JCBI
Journal of Computing & Biomedical Informatics
ISSN: 2710 - 1606
Volume 07 Issue 02
2024

Research Article
https://doi.org/10.56979/702/2024

Integrative QSPR and VIKOR Multi-Criteria Decision Analysis for Optimizing Anti-Parkinson Drug Candidates

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Received: April 22, 2024 **Accepted**: August 04, 2024 **Published**: September 01, 2024

Abstract: Developing efficient anti-Parkinson medications poses a considerable challenge in the field of pharmacology, necessitating sophisticated techniques for assessing and refining potential therapeutic agents. This research presents a unified method that merges Quantitative Structure-Property Relationship (QSPR) analysis with VIKOR Multi-Criteria decision-making (MCDM) to enhance the selection and refinement of anti-Parkinson drug candidates. QSPR analysis aims to elucidate the connection between molecular descriptors and the pharmacological characteristics of different anti-Parkinson compounds. By pinpointing essential molecular elements that influence both drug efficacy and safety, QSPR models yield predictive insights that direct the design and choice of new drug candidates. Subsequently, the VIKOR method is utilized to prioritize and choose the most promising drug candidates according to their anticipated performance. This method incorporates a range of pharmacological and safety considerations, enabling a balanced evaluation that weighs therapeutic advantages against potential risks. The collaborative QSPR-VIKOR approach facilitates a thorough assessment of drug candidates, reconciling conflicting goals and offering a definitive ranking system for decision-making. By integrating the benefits of both strategies, this study seeks to identify ideal anti-Parkinson drug candidates with improved efficacy and safety profiles. The results offer a solid groundwork for the systematic assessment and enhancement of new therapeutic agents, potentially hastening the creation of more effective treatments for Parkinson's disease and enhancing patient outcomes and their quality of life.

Keywords: Parkinson's Disease; Drugs; Molecular Structure; Topological Index; Linear Regression Model; VIKOR Method.

1. Introduction

Parkinson's is a neurological disorder presented with postural disturbances, resting tremors, and problems with balance and coordination [1]. Parkinson's disorder highly affects the central and peripheral systems of the human body nervous system [2]. It can be recognized as an age-related disease, with its incidence and prevalence rising in tandem with age. The multifactorial interplay between environmental factors and genetics, for example, exposure to environmental toxins, is supposed to play a part in the development of Parkinson's disorder [3]. Therefore, it is thought that genetics and environment contribute to the development of Parkinson's disease [4]. Parkinson's disease is more likely to develop in People having family history of Parkinson's disease, as certain genes are recognized as inheritable risk factors [5]. Other possibilities that increase the accessibility of Parkinson's disease comprise pesticide exposure and a history of head trauma. However, consumption of coffee, tea, or tobacco might reduce the risk of developing Parkinson's [6]. Parkinson's disease typically arises in people above the era of 60, and when it manifests in people under 50 years of age, it is classified as early-onset PD [7]. As of 2015, Parkinson's disease affected approximately 6.2

million individuals and led to roughly 117,400 deaths worldwide [8-9]. The living period of a person after being diagnosed with Parkinson's is 7 to 15 years [10]. The accuracy and precision of early diagnosis of non-physical symptoms such as depression, constipation, eye movement, fatigue, dementia and others can be increased [11].

Quantitative structural property relationship (QSPR) analysis is energetic in the discovery and development of drugs, utilizing mathematical models to forecast properties and activities of molecules based on their chemical structures. QSPR has become indispensable for understanding the connections between molecular descriptors and drug effectiveness, safety, and physicochemical features. This review summarizes recent advancements and research in QSPR analysis for pharmaceuticals, highlighting the newest developments and practical uses. A recent study conducted by Abubakar et al. [12] discovered the usage of degree-based structural indices in QSPR analysis focused on anti-tuberculosis drugs. The findings demonstrated that distance-based indices can accurately predict these properties, revealing insights into the molecular aspects that influence drug behavior under different conditions. The study identified significant correlations between the topological indices and drug characteristics, providing a useful framework for the assessment and improvement of new malaria treatments.

The topological index is a mathematical parameter which converts a structural configuration into a numeric value. Topological indices serve as a crucial instrument for analyzing the physicochemical characteristics of chemical substances, offering insights into their molecular structures. In the following research, degree-based topological indices were applied to explore medications used for Parkinson's disease. The formulas of these drugs were modelled as graphs, where the elements represented by vertices and the bond between elements are signified the bonds. The calculation of these indices enables chemists and pharmacists to use graph theory in the process of new drug discoveries. Furthermore, assessing the topological indices of a drug's structure can yield useful insights into its physical and biological properties [13-15].

The results underscored the effectiveness of linear regression in deciphering the connection between molecular structure and these physical characteristics, which assists in pinpointing potential drug candidates.

Also, Aslam et al. [16], utilized linear regression models in their QSPR assessment to examine hexagonal close-packed crystal lattices. Therefore, chemical graph theory emerges as a potent method for determining topological indices, acting as a reliable predictor for the physicochemical and biological behaviors of molecular compounds [17- 26].

Multi-criteria decision-making (MCDM) methods can be categorized in several ways, including linear/non-linear models and interplanetary decision individualities[27].In our research, we use a highly compatible technique known as VIKOR. The VIKOR method was established for multi-criteria optimization of complex systems. It controls the trade-off list and the trade-off solution achieved with the initial known weights. For the best ranking of Parkinson's targeting drug VIKOR method employs the QSRP study analysis. The VIKOR method is used in various fields, such as Engineering and manufacturing for selecting the best design or process. Environmental management for evaluating sustainability options. Healthcare for prioritizing treatment plans. Business and economics for strategic planning and investment decisions.

Hui et al. [28] Implement QSPR analysis through multiple regression modelling toward nanotubes. Farooq, F. B [29] utilized multi-criteria decision-making for the ranking of treatments for bone cancer. Yali li *et al*. used the VIKOR method for the decision-making of anticancer drugs [30].

The recent trend in drug development has seen an increasing reliance on multiple-choice decision-making frameworks [31-33]. Recent advancements in QSPR analysis have significantly improved the technique's predictive capabilities and its application in new pharmaceutical candidates, ultimately aiding in the growth of more effective and safer therapeutic cures. The combination of various topological indices with sophisticated modelling techniques, such as multigraph representations and linear regression, has deepened our insight into the assembly between molecular structure and drug characteristics. For example, Zaman et al. [34] explored new medications for treating blood cancer by employing degree-based topological indices and regression analysis.

Similarly, Mahboob et al [35] utilized QSPR methodologies to evaluate the physicochemical traits of anti-hepatitis drugs through linear regression. Additionally, Zhang et al. [36] conducted a QSPR analysis using

topological indices to investigate treatments for schizophrenia. Such methodologies streamline the selection process, allowing researchers to assess drug candidates against defined criteria, thus enhancing efficiency and promoting informed decision-making.

