

FULL PAPER

Ve-degree and Ev-degree topological analysis of some anticancer drugs

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Computing topological indices of drug structures provides the chemical information about the underlying topology of the drug's structures. Novel anticancer drug studies have been conducting by researches to design and produce ideal drugs. Chemical properties of these new drug candidates investigated using the simulation methods. Topological indices also have been used to investigate the chemical properties of some drug structures. Ve-degree and Ev-degree topological indices have been defined recently in chemical graph theory. In this study we evaluated the ev-degree and ve-degree topological indices of some newly defined anticancer drug candidates which are based on alkylating agent.

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KEYWORDS

Alkylating agents; Ev-degree topological indices; Ve-degree topological indices.

Introduction

Graph theory applications to medicine and pharmacology have been rising in recent years. Especially computing topological indices of drug structures drag attention of many chemical graph theoretician. Nada et. al. have modeled the blood circulation in heart by using the digraphs and investigating the topological properties of this model via using this digraph model [1]. Zhao and Wu computed some topological indices value of star such as trees and heterofunctional dendrimers, which are constituted of many drug structures [2]. In 2016, Gao, Farahani and Shi studied the forgotten topological index of some drug structures [3]. Again the forgotten topological index of some other chemical drug structures have been determined by Gao *et al.* [4]. Some topological indices of molecular structures in anti cancer drugs have been computed by Gao *et al.* [5]. The first multiplication atom-bond connectivity index of some drug structures and some distance based topological indices of

hexagonal jagged-rectangle in some drug structures have been determined in 2017 [6, 7]. In 2015, Keshavarz and Mohammad-Aghaie studeid the rational design and simulation studies of dual-target anticancer drug candidates [12]. Anticancer drugs is classified into seven groups including, alkylating agents, cytotoxic antibiotics, antimetabolites, microtubule inhibitors, monoclonal antibodies, and steroid hormones and their antagonists [13]. Alkylating agents are the the most commonly used anticancer drug structures [12]. ThioTEPA (N,N',N"-triethylene thiophosphoramidate) and its main metabolite, i.e. TEPA (Figure 1), are trifunctional alkylating agents [13].

ThioTEPA is mainly used for treating the ovarian and breast cancer tumors [14-16]. The authors designed nine novel thioTEPA based anticancer drug candidates and investigated some pharmacological properties of these drugs by using the simulation methods [12].

Classical degree based topological indices such as Zagreb and Randić indices have many

applications in chemistry, physics and pharmacology. Ev-degree and ve-degree concepts have been defined by Chellali et al. in 2017 [8]. The difference between the classical degree concept and ve-degree concept is classical degree is related to only first neighbors of vertices however, the ve-degree is related to both first and second neighbors of vertices. After given the relation between the Zagreb index and total ve-degree concept, the authors suggested that the ve-degree based topological indices were interesting problems to investigate in view of chemical graph theory.

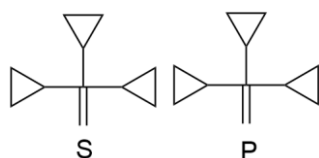


FIGURE 1 Chemical structures of thioTEPA and TEPA.

Ve-degree and ev-degree based molecular topological indices have been defined by Ediz in 2017 [9-11]. These novel ev-degree and ve-degree based indices gave better correlation than classical degree counterparts modeling for entropy and acentric factor of octanes.

Ve-degree harmonic, sum-connectivity, atom-bond connectivity and geometric-arithmetic indices for alkylating agents based the dual-target anticancer drug candidates have been computed in [19].

As a continuation of this last study, in this research study, we computed the ev-degree and ve-degree Zagreb and Randić indices for alkylating agents based the dual-target anticancer drug candidates. For related studies see the references [20-26].

Preliminaries

Let $G=(V,E)$ be a connected graph and where v is a vertex of G . The number of edges incident to v is defined as the degree of v and denoted as $deg(v)$. The set which is consisted of v and

the vertices of the first neighbors of v is called the closed neighborhood of v .

Definition 1 (ve-degree): The number of different edges which is adjacent to v and the first neighbors of v is defined as **ve-degree of v** and denoted as $deg_{ve}(v)$.

Definition 2 (ev-degree): The number of vertices in the closed neighborhood of the end vertices of an edge e is defined as **ev-degree of e** and denoted as $deg_{ev}(e)$.

