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Research Article

Topological Indices of Drugs Used in Rheumatoid Arthritis Treatment and Its QSPR Modeling

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A topological index is a molecular descriptor derived from the molecular structure of a chemical substance. These indices can be used to analyze mathematical values and predict various physical properties of drugs. This article discusses tofacitinib, leflunomide, upadacinib, baricitinib, filgotinib, methotrexate, and other drugs used to treat rheumatoid arthritis, and the goal of the QSPR study is to calculate the relationship between the properties under investigation (e.g., boiling point, polarity, and molar volume) and molecular descriptors. Topological indices (TIs) were imposed on said drugs to calculate the correlation with physicochemical properties in this course.

1. Introduction

Topological indices (TIs) are numeric descriptors obtained through a molecular graph in order to fully examine the drugs and are widely used in the investigation and prediction of many drugs' physicochemical properties. There are various types of polynomials and topological indices that are extensively calculated, represent the chemical structure, and play an important role in chemical graph theory. Among these families, degree-based topological indices are extremely important and play an important role in chemical graph theory. Among these techniques, the QSPR approach correlates a molecule's biological activity with its physicochemical properties using a variety of descriptors, and it is used on drugs used in the treatment of rheumatoid arthritis. The QSPR approach has recently been used to develop models to predict drug properties. QSAR is a drug design source that specifies a relationship between molecules' physicochemical properties and biological activities that affect drug response. The augmented Zagreb index in [1] is the best predictor of alkane heat of formation. The ABC index and Randic index are useful for calculating drug bioactivity. These properties are being researched because of their substantial impact on bioactivity and drug transit in the human body. In this paper, we compute TIs for drugs used in the treatment of rheumatoid arthritis. Similarly, anti-RA drugs are chemical compounds with carefully defined topological indices and deliberate QSPR analysis. Using linear regression is highly correlated with the characteristic of RA drugs based on mathematical observation. Rheumatoid arthritis (RA) is a chronic, autoimmune, and inflammatory joint disease. Estimates from North America and Northern Europe range from 20 to 50 cases per 100,000 people. The prevalence of RA in developing countries is unknown [2–5]. Scientists are constantly looking for the latest ways to treat people suffering from RA. One method is to create new drugs. Drug detection remains difficult to work because it is expensive, needs much time, and is much more difficult in some situations. This disease will cause functional impairment, premature mortality, joint erosions, and decreased

