

Analysis of Antiviral Drugs Using Topological Descriptors

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Abstract: This study conducted a comprehensive analysis of the data derived from the various topological descriptors of antiviral drugs using a range of statistical parameters. Quantitative structure-property relationships for the antiviral drugs Remdesivir, Favipiravir, Ribavirin, Lopinavir, Ritonavir, Darunavir, Oseltamivir, and Umifenovir are derived and studied using degree-based topological descriptors. This QSPR study provides the mathematical relationship between the physical-chemical properties and different topological descriptors. The statistical analysis also provides a deeper insight into the relationship between topological descriptors and the physicochemical characteristics of the above-mentioned antiviral drugs. The analysis aims to provide a deeper understanding of how chemical graph-theoretical analysis can predict the properties of antiviral drugs. In this analysis, linear, quadratic, and cubic regression models are used to investigate QSPR for potential degree-based topological indices.

Keywords: antiviral drugs; topological descriptors; QSPR analysis; correlation.

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1. Introduction

Viruses are major sources of infection in both humans and animals. The earliest evidence of viruses came from experiments using filters with pores large enough to retain bacteria. One of these filters was first used by Dmitri Ivanovsky in 1892 to demonstrate that healthy plants can be infected by sap from plants that carry the virus. This was followed by the 1898 discovery of the Tobacco Mosaic Virus by Martinus. When a virus is present in a host cell, the host cell is often compelled to replicate into thousands of copies of the initial virus rapidly. When the virus is not present in the host cell, it exists as independent viral particles, or virions. Antivirals result from extensive research into how viruses work. They are made up of two main parts: the genetic material, which consists of long molecules such as DNA or RNA that tell the virus how to act, and a protein coat called the capsid that protects the genetic material. In some cases, there is also an outer layer of lipids. All of this knowledge has helped scientists understand how viruses work, leading to significant progress in developing new drugs. The 1960s saw the emergence of experimental antivirals, primarily designed to combat the human immunodeficiency virus (HIV), which is the underlying cause of acquired

immunodeficiency syndrome (AIDS). These drugs were discovered using traditional drug discovery methods, which involved growing cultures of cells and infecting them with the desired virus. Subsequently, chemicals were added to the cultures thought to inhibit viral activity, and the levels of the virus in the cultures were monitored to determine whether they increased or decreased. Chemicals that were found to be effective were selected for further study.

The global health crisis caused by COVID-19 continues to pose a wide range of threats to global health. Clinical trials for vaccines, small-molecule drugs, and therapeutic antibodies are summarized by Kumari *et al.* [1,2]. Comparing the molecular structures of various antiviral drugs is a key factor in understanding their activity against viruses. This is because molecular similarities are really important when it comes to drug discovery. It is based on the fact that structurally similar molecules often share properties. So, it is important to determine whether there are similarities among small molecules. Two-dimensional similarity approaches have become popular because they are simple, accurate, and efficient. There are many methods for describing molecular shapes and figuring out the structural similarity of molecules. The most popular methods are based on atomic distance. Structurally, molecular similarity is associated with their shared physical and biological characteristics. This similarity principle was widely used in the early days of drug development to identify new drug molecules [3].

In molecular graph theory, the structure of a chemical compound is associated with a graph having vertices and edges. The vertices of a molecular graph correspond to the molecules of the compound, while the edges of the graph correspond to the chemical bonds between the molecules. As a new field of study, cheminformatics combines chemistry, mathematics, and information science. QSAR (quantitative structure-activity relationship) and QSPR (quantitative structure-property relationship) are methods for predicting the biological activity and properties of different chemicals. In fact, Wiener was the first to show a correlation between the Wiener index and the boiling points of alkane molecules [4]. Further investigation of quantitative structure-activity relationships showed that it is also associated with other parameters, such as van der Waals surface area [5], viscosity [6], surface tension [7], and the critical point (CP) density [8] of the molecule.

In Section 2, the molecular structures of eight antiviral drugs are studied and graphically represented. The topological indices of the following eight antiviral drugs are calculated using twelve different indices. Antiviral drugs are used in the treatment of a variety of diseases.

Remdesivir: Remdesivir is a prodrug with broad-spectrum antiviral activity *in vitro*, demonstrated to be effective against a variety of RNA viruses, including Ebola virus, Marburg virus, severe acute respiratory syndrome coronavirus (SARS-CoV), and SARS-CoV-2. Currently, it is being studied in phase III clinical trials in adults, with potential as a therapeutic agent, prodrug, and anticoagulant. A topological analysis of a line graph of a substance used in the treatment of coronavirus disease has been performed [9]. Additionally, topological indices of certain chemical structures used to treat COVID-19 have been extensively studied.

Favipiravir [10,11]: It is an antiviral agent that has been approved in Japan to treat influenza (flu) due to its role as an anti-coronavirus agent. It works by inhibiting RNA-dependent RNA polymerase, which is involved in the metabolism of a variety of RNA viruses.

Ribavirin [12,13]: It functions as an antineoplastic agent, antiviral agent, anti-infectious agent, an inhibitor of RNA-dependent DNA polymerase, and an anticonviral agent.

Lopinavir [14]: It is a type of drug that fights HIV infection by blocking proteins in the body. It is usually used in combination with a protein-based drug to treat HIV infection. It is an antiviral drug, an HIV-protein-inhibitor, and an anticoagulant.

Ritonavir [15]: A fixed-dose combination of a cytochrome P450 IIA (CYP3A) inhibitor and an anti-retroviral drug. It belongs to the class of drugs known as protease inhibitors, which are used to treat HIV infections and AIDS.

Darunavir [16,17]: The active substance in this product is furofuran, which is a carbamate ester, a sulfonamide. This product is the second generation of an HIV Protease Interferon designed for the treatment of HIV infection. It functions as an HIV protease inhibitor as well as an antiviral drug.

Oseltamivir [18,19]: This drug helps fight and stop flu and other flu-like illnesses caused by viruses like H1N1 and B. It does this by blocking the virus' neuraminidase, a viral enzyme.

Umifenovir [20,21]: This medicinal product is currently being studied as a potential therapy and prophylaxis agent for the COVID-19 coronavirus caused by SARS-CoV-2 infections in combination with conventional and experimental HIV therapies.

Section 3 results and discussions. Finally, the conclusions are presented in Section 4 based on the analysis. This analysis looks at how antiviral drugs are structured and how they are represented graphically. Also, the values of 12 topological indices for the above 8 antiviral drugs are calculated for further analysis.

