Computation of Zagreb and Randić indices of two biodegradable dendrimers used in cancer therapy

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Abstract: Chemical characteristics of molecules are closely related to their structures. Molecular structures have been studied by the topological indices for the last forty years. The degree-based topological indices are the most studied and commonly used topological indices, which play a significant role in characterizing molecular structures. Dendrimers have been used in cancer therapy for the last few years. This research focused on calculating the different versions of the Zagreb index and the Randić index of two well-known dendrimers which are used in cancer therapy.

Keywords: Topological index, Zagreb index, Randić index, Dendrimers.

INTRODUCTION

Topological indices are numerical representations of the topology of a molecule. They are calculated from the heavy atom graphical depiction of the molecule. One of the first topological indices was the Wiener index which was developed in 1947 by the mathematical chemist Wiener (Wiener, 1947). He showed that the Wiener index correlated well with boiling points of alkanes. In the field of drug design and development, Wiener index, Kosoya index or Z index, Zagreb index, Randić index and Balaban J index are the mostly used indices (Dearden, 2017, Estrada et al., 2003, Gozalbes et al., 2002). Wiener index, Kosoya index or Z index and Balaban J index are non-degree based topological indices; Wiener index is a distance-based topological index and Balaban J index is a distance sums index. The mostly used vertex degree based topological indices in the field of drug design and developments are the Zagreb index and the Randić index.

In molecular graphs, atoms and chemical bonds between them are represented by vertices and edges, respectively, in graph theory. A graph $G=V(G),E)$ is a pair of nonempty set of vertices and $E=E(G)$ of the set of connected edges if there exists a connection between any pair of vertices in $G$. For a connected graph $G$ and vertices $u,v$ in the set of vertices $V(G)$, The number of vertices of $G$, adjacent to a given vertex $v$, is called the degree of this vertex, and is denoted by $d_u(G)$ or $d_v$. It is noted that the degree of any vertex in a chemical graph is at most four [Gutman, 2013]. The concept of degree is closely related to the concept of valence bond in chemistry. The distance between two vertices $u$ and $v$ is the length of shortest path between these vertices and is denoted by $d(u,v)$ or $d_G(u,v)$.

The vertex degree-based topological indices are the most studied type of topological indices which play a prominent role in chemical graph theory. One of the oldest degree-based topological indices is the Zagreb index which was introduced by Gutman and Trinajstić (Gutman and Trinajstić1972) during the analysis of the structure-dependency of total-electron energy. The first Zagreb index $M_1(G)$ was defined as

$$M_1(G) = \sum_{v \in V(G)} (d_v)^2 = \sum_{u \in E(G)} (d_u+d_v)$$

and the second Zagreb index $M_2(G)$ was defined as

$$M_2(G) = \sum_{u \in E(G)} d_u d_v.$$ 

The second modified Zagreb index which was introduced by Hao (Hao, 2011) and is defined as

$$M_2'(G) = \sum_{u \in V(G)} \frac{1}{d_u d_v}$$

one of the oldest topological indices introduced by Randić (Randić, 1974). This was defined as

$$R(G) = \sum_{u \in V(G)} \frac{1}{d_u d_v}.$$ 

The Randić index is one of the most studied, most often applied and most popular degree-based topological indices in the field of drug design.

This index was globalized and recognized as the generalized Randić index and defined as

$$R_\alpha(G) = \sum_{u \in V(G)} (d_u d_v)^\alpha.$$ 

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where $\alpha$ is an arbitrary real number (Li and Shi, 2008). When $\alpha = -1/2$, the above generalized Randić index becomes the (original) Randić index.

The reciprocal Randić index is defined as

$$RR(G) = \sum_{uv \in E(G)} \frac{1}{d_u d_v}.$$ 

It is, of course, a special case of the earlier much examined generalized Randić index when $\alpha = 1/2$. The invariant $RR$ seems to be first encountered in a paper by Favaron, Mahéco, and Saclé (Favaron et al., 1993).

The reduced second Zagreb index is defined as

$$RM_2(G) = \sum_{uv \in E(G)} (d_u - 1)(d_v - 1).$$

The reduced reciprocal Randić index is defined as

$$RRR(G) = \sum_{uv \in E(G)} \frac{1}{(d_u - 1)(d_v - 1)}.$$

Even though the reciprocal Randić index, the reduced second Zagreb index and the reduced second Zagreb index appeared in the literature earlier, they were presented again by Gutman (Gutman et al., 2014) by establishing the correlating abilities with respect to the chemical and physical properties of chemical compounds especially with alkanes.

