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Quantitative Structural Property Relationship of Quinolone Antibiotics by VL-Indices

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Abstract: ***Quinolones, a class of synthetic antibiotics, have evolved from being minor ther- apeutic agents to playing a significant role in the treatment of bacterial infections, including those affecting the urinary tract. In this study, three variants of the Veer- abhadraiah Lokesha (VL) index: the Sombor-type VL index (SVL), the neighbor- hood degree sum VL index (NVL), and the Sombor-type neighborhood degree sum VL index (SNVL) are introduced. These indices, derived from molecular graph the- ory, are analyzed in relation to the physicochemical properties of various Quinolone antibiotics. Regression analyses, including linear, quadratic, logarithmic, and cubic models, are employed to examine the correlation between the VL index, its vari- ants, and the physicochemical properties. The correlation coefficient (r) and scatter plots for each model are discussed to determine the most significant relationships between the indices and the drug properties, providing valuable insights into the structural characteristics of Quinolone antibiotics.***

Keywords: Quinolone antibiotic drugs, degree-based topological indices, QSPR analysis, curvilinear regression models

1. Introduction

Topological indices are quantitative measures obtained using specific rules and are im- portant in understanding chemical properties of compounds through mathematical and computational methods. These indices are widely used in QSPR/QSAR (Quantitative Structure-Property/Activity Relationship) analysis, playing a significant role in drug de- sign. Quinolone antibiotics, synthetic antibacterial agents, are used to treat a broad range of bacterial infections, including both gram-positive and gram-negative bacteria. They are effective against infections such as urinary tract, respiratory, bone and joint, skin, and sexually transmitted infections. Nalidixic acid, the first quinolone antibiotic, was initially used to treat urinary tract infections and contains two nitrogen atoms in its nu- cleus, distinguishing it from other quinolones. Discovered in the 1960s by George Lesher, quinolone byproducts like nalidixic acid were clinically introduced in 1967. Quinolones inhibit bacterial enzymes such as gyrase and topoisomerase IV, blocking DNA replica- tion, leading to rapid cell death. However, long-term use must be restricted to prevent mutations. More recent quinolone drugs, such as norfloxacin and ciprofloxacin, have im- proved pharmacokinetics and pharmacodynamics, making them more effective against gram-positive organisms. Ciprofloxacin, for example, was the first quinolone to treat bacterial infections outside the urinary tract. Levofloxacin and other newer quinolones have shown effectiveness against respiratory tract infections, with levofloxacin showing improved pharmacokinetics and efficacy with a single daily dose. Some quinolones are now used to treat skin, bronchitis, prostatitis, pneumonia, and even tuberculosis, which remains a major global health threat.

QSPR analysis involves establishing correlations between topological indices and tar- geted properties, commonly through curvilinear regression. Curvilinear regression, which models non-linear relationships between variables, is widely used in medicinal chem- istry and environmental science. It allows for quadratic, cubic, and logarithmic models, providing greater flexibility and more accurate representation of complex data than lin- ear regression. This method is particularly useful for studying relationships that follow non-linear patterns, such as the dosage-efficacy relationship in drug design, or stress- performance dynamics in psychological research. Curvilinear regression provides better fit and interpretation of data, making it a valuable tool in understanding complex rela- tionships like molecular structure and biological activity, drug exposure, and toxicity.

T. Deepika [4] introduced a new molecular descriptor called the Veerabhadraiah Loke- sha (VL) index for a graph G. In this work, we present three additional variants of the VL index: the Sombor-type VL index, the neighborhood degree VL index, and the Sombor-type neighborhood degree VL index. A regression analysis is performed to exam- ine the relationship between these indices and the physicochemical properties of various Quinolone antibiotic drugs. For more study on topological indices and QSPR analysis refer [1–3, 7–11].

1.1 Basic terminology and topological indices

Let G (V, E) be a simple graph with vertex set $|V| = n$ and edge set $|E| = m$ representing atoms and bonds of a molecular graph drawn from chemical compound or drug. The open neighborhood of a vertex $v \in V$ is $N(v) = \{u/uv \in E\}$ and closed if $N[v] = N(v) \cup v$. Let d_v be the degree of the vertex v representing the number of edges incident to vertex v and n_v be the sum of degrees of vertices that are incident to vertex v. For more study on basic definition and notations refer [5].

Molecular descriptors

1) VL Index

$$VL(G) = \sum_{uv \in G} (d_u + d_v + d_u d_v)$$

2) Sombor type VL Index

$$SVL(G) = \sum_{uv \in G} \sqrt{(d_u + d_v + d_u d_v)}$$

3) Neighborhood degree sum VL Index

$$NVL(G) = \sum_{uv \in G} (n_u + n_v + n_u n_v)$$

4) Sombor type Neighborhood degree sum VL Index

$$SNVL(G) = \sum_{uv \in G} \sqrt{(n_u + n_v + n_u n_v)}$$

2. Data Set

The physicochemical properties of various Quinolone antibiotics are listed in Table 1, while Table 2 provides the computed values of the topological indices for these antibiotics.

Table 1: Physicochemical properties of various Quinolone antibiotic drugs [6].

Drug	BP	MP	MR	TPSA
Nalidixic Acid	397.21	229.5	60.1	71
Ciprofloxacin	581.8	316.67	83.3	73
Norfloxacin	555.8	227	80.7	73
Sparfloxacin	640.4	324.9	96.9	99
Moxifloxacin	636.4	325	101.8	82
Gatifloxacin	607.8	321.32	94.6	82
Ofloxacin	571.5	317.69	91.1	73
Pefloxacin	529.1	313.93	85.6	64
Temafloxacin	608.9	324	100.5	73
Fleroxacin	535.3	313.71	85.8	64
Lomefloxacin	542.7	315.5	85.4	73
Mepron	535	226.87	99.5	54
Fluoroquinolone	343.2	116.93	42.2	29
Gemifloxacin	638.9	324.18	99.2	121

Table 2: Computed values of topological indices for various Quinolone antibiotic drugs.

