

Polynomial Regression Analysis for Some Anticancer Drugs with Degree Based Topological Indices

Sujata Timmanaikar

Department of Mathematics, Govt. Engineering College, Haveri-581 110, India

Abstract

The topological index is a numerical value associated with the molecular graph. These are also called molecular descriptors. Molecular descriptors plays vital role in QSPR-studies of predicting anti-cancer drugs. In this paper, we consider thirteen degree-based molecular descriptors for the QSPR-analysis of anti-cancer drugs.

Keywords: Molecular descriptor, molecular graph, anticancer drug, QSPR-analysis.

Subject Classification: 05C90; 05C35; 05C69.

Introduction

Cancer is one of the leading causes of disease-related death in the world. Despite the discovery of numerous chemotherapeutic drugs that inhibit uncontrolled cell division processes for the treatment of various cancers, serious side effects are a significant disadvantage. Furthermore, multi-drug resistance is a significant issue in anticancer treatment. Many studies are being conducted to discover and develop effective anticancer drugs due to issues such as cytotoxicity and drug resistance. This disease's symptoms include a lump, abnormal bleeding, a longer cough, weight loss, and so on. Chewing tobacco, obesity, poor diet, laziness, and excessive alcohol consumption are the main causes of this cancerous disease. Several treatments, including surgery, radiotherapy, chemotherapy, hormone therapy, targeted therapy, and others, are available to treat this dangerous disease. Anticancer drugs, which include alkylates and metabolites, are those used to treat the disease known as cancer.

Chemical graph theory is a branch of mathematical chemistry, which is found to be useful in study of QSAR (Quantitative Structure-Activity Relationships) and QSPR (Quantitative Structure-Property Relationship) analysis. Numerous studies have been made relating to the above mentioned fields by using what are called molecular descriptors.

There are mainly three types of descriptors:

1. Degree based molecular descriptors
2. Distance based molecular descriptors
3. Eigenvalue based molecular descriptors

A pair of molecular descriptors known as the first Zagreb index $M_1(G)$ and the second Zagreb index $M_2(G)$, are the first degree-based molecular descriptors and they first appeared in the topological formula for the total π -electron energy of conjugated molecules that has been derived by Gutman and Trinajstić[7], the first and second Zagreb indices are defined as:

$$M_1(G) = \sum_{uv \in E(G)} (d_u + d_v) M_2(G) = \sum_{uv \in E(G)} (d_u \cdot d_v)$$

In [14] several degree based topological indices to study QSPR-analysis of anticancer drugs. To conduct QSPR analysis low intercorrelation between the variables should be verified. If there is a high intercorrelation between the variables, then we have to choose different variables for QSPR-study. In this paper, we proved that there is a high intercorrelation between the topological indices for the study carried out in[14].

We have considered the following topological indices [6, 9, 12, 20, 19, 10, 11, 7, 5, 15, 2, 8, 1] for the study:

$$ABC(G) = \sum_{uv \in E(G)} \sqrt{\frac{d_u + d_v - 2}{d_u d_v}} \quad (1)$$

$$ABC_4(G) = \sum_{uv \in E(G)} \sqrt{\frac{s_u + s_v - 2}{s_u s_v}} \quad (2)$$

$$\chi(G) \sum_{u \sim v} \frac{1}{\sqrt{d_G(u) d_G(v)}} \quad (3)$$

$$S(G) = \sum_{u \sim v} \frac{1}{d_u(G) + d_v(G)} \quad (4)$$

$$GA(G) = \sum_{u \sim v} \frac{2\sqrt{d_u(G) d_v(G)}}{d_u(G) + d_v(G)} \quad (5)$$

$$GA_5(G) = \sum_{u \sim v} \frac{2\sqrt{s_u(G) s_v(G)}}{s_u(G) + s_v(G)} \quad (6)$$

$$M_1(G) = \sum_{u \in V(G)} d_G(u)^2 \quad (7)$$

$$M_2(G) = \sum_{uv \in E(G)} d_G(u) d_G(v) \quad (8)$$

$$H(G) = \sum_{u \sim v} \frac{2}{d_u(G) + d_v(G)} \quad (9)$$

$$HM(G) = \sum_{u \sim v} (d_u(G) + d_v(G))^2 \quad (10)$$

$$ZG_3(G) = \sum_{uv \in E(G)} |d_G(u) - d_G(v)| \quad (11)$$

$$F(G) = \sum_{u \in V(G)} d_G(u)^3 \quad (12)$$

$$SSD(G) = \sum_{uv \in E(G)} \left[\frac{P}{Q} + \frac{Q}{P} \right] \quad (13)$$

