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AI-ASSISTED QSPR ANALYSIS OF RHEUMATOID ARTHRITIS DRUGS USING THE VL TOPOLOGICAL INDEX

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ABSTRACT:

Artificial Intelligence (AI)-supported computational methods play an important role in modern scientific research by helping researchers analyse molecular data and predict physio-chemical properties efficiently. In the present work, a quantitative structure-property relationship (QSPR) study of ten rheumatoid arthritis (RA) drugs was performed using the VL topological index and its transformed forms, namely $\sqrt{VL(G)}$, $[VL(G)]^2$, $1/VL(G)$, and $1/\sqrt{VL(G)}$. The study investigates the relationship between these descriptors and selected physio-chemical properties, including molar volume (MV), polarity (P), refractive index (RI), complexity (C), boiling point (BP), and enthalpy (E). Correlation analysis revealed that VL(G), $\sqrt{VL(G)}$, and $[VL(G)]^2$ exhibited strong positive associations with MV, P, RI, and C, whereas inverse descriptors showed negative correlations with the same properties. Among the descriptors, $\sqrt{VL(G)}$ showed the strongest correlations with MV ($r = 0.8645$), P ($r = 0.7996$), RI ($r = 0.7992$), and C ($r = 0.7160$). Regression analysis further indicated that VL(G) effectively predicted MV ($R^2 = 0.7136$), P ($R^2 = 0.6079$), RI ($R^2 = 0.6070$), and C ($R^2 = 0.5060$), while $\sqrt{VL(G)}$ demonstrated the best predictive performance with MV ($R^2 = 0.7473$), P ($R^2 = 0.6394$), RI ($R^2 = 0.6387$), and C ($R^2 = 0.5127$). Similarly, $[VL(G)]^2$ also showed statistically significant predictive relationships with MV ($R^2 = 0.6319$), P ($R^2 = 0.5291$), RI ($R^2 = 0.5280$), and C ($R^2 = 0.4847$). In contrast, BP and enthalpy exhibited weak correlations and statistically insignificant regression performance, indicating limited predictive capability for these parameters. The findings suggest that VL(G)-based descriptors may serve as useful computational tools for predicting selected molecular properties of RA medications and highlight the role of AI-assisted QSPR methodologies in molecular property prediction studies.

Keywords: Artificial Intelligence (AI), QSPR Analysis, Rheumatoid Arthritis Drugs, VL Topological Index, Molecular Descriptors, Linear Regression, Computational Chemistry, Physio-Chemical Properties.

INTRODUCTION

Topological indices are important mathematical descriptors widely used in graph theory, mathematical chemistry, and computational drug analysis [1]. These descriptors convert the structural information of chemical compounds into numerical values that help in understanding and predicting different physio-chemical and biological properties of molecules [2]. In recent years, topological indices have gained significant importance in quantitative structure-property relationship (QSPR) and quantitative structure-activity relationship (QSAR) studies because they provide efficient and cost-effective alternatives to extensive experimental investigations [3]. Degree-based topological descriptors, in particular, have shown promising applications in pharmaceutical chemistry, nanotechnology, and molecular property prediction [4-5]. Among such descriptors, the VL topological index has attracted attention due to its ability to characterize molecular structures and establish meaningful relationships with molecular properties [6]. Earlier studies have also

demonstrated the usefulness of topological indices in QSPR modelling of therapeutic drugs, including rheumatoid arthritis medications and other pharmaceutical compounds.

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease that mainly affects the joints and surrounding tissues, leading to pain, stiffness, swelling, and gradual joint damage [7]. Epidemiological investigations have reported the occurrence and prevalence of RA in different populations, emphasizing its significance as a major health concern [8]. The treatment of RA generally involves long-term administration of therapeutic drugs such as Methotrexate, Leflunomide, Hydroxychloroquine, Tofacitinib, and related medications [9]. Figure 1 illustrates their corresponding molecular structures. Since the effectiveness and chemical behaviour of these drugs depend strongly on their molecular structure and physio-chemical characteristics, the prediction of molecular properties has become an important area of research in computational chemistry and pharmaceutical sciences [10].

