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QSPR-Based Statistical Study of Uphill Topological Indices for Anti-Tuberculosis Drugs

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ABSTRACT: Tuberculosis (TB) is still one of the most infectious and lethal diseases in the world, with mortality rates surpassing even HIV/AIDS. In response to the urgent need for more effective treatments, the pharmaceutical industry is increasingly turning to Quantitative Structure-Property Relationship (QSPR) models. These models play an important role in drug discovery and development because they allow for the design of compounds with specific biological activities. Researchers hope to use QSPR techniques to better control the spread of tuberculosis and combat emerging syndromes and genetic disorders. This study aims to develop a QSPR model for tuberculosis medications utilizing nine physicochemical properties through Uphill degree-based topological indices. Our research and predictive models have the potential to make a significant contribution to the development of novel tuberculosis treatments.

Key Words: Molecular graph, topological indices, uphill degree, uphill topological indices.

Contents

1. Introduction

The branch of graph theory that deals with the molecular structure of chemical compounds and their related properties is chemical graph theory (CGT). CGT plays crucial roles in various areas of scientific disciplines, especially in chemistry, materials science, pharmaceutical science, and cheminformatics. CGT involves the representation of molecules as simple graphs, where chemical bonds between atoms are shown as edges, and atoms themselves are shown as vertices. A molecular descriptor, also known as a topological index (TI), is a numerical invariant/value associated with a chemical graph in some specific manner that is being used to characterize its structure and topology. In CGT, these indices are essentially useful, as they provide a means to quantify and compare the structural features of distinct chemical compounds. The relationship between TIs and CGT lies in the use of TIs as numerical descriptors to characterize the structural and physical features of several compounds [1,2,3].

Tuberculosis (TB) is an airborne disease caused by Mycobacterium tuberculosis. It primarily affects the lungs but can spread to other organs. TB affects approximately one-third of the global population [4]. While most infections remain dormant, some develop into active disease, particularly among individuals with HIV [5]. TB disproportionately affects men and remains one of the leading causes of death worldwide.

Although antibiotics are usually adequate, surgery may be required in cases of drug resistance or severe pulmonary complications. Since the Cape Town Declaration in 2000, interest in anti-TB drugs has increased, leading to the development of safer and faster therapies [6]. Medications commonly prescribed include Bedaquiline, Ciprofloxacin, Clofazimine, Delamanid, Ethambutol, Ethionamide, Levofloxacin, Moxifloxacin, Ofloxacin, p-Aminosalicylic acid, and Pyrazinamide [7]. Despite available treatments,

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there is currently no vaccine that provides effective protection against tuberculosis [8]. The disease is unlikely to be eradicated without improved vaccines [9].

Dwivedi et al. [10] investigated anti-tuberculosis drug molecules using QSAR. Shenoy et al. [11] created a QSPR model for tuberculosis drugs with Revan topological indices. Abdullahi et al. [12] used QSAR modelling to predict the biological activity of new drugs against Mycobacterium tuberculosis (TB). Kovalishyn et al. [13] used machine learning to develop effective QSAR models for tuberculosis treatment. Naz et al. [14] investigated the physicochemical properties of six tuberculosis (TB) drugs using extended topological indices. Arockiaraj [15] et al. developed a QSPR model between a few distance-based topological indices and their physicochemical properties. More work on QSPR, QSAR models, and related topics on topological indices in chemical graph theory can be found in [16,17,18,19,20,21]. Motivated by these, we use uphill topological indices to conduct QSPR analysis for several medicines used in tuberculosis treatment. Topological invariants serve as mathematical functions that assign real-number values to a set of graphs, effectively characterizing the underlying graph topology. These invariants find crucial applications in the analysis of Quantitative Structure-Property Relationships (QSPR) and Quantitative Structure-Activity Relationships (QSAR) within the realm of chemical research.

Definition 1.1 [22] For any graph, $G = (V, E)$. A path $u - v$ is a sequence of vertices in G, initialing with u and terminal at v, such that sequential vertices are adjacent, and no vertex is repeated. A path $P = v_1, v_2, \ldots, v_{k+1}$ in G is an uphill path if for every i, $1 \leq I \leq k$, $deg(v_i) \leq deg(v_{i+1})$.

For any vertices u and v in G, if there is an uphill path from u to v we say that u is uphill adjacent to v.

Definition 1.2 [23] A vertex v is uphill dominates a vertex u in a graph G if v uphill adjacent to u. An uphill neighborhood of the vertex v is denoted by $N_{up}(v)$ and described as: $N_{up}(v) = \{u :$ v uphill adjacent to u$\}$. The uphill degree of the vertex v, denoted by $d_{up}(v)$, is the number of vertices which v uphill adjacent them, that means $d_{up}(v) = |N_{up}(v)|$.

The uphill closed neighborhood, $N_{up}[v]$, of the vertex v is the uphill open neighborhood of v together with the vertex v.

Saleh et al. in [23] defined novel graph indices based on the uphill degree of the vertices, termed as uphill Zagreb topological indices. Some of the uphill topological indices are given in Table 1.

Motivated by their work, we define some novel uphill topological indices, as listed in Table 2.