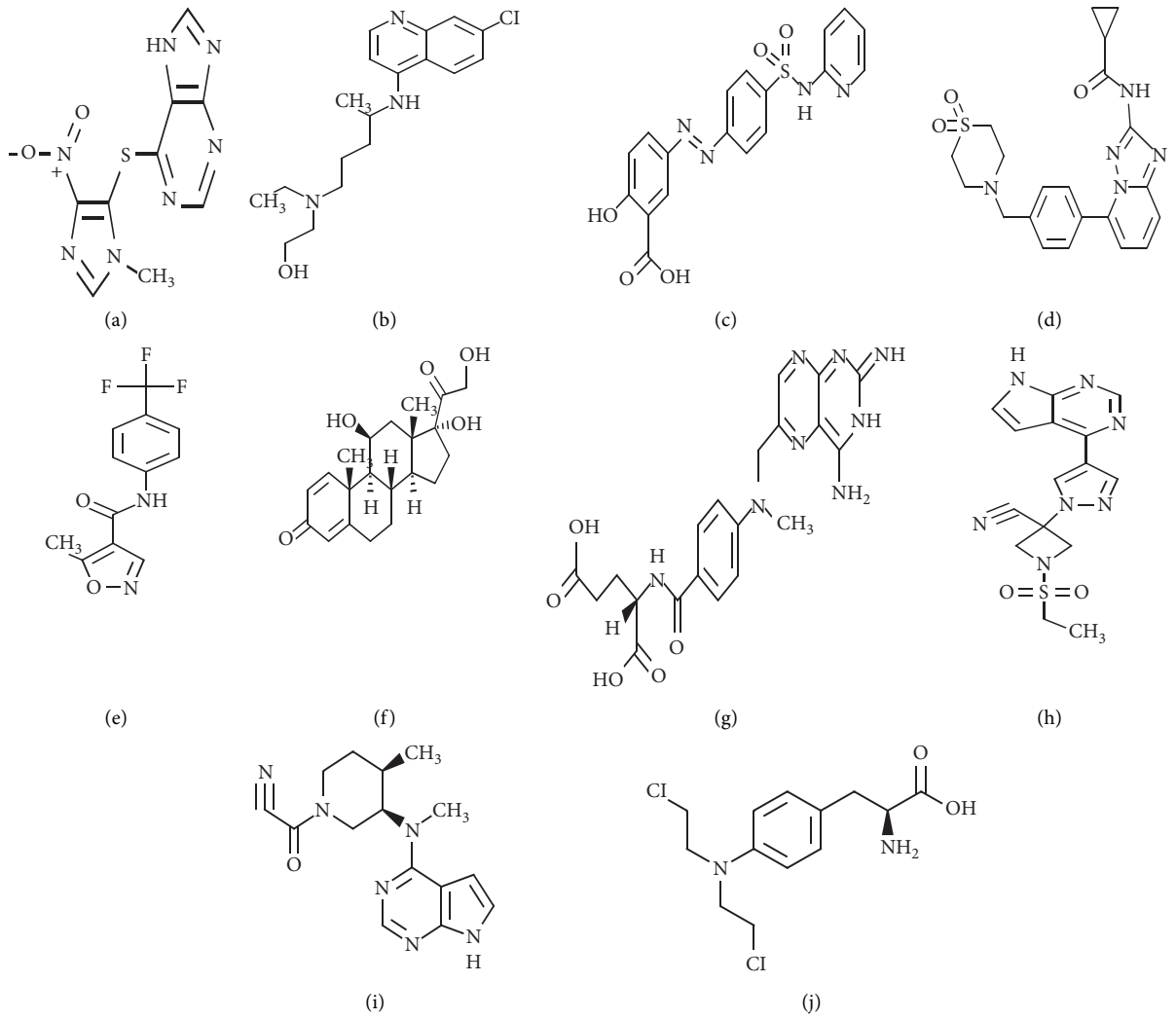

Figure 1: Structure of drugs. (a) Azathioprine. (b) Hydroxycholoquine. (c) Sulfasalazine. (d) Filgothinib. (e) Leflunomide. (f) Prednisolone. (g) Methotrexate. (h) Baricitinib. (i) Tofacitinib. (j) Upadacitinib.

quality of life over time. This necessitates prompt screening, diagnosis, and treatment which helps in order to control the disease. This work investigates ten drugs medicines tofacitinib, leflunomide, upadacinib, baricitinib, filgotinib, methotrexate, prednisolone, sulfasalazine, azathioprine, and hydroxychloroquine that are secure and reliable remedies which are the need of the community well-being. Figure 1 depicts the chemical structure of said drugs.

2. Material and Method

Elements denote vertices in drug structure, and the corresponding bonds of atoms are referred to as edges. Graph $G(V, E)$ is simple, finite, and connected, whereas V and E in the chemical graph are referred to as vertex and edge set, respectively. The degree of a vertex in a graph G is denoted by d_u and is the number of vertices adjacent to it. Degree-based topological indices used are given as follows.

Definition 1. The *ABC* indices [6] is

$$ABC(G) = \sum_{uv \in E(G)} \sqrt{\frac{d_{u+}d_v - 2}{d_u d_v}}. \tag{1}$$

Definition 2. The Randic index $RA(G)$ [7] is

$$RA(G) = \sum_{uv \in E(G)} \sqrt{\frac{1}{d_u d_v}}. \tag{2}$$

Definition 3. The sum connectivity index [8] is

$$S(G) = \sum_{uv \in E(G)} \sqrt{\frac{1}{d_u + d_v}}. \tag{3}$$

Definition 4. The GA index [9] of a molecular graph G is

Table 1: The TI values of drugs.

Name of drug	$F(G)$	$ABC(G)$	$RA(G)$	$S(G)$	$M2(G)$	$GA(G)$	$M1(G)$	$H(G)$	$HM(G)$
Azatjoprine	410	20.54	12.00	12.45	174	26.38	144	11.15	758
Hydroxycholoqoine	916	37.92	21.41	21.59	353	45.07	278	18.88	1622
Sulfasatazne	626	31.29	18.94	19.34	273	20.60	220	17.60	1172
Filgotinib	1050	42.41	23.52	24.38	426	52.26	322	21.08	1902
Leflumomide	454	21.65	12.60	12.82	184	26.80	152	11.43	822
Predisolane	1176	42.46	23.59	24.12	469	51.53	336	20.81	2114
Methotrexate	906	42.19	24.90	25.29	373	52.88	300	22.71	1652
Bracitinib	824	34.12	19.21	19.84	334	42.32	256	17.33	1492
Tofacitinib	828	33.80	18.94	19.35	325	40.88	252	16.85	1478
Upadacinib	902	36.66	16.33	20.98	361	44.74	276	18.14	1624

$$GA(G) = \sum_{uv \in E(G)} \frac{2\sqrt{d_u d_v}}{d_u + d_v}. \tag{4}$$

Definition 5. The first and second Zagreb indices [10] are

$$\begin{aligned} M1(G) &= \sum_{uv \in E(G)} (d_u + d_v), \\ M2(G) &= \sum_{uv \in E(G)} (d_u d_v). \end{aligned} \tag{5}$$

Definition 6. The harmonic index [11] is

$$H(G) = \sum_{uv \in E(G)} \frac{2}{d_u + d_v}. \tag{6}$$

Definition 7. The hyper Zagreb index [12] is

$$HM(G) = \sum_{uv \in E(G)} (d_u + d_v)^2. \tag{7}$$

Definition 8. The forgotten index [13] is

$$F(G) = \sum_{uv \in E(G)} \left[(d_u)^2 + (d_v)^2 \right]. \tag{8}$$

Physical property values are obtained from Chemspider. The data in Table1 show that they are normally distributed. As a result, the linear regression model is best to examine and use in this analysis. We recommend that the reader read the following research articles [1, 14–32] for more information on TIs.

The molecular formula of methotrexate is $C_{20}H_{22}N_8O_5$. A wide range of cancers and rheumatoid arthritis are treated with methotrexate. Lymphocytic leukemia is also treated with this medicine. The molecular formula of baricitinib is $C_{16}H_{17}N_7O_2S$. Baricitinib is used in severe rheumatoid arthritis. The molecular formula of tofacitinib is $C_{16}H_{20}N_6O$. The molecular formula of Upadacitinib is $C_{17}H_{19}F_3N_6O$. Upadacitinib is used to cure moderate to severe RA and slow down disease progression. The molecular formula of azathioprine is $C_9H_7N_7O_2S$. Azathioprine has a long duration of action. The molecular formula of hydroxychloroquine is $C_{18}H_{26}ClN_3O$ and is helpful in RA treatment. The molecular formula of sulfasatazne is $C_{18}H_{14}N_4O_5S$. Ulcerative colitis and rheumatoid arthritis are treated with the anti-inflammatory drug sulfasalazine. The molecular formula of filgotinib is $C_{21}H_{23}N_5O_3S$. Methotrexate is used alone or in combination with filgotinib to treat rheumatoid arthritis. More than 50% of patients suffering from RA are incapable to accomplish the availability of numerous cures including disease-modifying anti-rheumatic drugs (DMARS) like methotrexate. The molecular formula of leflunomide is $C_{12}H_9F_3N_2O_2$. The use of this medical treatment retards the progression of structural damage and improves physical function.