The rapid development of Artificial Intelligence (AI) and computational technologies has strengthened modern QSPR and QSAR investigations [11]. In computational chemistry, AI-assisted approaches involve the use of statistical prediction methods, regression analysis, computational data processing, and digital visualization techniques to study relationships between molecular descriptors and chemical properties. Such methods help researchers analyse molecular data efficiently, reduce experimental effort, and develop reliable predictive models [12]. These approaches support data-driven research and demonstrate the growing role of AI-assisted methodologies in interdisciplinary scientific studies and higher education research [13].

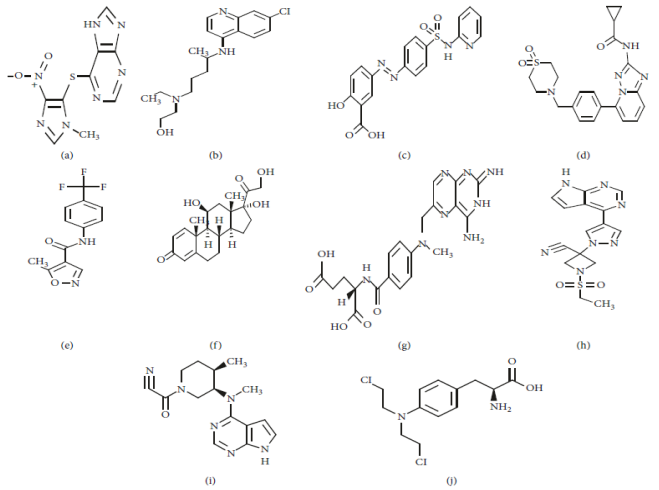

Figure 1. Molecular structure of Rheumatoid Arthritis drugs

(a) Azathioprine. (b) Hydroxychloroquine. (c) Sulfasalazine. (d) Filgotinib. (e) Leflunomide.

(f) Prednisolone. (g) Methotrexate. (h) Baricitinib. (i) Tofacitinib. (j) Upadacitinib.

MATERIALS AND METHODS

The present study applies an AI-assisted quantitative structure-property relationship (QSPR) approach to investigate the molecular properties of selected rheumatoid arthritis (RA) medications. Ten widely prescribed RA drugs, namely Azathioprine, Hydroxychloroquine, Sulfasalazine, Filgotinib, Leflunomide, Prednisolone, Methotrexate, Baricitinib, Tofacitinib, and Upadacitinib, were considered for the analysis. The physio-chemical properties selected for this investigation include molar volume (MV), polarity (P), refractive index (RI),

complexity (C), boiling point (BP), and enthalpy (E). The required data for these properties were collected from published literature sources, mainly from Parveen et al. [7] and partially obtained from the ChemSpider database.

The molecular structures of the selected RA drugs were transformed into molecular graphs in which atoms are represented by vertices and chemical bonds by edges, following graph-theoretical approaches commonly employed in mathematical chemistry and QSPR studies [15]. Using these graph structures, the VL topological index and its transformed forms, namely $\sqrt{VL(G)}$, $[VL(G)]^2$, $1/VL(G)$, and $1/\sqrt{VL(G)}$, were computed for each molecular structure based on the methodology proposed for the VL descriptor [16]. These descriptors were utilized to establish predictive relationships between molecular topology and the selected physio-chemical parameters.

To examine the effectiveness of the descriptors, correlation analysis and linear regression techniques were employed. Regression models of the form A = a + bB were developed, where A represents the physio-chemical property and B denotes the VL topological descriptor. Statistical measures such as correlation coefficient (R), coefficient of determination (R^2), p-value, F-test, t-test, confidence intervals, and residual standard deviation were used to evaluate the accuracy and significance of the predictive models [17].

