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Open Neighbourhood Sombor Degree Based Topological Indices Of Fungal Infection Drugs

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ABSTRACT :

A topological index is a molecular descriptor based on the molecular structure of a chemical substance. In this article, we introduce some Open Neighbourhood Sombor Indices and discuss several antifungal drugs like Ketoconazole, Clotrimazole, Miconazole, Fluconazole, Itraconazole, Posaconazole, Voriconazole, and Isavuconazole, along with their physicochemical properties, to analyse the QSPR model and forecast the best fit.

Keywords: Fungal disease drug, open neighbourhood, QSPR model.

1. Introduction :

Topological indices are quantitative descriptors derived from a chemical graph, offering a comprehensive characterization of a chemical system. They are widely used to investigate the physicochemical properties of a variety of drugs. In pharmaceutical research, the development of novel antifungal drugs has become increasingly important, particularly due to the growing resistance of fungi to existing treatments. One of the key tools in this area is Quantitative Structure-Property Relationship (QSPR) modeling, which is essential for predicting the biological activity of drugs based on their molecular structures. A central feature of QSPR modeling involves the use of topological descriptors, which reflect a molecule's connectivity and can significantly assist in forecasting drug properties. These descriptors are mathematical representations that capture essential aspects of a molecule's structure, excluding the three-dimensional spatial arrangement of atoms. By analyzing the molecular graph, where atoms are nodes and bonds are edges, researchers can derive valuable insights into both the physicochemical properties and biological efficacy of antifungal drugs.

In 2019, S.Mondal et al.,[7,8] introduced the neighbourhood degree based topological indices. In 2021, V.Ravi et al.,[11] introduced some open neighbourhood degree based topological indices. In 2021, I.Gutman[5] introduced the Sombor index. In 2021, V.R.Kulli [6] introduced the Banhatti-Sombor index. In 2024, I.Gutman et al.,[4] discussed the Elliptic Sombor index. In 2021, I.Gutman introduced the Reduced Sombor index. In 2024, I.Gutman[3] discussed the Euler Sombor index.

The aforementioned studies motivated us to undertake the present investigation**.** In this article, we introduce some Open Neighbourhood Sombor Indices and discuss several antifungal drugs like Ketoconazole, Clotrimazole, Miconazole, Fluconazole, Itraconazole, Posaconazole, Voriconazole, and Isavuconazole, along with their physicochemical properties, to analyse the QSPR model and forecast the best fit.

2. Results and discussion :

Let u and v are the vertices of a graph G, then u is adjacent to v if there is an edge between u and v. Adjacent vertices are called neighbors. The set of neighbors of vertex u is the neighborhood of u, denoted $N(u)$.

We define the Open Neighbourhoods of Degree Sum Based Sombor Indices, where the open neighbourhood index is given by $\alpha(q) = \sum_{q \in N_G(r)} d(q)$, $N_G(r)$ represents the neighbourhood of vertex r in the graph G and $d(q)$ denotes the degree of the vertex q.

- The Open Neighbourhood Sombor Index is defined as

$$N_oSO = \sum_{qr \in E(G)} \frac{\sqrt{\alpha(q)^2 + \alpha(r)^2}}{2}$$

- The Open Neighbourhood Banhatti Sombor Index is defined as

$$N_oBSO = \sum_{qr\in E(G)} \frac{\sqrt{\frac{1}{(\alpha(q))^2}+\frac{1}{(\alpha(r))^2}}}{2}$$

- The Open Neighbourhood Elliptic Sombor Index is defined as

$$N_oESO = \sum_{qr\in E(G)} \frac{(\alpha(q)+\alpha(r))\sqrt{\alpha(q)^2+\alpha(r)^2}}{2}$$

- The Open Neighbourhood Reduced Sombor Index is defined as

$$N_oRSO = \sum_{qr\in E(G)} \frac{\sqrt{(\alpha(q)-1)^2+(\alpha(r)-1)^2}}{2}$$

- The Open Neighbourhood of Euler Sombor Index is defined as

$$N_oEUSO = \sum_{qr\in E(G)} \frac{\sqrt{\alpha(q)^2+\alpha(r)^2+\alpha(q)\alpha(r)}}{2}$$