Note: $s_u = \sum_{u \in V(G)} \deg(N(u))$, where $N(u)$ denote the neighborhood of the vertex u ; $P = \min\{d_G(u), d_G(v)\}$ and $Q = \max\{d_G(u), d_G(v)\}$

2 Data Sets

We studied 17 anticancer drugs from Amathaspiramide-E to Tambjamine-K. The values for these properties are taken from Chem Spider. The physico-chemical properties of these anticancer drugs are mentioned in Table 2.

Structures belonging to these sets are conveniently displayed in Table 3.

We list in Table 3, the above mentioned topological indices values of molecular graphs of 17 anticancer drugs. The considered topological indices values of anticancer drugs were computed manually by employing definition of each topological index mentioned in (1)-(13).

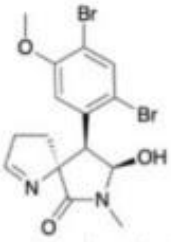
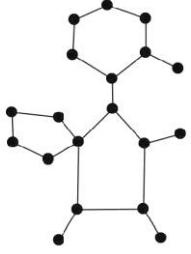
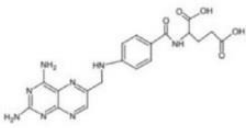
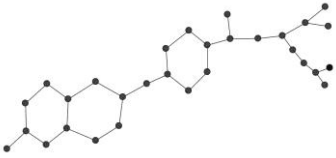
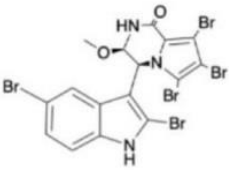
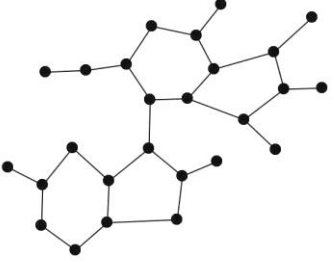
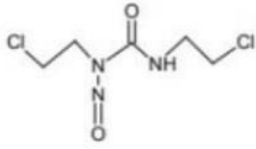
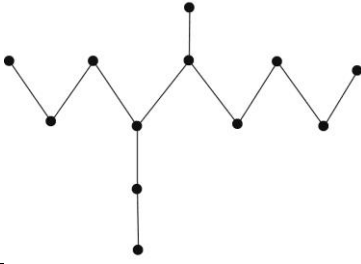
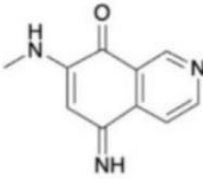
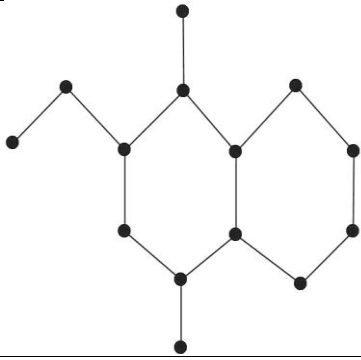
3 Statistical Parameters

