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Graph Theoretic Modeling of Antibiotic Drugs - Correlating Topological Indices with Physicochemical Properties

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Abstract. QSPR establishes a mathematical relationship between a molecular structure and its physicochemical characteristics. Topological indices can serve as effective tools for predicting the physicochemical properties of chemical compounds, providing a useful alternative to time-consuming and laboratory testing. In this study, we established a QSPR relationship between topological indices and antibacterial medications. Our analysis indicates that these properties can be predicted with high accuracy. Additionally, we computed the topological indices of antimicrobial drugs. By combining these metrics with statistical modeling, this study aims to predict

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antibacterial efficacy and potentially aid in the discovery of novel antibiotic compounds that are more effective and less prone to resistance. This study highlights that topological indices can inform the rational development and selection of antibiotics for future medical and therapeutic applications.

Keywords: Antibiotic drugs, Correlation, Degree, Distance, Topological index.

2000 Mathematics subject classification: 05C10, O5C90, 05C12

1. Introduction

Topological indices and physicochemical properties are closely connected with drug discovery. In 1982, Alexandru T. Balaban introduced an index to measure the connectivity and branching of molecular graphs. [7].

$$G_1 = B = \frac{m}{m-n+2} \sum_{uv \in E(G)} \frac{1}{\sqrt{\rho_u \rho_v}}$$

In 2021, Ivan Gutman proposed the Sombor index G_2, which utilizes the Euclidean distance between degree pairs of vertices. Several physicochemical properties, including enthalpy of vaporization, flash point, and molar refractivity in benzenoid hydrocarbons, have been found to correlate significantly with the Sombor index [6, 14]. To enhance its applicability in both theoretical and practical contexts, researchers have also investigated the reduced Sombor index G_3 and the average Sombor index G_4 [3].

$$G_2 = SO(G) = \sum_{uv \in E(G)} \sqrt{\rho_u^2 + \rho_v^2}$$

$$G_3 = RSO(G) = \sum_{uv \in E(G)} \sqrt{(\rho_u - 1)^2 + (\rho_v - 1)^2}$$

$$G_4 = ASO(G) = \sum_{uv \in E(G)} \sqrt{\left(\rho_u - \frac{2m}{n}\right)^2 + \left(\rho_v - \frac{2m}{n}\right)^2}$$

Ivan Gutman introduced the Zagreb indices, which have found important applications in cancer research and in the prediction of boiling points [12, 13, 18].

$$G_5 = M_1(G) = \sum_{uv \in E(G)} (\rho_u + \rho_v)$$

$$G_6 = M_2(G) = \sum_{uv \in E(G)} (\rho_u \cdot \rho_v)$$

The Randić index, introduced by the chemist Milan Randić in 1975, is used in the study of molecular structures, particularly in chemistry, to quantitatively evaluate branching in molecular graphs [8]. It is commonly used in pharmaceutical design as an indicator of molecular complexity.

$$G_7 = R(G) = \sum_{uv \in E(G)} \frac{1}{\sqrt{\rho_u \cdot \rho_v}}$$

The Forgotten topological index (F-index), introduced by Boris Furtula and Ivan Gutman, measures molecular complexity by incorporating higher powers of vertex degrees along with distance-related structural information [9].

$$G_8 = F(G) = \sum_{v \in V(G)} \rho_v^3$$

The Atom-Bond Connectivity (ABC) index, introduced by Iván Gutman in 1998, was developed to elucidate structure-property relationships in molecular entities by incorporating contributions from both atoms and bonds [10, 16].It is widely used to evaluate molecular stability, reactivity, and biological activity.

$$G_9 = ABC(G) = \sum_{uv \in E(G)} \sqrt{\frac{\rho_u + \rho_v - 2}{\rho_u \cdot \rho_v}}$$

Harold Wiener introduced the Wiener index in his seminal 1947, structural determination of paraffin boiling points. The Wiener index serves as a topological descriptor specifically tailored for paraffins (alkanes), demonstrating a significant correlation with their boiling points. It is widely used in chemistry, pharmacology, and ecology for modeling purposes, particularly in predicting boiling points and solubility [1].

$$G_{10} = W(G) = \sum_{u,v \in V(G)} \rho_G(u, v)$$

Ernesto Estrada and M. A. M. P. Oliveira expanded the Hyper-Wiener index in 2001 [19], extension of Wiener index. In 2014, Ivan Gutman developed the Augmented Zagreb index that improves the analytical power of molecular structure quantification.

$$G_{11} = HW(G) = W + \frac{1}{2} \sum_{u,v \in V(G)} [\rho_G(u, v)]^2$$

$$G_{12} = AZI(G) = \sum_{uv \in E(G)} \left(\frac{\rho_u \cdot \rho_v}{\rho_u + \rho_v - 2} \right)^3$$

The primary purpose of the Gutman molecular topological index is to describe the branching patterns and topological complexity of molecular structures [11].