In this study, we familiarize readers with several topological indices relevant to understanding the physicochemical properties of medications necessary for Parkinson's disease. In the realm of chemical graph theory, drugs are depicted using molecular graphs, with vertices symbolizing atoms and edges representing the bonds between them. We can view the drug structure as a graph $\Theta = \Theta(V, E)$, where the degree of vertices is represented by d_u, indicating the number of connections for vertex u, and d_v for vertex v. The indices we utilized are described by the subsequent formulas, which are based on the degrees of the vertices:

- First and Second Zagreb [$M_1(\Theta)$ and $M_2(\Theta)$] indices were proposed by Trinajestic and Gutman [37]:

$$M_1(\Theta) = \sum_{uv \in E} [d_u + d_v],$$

$$M_2(\Theta) = \sum_{uv \in E} [d_u d_v],$$

- Randic index [$\chi(\Theta)$] was the invention of Milan Randič [38]:

$$\chi(\Theta) = \sum_{uv \in E} \frac{1}{\sqrt{d_u d_v}},$$

- Atom Bond Connectivity index [ABC(Θ)] was proposed by a mathematician Estrada et al.[39]:

$$\sum_{uv \in E} \sqrt{\frac{d_u + d_v + 2}{d_u d_v}}$$

- Sum Connectivity index [SCI(Θ)] introduced by Zhou and Trinjstic[40]:

$$SCI(\Theta) = \sum_{uv \in E} \frac{1}{\sqrt{d_u + d_v}},$$

- Geometric Arithmetic index [$GA(\Theta)$] introduced by Vukicevic et al.[41]:

$$GA(\Theta) = \sum_{uv \in E} \frac{2\sqrt{d_u d_v}}{d_u + d_v},$$

- Harmonic index [$H(\Theta)$] proposed by Fajtlowicz[42]:

$$H(\Theta) = \sum_{uv \in E} \frac{2}{[d_u + d_v]},$$

- Hyper Zagreb index [HM(Θ)] was proposed by Shirdel et al.[43]:

$$HM(\Theta) = \sum_{uv \in E} (d_u + d_v)^2,$$

- Forgotten index [F(Θ)] proposed by Furtula et al. [44]:

$$F(\Theta) = \sum_{uv \in E} \left({d_u}^2 + {d_v}^2\right),$$

Topological indices (TIs) were first explored for the coding of alkenes [45]. QSAR and QSPR models play a vibrant role in anticipating new ideal compounds' biological activity or properties grounded on their chemical arrangements. This predictive capability reduces the necessity for extensive and costly lab experiments, enabling researchers to focus their efforts on the most promising candidates. By shedding light on the connection between chemical structure and biological activity or physical properties, QSAR and QSPR models assist in refining drug candidates to improve effectiveness and reduce side effects. They allow for the early evaluation of compound libraries, helping researchers to prioritize those with a greater chance of success, thereby speeding up the drug discovery process. Furthermore, regulatory bodies may require QSPR assessments to estimate the potential toxicity or environmental effects of drug candidates. QSAR and QSPR analyses are essential tools in drug development, enhancing efficiency, lowering costs, and boosting the overall success rate of new drug creation. Recent research continues to utilize topological indices and QSPR analysis

in drug discovery and development [46-48]. These studies underscore the ongoing consequence and promise of QSPR analysis in field of drug development and discovery.

2. Material and Methods

2.1. QSPR analysis using Linear Regression:

In this section, we discussed the degree-based topological indices computed for chemical structures of treatments for Parkinson's disease. The discussion centers on QSPR analysis concerning specific topological descriptors, which have been found to correlate strongly with the properties of the biochemical compounds utilized in Parkinson's treatment. The current study developed QSPR analysis through linear regression to explore the connection between the physicochemical properties of Parkinson's drugs with topological indices. The molecular structures of Parkinson's drugs were retrieved from the PubChem database.

The PubChem CID number was used as an identifier to obtain the 2D structure in SDF format from PubChem. The SDF files of the molecules were then imported into the ChemBioDraw [49] software to evaluate the degree-based topological indices via built-in Topological Indices Calculator.

For this analysis, we considered the drugs with their drug bank IDs Apomorphine(DB00714), Biperiden(DB00810), Carbidopa(DB00190), Entacapone(DB00494), Lergotrile(D04693), levodopa(DB00190), Orphenadrine(DB01173), Pergolide(DB01186), Pramipexole(DB00413), Rasagiline(DB01367), Ropinirole(DB00268), Selegiline(DB01037), Tolcapone(DB00323), and Trihexyphenidyl(DB00376) which are being used for Parkinson's treatment. These drugs with their chemical structure are shown in Figure 1.

These molecular structures of Parkinson's drug are considered as a chemical diagram having elements taken as vertices and the bonds between elements are taken as edges.Physicochemical properties are vital in QSPR modelling for drug design, impacting drug absorption, distribution, metabolism, and toxicity prediction [50]. They guide formulation design, affecting bioavailability and stability, and are crucial for regulatory compliance and predicting drug interactions [51] QSPR modelling utilizes these properties to optimize drug efficacy, safety, and development processes. The physic-chemical properties which are used to build QSPR model are Boiling point (BP), Melting point (MP), Flashpoint (FP), Complexity(C), Enthalpy of vaporization (EV), Molar refractivity (MR), Refractive index (RI), Molecular weight (MW), Density(D) and Molar volume (MV) extracted from ChemSpider [52-26] and PubChem [53] are summarized in Table 1.

The calculated degree-based topological descriptors were then used as independent variables, while physio-chemical attributes of the Parkinson's drugs were used as the dependent variable in the linear regression modelling. The linear regression model was developed by SPSS [54] and validated using the test set under the following equation:

$$Y = A + b(TI)$$

Here Y is the indication of physicochemical property, TI is an abbreviation of topological index, A is being a constant with b as regression coefficient. The performance of the model was evaluated using certain statistical parameters such as correlation coefficient (r), F-test value (F), significance level (P), number of sample (N) and coefficient of determination (r^2).

Table 1. Physical properties associated with treatments for Parkinson's disease.

Drug's name	BP ^oC	MP ^oC	FP ^oC	C	EV kJ/mol	MR cm^3	RI	MW g/mol	D g/cm^3	MV cm^3
Apomorphine	473.4	195	268.8	374	76.5	77.9	1.682	267.32	1.3	205.6
Biperiden	462.1	114	224.5	422	76.2	94.1	1.583	311.5	1.1	281.7
Carbidopa	528.7	203	273.5	261	84.6	57.5	1.641	226.23	1.4	159.3
Entacapone	526.6	162	272.3	500	83.1	79.1	1.642	305.286	1.4	219.2
Lergotrile	528		273.1	458	80.3	85.0	1.637	299.798	1.265	236.9

levodopa	448.4	295	225	209	74.5	49.3	1.654	197.19	1.5	134.3
Orphenadrine	363	132	107.1	260	60.9	84.4	1.549	269.4	1.027	265.5
Pergolide	491.3	207.5	250.9	388	75.8	97.4	1.614	314.5	1.1	279.6
Pramipexole	378	288	182.4	188	62.6	60.3	1.583	211.33	1.2	180.5
Rasagiline	305.5	155	146.8	212	54.6	53.9	1.577	171.24	1.1	162.7
Ropinirole	410.5	246.5	202.0	287	66.3	78.4	1.539	260.37	1.0	250.2
Selegiline	272.5	141	108.4	195	51.1	60.5	1.529	187.28	1.0	196.2