Drug	VL	SVL	NVL	SNVL
Nalidixic Acid	96.5000	29.1144	421.0000	60.0622
Ciprofloxacin	149.0000	44.4376	539.0000	73.9534
Norfloxacin	134.5000	40.5466	569.5000	80.6685
Sparfloxacin	169.5000	49.8818	831.5000	111.0287
Moxifloxacin	186.5000	54.9259	810.0000	109.5083
Gatifloxacin	167.5000	49.5814	777.0000	105.2773
Ofloxacin	165.0000	48.4061	729.5000	98.7649
Pefloxacin	140.0000	42.1477	595.5000	84.4385
Temafloxacin	179.0000	53.8694	854.0000	119.9048
Fleroxacin	152.5000	45.6512	645.0000	90.8465
Lomefloxacin	141.0000	42.3577	671.5000	92.7927
Mepron	157.0000	47.2661	696.5000	98.8171
Fluoroquinolone	67.0000	20.7112	269.5000	41.4031
Gemifloxacin	171.5000	51.0008	783.5000	107.7926

3. Results and Discussion

The correlation coefficient (r) is a statistical measure that indicates the strength and direction of the linear relationship between two variables. In regression analysis, it is used to quantify how well a model fits the data. Different models-linear, quadratic, logarithmic, and cubic-can be used to explore the relationship between variables depending on the nature of the data.

Table 3: The correlation coefficient r for linear regression model between topological indices and physical properties of Quinolone antibiotic drugs.

	BP	MP	**MR**	TPSA
VL Index	**0.957**	0.846	0.978	0.654
SVL Index	**0.954**	0.841	**0.982**	0.643
NVL Index	**0.915**	0.801	**0.953**	0.678
SNVL Index	0.899	0.781	**0.956**	0.649

Table 4: The correlation coefficient r for quadratic regression model between topological indices and physical properties of Quinolone antibiotic drugs

	BP	MP	**MR**	TPSA
VL Index	**0.958**	0.875	**0.983**	0.656
SVL Index	**0.955**	0.871	**0.985**	0.647
NVL Index	**0.927**	0.858	**0.977**	0.682
SNVL Index	**0.915**	0.845	**0.978**	0.661

Table 5: The correlation coefficient r for logarithmic regression model between topological indices and physical properties of Quinolone antibiotic drugs

	BP	MP	**MR**	TPSA
VL Index	**0.952**	0.872	**0.981**	0.661
SVL Index	**0.950**	0.866	**0.984**	0.652
NVL Index	**0.927**	0.847	**0.975**	0.689
SNVL Index	**0.915**	0.826	**0.976**	0.666

Table 6: The correlation coefficient r for cubic regression model between topological indices and physical properties of Quinolone antibiotic drugs

	BP	MP	**MR**	TPSA
VL Index	**0.959**	0.880	**0.983**	0.684
SVL Index	**0.955**	0.871	**0.985**	0.647
NVL Index	**0.928**	0.872	**0.977**	0.718
SNVL Index	**0.915**	0.862	**0.978**	0.675

4. Observations

- For the VL index, the correlation coefficient demonstrates a strong linear relation- ship for both **BP** (**r = 0.957**) and **MR** (**r = 0.978**). In contrast, the relationship is moderate for **MP** (r = 0.846) and weaker for **TPSA** (r = 0.654).
- The SVL index shows a high correlation with **BP** (**r = 0.954**) and **MR** (**r = 0.982**), signifying a robust linear relationship, while the correlations with **MP** (r = 0.841) and **TPSA** (r = 0.643) are noticeably weaker.
- With the NVL index, a strong correlation is seen with **MR** (**r = 0.953**), while the relationship is somewhat moderate for **BP** (**r = 0.915**) and notably weaker for **MP** (r = 0.846) and **TPSA** (r = 0.678).
- The SNVL index reflects a strong linear correlation with **MR** (**r = 0.956**), but lower correlations are found with **BP** (r = 0.899), **MP** (r = 0.781), and **TPSA** (r = 0.649).
- For the VL index in the quadratic model, there is a high correlation with **BP** (**r = 0.958**) and **MR** (**r = 0.983**), indicating a robust quadratic relationship, whereas **MP** (r = 0.875) and **TPSA** (r = 0.656) show weaker correlations.
- The SVL index in quadratic regression also shows a strong association with **BP** (**r = 0.955**) and **MR** (**r = 0.985**), but lower values for **MP** (r = 0.871) and **TPSA** (r = 0.647).