$$G_{13} = Gut(G) = \sum_{\{u,v\}\subseteq V(G)} (\rho_u + \rho_v - 2)$$

Ernesto Estrada developed the Estrada index in 2000, which uses the eigenvalues of the adjacency matrix of a molecular graph to quantify molecular structure. It is useful in network research, protein folding, and pharmacokinetics, providing insights into connectivity and structural characteristics.

$$G_{14} = EE(G) = \sum_{j=1}^{n} e^{\lambda_j},$$

where $|V| = n$, where $\lambda_1 \geq \lambda_2 \geq \lambda_3 \geq \cdots \geq \lambda_n$, are eigenvalues of the adjacency matrix. H. J. Schultz developed the Schultz index in the 1980s as a topological metric specifically designed to measure molecular complexity. The Harary index is employed to calculate network resilience, molecular connectivity studies, and reliability engineering.

$$G_{15} = S(G) = \sum_{\{u,v\}\subseteq V(G)} (\rho_G(u) + \rho_G(v))\, \rho_G(u,v)$$

$$G_{16} = H(G) = \sum_{\{u,v\}\subseteq V(G)} \frac{1}{\rho_G(u,v)}$$

Topological indices serve as powerful tools for modeling and predicting molecular activity across various applications. Over time, they have become more specialized, focusing on specific characteristics such as branching, connectivity, and molecular structure. Consequently, they have enhanced QSAR/QSPR prediction accuracy and provided valuable insights for drug design [15, 17].

2. Antibiotic Drugs

The selection of antibiotics is based on the patient's medical history, the site of infection, and the causative microorganisms, taking into account their specific spectrum of activity and resistance profiles [2]. Ampicillin and Amoxicillin are commonly prescribed for gastrointestinal, ear, urinary, and respiratory tract infections. Cefalexin is used to treat skin infections, urinary tract infections, and respiratory tract infections. Cefuroxime is effective against Lyme disease, skin infections, and respiratory tract infections. Cefotetan is used for the treatment of intra-abdominal infections and urinary tract infections (UTIs). Cefotaxime is indicated for meningitis, respiratory tract infections, and severe UTIs.

Cefixime is prescribed for respiratory tract infections, UTIs, and gonorrhea. Ceftriaxone is effective in treating meningitis, respiratory tract infections, skin infections, and sexually transmitted infections (STIs). Cefepime is a broad-spectrum antibiotic indicated for severe hospital-acquired infections, UTIs, and pneumonia.

Ciprofloxacin and Levofloxacin are indicated for the treatment of urinary tract infections, respiratory infections, and infections caused by foodborne pathogens such as Salmonella. Azithromycin is frequently prescribed for respiratory infections, skin infections, and sexually transmitted infections, particularly Chlamydia. Clarithromycin is employed for respiratory and skin infections and serves as a component of treatment regimens for Helicobacter pylori. Erythromycin is commonly indicated for respiratory infections, skin infections, and STIs, and it can also serve as an alternative for patients with penicillin allergies.

Tetracyclines and Doxycycline are effective against a wide range of infections, including respiratory infections, Lyme disease, malaria prophylaxis, acne, and certain STIs. Oxazolidinones, including Linezolid, are typically reserved for the treatment of severe infections caused by multidrug-resistant bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE). Lincosamides, including Clindamycin, are indicated for the management of anaerobic infections, skin infections, and respiratory infections, and are also used as prophylaxis in surgical patients with penicillin allergies. Monobactams, such as Aztreonam, are generally prescribed for Gram-negative infections in patients with severe penicillin allergies, including UTIs and lower respiratory tract infections. Nitroimidazoles, including Metronidazole, are commonly used for the treatment of anaerobic bacterial infections, certain parasitic infections, and infections of the abdominal and reproductive systems.

In general, antibiotics are used to treat infections caused by bacteria [4]. Some antibiotics are administered prophylactically before surgery to prevent bacterial infections, particularly in patients with compromised immune systems or specific medical conditions [5]. However, antibiotics are not effective against viral illnesses such as the common cold or influenza, as they are specifically designed to target bacterial infections. The selection of an appropriate antibiotic requires careful consideration of several factors, including the type of infection, the patient's overall health, bacterial resistance patterns, and any known allergies.

3. Methodology

The molecular structure of an antibiotic can be mapped to a unique real number using a topological index, which may be regarded as a real-valued function $\mathcal{S} : G \to \mathbb{R}^+$ defined on a molecular graph. In a chemical structure, atoms are represented as vertices, while the chemical bonds connecting them are represented as edges. Generally, topological indices are classified into two categories: degree-based and distance-based indices. A degree-based topological index depends on the number of bonds associated with each atom, whereas a distance-based topological index considers the distances between atoms in a molecular graph.

