \tag{3}$$

Definition 4. Vukicevic et al., [26] proposed the GA index as

$$GA(G) = \sum_{e=st\in E(G)} \frac{2\sqrt{d_s d_t}}{d_s + d_t}. \tag{4}$$

Definition 5. Gutman et al., [27] proposed the first and second Zagreb indices as

$$M_1(G) = \sum_{e=st\in E(G)} (d_s + d_t). \tag{5}$$

$$M_2(G) = \sum_{e=st\in E(G)} (d_s \cdot d_t). \tag{6}$$

Definition 6. Harmonic index is proposed by Fajtlowicz [28] as,

$$H(G) = \sum_{e=st\in E(G)} \frac{2}{d_s + d_t}. \tag{7}$$

Definition 7. The third Zagreb index is proposed by Fath-Tabar et al., [29] as

$$ZG_3(G) = \sum_{e=st\in E(G)} |d_s - d_t|. \tag{8}$$

Definition 8. Symmetric division index is proposed by V. Alexander [30] and can be stated as

$$SSD(G) = \sum_{e=st\in E(G)} \left[\frac{X}{Y} + \frac{Y}{Z}\right], \tag{9}$$

where $X = min\,[d_s, d_t]$ and $Y = max\,[d_s, d_t]$.

Definition 9. The inverse sum index is the topological index used in [31] is stated as

$$I(G) = \sum_{e=st\in E(G)} \frac{d_s \times d_t}{d_s + d_t}. \tag{10}$$

Definition 10. Furtula et al. proposed the Augmented Zagreb index [32] and is stated as

$$A(G) = \sum_{e=st\in E(G)} \left\{\frac{d_s \times d_t}{d_s + d_t - 2}\right\}^3. \tag{11}$$

Definition 11. The modified second Zagreb index [33] is stated as

$${}^{m}M_2(G) = \sum_{e=st\in E(G)} \frac{1}{d_s \times d_t}. \tag{12}$$

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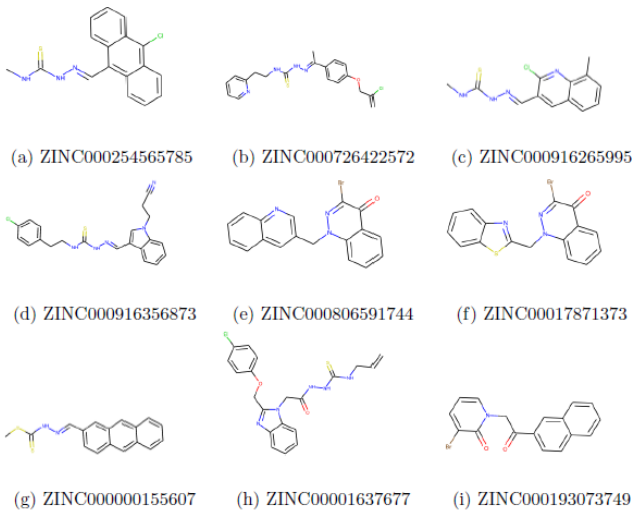


(a) ZINC000254565785 (b) ZINC000726422572 (c) ZINC000916265995

(d) ZINC000916356873 (e) ZINC000806591744 (f) ZINC00017871373

(g) ZINC000000155607 (h) ZINC00001637677 (i) ZINC000193073749

Figure 1: Various structures of the top-ranked ZINC databased molecules by ChemAI

III. Results and Discussion

Theorem 1. *Let G denotes the graph of molecular structure of (a)$ZINC000254565785$, then*

$$\chi(G) = 10.2192,\ GA(G) = 22.533,\ SCI(G) = 10.6573,$$
$$HI(G) = 9.9667,\ M_1(G) = 110,\ M_2(G) = 132,$$
$$^{m}M_2(G) = 4.75,\ IS(G) = 26.567,\ ABC(G) = 16.2396,$$
$$SSD(G) = 56.3333,\ AZI(G) = 195.094,\ ZG_3(G) = 12.$$

Proof. The structure (a)$ZINC000254565785$ has five different types of edges which are given below. It is obvious from the Figure 1, that the total number of vertices are 21 while edges are 23.