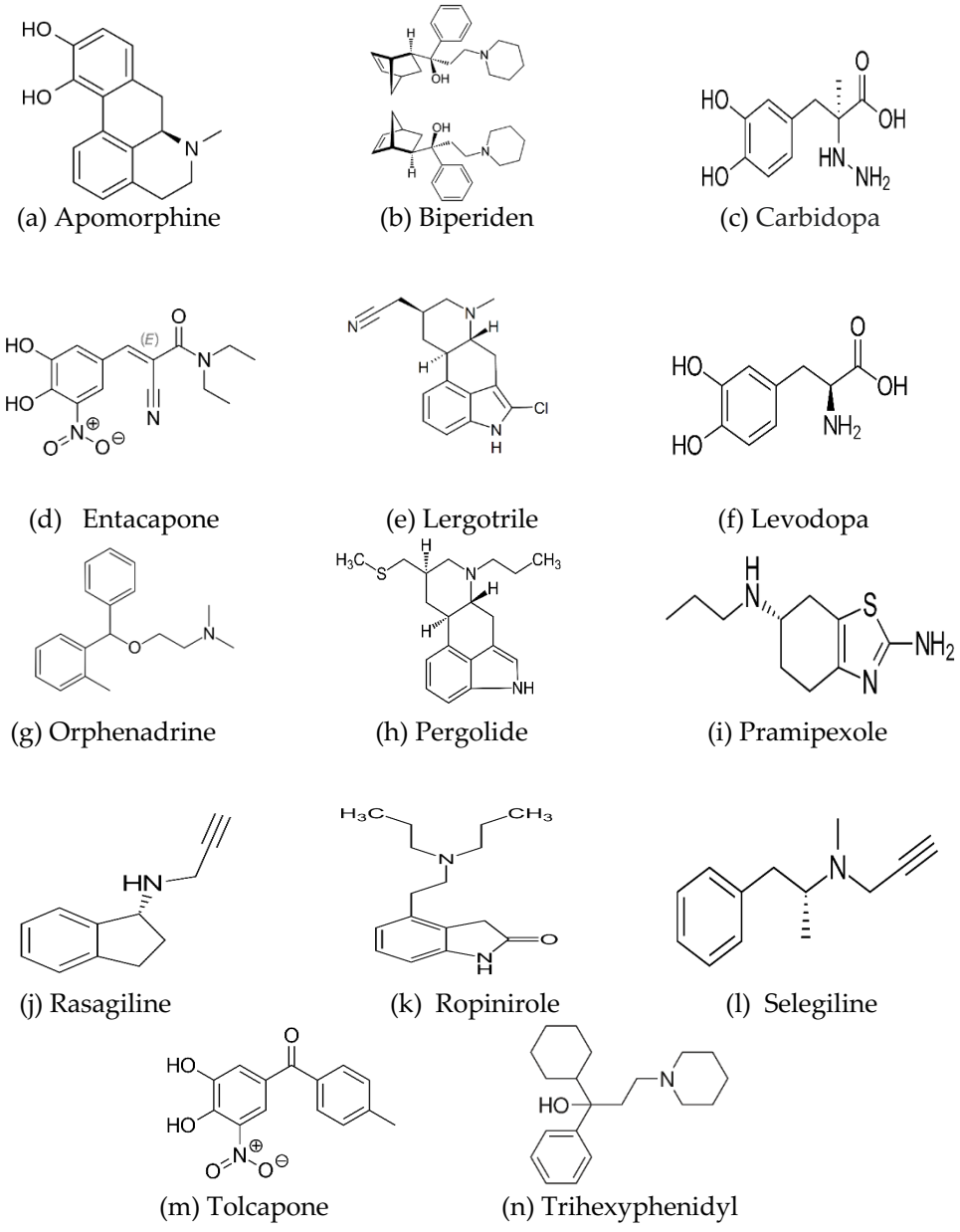


Figure 1. Parkinson's drugs with their chemical structures.

2.2. MCDM techniques

The main idea of VIKOR is to identify an ideal closest solution, considering a compromise among the criteria. This means finding a solution that provides the best trade-off. VIKOR ranks the alternatives and

suggests a compromise solution by considering the distance of each alternative from the ideal and the anti-ideal solutions. The VIKOR method has following steps for completion.

- Determine t_i^+(ideal best) and t_i^-(ideal worst) values for all function models that we consider as estimation tools, where $\{i = P_i, i = 1,\ldots., 6\}$.
  - $t_i^+ := \{\max\{t_{ij}, j = 1,\ldots., j\}, \min\{t_{ij}, j = 1,\ldots., j\}$:if beneficial is ith function$\}$
  - $t_i^- := \{\min\{t_{ij}, j = 1,\ldots., j\}, \max\{t_{ij}, j = 1,\ldots., j\}$:if unbeneficial is ith function$\}$
- Determine the S_j and R_j values where , $j = 1,\ldots.,$ j. we have the following parameters.
  - $S_j := \sum_{j=1}^{m} \left[w_i \times \frac{(t_i^+ - t_{ij})}{(t_i^+ - t_i^-)}\right]$
  - $R_j := max\left[w_i \times \frac{(t_i^+ - t_{ij})}{(t_i^+ - t_i^-)}\right]$
- Determine the Q_j values where , $j = 1,\ldots.,$ j , through the following formulation.
  - $Q_j := \left[v \times \frac{(S_j - S^+)}{(S^- - S^+)}\right] + \left[(1 - v) \times \frac{(R_j - R^+)}{(R^- - R^+)}\right]$

Whereas $(1 - v)$ is the weight of the distinct regret. This tactic might be demoralized by $v = 0.5$
Sort the options according to S, R, and Q values., starting from the smallest value.
Furthermore, Microsoft Excel uses the VIKOR techniques to attain outcomes generated from QSPR modelling through regression analysis.

3. Results and Discussion

We have considered two-dimensional graphs of drugs because they offer a simplified yet informative representation of molecular geometry, facilitating the calculation of topological indices. Topological indices computed for these drugs are shortened in Table 2. Figure 2 represents the 2D graph of topological indices vs the drugs used for Parkinson's. The models are investigated using fourteen medications and nine topological indices. A linear regression model correlation coefficient (R) is attained among these indices and physicochemical properties. The model with the maximum correlation coefficient (R) is considered the most accurate predictor of the regression model.

Table 2. Topological indices related to Drugs for Parkinson's.

Drug's name	$ABC(\Theta)$	$RA(\Theta)$	$M_1(\Theta)$	$M_2(\Theta)$	$HM(\Theta)$	$H(\Theta)$	$SCI(\Theta)$	$F(\Theta)$	$GA(\Theta)$
Apomorphine	16.268	9.665	116	145	600	9.366	10.343	310	22.436
Biperiden	18.380	11.254	126	151	630	11.04	11.938	328	25.500
Carbidopa	11.808	7.386	78	89	396	6.852	7.363	218	14.981
Entacapone	15.901	10.348	104	120	512	9.767	10.298	272	20.976
Lergotrile	16.906	10.185	120	149	616	9.9	10.855	318	23.453
Levodopa	10.365	6.5029	66	73	318	6.067	6.499	172	13.208
Orphenadrine	15.056	9.682	96	108	450	9.4	9.908	234	20.476
Pergolide	17.435	10.813	122	150	614	10.63	11.470	314	24.643
Pramipexole	10.675	6.7920	70	80	334	6.6	7.011	174	14.627
Rasagiline	9.818	6.415	64	74	302	6.334	6.629	154	13.842
Ropinirole	14.170	9.2407	92	105	436	9	9.443	226	19.549
Selegiline	9.8707	6.736	62	67	282	6.5	6.722	148	13.574
Tolcapone	15.303	9.396	102	119	508	8.867	9.618	270	20.034
Trihexyphenidyl	17.006	10.788	112	130	542	10.60	11.241	282	23.580

3.1. Regression Models and Computation of Statistical Parameters

The nine degree-based topological indices are used to model ten physical properties of the fourteen drugs for Parkinson's. The following are the linear regression models of the physical properties of different drugs used to treat Parkinson's. This section uses the QSPR model to establish a connection between the statistical parameter for Parkinson's medication computation and its physicochemical characteristics.

Topological indices are considered independent variables, while the physicochemical properties are dependent. Tables 3-11 include the statistical parameters of the linear regression model of topological indices with statistical parameters N, A, b, r, F and P.

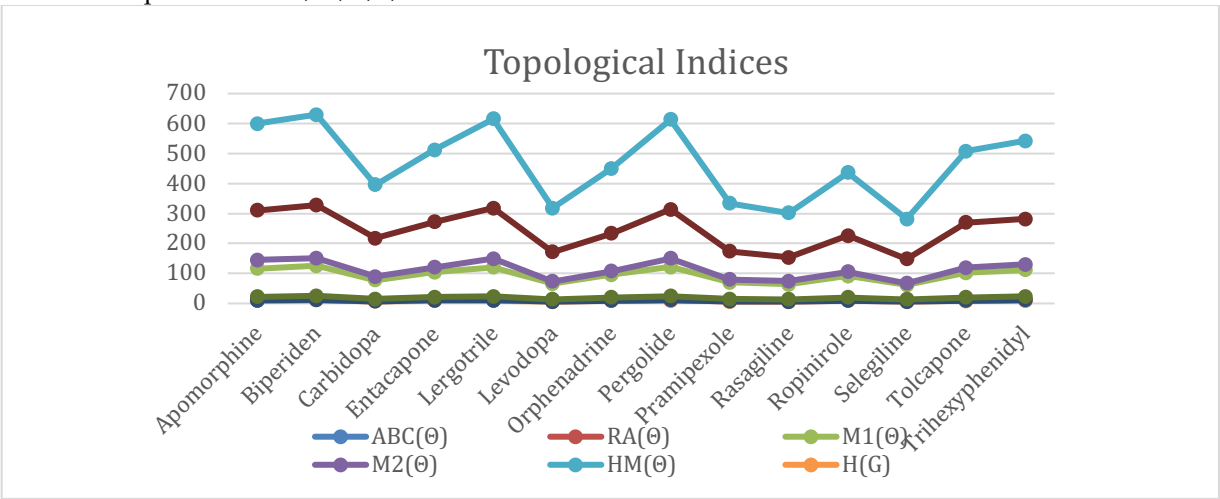


Figure 2. 2D graph of TIs with drug.

