Analysis of Degree-Based Topological Indices for Stroke Treatment Drugs: A Study on the Physicochemical Features

S Shenbaga Devi and S Dhanalakshmi

***Abstract*—Topological indices are numerical descriptors obtained using a molecular graph in order to study the medications thoroughly. They are used in the analysis and forecasting of various pharmaceuticals' physicochemical features. In this paper, a few degree-based topological indices of drugs - Apixaban, Betrixaban, Rivaroxaban, Edoxaban Warfarin, Clopidogrel, Rosuvastatin, Simvastatin, and Atorvastatin which are used in the treatment of stroke have been computed. Also, we have shown the correlation and standard error of the estimate with the physico-chemical properties of medications used in the treatment of stroke. This will help the pharmaceutical people to understand the properties of drugs without the process of experimentation.**

***Index Terms*—Topological indices, stroke, degree-based topological indices**

I. Introduction

A Stroke is a brain attack when there is an interruption in the blood supply to a particular brain region. It is one of the dangerous medical conditions, which is life-threatening. It occurs when a blockage or bleeding in the blood vessels causes the blood supply to the brain to be diminished or disturbed. As a result, the brain receives insufficient oxygen and nutrients, which leads to the degeneration of brain cells. Stroke represents one form of cerebrovascular disease. This suggests that it affects the blood vessels that supply the brain with oxygen. A medical emergency may result from brain injury caused by inadequate oxygen delivery to the brain. While there is a cure for many strokes, some can be deadly or leave a person incapacitated. There are two distinct types of strokes: hemorrhagic and ischemic. The most frequent kind of strokes are ischemic ones. Blood clots or foreign objects blocking the blood vessels in the brain cause an ischemic stroke. When a brain artery rupture or leaks blood, it can cause a hemorrhagic stroke. The high pressure brought on by the brain leak damages the brain's cells.

A stroke has long-lasting physical and psychological symptoms that may change one's life. The main signs of stroke are: slanting of face, lacking ability to grin, dropping of jaw or eyes; also, struggling in lifting the arms, slurring and garbling speech, communicating and comprehending difficulty. Excessive weight especially, after 55 years of age, high blood pressure, family history of stroke, diabetes, high cholesterol, heart problem, excessive drinking, excessive smoking, and use of illegal drugs are also reasons for stroke. According to a study published by Neurology India in 2021, the prevalence of stroke is relatively high in India, and more than 80 percent of all stroke cases is ischemic stroke. Furthermore, the sharp increase in stroke cases in India over the past ten years can be related to several socio-economic factors that altered the lifestyle reducing physical activity, consuming too much processed food, and experiencing stress at work. For further details see [1], [2], [3].

The treatment for the stroke depends on the kind of the stroke and identifying the part of the brain that is hurt. This group includes the use of medications to treat blood clots, lower blood pressure, and lower cholesterol. In some cases, procedures to get rid of blood clots should be done. Surgery is necessary to treat stroke caused by brain enlargement and reduce the risk of bleeding. In any of the cases, some drugs stop a stroke from recurring, while others from happening in the first place. The most typical stroke treatments are done using Anticoagulants, Antiplatelet drugs, and Statins. The blood's capacity to clot is decreased by anticoagulant medications. The most typical anticoagulants are Apixaban, Betrixaban, Rivaroxaban, Edoxaban and Warfarin. Figure (1) depicts the drug structures. The molecular formula for Apixaban is $C_{25}H_{25}N_5O_4$. Apixaban is prescribed to patients with atrial fibrillation as a preventive against stroke and as a postoperative measure for deep vein thrombosis to prevent pulmonary embolism. The molecular formula for Betrixaban is $C_{23}H_{22}ClN_5O_3$. Betrixaban is used to lower the risk of pulmonary embolism and deep vein thrombosis in hospitalized patients with an acute medical condition and who are at high risk for venous thromboses. The molecular formula for Rivaroxaban is $C_{19}H_{18}ClN_3O_5S$. Rivaroxaban treats and prevents deep vein thrombosis, a condition in which harmful blood clots develop in the leg arteries. Moreover, it is used to prevent blood clots and stroke in people with specific heart rhythm issues. The molecular formula for Edoxaban is $C_{24}H_{30}ClN_7O_4S$. In people without heart valve issues, edoxaban is used to treat atrial fibrillation, a condition in which the heart beats irregularly, increasing the risk of blood clots developing in the body and possibly causing strokes. The molecular formula for Warfarin is $C_{19}H_{16}O_4$. Warfarin is used to prevent the formation or growth of blood clots in blood vessels. It is administered to those who have experienced a heart attack, have artificial heart valves, or exhibit specific types of irregular heartbeat. Antiplatelet medications prevent blood clots by making it harder for the platelets in the blood to cling to one another. Clopidogrel is the most popular antiplatelet medication. The molecular for-