3. Results and Discussion

TIs are carried out on RA drugs in this section. The relationship between QSPR analysis and TIs shows that properties under discussion are highly correlated as regards of the disease's physicochemical properties. Tofacitinib, leflunomide, upadacinib, baricitinib, filgotinib, methotrexate, neoral, prednisolone, sulfasalazine, azathioprine, and hydroxychloroquine are the ten medications used in the RA analysis. Figure 1 depicts the drug structure. For drug research, we use regression analysis calculations.

3.1. Regression Model. In this article, the tenacity of QSPR modelling is tested using a drug computable structure analysis of nine topological indices. Table 2 shows the four physical properties of ten RA medications: polarity, molar volume (MV), refractive index (R), and complexity. We run the regression analysis for the drugs, and the validated linear regression model is as follows:

$$P = A + b(TI). \tag{9}$$

P denotes physicochemical property. Letters A, TI, and b represent the topological index, constant, and regression coefficient, respectively. The software packages Statistix, Python, and MATLAB are helpful in determining the results. The physiochemical properties of nine TIs of RA drugs are investigated using a linear QSPR model. For the aforementioned calculation, equation (1) is appropriate.

Table 2: Correlation coefficients.

Topological index	Correlation coefficient of			
	Polarity	Refractive index	Molar volume	Complexity
ABC (*G*)	0.872	0.872	0.898	0.709
RA (*G*)	0.909	0.909	0.914	0.729
S (*G*)	0.933	0.933	0.908	0.735
GA (*G*)	0.907	0.907	0.897	0.761
M1 (*G*)	0.818	0.818	0.867	0.709
M2 (*G*)	0.754	0.754	0.83	0.707
HM (*G*)	0.728	0.727	0.82	0.677
F (*G*)	0.722	0.721	0.821	0.649
H (*G*)	0.931	0.93	0.909	0.755

Theorem 1. *Let G_1 be a graph of Sulfasatazne. The TIs of G_1 are*

$$\begin{aligned} ABC(G_1) &= 31.29,\\ RA(G_1) &= 18.95,\\ S(G_1) &= 19.34,\\ GA(G_1) &= 40.60,\\ M1(G_1) &= 220,\\ M2(G_1) &= 273,\\ F(G_1) &= 626,\\ H(G_1) &= 17.60,\\ HM(G_1) &= 1172. \end{aligned} \tag{10}$$

Proof. Let G_1 be the graph of sulfasatazne, with edge set E and $E_{m,n}$ partition of G_1 vertices with degrees m and n. $|E_{1,2}| = 2$,, ,$|E_{1,3}| = 13$,$|E_{1,4}| = 2$,$|E_{2,3}| = 6$,$|E_{3,3}| = 18$, and $|E_{3,4}| = 2$.

(i) Using Definition 1 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} ABC(G_1) &= 2\sqrt{\frac{1+2-2}{1\times 2}} + 13\sqrt{\frac{1+3-2}{1\times 3}}\\ &\quad + 2\sqrt{\frac{1+4-2}{1\times 4}} + 6\sqrt{\frac{2+3-2}{2\times 3}}\\ &\quad + 18\sqrt{\frac{3+3-2}{3\times 3}} + 2\sqrt{\frac{3+4-2}{3\times 4}} = 31.29. \end{aligned} \tag{11}$$

(ii) Using Definition 2 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} RA(G_1) &= 2\sqrt{\frac{1}{1\times 2}} + 13\sqrt{\frac{1}{1\times 3}} + 2\sqrt{\frac{1}{1\times 4}} + 6\sqrt{\frac{1}{2\times 3}}\\ &\quad + 18\sqrt{\frac{1}{3\times 3}} + 2\sqrt{\frac{1}{3\times 4}} = 18.95. \end{aligned} \tag{12}$$

(iii) Using Definition 3 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} S(G_1) &= 2\sqrt{\frac{1}{1+2}} + 13\sqrt{\frac{1}{1+3}} + 2\sqrt{\frac{1}{1+4}} + 6\sqrt{\frac{1}{2+3}}\\ &\quad + 18\sqrt{\frac{1}{3+3}} + 2\sqrt{\frac{1}{3+4}} = 19.34. \end{aligned} \tag{13}$$

(iv) Using Definition 4 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} GA(G_1) &= \frac{2\sqrt{1\times 2}}{1+2} + \frac{13\sqrt{1\times 3}}{1+3} + \frac{2\sqrt{1\times 4}}{1+4} + \frac{6\sqrt{2\times 3}}{2+3}\\ &\quad + \frac{18\sqrt{3\times 3}}{3+3} + \frac{2\sqrt{3\times 4}}{3+4} = 40.60. \end{aligned} \tag{14}$$

(v) Using Definition 5 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} M1(G_1) &= 2(1+2) + 13(1+3) + 2(1+4) + 6(2+3)\\ &\quad + 18(3+3) + 2(3+4) = 220. \end{aligned} \tag{15}$$