$$E_{1,2} = \{e = st \in E(G) | d_s = 1,\ d_t = 2\},$$
$$E_{1,3} = \{e = st \in E(G) | d_s = 1,\ d_t = 3\},$$
$$E_{2,2} = \{e = st \in E(G) | d_s = 2,\ d_t = 2\},$$
$$E_{2,3} = \{e = st \in E(G) | d_s = 2,\ d_t = 3\},$$
$$E_{3,3} = \{e = st \in E(G) | d_s = 3,\ d_t = 3\},$$

such that

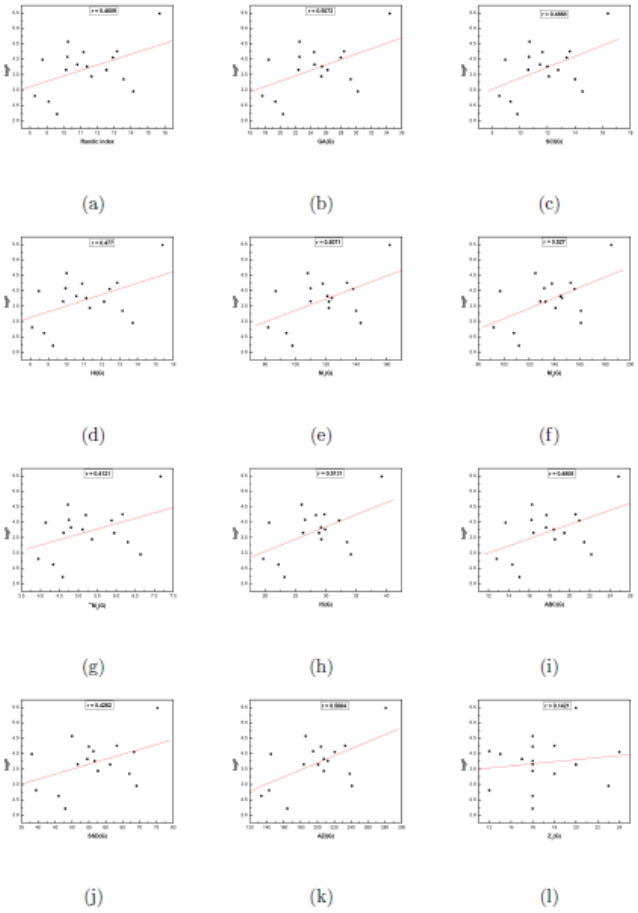
$$|E_{1,2}| = 1,\ |E_{1,3}| = 2,\ |E_{2,2}| = 7,\ |E_{2,3}| = 7,\ |E_{3,3}| = 6.$$

Thus, with the above background study and employing equations 1-12, we obtain the required results. □

Similarly, we obtained the following results for other structures as depicted in Table 1 & Table 2. The 12 topological indices are plotted against logP individually. The correlation coefficient is determined for each of these cases and is shown in Figure 2.

$Molecules$	$\chi(G)$	$GA(G)$	$SCI(G)$	$HI(G)$	$M_1(G)$	$M_2(G)$
$ZINC000254565785$	10.2192	22.533	10.6573	9.9667	110	132
$ZINC000726422572$	12.5417	26.2216	12.7748	12.133	122	133
$ZINC000916265995$	9.1134	19.359	9.327	8.7667	94	108
$ZINC000916356873$	13.169	28.4122	13.6159	12.8667	134	153
$ZINC000806591744$	11.387	25.4896	11.9995	11.1333	124	146
$ZINC000178971373$	10.8121	24.5098	11.4606	10.5667	121	145
$ZINC000000155607$	10.2584	22.5462	10.7076	10.0333	108	125
$ZINC000016317677$	14.1378	30.2176	14.5493	13.7333	143	161
$ZINC000193073749$	10.1479	22.396	10.6051	9.8333	110	129
$ZINC000755523869$	11.6479	25.396	12.1051	11.3333	122	141
$ZINC000763345954$	9.6134	20.359	9.827	9.627	98	112
$ZINC000001448699$	11.1859	24.4526	11.6297	10.9	118	138
$ZINC000016940508$	13.5586	29.2621	14.0134	13.1667	140	161
$ZINC000005527649$	8.298	17.627	8.5105	8.1	82	92
$ZINC000746495682$	12.9216	27.9866	13.394	12.4333	138	156
$ZINC000005719506$	8.7565	18.4566	8.947	8.467	87	97
$ZINC000002149503$	15.6867	34.4088	16.3802	15.4	162	185

