



Degree-based Topological indices of Top Ranked Zinc Databased Inhibitors of SARS-CoV-2

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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, log P 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.

Keywords: Topological indices, ZINC databased molecules, Partition coefficient

AMS Mathematical Subject Classification [2010]: 05C07, 05C10, 05C90

1 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

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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 treatment 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 [29], pubchem[16] 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, log P 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(atom) s in G . In this work the graphs considered are simple graphs with no cycles and multiple edges [1, 10, 28].

In this paper, a large number of molecules were considered for inference with ChemAI [17] 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 [21, 22, 26, 27, 24, 14]. 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, log P of these inhibitors.

log P is extensively used in drug discovery/drug design as log P 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.

log P 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 [16, 18, 23, 32]

2 Materials and Methods

The materials used for this work are [17, 25, 31] 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 [29]. In order 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 [2, 8, 11, 12]. The degree of every vertex and the types of edges are studied for each molecule. This data is clearly explained in the first theorem 3.12 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 $\log P$. 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 2.1. Degree-based topological index ABC was introduced by Estrada et al., [6] as

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

Definition 2.2. Milan Randic defined Randic index [20] as

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

Definition 2.3. Zhou et al., [33] proposed the sum-connectivity index and is defined as

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

Definition 2.4. Vukicevic et al., [30] proposed the GA index as

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

Definition 2.5. Gutman et al., [13] proposed the first and second Zagreb indices as

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

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

Definition 2.6. Harmonic index is proposed by Fajtlowicz [7] as,

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

Definition 2.7. The third Zagreb index is proposed by Fath-Tabar et al., [3] as

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

Definition 2.8. Symmetric division index is proposed by V. Alexander [4] and can be stated as

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

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

Definition 2.9. The inverse sum index is the topological index used in [5] is stated as

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

Definition 2.10. Furtula et al. proposed the Augmented Zagreb index [9] and is stated as

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

Definition 2.11. The modified second Zagreb index [19] is stated as

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

3 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(a), that the total number of vertices of Figure 1(a) are 21 while edges are 23.

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

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

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

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

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

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. \square

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

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

<i>Molecules</i>	$\chi(G)$	$GA(G)$	$SCI(G)$	$HI(G)$	$M_1(G)$	$M_2(G)$
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