The statistical computations and regression analysis were carried out using Google Sheets, while graphical visualizations and predictive plots were generated through Python coding techniques [18]. The entire methodology integrates AI-supported computational analysis, mathematical modelling, and statistical prediction methods to provide an efficient framework for studying molecular properties of rheumatoid arthritis medications and demonstrates the role of AI-assisted approaches in modern QSPR investigations [19].

RESULTS AND DISCUSSION

The obtained results demonstrate the applicability of VL(G)-based descriptors in predicting selected physio-chemical properties of rheumatoid arthritis drugs through AI-assisted QSPR analysis.

1.1 Physio-Chemical Properties and Descriptor Calculation

Table 1. Physio-chemical properties of selected rheumatoid arthritis (RA) medications

NameofMedications	Molar Volume (MV)	Polarity (P)	Refractiveindex (RI)	Complexity (C)	Boilingpoint (BP)	Enthalpy (E)
Azatjoprine	145.40	27.30	68.90	354.00	555.80	368.50
Hydroxycholoqoine	285.40	39.20	99.00	331.00	516.70	266.30
Sulfasatazne	267.70	40.60	102.40	657.00	689.30	370.70
Filgotinib	281.10	45.30	114.30	715.00	-	-
Leflumomide	194.10	24.20	61.00	327.00	289.30	129.00
Predisolane	274.70	37.90	95.50	724.00	570.60	314.80
Methotrexate	275.7	47.20	119.00	704.00	-	-

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Bracitinib	238.10	38.90	98.20	678.00	707.00	-
Tofacitinib	241.00	34.70	87.50	-	585.80	308.10
Upadacinib	243.00	36.30	91.60	561.00	189.00	-

Table 2. Computed values of the VL topological index and its transformed forms for RA medications

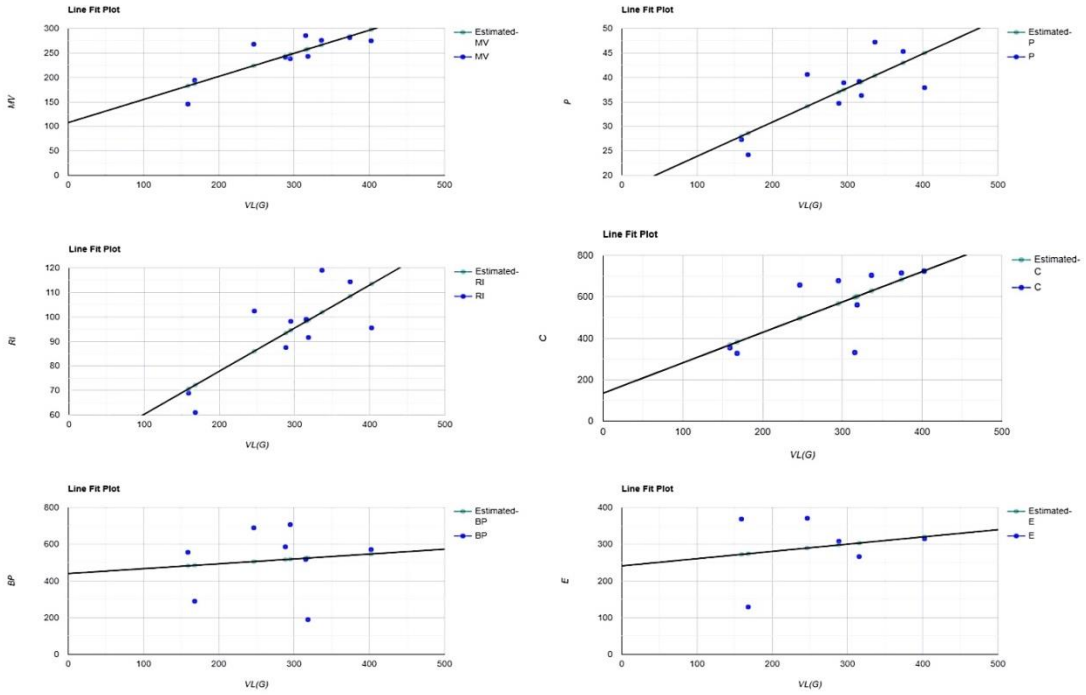
Drugs of RA Drugs	VL(G)	$\sqrt{VL(G)}$	$[VL(G)]^2$	$\frac{1}{VL(G)}$	$\frac{1}{\sqrt{VL(G)}}$
Azatjoprine	159	12.60952	25281	0.00629	0.07931
Hydroxycholoqoine	315.5	17.76232	99540.25	0.00317	0.0563
Sulfasatazne	246.5	15.70032	60762.25	0.00406	0.06369
Filgotinib	374	19.33908	139876	0.00267	0.05171
Leflumomide	168	12.96148	28224	0.00595	0.07715
Predisolane	402.5	20.0624	162006.25	0.00248	0.04984
Methotrexate	336.5	18.34394	113232.25	0.00297	0.05451
Bracitinib	295	17.17556	87025	0.00339	0.05822
Tofacitinib	288.5	16.98529	83232.25	0.00347	0.05887
Upadacinib	318.5	17.84657	101442.25	0.00314	0.05603