(iii) Using Definition 5 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} M2(G_1) &= 2(1\times 2) + 13(1\times 3) + 2(1\times 4) + 6(2\times 3)\\ &\quad + 18(3\times 3) + 2(3\times 4) = 273. \end{aligned} \tag{16}$$

(vi) Using Definition 6 and the partitions $E_{m,n}$, we obtain

$$\begin{aligned} H(G_1) &= 2\left(\frac{1}{1+2}\right) + 13\left(\frac{1}{1+3}\right) + 2\left(\frac{1}{1+4}\right) + 6\left(\frac{1}{2+3}\right)\\ &\quad + 18\left(\frac{1}{3+3}\right) + 2\left(\frac{1}{3+4}\right) = 17.60. \end{aligned} \tag{17}$$

(vii) Using Definition 7 and the partitions $E_{m,n}$, we obtain

$$HM(G_1) = 2(1+2)^2 + 13(1+3)^2 + 2(1+4)^2 + 6(2+3)^2 + 18(2+4)^2 + 2(3+4)^2 = 1172. \tag{18}$$

(viii) Using Definition 8 and the partitions $E_{m,n}$, we obtain

$$F(G_1) = 2(1+4) + 13(1+9) + 2(1+16) + 6(4+9) + 18(4+16) + 2(9+9) + 2(9+16) = 626. \tag{19}$$

□

Theorem 2. *Let G_2 be graph of Upadacinib. The TIs of G_2 are as follows:*

$$\begin{aligned} ABC(G_2) &= 36.66, \\ RA(G_2) &= 20.33, \\ S(G_2) &= 20.98, \\ GA(G_2) &= 44.74, \\ M1(G_2) &= 276, \\ M2(G_2) &= 361, \\ F(G_2) &= 902, \\ H(G_2) &= 18.14, \\ HM(G_2) &= 1624. \end{aligned} \tag{20}$$

Proof. Let G_2 be graph of upadacinib having edge set E and $E_{m,n}$ partition of G_2 vertices with degrees m and n. With $|E_{1,3}| = 7, |E_{1,4}| = 16, |E_{2,3}| = 4, |E_{3,3}| = 12, |E_{3,4}| = 4,$ and $|E_{4,4}| = 6$.

(i) Using Definition 1 and the partitions $E_{m,n}$, we obtain

$$ABC(G_2) = 7\sqrt{\frac{1+3-2}{1\times 3}} + 16\sqrt{\frac{1+4-2}{1\times 4}} + 4\sqrt{\frac{2+3-2}{2\times 3}} + 12\sqrt{\frac{3+3-2}{3\times 3}} + 4\sqrt{\frac{3+4-2}{3\times 4}} + 6\sqrt{\frac{1}{4\times 4}} = 36.66. \tag{21}$$

(ii) Using Definition 2 and the partitions $E_{m,n}$, we obtain

$$RA(G_2) = 7\sqrt{\frac{1}{1\times 3}} + 16\sqrt{\frac{1}{1\times 4}} + 4\sqrt{\frac{1}{2\times 3}} + 12\sqrt{\frac{1}{3\times 3}} + 4\sqrt{\frac{1}{3\times 4}} + 6\sqrt{\frac{1}{4\times 4}} = 20.33. \tag{22}$$

(iii) Using Definition 3 and the partitions $E_{m,n}$, we obtain

$$S(G_2) = 7\sqrt{\frac{1}{1+3}} + 16\sqrt{\frac{1}{1+4}} + 4\sqrt{\frac{1}{2+3}} + 12\sqrt{\frac{1}{3+3}} + 4\sqrt{\frac{1}{3+4}} + 6\sqrt{\frac{1}{4+4}} = 20.98. \tag{23}$$

(iv) Using Definition 4 and the partitions $E_{m,n}$, we obtain

$$GA(G_2) = \frac{7\sqrt{1\times 3}}{1+3} + \frac{16\sqrt{1\times 4}}{1+4} + \frac{4\sqrt{2\times 3}}{2+3} + \frac{12\sqrt{3\times 3}}{3+3} + \frac{4\sqrt{3\times 4}}{3+4} + \frac{6\sqrt{4\times 4}}{4+4} = 44.74. \tag{24}$$

(v) Using Definition 5 and the partitions $E_{m,n}$, we obtain

$$M1(G_2) = \sum_{uv\in E(G_1)} (s_{u+}s_v) = 7(1+3) + 16(1+4) + 4(2+3) + 12(3+3) + 4(3+4) + 6(4+4) = 276. \tag{25}$$

(vi) Using Definition 5 and the partitions $E_{m,n}$, we obtain

$$M2(G_2) = 7(1\times 3) + 16(1\times 4) + 4(2\times 3) + 12(3\times 3) + 4(3\times 4) + 6(4\times 4) = 361. \tag{26}$$

(vii) Using Definition 5 and the partitions $E_{m,n}$, we obtain

$$H(G_2) = 7\left(\frac{1}{1+3}\right) + 16\left(\frac{1}{1+4}\right) + 4\left(\frac{1}{2+3}\right) + 12\left(\frac{1}{3+3}\right) + 4\left(\frac{1}{3+4}\right) + 6\left(\frac{1}{4+4}\right) = 18.14. \tag{27}$$

(viii) Using Definition 6 and the partitions $E_{m,n}$, we obtain

$$HM(G_2) = 3(1+2)^2 + 3(1+3)^2 + 6(1+4)^2 + 4(2+3)^2 + 5(2+4)^2 + 3(3+3)^2 + 1(3+4)^2 + 4(4+4)^2 = 1624. \tag{28}$$

(ix) Using Definition 7 and the partitions $E_{m,n}$, we obtain

$$F(G_2) = 3(1+4) + 4(1+9) + 6(1+16) + 4(4+9) + 5(4+16) + 3(9+9) + 1(9+16) + 4(16+16) = 902. \tag{29}$$

Table 3: RA immune system drugs physical properties.