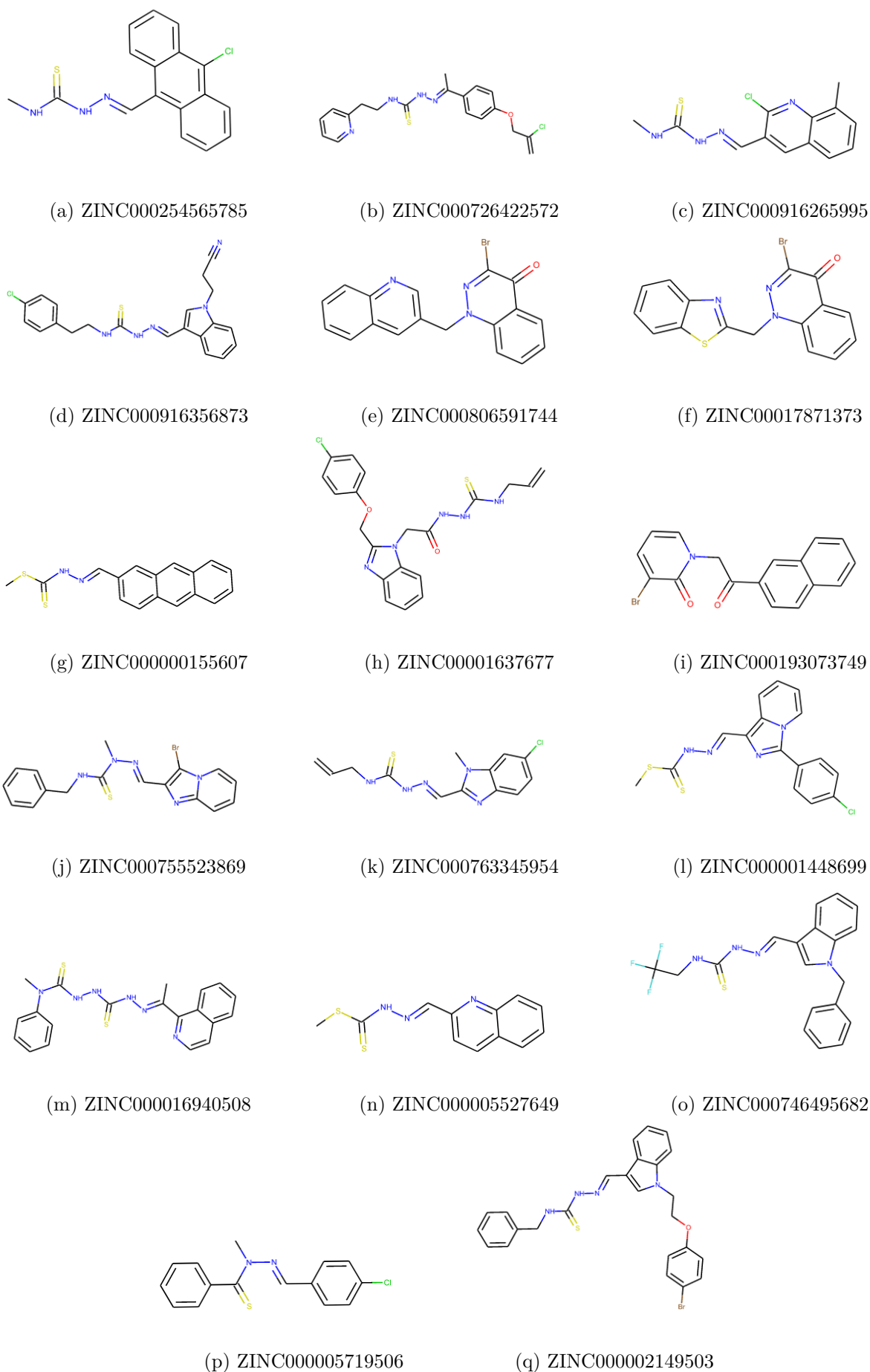


Figure 1: Various structures of the top-ranked ZINC databased molecules by ChemAI.

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

<i>Molecules</i>	${}^m M_2(G)$	$IS(G)$	$ABC(G)$	$SSD(G)$	$AZI(G)$	$ZG_3(G)$
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 3: Various top ranked Zinc databased molecules of SARS-COV-2 with log P [17]

<i>Molecules</i>	<i>logP</i>
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 4: Correlation coefficient of logP with topological indices