Let $Gr(V, E)$ be a graph with vertex set $V = Ver(G)$ and edge set $E = Ed(G)$. The graph $Gr(V, E)$ is connected if there is a connection between any pair of vertices in graph Gr . The distance $d(x, y) = dGr(x, y)$ between any two vertices x and y is defined as the length of the shortest path between x and y in graph Gr . The number of vertices adjacent to a given vertex y in Gr is defined as the “degree” of the vertex y and is denoted by $dy(Gr)$ or dy . The degree is related to valence a bit in chemistry. Here are some degree-related topological indices that we define and use in our work.

Definition 1. The topological indices used in this study are as follows:

ABC index [22] is defined as:

$$ABC(Gr) = \sum_{e=xy \in Ed(G)} \sqrt{\frac{d_x + d_y}{d_x d_y}} \quad (1)$$

The Randic index [23] is defined as:

$$R(Gr) = \sum_{e=xy \in Ed(G)} \sqrt{\frac{1}{d_x d_y}} \quad (2)$$

The sum connectivity index [24] is defined as:

$$S(Gr) = \sum_{e=xy \in Ed(G)} \sqrt{\frac{1}{d_x + d_y}} \quad (3)$$

The GA index [25] is defined as:

$$GA(Gr) = \sum_{e=xy \in Ed(G)} \frac{2\sqrt{d_x d_y}}{d_x + d_y} \quad (4)$$

The first and second Zagreb indices [26,27] are defined as

$$M1(Gr) = \sum_{e=xy \in Ed(G)} d_x + d_y \quad (5)$$

$$M2(Gr) = \sum_{e=xy \in Ed(G)} d_x d_y \quad (6)$$

The harmonic index [28, 29] is defined as:

$$H(Gr) = \sum_{e=xy \in Ed(G)} \frac{2}{d_x + d_y} \quad (7)$$

The hyper-Zagreb index [30, 31] is defined as:

$$HM(Gr) = \sum_{e=xy \in Ed(G)} (d_x + d_y)^2 \quad (8)$$

The third Zagreb index [32] is defined as:

$$ZG3(Gr) = \sum_{e=xy \in Ed(G)} |d_x - d_y| \quad (9)$$

The forgotten index [33, 34] is defined as

$$F(Gr) = \sum_{e=xy \in Ed(G)} [(d_x)^2 + (d_y)^2] \quad (10)$$

The symmetric division index [35, 36] is defined as:

$$(Gr) = \sum_{e=xy \in Ed(G)} \left[\frac{J}{K} + \frac{K}{J} \right] \quad (11)$$

Where $J = \min[d_x, d_y]$ and $K = \max[d_x, d_y]$.

The augmented Zagreb index [37, 38] is defined as:

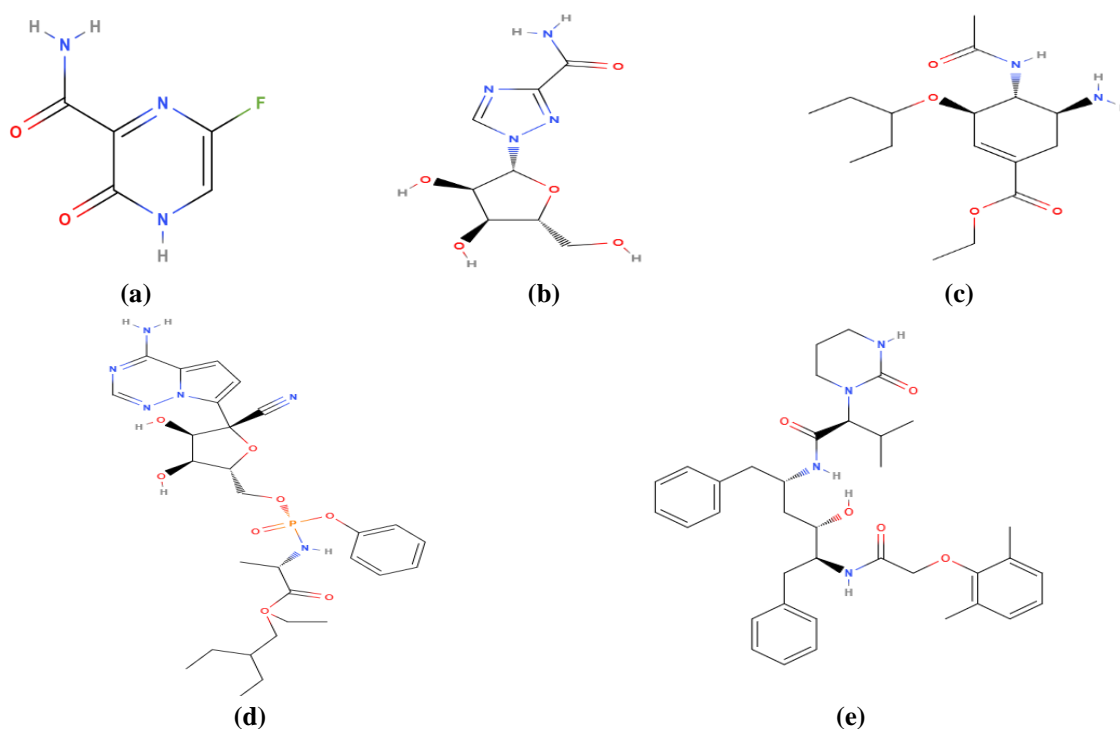
$$AUZI(Gr) = \sum_{e=xy \in Ed(G)} \left\{ \frac{d_x d_y}{d_x + d_y - 2} \right\}^3 \quad (12)$$

2. Materials and Methods

The above-mentioned twelve topological indices are used to model seven physical properties such as boiling point (BP), flash point (FP), enthalpy of vapor (EV), molar refractivity (MR), molar volume (MV), and polarizability (P) and free rotating bond (FRB) of the eight antiviral drugs (Remdesivir; Favipiravir; Ribavirin; Lopinavir; Ritonavir; Darunavir; Oseltamivir; Umifenovir). Materials and all techniques in the calculations are according to [39].

2.1. Topological indices of antiviral drugs.

In this section, the topological indices for the eight selected antiviral drugs are calculated.