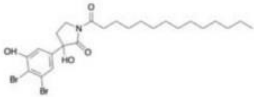
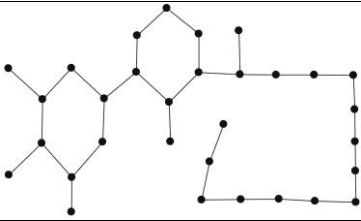
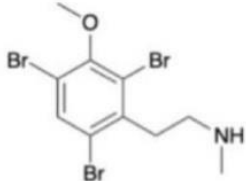
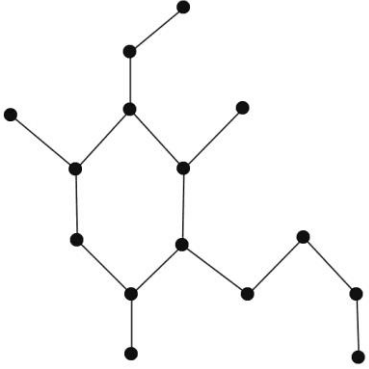
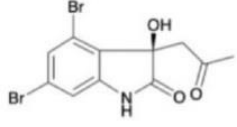
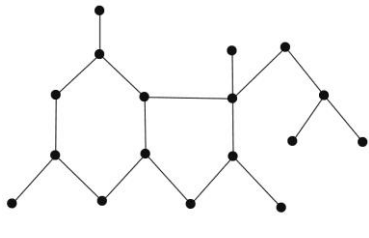
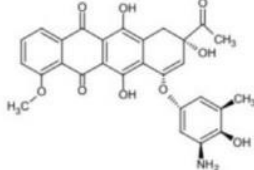
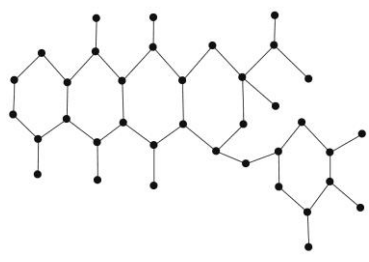
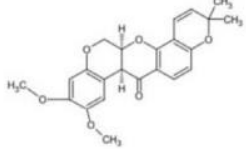
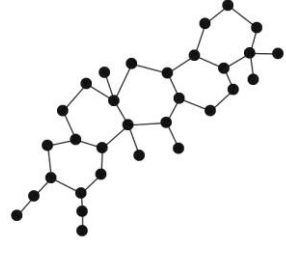
The ability of considered topological indices to correlate with normal[Boiling point (BP), Melting point (MP), Enthalpy (E), Flash point (FP), Molar refraction (MR)] of the 17 anticancer drugs from Amathaspiramide-E to Tambjamine-K were tested through linear correlations using the SAS procedure.

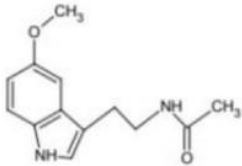
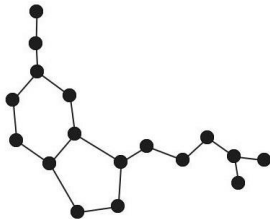
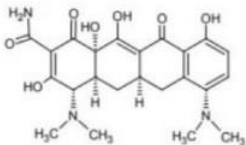
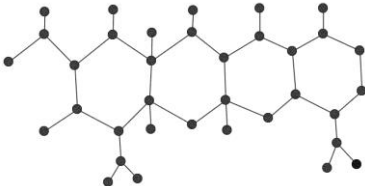
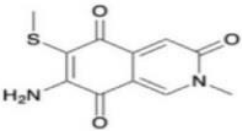
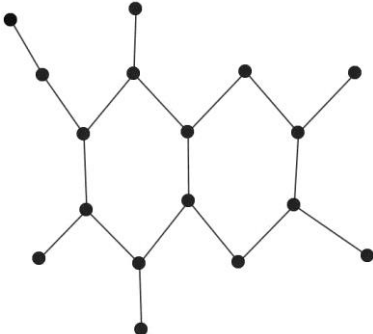
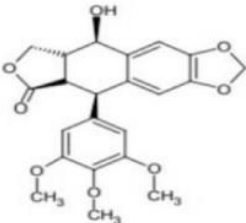
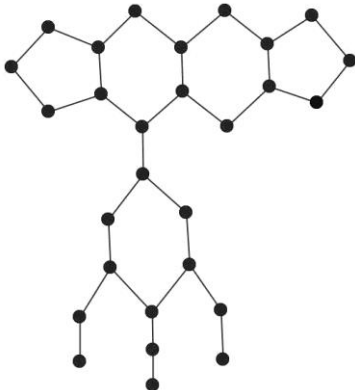
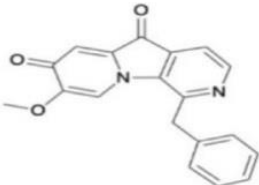
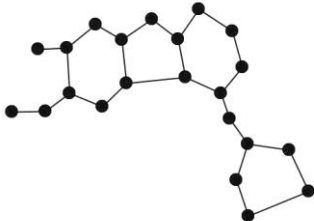
Table 1. Various anticancer drugs with physico-chemical properties.