Name of drug	Molar volume (cm^3)	Polarity (m^3mol^{-1})	Refractive index (m^3mol^{-1})	Complexity	Boiling point (°C)	D (cm^3)	Enthalpy (°C)
Azatjoprine	145.40	27.30	68.90	354.00	555.80	145.40	368.50
Hydroxycholoqoine	285.40	39.20	99.00	331.00	516.70	285.40	266.30
Sulfasatazne	267.70	40.60	102.40	657.00	689.30	267.70	370.70
Filgotinib	281.10	45.30	114.30	715.00		281.10	
Leflumomide	194.10	24.20	61.00	327.00	289.30	194.10	129.00
Predisolane	274.70	37.90	95.50	724.00	570.60	274.70	314.80
Methotrexate	275.70	47.20	119.00	704.00		275.70	
Bracitinib	238.10	38.90	98.20	678.00	707.00	238.10	
Tofacitinib	241.00	34.70	87.50		585.80	241.00	308.10
Upadacinib	243.00	36.30	91.60	561.00	189.00	243.00	

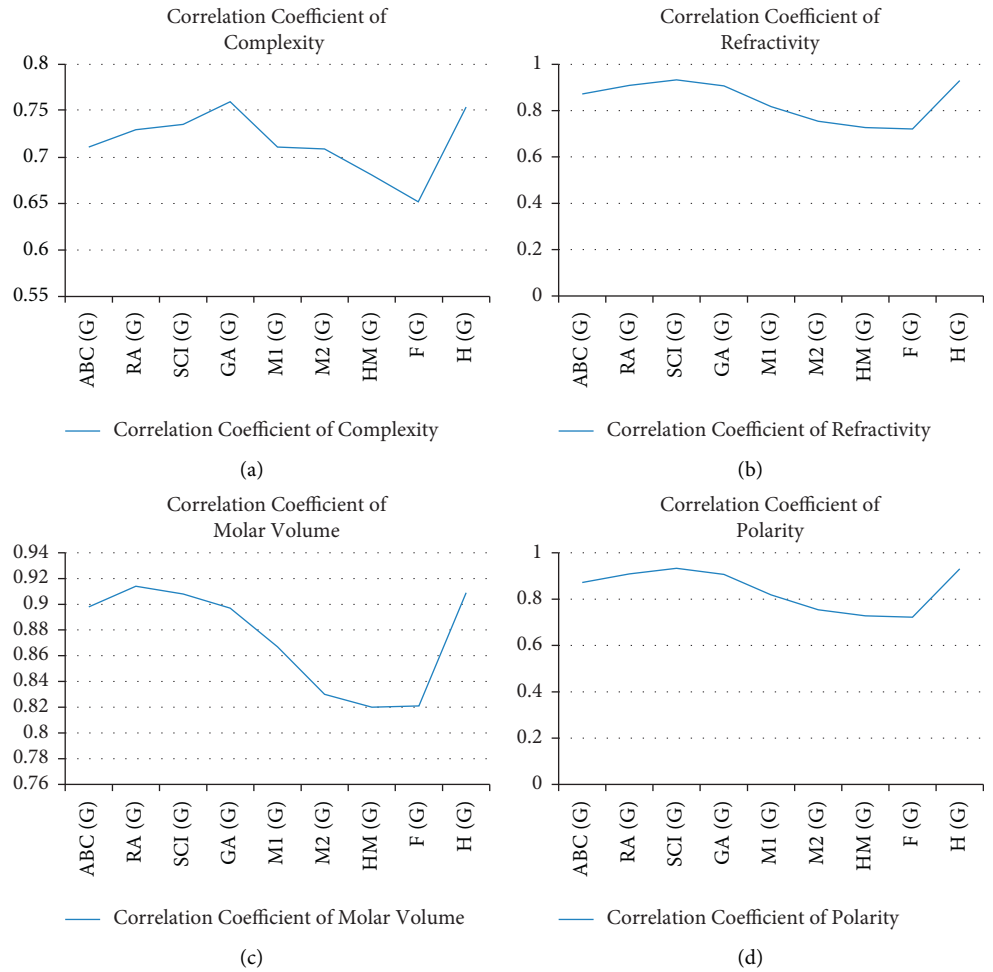

Figure 2: Physicochemical properties and TIs.

The remaining drugs topological indices can be calculated using the same procedure as applied in Theorem 2, Theorem 1, and Definitions 1–8. Table 1 contains values for each drug.

Applying (1), we calculated the linear models for all TIs written as follows:

(1) Regression models for $ABC\ (G)$ are as follows:

$$\text{Polarity} = 10.364 + 0.781\ [ABC\ (G)]$$
$$\text{Refractive index} = 26.174 + 1.970\ [ABC\ (G)]$$
$$\text{Complexity} = 57.998 + 14.646\ [ABC\ (G)]$$
$$\text{MV} = 72.605 + 5.014\ [ABC\ (G)]$$

(2) Regression models for $RA\ (G)]$ are as follows:

$$\text{Polarity} = 8.149 + 1.483\ [RA\ (G)]$$
$$\text{Refractive index} = 20.601 + 3.739\ [RA\ (G)]$$
$$\text{Complexity} = 21.629 + 27.488\ [RA\ (G)]$$
$$\text{MV} = 62.686 + 9.01\ [RA\ (G)]$$

Table 4: QSPR model of ABC (G).