2. Methods and Techniques

This paper employs uphill degree counting, vertex division based on uphill degree, and edge partitioning according to the uphill degree of end vertices. The topological indices presented in Table 1 and Table 2 are computed using uphill degree counting and the edge partitioning method. The correlation coefficients were computed using Python. The two-dimensional chemical structure of tuberculosis medications is referred to in PubChem [29].

3. Results and Interpretation

The study examines the physicochemical properties of eleven tuberculosis drugs: Bedaquiline, Ciprofloxacin, Clofazimine, Delamanid, Ethambutol, Ethionamide, Levofloxacin, Moxifloxacin, Ofloxacin, p-Aminosalicyclic acid, and Pyrazinamide. Table 3 shows the properties of tuberculosis drugs, including boiling point (BP), flash point (FP), enthalpy of vaporization (EV), molar refractivity (MR), polarizability (P), molar volume (MV), molecular weight (MW), heavy atom count (HAC), and complexity (CO). These values are obtained from ChemSpider and PubChem [29,30]. Figures 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11 illustrates the molecular structure of these drugs.

Index	Notation	Expression
First uphill Zagreb Index [23]	$UPM_1(G)$	$\sum_{v\in V(G)} (d_{up}(v))^2$
Second uphill Zagreb Index [23]	$UPM_2(G)$	$\sum_{u,v\in E(G)} d_{up}(u)d_{up}(v)$
Forgotten uphill Zagreb Index [23]	$UPF(G)$	$\sum_{v\in V(G)} (d_{up}(v))^3$
Uphill Inverse Sum Index [24]	$UPI(G)$	$\sum_{u,v\in E(G)} \frac{d_{up}(u)\cdot d_{up}(v)}{d_{up}(u)+d_{up}(v)}$
Uphill Sombor Index [25]	$UPSO(G)$	$\sum_{u,v\in E(G)} \sqrt{d_{up}(u)^2 + d_{up}(v)^2}$
Uphill Harmonic Index [26]	$UPH(G)$	$\sum_{u,v\in E(G)} \frac{2}{d_{up}(u)+d_{up}(v)}$
Uphill Geometric Arithmetic Index [28]	UPGA(G)	$\sum_{u,v\in E(G)} \frac{2\sqrt{d_{up}(u)\times d_{up}(v)}}{d_u(u)+d_{up}(v)}$
Uphill Nirmala Index [27]	$UPN(G)$	$\sum_{u,v\in E(G)} \sqrt{d_{up}(u) + d_{up}(v)}$

Table 1: Uphill Topological Indices

Index	Notation	Expression
First uphill Hyper Zagreb Index	$UPHM_1(G)$	$\sum_{u,v\in E(G)} (d_{up}(u) + d_{up}(v))^2$
Second uphill Hyper Zagreb Index	$UPHM_2(G)$	$\sum_{u,v\in E(G)} (d_{up}(u) \times d_{up}(v))^2$
Uphill Sum Connectivity Index	$UPSCI(G)$	$\sum_{u,v\in E(G)} \frac{1}{\sqrt{d_{up}(u)+d_{up}(v)}}$

Table 2: Newly defined Uphill Topological Indices

Table 3: Physicochemical Properties of Selected Drug Compounds

Compound	**BP**	**FP**	**EV**	**MR**	**PO**	**MV**	**MW**	**HAC**	**CO**
Bedaquiline	702.7	378.8	108	156.2	61.9	420.1	555.5	37	715
Ciprofloxacin	581.8	305.6	91.5	83.3	33	226.8	331.3	24	571
Clofazimine	566.9	296.7	85.1	136.2	54	366.1	473.4	33	829
Delamanid	653.7	349.1	96.3	127.7	50.6	368	534.5	38	795
Ethambutol	345.3	113.7	68.3	58.6	23.2	207	204.3	14	109
Ethionamide	247.9	103.7	46.5	49	19.4	142	166.3	11	147
Levofloxacin	571.5	299.4	90.0	91.1	36.1	244	361.4	26	634
Moxifloxacin	636.4	338.7	98.8	101.8	40.4	285	401.4	29	727
Ofloxacin	571.5	299.4	90.1	91.1	36.1	244	361.4	26	634

Table 4 displays the computation of the 11 topological indices of Bedaquiline, Ciprofloxacin, Clofazimine, Delamanid, Ethambutol, Ethionamide, Levofloxacin, Moxifloxacin, Ofloxacin, p-Aminosalicyclic acid, and Pyrazinamide molecules.