Development of anticancer therapeutic agents is of tremendous interest and importance for many researchers over many decades. Biodegradable nanopolymers are used as potential drug delivery systems, especially for cancer therapy. Among the biodegradable nanopolymers, dendrimers are one of the promising structures which could be used in cancer therapy (Kesharwani et al., 2016). Dendrimers are nano-sized macromolecules with a particular architecture (Luo et al., 2015.). The characteristic architecture of dendrimers provides a well-defined branched structure with a globular shape which renders large number of surface groups that could be used as active sites for many biological applications, especially in cancer therapy (Kesharwani et al., 2012).

There are various types of dendrimers used in cancer therapy and therefore, many studies have been focused on the development of new techniques to synthesize different types of dendrimers. Properties of materials depend on their molecular structure and applications of materials are based on their properties. Therefore, the characterization of materials is important to use them in various applications. Topological indices are the numerical graph invariants that quantitatively characterize the molecular structure and therefore, topological index can be considered as the transformation of a chemical structure into a real number. Hence, molecular descriptors are playing a significant role in characterizing dendrimeric molecules which are used in various applications. Therefore, this study focused on determining the different versions of the Zagreb index and the Randić index for two types of dendrimers which are used in cancer therapy.

**METHODOLOGY**

The structures of the dendrimers were observed and using the methodologies in the chemical graph theory, the edge partitions were calculated. The $n^{th}$ growth of the dendrimers was identified by chemical theories and using these, the edge partitions were calculated for their $n^{th}$ growth. Finally, the Zagreb and Randić indices were calculated by respective formulas.

**RESULTS AND DISCUSSION**

In this paper, we considered two biodegradable dendrimers, namely (1) a fourth-generation poly(amidoamine) dendrimer (Figure 1) and (2), a dendrimer based on glycerol and succinic acid (Figure 2), and both are used for cancer therapy. The edge partitions of these dendrimers are constructed by the methods used in the work of Kang [Kang et al., 2018] and Aslam [Aslam et al., 2017].

By observing the structure, we inferred four partitions of the edge set which are:

$$E_1(G) = \{e = uv \in E(G) : d_u = 1 \text{ and } d_v = 2\}$$

$$E_2(G) = \{e = uv \in E(G) : d_u = 1 \text{ and } d_v = 3\}$$

$$E_3(G) = \{e = uv \in E(G) : d_u = d_v = 2\}$$

$$E_4(G) = \{e = uv \in E(G) : d_u = 2 \text{ and } d_v = 3\}$$

and

$$|E_1(G)| = 2^{n+1}, |E_2(G)| = 4 \times 2^n - 4,$$

$$|E_3(G)| = 12 \times 2^n - 11, |E_4(G)| = 14 \times 2^n - 14.$$ 

where $n$ is the steps of growth of the dendrimers.

**Theorem 1.**

Let $G$ be the Schematic representation of the fourth-generation poly (amidoamine) dendrimer. Then the first Zagreb index $M_1(G)$, the second Zagreb index $M_2(G)$, the second modified Zagreb index $\overline{M}_2(G)$ and the reduced second Zagreb index $RM_2(G)$ for $G$ are

1. $M_1(G) = 140 \times 2^n - 130.$
2. $M_2(G) = 148 \times 2^n - 140.$
3. $\overline{M}_2(G) = \frac{23}{3} \times 2^n - \frac{77}{12}.$
4. $RM_2(G) = 40 \times 2^n - 39.$
Figure 1: Molecular structure of fourth-generation poly(amidoamine) dendrimer (Kesharwani et al., 2015).

Proof:
Using this edge partition of the schematic representation of a fourth-generation poly (amidoamine) dendrimer and by the formulas of different versions of the Zagreb indices, we get

1. $M_1(G) = \sum_{u \neq v \in E(G)} (d_u + d_v)$
   
   \[
   = \sum_{u \neq v \in E_1(G)} (d_u + d_v) + \sum_{u \neq v \in E_2(G)} (d_u + d_v) + \sum_{u \neq v \in E_3(G)} (d_u + d_v) + \sum_{u \neq v \in E_4(G)} (d_u + d_v)
   \]
   
   \[
   = |E_1(G)|(1 + 2) + |E_2(G)|(1 + 3) + |E_3(G)|(2 + 2) + |E_4(G)|(2 + 3)
   \]
   
   \[
   = 2^{n+1} \times 3 + (4 \times 2^n - 4) \times 4 + (12 \times 2^n - 11) \times 4 + (14 \times 2^n - 14) \times 5
   \]
   
   \[
   = 140 \times 2^n - 130.
   \]