In this study, we collected antibiotic drugs including Ampicillin, Amoxicillin, Doxycycline, Cefalexin, Ciprofloxacin, Levofloxacin, Cefotetan, Metronidazole, Cefuroxime, Azithromycin, Clarithromycin, Cefdinir, Meropenem, Imipenem, Linezolid, Clindamycin, Cefotaxime, Erythromycin, Cefixime, Fosfomycin, Nitrofurantoin, Ertapenem, Ceftriaxone, Cefepime, Ceftazidime, Moxifloxacin, Aztreonam, Piperacillin, Fusidic Acid, and Virginiamycin M1, and calculated their corresponding topological index values.

SMILES (Simplified Molecular Input Line Entry System) provides a compact, readable, and standardized method for representing chemical structures as strings of characters, enabling efficient storage, exploration, and manipulation of molecular information in cheminformatics software and databases. This representation facilitates the sharing of chemical information across digital platforms and supports computational tasks such as molecular modeling and structure–property relationship analysis. In SMILES notation, each atom is represented by its chemical element symbol, and chemical bonds are encoded through character-based connections between atoms.

The antibiotic molecules were converted into their corresponding SMILES codes using a Python program, and the associated topological index values were subsequently computed. The antibiotic drugs and their calculated topological indices are presented in Table 1.

4. The physical-chemical characteristics of antibacterial medications

Antibiotic medications possess physicochemical properties that influence their toxicity, distribution, metabolism, excretion, and absorption. These characteristics also determine drug effectiveness, stability, solubility, and interactions with bacterial targets. In this study, Tables 2, 3, and 4 present the physicochemical parameters collected from PubChem.

TABLE 1. Topological indices of antibiotic drugs

Antibiotic Drugs	G_1	G_2	G_3	G_4	G_5	G_6	G_7	G_8	G_9	G_{10}	G_{11}	G_{12}	G_{13}	G_{14}	G_{15}	G_{16}
Ampicillin	73.04	96.81	62.23	29.99	132	161	11.24	370	18.86	1365	10302	65.33	5833	61.02	5657	87.06
Amoxicillin	78.51	101.53	65.88	32.75	138	168	11.63	390	19.68	1551	12264	65.33	6572	63.51	6401	92.03
Doxycycline	104.07	134.66	88.37	44.54	184	237	14.87	532	25.28	2336	16012	72.16	9891	81.84	9646	148.40
Cefalexin	74.19	92.93	57.94	25.49	128	155	11.41	340	18.68	1383	10562	42.14	5960	60.47	5754	86.24
Ciprofloxacin	62.42	96.79	60.06	23.99	134	164	11.56	354	19.21	1234	8270	38.77	5728	62.89	5330	90.59
Levofloxacin	71.80	105.94	66.89	28.60	146	180	12.38	394	20.76	1484	10200	42.14	6643	66.52	6298	104.30
Cefotaxime	132.69	143.04	91.07	43.87	196	241	17.01	540	28.03	4350	45046	85.79	18754	91.47	18098	153.60
Metronidazole	33.98	40.92	25.02	12.49	56	64	5.66	144	8.69	193	884	50.14	645	28.56	712	30.18
Cefixime	107.30	108.81	67.07	29.71	150	179	13.85	392	22.21	2349	20346	46.77	9726	72.17	9584	112.06
Azithromycin	322.77	203.33	133.21	74.73	274	327	23.91	786	39.75	9356	90216	92.78	37245	127.59	37382	280.55
Clarithromycin	323.81	202.95	132.73	74.98	274	330	23.99	786	39.55	9201	87272	92.78	36484	127.62	36694	283.13
Cefdinir	86.68	100.18	62.65	29.29	138	168	12.38	368	19.98	1701	13420	54.77	7145	65.35	6990	97.13
Meropenem	85.02	103.83	66.77	32.62	142	175	12.15	392	20.30	1652	12624	42.14	6758	65.88	6708	98.54
Imipenem	66.40	74.12	45.99	21.68	102	123	9.49	270	15.07	843	5742	50.14	3196	49.50	3303	64.84
Linezolid	75.02	89.86	54.63	22.06	124	144	11.54	316	18.66	1467	12084	42.14	6367	59.61	6126	84.48
Clindamycin	118.58	99.43	62.40	31.95	136	161	12.70	362	20.24	1843	14356	54.77	7131	65.63	7269	102.29
Cefotaxime	113.91	113.53	70.71	32.56	156	186	14.24	412	23.03	2584	22940	50.14	10635	74.67	10420	117.26
Erythromycin	310.39	200.31	131.56	74.13	270	324	23.43	778	39.90	8842	84094	92.78	35135	125.32	35309	274.06
Cefixime	113.91	113.53	70.71	32.56	156	186	14.24	412	23.03	2584	22940	50.14	10549	74.67	10420	117.54
Fosfomycin	14.06	31.99	21.91	13.77	42	48	3.52	130	6.14	261	220	38.96	191	20.84	220	16.08
Nitrofurantoin	48.35	62.85	38.85	17.43	86	98	8.06	222	13.08	580	3894	38.77	2380	41.77	2356	49.92
Ertapenem	112.28	131.12	83.02	37.65	180	219	15.60	486	25.96	3464	34260	42.14	15200	83.79	14537	135.64
Ceftriaxone	133.51	139.60	87.31	39.30	192	231	17.12	510	28.01	4386	45640	50.14	19120	90.53	18340	152.67
Cefepime	106.66	126.80	79.79	36.30	174	210	15.24	472	25.09	3029	27590	57.14	13425	81.28	12774	131.43
Ceftazidime	139.93	144.71	91.19	41.61	198	236	17.49	536	28.94	4573	46076	65.33	19839	93.02	19083	159.80
Moxifloxacin	76.95	119.74	74.84	30.07	166	207	13.99	444	23.33	2006	14662	46.77	9587	76.58	8788	121.88
Aztreonam	123.28	110.41	72.82	40.35	148	174	12.75	430	21.59	2092	16898	80.16	8052	69.23	8232	106.11
Piperacillin	132.39	143.20	91.14	43.23	196	239	16.97	540	28.11	4075	38320	70.96	17678	91.01	17001	156.63
Fusidic Acid	137.35	153.37	100.73	52.52	208	260	17.17	608	29.12	3804	31748	107.12	15759	93.77	15540	175.63
Virginiamycin	180.45	138.62	85.12	37.65	190	217	18.04	488	29.03	4665	43402	42.14	19637	92.67	19165	165.47