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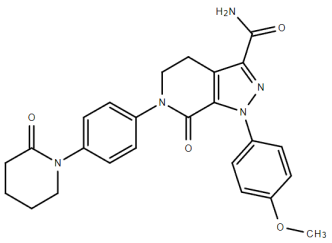
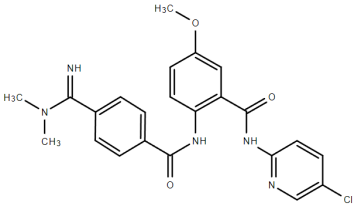
mula is $C_{16}H_{16}ClNO_2S$. Clopidogrel keeps platelets from adhering to one another and creating a potentially fatal blood clot. Statins are used to decrease high blood cholesterol. Atorvastatin, Simvastatin, and Rosuvastatin are examples of common statins. The molecular formula for Rosuvastatin, Simvastatin, and Atorvastatin are: $C_{22}H_{28}FN_3O_6S$, $C_{25}H_{38}O_5$ and $C_{33}H_{35}FN_2O_5$. Rosuvastatin, Simvastatin, and Atorvastatin are taken in combination with a healthy diet, to reduce weight and start an exercise regimen to lessen your chance of having a heart attack, stroke, or needing heart surgery. Triglycerides and low-density lipoprotein cholesterol are lowered and high-density lipoprotein cholesterol is raised in the blood by their use. They're also used to reduce blood levels of cholesterol and other fatty substances in kids and teenagers with familial heterozygous hypercholesterolemia, who are between the ages of 10 and 17. They also help to reduce the amount of cholesterol that may accumulate on the artery walls and obstruct blood flow to the heart, brain and other regions of the body by inhibiting the body's creation of cholesterol [4], [5].

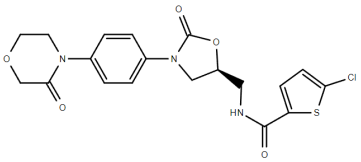
Analysis and forecasting of pharmaceuticals' physiochemical features help in studying the medications thoroughly. At this point, examination of molecular properties of the compounds is very imperative and it involves a lot of time. This can be avoided by employing quantitative structure activity relationship models to identify how topological descriptors are utilized to describe various properties of distinct chemical compounds. A numerical value connected to a molecular graph is called a topological index. Correlation analysis has been performed using a number of determined indices. The degree-based topological indices are useful in testing the drug properties and compounds and they are extensively used in pharmacy and in chemical engineering. They are employed to evaluate the pharmacological and medicinal properties of drugs. To anticipate the bioactivity of medications, indices like the ABC index, Randic index, and Weiner index are helpful [6], [7]. The three main aims of this study are: to calculate topological indices for the medications being considered, to compare topological indices to the correlations of a few physical and statistical properties, and to employ regression models for the nine stroke medications to do a QSPR analysis of the topological indices [8], [9], [10].



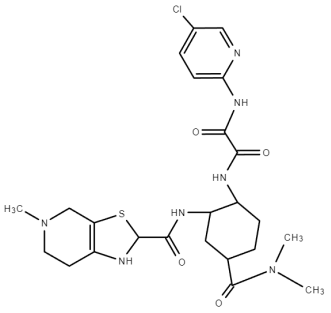
(a) Apixaban



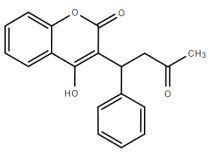
(b) Betrixaban



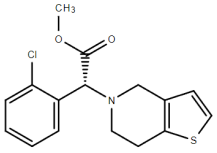
(c) Rivaroxaban



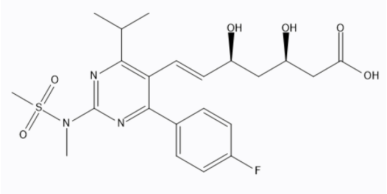
(d) Edoxaban



(e) Warfarin



(f) Clopidogrel



(g) Rosuvastatin

II. Basic Concepts and Terminologies

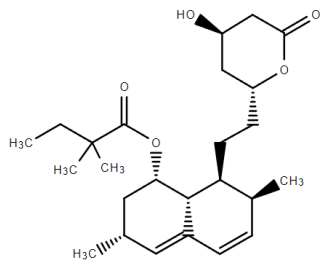
Assume G be a simple drug structure with vertex set $V(G)$ which corresponds to the atoms of the drug and the edge set $E(G)$ corresponds to the bonds connecting the atoms respectively. The degree of a vertex, denoted by d_p, where $p \in V(G)$, is determined by counting the edges that coincide with it.

