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Investigation of Molecular Descriptors and Thermodynamic Properties of Anti-Tuberculosis Drugs Used in Tuberculosis Disease through QSPR Analysis

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ABSTRACT: Tuberculosis remains a significant public health challenge due to its widespread prevalence and severe health implications. The development of effective therapeutic agents is crucial for combating this disease. This study focuses on analyzing the structural and physicochemical characteristics of 13 key anti-tuberculosis drugs, including Isoniazid, Levofloxacin, Cycloserine, Ciprofloxacin, Pyrazinamide, Amikacin, 4-Aminosalicylic Acid, Bedaquiline, Streptomycin, Ethionamide, Ofloxacin, Ethambutol, and Kanamycin. Using a computational approach, distance-based topological descriptors, specifically the Mostar index, were investigated to explore their potential as predictors of these drugs' physicochemical properties. The methodology involved calculating the Mostar index and performing Quantitative Structure-Property Relationship (QSPR) analysis to evaluate its correlation with critical parameters such as melting point and molar mass. The results demonstrated a strong correlation (melting point $R > 0.990$, molar mass $R > 0.970$), highlighting the predictive power of the Mostar index. These findings provide valuable insights into the structural properties of anti-tuberculosis medications and support the development of novel therapeutic agents leveraging the Mostar index for enhanced drug design.

Key Words: Mycobacterium, Tuberculosis drugs, structural descriptors, QSPR analysis, regression models, correlation coefficients.

Contents

1. Introduction

Tuberculosis (TB) is a contagious bacterial infection caused by Mycobacterium tuberculosis, primarily affecting the lungs, but it can also spread to other organs through the bloodstream. It is one of the top 10 causes of death worldwide, especially in low- and middle-income countries. TB spreads through airborne droplets when an infected person coughs, sneezes, or talks. Symptoms include a persistent cough, chest pain, fever, night sweats, and weight loss. The disease is particularly dangerous for immunocompromised individuals, such as those with HIV/AIDS. Treatment involves a combination of antibiotics over a long duration, typically six months, but drug-resistant strains pose significant challenges to TB control. Efforts such as early detection, vaccination (BCG), and improved public health strategies are crucial in curbing its spread. According to the World Health Organization, TB claimed 1.5 million lives in 2020, making it a persistent global health threat [1, 2].

The management of tuberculosis (TB) entails a regimen of multiple drugs, each serving a distinct function in suppressing the proliferation of Mycobacterium tuberculosis, the bacterium that causes TB. Isoniazid (S1) is a highly effective first-line medication that inhibits bacterial cell wall formation. Pyrazinamide (S2) and Ethionamide (S3) are essential in early treatment by impairing bacterial metabolism, particularly during the latent phase of tuberculosis [3, 4, 5]. Fluoroquinolones such as Levofloxacin (S4) and Ofloxacin (S6) impede bacterial DNA replication, whereas Amikacin (S5) and Kanamycin (S12), classified as aminoglycosides, function by obstructing protein synthesis in bacteria. These medications

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are crucial for cases of multidrug-resistant tuberculosis, in which the germs exhibit resistance to standard therapies [6, 7, 8, 19].

Additional second-line medications are essential for managing more intricate or drug-resistant tuberculosis cases. Cycloserine (S7) disrupts cell wall production, whereas 4-aminosalicylic acid (S8) functions as a bacteriostatic agent, impeding bacterial proliferation. Ethambutol (S9) impedes cell wall synthesis and is frequently employed in combination therapy to avert resistance. Ciprofloxacin (S10), a fluoroquinolone, inhibits bacterial DNA gyrase, resulting in bacterial mortality [9, 10, 11]. Bedaquiline (S11) is a novel pharmaceutical agent designed for drug-resistant tuberculosis, functioning by obstructing ATP generation in the bacterium. Streptomycin (S13), an antiquated antibiotic, is predominantly utilized against more resistant types of tuberculosis, functioning by obstructing bacterial protein synthesis. The appropriate utilization of this drug combination is essential for the successful treatment of tuberculosis, especially in complex or resistant cases [12, 13, 14]. Topological indices are numerical values derived from the structural properties of molecular graphs and have found extensive applications in chemistry and materials science. They serve as essential tools in Quantitative Structure-Property Relationship (QSPR) and Quantitative Structure-Activity Relationship (QSAR) studies, enabling researchers to predict a wide range of physicochemical, biological, and pharmacological properties of chemical compounds without the need for exhaustive experimental testing. For instance, valency-based and spectrum-based descriptors have proven effective in predicting physical and pharmacological properties of polycyclic compounds, aiding in drug discovery and development [15, 16]. Moreover, topological indices such as distance-based entropy measures have been utilized to explore the structural characteristics of dendrimers, enhancing the understanding of their chemical behavior [17]. Additionally, newly introduced topological invariants have demonstrated significant correlations with the properties of polycyclic compounds, further broadening their applicability in chemical and mathematical studies [18].