TABLE 2. Predicted solubility, absorption, and P-gp substrate properties of antibiotic drugs

Antibiotic drugs	**ESOL Class**	**Ali Log S**	**Ali Solubility (mg/ml)**	**Ali Solubility (mol/l)**	**Ali Class**	**Silicos-IT LogSw**	**Silicos-IT Solubility (mg/ml)**	**Silicos-IT Class**	**GI absorption**	**Pgp substrate**
Ampicillin	4	-1	18.5	0.05	4	-2	2.15	3	1	1
Amoxycillin	4	-1	56.6	0.16	4	-2	8.67	3	1	1
Doxycycline	3	-4	0.05	0	3	-1	18.8	3	1	2
Cefalexine	3	-3	0.26	0	3	-2	1.68	3	2	2
Ciprofloxacine	4	0	334	1.01	4	-4	0.10	3	2	2
Levofloxacine	4	-1	68.6	0.19	4	-3	0.36	3	2	2
Cefotetan	3	-6	0	0	1	0	501	3	1	2
Metronidazole	4	-1	8.74	0.05	4	0	66.9	3	2	1
Cefuroxime	4	-4	0.12	0	3	-1	19.1	3	1	1
Azithromycin	1	-8	0	0	1	-2	4.48	3	1	2
Clarithromycin	2	-7	0	0	1	-3	0.61	3	1	2
Cefdinir	3	-4	0.04	0	3	-1	77.8	3	1	1
Meropenem	4	0	433	1.13	4	0	129	3	1	1
Imipenem	4	-2	4.78	0.02	4	0	210	3	1	1
Linezolid	3	-2	5.86	0.02	4	-3	0.22	3	2	2
Clindamycin	3	-4	0.01	0	2	-1	26.9	3	2	2
Cefotaxime	4	-3	0.56	0	3	-1	18.7	3	1	1
Erythromycin	2	-7	0	0	1	-2	2.85	3	1	2
Cefixime	4	-4	0.06	0	3	-1	81.4	3	1	1
Fosfomycin	3	0	221	1.60	4	1	16	3	2	1
Nitrofurantoin	4	-2	6.00	0.03	4	-1	19.4	3	2	1
Ertapenem	4	-2	6.73	0.01	4	-2	2.89	3	1	1
Ceftriaxone	3	-4	0.02	0	2	-2	4.56	3	1	1
Cefepime	4	-3	0.39	0	3	-3	0.70	3	1	1
Ceftazidime	4	-2	2.41	0	3	-2	2.51	3	1	1
Moxifloxacin	3	-2	4.57	0.01	4	-4	0.05	3	2	2
Aztreonam	3	-5	0.01	0	2	0	282	3	1	2
Piperacillin	3	-4	0.07	0	3	-3	0.90	3	1	2
Fusidic Acid	1	-7	0	0	1	-4	0.03	2	1	2
Virginiamycin M1	2	-5	0	0	2	-4	0.03	2	2	2

5. Correlation analysis for Topological indices and physico chemical properties

Correlation is a statistical measure that indicates the strength of the linear relationship between variables. The strength of this relationship is quantified by the correlation coefficient r. The statistical significance