Also, we proposed reciprocal of Open Neighbourhoods Degree Sum Based Sombor Indices are given below

- The Reciprocal Open Neighbourhood Sombor Index is defined as

$$RN_oSO = \sum_{qr\in E(G)} \frac{2}{\sqrt{(\alpha(q)+\alpha(r))^2}}$$

- The Reciprocal Open Neighbourhood Banhatti Sombor Index is defined as

$$RN_oBSO = \sum_{qr\in E(G)} \frac{2}{\sqrt{\frac{1}{(\alpha(q))^2}+\frac{1}{(\alpha(r))^2}}}$$

- The Reciprocal Open Neighbourhood Elliptic Sombor Index is defined as

$$RN_oESO = \sum_{qr\in E(G)} \frac{2}{(\alpha(q)+\alpha(r))\sqrt{\alpha(q)^2+\alpha(r)^2}}$$

- The Reciprocal Open Neighbourhood Reduced Sombor Index is defined as

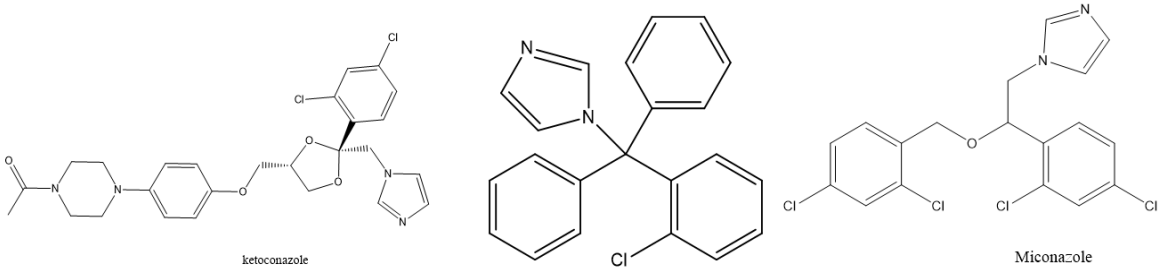
$$RN_oRSO = \sum_{qr\in E(G)} \frac{2}{\sqrt{(\alpha(q)-1)^2+(\alpha(r)-1)^2}}$$

- The Reciprocal Open Neighbourhood of Euler Sombor Index is defined as

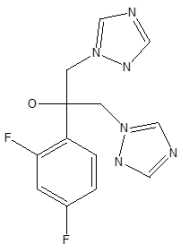
$$RN_oESO = \sum_{qr\in E(G)} \frac{2}{\sqrt{\alpha(q)^2+\alpha(r)^2+\alpha(q)\alpha(r)}}$$

In this section, we analyze the topological indices of several antifungal medications. The relationship between QSPR analysis and topological indices shows that the properties are correlated with physicochemical properties such as Boiling Point (BP), Enthalpy (E), Flash Point (FP), Molar Refractivity (MR), and Polarizability (P). The information presented in Table 1 was obtained from ChemSpider and PubChem. The structures of the drugs are provided in Figure 1 below.

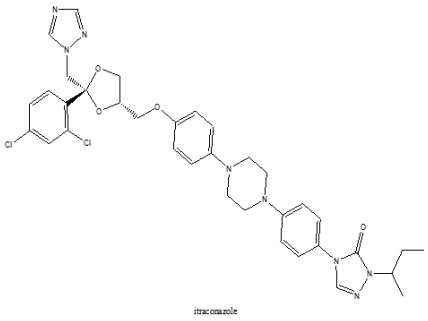
We have assessed the open neighbourhood edge partition values for various drugs as shown in Tables 2 to 9, and the Open Neighbourhood Sombor Index degree based topological indices values are presented in Table 10.