1. **Regression model and statistical parameter of Atom Bond Connectivity index [ABC(Θ)]:**

BP=205.161+ 16.331 [ABC(Θ)]
MP = 270.836-5.478 [ABC(Θ)]
FP =83.077+8.989 [ABC(Θ)]
C= -84.189+28.239 [ABC(Θ)]
EV =43.080+1.989 [ABC(Θ)]
MR= 6.093+4.803 [ABC(Θ)]
RI=1.562+0.003 [ABC(Θ)]
MW= 34.185+15.669 [ABC(Θ)]
D=1.285-0.006 [ABC(Θ)]
MV=29.167+13.297 [ABC(Θ)]

Table 3. Statistical parameters of linear regression model for ABC(Θ) index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	205.161	16.331	.617	.380	7.370	.019
Melting Point	13	270.836	-5.478	.273	.074	.885	.367
Flash Point	14	83.077	8.989	.480	.230	3.587	.083
Complexity	14	-84.189	28.239	.846	.715	30.116	.000
Enthalpy	14	43.080	1.989	.584	.341	6.202	.028
Molar Refractivity	14	6.093	4.803	.938	.881	88.536	.000
Refractive index	14	1.562	.003	.175	.030	.377	.551
Molecular weight	14	34.185	15.669	.975	.951	230.688	.000
Density	14	1.285	-.006	.103	.011	.129	.726
Molar volume	14	29.167	13.297	.814	.662	23.548	.000

2. **Regression model and statistical parameter of Randic index [RA(Θ)]:**

BP =209.013+25.520 [RA(Θ)]
MP =281.614-9.889 [RA(Θ)]
FP=92.445+13.236 [RA(Θ)]
C =-110.740+47.843 [RA(Θ)]
EV=43.724+3.089 [RA(Θ)]

MR= -1.394+8.469 [RA(Θ)]
RI= 1.585+0.002 [RA(Θ)]
MW= 13.926+27.164 [RA(Θ)]
D=1.359-0.018 [RA(Θ)]
MV=.289+24.358 [RA(Θ)]

Table 4. Statistical parameters of linear regression model for RA(Θ) index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	209.013	25.520	.559	.313	5.457	.038
Melting Point	13	281.614	-9.889	.289	.084	1.004	.338
Flash Point	14	92.445	13.236	.410	.168	2.421	.146
Complexity	14	-110.740	47.843	.831	.690	26.772	.000
Enthalpy	14	43.724	3.089	.526	.276	4.584	.053
Molar Refractivity	14	-1.394	8.469	.960	.921	140.390	.000
Refractive index	14	1.585	.002	.069	.005	.057	.816
Molecular weight	14	13.926	27.164	.980	.961	296.561	.000
Density	14	1.359	-.018	.181	.033	.404	.537
Molar volume	14	.289	24.358	.865	.748	35.595	.000

3. Regression model and statistical parameter of Sum connectivity index [SCI(Θ)]:

BP=230.390+22.390 [SCI(Θ)]
MP=272.368-8.585 [SCI(Θ)]
FP =99.381+12.062 [SCI(Θ)]
C=-75.341+42.482 [SCI(Θ)]
EV=46.545+2.685 [SCI(Θ)]
MR=3.320+7.688 [SCI(Θ)]
RI=1.584+0.002 [SCI(Θ)]
MW= 33.321+24.197 [SCI(Θ)]
D =1.365-0.018 [SCI(Θ)]
MV=14.890+21.999 [SCI(Θ)]

Table 5. Statistical parameters of linear regression model for SCI(Θ) index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	230.390	22.390	.544	.296	5.057	.044
Melting Point	13	272.368	-8.585	.277	.076	.911	.360
Flash Point	14	99.381	12.062	.414	.172	2.489	.141
Complexity	14	-75.341	42.482	.819	.671	24.448	.000
Enthalpy	14	46.545	2.685	.507	.257	4.157	.064
Molar Refractivity	14	3.320	7.688	.967	.935	173.605	.000
Refractive index	14	1.584	.002	.078	.006	.074	.790
Molecular weight	14	33.321	24.197	.969	.940	186.515	.000
Density	14	1.365	-.018	.202	.041	.509	.489
Molar volume	14	14.890	21.999	.867	.752	36.307	.000

4. Regression model and statistical parameter of First Zagreb index [M_1(Θ)]:

BP =223.717+2.248 [M1(Θ)]
MP =259.723-0.705 [M1(Θ)]
FP = 84.124+1.334 [M1(Θ)]
C=-42.987+3.791 [M1(Θ)]
EV = 45.515+0.272 [M1(Θ)]

MR=15.268+0.622 [M1(Θ)]
RI= 1.552+0.001 [M1(Θ)]
MW= 63.957+2.031 [M1(Θ)]
D =1.251-0.001 [M1(Θ)]
MV=59.823+1.666 [M1(Θ)]

Table 6. Statistical parameters of linear regression model for $M_1(\Theta)$ index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	223.717	2.248	.640	.409	8.321	.014
Melting Point	13	259.723	-.705	.260	.068	.797	.391
Flash Point	14	84.124	1.334	.536	.288	4.849	.048
Complexity	14	-42.987	3.791	.856	.732	32.784	.000
Enthalpy	14	45.515	.272	.601	.362	6.802	.023
Molar Refractivity	14	15.268	.622	.916	.839	62.468	.000
Refractive index	14	1.552	.001	.245	.060	.766	.399
Molecular weight	14	63.957	2.031	.952	.907	116.993	.000
Density	14	1.251	-.001	.068	.005	.056	.816
Molar volume	14	59.823	1.666	.769	.591	17.347	.001

5. Regression model and statistical parameter of Second Zagreb index [$M_2(\Theta)$]:

BP =248.777+1.691 [M2(Θ)]
MP =249.125-0.507 [M2(Θ)]
FP =93.106+1.056 [M2(Θ)]
C =2.143+ 2.827 [M2(Θ)]
EV=48.712+0.203 [M2(Θ)]
MR=23.968+0.452 [M2(Θ)]
RI=1.549+0.000 [M2(Θ)]
MW=92.730+1.473 [M2(Θ)]
D=1.231+0.000 [M2(Θ)]
MV=86.538+1.181 [M2(Θ)]

Table 7. Statistical parameters of linear regression model for $M_2(\Theta)$ index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	248.777	1.691	.643	.413	8.459	.013
Melting Point	13	249.125	-.507	.246	.061	.709	.418
Flash Point	14	93.106	1.056	.567	.322	5.698	.034
Complexity	14	2.143	2.827	.852	.726	31.774	.000
Enthalpy	14	48.712	.203	.600	.360	6.750	.023
Molar Refractivity	14	23.968	.452	.889	.791	45.292	.000
Refractive index	14	1.549	.000	.292	.085	1.118	.311
Molecular weight	14	92.730	1.473	.922	.851	68.523	.000
Density	14	1.231	.000	.047	.002	.026	.874
Molar volume	14	86.538	1.181	.728	.529	13.497	.003

6. Regression model and statistical parameter of Forgotten Zagreb index [$F(\Theta)$]:

BP=212.209+0.921 [F(Θ)]
MP=253.226-0.248 [F(Θ)]
FP=72.519+0.566 [F(Θ)]
C=-27.118+1.409 [F(Θ)]

EV=43.670+0.113 [F(Θ)]
MR=22.753+0.211 [F(Θ)]
RI=1.533+0.000 [F(Θ)]
MW=80.297+0.723 [F(Θ)]
D =1.168+0.000 [F(Θ)]
MV=87.106+0.536 [F(Θ)]

Table 8. Statistical parameters of linear regression model for [F(Θ)].