Streptomycin, a well-known antibiotic used to combat bacterial infections, serves as an excellent candidate for topological analysis. By examining the molecular graph of Streptomycin through the lens of the Mostar and edge Mostar indices, we aim to uncover how the drug's structure correlates with its function. The Mostar index is determined by comparing the number of vertices closer to each endpoint of an edge, highlighting the local asymmetry within the graph. The edge Mostar index extends this concept, focusing specifically on the edge based asymmetry.

During the year 1947, Harold Wiener made the initial suggestion for topological indices, which was subsequently mentioned in Wiener's work [20]. Over the course of the succeeding time period, he proceeded to publish a series of articles that shed light on the relationship between the wiener index and the physicochemical properties of carbon-based compounds [21]. According to the reference [22], this decade of the 20th century saw the computation of a considerable number of topological indices that are connected to the Wiener index. These indices were computed during the final decade of the century. Researchers have been estimating irregularity topological indices for a variety of chemical structures [23] from the beginning of the 21st century and continuing to do so during the second decade of the century. A number of new banhatti indices were introduced in the year 2016 by V. R. Kulli [24]. These new banhatti indices included modified Banhatti indices, super K Banhatti indices, and K Banhatti indices.

A lot of people in the area of chemical graph theory have been interested in studying degree-based, irregular, and distance-based topological indices in the last ten years. These indices have recently attracted a lot of attention from researchers looking to better understand molecular structures. As an example, A. Fahad and M. I. Qureshi [25, 26] examined polynomials of Poly(EThyleneAmidoAmine) (PETAA) dendrimers and eccentricity-based topological indices in 2019. Their research brought attention to novel methods for describing molecular graphs. In November 2020, A. Fahad further investigated the topological characteristics of PETIM dendrimers, contributing important information to this expanding area of study. In the same year, M. I. Qureshi shifted his attention to the Zagreb connection index, particularly as it pertained to chemical structures associated with drugs. Adding to our understanding of the behavior of these structures, Yu-Ming Chu continued to investigate topological indices in 2021 by computing irregular indices for specific metal-organic frameworks [27, 28].

Also, bond-additive topological descriptors are being used more and more to describe the features of chemical graphs and the parts that make them up. The Wiener index is a new bond-additive index that gives each bond an input based on the number of atoms on both sides. This gives a clear measure

of how connected molecules are. Since this start, many better descriptors have been created, such as the Szeged, revised-Szeged, PI, irregularity, and Zagreb indices [29]. The Mostar index is a new bond-additive topological measure that was just released by Došlic and his colleagues [30]. This index gives information about how peripheral certain bonds are, and then adds up their effects to make a full measure of peripherality in the chemical structure. Understanding the peripherality of bonds is important in chemistry because it has a big effect on predicting the physicochemical features of molecules, which in turn changes how they behave in different situations. Tratnik significantly advanced [32] by demonstrating that the Mostar index of a weighted graph may be determined by comparing it to the quotient graphs. This discovery simplified index calculation for complex weighted structures. According to [33], Arockiaraj and his team accurately calculated the Mostar index for molecular shapes like carbon nanocones and coronoid structures. The exact numbers revealed new aspects of these unusual molecular configurations. Arockiaraj et al. extended on their work in [34] by determining weighted Mostar indices for molecular peripheral forms. These indices can be employed in graphene, graphyne, and graphdiyne nanoribbons. Došlic et al. calculated the Mostar index for benzenoid systems using the techniques outlined in [30]. They also found exceptional Mostar index values for trees and unicyclic networks. This improved their understanding of this index for more molecule forms. Later, [31] introduced formulas for bicyclic graph Mostar index. These extended graph analysis to more complex structures. In [35], Hayat and Zhou made a big addition by finding the extreme Mostar index values for cacti and structures that look like trees. They showed how the Mostar index can be used to look at different types of molecular graphs and how extremal behavior works in both simple and complex structures.