Table 4: Uphill Topological Indices of Selected Drug Compounds

Drugs	UPM_1	UPM_2	UPF	UPI	$UPSO$	UPH	$UPGA$	UPN	$UPHM_1$	$UPHM_2$	$UPSCI$
Bedaquiline	1024	912	7244	74.5789	258.4614	19.1928	29.4676	112.5068	3925	44420	17.7234
Ciprofloxacin	1042	984	7674	76.1554	235.4636	5.1792	26.0346	92.4266	4160	43364	8.1636
Clofazimine	954	847	7122	64.9686	240.4628	18.4592	23.7895	101.4404	3750	43559	16.3967
Delamanid	258	136	898	23.2333	135.3795	29.8667	20.0177	79.7707	782	1424	23.9399
Ethambutol	120	83	536	10.1667	44.1575	12.0667	6.7712	24.8872	390	1891	8.1525
Ethionamide	99	65	429	9.0833	39.5259	7.3	7.4398	22.3525	318	1297	6.0044
Levofloxacin	2912	2972	32562	138.3563	419.9995	4.7577	25.9644	128.2452	12262	349358	7.1945
Moxifloxacin	2819	2878	30397	142.6192	431.4111	4.9355	31.4843	137.9152	11868	311924	8.4629
Ofloxacin	2912	2972	32562	138.3563	419.9995	4.7577	25.9644	128.2452	12262	349358	7.1945
p-Aminosalicylic acid	106	69	420	10.8619	43.4019	5.919	7.7857	24.2018	334	929	5.3913
Pyrazinamide	190	161	1098	15.5476	51.993	3.5714	8.2853	24.0262	696	5265	3.7724

4. Regression Models

This study focuses on the following regression models.

1. Linear regression model

$$\mathcal{P} = a(TI) + b \tag{4.1}$$

2. Quadratic regression model

$$\mathcal{P} = c(TI)^2 + d(TI) + e \tag{4.2}$$

where $\mathcal{P}$ refers to the physicochemical property of the drug, TI denotes the topological index, a, c, d are regression coefficients, and b, e are constants specific to the model type.

4.1. Linear regression

The topological indices linear regression model is as follows:

1. First Uphill Zagreb Index $UPM_1(G)$

$$\begin{aligned}
BP &= 0.0757 \quad UPM_1(G) + 417.3084 \\
FP &= 0.0493 \quad UPM_1(G) + 197.7416 \\
EV &= 0.0095 \quad UPM_1(G) + 70.6291 \\
MR &= 0.0112 \quad UPM_1(G) + 75.1890 \\
PO &= 0.0044 \quad UPM_1(G) + 29.8019 \\
MV &= 0.0254 \quad UPM_1(G) + 216.1167 \\
MW &= 0.0482 \quad UPM_1(G) + 278.7544 \\
HAC &= 0.0037 \quad UPM_1(G) + 19.3189 \\
CO &= 0.1415 \quad UPM_1(G) + 334.1619
\end{aligned}$$

2. Second Uphill Zagreb Index $UPM_2(G)$

$$\begin{aligned}
BP &= 0.0689 \quad UPM_2(G) + 427.2300 \\
FP &= 0.0449 \quad UPM_2(G) + 204.1530 \\
EV &= 0.0087 \quad UPM_2(G) + 71.8303 \\
MR &= 0.0096 \quad UPM_2(G) + 77.2924 \\
PO &= 0.0038 \quad UPM_2(G) + 30.6356 \\
MV &= 0.0214 \quad UPM_2(G) + 221.3260 \\
MW &= 0.0421 \quad UPM_2(G) + 287.0212 \\
HAC &= 0.0032 \quad UPM_2(G) + 19.9102 \\
CO &= 0.1287 \quad UPM_2(G) + 352.8788
\end{aligned}$$

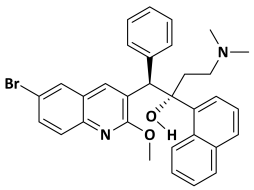

Figure 1: Bedaquiline

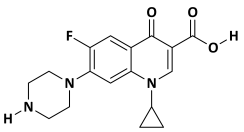

Figure 2: Ciprofloxacin

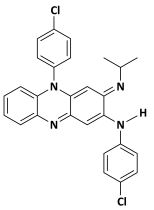

Figure 3: Clofazimine

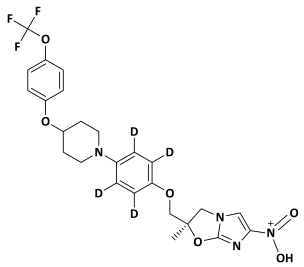

Figure 4: Delamanid

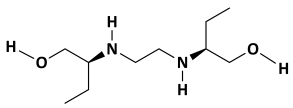

Figure 5: Ethambutol

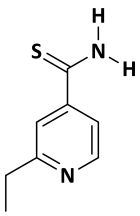

Figure 6: Ethionamide

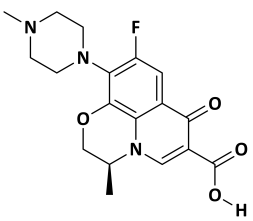

Figure 7: Levofloxacin

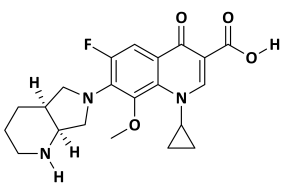

Figure 8: Moxifloxacin

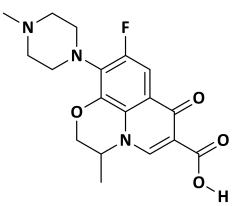

Figure 9: Ofloxacin

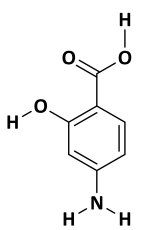

Figure 10: p-Aminosalicyclic acid

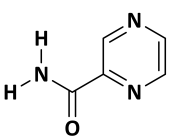

Figure 11: Pyrazinamide

3. Modified First Uphill Zagreb Index $UPF(G)$

$$\begin{aligned}
BP &= 0.0057 \quad UPF(G) + 440.4557 \\
FP &= 0.0037 \quad UPF(G) + 212.7317 \\
EV &= 0.0007 \quad UPF(G) + 73.4766 \\
MR &= 0.0007 \quad UPF(G) + 79.8603 \\
PO &= 0.0003 \quad UPF(G) + 31.6538 \\
MV &= 0.0016 \quad UPF(G) + 227.4637 \\
MW &= 0.0033 \quad UPF(G) + 296.7962 \\
HAC &= 0.0003 \quad UPF(G) + 20.6106 \\
CO &= 0.0107 \quad UPF(G) + 376.5217
\end{aligned}$$