S.No	Drugs	BP	MP	E	FP	MR
1.	Amathaspiramide E	572.7	209.72	90.3	300.2	89.4
2.	Aminopterin	782.27	344.45			114
3.	Aspidostomide E	798.8		116.2	436.	9 116
4.	Carmustine	309.6	120.99	63.8	141	46.6
5.	Caulibugulone E	373	129.46	62	179.4	52.2
6.	Convolutamide A	629.9		97.9	334.7	130.1
7.	Convolutamine F	387.7	128.67	63.7	188.3	73.8
8.	Convolutamydine A	504.9	199.2	81.6	259.2	68.2
9.	Daunorubicin	770	208.5	117.6	419.5	130
10.	Deguelin	560.1	213.39	84.3	244.8	105.1
11.	Melatonin	512.8	182.51	78.4	264	67.6
12.	Minocycline	803.3	326.3	122.5	439.6	116
13.	Perfragilin A	431.5	187.62	68.7	214.8	63.6
14.	Podophyllotoxin	597.9	235.86	93.6	210.2	104.3
15.	Pterocellin B	521.6	199.88	79.5	269.2	87.4
16.	Raloxifene	728.2	289.58	110.1	394.2	136.6
17.	Tambjamine K	391.7		64.1	3190.7	76.6

Table 2. Various anticancer drugs with their molecular graphs.

Cancer Drug	Molecular Graphs
 (a) Amathaspiramide E	
 (b) Aminopterin	
 (c) Aspidostomide E	
 (d) Carmustine	
 (e)Caulibugulone E	

 (f) Convolutamide A	
 (g) Convolutamine F	
 (h) Convolutamydine A	
 (i) Daunorubicin	
 (j) Deguelin	

 (k) Melatonin	
 (l) Minocycline	
 (m) Perfragilin A	
 (n) Podophyllotoxin	
 (o) Pterocellin B	

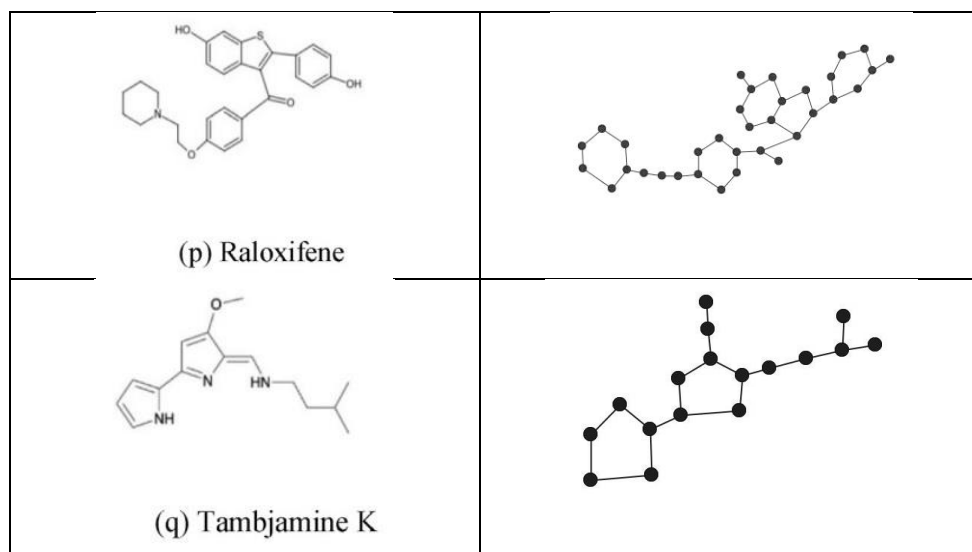


Table 3. Various Anticancer drugs with Topological Indices values.