The graph theoretical results of the novel degree concepts were investigated by Żyliński and Horoldogva et al [17,18].

Definition 3 (ev-degree Zagreb index): The closed formula of the ev-degree Zagreb index of a connected graph G given as:

$$M^{ev}(G) = \sum_{e \in E(G)} deg_{ev} e^2$$

Definition 4 (the first ve-degree Zagreb alpha index): The closed formula of the first ve-degree Zagreb alpha index of a connected graph G given as: $M_1^{\alpha ve}(G) = \sum_{v \in V(G)} deg_{ve} v^2$

Definition 5 (the first ve-degree Zagreb beta index): The closed formula of the first ve-degree Zagreb beta index of a connected graph G defined as:

$$M_1^{\beta ve}(G) = \sum_{uv \in E(G)} (deg_{ve} u + deg_{ve} v)$$

Definition 6 (the second ve-degree Zagreb index): The closed formula of the second ve-degree Zagreb index of a connected graph G given as: $M_2^{ve}(G) = \sum_{uv \in E(G)} deg_{ve} u deg_{ve} v$.

Definition 7 (ve-degree Randić index): The closed formula of the ve-degree Randić index of a connected graph G given as:

$$R^{ve}(G) = \sum_{uv \in E(G)} (deg_{ve} u deg_{ve} v)^{-1/2}$$

Definition 8 (ev-degree Randić index): The closed formula of the ev-degree Randić index of a connected graph G defined as:

$$R^{ev}(G) = \sum_{e \in E(G)} deg_{ev} e^{-1/2}$$

After this definitions we can start to compute these molecular topological indices for the some alkalyting agents.

Results and discussion

In this section we discuss the molecular graphs of the novel nine proposed thioTEPA based anticancer drugs and compute the Ev-degree and Ve-degree topological indices for these novel drug structures.

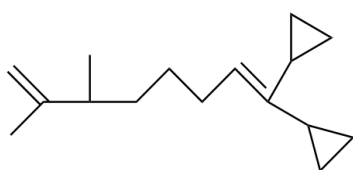


FIGURE 2 Chemical structure of the first (Arg based) alkylating agent

Theorem 1. The ev-degree and ve-degree topological indices of the first Arg based alkylating agent Figure 2 are:

ev-degree Zagreb index: $M^{ev}(Arg) = 336$

the first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Arg) = 370$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Arg) = 170$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Arg) = 428$$

ve-degree Randić index: $R^{ve}(Arg) = 3,577$

ev-degree Randić index: $R^{ev}(Arg) = 8,273$

Proof: We firstly present the molecular graph of the first (Arg based) alkylating agent in Figure 3 for to facilitate our computations.

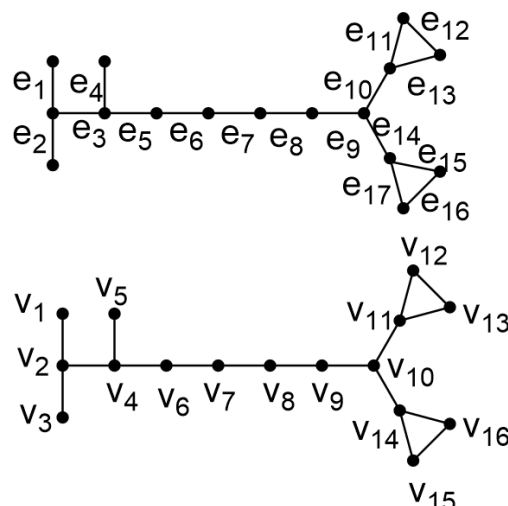


FIGURE 3 Chemical graph of the first (Arg based) alkylating agent

We give the ev-degree of the edges and ve-degree of the vertices of the chemical graph of the first (Arg based) alkylating agent in the Table1 and Table 2.

TABLE 1 The ev-degree of the edges of the chemical graph of the first (Arg based) alkylating agent

Ev-degree	Edges
3	e ₁₂ , e ₁₆
4	e ₁ , e ₂ , e ₄ , e ₆ , e ₇ , e ₈ , e ₁₁ , e ₁₃ , e ₁₅ , e ₁₇
5	e ₅ , e ₉ ,
6	e ₃ , e ₁₀ , e ₁₄

Table 2 The ve-degree of the vertices of the chemical graph of the first (Arg based) alkylating agent.