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	212.209	.921	.723	.523	13.179	.003
Melting Point	13	253.226	-.248	.250	.063	.734	.410
Flash Point	14	72.519	.566	.628	.395	7.823	.016
Complexity	14	-27.118	1.409	.877	.770	40.140	.000
Enthalpy	14	43.670	.113	.691	.478	10.985	.006
Molar Refractivity	14	22.753	.211	.858	.736	33.498	.000
Refractive index	14	1.533	.000	.359	.129	1.777	.207
Molecular weight	14	80.297	.723	.935	.874	83.569	.000
Density	14	1.168	.000	.052	.003	.032	.861
Molar volume	14	87.106	.536	.683	.466	10.472	.007

7. Regression model and statistical parameter of Harmonic Index [H(Θ)]:

BP =238.035+23.063 [H(Θ)]
MP =275.771-9.561 [H(Θ)]
FP = 107.841+11.922 [H(Θ)]
C =-80.518+46.038 [H(Θ)]
EV=47.574+2.753 [H(Θ)]
MR=0.137+8.591 [H(Θ)]
RI=1.599+0.000 [H(Θ)]
MW=26.021+26.726 [H(Θ)]
D=1.410-0.024 [H(Θ)]
MV=1.084+25.128 [H(Θ)]

Table 9. Statistical parameters of linear regression model for H(Θ) index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	238.035	23.063	.507	.257	4.142	.065
Melting Point	13	275.771	-9.561	.280	.079	.937	.354
Flash Point	14	107.841	11.922	.370	.137	1.903	.193
Complexity	14	-80.518	46.038	.802	.643	21.582	.001
Enthalpy	14	47.574	2.753	.470	.221	3.397	.090
Molar Refractivity	14	.137	8.591	.976	.953	243.350	.000
Refractive index	14	1.599	.000	.015	.000	.003	.961
Molecular weight	14	26.021	26.726	.967	.935	172.959	.000
Density	14	1.410	-.024	.249	.062	.793	.391
Molar volume	14	1.084	25.128	.894	.800	48.005	.000

8. Regression model and statistical parameter of Hyper Zagreb index [HM(Θ)]:

BP =229.544+0.445 [HM(Θ)]
MP =251.514-0.126 [HM(Θ)]
FP =82.211+0.275 [HM(Θ)]
C =-14.197+0.709 [HM(Θ)]

EV =46.080+0.054 [HM(Θ)]
MR=23.074+0.110 [HM(Θ)]
RI=1.541+0.000 [HM(Θ)]
MW=85.612+0.367 [HM(Θ)]
D=1.200+(4.494E-6) [HM(Θ)]
MV=86.058+0.283 [HM(Θ)]

Table 10. Statistical parameters of linear regression model for HM(Θ) index.

Physiochemical Property	N	A	b	r	r^2	F	P
Boiling Point	14	229.544	.445	.686	.470	10.641	.007
Melting Point	13	251.514	-.126	.249	.062	.726	.412
Flash Point	14	82.211	.275	.600	.360	6.742	.023
Complexity	14	-14.197	.709	.867	.752	36.332	.000
Enthalpy	14	46.080	.054	.648	.420	8.686	.012
Molar Refractivity	14	23.074	.110	.875	.766	39.383	.000
Refractive index	14	1.541	.000	.327	.107	1.435	.254
Molecular weight	14	85.612	.367	.931	.867	78.284	.000
Density	14	1.200	4.494E-6	.003	.000	.000	.991
Molar volume	14	86.058	.283	.706	.499	11.956	.005

9. Regression model and statistical parameter of Arithmetic Geometric index [GA(Θ)]:

BP =245.781+9.896 [GA(Θ)]
MP =264.509-3.698 [GA(Θ)]
FP =103.532+5.545 [GA(Θ)]
C=-45.919+18.764 [GA(Θ)]
EV=48.559+1.178 [GA(Θ)]
MR=8.456+3.405 [GA(Θ)]
RI=1.580+0.001 [GA(Θ)]
MW=51.446+10.617 [GA(Θ)]
D=1.355-0.008 [GA(Θ)]
MV=31.441+9.649 [GA(Θ)]

Table 11. Statistical parameters of linear regression model for GA(Θ) index.θ

Physiochemical Property	N	A	b	r	r^2	F	p
Boiling Point	14	245.781	9.896	.541	.292	4.954	.046
Melting Point	13	264.509	-3.698	.265	.070	.834	.381
Flash Point	14	103.532	5.545	.428	.183	2.691	.127
Complexity	14	-45.919	18.764	.813	.660	23.325	.000
Enthalpy	14	48.559	1.178	.500	.250	3.997	.069
Molar Refractivity	14	8.456	3.405	.962	.926	150.266	.000
Refractive index	14	1.580	.001	.101	.010	.124	.731
Molecular weight	14	51.446	10.617	.955	.913	125.459	.000
Density	14	1.355	-.008	.203	.041	.514	.487
Molar volume	14	31.441	9.649	.854	.730	32.370	.000

The correlation coefficients between physicochemical properties and Tis are depicted in table 12 and Figure 3 depicts a graph of the correlation coefficient of Parkinson's drugs.

Table 12. Correlation coefficient for physical properties of the drugs.

TIs	BP	MP	FP	C	EV	MR	RI	MW	D	MV
ABC(Θ)	.617	-.273	.480	.846	.584	.938	.175	.975	-.103	.814

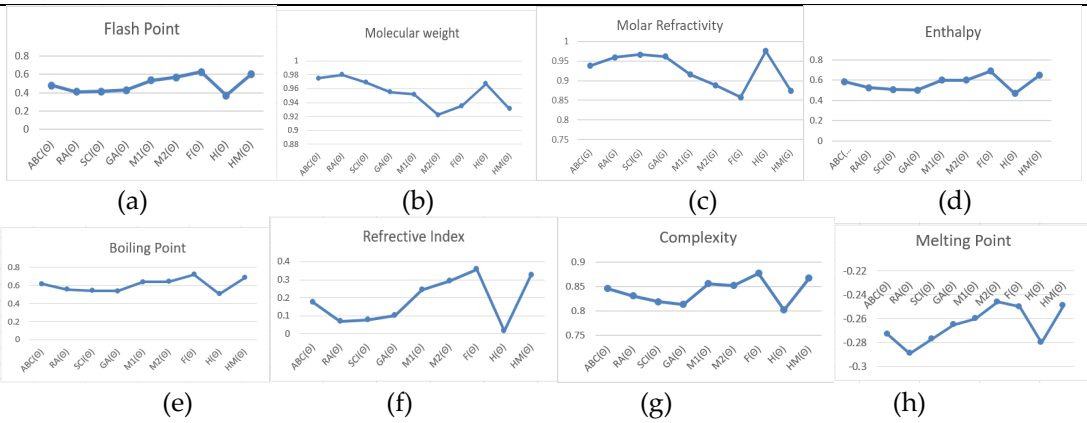
RA(Θ)	.559	-.289	.410	.831	.526	.960	.069	.980	-.181	.865
SCI(Θ)	.544	-.277	.414	.819	.507	.967	.078	.969	-.202	.867
GA(Θ)	.541	-.265	.428	.813	.500	.962	.101	.955	-.203	.854
M1(Θ)	.640	-.260	.536	.856	.601	.916	.245	.952	-.068	.769
M2(Θ)	.643	-.246	.567	.852	.600	.889	.292	.922	-.047	.728
F(Θ)	.723	-.250	.628	.877	.691	.858	.359	.935	.052	.683
H(Θ)	.507	-.280	.370	.802	.470	.976	.015	.967	-.249	.894
HM(Θ)	.686	-.249	.600	.867	.648	.875	.327	.931	.003	.706

3.2. Calculation of Standard Error of Estimation

As seen in Table 13, a standard error of estimate is an indicator of deviation for an observation computed around the computed regression line that evaluates the degree of accuracy of predictions computed around the regression line.