Drugs	ABC	ABC_4	χ	S	GA	GA_5	M_1	M_2	H	HM	ZG_3	F	SSD
Amathaspiramide E	10.773	9.079	7.112	7.076	14.403	11.748	70	81	6.767	343	12	180	35.667
Aminopterin	24.65	18.96	15.23	15.68	32.7	33.63	162	185	14.53	786	32	416	80.33
Aspidostomide E	18.813	11.346	12.35	13	17.548	26.906	148	186	11.767	778	22	406	55
Carmustine	7.847	6.775	5.757	5.482	10.634	10.738	46	48	5.533	202	8	106	25.331
Caulibugulone E	10.664	8.342	6.736	6.946	14.574	18.966	72	86	6.5	358	10	186	29.5
Convolutamide A	24.463	19.369	17.93	17.74	35.702	34.208	167	167	17.205	793	21	419	86.583
Convolutamine F	10.773	8.616	7.113	7.077	14.403	14.599	70	81	6.767	522	12	432	29.167
Convolutamydine A	12.016	8.962	7.93	7.544	16.273	15.753	88	109	6.738	468	20	250	40.083
Daunorubicin	32.295	22.564	17.89	18.89	40.19	33.116	216	270	16.919	1146	38	606	101.666
Deguelin	23.398	17.507	13.91	14.8	31.954	32.5264	168	208	13.4	878	28	462	76.166
Melatonin	12.865	9.676	8.203	8.419	17.493	17.809	84	96	7.933	402	14	210	40.666
Minocycline	26.081	19.093	15.54	16.12	34.271	35.014	184	229	14.567	970	30	512	89
Perfragilin A	12.992	9.836	7.968	8.171	17.172	17.491	90	110	7.5	466	16	246	44

Podophyllotoxin	22.02	16.42	12.95	13.86	30.09	30.53	158	198	12.47	824	22	428	70.66
Pterocellin B	19.027	11.25	11.69	12.93	26.452	20.788	132	161	11.4	664	16	342	58.999
Raloxifene	26.956	20.862	16.58	17.5	37.234	37.684	182	215	16.2	890	24	460	83
Tambjamine K	14.28	9.654	9.203	9.419	19.493	19.774		104	8.933	434	14	226	44.667

4 Intercorrelation between considered topological indices

The intercorrelation between the thirteen degree based topological indices was carried out on the data set depicted in Table 5. The degree of the intercorrelation was judged by the correlation coefficient r . We considered pairs of indices with $r \geq 0.950$ highly intercorrelated, those with $0.9 < r < 0.95$ appreciably intercorrelated, those with $8.5 < r < 0.9$ weakly intercorrelated and indices with $r < 0.5$ not intercorrelated.

From Table 5, we learn that ABC index is highly intercorrelated with ABC_4 , χ , S , GA , M_1 , M_2 , H , HM and SSD with correlation coefficient $r > 0.950$ respectively. However, the ABC index is appreciably intercorrelated with GA_5 and ZG_3 with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the ABC index is weakly intercorrelated with F index with $r = 0.888$.

We observe that ABC_4 index is highly intercorrelated with χ , S , GA , M_1 , H and SSD with correlation coefficient $r > 0.950$ respectively. However, the ABC_4 index is appreciably intercorrelated with GA_5 , M_2 and HM with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the ABC_4 index is weakly intercorrelated with ZG_3 and F with correlation coefficient ranging from $8.5 < r < 0.9$.

The Randic' index χ is highly intercorrelated with S , GA , GA_5 , M_1 , H and SSD with correlation coefficient $r > 0.950$ respectively. However, the χ index is appreciably intercorrelated with M_2 and HM with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the χ index is weakly intercorrelated with ZG_3 and F with correlation coefficient ranging from $8.5 < r < 0.9$.