Although the above literature review discusses extensive work related to the Moster index, this research primarily focuses on its mathematical aspects. Mathematicians have extensively studied the mathematical properties of the Moster index, exploring its theoretical foundations and implications within pure mathematics. However, our work is the first to investigate the chemical applicability of the Moster index. We achieved this by performing a detailed sensitivity analysis to evaluate its behavior and subsequently conducting a QSPR (Quantitative Structure-Property Relationship) analysis to explore its relevance in chemical studies. The Mostar index of a graph G is defined as

$$Mo(G) = \sum_{uv \epsilon E(G)} |n_u - n_v| \tag{1.1}$$

where n_u and n_v are the number of vertices of G closer to u than v and the number of vertices of G closer to v than u respectively. The edge version of mostar index is defined as

$$Mo_e(G) = \sum_{e=uv \epsilon E(G)} |m_u - m_v| \tag{1.2}$$

where m_u and m_v are the number of edges of G closer to u than v and the number of edges of G closer to v than u respectively.

In this paper, we derive explicit formulas for both indices as applied to Streptomycin and discuss their implications in terms of molecular structure and drug activity, but before this, we analyzed the implacability of these descriptors by applying Smoothness, Abruptness and QSPR regression analysis. This analysis contributes to the broader application of topological indices in pharmaceutical chemistry, providing insights that may assist in the development of more effective drugs. In our work, Matlab is utilized for mathematical calculations and verifications whereas Maple is used for graphically analyzing and plotting these results and ChemSketch is used to draw the molecular graphs.

2. Structure-Sensitivity Analysis

Several parameters were introduced to reduce randomness in constructing a new topological index. One key parameter is smoothness, which ensures a molecular descriptor's value changes uniformly with gradual structural changes [36, 37, 38]. However, assessing smoothness is challenging and often overlooked by researchers. This section explores the smoothness of some novel degree based topological indices and compares them with existing results. Two graph structural measures, denoted as structural sensitivity

(Ψ_s) and abruptness (Δ_a), were proposed to evaluate smoothness. The structural sensitivity of eigenvalue-based indices and the smoothness of graph energy in chemical graphs have been studied. An existing algorithm for calculating Ψ_s and Δ_a is also outlined.

1. **Initialize Variables:**
   - Matrices for trees, GED, topological indices, and results are initialized.
   - Tree set Ω and GED for all trees are computed using a Python package.
2. **Calculate TIs for Each Tree:**
   - Loop through each tree T_i in the dataset.
   - Compute structure sensitivity $\Psi_s(T_i, \text{TIs})$ and abruptness $\Delta_a(T_i, \text{TIs})$ for each TI.
   - Store all Ψ_s and Δ_a values for each tree.
3. **Final Calculation for the Dataset:**
   - Compute the average Ψ_s and Δ_a for all trees in Ω.
   - Output the results for all trees in the dataset.

The structure sensitivity and abruptness of a topological index T for a graph G can be assessed through the following mathematical formulas. To measure the structure sensitivity:

$$\Psi_s(T, G) = \frac{1}{|S(G)|} \sum_{H \in S(G)} \left| \frac{T(H) - T(G)}{T(G)} \right| \tag{2.1}$$

Here, $|S(G)|$ is the total number of graphs in the set $S(G)$, H is a graph from the set $S(G)$, and $T(H)$ and $T(G)$ are the values of the topological index T for graphs H and G, respectively. To capture the abruptness:

$$\Delta_a(T, G) = \max_{H \in S(G)} \left| \frac{T(H) - T(G)}{T(G)} \right| \tag{2.2}$$

Here, $\Delta_a(T, G)$ measures the maximum relative change of T between the graph G and any graph H in the set $S(G)$. By calculating the average values of Ψ_s (structure sensitivity) and Δ_a (abruptness) for a topological index T across all graphs in a given class O, we obtain the overall structure sensitivity and abruptness of T for that class of connected graphs. Specifically,

$$\Psi_s(T) = \frac{1}{|O|} \sum_{G \in O} \Psi_s(T, G) \tag{2.3}$$

Here, $|O|$ is the total number of graphs in the set O, and $\Psi_s(T, G)$ is the structure sensitivity of the index T for a graph G. Similarly

$$\Delta_a(T) = \frac{1}{|O|} \sum_{G \in O} \Delta_a(T, G) \tag{2.4}$$

Here, $|O|$ is the total number of graphs in the set O, and $\Delta_a(T, G)$ is the abruptness of the index T for a graph G. Utilizing these (TIs) and definitions of sensitivity and abruptness, we generated the Table 2 for better understanding of applicability of Moster index. We used the following algorithm to generate the mentioned tables.