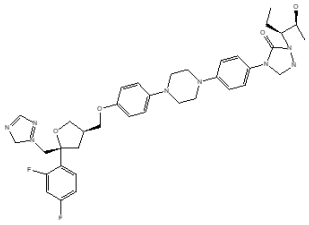
(a) Ketoconazole **(b)Clotrimazole** **(c)Miconazole**



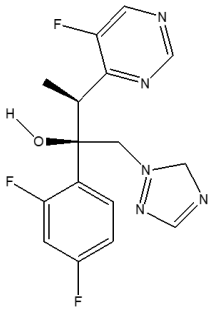
(d)Fluconazole



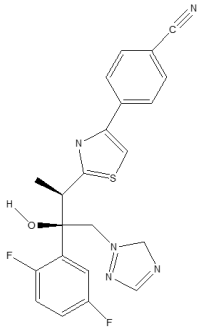
(e)Itraconazole



(f)Posaconazole



(g)Voriconazole



(h)Isavuconazole

Figure 1. Molecular structure of fungal infection drugs

Table 1. Physicochemical properties and biological activity of fungal infection drugs

Drugs	BP	E	FP	MR	P	MV
Ketoconazole	753.4	109.8	409.4	139.1	55.2	385
Clotrimazole	482.3	71.9	245.5	105.9	42	302.8
Miconazole	555.1	80.5	289.5	104.7	41.5	296
Fluconazole	579.8	91.2	304.4	76.1	30.2	205.3
Itraconazole	850	123.5	467.9	189.3	75.1	502
Posaconazole	850.7	129.5	468.3	188.6	74.8	512
Voriconazole	508.6	82	261.4	85.6	33.9	244.7
Isavuconazole	678	104.5	363.8	117.5	46.6	316.2

Table 2. Open Neighbourhood Edge partition of Ketoconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	Number of edges
(4,4)	1
(4,5)	4
(6,5)	7
(6,7)	1
(7,9)	2
(9,9)	1
(6,9)	2
(6,6)	1
(9,5)	1

(5,5)	7
(7,4)	1
(6,3)	1
(5,3)	3
(7,5)	7
(7,7)	1

Table 3. Open Neighbourhood Edge partition of Clotrimazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(4,4)	6
(4,5)	8
(5,8)	6
(8,12)	3
(12,9)	1
(9,5)	1
(6,5)	1
(9,6)	1
(3,6)	1

Table 4. Open Neighbourhood Edge partition of Miconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(6,5)	4
(5,5)	5
(6,7)	2
(5,3)	2
(6,3)	2
(7,5)	4
(6,6)	2
(4,5)	2
(4,4)	1
(6,8)	1
(7,8)	1
(5,8)	1

Table 5. Open Neighbourhood Edge partition of Fluconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(4,4)	2
(4,5)	4
(5,5)	2
(5,6)	6
(9,5)	2
(7,8)	2
(9,8)	1
(6,7)	2
(5,3)	2

Table 6. Open Neighbourhood Edge partition of Itraconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(4,4)	1
(4,5)	2
(9,9)	1

(6,9)	1
(7,9)	2
(9,5)	1
(9,6)	1
(6,7)	2
(6,5)	9
(5,5)	10
(6,6)	1
(5,3)	1
(6,3)	2
(6,8)	1
(6,4)	1
(4,2)	1
(7,7)	2
(7,5)	10
(7,8)	2
(8,7)	1
(7,3)	1
(8,5)	2

Table 7. Open Neighbourhood Edge partition of Posaconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(4,4)	1
(4,5)	2
(9,9)	1
(6,9)	1
(7,9)	2
(9,5)	1
(9,6)	1
(6,7)	2
(7,3)	1
(6,6)	1
(3,6)	1
(5,3)	3
(5,5)	10
(6,5)	9
(7,5)	10
(7,7)	2
(7,8)	3
(8,5)	3
(8,8)	1
(8,4)	1
(2,4)	1

Table 8. Open Neighbourhood Edge partition of Voriconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(5,4)	4
(6,5)	4
(4,4)	2
(6,7)	1
(8,8)	1
(3,6)	2
(3,8)	1

(5,3)	1
(9,5)	2
(9,8)	1
(9,9)	1
(5,5)	2
(6,8)	1
(8,5)	1
(6,6)	1
(9,7)	1
(9,4)	1

Table 9. Open Neighbourhood Edge partition of Isavuconazole

$\alpha(q), \alpha(r) : qr \in E(G)$	**Number of edges**
(7,5)	4
(9,9)	1
(9,7)	1
(9,4)	1
(9,8)	1
(7,8)	1
(6,7)	3
(7,7)	1
(6,9)	2
(4,2)	1
(6,4)	1
(6,5)	6
(5,5)	5
(4,5)	2
(5,3)	1
(6,3)	1
(3,8)	1
(4,4)	1