4. Uphill Inverse Sum Index $UPI(G)$

$$\begin{aligned}
BP &= 1.9105 \quad UPI(G) + 380.6327 \\
FP &= 1.2425 \quad UPI(G) + 173.9727 \\
EV &= 0.2381 \quad UPI(G) + 66.1263 \\
MR &= 0.3197 \quad UPI(G) + 67.3793 \\
PO &= 0.1268 \quad UPI(G) + 26.7062 \\
MV &= 0.7477 \quad UPI(G) + 197.0064 \\
MW &= 1.3115 \quad UPI(G) + 249.3221 \\
HAC &= 0.0971 \quad UPI(G) + 17.2431 \\
CO &= 3.5164 \quad UPI(G) + 269.1538
\end{aligned}$$

5. Uphill Sombor Index $UPSO(G)$

$$\begin{aligned}
BP &= 0.7304 \quad UPSO(G) + 348.8178 \\
FP &= 0.4736 \quad UPSO(G) + 153.5798 \\
EV &= 0.0898 \quad UPSO(G) + 62.4242 \\
MR &= 0.1350 \quad UPSO(G) + 59.3661 \\
PO &= 0.0535 \quad UPSO(G) + 23.5307 \\
MV &= 0.3258 \quad UPSO(G) + 176.1404 \\
MW &= 0.5467 \quad UPSO(G) + 217.9353 \\
HAC &= 0.0399 \quad UPSO(G) + 15.0313 \\
CO &= 1.3646 \quad UPSO(G) + 206.3378
\end{aligned}$$

6. Uphill Harmonic Index $UPH(G)$

$$\begin{aligned}
BP &= 8.2337 \quad UPH(G) + 416.0580 \\
FP &= 4.8768 \quad UPH(G) + 202.0512 \\
EV &= 0.9000 \quad UPH(G) + 71.8732 \\
MR &= 3.2580 \quad UPH(G) + 53.4778 \\
PO &= 1.2902 \quad UPH(G) + 21.2120 \\
MV &= 9.3855 \quad UPH(G) + 145.8752 \\
MW &= 12.2992 \quad UPH(G) + 203.5426 \\
HAC &= 0.8249 \quad UPH(G) + 14.7547 \\
CO &= 16.3218 \quad UPH(G) + 322.0521
\end{aligned}$$

7. Uphill Geometric Arithmetic Index $UPGA(G)$

$$\begin{aligned}
BP &= 15.0630 \quad UPGA(G) + 211.2102 \\
FP &= 9.7528 \quad UPGA(G) + 64.6279 \\
EV &= 1.8220 \quad UPGA(G) + 46.0837 \\
MR &= 3.2622 \quad UPGA(G) + 24.6666 \\
PO &= 1.2931 \quad UPGA(G) + 9.7794 \\
MV &= 8.1745 \quad UPGA(G) + 86.5633 \\
MW &= 12.7436 \quad UPGA(G) + 86.4831 \\
HAC &= 0.9027 \quad UPGA(G) + 5.9742 \\
CO &= 27.2911 \quad UPGA(G) - 34.2841
\end{aligned}$$

8. Uphill Narumi Index $UPN(G)$

$$\begin{aligned}
BP &= 2.9711 \quad UPN(G) + 266.2768 \\
FP &= 1.9171 \quad UPN(G) + 100.8103 \\
EV &= 0.3596 \quad UPN(G) + 52.7292 \\
MR &= 0.6285 \quad UPN(G) + 37.7841 \\
PO &= 0.2491 \quad UPN(G) + 14.9788 \\
MV &= 1.5719 \quad UPN(G) + 119.6751 \\
MW &= 2.4844 \quad UPN(G) + 135.3935 \\
HAC &= 0.1776 \quad UPN(G) + 9.3099 \\
CO &= 5.5340 \quad UPN(G) + 53.4640
\end{aligned}$$

9. Uphill Hyper Zagreb Index $UPHM_1(G)$

$$\begin{aligned}
BP &= 0.0172 \quad UPHM_1(G) + 423.6012 \\
FP &= 0.0112 \quad UPHM_1(G) + 201.8032 \\
EV &= 0.0022 \quad UPHM_1(G) + 71.4001 \\
MR &= 0.0025 \quad UPHM_1(G) + 76.4897 \\
PO &= 0.0010 \quad UPHM_1(G) + 30.3175 \\
MV &= 0.0055 \quad UPHM_1(G) + 219.3258 \\
MW &= 0.0107 \quad UPHM_1(G) + 283.8714 \\
HAC &= 0.0008 \quad UPHM_1(G) + 19.6839 \\
CO &= 0.0322 \quad UPHM_1(G) + 345.6327
\end{aligned}$$