TABLE 3. Physicochemical and solubility properties of antibiotic drugs

Antibiotic drug	MW	Heavy atoms	Rotatable bonds	H-bond acceptors	H-bond donors	MR	TPSA	iLOGP	ESOL Solubility	ESOL Solubility
Ampicillin	349	24	5	5	3	93	138	1	24.8	0.07
Amoxicillin	365	25	5	6	4	95	158	1	73	0.20
Doxycycline	444	32	2	9	6	111	182	2	0.51	0.00
Cefalexin	347	24	5	5	3	92	138	2	1.92	0.01
Ciprofloxacin	331	24	3	5	2	95	75	2	15.7	0.05
Levofloxacin	361	26	2	6	1	102	75	2	3.72	0.01
Cefotetan	576	36	10	11	4	131	321	1	0.71	0.00
Metronidazole	171	12	3	4	1	43	84	1	17.2	0.10
Cefixime	424	29	9	9	3	100	199	2	5.29	0.01
Azithromycin	749	52	7	14	5	201	180	5	0	0.00
Clarithromycin	748	52	8	14	4	194	183	5	0	0.00
Cefdinir	395	26	6	7	4	98	212	1	3.90	0.01
Meropenem	383	26	6	6	3	104	135	2	177	0.46
Imipenem	299	20	5	5	3	79	142	2	41.4	0.14
Linezolid	337	24	5	5	1	91	71	2	2.03	0.01
Clindamycin	425	27	8	6	4	111	128	3	0.21	0.00
Cefotaxime	455	30	9	9	3	110	227	2	21	0.05
Erythromycin	734	51	7	14	5	189	194	5	0	0.00
Cefixime	453	30	9	9	4	110	238	1	8.02	0.02
Fosfomycin	138	8	1	4	2	26	80	0	240	1.74
Nitrofurantoin	238	17	3	6	1	63	121	0	21.7	0.09
Ertapenem	476	33	8	8	5	128	182	1	15.9	0.03
Ceftriaxone	555	36	9	10	4	134	294	1	4.30	0.01
Cefepime	481	32	8	7	2	127	204	-4	5.27	0.01
Ceftazidime	547	37	10	9	3	136	245	-3	23.2	0.04
Moxifloxacin	401	29	4	6	2	114	84	3	0.79	0.00
Aztreonam	435	28	8	10	4	100	238	0	2.11	0.00
Piperacillin	518	36	9	7	3	139	182	1	0.66	0.00
Fusidic Acid	517	37	6	6	3	146	104	4	0	0.00
Virginiamycin M1	526	38	1	8	2	148	139	2	0.01	0.00

TABLE 4. Drug-likeness, bioavailability, and synthetic accessibility parameters of antibiotic drugs

Antibiotic drugs	log K_p (cm/s)	Lipinski violations	Ghose violations	Veber violations	Egan violations	Muegge violations	Bioavailability Score	Brenk alerts	Leadlikeness violations	Synthetic Accessibility
Ampicillin	-9	0	0	0	1	0	1	0	0	4
Amoxycillin	-10	0	1	1	1	1	1	0	1	4
Doxycycline	-9	1	1	1	1	2	0	1	1	5
Cefalexine	-8	0	0	0	1	0	1	0	0	4
Ciprofloxacine	-9	0	0	0	0	0	1	0	0	3
Levofloxacine	-9	0	0	0	0	0	1	0	1	4
Cefotetan	-10	2	3	1	1	2	0	4	2	5
Metronidazole	-7	0	0	0	0	1	1	2	1	2
Cefuroxime	-9	1	1	1	1	1	0	2	2	5
Azithromycin	-8	2	3	1	1	3	0	0	2	9
Clarithromycin	-9	2	3	1	1	3	0	0	2	9
Cefdinir	-9	0	1	1	1	1	0	3	1	5
Meropenem	-10	0	1	0	1	1	1	0	1	5
Imipenem	-9	0	1	1	1	0	1	2	0	4
Linezolid	-8	0	0	0	0	0	1	0	0	3
Clindamycin	-7	0	0	0	0	0	1	1	2	6
Cefotaxime	-10	1	1	1	1	1	0	2	2	5
Erythromycin	-9	2	3	1	1	3	0	0	1	9
Cefixime	-10	1	1	1	1	1	0	2	2	5
Fosfomycin	-8	0	3	0	0	2	1	2	1	4
Nitrofurantoin	-8	0	1	0	0	0	1	4	1	3
Ertapenem	-10	0	0	1	1	1	0	0	2	5
Ceftriaxone	-11	2	3	1	1	1	0	3	2	5
Cefepime	-10	1	2	1	1	1	1	3	2	5
Ceftazidime	-11	2	3	1	1	2	0	3	2	5
Moxifloxacin	-8	0	0	0	0	0	1	0	1	4
Aztreonam	-9	1	1	1	1	1	0	3	2	4
Piperacillin	-9	2	3	1	1	1	0	1	2	5
Fusidic Acid	-6	1	4	0	0	1	1	2	2	7
Virginiamycin M1	-8	1	3	0	1	0	1	0	1	7

of correlations is examined to determine their reliability. A weaker correlation is indicated when r is close to zero. A positive correlation is represented by a positive r value, meaning that the values of both variables tend to increase together. Conversely, a negative correlation is indicated by a negative r value, meaning that when the value of one variable decreases, the value of the other variable tends to increase. Tables 5 and 6 display the correlations between the topological indices and their physicochemical characteristics.