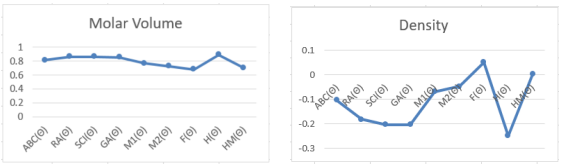
Table 13. Std. error of the estimate for physical properties of the drugs.

TIs	BP	MP	FP	C	EV	MR	RI	MW	D	MV
ABC(Θ)	66.726	62.509	52.647	57.079	8.860	5.662	.05206	11.443	0.179	30.394
RA(Θ)	70.287	62.197	54.734	59.490	9.282	4.598	.05275	10.148	0.177	26.267
SCI(Θ)	71.107	62.440	54.606	61.357	9.404	4.166	.05271	12.653	0.176	26.073
GA(Θ)	71.323	62.645	54.228	62.325	9.451	4.456	.05260	15.205	0.176	27.205
M_1(Θ)	65.146	62.741	50.636	55.353	8.717	6.578	.05126	15.696	0.179	33.451
M_2(Θ)	64.926	62.978	49.406	55.988	8.729	7.499	.05056	19.866	0.180	35.888
F(Θ)	58.525	62.910	46.684	51.300	7.884	8.416	.04935	18.236	0.179	38.227
H(Θ)	73.093	62.372	55.743	63.922	9.634	3.552	.05286	13.108	0.174	23.394
HM(Θ)	61.718	62.932	48.011	53.283	8.311	7.919	.04996	18.762	0.180	37.024



(a) (b) (c) (d)

(e) (f) (g) (h)



(i) (j)

Figure 3. Correlation coefficient graphs of physiochemical properties: (a) Flash point (b) Molecular weight(c) Molar refractivity (d) enthalpy(e) Boiling point (f) Refractive index (i) Complexity (h) Melting point (i) Molar volume (j) density with topological indices.

4. Implementation of VIKOR Method

In this technique of VIKOR, we will utilize the main results obtained from the QSPR model. Here we have considered the regression standard error (SE) and correlation coefficients (r) values among the properties MW (molecular weight) and MV (molar volume) with all topological indices each numerically representing some correlation value shown in Table 1A. if the r value is closer to 1 with a low standard error, then there will be a good correlation between chemical indices to envisage targeted properties.

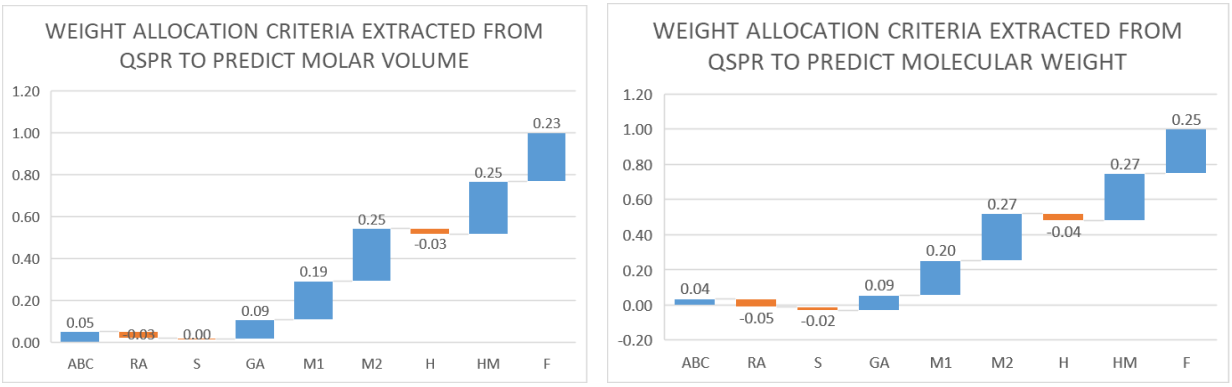
Table 14. Correlation coefficient(r) and standard error (SE) between Parkinson's drugs and physical property.

Topological index	MV Correlation Coefficient	MV Standard Error	MW Correlation Coefficient	MW Standard Error
ABC(Θ)	.814	30.394	.975	11.443
RA(Θ)	.865	26.267	.980	10.148
SCI(Θ)	.867	26.073	.969	12.653
GA(Θ)	.854	27.205	.955	15.205
M_1(Θ)	.769	33.451	.952	15.696
M_2(Θ)	.728	35.888	.922	19.866
F(Θ)	.683	38.227	.935	18.236
H(Θ)	.894	23.394	.967	13.108
HM(Θ)	.706	37.024	.931	18.762

From Table 14, we will dictate correlation coefficient as weight allocation criteria for molar volume and molecular weight in Fig.5(a, b). For both cases standard error criteria as beneficial and non-beneficial corresponding to each drug and its chemical indices is shown in Table 15. Beneficial criteria are chosen for numerical values that are bold.

4.1. VIKOR analysis for Molar Weight QSPR extrications

To extract the correlation and standard error results for QSPR analysis within the molecular weight study, we obtained the calculation steps as, step 1 is obtained through topological indices and correlation coefficients and Table 16 provides the final computations for steps 2, 3, and 4. Weights are allocated by entropy method.



(a) Molar Volume (b) Molecular weight

Figure 4. Weight allocation from QSPR extractions for (a) molar volume and (b) molecular weight.

Table 15. Beneficial and non-beneficial criteria for molecular weight and molar volume.

Topological index	MV	MW
ABC(Θ)	30.394	**11.443**
RA(Θ)	**26.267**	**10.148**
SCI(Θ)	**26.073**	**12.653**
GA(Θ)	**27.205**	15.205
M_1(Θ)	33.451	15.696
M_2(Θ)	35.888	19.866
F(Θ)	38.227	18.236
H(Θ)	**23.394**	**13.108**
HM(Θ)	37.024	18.762

4.2. VIKOR analysis for Molar Volume QSPR extrications

To extract the correlation and standard error results for QSPR analysis within molar volume study, step 1 is obtained through topological indices and correlation coefficients and table 17 comprises final computations for steps 2, 3 and 4.

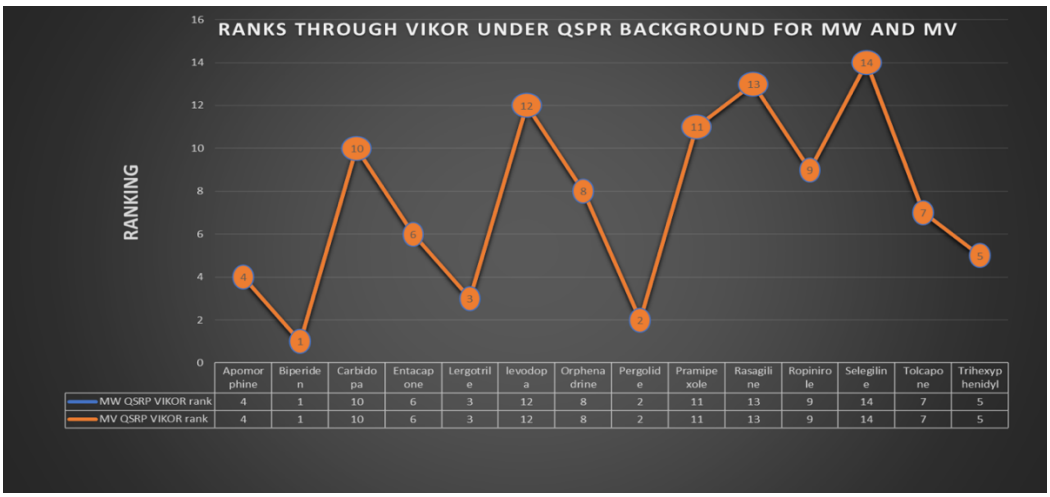


Figure 5. Ranking 14 Parkinson's drugs through VIKOR method keeping in concern with their values for Molecular weight and Molar volume.

Table 16. Outputs for S_j, R_j, Q_j and the rank (Molecular weight case).