The physio-chemical properties and computed topological descriptors of the selected rheumatoid arthritis (RA) drugs are presented in Tables 1 and 2. The observed variation in molar volume, polarity, refractive index, complexity, boiling point, and enthalpy reflects structural diversity among the selected compounds. Similarly, noticeable differences in the values of VL(G), $\sqrt{VL(G)}$, and $[VL(G)]^2$ indicate variations in molecular connectivity and structural arrangement. These computed descriptors provide a mathematical representation of molecular structure, making them suitable for QSPR-based prediction of selected physio-chemical parameters.

3.2 Correlation Analysis of VL-Based Descriptors

Table 3. Correlation coefficients between VL-based descriptors and physio-chemical properties of RA

Drugs of RA Drugs	VL(G)	$\sqrt{VL(G)}$	$[VL(G)]^2$	$\frac{1}{VL(G)}$	$\frac{1}{\sqrt{VL(G)}}$
MV	0.845	0.8645	0.7949	-0.9015	-0.8926
P	0.7797	0.7996	0.7274	-0.8328	-0.8259
RI	0.7791	0.7992	0.7266	-0.8326	-0.8256
C	0.7113	0.716	0.6962	-0.7197	-0.72
BP	0.1175	0.1306	0.09362	-0.1671	-0.1562
E	0.2042	0.2139	0.1825	-0.2324	-0.2287



The correlation analysis presented in Table 3 indicates that VL(G) and its transformed forms exhibit meaningful relationships with several physio-chemical properties of RA medications. Among the investigated descriptors, $\sqrt{VL(G)}$ showed comparatively stronger positive correlations with molar volume, polarity, refractive index, and complexity, while VL(G) and $[VL(G)]^2$ also demonstrated notable positive associations with these properties. In contrast, boiling point and enthalpy exhibited weak correlations, suggesting limited dependence on topological descriptors. Since reciprocal descriptors showed negative correlations, only positively correlated descriptors were considered for further regression analysis.

3.3 Regression Analysis and Predictive Modeling

Linear regression analysis confirmed the predictive ability of VL-based descriptors for selected physio-chemical properties. Among the tested models, $\sqrt{VL(G)}$ produced the strongest predictive performance for molar volume with an R^2 value of 0.7473, indicating that nearly 74.7% of the variation in molar volume is explained by the descriptor. Polarity and refractive index also demonstrated statistically significant models with R^2 values of 0.6394 and 0.6387, respectively. Complexity exhibited moderate predictive performance (R^2 = 0.5127). In contrast, boiling point and enthalpy showed weak predictive relationships with low R^2 values and statistically insignificant p-values. These findings suggest that VL(G)-based descriptors are more effective in predicting structural and electronic properties than thermodynamic properties of RA drugs.

The present study highlights the usefulness of AI-assisted computational methodologies in QSPR analysis of rheumatoid arthritis drugs. By integrating topological descriptors with statistical regression models, supported through digital computational tools and Python-based visualization, meaningful predictive relationships between molecular structure and physio-chemical properties were identified. Such data-driven approaches may support faster molecular assessment and property prediction in pharmaceutical research.