TABLE 5. Correlation between physicochemical properties of antibiotic drugs and graph indices

Physicochemical Properties	G_1	G_2	G_3	G_4	G_5	G_6	G_7	G_8
MW	0.93	0.98	0.98	0.95	0.98	0.97	0.99	0.97
Heavy atoms	0.94	0.99	0.99	0.95	0.99	0.98	1.00	0.98
Rotatable bonds	0.38	0.46	0.44	0.41	0.46	0.45	0.49	0.44
H-bond acceptors	0.89	0.85	0.85	0.87	0.84	0.83	0.86	0.85
H-bond donors	0.53	0.58	0.60	0.64	0.58	0.60	0.55	0.61
MR	0.92	0.99	0.98	0.94	0.99	0.98	0.99	0.98
TPSA	0.37	0.46	0.44	0.41	0.46	0.45	0.48	0.44
iLOGP	0.53	0.42	0.43	0.48	0.41	0.41	0.41	0.43
ESOL Solubility (mg/ml)	0.35	0.46	0.43	0.33	0.47	0.46	0.49	0.42
ESOL Solubility (mol/l)	0.33	0.47	0.44	0.33	0.48	0.48	0.50	0.43
ESOL Class	0.68	0.62	0.64	0.69	0.61	0.60	0.60	0.64
Ali Log S	0.79	0.77	0.78	0.80	0.77	0.76	0.78	0.78
Ali Solubility (mg/ml)	0.28	0.29	0.27	0.25	0.29	0.27	0.32	0.27
Ali Solubility (mol/l)	-0.34	-0.41	-0.38	-0.32	-0.41	-0.40	-0.45	-0.38
Ali Class	-0.80	-0.76	-0.77	-0.81	-0.76	-0.74	-0.77	-0.77
Silicos-IT LogSw	-0.32	-0.49	-0.47	-0.34	-0.50	-0.50	-0.50	-0.47
Silicos-IT Solubility (mg/ml)	-0.27	-0.40	-0.38	-0.27	-0.42	-0.42	-0.44	-0.37
Silicos-IT Class	-0.14	-0.19	-0.18	-0.15	-0.19	-0.18	-0.20	-0.18
GI absorption	-0.41	-0.52	-0.53	-0.54	-0.52	-0.54	-0.50	-0.54
Pgp substrate	0.41	0.45	0.46	0.44	0.45	0.46	0.43	0.46
log K_p (cm/s)	0.03	-0.11	-0.09	0.00	-0.12	-0.12	-0.12	-0.08
Lipinski violations	0.75	0.79	0.78	0.77	0.79	0.77	0.80	0.78
Ghose violations	0.57	0.57	0.58	0.61	0.57	0.55	0.56	0.58
Veber violations	0.44	0.50	0.49	0.49	0.50	0.49	0.50	0.49
Egan violations	0.42	0.47	0.46	0.44	0.47	0.46	0.48	0.45
Muegge violations	0.70	0.62	0.65	0.74	0.61	0.60	0.58	0.65
Bioavailability Score	-0.47	-0.53	-0.53	-0.51	-0.53	-0.53	-0.54	-0.52
Brenk alerts	-0.24	-0.22	-0.23	-0.21	-0.22	-0.23	-0.21	-0.22
Leadlikeness violations	0.42	0.48	0.48	0.47	0.48	0.47	0.49	0.48

Molecular weight (MW) shows strong correlations with the Estrada index, atom–bond connectivity index, and Randić index, indicating that

TABLE 6. Correlation of physicochemical properties of antibiotic drugs with graph indices G_9–G_{16}