The sum connectivity index S is highly intercorrelated with GA , GA_5 , M_1 , H and SSD with correlation coefficient $r > 0.950$ respectively. However, the S index is appreciably intercorrelated with M_2 and HM with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the S index is weakly intercorrelated with ZG_3 and F with correlation coefficient ranging from $8.5 < r < 0.9$.

The geometric-arithmetic index GA is highly intercorrelated with H and SSD with correlation coefficient $r > 0.950$ respectively. However, the GA index is appreciably intercorrelated with GA_5 , M_1 , M_2 and HM with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the GA index is weakly intercorrelated with ZG_3 and F with correlation coefficient ranging from $8.5 < r < 0.9$.

The GA_5 is highly intercorrelated with harmonic index H with correlation coefficient $r = 0.955$. However, the GA_5 index is appreciably intercorrelated with M_1 , M_2 , HM and SSD with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the GA_5 index is weakly intercorrelated with ZG_3 and F with correlation

coefficient ranging from $0.5 < r < 0.9$.

The first Zagreb index M_1 is highly intercorrelated with harmonic index M_2 , H , HM and SSD with correlation coefficient $r > 0.950$ respectively. However, the M_1 index is appreciably intercorrelated with ZG_3 with correlation coefficient $r = 0.914$. Whereas the M_1 index is weakly intercorrelated with F index with $r = 0.899$.

The second Zagreb index M_2 is neither highly intercorrelated nor weakly intercorrelated with any of the topological indices. However, the M_2 index is appreciably intercorrelated with H , HM , ZG_3F and SSD with correlation coefficient ranging from $0.9 < r < 0.95$.

The hyper Zagreb index HM is highly intercorrelated with the F index with $r = 0.962$. However, the HM index is appreciably intercorrelated with ZG_3 and SSD with correlation coefficient ranging from $0.9 < r < 0.95$. Whereas the HM index is not weakly intercorrelated with any of the topological indices.

The ZG_3 index is not highly intercorrelated with any of the topological indices. However, the ZG_3 index is appreciably intercorrelated with SSD with $r = 0.908$. Whereas the ZG_3 weakly intercorrelated with F index with $r = 0.850$.

The forgotten index F is weakly intercorrelated with SSD index with $r = 0.856$.

In Figure 1, intercorrelation between the topological indices is depicted and in Figure 2, hierarchical cluster analysis of topological indices is shown.

Table 4. Correlation matrix of selected topological indices.

	ABC	ABC_4	χ	S	GA	GA_5	M_1	M_2	H	HM	ZG_3	F	SSD
ABC	1	0.975	0.977	0.986	0.974	0.944	0.991	0.969	0.974	0.967	0.913	0.888	0.990
ABC_4		1	0.966	0.963	0.979	0.948	0.953	0.914	0.963	0.922	0.887	0.853	0.979
χ			1	0.996	0.964	0.953	0.970	0.920	0.998	0.930	0.857	0.852	0.981
S				1	0.968	0.956	0.982	0.941	0.996	0.944	0.860	0.863	0.982
GA					1	0.932	0.950	0.910	0.964	0.913	0.851	0.836	0.980
GA_5						1	0.949	0.914	0.955	0.911	0.836	0.829	0.939
M_1							1	0.987	0.965	0.981	0.914	0.899	0.979
M_2								1	0.912	0.984	0.922	0.901	0.947
H									1	0.922	0.835	0.843	0.975
HM										1	0.915	0.962	0.944
ZG_3											1	0.850	0.908
F												1	0.856
SSD													1