10. Second Uphill Hyper Zagreb Index $UPHM_2(G)$

$$\begin{aligned}
BP &= 0.0005 \quad UPHM_2(G) + 455.2389 \\
FP &= 0.0003 \quad UPHM_2(G) + 222.3348 \\
EV &= 0.0001 \quad UPHM_2(G) + 75.3046 \\
MR &= 0.0000 \quad UPHM_2(G) + 82.6541 \\
PO &= 0.0000 \quad UPHM_2(G) + 32.7615 \\
MV &= 0.0001 \quad UPHM_2(G) + 234.1054 \\
MW &= 0.0002 \quad UPHM_2(G) + 307.6152 \\
HAC &= 0.0000 \quad UPHM_2(G) + 21.3952 \\
CO &= 0.0009 \quad UPHM_2(G) + 403.9158
\end{aligned}$$

11. Uphill Sum Connectivity Index $UPSCI(G)$

$$
\begin{aligned}
BP &= 16.7549 \quad UPSCI(G) + 331.6923 \\
FP &= 10.3891 \quad UPSCI(G) + 147.3277 \\
EV &= 1.8882 \quad UPSCI(G) + 62.0714 \\
MR &= 5.4216 \quad UPSCI(G) + 32.4399 \\
PO &= 2.1476 \quad UPSCI(G) + 12.8748 \\
MV &= 15.0202 \quad UPSCI(G) + 91.3802 \\
MW &= 20.7553 \quad UPSCI(G) + 121.1755 \\
HAC &= 1.4150 \quad UPSCI(G) + 8.9962 \\
CO &= 32.2774 \quad UPSCI(G) + 164.3773
\end{aligned}
$$

Table 5: Linear regression model correlation coefficients between topological indices and drug physicochemical properties

TI	BP	FP	EV	MR	PO	MV	MW	HAC	CO
UPM_1	0.5585	0.5679	0.5724	0.3244	0.3247	0.2755	0.3710	0.4060	0.5668
UPM_2	0.5303	0.5397	0.5459	0.2904	0.2907	0.2422	0.3379	0.3737	0.5375
UPF	0.4850	0.4941	0.5006	0.2435	0.2438	0.1984	0.2953	0.3323	0.4960
UPI	0.6545	0.6645	0.6665	0.4304	0.4307	0.3763	0.4686	0.5002	0.6538
$UPSO$	0.7280	0.7369	0.7312	0.5287	0.5290	0.4769	0.5683	0.5987	0.7381
UPH	0.4355	0.4026	0.3889	0.6772	0.6768	0.7292	0.6785	0.6564	0.4685
$UPGA$	**0.9185**	**0.9283**	**0.9077**	**0.7817**	**0.7821**	0.7322	0.8105	0.8281	**0.9032**
UPN	0.8737	0.8800	0.8639	0.7263	0.7266	0.6790	0.7620	0.7857	0.8832
$UPHM_1$	0.5414	0.5508	0.5558	0.3045	0.3048	0.2560	0.3516	0.3873	0.5505
$UPHM_2$	0.4262	0.4348	0.4428	0.1821	0.1824	0.1412	0.2391	0.2771	0.4381
$UPSCI$	0.6562	0.6351	0.6041	0.8344	0.8342	**0.8641**	**0.8478**	**0.8337**	0.6860

Bolded values indicate the highest correlation coefficients in each category.

Table 5 displays the correlation coefficients obtained by the linear regression model between the topological indices and the physicochemical properties of drugs. Table 5 indicates that $UPGA(G)$ (for BP, FP, EV, MR, PO, and CO) and $UPSCI(G)$ (for MV, MW, and HAC) serve as the best estimator

topological indices in linear regression models.

$$\begin{aligned} BP &= 15.0630 \quad UPGA(G) + 211.2102 \\ FP &= 9.7528 \quad UPGA(G) + 64.6279 \\ EV &= 1.8220 \quad UPGA(G) + 46.0837 \\ MR &= 3.2622 \quad UPGA(G) + 24.6666 \\ PO &= 1.2931 \quad UPGA(G) + 9.7794 \\ MV &= 15.0202 \quad UPSCI(G) + 91.3802 \\ MW &= 20.7553 \quad UPSCI(G) + 121.1755 \\ HAC &= 1.4150 \quad UPSCI(G) + 8.9962 \\ CO &= 27.2911 \quad UPGA(G) - 34.2841 \end{aligned}$$

The correlation coefficient represents the proportion of the variation in the dependent variable that can be explained by a linear model.

For TIs and the physicochemical characteristics of the drugs, the best fit linear regression models are shown in Figures 12, 13, 14, 15, 18, and 20.