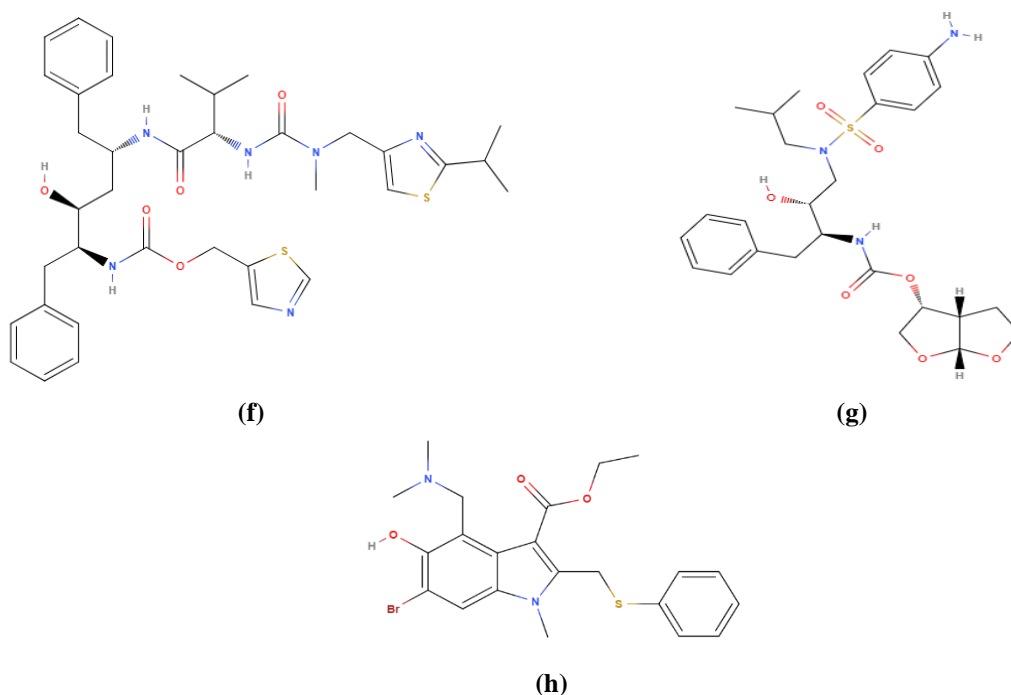


Figure 1. Chemical structures of (a) Favipiravir; (b) Ribavirin; (c) Oseltamivir; (d) Remdesivir; (e) Lopinavir; (f) Ritonavir; (g) Darunavir; (h) Umifenovir (Arbidol).

The molecular structures of the eight antiviral drugs are shown in Figure 1, and the graphical representations of the classes of vertices with varying degrees are shown in Figures 2 to 9. The procedure for calculating the topological indices for the antiviral drug ribavirin is derived in Theorem 1. The topological indices can be calculated for other antiviral drugs using the same procedure outlined in Theorem 1.

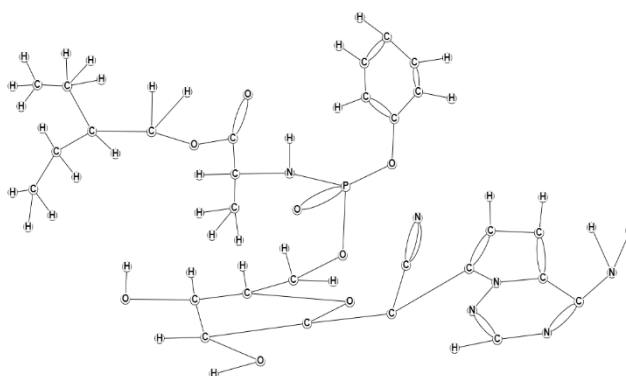


Figure 2. Molecular graph of Remdesivir.

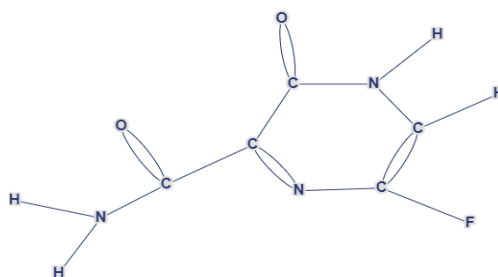


Figure 3. Molecular graph of Favipiravir.

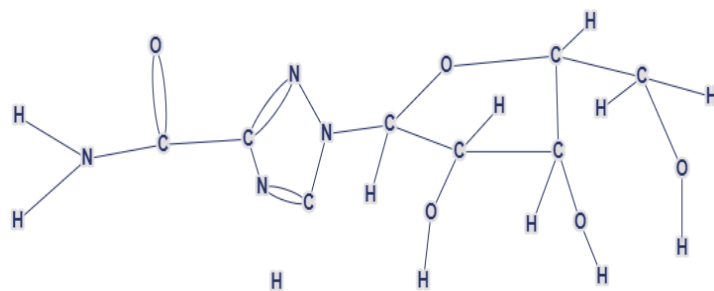


Figure 4. Molecular graph of Ribavirin.

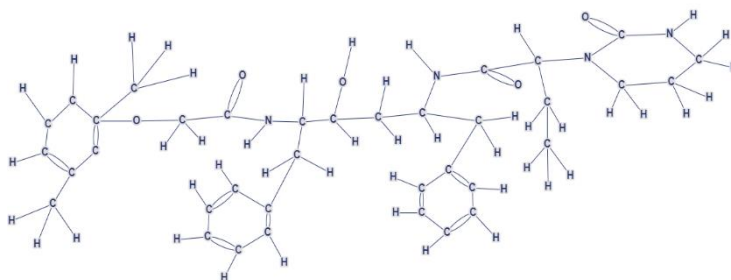


Figure 5. Molecular graph of Lopinavir.

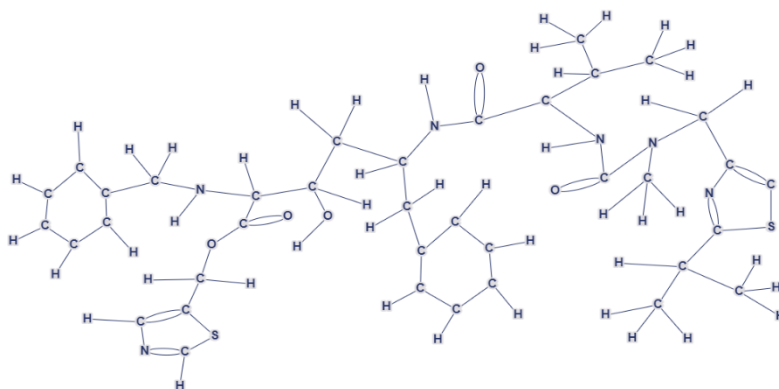


Figure 6. Molecular graph of Ritonovir.