This section covers an overview of the basic definitions of the Degree-based topological indices used in the study:

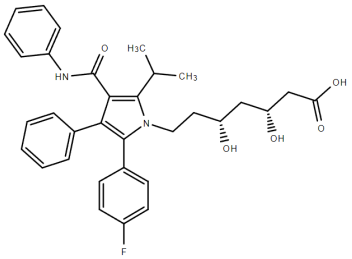
Definition 2.1

The ABC index [11] of a molecular graph G is defined as:

$$ABC(G) = \sum_{pq \in E(G)} \sqrt{\frac{d_p + d_q - 2}{d_p d_q}} \qquad (1)$$



(h) Simvastatin



(i) Atorvastatin

Fig. 1. Drugs molecular structure

Definition 2.2

The Randic index [12] of a molecular graph G is defined as:

$$RA(G) = \sum_{pq \in E(G)} \sqrt{\frac{1}{d_p d_q}} \tag{2}$$

Definition 2.3

The sum connectivity index [13] of a molecular graph G is defined as:

$$S(G) = \sum_{pq \in E(G)} \sqrt{\frac{1}{d_p + d_q}} \tag{3}$$

Definition 2.4

The Geometric-Arithmetic index [14] of a molecular graph G is defined as:

$$GA(G) = \sum_{pq \in E(G)} 2\frac{\sqrt{d_p d_q}}{d_p + d_q} \tag{4}$$

Definition 2.5

The first Zagreb index [15] of a molecular graph G is defined as:

$$M_1(G) = \sum_{p \in V(G)} d_p^2 \tag{5}$$

The second Zagreb index of a molecular graph G is defined as:

$$M_2(G) = \sum_{pq \in E(G)} d_p d_q \tag{6}$$

Definition 2.6

The harmonic index [16] of a molecular graph G is defined as:

$$H(G) = \sum_{pq \in E(G)} \frac{2}{d_p + d_q} \tag{7}$$

Definition 2.7

The hyper-Zagreb index [17] of a molecular graph G is defined as:

$$HM(G) = \sum_{pq \in E(G)} (d_p + d_q)^2 \tag{8}$$

Definition 2.8

The forgotten index [18] of a molecular graph G is defined as:

$$F(G) = \sum_{pq \in E(G)} (d_p^2 + d_q^2) \tag{9}$$

III. Results and Discussion

In this study, the above defined 9 topological indices to model 6 physical properties have been used: molar refractivity (MR), polarizability (P), enthalpy of vaporization (EV), boiling point (BP), flash point (FP), and molar volume (MV) of 9 drugs: Apixaban, Betrixaban, Rivaroxaban, Edoxaban, Warfarin, Clopidogrel, Rosuvastatin, Simvastatin and Atorvastatin. ChemSpider and PubChem are used to obtain the physicochemical characteristics of the eight medications and the values are listed in Table I.

TABLE I
PHYSICOCHEMICAL PROPERTIES OF DRUGS IN TREATMENT OF STROKE

Name of the medicine	BP	FP	EV	MR	PY	MV
Apixaban	770.5	419.8	112.2	125.6	49.8	323.4
Betrixaban				123.1	48.8	346.4
Rivaroxaban	732.6	396.9	106.9	106.7	42.3	298.5
Edoxaban				139.1	55.2	383.2
Warfarin	515.2	188.8	82.9	84.4	33.5	235.8
Clopidogrel	423.7	210.0	67.8	85.5	33.9	244.3
Rosuvastatin	745.6	404.7	114.1	120.0	47.6	351.9
Simvastatin	564.9	184.8	97.5	116.4	46.1	376.6
Atorvastatin	722.2	390.6	110.7	155.2	61.5	451.9

A. Topological Indices of drugs

Theorem: Let G_1 be the graph of Apixaban, the various topological indices of G_1 are given as follows:
i. $ABC(G_1) = 26.9032$
ii. $RA(G_1) = 16.4736$
iii. $S(G_1) = 17.3680$
iv. $GA(G_1) = 37.1038$
v. $M_1(G_1) = 186$
vi. $M_2(G_1) = 226$
vii. $H(G_1) = 16$
viii. $HM(G_1) = 936$
ix. $F(G_1) = 484$

Proof: Let G_1 be the graph of Apixaban. Let $E_(p,q))$ denote the edges which connects the vertices of degrees d_p and d_q. The edge set of G_1 has the partition as shown in Table II.

i. By using definition 2.1. and Table 2 we get,

$$ABC(G_1) = 1\sqrt{\tfrac{1+2-2}{1\times 2}} + 4\sqrt{\tfrac{1+3-2}{1\times 3}} + 8\sqrt{\tfrac{2+2-2}{2\times 2}} + 15\sqrt{\tfrac{2+3-2}{2\times 3}} + 10\sqrt{\tfrac{3+3-2}{3\times 3}} = 26.9032 \tag{10}$$