Physiochemical property	N	A	b	r	r^2	F	p	Indicator
Polarity	10	10.364	0.8	0.781	0.872	25.479	0.001	Significant
Refractive index	10	26.174	1.970	0.782	0.760	25.364	0.001	Significant
Molar volume	10	72.605	5.014	0.898	0.806	33.157	0.000	Significant
Complexity	9	57.998	14.646	0.709	0.502	7.064	0.033	Significant

Table 5: QSPR model of RA (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	8.149	1.483	0.909	0.827	38.129	0.000	Significant
Refractive index	10	20.601	3.739	0.909	0.825	37.829	0.000	Significant
Molar volume	10	62.686	9.301	0.914	0.835	40.511	0.000	Significant
Complexity	9	21.629	27.488	0.729	0.532	7.959	0.026	Significant

Table 6: QSPR model of S (G).

Physiochemical property	N	A	B	R	r^2	F	p	Indicator
Polarity	10	6.574	1.536	0.933	0.871	53.979	0.000	Significant
Refractive index	10	16.611	3.874	0.933	0.870	53.595	0.000	Significant
Molar volume	10	58.881	9.330	0.908	0.825	37.724	0.000	Significant
Complexity	9	2.985	27.955	0.735	0.540	8.233	0.024	Significant

Table 7: QSPR model of GA (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	8.253	0.683	0.907	0.823	37.292	0.000	Significant
Refractive index	10	20.859	1.721	0.907	0.822	37.020	0.000	Significant
Molar volume	10	66.421	4.207	0.897	0.804	32.770	0.000	Significant
Complexity	9	−1.382	13.231	0.761	0.580	9.650	0.017	Significant

Table 8: QSPR model of $M1$ (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	14.306	0.090	0.818	0.669	16.188	0.004	Significant
Refractive index	10	36.118	0.227	0.818	0.668	16.130	0.004	Significant
Molar volume	10	93.419	0.597	0.867	0.753	24.328	0.001	Significant
Complexity	9	104.000	1.804	0.709	0.503	7.073	0.032	Significant

(3) Regression models for sum S (G) are as follows:

$$\text{Polarity} = 6.574 + 1.536\ [S\ (G)]$$
$$\text{Refractive index} = 16.611 + 3.874\ [S\ (G)]$$
$$\text{Complexity} = 2.985 + 27.955\ [S\ (G)]$$
$$\text{MV} = 58.881 + 9.330\ [S\ (G)]$$

(4) Regression models for GA (G) are as follows:

$$\text{Polarity} = 8.253 + 0.683\ [GA\ (G)]$$
$$\text{Refractive index} = 20.859 + 1.721\ [GA\ (G)]$$
$$\text{Complexity} = -1.382 + 13.231\ [GA\ (G)]$$
$$\text{MV} = 66.421 + 4.207\ [GA\ (G)]$$

(5) Regression models for $M1$ (G) are as follows:

$$\text{Polarity} = 14.306 + 0.090\ [M1\ (G)]$$
$$\text{Refractive index} = 36.118 + 0.227\ [M1\ (G)]$$
$$\text{Complexity} = 104.000 + 1.804\ [M1\ (G)]$$
$$\text{MV} = 93.419 + 0.597\ [M1\ (G)]$$

(6) Regression models for HM (G) are as follows:

$$\text{Polarity} = 19.733 + 0.023\ [HM\ (G)]$$
$$\text{Refractive index} = 49.809 + 0.030\ [HM\ (G)]$$
$$\text{Complexity} = 187.760 + 0.255\ [HM\ (G)]$$
$$\text{MV} = 122.143 + 0.084\ [HM\ (G)]$$

(7) Regression models for $M2$ (G) are as follows:

$$\text{Polarity} = 18.556 + 0.057\ [M2\ (G)]$$
$$\text{Refractive index} = 46.844 + 0.143\ [M2\ (G)]$$
$$\text{Complexity} = 158.746 + 1.228\ [M2\ (G)]$$
$$\text{MV} = 116.976 + 0.390\ [M2\ (G)]$$

(8) Regression models for F (G) are as follows:

$$\text{Polarity} = 19.971 + 0.021\ [F\ (G)]$$

Table 9: QSPR model of $M2$ (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	18.556	0.057	0.754	0.569	10.570	0.012	Significant
Refractive index	10	46.844	0.143	0.754	0.568	10.530	0.012	Significant
Molar volume	10	116.976	0.390	0.830	0.688	17.669	0.003	Significant
Complexity	9	158.746	1.228	0.707	0.500	6.988	0.033	Significant

Table 10: QSPR model of HM (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	19.733	0.023	0.728	0.530	9.009	0.017	Significant
Refractive index	10	49.809	0.030	0.727	0.529	8.979	0.017	Significant
Molar volume	10	122.143	0.084	0.820	0.672	16.394	0.004	Significant
Complexity	9	187.760	0.255	0.677	0.458	5.909	0.045	Significant

Table 11: QSPR model of F (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	19.971	0.021	0.722	0.521	8.695	0.018	Significant
Refractive index	10	50.401	0.054	0.721	0.520	8.673	0.019	Significant
Molar volume	10	122.674	0.151	0.821	0.673	16.491	0.004	Significant
Complexity	9	205.354	0.442	0.649	0.421	5.097	0.059	Significant

Table 12: QSPR model of H (G).