Algorithm 1 Computation of SS and Abr Values for Trees

Require: Ω *(set of all trees with a given number of vertices)*

$A \leftarrow \texttt{zeros}(|\Omega|, 23)$
$B \leftarrow \texttt{zeros}(|\Omega|, 23)$
$C \leftarrow \texttt{zeros}(1, 23)$
$D \leftarrow \texttt{zeros}(1, 23)$
for $i = 1$ **to** $|\Omega|$ **do**
    Let T_i be the i-th tree in Ω.
    $S \leftarrow \{\text{trees with GED } = 2 \text{ from } T_i\}$ ▷ GED via `networkx` in Python
    $E \leftarrow [\text{23 TIs for } T_i]_{1\times 23}$ ▷ Step 1
    $F \leftarrow [\text{23 TIs for each tree in } S]_{23\times|S|}$ ▷ Step 2
    $G \leftarrow \texttt{zeros}(23, |S|)$
    $H \leftarrow \texttt{zeros}(1, 23)$ ▷ SS for T_i per TI
    $I \leftarrow \texttt{zeros}(1, 23)$ ▷ Abr for T_i per TI
    for $j = 1$ to 23 **do**
        $p \leftarrow 0$
        for $k = 1$ to $|S|$ **do**
            $q \leftarrow \left|\dfrac{F(j,k) - E(j)}{E(j)}\right|$
            $G(j,k) \leftarrow q$
            $p \leftarrow p + q$
        end for
        $\mathrm{SS}(T_i, \mathrm{TI}_j) \leftarrow \dfrac{p}{|S|}$ ▷ Step 3
        $\mathrm{Abr}(T_i, \mathrm{TI}_j) \leftarrow \max\big(G(j, 1{:}|S|)\big)$ ▷ Step 3
        $H(j) \leftarrow \mathrm{SS}(T_i, \mathrm{TI}_j)$
        $I(j) \leftarrow \mathrm{Abr}(T_i, \mathrm{TI}_j)$
    end for
    $A(i, :) \leftarrow H(1, :)$
    $B(i, :) \leftarrow I(1, :)$
end for
Display: A, B
for $\ell = 1$ to 23 **do**
    $r \leftarrow 0; \quad t \leftarrow 0$
    for $m = 1$ to $|\Omega|$ **do**
        $r \leftarrow r + A(m, \ell)$
        $t \leftarrow t + B(m, \ell)$
    end for
    $\mathrm{SS}(\Omega, \mathrm{TI}_\ell) \leftarrow \dfrac{r}{|\Omega|}$
    $\mathrm{Abr}(\Omega, \mathrm{TI}_\ell) \leftarrow \dfrac{t}{|\Omega|}$
    $C(\ell) \leftarrow \mathrm{SS}(\Omega, \mathrm{TI}_\ell)$
    $D(\ell) \leftarrow \mathrm{Abr}(\Omega, \mathrm{TI}_\ell)$
end for
Display: C, D ▷ average SS and Abr for all TIs over Ω