TABLE II
PARTITION OF EDGES

$E[d_p, d_q]$	$E_{(1,2)}$	$E_{(1,3)}$	$E_{(2,2)}$	$E_{(2,3)}$	$E_{(3,3)}$
No. of edges	1	4	8	15	10

ii. By using definition 2.2. and Table 2 we get,

$$RA(G_1) = 1\sqrt{\tfrac{1}{1\times2}} + 4\sqrt{\tfrac{1}{1\times3}} + 8\sqrt{\tfrac{1}{2\times2}} + 15\sqrt{\tfrac{1}{2\times3}} + 10\sqrt{\tfrac{1}{3\times3}} = 16.4736 \quad (11)$$

iii. By using definition 2.3. and Table 2 we get,

$$S(G_1) = 1\sqrt{\tfrac{1}{1+2}} + 4\sqrt{\tfrac{1}{1+3}} + 8\sqrt{\tfrac{1}{2+2}} + 15\sqrt{\tfrac{1}{2+3}} + 10\sqrt{\tfrac{1}{3+3}} = 17.3680 \quad (12)$$

iv. By using definition 2.4. and Table 2 we get,

$$GA(G_1) = 2\tfrac{\sqrt{1\times2}}{1+2} + 8\tfrac{\sqrt{1\times3}}{1+3} + 16\tfrac{\sqrt{2\times2}}{2+2} + 30\tfrac{\sqrt{2\times3}}{2+3} + 20\tfrac{\sqrt{3\times3}}{3+3} = 37.1038 \quad (13)$$

v. By using definition 2.5. and Table 2 we get,

$$M_1(G_1) = 1(1+2) + 4(1+3) + 8(2+2) + +15(2+3) + 10(3+3) = 186. \quad (14)$$

vi. By using definition 2.5. and Table 2 we get,

$$M_2(G_1) = 1(1\times2) + 4(1\times3) + 8(2\times2) + +15(2\times3) + 10(3\times3) = 226. \quad (15)$$

vii. By using definition 2.6. and Table 2 we get,

$$H(G_1) = 1\tfrac{2}{1+2} + 4\tfrac{2}{1+3} + 8\tfrac{2}{2+2} + +15\tfrac{2}{2+3} + 10\tfrac{2}{3+3} = 16. \quad (16)$$

viii. By using definition 2.7. and Table 2 we get,

$$HM(G_1) = 1(1+2)^2 + 4(1+3)^2 + 8(2+2)^2 + 15(2+3)^2 + 10(3+3)^2 = 936. \quad (17)$$

ix. By using definition 2.8. and Table 2 we get,

$$F(G_1) = 1(1^2+2^2) + 4(1^2+3^2) + 8(2^2+2^2) + + 15(2^2+3^2) + 10(3^2+3^2) = 484. \quad (18)$$

Similarly, the topological indices of the remaining drugs are computed and the results are displayed in the Table III.

B. Regression Models

Regression models are utilised to correlate some topological indices with the various drugs used to treat stroke. The most basic statistical technique for figuring out the relationship between a dependent and an independent variable is the linear regression model. This model is a best suit for the people who are working in pharmaceutical industry to reveal the risk factors associated with diseases by identifying the relationship between the topological indices such as ABC index, Randic index, etc and dependent ones, such as boiling point, flash point, etc. The linear regression model is verified by the equation given as

$$P = C + b(TI) \quad (19)$$

TABLE III
TOPOLOGICAL INDICES OF DRUGS IN TREATMENT OF STROKE

Medicine	$ABC(G)$	$RA(G)$	$S(G)$	$GA(G)$	$M_1(G)$	$M_2(G)$	$H(G)$	$HM(G)$	$F(G)$
Apixaban	26.9032	16.4736	17.3680	37.1038	186	226	16	936	484
Betrixaban	24.4958	15.2781	15.7212	32.7955	162	187	14.6333	790	416
Rivaroxaban	22.8628	14.0080	14.6967	31.1408	154	181	13.5667	756	394
Edoxaban	28.9167	17.6003	18.2882	38.4837	194	226	16.8	958	506
Warfarin	17.8726	11.0754	11.5272	24.3025	120	142	10.7	592	308
Clopidogrel	16.28	10.2027	10.6435	22.4930	110	131	9.9333	542	280
Rosuvastatin	25.1297	15.2896	15.5218	32.0351	166	189	14.2524	830	452
Simvastatin	23.2688	14.1014	14.5464	30.4822	158	185	13.3190	800	430
Atorvastatin	31.6239	19.6508	20.3297	42.6049	210	245	18.9	1028	538

where P is the physical property of drugs used in the treatment of stroke, TI is the topological index, b is the regression coefficient and C is a constant. The data is calculated using SPSS software. The degree-based topological indices that can be defined using (19) have the following linear regression models:

1) Atom bond connectivity index Regression Models:
Boiling Point = $139.936 + 21.320[ABC(G)]$
Flash Point = $-51.282 + 15.582[ABC(G)]$
Enthalpy of Vaporization = $31.125 + 2.893[ABC(G)]$
Molar refractivity = $5.327 + 4.638[ABC(G)]$
Polarizability = $2.137 + 1.838[ABC(G)]$
Molar Volume = $26.318 + 12.768[ABC(G)]$

2) Randic index Regression Models: $RA(G)$: Boiling Point = $146.942 + 34.187[RA(G)]$
Flash Point = $-51.434 + 25.353[RA(G)]$
Enthalpy of Vaporization = $32.437 + 4.613[RA(G)]$
Molar refractivity = $3.817 + 7.642[RA(G)]$
Polarizability = $1.540 + 3.028[RA(G)]$
Molar Volume = $23.315 + 20.962[RA(G)]$

3) Sum Connectivity index Regression Models: $S(G)$:
Boiling Point = $141.703 + 33.286[S(G)]$
Flash Point = $-57.126 + 24.805[S(G)]$
Enthalpy of Vaporization = $32.439 + 4.444[S(G)]$
Molar refractivity = $4.020 + 7.356[S(G)]$
Polarizability = $1.620 + 2.915[S(G)]$
Molar Volume = $27.685 + 19.928[S(G)]$

4) Geometric-Arithmetic index Regression Models: $GA(G)$: Boiling Point = $139.864 + 15.878[GA(G)]$
Flash Point = $-59.681 + 11.870[GA(G)]$
Enthalpy of Vaporization = $32.775 + 2.102[GA(G)]$
Molar refractivity = $4.739 + 3.477[GA(G)]$
Polarizability = $1.905 + 1.378[GA(G)]$
Molar Volume = $32.999 + 9.316[GA(G)]$

5) First Zagreb index Regression Models: $M_1(G)$:
Boiling Point = $132.041 + 3.216[M_1(G)]$
Flash Point = $-54.756 + 2.336[M_1(G)]$
Enthalpy of Vaporization = $30.392 + 0.434[M_1(G)]$
Molar refractivity = $5.248 + 0.691[M_1(G)]$
Polarizability = $2.107 + 0.274[M_1(G)]$
Molar Volume = $29.059 + 1.884[M_1(G)]$

6) Second Zagreb index Regression Models: $M_2(G)$:
Boiling Point = $134.890 + 2.718[M_2(G)]$
Flash Point = $-54.070 + 1.982[M_2(G)]$
Enthalpy of Vaporization = $31.654 + 0.362[M_2(G)]$
Molar refractivity = $6.624 + 0.582[M_2(G)]$
Polarizability =$2.654 + 0.231[M_2(G)]$
Molar Volume = $38.536 + 1.557[M_2(G)]$

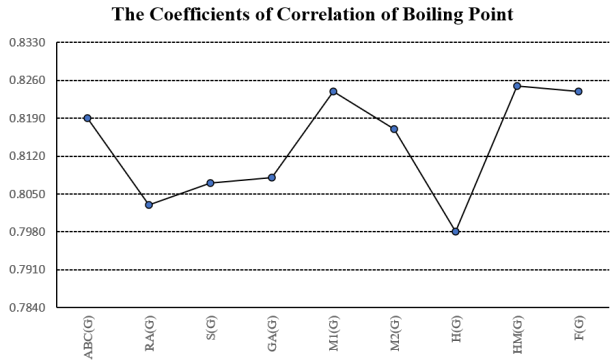
7) Harmonic index Regression Models: $H(G)$: Boiling Point = $147.146 + 35.633[H(G)]$
Flash Point = $-56.305 + 26.789[H(G)]$
Enthalpy of Vaporization = $33.409 + 4.740[H(G)]$
Molar refractivity = $3.571 + 7.992[H(G)]$
Polarizability = $1.443 + 3.167[H(G)]$
Molar Volume = $27.178 + 21.603[H(G)]$

8) Hyper-Zagreb index Regression Models: $HM(G)$:
Boiling Point = $132.327 + 0.647[HM(G)]$
Flash Point = $-48.444 + 0.462[HM(G)]$
Enthalpy of Vaporization = $29.912 + 0.088[HM(G)]$
Molar refractivity = $6.314 + 0.138[HM(G)]$
Polarizability = $2.531 + 0.055[HM(G)]$
Molar Volume = $30.631 + 0.378[HM(G)]$