Ve-degree	Vertices
3	v ₁ , v ₃ , v ₅
4	v ₇ , v ₈ , v ₁₂ , v ₁₃ , v ₁₅ , v ₁₆
5	v ₂ , v ₆ , v ₉
6	v ₄ , v ₁₁ , v ₁₄
8	v ₁₀

We computed ev-degree and ve-degree topological indices as follows.

ve-degree Zagreb index: From the Definition 3 and Table 1:

$$M^{ev}(Arg) = \sum_{e \in E(Arg)} deg_{ev} e^2$$

$$= 10x^4 + 2x^5 + 3x^6 + 2x^3 = 336$$

The first ve-degree Zagreb alpha index:

From the Definition 4 and Table 2:

$$M_1^{\alpha ve}(Arg) = \sum_{v \in V(Arg)} deg_{ve} v^2$$

$$= 3x^3 + 6x^4 + 3x^5 + 3x^6 + 8^2 = 370$$

The first ve-degree Zagreb beta index:

From the Definition 5 and Table 2:

$$M_1^{\beta ve}(Arg) = \sum_{uv \in E(Arg)} (deg_{ve} u + deg_{ve} v) = 170.$$

The second ve-degree Zagreb index: From the Definition 6 and Table 2:

$$M_2^{ve}(Arg) = \sum_{uv \in E(G)} deg_{ve} u deg_{ve} v = 428.$$

ve-degree Randić index: From the Definition 7 and Table 2:

$$R^{ve}(Arg) = \sum_{uv \in E(G)} (deg_{ve} u deg_{ve} v)^{-1/2} = 3,577$$

ev-degree Randić index: From the Definition 8 and Table 1:

$$R^{ev}(Arg) = \sum_{e \in E(G)} deg_{ev} e^{-1/2} = 8,273$$

The proof is completed. ■

Since the proof of the following theorems are the similar the proof of the Theorem 1, we omit the proofs.

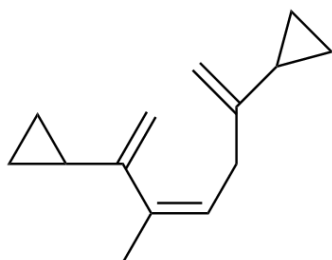


FIGURE 4 Chemical structure of the second (Asp based) alkylating agent

Theorem 2. The ev-degree and ve-degree topological indices of the second Asp based alkylating agent Figure 4 are:

The ev-degree Zagreb index:

$$M^{ev}(Asp) = 304$$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Asp) = 334$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Asp) = 154.$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Asp) = 390.$$

ve-degree Randić index: $R^{ve}(Asp) = 3,104.$

ev-degree Randić index: $R^{ev}(Asp) = 7,273.$

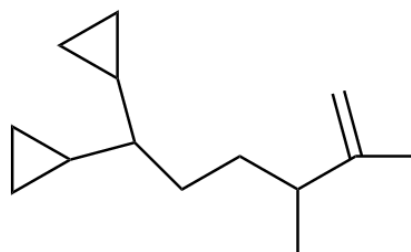


FIGURE 5 Chemical structure of the third (Cys based) alkylating agent

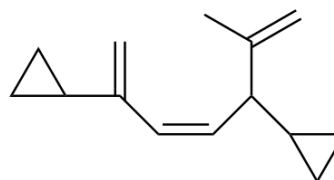


FIGURE 6 Chemical structure of the fourth (Gln based) alkylating agent

Theorem 3. The ev-degree and ve-degree topological indices of the third Cys based alkylating agent Figure 5 are:

ev-degree Zagreb index: $M^{ev}(Cys) = 432$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Cys) = 338$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Cys) = 154$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Cys) = 405$$

ve-degree Randić index: $R^{ve}(Cys) = 2,732.$

ev-degree Randić index: $R^{ev}(Cys) = 7,273.$

Theorem 4. The ev-degree and ve-degree topological indices of the fourth Gln based alkylating agent Figure 6 are:

ev-degree Zagreb index: $M^{ev}(Gln) = 404$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Gln) = 310$$