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- In the case of the NVL index, a solid quadratic correlation is found for **MR** (**r = 0.977**), with moderate correlation for **BP** (**r = 0.927**) and weaker connections with **MP** (r = 0.858) and **TPSA** (r = 0.682).
- The SNVL index exhibits a strong quadratic correlation with **MR** (**r = 0.978**), a moderate correlation with **BP** (**r = 0.915**), and lower values for **MP** (r = 0.845) and **TPSA** (r = 0.661).
- The VL index shows strong logarithmic relationships with **BP** (**r = 0.952**) and **MR** (**r = 0.981**), but **MP** (r = 0.875) and **TPSA** (r = 0.661) exhibit weaker correlations.
- For the SVL index in the logarithmic model, the correlation is high for **BP** (**r = 0.950**) and **MR** (**r = 0.984**), while the relationships with **MP** (r = 0.866) and **TPSA** (r = 0.652) are less pronounced.
- The NVL index shows a strong logarithmic relationship with **MR** (**r = 0.975**), with a moderate relationship for **BP** (**r = 0.927**) and weaker correlations for **MP** (r = 0.847) and **TPSA** (r = 0.689).
- For the SNVL index, the logarithmic regression yields a strong correlation with **MR** (**r = 0.976**), while **BP** (**r = 0.915**) shows a moderate correlation, and **MP** (r = 0.826) and **TPSA** (r = 0.666) exhibit weaker correlations.
- In the cubic model, the VL index has high correlations with **BP** (**r = 0.959**) and **MR** (**r = 0.983**), while **MP** (r = 0.880) and **TPSA** (r = 0.684) show weaker relationships.
- The SVL index exhibits strong cubic correlations with **BP** (**r = 0.955**) and **MR** (**r = 0.985**), whereas **MP** (r = 0.871) and **TPSA** (r = 0.647) display weaker correlations.
- For the NVL index, the cubic model shows a robust relationship with **MR** (**r = 0.977**), moderate correlation with **BP** (**r = 0.928**), and weaker correlations with **MP** (r = 0.872) and **TPSA** (r = 0.718).
- The SNVL index in the cubic model demonstrates a strong correlation with **MR** (**r = 0.978**), moderate correlation with **BP** (**r = 0.915**), and lower correlations for **MP** (r = 0.862) and **TPSA** (r = 0.675).
- For all the above models the significance is 0.000

5. Regression Models

Linear, quadratic, logarithmic, and cubic regression models are different approaches used to capture relationships between variables, depending on the nature of their interaction. Linear regression assumes a straight-line relationship, where the dependent variable changes at a constant rate with respect to the independent variable. When the relationship shows curvature, quadratic regression is more suitable, modeling a parabolic trend where the variable increases or decreases at a non-constant rate. Logarithmic regression is useful when the dependent variable grows rapidly at first and then stabilizes, captur- ing exponential-like growth that slows over time. For more complex relationships, cubic regression introduces greater flexibility, allowing the curve to change direction up to two times, capturing oscillations or multiple trends in the data. Each of these models provides different insights based on the underlying patterns between variables and can be selected based on the best fit for the observed data.

The linear regression model is given by $PP = a(TI) + b$

For VL index

$$BP = 2.567(VL) + 170.985$$
$$n = 14, F = 130.096, SF = 26.376$$
$$MR = 0.505(VL) + 11.317$$
$$n = 14, F = 263.860, SF = 3.642$$

For SVL index

$$BP = 8.863(SVL) + 159.287$$
$$n = 14, F = 130.096, SF = 26.376$$
$$MR = 1.755(SVL) + 8.488$$
$$n = 14, F = 320.319, SF = 3.319$$

For NVL index

$$BP = 0.479(NVL) + 237.352$$
$$n = 14, F = 62.073, SF = 36.532$$
$$MR = 0.096(NVL) + 23.214$$
$$n = 14, F = 119.148, SF = 5.283$$

For SNVL index

$$BP = 3.636(SNVL) + 220.526$$
$$n = 14, F = 50.696, SF = 39.709$$
$$MR = 0.743(SNVL) + 18.478$$
$$n = 14, F = 126.034, SF = 5.149$$