Invariant	Symbol	Formula
First Zagreb Index	$M_1(G)$	$\sum_{v\in V(G)} d_G(v)^2 = \sum_{uv\in E(G)}(d_G(u)+d_G(v))$
Second Zagreb Index	$M_2(G)$	$\sum_{uv\in E(G)} d_G(u)d_G(v)$
Modified Second Zagreb	$mM_2(G)$	$\sum_{uv\in E(G)} \frac{1}{d_G(u)d_G(v)}$
Forgotten Index	$F(G)$	$\sum_{v\in V(G)} d_G(v)^3 = \sum_{uv\in E(G)}\left(d_G(u)^2+d_G(v)^2\right)$
Randic Index	$R_{-1/2}(G)$	$\sum_{uv\in E(G)} \frac{1}{\sqrt{d_G(u)d_G(v)}}$
Reciprocal Randic Index	$RR_{-1/2}(G)$	$\sum_{uv\in E(G)} \sqrt{d_G(u)d_G(v)}$
Sum Connectivity Index	$SCI(G)$	$\sum_{uv\in E(G)} \frac{1}{\sqrt{d_G(u)+d_G(v)}}$
Symmetric Division Deg	$SDD(G)$	$\sum_{uv\in E(G)} \left(\frac{d_G(u)}{d_G(v)}+\frac{d_G(v)}{d_G(u)}\right)$
Harmonic Index	$H(G)$	$\sum_{uv\in E(G)} \frac{2}{d_G(u)+d_G(v)}$
Inverse Sum Index	$ISI(G)$	$\sum_{uv\in E(G)} \frac{d_G(u)d_G(v)}{d_G(u)+d_G(v)}$
Atom-Bond Connectivity	$ABC(G)$	$\sum_{uv\in E(G)} \frac{\sqrt{d_G(u)+d_G(v)-2}}{d_G(u)d_G(v)}$
Augmented Zagreb Index	$AZI(G)$	$\sum_{uv\in E(G)} \left(\frac{d_G(u)d_G(v)}{d_G(u)+d_G(v)-2}\right)^3$
First Hyper-Zagreb Index	$HM_1(G)$	$\sum_{uv\in E(G)}(d_G(u)+d_G(v))^2$
Second Hyper-Zagreb Index	$HM_2(G)$	$\sum_{uv\in E(G)}(d_G(u)d_G(v))^2$
Geometric-Arithmetic Index	$GA(G)$	$\sum_{uv\in E(G)} \frac{2\sqrt{d_G(u)d_G(v)}}{d_G(u)+d_G(v)}$
Arithmetic-Geometric Index	$AG(G)$	$\sum_{uv\in E(G)} \frac{d_G(u)+d_G(v)}{2\sqrt{d_G(u)d_G(v)}}$
Sombor Index	$SO(G)$	$\sum_{uv\in E(G)} \sqrt{d_G(u)^2+d_G(v)^2}$
Modified Sombor Index	$mSO(G)$	$\sum_{uv\in E(G)} \frac{1}{\sqrt{d_G(u)^2+d_G(v)^2}}$
Nirmala Index	$N(G)$	$\sum_{uv\in E(G)} \sqrt{d_G(u)+d_G(v)}$
First Inverse Nirmala Index	$IN_1(G)$	$\sum_{uv\in E(G)} \sqrt{\frac{1}{d_G(u)}+\frac{1}{d_G(v)}}$
Second Inverse Nirmala Index	$IN_2(G)$	$\sum_{uv\in E(G)} \frac{1}{\sqrt{\frac{1}{d_G(u)}+\frac{1}{d_G(v)}}}$
Geometric-Quadratic Index	$GQ(G)$	$\sum_{uv\in E(G)} \frac{\sqrt{2d_G(u)d_G(v)}}{\sqrt{d_G(u)^2+d_G(v)^2}}$
Quadratic-Geometric Index	$QG(G)$	$\sum_{uv\in E(G)} \frac{\sqrt{d_G(u)^2+d_G(v)^2}}{\sqrt{2d_G(u)d_G(v)}}$

Table 1: Topological indices with their symbols and formulas

Descriptors		$n=4$	$n=5$	$n=6$	$n=7$	$n=8$	$n=9$	$n=10$
SO	Sensitivity	0.2691	0.2398	0.1864	0.1595	0.1263	0.1101	0.0939
	Abruptness	0.2667	0.2762	0.2781	0.2901	0.2394	0.2228	0.2091
$RR_{-1/2}$	Sensitivity	0.0754	0.0813	0.0707	0.0631	0.0587	0.0501	0.0447
	Abruptness	0.0722	0.0854	0.1011	0.7198	0.1372	0.1087	0.1078
GQ	Sensitivity	0.1857	0.1676	0.1243	0.0978	0.0767	0.0632	0.0531
	Abruptness	0.1851	0.1805	0.1721	0.1456	0.1309	0.1177	0.1056
HM_1	Sensitivity	0.3562	0.3509	0.2809	0.2391	0.2041	0.1809	0.1596
	Abruptness	0.3534	0.3956	0.4333	0.4194	0.4029	0.3922	0.3799
AG	Sensitivity	0.1061	0.0982	0.0745	0.0613	0.0496	0.0426	0.0355
	Abruptness	0.1068	0.1103	0.1099	0.0984	0.0892	0.0829	0.0749
${}^{\mathrm{m}}SO$	Sensitivity	0.2795	0.2652	0.2039	0.0103	0.1289	0.1062	0.0882
	Abruptness	0.2814	0.2826	0.2794	0.2427	0.2225	0.1999	0.1797
IN_2	Sensitivity	0.0142	0.0121	0.0105	0.0221	0.0107	0.0093	0.0089
	Abruptness	0.0140	0.0144	0.0155	0.0967	0.0193	0.0207	0.0228
ISI	Sensitivity	0.0381	0.0320	0.0302	0.0286	0.0274	0.0257	0.0248
	Abruptness	0.0373	0.0385	0.0427	0.0482	0.0549	0.0584	0.0619
F	Sensitivity	0.5388	0.4899	0.3691	0.3077	0.2565	0.2243	0.1937
	Abruptness	0.5376	0.5669	0.5959	0.5572	0.5188	0.4912	0.4706
SDD	Sensitivity	0.3685	0.3191	0.2395	0.1957	0.1578	0.1343	0.1157
	Abruptness	0.3663	0.3688	0.3693	0.3302	0.3029	0.2809	0.2607
IN_1	Sensitivity	0.0051	0.0042	0.0037	0.0035	0.0033	0.0029	0.0028
	Abruptness	0.0045	0.0043	0.0047	0.0053	0.0057	0.0061	0.0164
${}^{\mathrm{m}}M_2$	Sensitivity	0.2283	0.2137	0.1645	0.1301	0.1027	0.0839	0.0692
	Abruptness	0.2281	0.2342	0.2267	0.1998	0.1769	0.1601	0.1444
N	Sensitivity	0.0954	0.0923	0.0715	0.0595	0.0493	0.0426	0.0367
	Abruptness	0.0957	0.1014	0.1049	0.0974	0.0902	0.0845	0.0794
QG	Sensitivity	0.1824	0.1613	0.1199	0.0967	0.0779	0.0663	0.0556
	Abruptness	0.1823	0.1808	0.1774	0.1576	0.1425	0.1307	0.1198
MoG	Sensitivity	0.1217	0.2548	0.3182	0.3217	0.3209	0.3032	0.2883
	Abruptness	0.0049	0.0045	0.0049	0.0055	0.0059	0.0064	0.0069