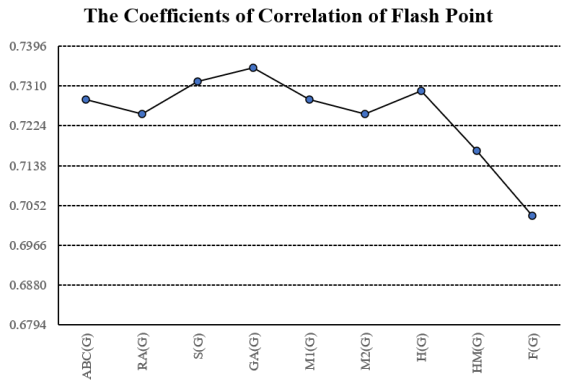
9) Forgotten index Regression Models: $F(G)$: Boiling Point = $139.429 + 1.212[F(G)]$
Flash Point = $-36.894 + 0.850[F(G)]$
Enthalpy of Vaporization = $29.668 + 0.168[F(G)]$
Molar refractivity = $7.833 + 0.259[F(G)]$
Polarizability = $3.133 + 0.103[F(G)]$
Molar Volume = $28.693 + 0.723[F(G)]$

TABLE IV
COEFFICIENT OF CORRELATION BETWEEN THE PHYSICOCHEMICAL PROPERTIES AND TI'S OF DRUGS

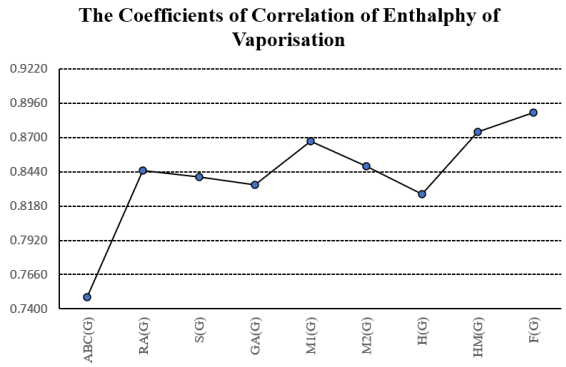
TI	BP	FP	EV	MR	PY	MV
$ABC(G)$	0.819	0.728	0.749	0.98	0.986	0.909
$RA(G)$	0.803	0.725	0.845	0.989	0.989	0.908
$S(G)$	0.807	0.732	0.840	0.983	0.983	0.892
$GA(G)$	0.808	0.735	0.834	0.975	0.975	0.875
$M_1(G)$	0.824	0.728	0.867	0.978	0.978	0.893
$M_2(G)$	0.817	0.725	0.848	0.961	0.961	0.861
$H(G)$	0.798	0.730	0.827	0.983	0.983	0.890
$HM(G)$	0.825	0.717	0.874	0.969	0.969	0.889
$F(G)$	0.824	0.703	0.889	0.969	0.969	0.907



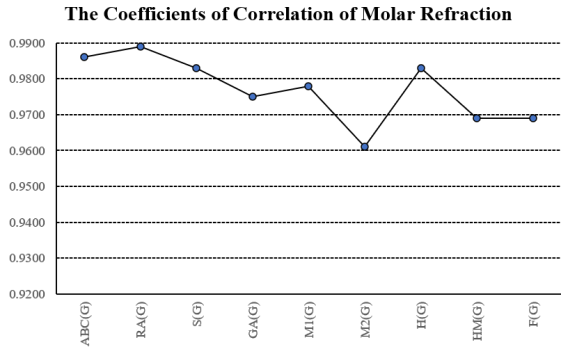
(j) The Coefficients of Correlation of Boiling Point



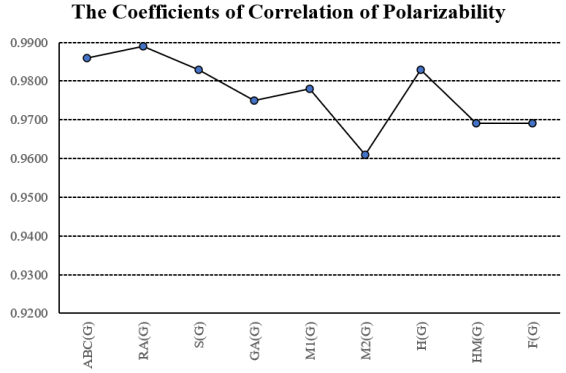
(k) The Coefficients of Correlation of Flash Point