Figure 2. Linear plots of $VL(G)$against the physicochemical properties of Rheumatoid Arthritis drugs

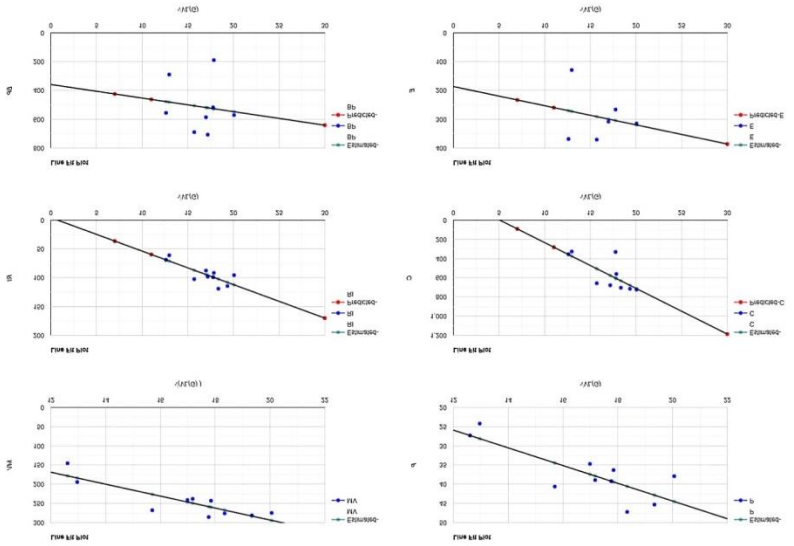


Figure 3. Linear plots of $\sqrt{VL(G)}$ against the physicochemical properties of Rheumatoid Arthritis drugs