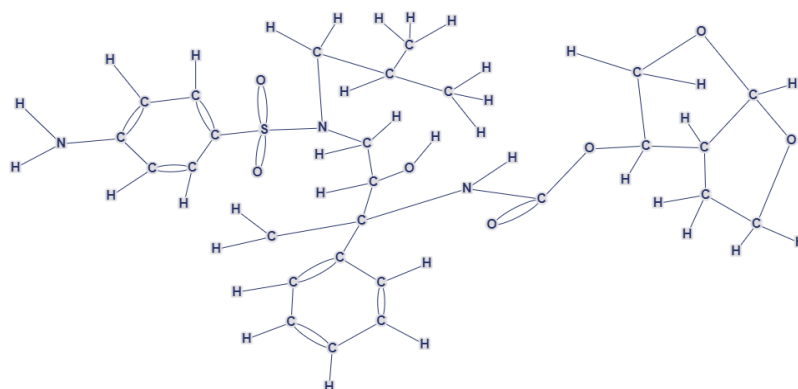


Figure 7. Molecular graph of Darunavir.

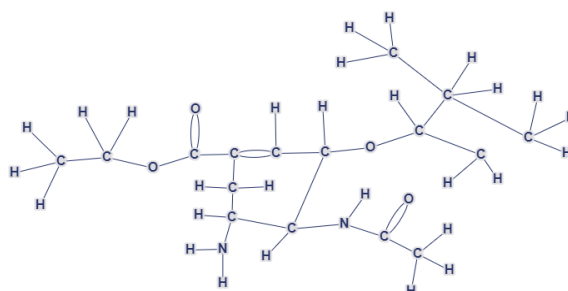


Figure 8. Molecular graph of Oseltamivir.

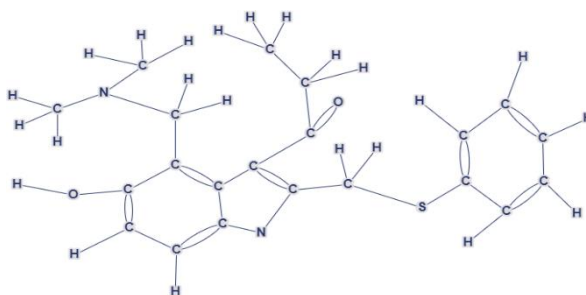


Figure 9. Molecular graph of Arbidol.

2.2. Molecular formula of antiviral drugs.

The molecular formula of antiviral drugs used in our study is as follows: Remdesivir- $C_{27}H_{35}N_6O_8P$; (b) Favipiravir- $C_5H_4FN_3O_2$; (c) Ribavirin- $C_8H_{12}N_4O_5$; Lopinavir- $C_{37}H_{48}N_4O_5$; (e) Ritonavir- $C_{37}H_{48}N_6O_5S_2$; (f) Darunavir- $C_{27}H_{37}N_3O_7S$; Oseltamivir- $C_{16}H_{28}N_2O_4$; (h) Arbidol- $C_{22}H_{25}BrN_2O_3S$.

2.3. Valence number of atoms.

In chemistry, the term "valence" refers to an element's property that determines its ability to form chemical bonds. This property is also referred to as the "power of combination" or "numerical power of combination". Valence was first introduced in 1868. The valence number of an atom may be considered as the degree of a vertex in the graphical representation of the chemical structure. The degree of chemical atoms in the selected antiviral structure graphs is as follows: degree (H) = $d(H) = 1$, degree (F) = $d(F) = 1$, degree (C) = $d(C) = 4$, degree (O) = $d(O) = 2$, degree (S) = $d(S) = 2$, degree (N) = $d(N) = 3$, degree (P) = $d(P) = 5$, degree (Br) = $d(Br) = 1$.

2.3.1 Theorem 1.

Let Gr1 be the graph of the antiviral drug lopinavir. Various topological indices of Gr1 are given as follows:

- (i) $ABC(Gr1) = 74.47$. (ii) $RA(Gr1) = 38.22$. (iii) $S(Gr1) = 41.18$.
- (iv) $GA(Gr1) = 92.93$. (v) $M1(Gr1) = 652$. (vi) $M2(Gr1) = 991$.
- (vii) $F(Gr1) = 2400$. (viii) $H(Gr1) = 33.74$. (ix) $HM(Gr1) = 4382$.
- (x) $AUZI(Gr1) = 1067.87$ (xi) $ZG3(Gr1) = 154$ (xii) $SDD(Gr1) = 303.75$

Proof. Let Gr1 be the graph of the antiviral drug lopinavir with edge set $Ed(Gr1)$. Let $Ed(x,y)$ represent the class of edges of Gr1 joining vertices of degrees x and y. From the molecular graph, we can obtain $|Ed(1,2)| = 1$, $|Ed(1,3)| = 3$, $|Ed(1,4)| = 40$, $|Ed(2,4)| = 9$, $|Ed(3,4)| = 9$, $|Ed(4,4)| = 40$.

From equation (1) and with respect to the edge partitions $Ed(x,y)$, we get:

$$\begin{aligned}
 ABC(Gr1) &= 1 \sqrt{\frac{1+2-2}{1 \times 2}} + 3 \sqrt{\frac{1+3-2}{1 \times 3}} + 40 \sqrt{\frac{1+4-2}{1 \times 4}} + \\
 &\quad 9 \sqrt{\frac{2+4-2}{2 \times 4}} + 9 \sqrt{\frac{3+4-2}{3 \times 4}} + 40 \sqrt{\frac{4+4-2}{4 \times 4}} \\
 &= 74.47 \qquad \qquad \qquad (13)
 \end{aligned}$$

From equation (2) and with respect to the edge partitions $Ed(x,y)$, we get:

$$RA(Gr1) = 1\sqrt{\frac{1}{1 \times 2}} + 3\sqrt{\frac{1}{1 \times 3}} + 40\sqrt{\frac{1}{1 \times 4}} + 9\sqrt{\frac{1}{2 \times 4}} + 9\sqrt{\frac{1}{3 \times 4}} + 40\sqrt{\frac{1}{4 \times 4}} = 38.22 \quad (14)$$

From equation (3) and with respect to the edge partitions $Ed(x,y)$, we get:

$$S(Gr1) = 1\sqrt{\frac{1}{1+2}} + 3\sqrt{\frac{1}{1+3}} + 40\sqrt{\frac{1}{1+4}} + 9\sqrt{\frac{1}{2+4}} + 9\sqrt{\frac{1}{3+4}} + 40\sqrt{\frac{1}{4+4}} = 41.18 \quad (15)$$