Table 1: Various top ranked Zinc databased molecules of SARS-COV-2 with topological indices values



(a) (b) (c)

(d) (e) (f)

(g) (h) (i)

(j) (k) (l)

Figure 2: logP with topological indices

IV. Conclusion

This work has highlighted the correlation coefficient of the topological indices with respect to the partition coefficient logP for the Zinc databased molecules. It is observed from the Table 4 that, there is a positive correlation between the degree-based indices considered and logP. It is low positive correlation as the values ponder between 0.4 to 0.566 except for the third Zagreb index with logP being least positive correlation. As per the correlation values, it shows that augmented Zagreb

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$Molecules$	${}^{m}M_2(G)$	$IS(G)$	$ABC(G)$	$SSD(G)$	$AZI(G)$	$ZG_3(G)$
$ZINC000254565785$	4.75	26.567	16.2396	56.3333	195.094	12
$ZINC000726422572$	5.9444	28.9	19.489	61.3333	200.891	20
$ZINC000916265995$	4.333	22.217	14.349	46	133.516	16
$ZINC000916356873$	6.167	29.767	20.6036	63.3333	232.922	18
$ZINC000806591744$	5.1111	29.9	18.4418	56.6666	212.313	16
$ZINC000178971373$	4.8055	29.2	17.6942	54.5	207.703	15
$ZINC000000155607$	4.7222	26.0167	16.292	50	186.156	16
$ZINC000016317677$	6.6389	34.1167	22.1676	69.1666	240.906	23
$ZINC000193073749$	4.6111	26.25	16.4299	51.6666	183.688	16
$ZINC000755523869$	5.3611	29.25	18.5511	57.6666	207.688	16
$ZINC000763345954$	4.5833	23.2167	15.056	48	164.297	16
$ZINC000001448699$	5.1944	28.367	17.7347	55	204.313	16
$ZINC000016940508$	6.3055	33.5	21.4486	67	238.453	18
$ZINC000005527649$	3.9444	19.7167	12.7969	39.3333	142.766	12
$ZINC000746495682$	5.875	32.1833	20.971	68.4166	220.658	24
$ZINC000005719506$	4.1389	20.65	13.6823	38.1111	144.906	13
$ZINC000002149503$	7.1667	39.2	24.8462	75.3333	280.922	20

Table 2: Various top ranked Zinc databased molecules of SARS-COV-2 with topological indices values

$Molecules$	$logP$
$ZINC000254565785$	4.074
$ZINC000726422572$	3.644
$ZINC000916265995$	2.624
$ZINC000916356873$	4.249
$ZINC000806591744$	3.756
$ZINC000178971373$	3.817
$ZINC000000155607$	4.564
$ZINC000016317677$	2.95
$ZINC000193073749$	3.647
$ZINC000755523869$	3.437
$ZINC000763345954$	2.211
$ZINC000001448699$	4.226
$ZINC000016940508$	3.349
$ZINC000005527649$	2.806
$ZINC000746495682$	4.05
$ZINC000005719506$	3.981
$ZINC000002149503$	5.481

Table 3: Various top ranked Zinc databased molecules of SARS-COV-2 with logP

Indices	Correlation coefficient(r)
$\chi(G)$	0.4609
$GA(G)$	0.5072
$SCI(G)$	0.4868
$HI(G)$	0.477
$M_1(G)$	0.5071
$M_2(G)$	0.527
${}^{m}M_2(G)$	0.4121
$IS(G)$	0.5131
$ABC(G)$	0.4805
$SSD(G)$	0.4262
$AZI(G)$	0.5664
$Z_3(G)$	0.1421

Table 4: Correlation coefficient of logP with topological indices

index is more correlated with logP compared to other indices which are considered in the study. Even though the correlation coefficient obtained is less, Zinc databased molecules play a vital role in the treatment and also as a supplementation for Covid-19 patients. Also, any variant of Covid-19 risk groups and patients can be cured soon.

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