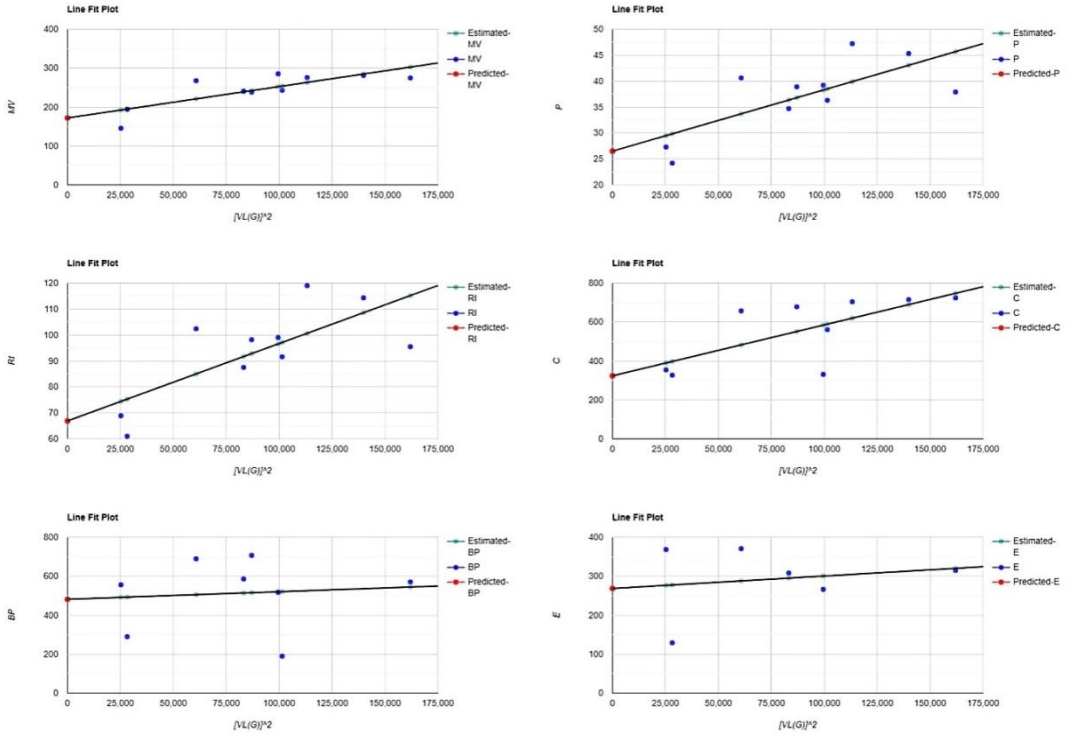


Figure 4. Linear plots of $[VL(G)]^2$against the physicochemical properties of Rheumatoid Arthritis drugs

The graphical representation (Figures 2,3 and 4) of the regression analysis is shown in the above figures. The regression equations obtained for the relationship between VL(G)-based descriptors and selected physio-chemical properties are presented below. Among the investigated descriptors, VL(G), $\sqrt{VL(G)}$, and $[VL(G)]^2$ demonstrated statistically significant

predictive ability for molar volume (MV), polarity (P), refractive index (RI), and complexity (C) ($p < 0.05$). In particular, $\sqrt{VL(G)}$ exhibited the strongest predictive performance, while VL(G) and $[VL(G)]^2$ also showed meaningful regression relationships with these properties. However, boiling point (BP) and enthalpy (E) exhibited weak correlations and low predictive accuracy; therefore, their regression equations were excluded from detailed discussion. Similarly, reciprocal forms of the VL(G) index were not considered further due to their negative correlations with the selected physio-chemical parameters.

$$MV = 107.6940 + 0.4715\,[VL(G)]$$
$$P = 16.9034 + 0.06975\,[VL(G)]$$
$$RI = 42.6739 + 0.1758\,[VL(G)]$$
$$C = 134.5016 + 1.4684[\,VL(G)]$$
$$MV = -17.9945 + 15.559\sqrt{VL(G)}$$
$$P = -1.7736 + 2.3067[\sqrt{VL(G)}\,]$$
$$RI = -4.4242 + 5.8159[\sqrt{VL(G)}\,]$$
$$C = -242.6683 + 47.6611[\sqrt{VL(G)}\,]$$
$$MV = 171.9959 + 0.0008064[VL(G)]^2$$
$$P = 26.5084 + 0.0001183[VL(G)]^2$$
$$RI = 66.8973 + 0.000298[VL(G)]^2$$
$$C = 323.6674 + 0.002616[VL(G)]^2$$

CONCLUSION

In the present study, an AI-assisted QSPR analysis of ten rheumatoid arthritis (RA) medications was carried out using the VL topological index and its transformed forms, namely $\sqrt{VL(G)}$ and $[VL(G)]^2$, to examine their relationship with selected physio-chemical properties. The correlation analysis revealed that $\sqrt{VL(G)}$ exhibited the strongest positive association with molar volume ($r = 0.8645$), followed by polarity ($r = 0.7996$), refractive index ($r = 0.7992$), and complexity ($r = 0.7160$). Regression analysis further indicated that $\sqrt{VL(G)}$ provided the best predictive performance for molar volume ($R^2 = 0.7473$), while statistically significant models were also obtained for polarity ($R^2 = 0.6394$), refractive index ($R^2 = 0.6387$), and complexity ($R^2 = 0.5127$). In contrast, boiling point and enthalpy exhibited weak correlations and statistically insignificant regression models, suggesting limited dependence on the selected topological descriptors. The findings indicate that VL(G)-based descriptors, particularly $\sqrt{VL(G)}$, may serve as useful computational tools for predicting selected molecular properties of RA drugs. Furthermore, the integration of regression-based computational analysis and Python-assisted visualization highlights the potential application of AI-assisted QSPR methodologies in pharmaceutical and molecular property prediction studies.