Table 2: Topological indices with their sensitivity and abruptness

For evaluating the quality of a topological index, it is crucial that the structural sensitivity (Ψ_s) is maximized, while the abruptness (Δ_a) is minimized. More details on these two measures are explored in [37, 38], where computational testing of the smoothness of several distance and degree-based indices was examined using data sets of trees with varying vertex counts. Table 2 leads to the following observations: the neighborhood face index, forgotten index, and first hyper-Zagreb index exhibit the highest, second-highest, and third-highest Ψ_s values, respectively. From Tables 2, we see for trees with $n = 10$ vertices that $\Psi_s\,(MoG) = 0.288$, $\Psi_s(F) = 0.192$, and $\Psi_s\,(\mathcal{HM}_1) = 0.157$, followed by $\Psi_s\,(\mathcal{AZI}) = 0.118$, $\Psi_s\,(\mathcal{SDD}) = 0.112$, $\Psi_s\,(\mathcal{M}_2) = 0.103$, $\Psi_s(\mathcal{SO}) = 0.093$, $\Psi_s\,({}^{m}\mathcal{SO}) = 0.086$, $\Psi_s\,(\mathcal{M}_1) = 0.073$, $\Psi_s\,({}^{m}\mathcal{M}_2) = 0.067$, and

$\Psi_s(H) = 0.067$, among others. These invariants maintain the following relationship:

$$\begin{aligned}
&\Psi_s\left(MoG\right) > \Psi_s(F) > \Psi_s\left(\mathcal{HM}_1\right) > \Psi_s(\mathcal{AZI}) > \Psi_s(\mathcal{SDD}) > \Psi_s\left(\mathcal{M}_2\right) > \Psi_s(\mathcal{GQ}) \\
&> \Psi_s(\mathcal{SO}) > \Psi_s\left({}^m\mathcal{SO}\right) > \Psi_s\left(\mathcal{M}_1\right) > \Psi_s\left({}^m\mathcal{M}_2\right) > \Psi_s(H) > \Psi_s(\mathcal{QG}) \\
&> \Psi_s\left(\mathcal{RR}_{-1/2}\right) > \Psi_s(N) > \Psi_s(\mathcal{SCI}) > \Psi_s\left(\mathcal{R}_{-1/2}\right) \approx \Psi_s(\mathcal{AG}) > \Psi_s(\mathcal{GA}) \\
&> \Psi_s(\mathcal{ABC}) > \Psi_s(\mathcal{ISI}) > \Psi_s\left(\mathcal{IN}_2\right) > \Psi_s\left(\mathcal{IN}_1\right)
\end{aligned}$$