Scatter diagrams of linear regression models

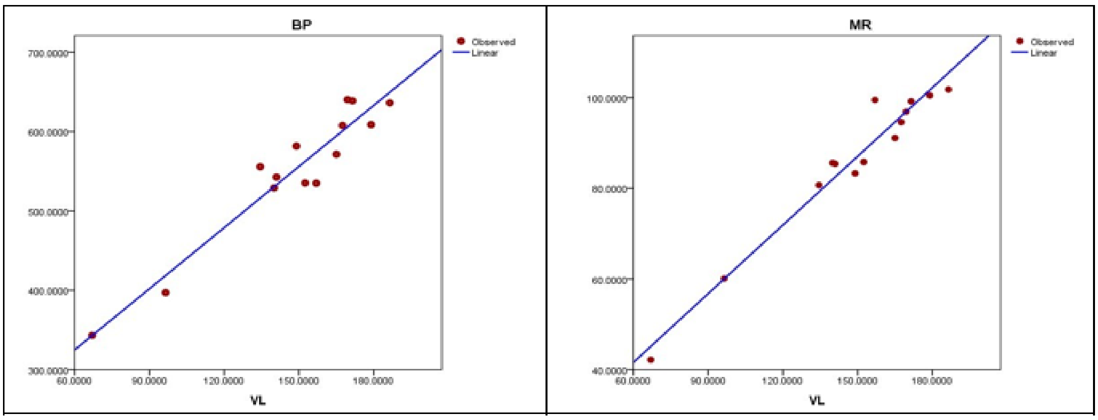

Figure 1: BP and MR with VL index

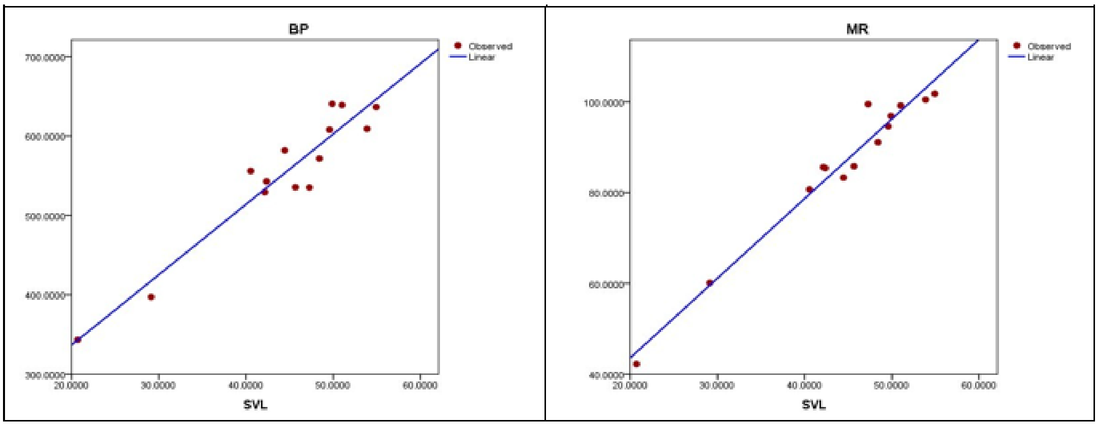

Figure 2: BP and MR with SVL index

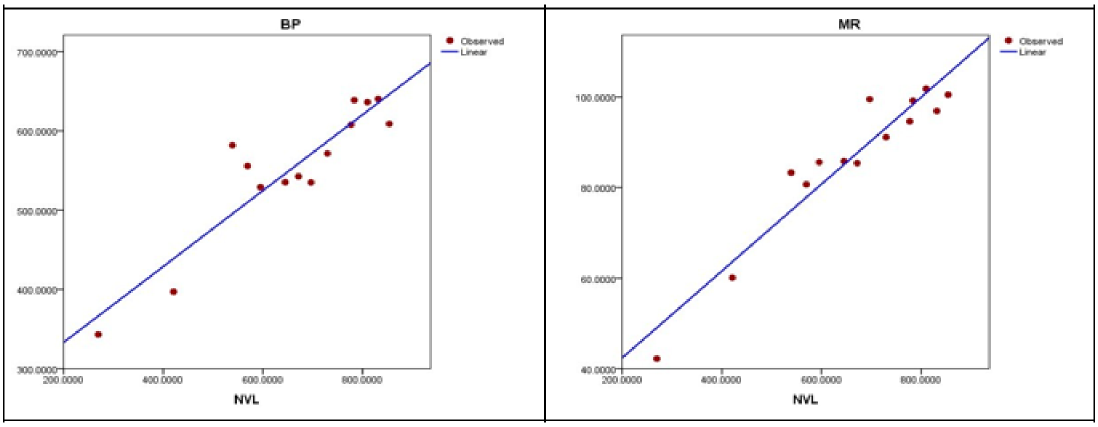

Figure 3: BP and MR with NVL index

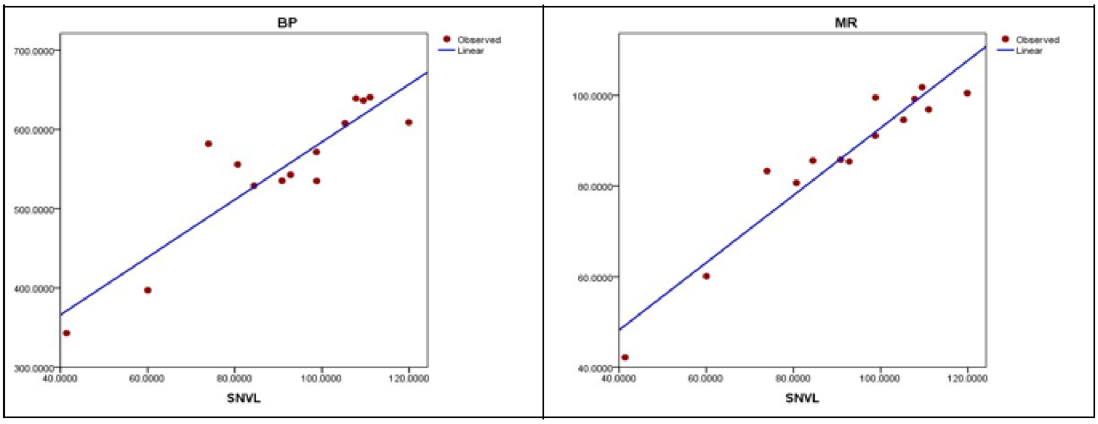

Figure 4: BP and MR with SNVL index

The quadratic regression model is given by $PP = a(TI)^2 + b(TI) + c$

For VL index
$BP = (-0.004)\,(VL)^2 + 3.476(VL) + 117.861$
$n = 14,\ F = 61.477,\ SF = 27.166$
$MR = (-0.001)\,(VL)^2 + 0.857(VL) + (-9.262)$
$n = 14,\ F = 156.037,\ SF = 3.366$

For SVL index
$BP = (-0.044)\,(SVL)^2 + 12.220(SVL) + 100.289$
$n = 14,\ F = 57.418,\ SF = 28.029$
$MR = (-0.014)\,(SVL)^2 + 2.845(SVL) + (-10.678)$
$n = 14,\ F = 183.596,\ SF = 3.111$

For NVL index
$BP = (0.000)\,(NVL)^2 + 0.953(NVL) + 111.517$
$n = 14,\ F = 33.379,\ SF = 35.656$
$MR = (0.000)\,(NVL)^2 + 0.232(NVL) + (-13.002)$
$n = 14,\ F = 183.596,\ SF = 3.111$

For SNVL index
$BP = (-0.028)\,(SNVL)^2 + 8.261(SNVL) + 46.040$
$n = 14,\ F = 28.232,\ SF = 38.280$
$MR = (-0.007)\,(SNVL)^2 + 1.852(SNVL) + (-23.353)$
$n = 14,\ F = 122.651,\ SF = 3.779$