From equation (4) and with respect to the edge partitions $Ed(x,y)$, we get:

$$GA(Gr1) = \left(1 \times \frac{2\sqrt{1 \times 2}}{1+2}\right) + \left(3 \times \frac{2\sqrt{1 \times 3}}{1+3}\right) + \left(40 \times \frac{2\sqrt{1 \times 4}}{1+4}\right) = \left(9 \times \frac{2\sqrt{2 \times 4}}{2+4}\right) + \left(9 \times \frac{2\sqrt{3 \times 4}}{3+4}\right) + \left(40 \times \frac{2\sqrt{4 \times 4}}{4+4}\right) = 92.93 \quad (16)$$

From equation (5) and with respect to the edge partitions $Ed(x,y)$, we get:

$$M_1(Gr1) = 1(1+2) + 3(1+3) + 40(1+4) + 9(2+4) + 9(3+4) + 40(4+4) = 652 \quad (17)$$

From equation (6) and with respect to the edge partitions $Ed(x,y)$, we get:

$$M_2(Gr1) = 1(1 \times 2) + 3(1 \times 3) + 40(1 \times 4) + 9(2 \times 4) + 9(3 \times 4) + 40(4 \times 4) = 991 \quad (18)$$

From equation (7) and with respect to the edge partitions $Ed(x,y)$, we get:

$$H(Gr1) = 1 \cdot \frac{2}{1+2} + 3 \cdot \frac{2}{1+3} + 40 \cdot \frac{2}{1+4} = 9 \cdot \frac{2}{2+4} + 9 \cdot \frac{2}{3+4} + 40 \cdot \frac{2}{4+4} = 33.74 \quad (19)$$

From equation (8) and with respect to the edge partitions $Ed(x,y)$, we get:

$$HM(Gr1) = 1(1+2)^2 + 3(1+3)^2 + 40(1+4)^2 + 9(2+4)^2 + 9(3+4)^2 + 40(4+4)^2 = 4382 \quad (20)$$

From equation (9) and with respect to the edge partitions $Ed(x,y)$, we get:

$$ZG_3(Gr1) = 1 \cdot |1-2| + 3 \cdot |1-3| + 40 \cdot |1-4| = 9 \cdot |2-4| + 9 \cdot |3-4| + 40 \cdot |4-4| = 154 \quad (21)$$

From equation (10) and with respect to the edge $Ed(x,y)$, we get:

$$F(Gr1) = 1(1^2 + 2^2) + 3(1^2 + 3^2) + 40(1^2 + 4^2) + 9(2^2 + 4^2) + 9(3^2 + 4^2) + 40(4^2 + 4^2) = 2400 \quad (22)$$

From equation (11) and with respect to the edge partitions $Ed(x,y)$, we get:

$$SDD(Gr1) = 1 \cdot \left(\frac{Min(1,2)}{Max(1,2)} + \frac{Max(1,2)}{Min(1,2)}\right) + 3 \cdot \left(\frac{Min(1,3)}{Max(1,3)} + \frac{Max(1,3)}{Min(1,3)}\right) = 40 \cdot \left(\frac{Min(1,4)}{Max(1,4)} + \frac{Max(1,4)}{Min(1,4)}\right) + 9 \cdot \left(\frac{Min(2,4)}{Max(2,4)} + \frac{Max(2,4)}{Min(2,4)}\right) = 9 \cdot \left(\frac{Min(3,4)}{Max(3,4)} + \frac{Max(3,4)}{Min(3,4)}\right) + 40 \cdot \left(\frac{Min(4,4)}{Max(4,4)} + \frac{Max(4,4)}{Min(4,4)}\right)$$

$$= 303.75 \tag{23}$$

From equation (12) and with respect to the edge partitions $Ed(x, y)$, we get:

$$\begin{aligned} AUZI(Gr1) &= 1 \left(\frac{1 \times 2}{1 + 2 - 2} \right)^3 + 3 \left(\frac{1 \times 3}{1 + 3 - 2} \right)^3 + 40 \left(\frac{1 \times 4}{1 + 4 - 2} \right)^3 \\ &= 9 \left(\frac{2 \times 4}{2+4-2} \right)^3 + 9 \left(\frac{3 \times 4}{3+4-2} \right)^3 + 40 \left(\frac{4 \times 4}{4+4-2} \right)^3 = 1067.87 \end{aligned} \tag{24}$$

2.4. Physical properties of antiviral drugs.

The boiling point (BP), flash point (FP), enthalpy of vapor (EV), molar refractivity (MR), molar volume (MV), Polarizability (P), and freely rotating bonds (FRB) are obtained from ChemSrc and ChemSpider for the eight different antiviral drugs: Remdesiver, Favipiravir, Ribavirin, Lopinavir, Ritonavir, Darunavir; Oseltamivir, and Umifenovir.

2.5. Regression models.

The correlation between physical properties and the topological indices is analyzed, and suitable regression models are used to establish the relationships.

The computations of topological indices and the physical properties of molecular structures are tabulated in Tables 1 and 2, respectively. With these values, regression models are used to fit the curves. This study aims to analyze the linear, quadratic, and cubic models. The regression models, including correlation coefficient (r) and coefficient of determination (r^2), have been analyzed.

Table 1. Antiviral drugs and their topological indices values.

Index	Remdesivir	Favipiravir	Ribavirin	Lopinavir	Ritonavir	Darunavir	Oseltamivir	Umifenovir
$ABC(Gr)$	66.11	13.11	23.66	74.47	83.44	62.86	40.27	41.84
$RA(Gr)$	34.29	7.14	13.14	38.22	42.90	32.16	21.43	20.87
$S(Gr)$	36.98	7.86	13.92	41.18	46.19	34.62	22.03	23.41
$GA(Gr)$	83.25	18.06	30.68	92.93	103.83	77.96	47.11	54.77
$M1(Gr)$	575.00	118.00	196.00	652.00	721.00	555.00	318.00	389.00
$M2(Gr)$	860.00	183.00	281.00	991.00	1075.00	841.00	433.00	618.00
$H(Gr)$	30.54	6.68	12.00	33.74	37.92	28.32	18.52	18.83
$HM(Gr)$	3819.00	778.00	1234.00	4382.00	4777.00	3783.00	2004.00	2677.00
$F(Gr)$	2099.00	412.00	672.00	2400.00	2627.00	2101.00	1138.00	1441.00
$AUZI(Gr)$	922.65	214.91	320.14	1067.87	1149.23	879.99	440.34	679.68
$ZG3(Gr)$	145.00	24.00	50.00	154.00	181.00	147.00	100.00	79.00
$SDD(Gr)$	265.62	47.33	90.08	303.75	339.33	259.42	170.50	164.00

Table 2. Physical properties of antiviral drugs.