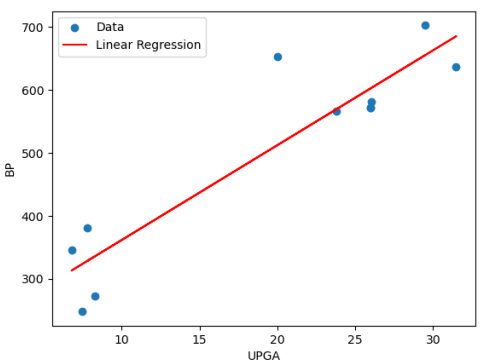

Figure 12: Correlation of $UPGA$ index with BP

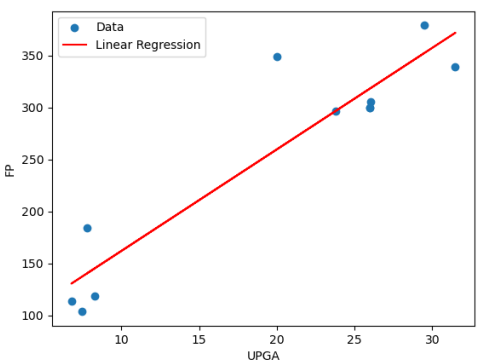

Figure 13: Correlation of $UPGA$ index with FP

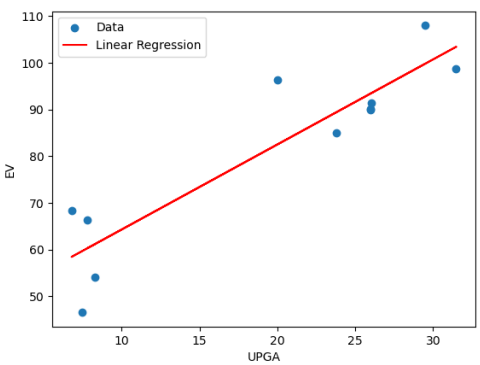

Figure 14: Correlation of $UPGA$ index with EV

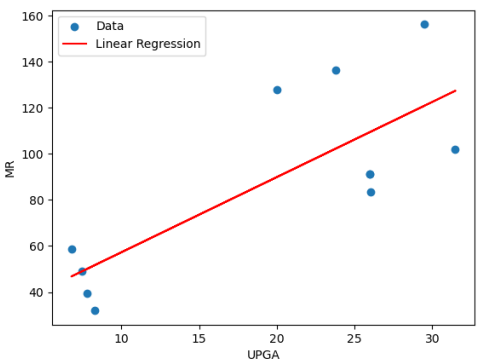

Figure 15: Correlation of $UPGA$ index with MR

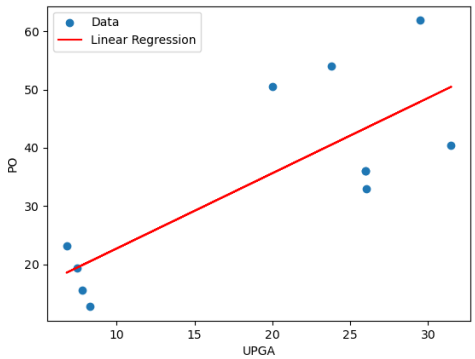

Figure 16: Correlation of $UPGA$ index with PO

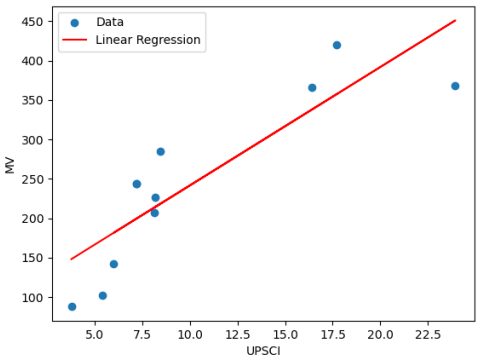

Figure 17: Correlation of $UPSCI$ index with MV

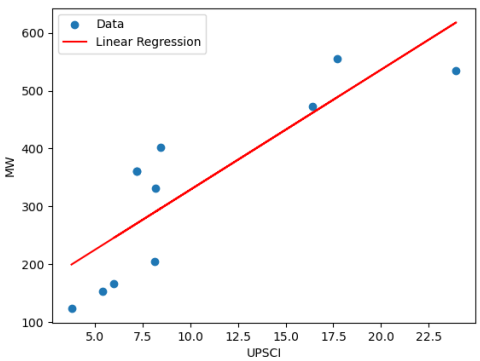

Figure 18: Correlation of $UPSCI$ index with MW

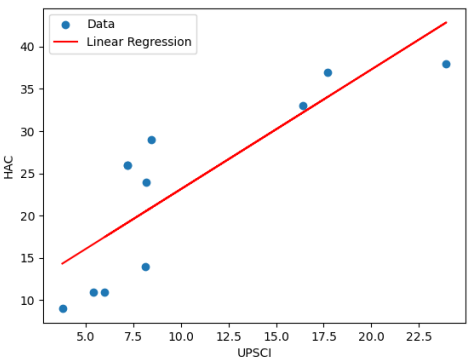

Figure 19: Correlation of $UPSCI$ index with HAC

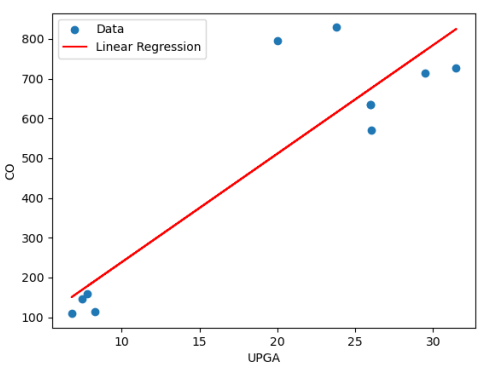

Figure 20: Correlation of $UPGA$ index with CO

4.2. Quadratic regression

By employing the quadratic regression model, we conduct a comprehensive investigation of nine physico-chemical parameters.