Physicochemical Properties	G_9	G_{10}	G_{11}	G_{12}	G_{13}	G_{14}	G_{15}	G_{16}
MW	0.99	0.95	0.94	0.69	0.96	0.99	0.95	0.97
Heavy atoms	1.00	0.95	0.94	0.68	0.96	1.00	0.96	0.99
Rotatable bonds	0.47	0.41	0.44	0.37	0.43	0.48	0.42	0.40
H-bond acceptors	0.85	0.89	0.89	0.63	0.88	0.85	0.89	0.87
H-bond donors	0.56	0.51	0.50	0.54	0.51	0.57	0.51	0.56
MR	0.99	0.94	0.93	0.66	0.95	0.99	0.95	0.98
TPSA	0.47	0.42	0.45	0.35	0.43	0.47	0.42	0.39
iLOGP	0.41	0.45	0.41	0.35	0.43	0.41	0.44	0.49
ESOL Solubility (mg/ml)	-0.48	-0.34	-0.32	-0.30	-0.35	-0.47	-0.34	-0.41
ESOL Solubility (mol/l)	-0.49	-0.30	-0.28	-0.26	-0.32	-0.49	-0.31	-0.40
ESOL Class	-0.61	-0.66	-0.64	-0.67	-0.65	-0.61	-0.66	-0.67
Ali Log S	-0.78	-0.77	-0.76	-0.78	-0.76	-0.78	-0.77	-0.79
Ali Solubility (mg/ml)	-0.30	-0.28	-0.28	-0.33	-0.29	-0.30	-0.28	-0.28
Ali Solubility (mol/l)	-0.43	-0.32	-0.31	-0.34	-0.33	-0.42	-0.32	-0.37
Ali Class	-0.77	-0.79	-0.78	-0.78	-0.78	-0.77	-0.78	-0.79
Silicos-IT LogSw	-0.50	-0.36	-0.33	-0.15	-0.39	-0.50	-0.37	-0.45
Silicos-IT Solubility (mg/ml)	-0.42	-0.24	-0.21	-0.11	-0.25	-0.42	-0.25	-0.35
Silicos-IT Class	-0.20	-0.14	-0.12	-0.22	-0.15	-0.19	-0.14	-0.19
GI absorption	-0.51	-0.43	-0.44	-0.56	-0.44	-0.51	-0.44	-0.46
Pgp substrate	0.44	0.38	0.34	0.42	0.38	0.44	0.38	0.46
log K_p (cm/s)	-0.12	-0.05	-0.09	0.21	-0.08	-0.12	-0.07	-0.03
Lipinski violations	0.79	0.81	0.83	0.66	0.82	0.79	0.82	0.78
Ghose violations	0.57	0.65	0.67	0.61	0.66	0.57	0.66	0.60
Veber violations	0.49	0.47	0.49	0.40	0.48	0.50	0.47	0.46
Egan violations	0.48	0.42	0.44	0.27	0.43	0.48	0.43	0.42
Muegge violations	0.60	0.73	0.74	0.66	0.72	0.60	0.73	0.68
Bioavailability Score	-0.54	-0.51	-0.52	-0.37	-0.52	-0.54	-0.51	-0.50
Brenk alerts	-0.22	-0.19	-0.15	0.05	-0.18	-0.21	-0.19	-0.25
Leadlikeness violations	0.49	0.46	0.48	0.41	0.47	0.49	0.47	0.45
Synthetic Accessibility	0.87	0.91	0.90	0.68	0.90	0.87	0.91	0.91

these indices effectively capture structural attributes related to molecular size. The number of heavy atoms also exhibits strong correlations with these indices. Molecular refractivity (MR) is highly correlated with the first Zagreb index, Estrada index, atom–bond connectivity index, and Randić index, reflecting the influence of structural features on electronic distribution, as presented in Table 7.

A heatmap of the correlation matrix provides a visual representation that illustrates the strength and direction of relationships among multiple variables in the dataset. This visualization is particularly useful in data analysis and model development, as it facilitates the identification

of highly correlated features and potential multicollinearity issues. The heatmap employs color gradients to represent correlation coefficients between variable pairs, enabling rapid identification of strong positive or negative associations.

As shown in Figure 1, the first Zagreb index and the Balaban index exhibit a near-perfect correlation. The reduced Sombor index, atom–bond connectivity index, Randić index, and first Zagreb index demonstrate strong correlations with several physicochemical properties. In contrast, the average Sombor index shows moderate correlation values ranging from 0.5 to 0.9.

TABLE 7. Inference values for Topological index and physicochemical properties

Properties	G_1	G_2	G_3	G_4	G_5	G_6	G_7	G_8	G_9	G_{10}	G_{11}	G_{12}	G_{13}	G_{14}	G_{15}	G_{16}
MW	0.93	0.98	0.98	0.95	0.98	0.97	0.99	0.97	0.99	0.95	0.94	0.69	0.96	0.99	0.95	0.97
Heavy atoms	0.94	0.99	0.99	0.95	0.99	0.98	1.00	0.98	1.00	0.95	0.94	0.68	0.96	1.00	0.96	0.99
H-bond acceptors	0.89	0.85	0.85	0.87	0.84	0.83	0.86	0.85	0.85	0.89	0.89	0.63	0.88	0.85	0.89	0.87
MR	0.92	0.99	0.98	0.94	0.99	0.98	0.99	0.98	0.99	0.94	0.93	0.66	0.95	0.99	0.95	0.98
Lipinski # violations	0.75	0.79	0.78	0.77	0.79	0.77	0.80	0.78	0.79	0.81	0.83	0.66	0.82	0.79	0.82	0.78
Synthetic Accessibility	0.93	0.87	0.88	0.92	0.86	0.84	0.87	0.87	0.87	0.91	0.90	0.68	0.90	0.87	0.91	0.91

The chemical properties, such as synthetic accessibility, veber violations, lipinski violations, and bioavailability score attains negative correlation. The figure 1 shows that the heatmap is symmetric, as expected for a correlation matrix, with the diagonal showing perfect correlation 1.0.