The first ve-degree Zagreb beta index:

$$M_1^{ve}(Gln) = 148$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Gln) = 363$$

ve-degree Randić index: $R^{ve}(Gln) = 3,232$

ev-degree Randić index: $R^{ev}(Gln) = 7,273$

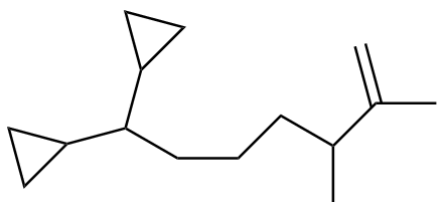


FIGURE 7 Chemical structure of the fifth (Met based) alkylating agent

Theorem 5. The ev-degree and ve-degree topological indices of the fifth Met based alkylating agent Figure 7 are:

ev-degree Zagreb index: $M^{ev}(Met) = 285$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Met) = 328.$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Met) = 170.$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Met) = 394.$$

ve-degree Randić index: $R^{ve}(Met) = 3.443.$

ev-degree Randić index: $R^{ev}(Met) = 7.967.$

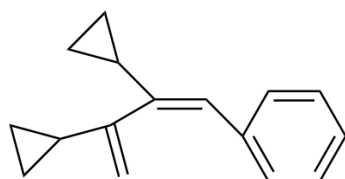


FIGURE 8 Chemical structure of the sixth (Phe based) alkylating agent

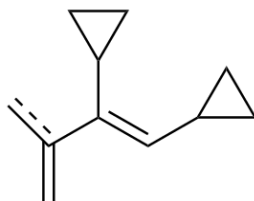


FIGURE 9 Chemical structure of the seventh (Ser based) alkylating agent

Theorem 6. The ev-degree and ve-degree topological indices of the sixth Phe based alkylating agent Fig.8 are:

ev-degree Zagreb index: $M^{ev}(Phe) = 262.$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Phe) = 418.$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Phe) = 190.$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Phe) = 511.$$

ve-degree Randić index: $R^{ve}(Phe) = 3.590$

ev-degree Randić index: $R^{ev}(Phe) = 8.668$

Theorem 7. The ev-degree and ve-degree topological indices of the seventh Ser based alkylating agent Figure 9 are:

ev-degree Zagreb index: $M^{ev}(Ser) = 222$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Ser) = 268$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Ser) = 122$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Ser) = 316$$

ve-degree Randić index: $R^{ve}(Ser) = 2.501$

ev-degree Randić index: $R^{ev}(Ser) = 5.225$

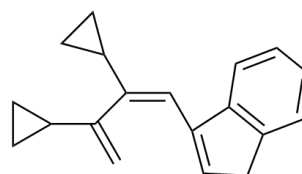


FIGURE 10 Chemical structure of the eighth (Trp based) alkylating agent

Theorem 8. The ev-degree and ve-degree topological indices of the eighth Ser based alkylating agent Figure 10 are:

ev-degree Zagreb index: $M^{ev}(Trp) = 492$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Trp) = 588$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Trp) = 250$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Trp) = 723$$

ve-degree Randić index: $R^{ve}(Trp) = 4.095$.

ev-degree Randić index: $R^{ev}(Trp) = 9.932$.

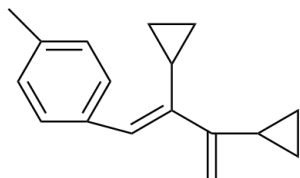


FIGURE 11 Chemical structure of the ninth (Tyr based) alkylating agent

Theorem 9. The ev-degree and ve-degree topological indices of the ninth Trp based alkylating agent Figure 11 are:

ev-degree Zagreb index: $M^{ev}(Tyr) = 434$

The first ve-degree Zagreb alpha index:

$$M_1^{\alpha ve}(Tyr) = 455$$

The first ve-degree Zagreb beta index:

$$M_1^{\beta ve}(Tyr) = 226$$

The second ve-degree Zagreb index:

$$M_2^{ve}(Tyr) = 554$$

ve-degree Randić index: $R^{ve}(Tyr) = 3,701$.

ev-degree Randić index: $R^{ev}(Tyr) = 9,062$.

Conclusion

Computing topological indices of new drug candidates enables to inspect the pharmacological properties of these novel drug candidates. In this study we evaluated the ev-degree and ve-degree topological indices of some newly defined anticancer drug candidates which are based on alkylating agent. The following studies are worth to study for future studies.

Computing and providing the relations between the novel drugs and their chemical properties by using ev-degree and ve-degree topological indices.

Evaluating the mathematical properties of the ev-degree and ve-degree topological indices.

Finding the extremal graph classes with respect to ev-degree and ve-degree topological indices.

Investigating the properties of ev-degree and ve-degree topological indices in some graph operations.

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