Scatter diagrams of quadratic regression models

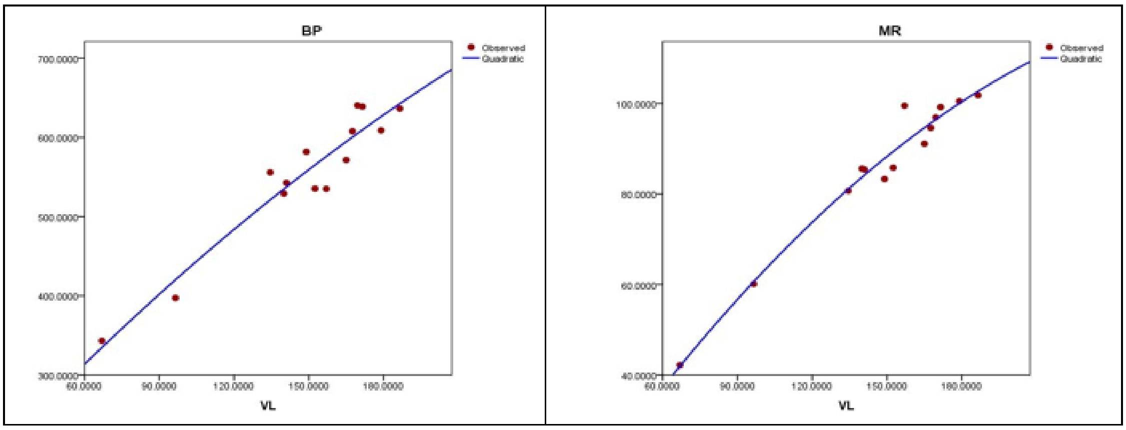

Figure 5: BP and MR with VL index

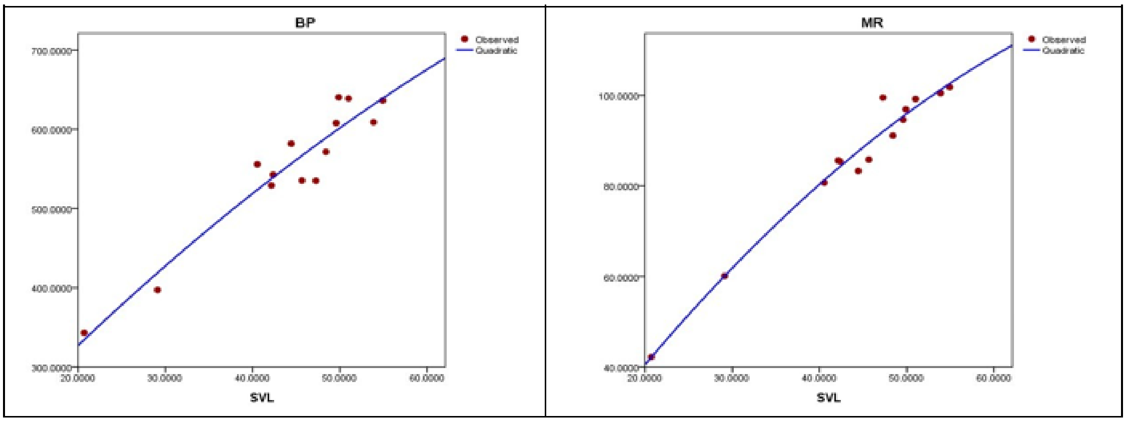

Figure 6: BP and MR with SVL index

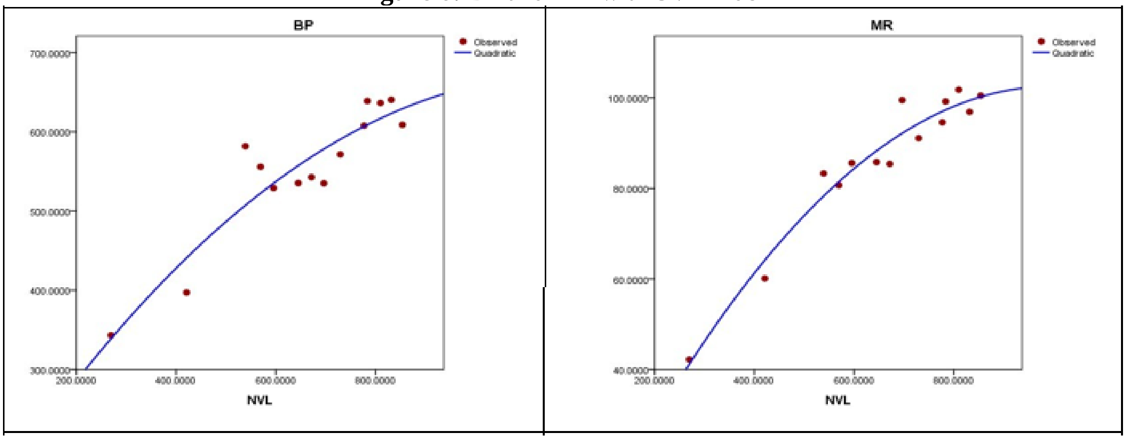

Figure 7: BP and MR with NVL index

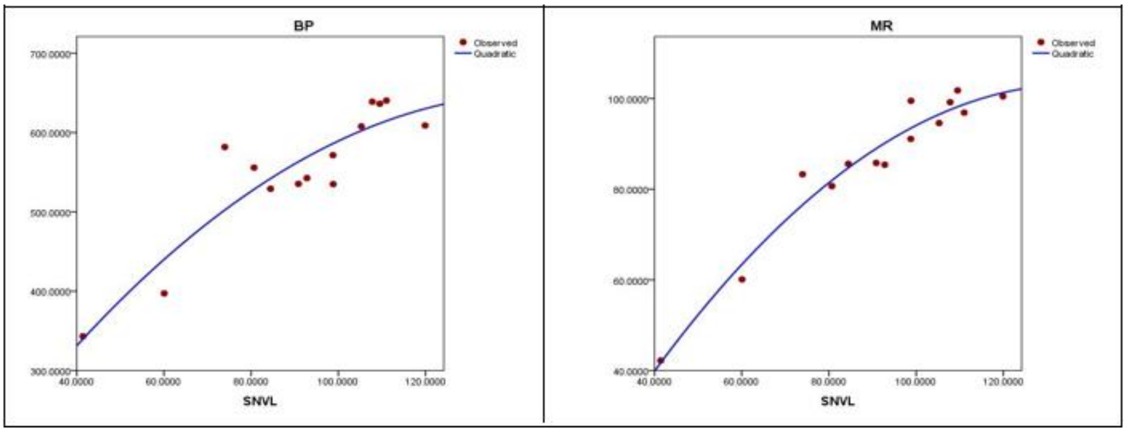

Figure 8: BP and MR with SNVL index

The logarithmic regression model is given by $PP = a\ln(TI) + b$ For VL index

$BP = 303.001 ln(VL) + (-954.067)$
$n = 14,\ F = 116.445,\ SF = 27.743$
$MR = 60.080 ln(VL) + (-212.376)$
$n = 14,\ F = 310.281,\ SF = 3.370$