Table. 10 Open Neighbourhood Degree sum based Topological indices of fungal infection drugs

Drugs	N_oSO	N_oBSO	N_oESO	N_oSOR	N_oEUSO
Ketoconazole	161.49	5.39	1903.30	133.57	196.42
Clotrimazole	117.83	3.87	1550.71	98.36	142.80
Miconazole	105.01	3.75	1175.06	86.17	127.75
Fluconazole	95.43	3.31	1115.07	78.68	116.04
Itraconazole	229.49	7.23	2780.28	191.14	279.03
Posaconazole	238.21	7.52	2896.18	198.49	289.52
Voriconazole	112.58	3.70	1382.68	93.88	136.33
Isavuconazole	141.85	4.58	1734.39	118.21	172.24
Drugs	RN_oSO	RN_oBSO	RN_oESO	RN_oSOR	RN_oEUSO
Ketoconazole	10.30	309.66	0.98	12.68	8.47
Clotrimazole	7.37	220.91	0.75	9.24	6.07
Miconazole	7.13	201.62	0.69	8.81	5.87
Fluconazole	6.33	182.72	0.62	7.86	5.21
Itraconazole	13.70	439.22	1.27	16.74	11.28
Posaconazole	14.22	454.83	1.33	17.40	11.71
Voriconazole	6.85	210.19	0.66	8.43	5.66
Isavuconazole	8.57	269.30	0.82	10.54	7.07

3. Regression model :

In this section, we examine the topological indices and using the regression model we investigate the relation between computed topological indices and physicochemical parameters.

Linear $$\mathrm{P} = a_1 X_i + b, i = 1$$

Quadratic $$\mathrm{P} = a_1 X_i + a_2 X_i^2 + b, i = 1,2$$

Cubic $$\mathrm{P} = a_1 X_i + a_2 X_i^2 + a_3 X_i^3 + b, i = 1,2,3$$

Here P is the physical property and $X_i, i = 1,2,3$ is the topological descriptor. b and a denote the co-efficient and constant respectively. The software packages MATLAB and SPSS are useful to determining the results.

Now, we present the SVR models for the physio-chemical properties in terms of our proposed indices where R^2, χ^2 denote the goodness of fit of the model with the p-value and SE denote the Standard error.

The hypothesis which we considered for checking the goodness of fit of the regression models are:

- H_0 : Proposed regression model is a good fit
- H_1 : Proposed regression model is not a good fit

3.1 Linear regression model

Using the linear regression equation, based on the R^2 and $RMSE$ values of the linear regression models, it is observed that six properties and the activity—BP, E, MR, P, and MV—are predicted using the open neighbourhood Sombor index degree-based indices. The best predictive models are as follows:

$$BP = 44.419(RN_oSO) + 243.66$$

$$E = 0.0717(N_oBSO) - 2.185$$

$$FP = 26.869(RN_oSO) + 101.11$$

$$MR = 155.16(RN_oESO) - 12.442$$

$$P = 61.58(RN_oESO) - 4.9735$$

$$MV = 401.32(RN_oESO) - 12.2$$

Table 11. Statistical Summary of $ONSO$ Linear Models for Fungal Infection Drugs

Property	*Best Predictor*	R^2	*RMSE*	*Chi square*
BP	RN_oSO	0.8782	55.810	33.24
E	N_oBSO	0.8397	9.105	5.9675
FP	RN_oSO	0.8784	33.726	23.355
MR	RN_oESO	0.9821	6.256	2.3165
P	RN_oESO	0.9822	2.478	0.9144
MV	RN_oESO	0.9738	19.674	9.333

Additionally, we conduct quadratic regression analysis to determine whether the additional properties can be predicted by the proposed descriptors. Also, we investigate if the quadratic regression models offer improvements in terms of R^2 and $RMSE$ values.