Parkinson's drugs	S_j	R_j	Q_j	MW QSRP VIKOR rank
Apomorphine	0.925827	0.24826	0.109149	4
Biperiden	1.072317	0.269293	0	1
Carbidopa	0.256087	0.097382	0.724198	10
Entacapone	0.689371	0.177981	0.362366	6
Lergotrile	0.990377	0.260992	0.053709	3
levodopa	0.018904	0.033495	0.96418	12
Orphenadrine	0.514647	0.130496	0.540048	8
Pergolide	1.013387	0.264174	0.036821	2
Pramipexole	0.086603	0.041377	0.917636	11
Rasagiline	-0.01288	0.035781	0.97334	13
Ropinirole	0.45855	0.120947	0.585014	9
Selegiline	-0.06239	0.035563	0.995615	14
Tolcapone	0.650624	0.174886	0.386003	7
Trihexyphenidyl	0.81162	0.201196	0.259272	5
S_+, R_+	1.072316	0.269293		
S_-, R_-	-0.062385	0.033494		

Table 17. Outputs for S_j, R_j, Q_j and the rank (Molar volume case).

Parkinsons drugs	S_j	R_j	Q_j	MV QSRP VIKOR rank
Apomorphine	0.868904	0.233155	0.106546	4
Biperiden	0.970652	0.25109	0	1
Carbidopa	0.323891	0.091013	0.811809	10
Entacapone	0.661579	0.165184	0.415424	6
Lergotrile	0.9171	0.245112	0.045969	3
levodopa	0.119668	0.090299	0.922618	12
Orphenadrine	0.500933	0.122556	0.625439	8
Pergolide	0.921895	0.248101	0.034687	2
Pramipexole	0.162773	0.079881	0.930096	11
Rasagiline	0.075167	0.08565	0.959888	13
Ropinirole	0.456332	0.113589	0.675372	9
Selegiline	0.031467	0.087618	0.977404	14
Tolcapone	0.63952	0.162311	0.435557	7
Trihexyphenidyl	0.744557	0.188318	0.303689	5
S_+, R_+	0.970652	0.251090		
S_-, R_-	0.031466	0.079880		

5. Conclusions

The results of our study reveal significant correlations between topological indices (TIs) and various physicochemical properties of Parkinson's drugs. Among the TIs analyzed from Table.3-11, the S (Θ) index exhibited a remarkably high correlation with molar refractivity (r = 0.956), while the H index demonstrated the strongest correlation with molar volume (r = 0.883). The F (Θ) index displayed the highest correlation coefficient with boiling point (r = 0.697), and the harmonic F(Θ) index showed the maximum correlation with complexity (r = 0.852). Additionally, the harmonic RA (Θ) index exhibited the highest correlation with molecular weight (r = 0.972). However, no significant relationships were found between the TIs and properties

such as density, melting point, refractive index, enthalpy, and flash point. Our comprehensive analysis involved calculating TIs and integrating them with linear QSPR models specifically tailored for Parkinson's drugs. The utilization of the Multi-Criteria Decision-Making (MCDM) method, specifically VIKOR, has provided valuable insights into the comparative assessment of 14 Parkinson's drugs. Through this thorough analytical method, we have successfully assessed the molecular weight and molar volume of each medication, leading to a detailed ranking illustrated in Figure 5. Notably, all 14 anti-Parkinson medications received the same rankings for both characteristics, demonstrating the reliability of the VIKOR process in decision-making. The ranked list of these drugs, which includes ApomorphineRank 4), Biperiden (Rank 1), Carbidopa (Rank 10), among others, emphasizes the consistency of evaluations based on molecular weight and molar volume. This alignment of rankings highlights the significance of evaluating multiple criteria in drug assessment, ensuring a comprehensive view in the quest for effective treatments for Parkinson's disease. The progress of QSPR (Quantitative Structure-Property Relationship) analysis marks a notable shift, reflecting the increasing demand for chemical products across various fields, from chemical biology to physical sciences. This innovative approach provides essential insights into commercial models and enables detailed evaluations through different frameworks. It is important to note that QSPR analysis goes beyond simple chemical indices, capturing the complex relationship between chemical properties and desired outcomes, as seen in the values derived from correlation coefficients and errors produced in QSPR modelling.

These results carry significant implications for the pharmaceutical sector, offering crucial insights for the creation of new drugs targeting diseases. The strong correlation coefficients found within the range of TIs indicate their usefulness in estimating and predicting physicochemical properties for new Parkinson's treatment drugs, and possibly for other autoimmune diseases as well. These findings pave the way for pharmaceutical researchers and present a strategic pathway for advancing medication science and developing effective therapies.

References

1. Pringsheim, T., Jette, N., Frolkis, A., & Steeves, T. D. (2014). The Prevalence of Parkinson's Disease: A Systematic Review and Meta-Analysis, 29(13), 1583-1590.
2. Parkinson, J. (1969). An essay on the Shaking Palsy. Archives of Neurology, 20(4), 441-445.
3. Kalia, L. V., & Lang, A. E. (2015). Parkinson's disease. The Lancet, 386(9996), 896-912.
4. Bucher, M. L., Barrett, C. W., Moon, C. J., Mortimer, A. D., Burton, E. A., Greenamyre, J. T., & Hastings, T. G. (2020). Acquired dysregulation of dopamine homeostasis reproduces features of Parkinson's disease. npj Parkinson's Disease, 6(1), 34.
5. Quadri, M., Mandemakers, W., Grochowska, M. M., Masius, R., Geut, H., Fabrizio, E., & Melis, M. (2018). LRP10 genetic variants in familial Parkinson's disease and dementia with Lewy bodies: a genome-wide linkage and sequencing study. The Lancet Neurology, 17(7), 597-608.
6. Barranco Quintana, J. L., Allam, M. F., Del Castillo, A. S., & Navajas, R. F. C. (2009). Parkinson's disease and tea: a quantitative review. Journal of the American College of Nutrition, 28(1), 1-6.
7. Mosley, A. D. (2009). The encyclopedia of Parkinson's disease. Infobase Publishing.
8. Vos, T., Allen, C., Arora, M., Barber, R. M., Bhutta, Z. A., Brown, A., & Boufous, S. (2016). Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. The lancet, 388(10053), 1545-1602.
9. Wang, H., Naghavi, M., Allen, C., Barber, R. M., Bhutta, Z. A., Carter, A., & Bell, M. L. (2016). Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The lancet, 388(10053), 1459-1544.
10. Sveinbjornsdottir, S. (2016). The clinical symptoms of Parkinson's disease. Journal of neurochemistry, 139, 318-324.
11. Mhyre, T. R., Boyd, J. T., & Hamill, R. W. (2012). and Kathleen A. Maguire-Zeiss. Protein Aggregation and Fibrillogenesis in Cerebral and Systemic Amyloid Disease, 65, 389.
12. Abubakar, M. S., Aremu, K. O., Aphane, M., & Amusa, L. B. (2024). A QSPR analysis of physical properties of antituberculosis drugs using neighbourhood degree-based topological indices and support vector regression. Heliyon, 10(7).
13. Zaman, S., Mushtaq, M., Danish, M., Ali, P., & Rasheed, S. (2024). Topological Characterization of Some New Anti-Viral Drugs for Cancer Treatment. BioNanoScience, 1-13.
14. Siddique, I., Muhiuddin, G., Mahboob, A., & Rasheed, M. W. (2022). Various Uses of Topological Invariants in Jahangir Graph Jβ, α. Journal of Mathematics, 2022(1), 4321206.
15. Mahboob, A., Rasheed, M. W., Amin, L., & Hanif, I. (2023). A study of novel molecular descriptors and quantitative structure–property relationship analysis of blood cancer drugs. The European Physical Journal Plus, 138(9), 856.
16. Aslam, A., Saeed, S., Kanwal, S., & Tchier, F. (2024). Investigating hexagonal closed packed crystal lattice through QSPR modeling via linear regression analysis and Topsis. Physica Scripta, 99(2), 025201.
17. Shanmukha, M. C., Basavarajappa, N. S., & Anilkumar, K. N. (2020). Predicting physico-chemical properties of octane isomers using QSPR approach. Malaya Journal of Matematik, 8(01), 104-116.
18. RAJU, C., SHAIKH, A. B., & Vyshnavi, D. (2024). Statistical Analysis of Atom-Bond Connectivity related Descriptors and their Polynomials of some molecular structures of COVID-19 drugs. Authorea Preprints.
19. Ibrahim, H., Shewa, G. A., & Aderibigbe, B. A. (2024). On the QSPR Models of some Anti-Malaria Drugs using some Reversed Degree-Based Topological Indices. Lafia Journal of Scientific and Industrial Research, 82-89.
20. Kumar, K. A., Basavarajappa, N. S., & Shanmukha, M. C. (2020). QSPR analysis of Alkanes with certain degree based topological indices. Malaya Journal of Matematik, 8(02), 314-330.
21. Adnan, M., Bokhary, S. A. U. H., Abbas, G., & Iqbal, T. (2022). Degree-Based Topological Indices and QSPR Analysis of Antituberculosis Drugs. Journal of Chemistry, 2022(1), 5748626.
22. Mondal, S., De, N., & Pal, A. (2022). Topological indices of some chemical structures applied for the treatment of COVID-19 patients. Polycyclic Aromatic Compounds, 42(4), 1220-1234.
23. Shanmukha, M. C., Usha, A., Praveen, B. M., & Douhadji, A. (2022). Degree-Based Molecular Descriptors and QSPR Analysis of Breast Cancer Drugs. Journal of Mathematics, 2022(1), 5880011.