For SVL index
$BP = 314.979 ln(SVL) + (-633.502)$
$n = 14,\ F = 111.420,\ SF = 28.302$
$MR = 62.733 ln(SVL) + (-149.862)$
$n = 14,\ F = 354.933,\ SF = 3.158$

For NVL index
$BP = 257.357 ln(NVL) + (-1107.679)$
$n = 14,\ F = 72.895,\ SF = 34.124$
$MR = 52.086 ln(NVL) + (-249.647)$
$n = 14,\ F = 228.129,\ SF = 3.904$

For SNVL index
$BP = 280.005 ln(SNVL) + (-702.375)$
$n = 14,\ F = 61.589,\ SF = 36.652$
$MR = 57.491 ln(SNVL) + (-171.298)$
$n = 14,\ F = 243.503,\ SF = 3.785$

Scatter diagrams of logarithmic regression models

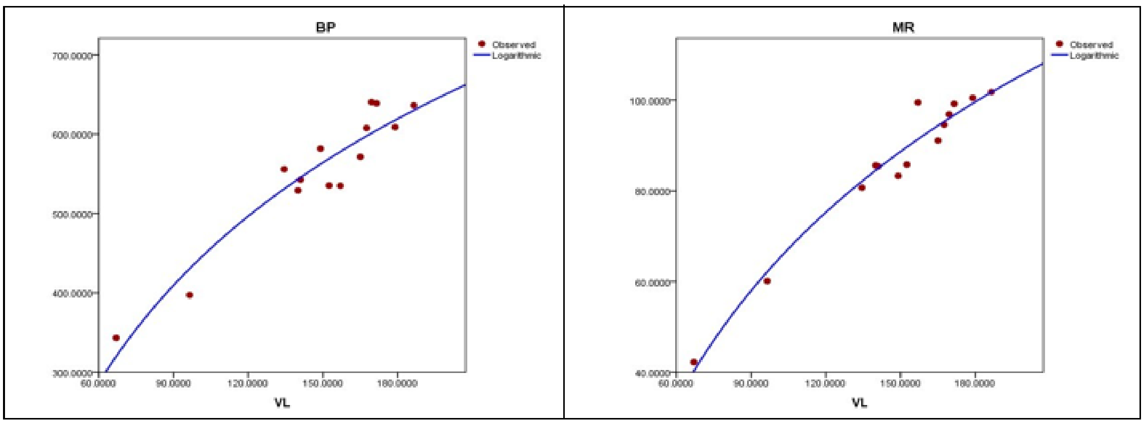

Figure 9: BP and MR with VL index

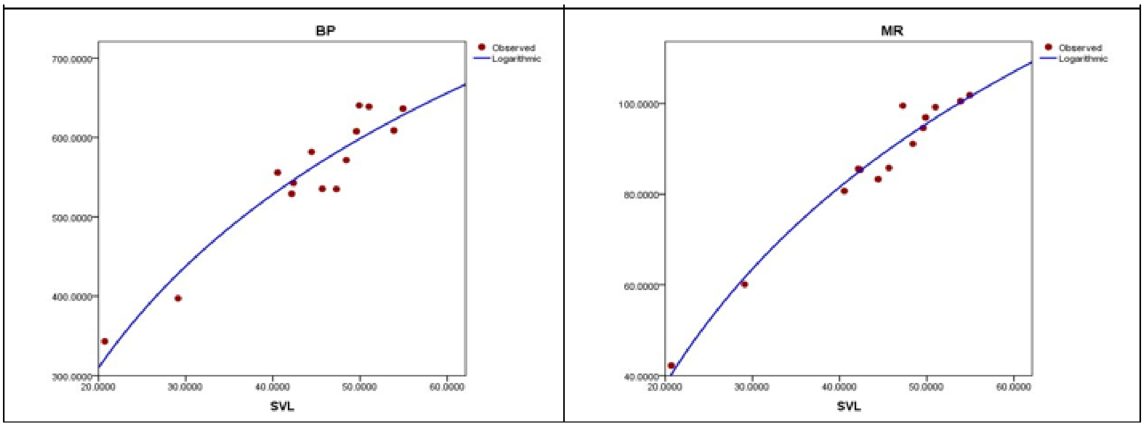

Figure 10: BP and MR with SVL index

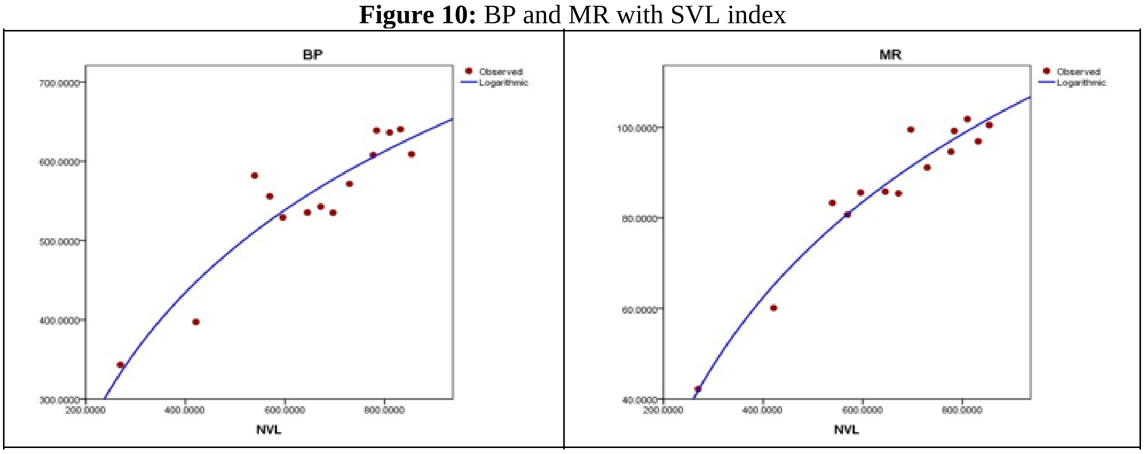

Figure 11: BP and MR with NVL index