Table 6: Correlation Coefficients Between Topological Indices and Physicochemical Properties Obtained via Quadratic Regression

TI	BP	FP	EV	MR	PO	MV	MW	HAC	CO
UPM_1	0.7973	0.8066	0.7946	0.7412	0.7414	0.6839	0.7069	0.7095	0.8018
UPM_2	0.7525	0.7626	0.7555	0.6845	0.6847	0.6238	0.6445	0.6475	0.7534
UPF	0.7501	0.7595	0.7526	0.6840	0.6844	0.6272	0.6423	0.6459	0.7556
UPI	0.8203	0.8316	0.8137	0.7621	0.7622	0.7018	0.7365	0.7397	0.8229
$UPSO$	0.9052	0.9131	0.8837	0.8610	0.8610	0.8150	0.8600	0.8668	0.9217
UPH	0.4484	0.4338	0.3936	0.6962	0.6958	0.7501	0.6785	0.6588	0.4834
$UPGA$	0.9313	0.9453	0.9102	0.8088	0.8089	0.7571	0.8521	0.8762	0.9545
UPN	**0.9423**	**0.9470**	**0.9137**	0.8663	0.8662	0.8310	0.9009	**0.9178**	**0.9634**
$UPHM_1$	0.7735	0.7834	0.7729	0.7128	0.7131	0.6537	0.6753	0.6783	0.7791
$UPHM_2$	0.7110	0.7186	0.7193	0.6331	0.6337	0.5869	0.5921	0.5978	0.7135
$UPSCI$	0.7533	0.7126	0.7303	**0.9417**	**0.9415**	**0.9634**	**0.9101**	0.8896	0.7722

Bolded values indicate the highest correlation coefficients in each category.

The quadratic regression model's correlation coefficients between the topological indices and the physicochemical characteristics are shown in Table 6. Table 6 indicates that $UPN(G)$ (for BP, FP, EV, HAC, and CO) and $UPSCI(G)$ (for MR, PO, MV, and MW) serve as the best estimator topological indices in quadratic regression models.

$$
\begin{aligned}
BP &= -0.0454 \quad UPN(G)^2 + 9.7550 \quad UPN(G) + 105.8648 \\
FP &= -0.0288 \quad UPN(G)^2 + 6.2226 \quad UPN(G) - 0.9987 \\
EV &= -0.0047 \quad UPN(G)^2 + 1.0597 \quad UPN(G) + 36.1733 \\
MR &= -0.5610 \quad UPSCI(G)^2 + 20.7302 \quad UPSCI(G) - 45.2602 \\
PO &= -0.2222 \quad UPSCI(G)^2 + 8.2108 \quad UPSCI(G) - 17.8993 \\
MV &= -1.4644 \quad UPSCI(G)^2 + 54.9835 \quad UPSCI(G) - 111.4553 \\
MW &= -1.6019 \quad UPSCI(G)^2 + 64.4717 \quad UPSCI(G) - 100.7090 \\
HAC &= -0.0041 \quad UPN(G)^2 + 0.7837 \quad UPN(G) - 5.0222 \\
CO &= -0.0912 \quad UPN(G)^2 + 19.1602 \quad UPN(G) - 268.7426
\end{aligned}
$$