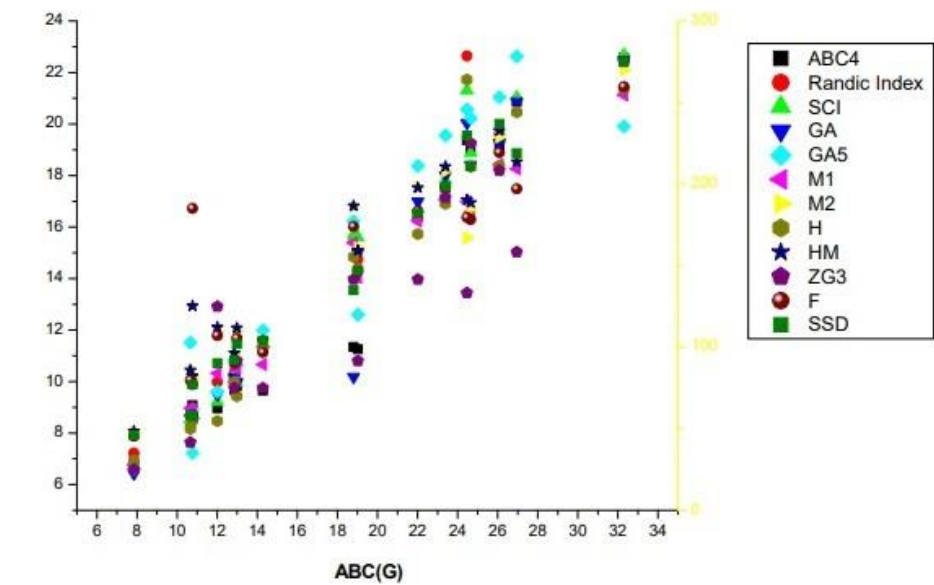


Figure 1. Intercorrelation between topological indices.

5 Hierarchical cluster analysis

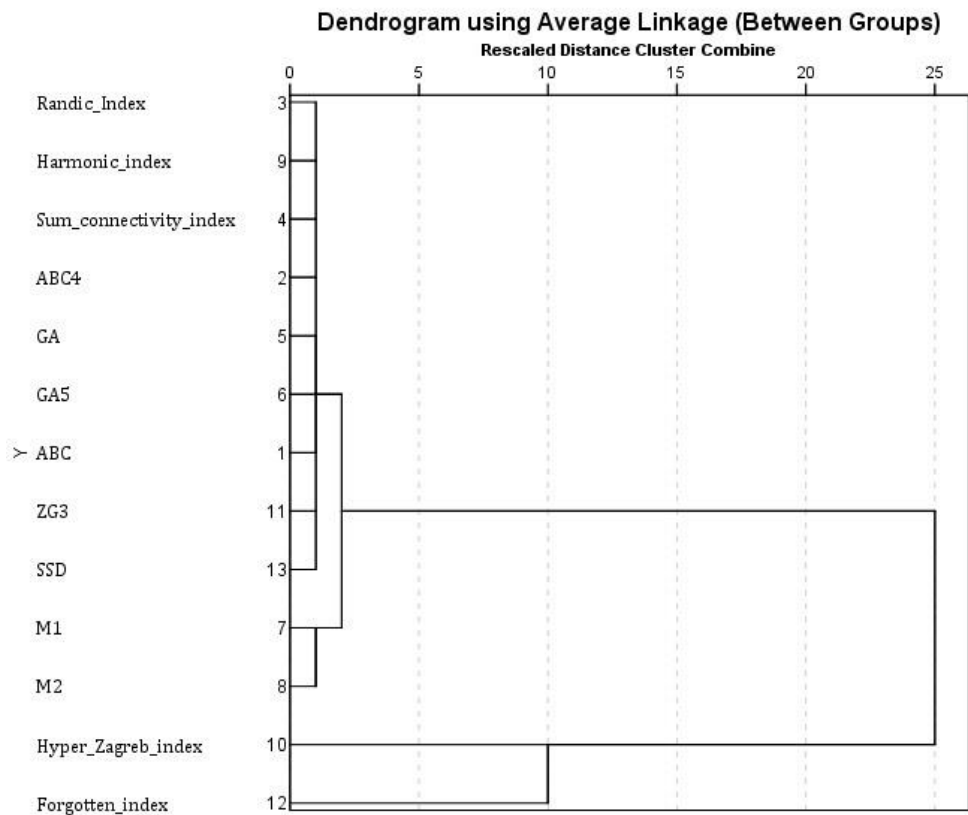


Figure 2. Hierarchical cluster analysis of topological indices

Hierarchical cluster analysis of these topological indices for a data set of seventeen anticancer drugs indicates that they are mutually highly intercorrelated.