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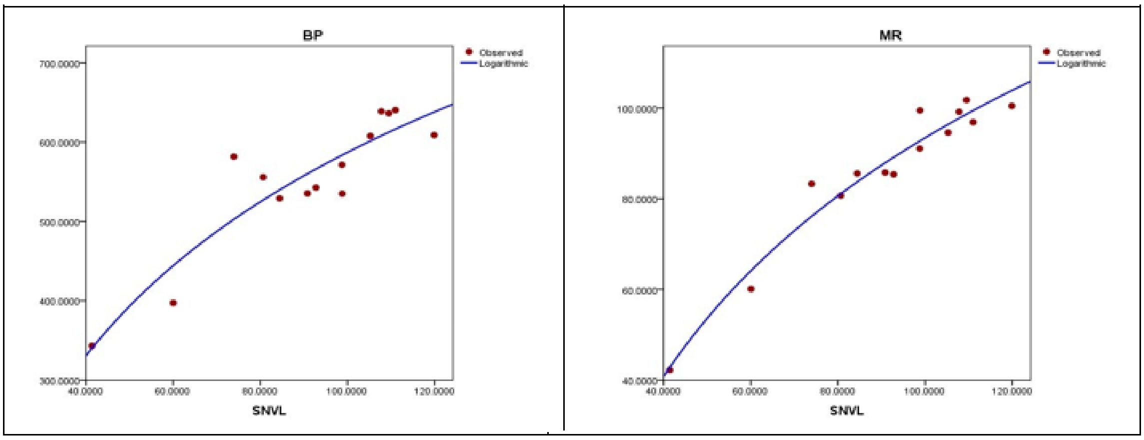

Figure 12: BP and MR with SNVL index

The cubic regression model is given by $PP = a(TI)^3 + b(TI)^2 + c(TI) + d$

For VL index

$$BP = 0.00(VL)^3 + 0.038(VL)^2 + (-1.582)(VL) + 308.300$$
$$n = 14,\ F = 38.148,\ SF = 28.185$$
$$MR = 0.000(VL)^3 + 0.001(VL)^2 + 0.611(VL) + (-0.007)$$
$$n = 14,\ F = 94.892,\ SF = 3.524$$

For SVL index

$$BP = 0.00(SVL)^3 + 4.769(SVL)^2 + 10.714(SVL) + 116.087$$
$$n = 14,\ F = 57.677,\ SF = 27.971$$
$$MR = 0.000(SVL)^3 + 0.409(SVL)^2 + 2.320(SVL) + (-4.703)$$
$$n = 14,\ F = 130.096,\ SF = 26.376$$

For NVL index

$$BP = 0.00(NVL)^3 + (-0.002)(NVL)^2 + 1.867(NVL) + (-34.755)$$
$$n = 14,\ F = 20.642,\ SF = 37.074$$
$$MR = 0.000(NVL)^3 + 0.000(NVL)^2 + 0.170(NVL) + (-2.961)$$
$$n = 14,\ F = 70.349,\ SF = 4.069$$