24. Nasir, S., Farooq, F. B., & Parveen, S. (2022). Topological indices of novel drugs used in blood cancer treatment and its QSPR modeling. AIMS Mathematics, 7(7), 11829-11850.
25. Naeem, M., Rauf, A., Akhtar, M. S., & Iqbal, Z. (2024). QSPR modeling with curvilinear regression on the reverse entropy indices for the prediction of physicochemical properties of benzene derivatives. Polycyclic Aromatic Compounds, 44(3), 1452-1469.
26. Parveen, S., Hassan Awan, N. U., Mohammed, M., Farooq, F. B., & Iqbal, N. (2022). Topological indices of novel drugs used in diabetes treatment and their QSPR modeling. Journal of Mathematics, 2022(1), 5209329.
27. Edwards, W. (1954). The theory of decision making. Psychological bulletin, 51(4), 380.
28. Hui, Z. H., Aslam, A., Kanwal, S., Saeed, S., & Sarwar, K. (2023). Implementing QSPR modeling via multiple linear regression analysis to operations research: a study toward nanotubes. The European Physical Journal Plus, 138(3), 200.
29. Farooq, Fozia Bashir. "Implementation of multi-criteria decision making for the ranking of drugs used to treat bone cancer.(2024)" AIMS Mathematics 9, no. 6: 15119-15131.
30. Li, Y., Aslam, A., Saeed, S., Zhang, G., & Kanwal, S. (2022). Targeting highly resisted anticancer drugs through topological descriptors using VIKOR multi-criteria decision analysis. The European Physical Journal Plus, 137(11), 1245.
31. Zuo, X., Akhtar, M., Aslam, A., Tawfiq, F. M., & Kanwal, S. (2023). Multiple-Criteria Decision-Making (MCDM) techniques to study the behavior of dendrimers using topological indices. Plos one, 18(11), e0294515.
32. Muneeb, F., Ramos, R. F., Wanke, P., & Lashari, F. (2023). Sustainable strategies for hyper-local restaurants: A multi-criteria decision-making approach.
33. Sultana, S., 2024. Prioritizing Asthma Treatment Drugs through Multicriteria Decision Making. International Journal of Analytical Chemistry, 2024.
34. Zaman, S., Yaqoob, H. S. A., Ullah, A., & Sheikh, M. (2024). QSPR analysis of some novel drugs used in blood cancer treatment via degree based topological indices and regression models. Polycyclic Aromatic Compounds, 44(4), 2458-247.
35. Mahboob, A., Rasheed, M. W., Dhiaa, A. M., Hanif, I., & Amin, L. (2024). On quantitative structure-property relationship (QSPR) analysis of physicochemical properties and anti-hepatitis prescription drugs using a linear regression model. Heliyon, 10(4).
36. Zhang, X., Saif, M. J., Idrees, N., Kanwal, S., Parveen, S., & Saeed, F. (2023). QSPR analysis of drugs for treatment of schizophrenia using topological indices. ACS omega, 8(44), 41417-41426.
37. Gutman, I., & Trinajstić, N. (1972). Graph theory and molecular orbitals. Total φ-electron energy of alternant hydrocarbons. Chemical physics letters, 17(4), 535-538.
38. Randic, M. (1975). Characterization of molecular branching. Journal of the American Chemical Society, 97(23), 6609-6615.
39. Estrada, E., Torres, L., Rodriguez, L., & Gutman, I. (1998). An atom-bond connectivity index: modelling the enthalpy of formation of alkanes.
40. Zhou, B., & Trinajstić, N. (2010). On general sum-connectivity index. Journal of mathematical chemistry, 47, 210-218.
41. Vukičević, D., & Furtula, B. (2009). Topological index based on the ratios of geometrical and arithmetical means of end-vertex degrees of edges. Journal of mathematical chemistry, 46, 1369-1376.
42. Fajtlowicz, S. (1987). On conjectures of Graffiti-II. Congr. Numer, 60(3), 187-97.
43. Shirdel, G. H., Rezapour, H., & Sayadi, A. M. (2013). The hyper-Zagreb index of graph operations, 4(2), 213-220.
44. Furtula, B., Gutman, I., & Dehmer, M. (2013). On structure-sensitivity of degree-based topological indices. Applied Mathematics and Computation, 219(17), 8973-8978.
45. Balaban, A. T. (1988). Topological indices and their uses: a new approach for the coding of alkanes. Journal of Molecular Structure: THEOCHEM, 165(3-4), 243-253.
46. Çolakoğlu, Ö. (2022). QSPR Modeling with Topological Indices of Some Potential Drug Candidates against COVID-19. Journal of Mathematics, 2022(1), 3785932**.**
47. Zhang, X., Idrees, N., Kanwal, S., Saif, M. J., & Saeed, F. (2022). Research Article Computing Topological Invariants of Deep Neural Networks..

48. Nasir, S., Farooq, F. B., Idrees, N., Saif, M. J., & Saeed, F. (2019). Topological characterization of nanosheet covered by C3 and C6. Processes, 7(7), 462.
49. Elmer, P. (2017). Chem Bio Draw Profeesional Version (15.0. 0.106). Cambridge Soft: Waltham, MA, USA.
50. Raevsky, O. A. (2004). Physicochemical descriptors in property-based drug design. Mini reviews in medicinal chemistry, 4(10), 1041-1052.
51. Salahshoori, I., Golriz, M., Nobre, M. A., Mahdavi, S., Malekshah, R. E., Javdani-Mallak, A., & Kargaran, F. (2023). Simulation-based approaches for drug delivery systems: navigating advancements, opportunities, and challenges. Journal of Molecular Liquids, 123888.
52. Pence, H. E., & Williams, A. (2010). ChemSpider: an online chemical information resource.
53. Kim, S., & Bolton, E. E. (2024). PubChem: A Large-Scale Public Chemical Database for Drug Discovery. Open Access Databases and Datasets for Drug Discovery, 39-66.
54. Kafle, S. C. (2019). Correlation and regression analysis using SPSS. Management, Technology & Social Sciences, 126.
55. Khan, M. F., Iftikhar, A., Anwar, H., & Ramay, S. A. (2024). Brain Tumor Segmentation and Classification using Optimized Deep Learning. Journal of Computing & Biomedical Informatics, 7(01), 632-640.
56. Khan, I. U., Khan, Z. A., Ahmad, M., Khan, A. H., Muahmmad, F., Imran, A., & Hamid, M. K. (2023, May). Machine Learning Techniques for Permission-based Malware Detection in Android Applications. In 2023 9th International Conference on Information Technology Trends (ITT) (pp. 7-13). IEEE.