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

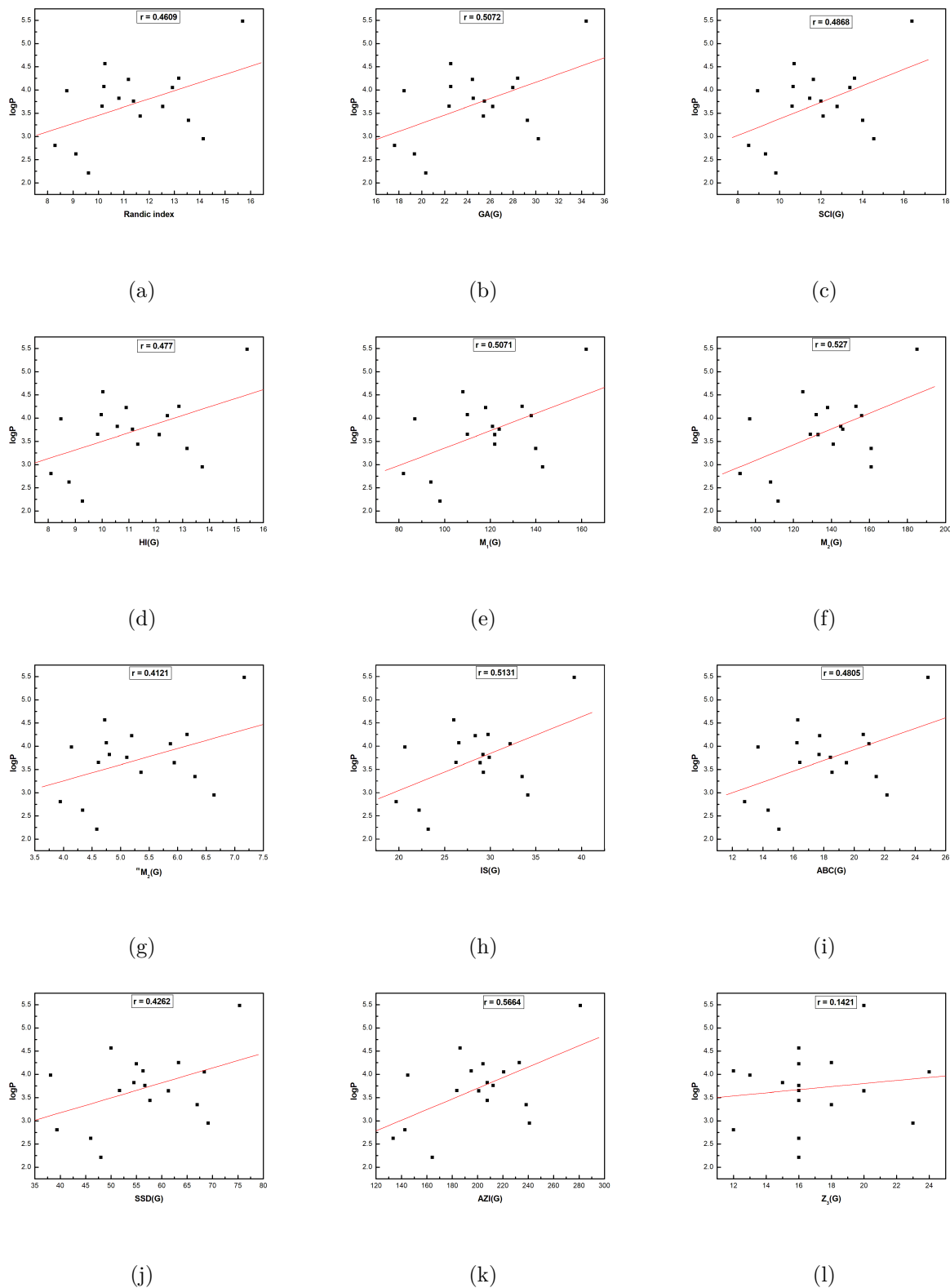


Figure 2: physico-chemical property with topological indices.

Conclusion

This work has highlighted the correlation coefficient of the topological indices with respect to the partition coefficient $\log P$ 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 $\log P$. It is low positive correlation as the values ponder between 0.4 to 0.566 except for the third Zagreb index with $\log P$ being least positive correlation. As per the correlation values, it shows that augmented Zagreb index is more correlated with $\log P$ 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.

References

- [1] Adnan Aslam, Safyan Ahmad, Wei Gao, *On Topological Indices of Boron Triangular Nanotubes*, Z. Naturforsch 72(8)(2017), PP. 711-716.
- [2] S. Ahmad, H.M. Afzal Siddiqui, A. Ali, M.R. Farahani, M. Imran, I.N. Cangul, *On Wiener index and Wiener polarity index of some polyomino chains*, Journal of Discrete Mathematical Sciences and Cryptography. 22(7)(2019), pp. 1151-1164.
- [3] Ali Astanesh-Asl, Fath-Tabar GH, *Computing the first and third Zagreb polynomials of certained product of graphs*, Iranian Journal of Mathematical Chemistry 2(2)(2011), PP. 73-78.
- [4] V. Alexander *Upper and lower bounds of symmetric division deg index*, Iranian Journal of Mathematical Chemistry 5(2)(2014), PP. 91-98.
- [5] A. T. Balaban, *Highly discriminating distance based numerical descriptor*, Chem. phys. Lett. 89 (1982), PP. 399-404.
- [6] E. Estrada, L. Torres, L. Rodriguez, I. Gutman, *An atom-bond connectivity index: Modeling the enthalpy of formation of alkanes*, Indian J. Chem. 37(A)(1998), PP. 849-855.
- [7] S. Fajtlowicz, *On Conjectures of Grafitti II*, Congr. Numer 60(1987), PP. 189-197.
- [8] Faryal Chaudhry, Iqra Shoukat, Deeba Afzal, Choonkil Park, Murat Cancan, Mohammad Reza Farahani, *M-Polynomials and Degree-Based Topological Indices of the Molecule Copper(I) Oxide*, Journal of Chemistry, vol. 2021, Article ID 6679819, 12 pages, 2021. <https://doi.org/10.1155/2021/6679819>
- [9] B. Furtula, A. Graovac, D. Vukicevic, *Augmented Zagreb index*, J. Math. Chem. 48(2)(2010), PP. 370-380.
- [10] B. Furtula, I. Gutman, *A forgotten topological index*, J. Math. Chem. 53(2015), PP. 213-220.
- [11] W. Gao, M.K. Siddiqui, M. Imran, M.K. Jamil, M.R. Farahani, *Forgotten topological index of chemical structure in drugs*, Saudi Pharm. J., 24 (2016), pp. 258-264.
- [12] W. Gao, L. Shi, M.R. Farahani, *Szeged Related Indices of TUAC6[p,q]*, Journal of Discrete Mathematical Sciences and Cryptography, 20(2)(2017), pp. 553-563.