For SNVL index

$$BP = 0.00(SNVL)^3 + (-0.093)(SNVL)^2 + 13.249(SNVL) + (-71.558)$$
$$n = 14,\ F = 17.246,\ SF = 40.016$$

$$MR = 0.000(SNVL)^3 + (-0.007)(SNVL)^2 + 1.860(SNVL) + (-23.536)$$
$$n = 14,\ F = 74.334,\ SF = 3.963$$

Scatter diagrams of cubic regression models

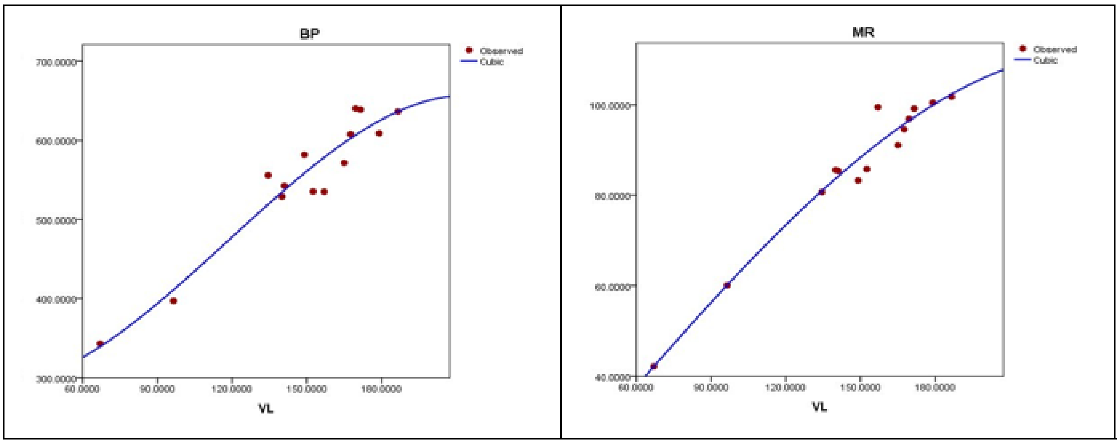

Figure 13: BP and MR with VL index

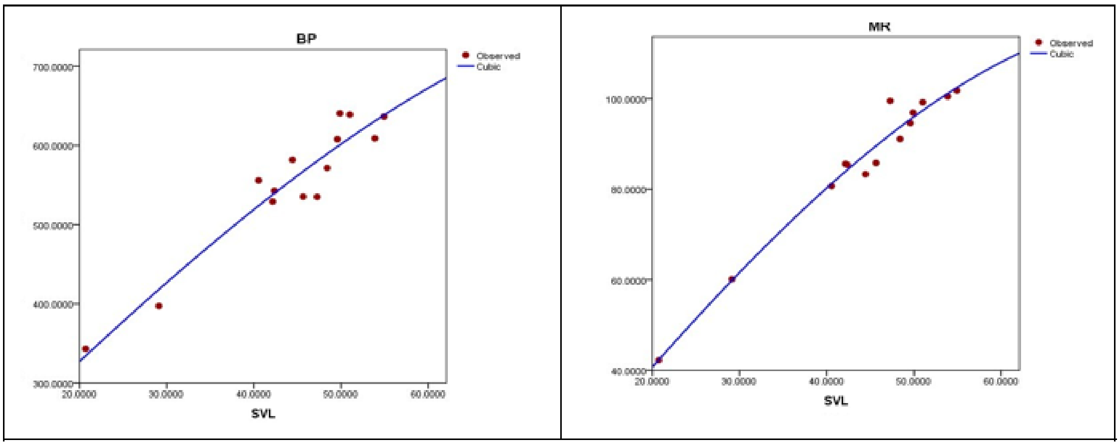

Figure 14: BP and MR with SVL index

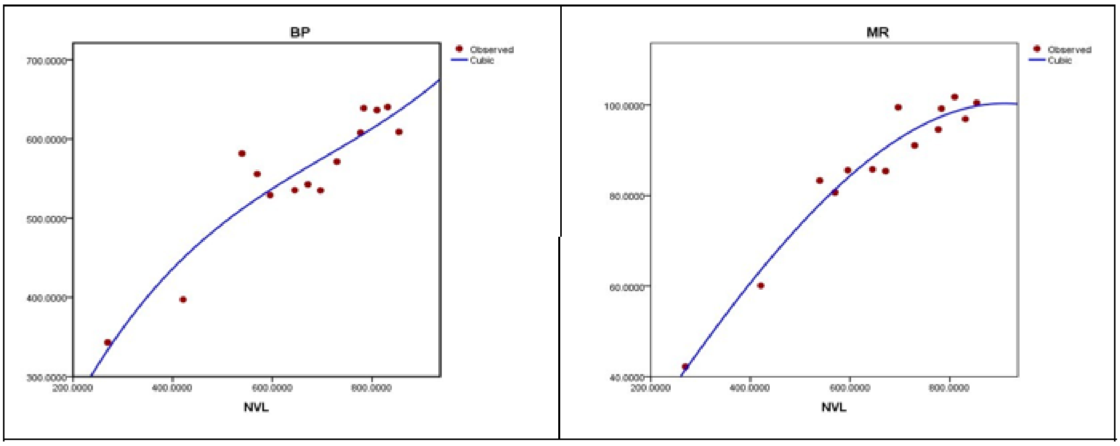

Figure 15: BP and MR with NVL index

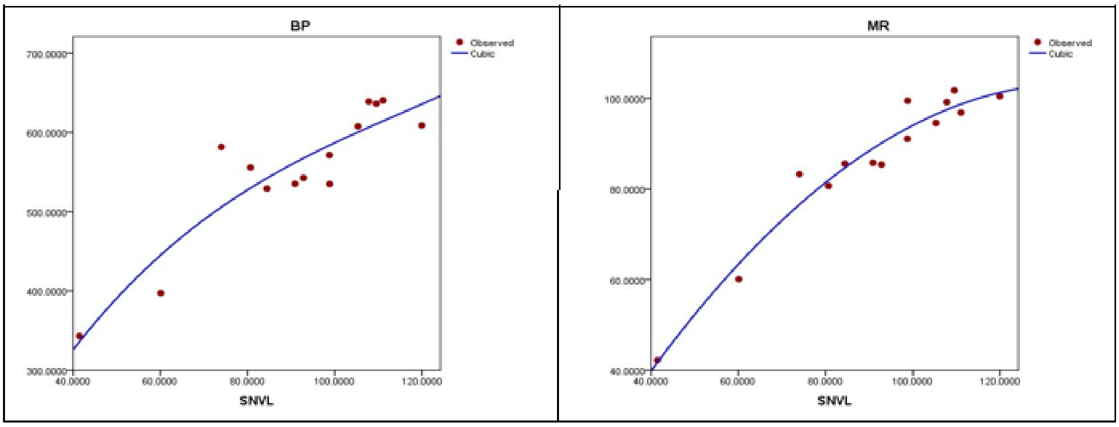

Figure 16: BP and MR with SNVL index

6. Conclusion

In this study, we analyzed the relationship between the Veerabhadraiah Lokesha (VL) index and its variants, Sombor type VL index (SVL), neighborhood degree sum VL index (NVL), and Sombor type neighborhood degree sum VL index (SNVL) with the physico- chemical properties of Quinolone antibiotics. Using regression models, including linear, quadratic, logarithmic, and cubic, we explored the correlation between these indices and drug properties. The analysis revealed that certain models provide a stronger fit for specific physicochemical properties, highlighting the usefulness of these topological indices in capturing the structural features of Quinolone antibiotics.

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