On the other hand, the topological indices with the lowest abruptness (Δ_a) are the (M_oG) and the first and second inverse Nirmala indices. For $n = 10$, Table 2 show that $\Delta_a\left(M_oG\right) = 0.005$, $\Delta_a\left(MoG\right) = 0.007$, $\Delta_a\left(\mathcal{IN}_2\right) = 0.021$, followed by $\Delta_a(\mathcal{ABC}) = 0.057$, $\Delta_a(\mathcal{ISI}) = 0.0604$, $\Delta_a(\mathcal{GA}) = 0.0671$, $\Delta_a\left(\mathcal{R}_{-1/2}\right) = 0.071$, and $\Delta_a(\mathcal{SCI}) = 0.0714$, among others. The following inequality relation holds for the degree based indices:

$$\begin{aligned}
&\Delta_a\left(M_oG\right) < \Delta_a\left(\mathcal{IN}_1\right) < \Delta_a\left(\mathcal{IN}_2\right) < \Delta_a(\mathcal{ABC}) < \Delta_a(\mathcal{ISI}) < \Delta_a(\mathcal{GA}) < \Delta_a\left(\mathcal{R}_{-1/2}\right) \\
&< \Delta_a(\mathcal{SCI}) < \Delta_a(\mathcal{AG}) < \Delta_a(N) < \Delta_a\left(\mathcal{RR}_{-1/2}\right) < \Delta_a(\mathcal{GQ}) < \Delta_a(\mathcal{QG}) \\
&< \Delta_a(H) < \Delta_a\left({}^m\mathcal{M}_2\right) < \Delta_a\left(\mathcal{M}_1\right) < \Delta_a\left({}^m\mathcal{SO}\right) < \Delta_a(\mathcal{AZI}) \\
&< \Delta_a(\mathcal{SDD}) < \Delta_a\left(\mathcal{M}_2\right) < \Delta_a\left(\mathcal{HM}_1\right) < \Delta_a(F) < \Delta_a\left(\mathcal{HM}_2\right)
\end{aligned}$$

Above sensitivity analysis depicts to assess how stable Moster and edge version of Mostar index are when small changes, such as adding or removing edges or nodes, occur in the graph.

3. Regression Analysis

We collected data on 13 tuberculosis (TB) drugs and their six physicochemical properties from reputable online sources such as PubChem and ChemSpider. Subsequently, we calculated the numerical results of ten degree-based reducible indices to analyze the molecular structure of these drugs using three techniques: edge partition, vertex degree, and counting degree. We employed Quantitative Structure–Activity Relationship (QSAR) analysis to establish a strong positive correlation between the indices and properties, utilizing linear, quadratic, and logarithmic regression equations for this purpose. The correlation coefficient (r) was one of the statistical parameters employed to assess the reliability and significance of the relationship between the physical properties and calculated numerical values of the TB drugs. Finally, we created line graphs to visually compare the correlation coefficients, facilitating a comprehensive discussion of the relationships between the properties and indices.

The physicochemical parameters of the specified pharmaceuticals are outlined in Table **??**, which provides exact values for the molar index, whereas experimental values for molar mass, XLOGP3, complexity, LOGP, melting temperature, and collision cross section were gathered from the PubChem database. We evaluated the regression models for each descriptor using the data supplied in Table **??** and investigated their chemical applicability.