3.2 Quadratic regression model

Using the quadratic regression equation, based on the R^2 and $RMSE$ values of the linear regression models, it is observed that six properties and the activity—BP, E, MR, P, and MV—are predicted using the open neighbourhood Sombor index degree-based indices. The best predictive models are as follows:

$$BP = -3.0728\,(RN_oSO)^2 + 108.14\,(RN_oSO) - 57.013$$

$$E = -0.0002(RN_oBSO)^2 + 0.3062\,(RN_oBSO) + 29.495$$

$$FP = -1.8563\ (RN_oSO)^2 + 65.362\ (RN_oSO) - 80.535$$

$$MR = -54.252\ (RN_oESO)^2 + 261.75\ (RN_oESO) - 60.713$$

$$P = -21.714\ (RN_oESO)^2 + 104.24\ (RN_oESO) - 24.294$$

$$MV = -179.48\ (RN_oESO)^2 + 753.96\ (RN_oESO) - 171.89$$

Table 12. Statistical Summary of $ONSO$ Quadratic Models for Fungal Infection Drugs

Property	*Best Predictor*	R^2	*RMSE*	*Chi square*
BP	RN_oSO	0.8914	57.710	31.316
E	RN_oBSO	0.8429	9.875	5.959
FP	RN_oSO	0.8916	34.875	22.143
MR	RN_oESO	0.9854	6.204	1.761
P	RN_oESO	0.9855	2.452	0.692
MV	RN_oESO	0.9791	19.280	6.933

Additionally, we conduct cubic regression analysis to determine whether the additional properties can be predicted by the proposed descriptors. Also, we investigate if the quadratic regression models offer improvements in terms of R^2 and $RMSE$ values.

3.3 Cubic regression model

Using the cubic regression equation, based on the R^2 and $RMSE$ values of the linear regression models, it is observed that six properties and the activity—BP, E, MR, P, and MV—are predicted using the open neighbourhood Sombor index degree-based indices. The best predictive models are as follows:

$$BP = -0.0009\ (N_oSO)^3 + 0.4234\ (N_oSO)^2 - 61.235\ (N_oSO) + 3318.3$$

$$E = -0.0002\ (N_oSOR)^3 + 0.0752\ (N_oSOR)^2 - 9.0421\ (N_oSOR) + 423.51$$

$$FP = -7E-05(RN_oBSO)^3 + 0.0659\ (RN_oBSO)^2 - 18.096\ (RN_oBSO) + 1837.3$$

$$MR = 0.1449\ (RN_oESO)^3 - 5.7155\ (RN_oESO)^2 + 83.723\ (RN_oESO) - 296.62$$

$$P = 0.0566\ (RN_oESO)^3 - 2.2362\ (RN_oESO)^2 + 32.858\ (RN_oESO) - 116.4$$

$$MV = 1079\ (RN_oESO)^3 - 3278.8\ (RN_oESO)^2 + 3609\ (RN_oESO) - 1017.3$$

Table 12. Statistical Summary of $ONSO$ Cubic Models for Fungal Infection Drugs

Property	*Best Predictor*	R^2	*RMSE*	*Chi square*
BP	N_oSO	0.9415	47.372	136.806
E	N_oSOR	0.8904	9.221	148.020
FP	RN_oBSO	0.9427	28.351	188.774
MR	RN_oESO	0.9868	6.589	1.444
P	RN_oESO	0.9868	2.614	0.574
MV	RN_oESO	0.9835	19.149	4.889