6 Conclusion

The intercorrelation between thirteen degree based topological indices is very high. Therefore, the work carried out in [9] should be reconsidered for the study by choosing other degree based topological indices with mutually less intercorrelation.

References

- [1] V. Alexander, Upper and lower bounds of symmetric division deg index, Iran. J. Math. Chem. 5 (2) (2014) 91-98.
- [2] Ali Astanesh-Asl, G. H Fath-Tabar, Computing the first and third Zagreb polynomials of certain product of graphs, Iran. J. Math. Chem. 2 (2) (2011) 73-78
- [3] B. Basavanagoud Shruti Policepatil, Topological indices of some anticancer drugs, Ratio Mathematica Volume 42, 29-59 (2022).
- [4] A. T. Balaban, O. Ivanciuc, Historical development of topological indices, in: J. Devillers, A. T. Balaban (Eds.), Topological Indices and Related Descriptors in QSAR and QSPR, Gordon and Breach, 1999, pp. 21-57.
- [5] A. T. Balaban, Topological indices based on topological distances in molecular graphs, Pure Appl. Chem. 55 (1983) 199-206.
- [6] E. Estrada, L. Torres, L. Rodriguez, I. Gutman, An atom-bond connectivity index: modeling the enthalpy of formation of alkanes, Indian J. Chem. 37A (1998) 849-855.
- [7] S. Fajtlowicz, On conjectures of graffiti II, Congr. Numerantium 60 (1987) 189-197
- [8] B. Furtula, I. Gutman, A forgotten topological index, J Math Chem, 53, 1184-1190 (2015).
- [9] M. Ghorbani, M.A. Hosseinzadeh, Computing ABC_4 index of Nanostar dendrimers, Optoelectron. Adv. Mater-Rapid Commun. 4 (9) (2010) 1419-1422.
- [10] A. Graovac, M. Ghorbani, M.A. Hosseinzadeh, Computing Fifth Geometric-Arithmetic index for nanostar dendrimers, J. Math. Nanosci. 1 (2011) 33-42
- [11] I. Gutman, N. Trinajstić, Graph theory and molecular orbitals. Total π -electron energy of alternant hydrocarbons, Chem. Phys. Lett. 17 (1972), 535-538.
- [12] M Randić, On characterization of molecular branching, J. Am. Chem. Soc., 97 (1975), 6609-6615.
- [13] M Randić, Generalized molecular descriptors, J. Math. Chem. 11 (1991), 155-168.
- [14] M. C. Shanmukha, N. S. Basavarajappa, K. C. Shilpa, A. Usha, Degreebased topological indices on anticancer drugs with QSPR analysis, Heliyon, 6, 2020, 1-9

- [15] G.H. Shirdel, H. RezaPour, A.M. Sayadi, The hyper-zagreb index of graph operations, Iran. J. Math. Chem. 4 (2) (2013) 213-220.
- [16] Shashank Kumar, Mohammad Kaleem Ahmad, Mohammad Waseem, Abhay K. Pandey, Drug targets for cancer treatment: an overview, Med. Chem. 5 (3) (2015) 115-123.
- [17] G. H. Shirdel, H. Rezapour, and A. M. Sayadi, The Hyper Zagreb Index of Graph Operations, Iranian J. Math. Chem. 4 (2013) 213-220.
- [18] Sumiya Nasir, Nadeem ul Hassan Awanr, Fozia Bashir Farooq, Saima Parveen, Topological indices of novel drugs used in blood cancer treatment and its QSPR modeling, AIMS Mathematics, 2022, 7(7): 11829-11850.
- [19] D. Vukicevic', B. Furtula, Topological index based on the ratios of geometrical and arithmetical means of end-vertex degrees of edges, J. Math. Chem. 46 (2009) 1369-1376.
- [20] B. Zhou, N. Trinajstić', On general sum-connectivity index, J. Math. Chem. 47 (2010) 210-218.