Physiochemical property	N	A	b	R	r^2	F	p	Indicator
Polarity	10	6.602	1.34	0.931	0.867	52.134	0.000	Significant
Refractive index	10	16.703	4.373	0.930	0.866	54.565	0.000	Significant
Molar volume	10	58.494	10.565	0.909	0.826	38.035	0.000	Significant
Complexity	9	−14.384	32.514	0.755	0.569	9.257	0.019	Significant

Table 13: SE of estimate.

Topological index	Std. error of the estimate for			
	Polarity	Refractive index	Complexity	Molar volume
ABC (G)	3.70109	9.35334	131.75522	20.82685
RA (G)	3.15306	7.98066	127.75416	19.18354
S (G)	2.72018	6.88389	126.59865	19.75959
GA (G)	3.18207	8.05203	121.09125	20.92556
$M1$ (G)	4.35128	10.9985	131.71405	23.49938
$M2$ (G)	4.96955	12.55069	132.1127	26.37188
HM (G)	54.9258	13.11165	137.52096	27.05248
F (G)	5.24112	13.23146	142.0393	26.9989
H (G)	2.76158	7.00027	122.54701	19.69254

Refractive index = 50.401 + 0.054 $[F\ (G)]$
Complexity = 205.354 + 0.442 $[F\ (G)]$
MV = 122.674 + 0.151 $[F\ (G)]$

(9) Regression models for H (G) are as follows:

Polarity = 6.602 + 1.34 $[H\ (G)]$
Refractive index = 16.703 + 4.373 $[H\ (G)]$
Complexity = −14.384 + 32.514 $[H\ (G)]$
MV = 58.494 + 10.565 $[H\ (G)]$ □

3.2. Quantitative Structure Analysis and Comparison between Topological Indices and Correlation Coefficient of Physicochemical Properties. Table 3 consists of physicochemical properties related to ten rheumatoid arthritis drugs. Their TIs values, on the other hand, are recorded in Table 1 and derived with the aid of their molecular structure. Table 2 shows the correlation coefficients among physicochemical properties and TIs. Figure 2 depicts a graph of the correlation coefficient of aforementioned drugs.

Table 14: Comparison of actual and computed values for refractive index from regression models.

Name of drug	Refractivity of drug ($m^3 \cdot mol^{-1}$)	Refractivity from regression model for								
		ABC (*G*)	*R* (*G*)	*S* (*G*)	*GA* (*G*)	*M*1 (*G*)	*M*2 (*G*)	*F* (*G*)	*H* (*G*)	*HM* (*G*)
Azathioprine	68.9 ± 0.5	66.6378	65.469	64.8423	66.25898	68.806	71.726	72.541	65.46195	72.549
Hydroxycholoquine	99 ± 0.3	100.8764	100.653	100.2507	98.42447	99.224	97.323	99.865	99.26524	98.469
Sulfasalazine	102.4 ± 0.5	87.8153	91.41766	91.53416	90.7316	86.058	85.883	84.205	93.6678	84.969
Filgotinib	114.3 ± 0.5	109.7217	108.5423	111.0591	110.7985	109.212	107.762	107.101	108.8858	106.869
Leflunomide	61 ± 0.3	68.8245	67.7124	66.27568	66.9818	70.622	73.156	74.917	66.68639	74.469
Prednisolone	95 ± 0.4	109.8202	108.804	110.0519	109.5421	112.39	113.911	113.905	107.7051	113.229
Methotrexate	119 ± 0.3	109.2883	113.7021	114.5845	111.8655	104.218	100.183	99.325	116.0138	99.369
Baricitinib	98.2 ± 0.5	93.3904	92.42719	93.47116	93.69172	94.23	94.606	94.897	92.48709	94.569
Tofacitinib	87.5 ± 0.3	92.76	91.41766	91.5729	91.21348	93.322	93.319	95.113	90.38805	94.149
Upadacitinib	91.6 ± 0.5	98.3942	96.61487	97.88752	97.85654	98.77	98.467	99.109	96.02922	98.529

Table 15: Comparision of actual and computed values for polarity from regression models.

Name of drug	Polarity of drug (cm^3)	Polarity computed from regression model for								
		ABC (*G*)	*R* (*G*)	*S* (*G*)	*GA* (*G*)	*M*1 (*G*)	*M*2 (*G*)	*F* (*G*)	*H* (*G*)	*HM* (*G*)
Azathioprine	27.3	26.40574	25.945	25.6972	26.27054	27.266	28.474	28.581	21.543	37.167
Hydroxycholoquine	39.2	39.97952	39.90003	39.7362	39.03581	39.326	38.677	39.207	31.9012	57.039
Sulfasalazine	40.6	34.80149	36.23702	36.2802	35.9828	34.106	34.117	33.117	30.186	46.689
Filgotinib	45.3	43.48621	43.02916	44.0217	43.94658	43.286	42.838	42.021	34.8492	63.479
Leflunomide	24.2	27.27265	26.8348	26.2655	26.5574	27.986	29.044	29.505	21.9182	38.639
Prednisolone	37.9	43.52526	43.13297	43.6223	43.44799	44.546	45.289	44.667	34.4874	68.355
Methotrexate	47.2	43.31439	45.0757	45.4194	44.37004	41.306	39.817	38.997	37.0334	57.729
Baricitinib	38.9	37.01172	36.63743	37.0482	37.15756	37.346	37.594	37.275	29.8242	54.049
Tofacitinib	34.7	36.7618	36.23702	36.2956	36.17404	36.986	37.081	37.359	29.181	53.727
Upadacitinib	36.3	38.99546	38.29839	38.7993	38.81042	39.146	39.133	38.913	30.9096	57.085

Table 16: Comparison of actual and computed values for complexity from regression models.