Physical property	Remdesivir	Favipiravir	Ribavirin	Lopinavir	Ritonavir	Darunavir	Oseltamivir	Umifenovir
Molar refractivity	149.5	33.2	51.1	179.2	198.9	143.6	84.7	121.9
Polarizability	59.3	13.2	20.3	71	78.9	56.9	33.6	48.3
Boiling point	N/A	552.6	639.8	924.2	947	N/A	473.3	591.8
Molar volume	409	97.2	117.1	540.5	581.7	408.4	286.8	347.3
Flash point	N/A	288	340.7	512.7	526.6	N/A	240	311.7
Freely rotating bonds	15	1	3	15	18	12	8	8
Enthalpy of vaporization	N/A	86.4	99.3	140.8	144.4	N/A	73.6	91.5

The regression model with the highest r^2 value is the most accurate. These models may be employed to evaluate the physicochemical characteristics of other antiviral drugs. The following are linear, quadratic, and cubic regression equations.

The linear regression model:

$$P = A + b(TOI) \tag{25}$$

The quadratic regression model:

$$P = A + b(TOI) + c(TOI)^2 \tag{26}$$

The cubic regression model:

$$P = A + b(TOI) + c(TOI)^2 + d(TOI)^3 \tag{27}$$

Where 'P' is the physical property of the drug, 'A' is the regression model constant, b, c, and d are the coefficients of the topological index, and 'TOI' is the topological index of the drug. SPSS Statistics version 24 was used for the computations. We analyze the 12 TOIs of selected antiviral drugs and their physico-chemical properties using the QSPR models using equations (13-15).

3. Results and Discussions

From the three QSPR model parameters and the topological indices ABC index, RA index, S index, and H index, it follows that these indices show a high correlation ($r = 0.99$) with freely rotating bonds. Also, the M2 and AUZI indices are well correlated ($r = 0.99$) for molar refractivity and polarizability. M1 index, HM index, and F index provide a high r-value of molar volume; that is, $r = 0.981$, and all the indices in our study depict the maximum correlation coefficient ($0.9 < r < 1$) with the physicochemical properties. Also, it is observed that the connectivity between the C and H atoms is very high in all the molecular structures of the selected antiviral drugs.

These results will help in the design and analysis of new drugs to fight infectious diseases in the world. The study of the correlation coefficient is an important tool in understanding the relationship between the various topological indices of these drugs and their properties. It could be used to analyze newer combinations for the design of antiviral drugs. The results would provide deeper insight for drug discovery researchers in the pharma industry and a better understanding of physical properties, enabling the discovery of antiviral drugs to treat other diseases. The following Figures 10-12 depict the correlation between the TOIs and the physicochemical properties of selected antiviral drugs.

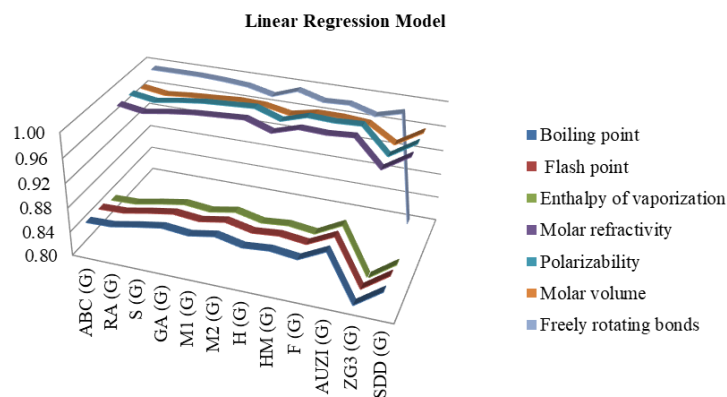


Figure 10. Linear regression model of physicochemical properties and TOI.

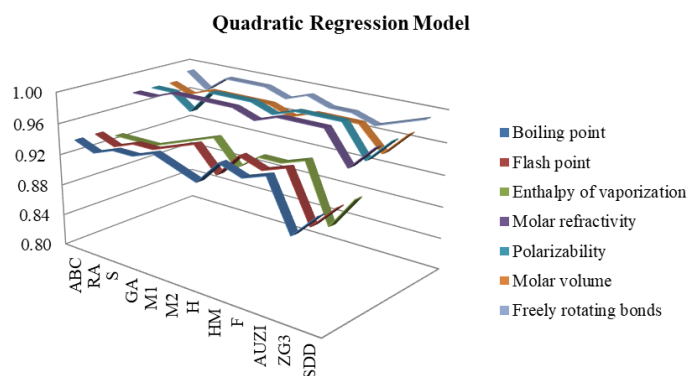


Figure 11. Quadratic regression model of physicochemical properties and TOI.

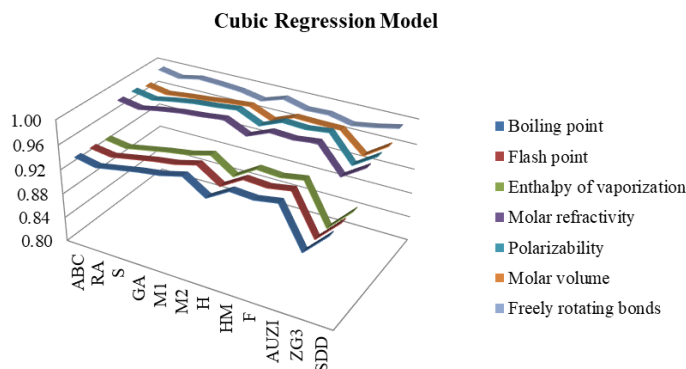


Figure 12. Cubic regression model of physicochemical properties and TOI.

The correlation coefficients analyzed here indicate how effectively the aforementioned indices predict the physical properties of antiviral drugs. The study specifically presents a quantitative structure-property relationship (QSPR) analysis of molecular descriptors (TOIs), which are tools used to predict a drug's chemical and physical properties, particularly in the context of pharmaceutical and medical applications. The physical characteristics, such as molar refractivity, polarizability, molar volume, and freely rotating bonds, have been predicted with great accuracy using the selected indices.

The molecular descriptors M2 (G), HM (G), and AUZI (G) in the cubic regression model are the most accurate predictors of variables such as polarizability and molar refractivity.