As shown in Table 7, the Sombor indices exhibit strong correlations with several molecular bulk properties, including molecular weight (MW), the number of heavy atoms, and molecular refractivity (MR). Notably, the Reduced Sombor Index demonstrates the highest overall correlation among these indices. In contrast, the Average Sombor Index shows greater relevance to synthetic accessibility, suggesting that it may be more suitable for evaluating drug-likeness or ease of synthesis. Furthermore, the comparatively lower correlation with hydrogen-bond acceptors indicates that these indices are less sensitive to hydrogen-bonding capacity.

6. FUTURE WORK

In future work, correlation analysis will be integrated with regression models, artificial intelligence techniques, and deep learning frameworks to enhance prediction accuracy. Furthermore, expanding the dataset to include a broader range of antibiotics and validating the results with

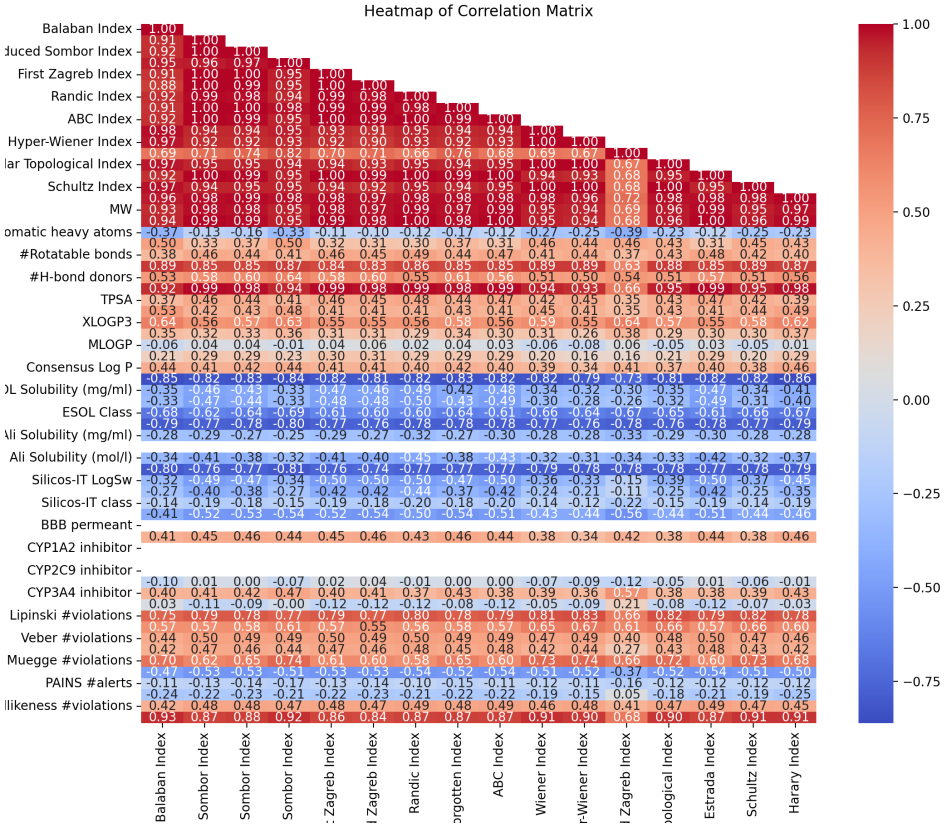


FIGURE 1. Correlation matrix of the topological indices

experimental or clinical data will help establish more reliable computational models. Such developments can significantly contribute to rational drug design, optimization of antibiotic efficacy, and the discovery of novel therapeutic agents.

7. CONCLUSION

The primary objective of this study is to evaluate the effectiveness of computational techniques in predicting the physicochemical characteristics of antibiotic drugs. The comparative analysis reveals that, although the computed topological indices demonstrate meaningful correlations with experimentally reported physicochemical properties, the predictive accuracy of the computational models varies across different drugs. Certain medications exhibit strong agreement between calculated values and

observed properties, whereas others show comparatively weaker consistency.

These observations highlight the necessity of careful validation of computational models employed for drug property prediction. While the computed indices provide useful preliminary estimations, further refinement and optimization of the computational methodologies are required to improve predictive reliability. Continuous research, model enhancement, and systematic validation will contribute to the development of more robust predictive frameworks, thereby supporting efficient drug design, development, and optimization processes.

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