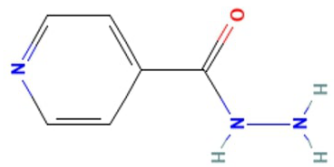

Figure 1: *
S1: Isoniazid

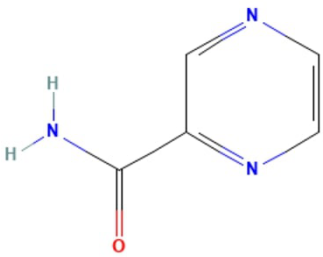

Figure 2: *
S2: Pyrazinamide

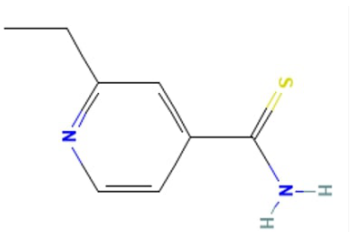

Figure 3: *
S3: Ethionamide

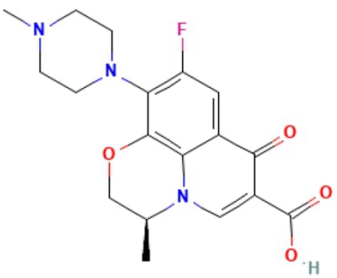

Figure 4: *
S4: Levofloxacin

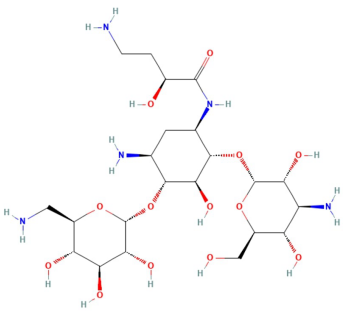

Figure 5: *
S5: Amikacin

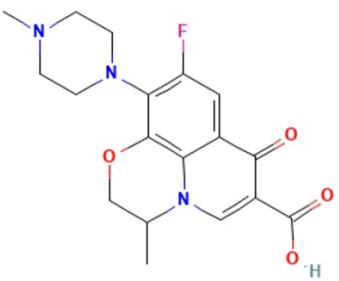

Figure 6: *
S6: Ofloxacin

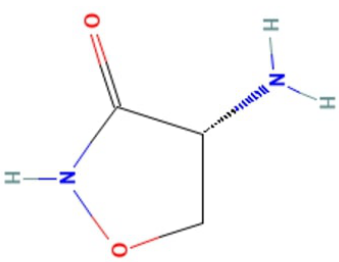

Figure 7: *
S7: Cycloserine

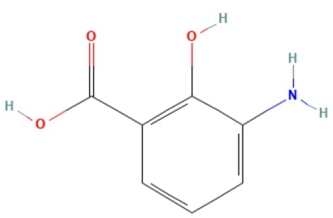

Figure 8: *
S8: 4-aminosalicylic acid

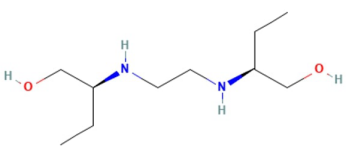

Figure 9: *
S9: Ethambutol

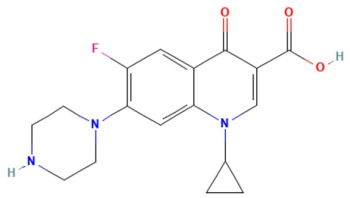

Figure 10: *
S10: Ciprofloxacin

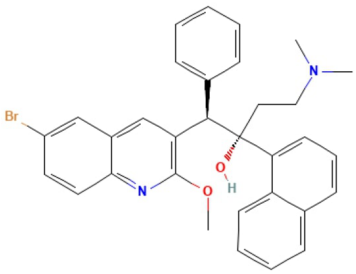

Figure 11: *
S11: Bedaquiline

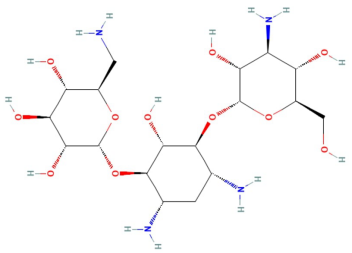

Figure 12: *
S12: Kanamycin

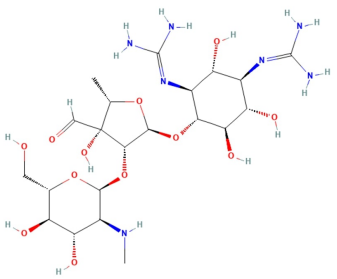

Figure 13: *
S13: Streptomycin

Figure: Comparison of anti-tuberculosis drugs (S1–S13), showcasing a visual representation of each drug for analysis and reference.

4. Conclusion

This study has conducted a comprehensive examination of essential anti-tuberculosis medications, including Isoniazid, Levofloxacin, Cycloserine, Ciprofloxacin, Pyrazinamide, Amikacin, 4-Aminosalicylic Acid, Bedaquiline, Streptomycin, Ethionamide, Ofloxacin, Ethambutol, and Kanamycin. The structural sensitivity investigation validated the relevance of the Mostar topological invariant for these pharmaceuticals, demonstrating optimal sensitivity and low abruptness. The QSPR research indicated that the Mostar index has a robust association with significant physicochemical parameters, including melting point (with correlation > 0.990) and molar mass (correlation > 0.970). The results demonstrate that the Mostar index is a very dependable predictor of the physicochemical qualities of pharmaceuticals utilized in the treatment of diseases such as tuberculosis. This discovery could greatly facilitate the creation of innovative therapeutic agents by utilizing the predictive capabilities of the Mostar index for pharmacological characteristics.

Declaration

- **Availabilty of data and materials:** The data is provided on request to the authors.
- **Authors Contribution:** All authors contributed equally in writing of this article.
- **Conflicts of interest:** The authors declare that they have no conflicts of interest and all agree to publish this paper under academic ethics.
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