When employing quadratic and cubic regression models, all the molecular descriptors are best for predicting molar refractivity, polarizability, molar volume, and freely rotating bonds.

All the molecular descriptors in the cubic regression model are moderate in predicting variables such as boiling point, flash point, and enthalpy of vaporization.

4. Conclusions

In summary, there is a significant and robust relationship between the structural characteristics of antiviral drugs and the topological indices. A clear comparison is made between the various regression models for predicting the physico-chemical characteristics using topological indices, and the best models are validated. The observed results show that the p-value is less than 0.05 and that the coefficients of determination are greater than 0.9. These observations validate our conclusions. Results from theoretical models and experimental values agree quite well. We assess the predictive capacity of degree-based TOIs by applying a range of physicochemical properties of these structures. The outcomes of this investigation will

improve our understanding of chemical structures. These indices have potential future use for numerous chemical graph exploration and drug discovery applications.

Author Contributions

Conceptualization, B.S. and V.R.; methodology, B.S. and V.R.; software, V.R.; validation, B.S. and V.R.; formal analysis, B.S. and V.R.; investigation, B.S.; resources, B.S.; data curation, V.R.; writing original draft preparation, B.S.; writing review and editing, B.S. and V.R.; visualization, V.R.; supervision, B.S.; project administration, B.S.; funding acquisition, not applicable. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement

Not applicable. This study did not involve humans or animals.

Informed Consent Statement

Not applicable. This study did not involve human participants.

Data Availability Statement

Data supporting the findings of this study are available upon reasonable request from the corresponding author.

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Conflicts of Interest

The authors declare no conflict of interest.

References

1. Kumari, M.; Lu, R.M.; Li, M.C.; Huang, J.L.; Hsu, F.F.; Ko, S.H.; Ke, F.Y.; Su, S.C.; Liang, K.H.; Yuan, J.P.; Chiang, H.L. A Critical Overview of Current Progress for COVID-19: Development of Vaccines, Antiviral Drugs, and Therapeutic Antibodies. *J. Biomed. Sci.* **2022**, *29*, 68, <https://doi.org/10.1186/s12929-022-00852-9>.
2. Xiang, Q.; Li, L.; Wu, J.; Tian, M.; and Fu, Y. Application of pseudovirus system in the development of vaccine, antiviral-drugs, and neutralizing antibodies. *Microbiol. Res.* **2022**, *258*, 126993, <https://doi.org/10.1016/j.micres.2022.126993>.
3. Gider, V.; Budak, C. Instruction of Molecular Structure Similarity and Scaffolds of Drugs Under Investigation in Ebola Virus Treatment by Atom-pair and Graph Network: A Combination of Favipiravir and Molnupiravir. *Comp. Bio. and Chem.* **2022**, *101*, 107778, <https://doi.org/10.1016/j.compbiolchem.2022.107778>.

4. Wiener, H. Structural Determination of Paraffin Boiling Points. *J. Am. Chem. Soc.* **1947**, *69*, 17-20, <https://doi.org/10.1021/ja01193a005>.
5. Estrada, E.; Torres, L.; Rodriguez, L.; Gutman, I. An Atom Bond Connectivity Index: Modeling the Enthalpy of Formation of Alkanes. *Indian J. Chem.* **1998**, *37*, 849–855, <https://nopr.niscpr.res.in/handle/123456789/40308>.
6. Gutmana, I.; Körtevényesi, T. Wiener Indices and Molecular Surfaces. *Z. Naturforsch. PT. B.* **1995**, *50*, 669-71.
7. Rouvray, D.H.; Crafford, B. The Dependence of Physico-Chemical Properties on Topological Factors. *S. Afr. J. Sci.* **1976**, *72*, 47.
8. Stiel, L.I.; Thodos G. The Normal Boiling Points and Critical Constants of Saturated Aliphatic Hydrocarbons. *Aiche J.* **1962**, *8*, 527-9, <https://doi.org/10.1002/aic.690080421>.
9. Rosary, M.S. Topological Study of Line graph of Remdesivir Compound Used in the Treatment of Corona Virus. *Polycycl. Aromat. Comp.* **2022**, *42*, 5731-47, <https://doi.org/10.1080/10406638.2021.1956552>.
10. Yavuz, S.; ÇELİKYURT, İ.K.F. An Update of Antiviral Treatment of COVID-19. *Turk. J. Med. Sci.* **2021**, *51*, 3372-3390, <https://doi.org/10.3906/sag-2106-250>.
11. Shah, P.L.; Orton, C.M.; Grinsztejn, B.; Donaldson, G.C.; Ramirez, B.C.; Tonkin, J.; Santos, B.R.; Cardoso, S.W.; Ritchie, A.I.; Conway, F.; Riberio, M.P. Favipiravir in patients hospitalised with COVID-19 (PIONEER trial): a multicentre, open-label, phase 3, randomised controlled trial of early intervention versus standard care. *Resp. Med.* **2023**, *11*, 415-424, [https://doi.org/10.1016/S2213-2600\(22\)00412-X](https://doi.org/10.1016/S2213-2600(22)00412-X).
12. Patterson, J.L.; Fernandez-Larsson, R. Molecular Mechanisms of Action of Ribavirin. *Rev. of infect. dis.* **1990**, *12*, 1139-46, <https://doi.org/10.1093/clinids/12.6.1139>.
13. Chiani, E.; Beaucamp, A.; Hamzeh, Y.; Azadfallah, M.; Thanusha, A.V.; Collins, M.N. Synthesis and characterization of gelatin/lignin hydrogels as quick release drug carriers for ribavirin. *Int. J. of Biol. Macromol.* **2023**, *224*, 1196-1205, <https://doi.org/10.1016/j.ijbiomac.2022.10.205>.
14. Chandwani, A.; Shuter, J. Lopinavir/Ritonavir in the Treatment of HIV-1 Infection: a Review. *Ther. clin. risk manag.* **2008**, *4*, 1023-33, <https://doi.org/10.2147/tcrm.s3285>.
15. Kaizer, A.M.; Shapiro, N.I.; Wild, J.; Brown, S.M.; Cwik, B.J.; Hart, K.W.; Jones, A.E.; Pulia, M.S.; Self, W.H.; Smith, C.; Smith, S.A. Lopinavir/ritonavir for treatment of non-hospitalized patients with COVID-19: a randomized clinical trial. *Int. J. Infect. Dis.* **2023**, *128*, 223-229, <https://doi.org/10.1016/j.ijid.2022.12.028>.
16. Deeks, E.D. Darunavir: A Review of its Use in the Management of HIV-1 Infection. *Drugs* **2014**, *74*, 99-125, <https://doi.org/10.1007/s40265-013-0159-3>.
17. Yu, K.; Shen, J.; Liu, J.; Tang, G.; Hu, X. Stability and Mechanical Properties of Darunavir Isostructural Solvates: An Experimental and Computational Study. *Cryst. Growth Des.* **2023**, *23*, 2905-2915, <https://doi.org/10.1021/acs.cgd.3c00057>.
18. Huang, D.; Yu, H.; Wang, T.; Yang, H.; Yao, R.; Liang, Z. Efficacy and Safety of Umifenovir for Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis. *J. Med. Vir.* **2021**, *93*, 481-90, <https://doi.org/10.1002/jmv.26256>.
19. Shiraiishi, C.; Kato, H.; Hagihara, M.; Asai, N.; Iwamoto, T.; Mikamo, H. Comparison of clinical efficacy and safety of baloxavir marboxil versus oseltamivir as the treatment for influenza virus infections: A systematic review and meta-analysis. *J. Infect. Chemother.* **2023**, *30*, 242-249, <https://doi.org/10.1016/j.jiac.2023.10.017>.
20. Parveen, S.; Hassan Awan, N.U.; Mohammed, M.; Farooq, F.B.; Iqbal, N. Topological Indices of Novel Drugs Used in Diabetes Treatment and Their QSPR Modeling. *J. of Math.* **2022**, *2022*, 1-7, <https://doi.org/10.1155/2022/5209329>.
21. Özok, H.İ.; Kiran, M.; Yunusoğlu, O.; Yardım, Y. The First Electroanalytical Study of Umifenovir (Arbidol) Used as A Potential Antiviral Drug for The Treatment of SARS-CoV-2: A Voltammetric Quantification on The Boron-Doped Diamond Electrode by Using Anionic Surfactant Media. *J. Electrochem. Soc.* **2023**, *170*, 016501, <https://doi.org/10.1149/1945-7111/acafa7>.
22. Ali, A.; Gutman, I.; Redžepović, I. Atom-bond sum-connectivity index of unicyclic graphs and some applications. *Electron. J. Math.* **2023**, *5*, 1-7, <http://dx.doi.org/10.47443/ejm.2022.039>.
23. Randić, M. Characterization of Molecular Branching. *J. Am. Chem. Soc.* **1975**, *97*, 6609-15, <https://doi.org/10.1021/ja00856a001>.