2. $M_2(G) = \sum_{u \neq v \in E(G)} (d_u \times d_v)$
   
   \[
   = \sum_{u \neq v \in E_1(G)} (d_u \times d_v) + \sum_{u \neq v \in E_2(G)} (d_u \times d_v) + \sum_{u \neq v \in E_3(G)} (d_u \times d_v) + \sum_{u \neq v \in E_4(G)} (d_u \times d_v)
   \]
   
   \[
   = |E_1(G)|(1 \times 2) + |E_2(G)|(1 \times 3) + |E_3(G)|(2 \times 2) + |E_4(G)|(2 \times 3)
   \]
   
   \[
   = 2^{n+1} \times 2 + (4 \times 2^n - 4) \times 3 + (12 \times 2^n - 11) \times 4 + (14 \times 2^n - 14) \times 6
   \]
   
   \[
   = 148 \times 2^n - 140.
   \]
Theorem 2

Let \( G \) be the Schematic representation of the fourth-generation poly(amidoamine) dendrimer. Then the Randić index \( R(G) \), the reciprocal Randić index \( RR(G) \) and the reduced reciprocal Randić index \( RRR(G) \) for \( G \) are

1. \( R(G) = \left( \sqrt{2} + \frac{4}{\sqrt{3}} + \frac{14}{\sqrt{6}} + 6 \right) \times 2^n - \left( \frac{4}{\sqrt{3}} + \frac{14}{\sqrt{6}} + \frac{11}{2} \right) \).
2. \( RR(G) = (2\sqrt{2} + 4\sqrt{3} + 14\sqrt{6} + 24)2^n - (16\sqrt{3} + 14\sqrt{6} + 22) \).
3. \( RRR(G) = (12 + 14\sqrt{2})2^n - (11 + 14\sqrt{2}) \).

Proof

Using this edge partition of the Schematic representation of the fourth-generation poly (amidoamine) dendrimer and by the formulas of different versions of the Randić indices, we get

1. \( R(G) = \sum_{uv \in E(G)} \frac{1}{d_ud_v} \)
   \[
   = \sum_{uv \in E_1(G)} \frac{1}{\sqrt{d_ud_v}} + \sum_{uv \in E_2(G)} \frac{1}{\sqrt{d_ud_v}} + \sum_{uv \in E_3(G)} \frac{1}{\sqrt{d_ud_v}} + \sum_{uv \in E_4(G)} \frac{1}{\sqrt{d_ud_v}} 
   = |E_1(G)| \frac{1}{\sqrt{2}} + |E_2(G)| \frac{1}{\sqrt{2}} + |E_3(G)| \frac{1}{\sqrt{6}} + |E_4(G)| \frac{1}{\sqrt{6}} 
   = 2^{n+1} \times \frac{1}{\sqrt{2}} + (4 \times 2^n - 4) \times \frac{1}{\sqrt{3}} + (12 \times 2^n - 11) \times \frac{1}{2} + (14 \times 2^n - 14) \times \frac{1}{\sqrt{6}} 
   = \left( \sqrt{2} + \frac{4}{\sqrt{3}} + \frac{14}{\sqrt{6}} + 6 \right) \times 2^n - \left( \frac{4}{\sqrt{3}} + \frac{14}{\sqrt{6}} + \frac{11}{2} \right) 
   \]
Now we consider the dendrimer based on glycerol and succinic acid. By observing the structure, we inferred three partitions of the edge set which are:

\[ |E_1(G)| = 10 \times 2^n - 6, \quad |E_2(G)| = 8 \times 2^n - 7, \quad |E_3(G)| = 20 \times 2^n - 18, \]

where \( n \) is the steps of growth of the dendrimers.

**Theorem 3**

Let \( G \) be the dendrimer based on glycerol and succinic acid. Then the first Zagreb index \( M_1(G) \), the second Zagreb index \( M_2(G) \), the second modified Zagreb index \( mM_2(G) \) and the reduced second Zagreb index \( RM_2(G) \) for \( G \) are,

1. \( M_1(G) = 172 \times 2^n - 142 \).
2. \( M_2(G) = 182 \times 2^n - 154 \).
3. \( mM_2(G) = \frac{26}{3} \times 2^n - \frac{27}{4} \).
4. \( RM_2(G) = 48 \times 2^n - 43 \).