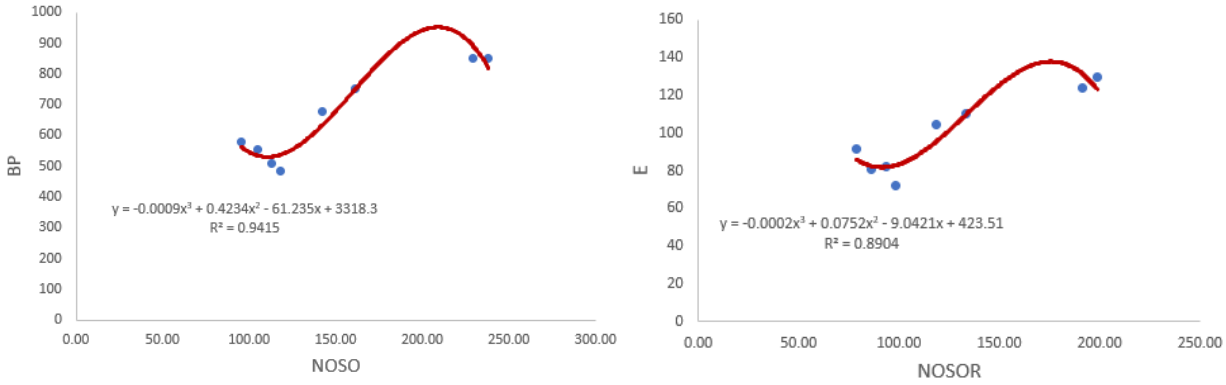


Fig. 2 Cubic Regression curve for BP and E

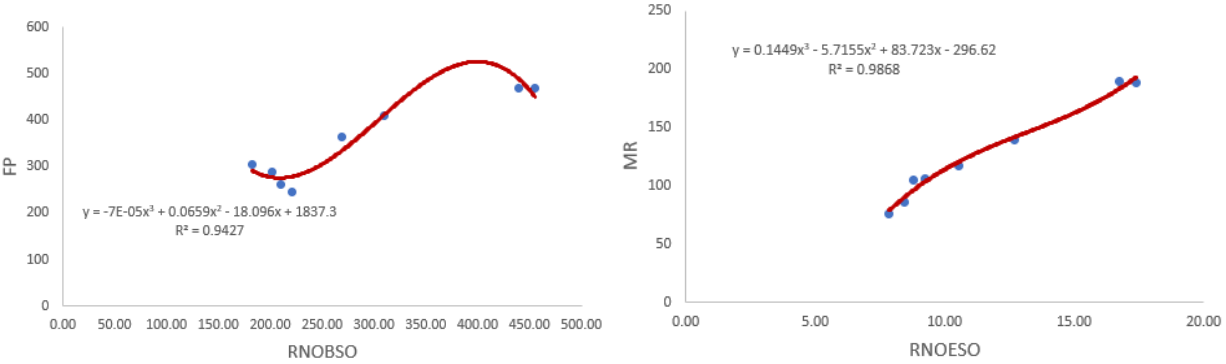


Fig. 3 Cubic Regression curve for FP and MR

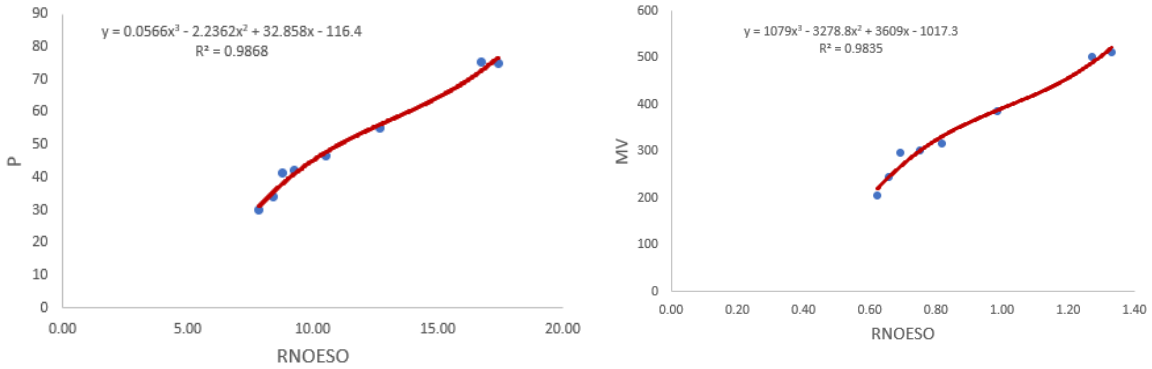


Fig. 4 Cubic Regression curve for P and MV

4. Conclusion :

In this paper, we introduced and computed the open neighbourhood sombor index of degree based topological indices for the fungal treatment drugs such as Ketoconazole, Clotrimazole, Miconazole, Fluconazole, Itraconazole, Posaconazole, Voriconazole and Isavuconazole.

QSPR analysis using curvilinear models indicates that cubic regression models offer more accurate predictions for the physicochemical properties of antifungal drugs.

- N_oSO is the best suited model for predicting the Boiling Point (BP), N_oSOR is the best fit model for Enthalpy (E) and RN_oBSO is the best model of Flash Point (FP) of the fungal infection drugs.
- RN_oESO is the best suited model for the Molar Refraction (MR), Polarizability (P), and Molar Volume (MV) of the fungal infection drugs

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