24. Zhou, B.; Trinajstić, N. On General Sum-Connectivity Index. *J. Math. Chem.* **2010**, *47*, 210-8, <https://doi.org/10.1007/s10910-009-9542-4>.
25. Vukičević, D.; Furtula, B. Topological Index Based on the Ratios of Geometrical and Arithmetical Means of End-Vertex Degrees of Edges. *J. Math. Chem.* **2009**, *46*, 1369-76, <https://doi.org/10.1007/s10910-009-9520-x>.
26. Gutman, I. Degree-Based Topological Indices. *Croat. Chem. Acta.* **2013**, *86*, 351-61, <https://doi.org/10.5562/cca2294>.
27. Islam, S.R.; Pal, M. Second Zagreb index for fuzzy graphs and its application in mathematical chemistry. *Iran. J. Fuzzy Syst.* **2023**, *20*, 119-136, <https://doi.org/10.22111/ijfs.2023.7350>.
28. Fajtlowicz, S. On conjectures of Grafitti II. *Ann. Discrete Math.* **1987**, *60*, 189-97, [https://doi.org/10.1016/S0167-5060\(08\)70776-3](https://doi.org/10.1016/S0167-5060(08)70776-3).
29. Wang, T.; Wu, B.; Wang, T. Harmonic index of a line graph. *Discrete Appl. Math.* **2023**, *325*, 284-296, <https://doi.org/10.1016/j.dam.2022.10.021>.
30. Shirdel, G.H.; RezaPour, H.; and Sayadi, A.M. The Hyperzagreb Index of Graph Operations, *Iranian J. Math. Chem.* **2013**, *4*, 213–220, <https://doi.org/10.22052/ijmc.2013.5294>.
31. Hayat, S.; Khan, M.A.; Khan, A.; Jamil, H.; Malik, M.Y.H. Extremal hyper-Zagreb index of trees of given segments with applications to regression modeling in QSPR studies. *Alexandria Engg. J.* **2023**, *80*, 259-268, <https://doi.org/10.1016/j.aej.2023.08.051>.
32. Astanesh-Asl, A.; Fath-Tabar, GH. Computing the First and Third Zagreb Polynomials of Curtained Product of Graphs. *Iranian J. Math. Chem.* **2011**, *2*, 73–78, <https://doi.org/10.22052/ijmc.2011.5177>.
33. Furtula, B.; Gutman, I. A Forgotten Topological Index. *J. Math. Chem.* **2015**, *53*, 1184-90, <https://doi.org/10.1007/s10910-015-0480-z>.
34. Mathivanan, A.; Joseph, M. Distance Version of Forgotten Topological Index of Some Graph Products. *Appl. And Comp. Math.* **2023**, *12*, 15-25, <https://doi.org/10.11648/j.acm.20231201.13>.
35. Alexander, V. Upper and lower bounds of symmetric division deg index. *Iranian J. Math. Chem.* **2014**, *5*, 91-98.
36. Naeem, M.; Atif, M.; Khalid, A.; Sajid, M.; Mustafa, M.A. Computation of degree-based topological indices for porphyrizine and tetrakis porphyrizine. *Mol. Phys.* **2023**, *121*, 13, <https://doi.org/10.1080/00268976.2023.2205534>.
37. Furtula, B.; Graovac, A.; Vukičević, D. Augmented Zagreb Index. *J. Math. Chem.* **2010**, *48*, 370-80, <https://doi.org/10.1007/s10910-010-9677-3>.
38. Shao, Y.; Gao, W. Complete characterization of chemical trees with maximal Augmented Zagreb index. *J. Appl. Math. and Comp.* **2023**, *69*, 3851-3870, <https://doi.org/10.1007/s12190-023-01904-5>.
39. Bokhary, S.A.; Adnan; Siddiqui, M.K.; Cancan, M. On Topological Indices and QSPR Analysis of Drugs Used for the Treatment of Breast Cancer. *Polycycl. Aromat. Comp.* **2022**, *42*, 6233-53, <https://doi.org/10.1080/10406638.2021.1977353>.