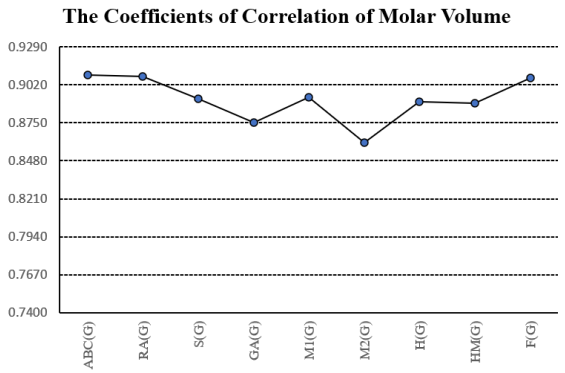
(l) The Coefficients of Correlation of Enthalphy of Vaporisation



(m) The Coefficients of Correlation of Molar Refraction



(n) The Coefficients of Correlation of Polarizability



(o) The Coefficients of Correlation of Molar Volume

Fig. 2. The Coefficients of Correlation of Physicochemical properties with Topological Indices

C. Statistical indicators for the linear QSPR model of the topological indices

The ABC index, Randic index, Sum Connectivity index, Geometric - Arithmetic index, First and Second Zagreb indices, harmonic index, hyper-Zagreb index, and Forgotten index are the statistical indicators for the linear QSPR model of the indices that are provided in the following tables.

TABLE V
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $ABC(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	139.936	21.320	0.819	0.670	10.165	0.024	Significant
Flash point	7	-51.282	15.582	0.728	0.530	5.637	0.064	Significant
Enthalpy of vaporization	7	31.125	2.893	0.749	0.699	14.946	0.012	Significant
Molar refraction	9	5.327	4.638	0.986	0.972	240.550	¡0.001	Significant
Polarizability	9	2.137	1.838	0.986	0.972	245.159	¡0.001	Significant
Molar volume	9	26.318	12.768	0.909	0.827	33.387	¡0.001	Significant

TABLE VI
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $RA(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	146.942	34.187	0.803	0.645	9.100	0.030	Significant
Flash point	7	-51.434	25.353	0.725	0.525	5.534	0.065	Significant
Enthalpy of vaporization	7	32.437	4.613	0.845	0.714	12.463	0.017	Significant
Molar refraction	9	3.817	7.642	0.989	0.977	299.367	¡0.001	Significant
Polarizability	9	1.540	3.028	0.989	0.978	305.470	¡0.001	Significant
Molar volume	9	23.315	20.962	0.908	0.825	33.037	¡0.001	Significant

TABLE VII
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $S(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	141.703	33.286	0.807	0.652	9.360	0.028	Significant
Flash point	7	-57.126	24.805	0.732	0.536	5.771	0.061	Significant
Enthalpy of vaporization	7	32.439	4.444	0.840	0.706	11.987	0.018	Significant
Molar refraction	9	4.020	7.356	0.983	0.966	198.227	¡0.001	Significant
Polarizability	9	1.620	2.915	0.983	0.966	200.966	¡0.001	Significant
Molar volume	9	27.685	19.928	0.892	0.796	27.272	0.001	Significant

TABLE VIII
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $GA(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	139.864	15.878	0.808	0.654	9.433	0.028	Significant
Flash point	7	-59.681	11.870	0.735	0.541	5.884	0.060	Significant
Enthalpy of vaporization	7	32.775	2.102	0.834	0.695	11.407	0.020	Significant
Molar refraction	9	4.739	3.477	0.975	0.951	135.366	¡0.001	Significant
Polarizability	9	1.905	1.378	0.975	0.951	136.660	¡0.001	Significant
Molar volume	9	32.999	9.316	0.875	0.766	22.935	0.002	Significant

TABLE IX
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $M_1(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	132.041	3.216	0.824	0.678	10.552	0.023	Significant
Flash point	7	-54.756	2.336	0.728	0.530	5.634	0.064	Significant
Enthalpy of vaporization	7	30.392	0.434	0.867	0.751	15.084	0.012	Significant
Molar refraction	9	5.248	0.691	0.978	0.956	152.180	¡0.001	Significant
Polarizability	9	2.107	0.274	0.978	0.956	153.817	¡0.001	Significant
Molar volume	9	29.059	1.884	0.893	0.798	27.619	0.001	Significant

TABLE X
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $M_2(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	134.890	2.718	0.817	0.667	10.035	0.025	Significant
Flash point	7	-54.070	1.982	0.725	0.525	5.529	0.065	Significant
Enthalpy of vaporization	7	31.654	0.362	0.848	0.720	12.850	0.016	Significant
Molar refraction	9	6.624	0.582	0.961	0.923	83.519	¡0.001	Significant
Polarizability	9	2.654	0.231	0.961	0.923	83.948	¡0.001	Significant
Molar volume	9	38.536	1.557	0.861	0.741	20.029	0.003	Significant