**Proof**

Using this edge partition of the dendrimer based on glycerol and succinic acid and by the formulas of different versions of the Zagreb indices, we get

1. \( M_1(G) = \sum_{u \neq v \in E(G)} (d_u + d_v) \)
   
   \[ = \sum_{u \in E_1(G)} (d_u + d_v) + \sum_{u \in E_2(G)} (d_u + d_v) + \sum_{u \in E_3(G)} (d_u + d_v) \]
   
   \[ = |E_1(G)|(1 + 3) + |E_2(G)|(2 + 2) + |E_3(G)|(2 + 3) \]
   
   \[ = (10 \times 2^n - 6) \times 4 + (8 \times 2^n - 7) \times 4 + (20 \times 2^n - 18) \times 5 \]
   
   \[ = 172 \times 2^n - 142 \]
Figure 2: Molecular structure of dendrimer based on glycerol and succinic acid (Wolinsky et al., 2008).

2. \( M_2(G) = \sum_{u \in E_1(G)} (d_u \times d_v) \)

\[
= \sum_{u \in E_1(G)} (d_u \times d_v) + \sum_{u \in E_2(G)} (d_u \times d_v) + \sum_{u \in E_3(G)} (d_u \times d_v)
\]

\[
= |E_1(G)|(1 \times 3) + |E_2(G)|(2 \times 2) + |E_3(G)|(2 \times 3) + \\
= (10 \times 2^n - 6) \times 3 + (8 \times 2^n - 7) \times 4 + (20 \times 2^n - 18) \times 6
\]

\[
= 182 \times 2^n - 154
\]
Theorem 4

Let $G$ be the dendrimer based on glycerol and succinic acid. Then the Randić index $R(G)$, the reciprocal Randić index $RR(G)$ and the reduced reciprocal Randić index $RRR(G)$ for $G$ are

4. $R(G) = \left( \frac{10}{\sqrt{3}} + \frac{20}{\sqrt{6}} + 4 \right) \times 2^n - \left( \frac{6}{\sqrt{3}} + \frac{18}{\sqrt{6}} + \frac{7}{2} \right)$

5. $RR(G) = \left( 10\sqrt{3} + 20\sqrt{6} + 16 \right) 2^n - \left( 6\sqrt{3} + 18\sqrt{6} + 14 \right)$

6. $RRR(G) = \left( 8 + 20\sqrt{2} \right) 2^n - \left( 7 + 18\sqrt{2} \right)$

Proof

Using this edge partition of the dendrimer based on glycerol and succinic acid and by the formulas of different versions of the Randić indices, we get

1. $R(G) = \sum_{uvw \in E(G)} \frac{1}{\sqrt{d_u d_v}}$

   $= \sum_{uv \in E_1(G)} \frac{1}{\sqrt{d_u d_v}} + \sum_{uv \in E_2(G)} \frac{1}{\sqrt{d_u d_v}} + \sum_{uv \in E_3(G)} \frac{1}{\sqrt{d_u d_v}}$

   $= |E_1(G)| \frac{1}{\sqrt{1 \times 3}} + |E_2(G)| \frac{1}{\sqrt{2 \times 2}} + |E_3(G)| \frac{1}{\sqrt{2 \times 3}}$

   $= (10 \times 2^n - 6) \times \frac{1}{\sqrt{3}} + (8 \times 2^n - 7) \times \frac{1}{2} + (20 \times 2^n - 18) \times \frac{1}{\sqrt{6}}$

   $= \left( \frac{10}{\sqrt{3}} + \frac{20}{\sqrt{6}} + 4 \right) \times 2^n - \left( \frac{6}{\sqrt{3}} + \frac{18}{\sqrt{6}} + \frac{7}{2} \right)$

2. $RR(G) = \sum_{uvw \in E(G)} \sqrt{d_u d_v}$

   $= \sum_{uv \in E_1(G)} \sqrt{d_u d_v} + \sum_{uv \in E_2(G)} \sqrt{d_u d_v} + \sum_{uv \in E_3(G)} \sqrt{d_u d_v}$

   $= |E_1(G)| \sqrt{1 \times 3} + |E_2(G)| \sqrt{2 \times 2} + |E_3(G)| \sqrt{2 \times 3}$

   $= (10 \times 2^n - 6) \times \sqrt{3} + (8 \times 2^n - 7) \times 2 + (20 \times 2^n - 18) \sqrt{6}$

   $= \left( 10\sqrt{3} + 20\sqrt{6} + 16 \right) 2^n - \left( 6\sqrt{3} + 18\sqrt{6} + 14 \right)$
CONCLUSION

In this work, we calculated the Zagreb index and the Randić index for the two well-known biodegradable dendrimers such as fourth-generation poly(amidoamine) dendrimer and the dendrimer based on glycerol and succinic acid which are used for cancer therapy. We also calculated the different versions of the Zagreb and the Randić indices for these dendrimers.

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