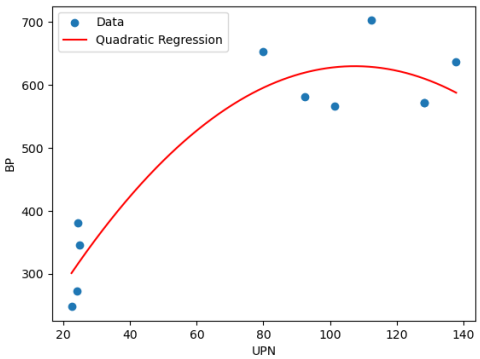

Figure 21: Correlation of UPN index with BP

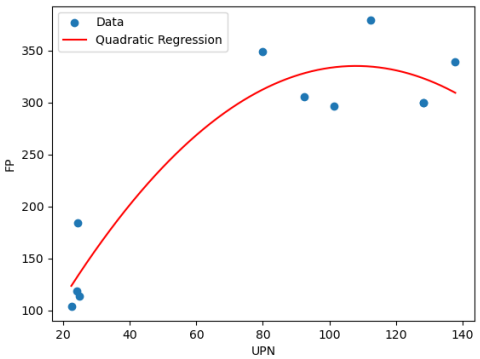

Figure 22: Correlation of UPN index with FP

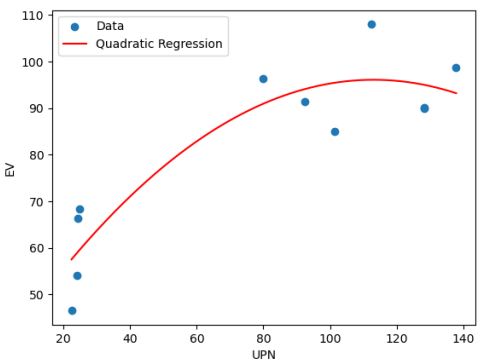

Figure 23: Correlation of UPN index with EV

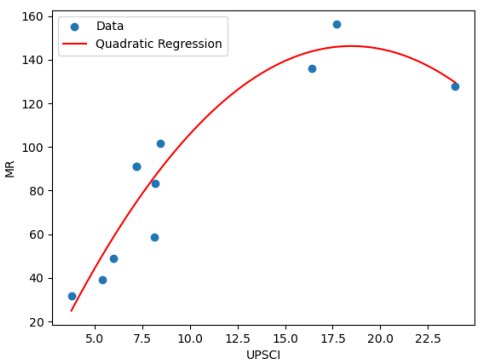

Figure 24: Correlation of $UPSCI$ index with MR

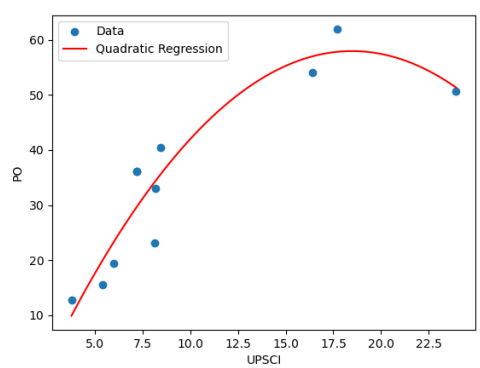

Figure 25: Correlation of $UPSCI$ index with PO

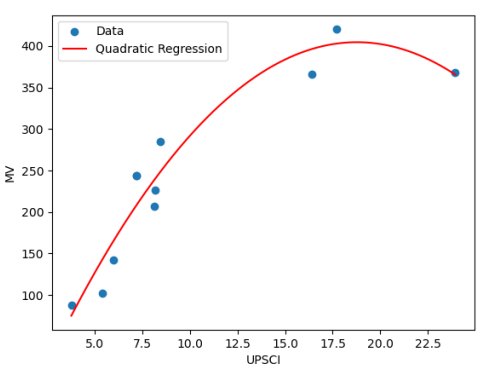

Figure 26: Correlation of $UPSCI$ index with MV

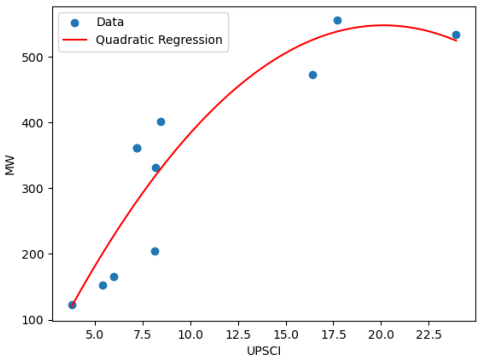

Figure 27: Correlation of $UPSCI$ index with MW

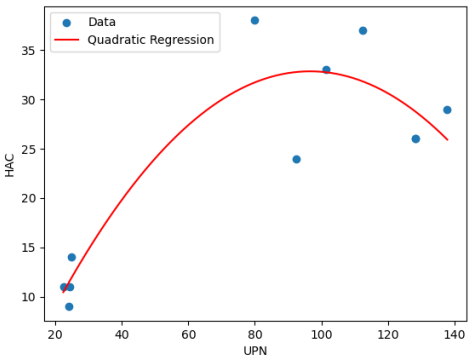

Figure 28: Correlation of UPN index with HAC

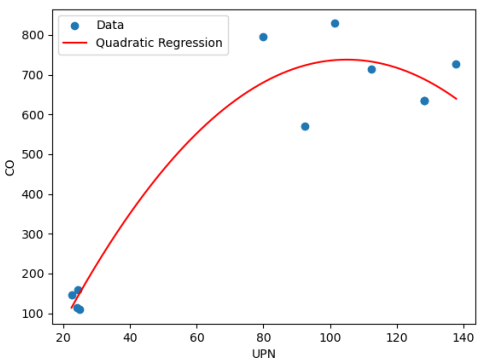

Figure 29: Correlation of UPN index with CO

Figures 21, 22, 23, 24, 25, 26, 27, 28 and 29 show the best-fit quadratic regression models that represent the relationship between TIs and drug physicochemical properties.

5. Conclusion

This study presented models for predicting the BP, FP, EV, MR, PO, MV, MW, HAC, and CO properties of key antitubercular drugs, including Bedaquiline, Ciprofloxacin, Clofazimine, Delamanid, Ethambutol, Ethionamide, Levofloxacin, Moxifloxacin, Ofloxacin, p-Aminosalicylic acid, and Pyrazinamide. These models, which were based on specific uphill topological indices, provided useful insights into the physicochemical properties of these drugs. This study employs linear and quadratic regression models to investigate the relationship between the physicochemical properties of antituberculosis drugs and their uphill topological indices. Each uphill topological index consistently demonstrated strong predictive performance when modelling the respective properties, emphasising its importance in QSPR-based drug characterisation. These findings provide valuable insights that may inform novel drug discovery efforts, particularly in the fields of medicinal chemistry, pharmaceutical sciences, and tuberculosis treatment.

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