TABLE XI
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $H(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	147.146	35.633	0.798	0.637	8.756	0.032	Significant
Flash point	7	-56.305	26.789	0.730	0.532	5.694	0.063	Significant
Enthalpy of vaporization	7	33.409	4.740	0.827	0.684	10.823	0.022	Significant
Molar refraction	9	3.571	7.992	0.983	0.965	195.295	¡0.001	Significant
Polarizability	9	1.443	3.167	0.983	0.966	197.726	¡0.001	Significant
Molar volume	9	27.178	21.603	0.890	0.792	26.604	0.001	Significant

TABLE XII
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $HM(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	132.327	0.647	0.825	0.680	10.645	0.022	Significant
Flash point	7	-48.444	0.462	0.717	0.514	5.285	0.070	Significant
Enthalpy of vaporization	7	29.912	0.088	0.874	0.765	16.243	0.010	Significant
Molar refraction	9	6.314	0.138	0.969	0.939	108.559	¡0.001	Significant
Polarizability	9	2.531	0.055	0.969	0.940	109.266	¡0.001	Significant
Molar volume	9	30.631	0.378	0.889	0.791	26.472	0.001	Significant

D. Standard error of the estimate

The standard error of the estimate is a measure of the standard deviation of the errors in a regression model.

TABLE XIII
STATISTICAL INDICATORS FOR THE LINEAR QSPR MODEL OF $F(G)$

Physical Property	N	C	b	ρ	ρ^2	F	p	**Indicator**
Boiling point	7	139.429	1.212	0.824	0.679	10.595	0.023	Significant
Flash point	7	-36.894	0.850	0.703	0.495	4.894	0.078	Significant
Enthalpy of vaporization	7	29.668	0.168	0.889	0.791	18.912	0.007	Significant
Molar refraction	9	7.833	0.259	0.969	0.939	108.027	¡0.001	Significant
Polarizability	9	3.133	0.103	0.969	0.940	108.720	¡0.001	Significant
Molar volume	9	28.693	0.723	0.907	0.823	32.574	¡0.001	Significant

The standard error of the sample mean depends on both the standard deviation and the sample size. The standard error is most useful in calculating confidence intervals and determining statistical significance. It measures the amount of accuracy of predictions made around computed regression line and is mentioned in Table XIV.

TABLE XIV
STANDARD ERROR OF THE ESTIMATE

Topological Index	**SE of BP**	**SE of FP**	**SE of EV**	**SE of MR**	**SE of PY**	**SE of MV**
$ABC(G)$	85.75006	84.15955	9.59518	4.13286	1.62229	30.53982
$RA(G)$	88.93102	84.57358	10.25469	3.71502	1.45734	30.67282
$S(G)$	88.12040	83.63782	10.39714	4.53904	1.78636	33.15233
$GA(G)$	87.89940	83.19884	10.57937	5.44977	2.14930	35.47277
$M_1(G)$	84.67717	84.17238	9.56215	5.15391	2.03142	32.98593
$M_2(G)$	86.12130	84.59139	10.14273	6.83467	2.70128	37.33079
$H(G)$	90.03599	83.93484	10.77301	4.57182	1.80044	33.48040
$HM(G)$	84.42465	85.59046	9.29751	6.04896	2.38912	33.54638
$F(G)$	84.56032	87.26610	8.76336	6.06292	2.39475	30.85169

IV. CONCLUSION

The topological indices of the drugs have been calculated and is related to the linear QSPR model for the drugs used in the treatment of stroke through this investigation. The development of a novel drug is based on the properties of its structures and they are attainable with the use of topological indices and QSPR modelling. The purpose of computing these 9 topological indices is that no single topological index is found yet that can be efficient for all physical properties of the drugs. The goal of the work is to gather information about the structure's topology using topological indices in the shortest amount of time and at the lowest possible cost. Table (4) includes the correlation coefficient between topological indices and physicochemical parameters. It is observed that Molar refractivity and Polarizability have good correlation with $RA(G)$ where $\rho = 0.989$. Also, MV has the highest correlation with $ABC(G)$ with $\rho = 0.909$. It is known that, if the value of $\rho \leq 0.1$, then it indicates the significance of the result. The correlation coefficient is more than 0.7 in all these models, causing the value of ρ to be less than 0.1, showing the significance of the findings.

V. IMPLICATIONS OF THE STUDY

By using the values of these topological indices, this study offers direction to chemists and those employed in the pharmaceutical business in the design of novel medications. It is also feasible to try different combinations of these medications based on the range of topological indices.

VI. FUTURE STUDIES

Similar to this work, research for various chemical structures is feasible, and conclusions may be drawn by figuring out how the physical characteristics of the medications and the values of the topological indices relate to one another. A multidisciplinary project can be adopted by researchers from various disciplines for a better result.

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