- [13] I. Gutman, *Degree Based Topological Indices*, Croat. Chem. Acta 86(2013), PP. 351-361.
- [14] S. M. Hosamani, Deepa Perigidad, Shruti Jamagoud Yallavva Maled, Sharada Gavade, *QSPR Analysis of Certain Degree Based Topological Indices*, Journal of Statistics Applications and Probability 6(2)(2017), PP. 1-11.
- [15] S. Kim, P.A. Thiessen, E.E. Bolton, J. Chen, G. Fu, A. Gindulyte, L. Han, J. He, S. He, B. A. Shoemaker, et al, *Pubchem substance and compound databases*, Nucleic acids research 44(D1)(2016), D1202-D1213.
- [16] S. A. Kirmani, P. Ali, F. Azam, *Topological indices and QSPR/QSAR analysis of some antiviral drugs being investigated for the treatment of COVID-19 patients*, International Journal of Quantum Chemistry, 121(9)(2021), e26594.
- [17] Markus Hofmarcher, Andreas Mayr and Elisabeth Rumetshofer et al, *Large-Scale Ligand-Based Virtual Screening for SARS-CoV-2 Inhibitors Using Deep Neural Networks*, SSRN Journal. DOI: 10.2139/ssrn.3561442.
- [18] S. Nagarajan, G. Priyadharsini, K. Pattabiraman, *QSPR Modeling of Status-Based Topological Indices with COVID-19 Drugs*, Polycyclic Aromatic Compounds, 2022, pp. 1-20.
- [19] A. Milicevic, S. Nikolic, N. Trinajstic, *On reformulated Zagreb indices*, Mol. Diversity 8(4)(2004), 393-399.
- [20] M. Randic, *On Characterization of molecular branching*, J. Amer. Chem. Soc. 97 (1975), PP. 6609-6615.
- [21] M. Randic, *Comparative structure-property studies: Regressions using a single descriptor*, Croat. Chem. Acta 66(1993), PP. 289-312.
- [22] M. Randic, *Quantitative Structure-Property Relationship: boiling points and planar benzenoids*, New. J. Chem. 20(1996), PP. 1001-1009.
- [23] V. Ravi V, M. K. Siddiqui, N. Chidambaram, K. Desikan, *On topological descriptors and curvilinear regression analysis of antiviral drugs used in COVID-19 treatment*, Polycyclic Aromatic Compounds, 2021, pp. 1-4.
- [24] Sakander Hayat, Muhammad Imran, Jia-Bao Liu *Correlation between the Estrada index and π -electronic energies for benzenoid hydrocarbons with applications to boron nanotubes*, Int J Quantum Chem, 2016, DOI:10.1002/qua.26016.
- [25] Sanjivanjit K. Bhal, *Log P- Making Sense of the Value*, Advanced Chemistry Development, Inc., Toronto, ON, Canada.
- [26] M. C. Shanmukha, N.S. Basavarajappa, K.N. Anilkumar, *Predicting physico-chemical properties of octane isomers using QSPR approach*, Malaya Journal of Matematik 8(1)(2020), PP. 104-116.
- [27] M. C. Shanmukha, N. S. Basavarajappa, K.C. Shilpa, A. Usha, *Degree-based topological indices on anticancer drugs with QSPR analysis*, Heliyon, 6(2020), PP. 1-9.

- [28] G. H. Shirdel, H. RezaPour H, A. M. Sayadi, *The Hyper-Zagreb Index of Graph Operations*, Iranian Journal of Mathematical Chemistry 4(2)(2013), PP. 213-220.
- [29] T. Sterling, J. J. Irwin, *Zinc 15-ligand discovery for everyone*, Journal of chemical information and modeling 55(11)(2015), PP. 2324-2337.
- [30] D. Vukicevic, B. Furtula, *Topological index based on the ratios of geometrical and arithmetical means of end-vertex degrees of edges*, J. Math. Chem. 46(2009), PP. 1369-1376.
- [31] Xue-Yan Zhang, Hao-Jie Huang, Dong-Lin Zhuang, Moussa Ide Nasser, Ming-Hua Yang, Ping Zhu, et al. *Biological, clinical and epidemiological features of COVID-19, SARS and MERS and AutoDock simulation of ACE2*, Infectious Diseases of Poverty 9(2020), PP. 1-11.
- [32] J.F. Zhong, A. Rauf, M. Naeem, J. Rahman and A. Aslam, *Quantitative structure-property relationships (QSPR) of valency based topological indices with Covid-19 drugs and application*, Arabian Journal of Chemistry, 14(7)(2021), pp.103240.
- [33] B. Zhou B, N. Trinajstic, *On general sum-connectivity index*, J. Math. Chem. 47(2010), PP. 210-218.

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