REFERENCES:

1. Haruo Hosoya, “Topological index: A newly proposed quantity characterizing the topological nature of structural isomers of saturated hydrocarbons,” Bulletin of the Chemical Society of Japan, vol. 44, no. 9, pp. 2332–2339, 1971.
2. Milan Randić, “On characterization of molecular branching,” Journal of the American Chemical Society, vol. 97, no. 23, pp. 6609–6615, 1975.
3. Lemont B. Kier and Lowell H. Hall, Molecular Connectivity in Chemistry and Drug Research. New York: Academic Press, 1986.

4. Alexei R. Katritzky, "QSPR: The correlation and quantitative prediction of chemical and physical properties from structure," Chemical Society Reviews, vol. 26, pp. 195–202, 1997.
5. Imran Gutman, "Degree-based topological indices," Croatica Chemica Acta, vol. 86, no. 4, pp. 351–361, 2013.
6. T. Deepika, "VL Index and Bounds for Tensor Products of F–Sum Graphs," TWMS Journal of Applied and Engineering Mathematics, vol. 11, no. 2, pp. 374–385, 2021.
7. S. Parveen, F. B. Farooq, N. U. H. Awan, R. Fanja, and M. F. Choudhary, "Topological indices of drugs used in rheumatoid arthritis treatment and its QSPR modeling," Journal of Mathematics, vol. 2022, Article ID 1562125, pp. 1–11, 2022.
8. J. S. Smolen, D. Aletaha, I. B. McInnes, et al., "Rheumatoid arthritis," Nature Reviews Disease Primers, vol. 6, pp. 1–23, 2020.
9. D. P. M. Symmons, E. M. Barrett, C. R. Bankhead, D. G. L. Scott, and A. J. Silman, "The incidence of rheumatoid arthritis in the United Kingdom: Results from the Norfolk Arthritis Register," Rheumatology, vol. 33, no. 8, pp. 735–739, 1994.
10. F. Guillemin, S. Briancon, J. M. Klein, E. Sauleau, and J. Pourel, "Low incidence of rheumatoid arthritis in France," Scandinavian Journal of Rheumatology, vol. 23, no. 5, pp. 264–268, 1994.
11. J. K. Pedersen, N. K. Kjær, A. J. Svendsen, and K. Hørslev-Petersen, "Incidence of rheumatoid arthritis from 1995 to 2001: Impact of ascertainment from multiple sources," Rheumatology International, vol. 29, no. 4, pp. 411–415, 2009.
12. Y. Alamanos, P. V. Voulgari, and A. A. Drosos, "Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: A systematic review," Seminars in Arthritis and Rheumatism, vol. 36, pp. 182–188, 2006.
13. Python Software Foundation, Python Language Reference, Version 3.x, 2024.
14. B. S. N. Urs and R. S. Kuntal, "Lower Bounds and Upper Bounds for the Topological Indices of ξ-Graph," AIP Conference Proceedings, vol. 3149, Article ID 140033, 2024. https://doi.org/10.1063/5.0224876.
15. B. S. N. Urs and S. Krishnamurthy, "Figuring of Some Degree-Based Topological Indices of Graphene," AIP Conference Proceedings, vol. 3258, Article ID 020002, 2025. https://doi.org/10.1063/5.0262225.
16. B. S. N. Urs and S. Krishnamurthy, "NM-polynomials of anti-cancer drugs," IAENG International Journal of Applied Mathematics, vol. 55, no. 12, pp. 3955–3967, 2025.
17. B. S. N. Urs, S. Krishnamurthy, A. S. Kamalakaran, and D. Togarichetu, "Evaluating Degree-Based Topological Indices in QSPR Modeling of Anticancer Drugs Using Linear and Multilinear Regression," International Journal of Quantum Chemistry, vol. 125, no. 22, Article e70123, 2025. https://doi.org/10.1002/qua.70123.
18. B. S. N. Urs, S. Krishnamurthy, and S. Maji, "Topological Indices of Certain Derived Graphs of Triglycerides," Boletim da Sociedade Paranaense de Matemática, vol. 44, no. 4, pp. 1–11, 2026. https://doi.org/10.5269/bspm.80157