Name of drug	Complexity of drug	Complexity computed from regression model for								
		ABC (*G*)	*R* (*G*)	*S* (*G*)	*GA* (*G*)	*M*1 (*G*)	*M*2 (*G*)	*F* (*G*)	*H* (*G*)	*HM* (*G*)
Azathioprine	354	358.8268	351.485	351.0248	347.6518	363.776	372.418	386.574	348.1471	381.05
Hydroxycholoquine	331	613.3743	610.1471	606.5335	594.9392	605.512	592.23	610.226	599.4803	601.37
Sulfasalazine	657	516.2713	542.2517	543.6347	535.7966	500.88	493.99	482.046	557.8624	486.62
Filgotinib	715	679.1349	668.1468	684.5279	690.0701	684.888	681.874	669.454	671.0111	672.77
Leflunomide	327	375.0839	367.9778	361.3681	353.2088	378.208	384.698	406.022	357.251	397.37
Prednisolone	724	679.8672	670.0709	677.2596	680.4114	710.144	734.678	725.146	662.2323	726.83
Methotrexate	704	675.9127	706.0802	709.967	698.2733	645.2	616.79	605.806	724.0089	609.02
Baricitinib	678	557.7195	549.6735	557.6122	558.5539	565.824	568.898	569.562	549.0836	568.22
Tofacitinib		553.0328	542.2517	543.9143	539.5013	558.608	557.846	571.33	533.4769	564.65
Upadacitinib	561	594.9204	580.46	589.4809	590.5729	601.904	602.054	604.038	575.42	601.88

Table 17: Comparison of actual and computed values for molar volume from regression models.

Name of drug	Molar volume molar volume of drug (cm^3)	Molar volume from regression model for								
		ABC (*G*)	*R* (*G*)	*S* (*G*)	*GA* (*G*)	*M*1 (*G*)	*M*2 (*G*)	*F* (*G*)	*H* (*G*)	*HM* (*G*)
Azathioprine	145.4 ± 7.0	175.5926	174.298	175.0395	177.4017	179.387	184.836	184.584	77.1802	185.815
Hydroxycholoquine	285.4 ± 3.0	262.7359	261.8204	260.3157	256.0305	259.385	254.646	260.99	95.94864	258.391
Sulfasalazine	267.7 ± 3.0	229.4931	238.8469	239.3232	237.2252	224.759	223.446	217.2	92.8408	220.591
Filgotinib	281.1 ± 7.0	285.2487	281.4455	286.3464	286.2788	285.653	283.116	281.224	101.2902	281.911
Leflunomide	194.1 ± 3.0	181.1581	179.8786	178.4916	179.1686	184.163	188.736	191.228	77.86004	191.191
Prednisolone	274.7 ± 5.0	285.4994	282.0966	283.9206	283.2077	294.011	299.886	300.25	100.6347	299.719
Methotrexate	275.7 ± 3.0	284.1457	294.2809	294.8367	288.8872	272.519	262.446	259.48	105.2479	260.911
Baricitinib	238.1 ± 7.0	243.6827	241.3582	243.9882	244.4612	246.251	247.236	247.098	92.18524	247.471
Tofacitinib	241 ± 3.0	242.0782	238.8469	239.4165	238.4032	243.863	243.726	247.702	91.0198	246.295
Upadacitinib	243 ± 7.0	256.4182	251.7753	254.6244	254.6422	258.191	257.766	258.876	94.15192	258.559

3.3. Calculation of Statistical Parameters. In this section, QSPR modelling is imposed in such a way to determine a relationship between the physicochemical properties of rheumatoid arthritis drugs that are tofacitinib, leflunomide, upadacinib, baricitinib, filgotinib, methotrexate, neoral, prednisolone, sulfasalazine, azathioprine, and hydroxychloroquine. TIs, b, r, and N are independent variables, regression model constants, correlation coefficients, and sample size. Such type of test is useful for comparing and deciding on model improvements. It is worth noting that the r value is larger than 0.6 and the p value is less than 0.05. As a result, it determines that all properties are significant as given in Tables 4–12.

3.4. Standard Error of Estimate (SE) and Comparision. A standard error of estimate is the measure of variation for an observation calculated around the computed regression line. This assesses degree of correctness of predictions computed around regression line as shown in Table 13. Tables 14–17 compare experimental and theoretical calculated values of the models.

4. Conclusions

According to the statistical parameters used in linear QSPR models and topological indices, the S (G) index has a high correlation with molar volume ($r = 0.908$). The H index has the highest correlated complexity value, $r = 0.755$. The S (G) index represents the highest correlation coefficient of the refractive index, $r = 0.933$. The maximum correlated value of flash polarity $r = 0.933$ is provided by harmonic S (G). TIs had no relationship with density, boiling point, or polar surface area.

In this paper, we calculated TIs and linked it with the linear QSPR model for rheumatoid arthritis drugs. The findings will aid in the development of new drugs and preventive measures for numerous disease in the pharmaceutical manufacturing industries. The correlation coefficient contributes significantly to the range of TIs for drugs. These findings are eye-opening of pharmaceutical researchers who work on medication science, and they provide a method to estimate and predict physicochemical properties for new RA treatment drugs to cure other specific autoimmune diseases.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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