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Article *in* Journal of the Indonesian Mathematical Society · July 2022

DOI: 10.22342/jims.28.2.1204.194-214

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J. Indones. Math. Soc.
Vol. 28, No. 02 (2022), pp. 194–214.

Calculating PI related indices and their polynomial of Hyaluronic Acid and Conjugates

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Abstract. A large number of medical experiments have confirmed that the features of drugs have a close correlation with their molecular structure. Drug properties can be obtained by studying the molecular structure of corresponding drugs. The calculation of the topological index of a chemical graph enables scientists to have a better understanding of the physical chemistry and biological characteristics of drugs. In this paper, we focus on Hyaluronic Acid-Curcumin/Paclitaxel conjugate which are widely used in the manufacture of anticancer drugs. Therefore in this paper we have computed the Padmakar-Ivan related indices and its polynomial of the Hyaluronic Acid-curcumin/paclitaxel conjugate by using edge partitioning technique.

Key words and Phrases: Padmakar-Ivan index, weighted Padmakar-Ivan index, Padmakar-Ivan related polynomial, Hyaluronic Acid, Hyaluronic Acid-Curcumin/Paclitaxel conjugate.

1. Introduction and Preliminaries

In a recent year, there is a rapid growth in pharmaceutical and chemical fields. Biological activity, as well as physical, physicochemical, and chemical features of organic molecules, are all inherent in molecular structure, according to the primary paradigm of medical chemistry. Crum-brown and Fraser pulished the first quantitative structure activity relationship in 1868 on the basis of this principle. Despite many advances in the field of theoretical drug design, a large number of chemical experiments are needed to determine the pharmacological, chemical, and biological properties of these new compounds and drugs, which significantly increases the workload of pharmaceutical and chemical researchers. The critical step

2020 Mathematics Subject Classification: 05-11, 05C05
Received: 25-04-2022, accepted: 31-07-2022.

in drug discovery remain the identification and optimization of lead compound in a rapid and cost effective way. Computational tool techniques have advanced rapidly over the past decade and accordingly have played a major role in the development of a number of drugs now on the market or going through clinical trials. These computational tool techniques are based on the use of a virtual world computer generated hypotheses, which are tested for practicality.

Developing structure-activity relationships for drug compounds using computational or theoretical methods, relies on appropriate representations of molecular structure. Which predict the properties of drug without using any weight lab by analyzing the molecular structure of the relevant drug using a well-known tool of chemical graph theory known as topological index or molecular descriptor. Topological indices are simply defined as numerical values associated with chemical graph which is used for correlation of molecular structure with numerous chacteristics such as chemical reactivity, pharmacological activity, and physical properties. Topological indices play a vital role in quantitative structure property relationship (QSPR) and the quantitative structure-activity relationship (QSAR) in predicting different physicochemical properties and bioactivity that contribute in the discovery of drugs. [10, 26]
In order to calculate topological indices, the structure of the drugs is represented as a graph known as chemical graph, where each vertex indicate an atom and each edge represents a chemical bond between the atoms. Let $G = (V, E)$ be a molecular graph with vertex set $V = V(G)$ and edge set $E = E(G)$. The number of vertices and edges in a graph G can be denoted by $|V(G)|$ and $|E(G)|$ respectively. The degree of vertex $u \epsilon V(G)$ is denoted by $deg_e^G(u)$ and is the number of vertices that are adjacent to u. The edge $e \epsilon E(G)$ connecting the vertices u and v is denoted by $e = uv$. We now recall the following quantities based on distances which will give the number of vertices, closer to the end vertices of $e = uv$ by $n_e^G(u) = |x \epsilon V(G) : d_G(u, x) < d_G(v, x)|$, $n_e^G(v) = |x \epsilon V(G) : d_G(v, x) < d_G(u, x)|$, where $d_G(u, v)$ is the distance between the vertex u and v. That is $n_e^G(u)$ denote the number of vertices that are lying closer to the vertex u than the vertex v of $e = uv$. Analogously, $n_e^G(v)$ denote the number of vertices that are lying closer to the vertex v than the vertex u of $e = uv$. Vertex equidistant from both ends of the edge are not counted. The concept of topological index was first introduced by Wiener 1947 [38] defined by $W(G) = \sum_{\{u,v\} \subseteq V(G)} d(u, v)$
while working on the boiling points of alkanes. Topological indices are classified into many classes such as degree-based, distance-based, and spectrum-based, etc. Out of these distance based topological indices plays a vital role in the drug designs and theoretical chemistry. Some important distance based indices are Padmakar-Ivan index, Szeged index, Mostar index and some degree-distance based indices are weighted Padmakar-Ivan index, weighted Szeged index, weighted Mostar index. The Padmakar-Ivan index (PI) is one of the important topological indices widely applied to study the proertics of molecular structure, introduced by Khadikar et

al. [21] Padmakar-Ivan index defined as $PI(G) = \sum_{e=uv\epsilon E(G)} (n_e^G(u) + n_e^G(v))$
The Padmakar-Ivan index is one of the highly correlated index with Wiener index and found many chemical applications see [22, 23].

Inspired by the extension of the Wiener index and in order to increase the bibartivity of graphs, illič and Milosavljevic, [16], proposed the modifications in the vertex-PI index as the weighted version of vertex-PI index, which are defined as the Additively weighted vertex PI index is
$PI_A(G) = \sum_{e=uv\epsilon E(G)} (deg_e^G(u) + deg_e^G(v))(n_e^G(u) + n_e^G(v))$ and
Multiplicatively weighted vertex-PI index is
$PI_M(G) = \sum_{e=uv\epsilon E(G)} (deg_e^G(u).deg_e^G(v))(n_e^G(u) + n_e^G(v))$
Recently the weighted vertex-PI index of the tensor and strong products of graphs have been studied in [13]. Extensively more applications on weighted version of PI index has been studied, see([19, 28, 29]).
Numerous graph polynomials have been developed for measuring structural information of molecular graphs. Graph polynomials found applications in chemistry in connection with the molecular orbital theory of unsaturated compounds and also an important source of structural descriptors used in developing structure property models [7, 14, 24]. Distance-based and degree-based graph polynomials are useful because they contain a wealth of information about topological indices, vertex-PI polynomial of a graph G is, $PI(G, x) = \sum_{e=uv\epsilon E(G)} x^{(n_e^G(u)+n_e^G(v))}$.
Various topological indices can be derived from polynomials by taking their value at some point directly, or by taking integrals or derivatives. For instance, the first derivative of the vertex PI polynomial evaluated at $x = 1$ equals to the PI index. In light of the preceding condition and the newly proposed weighted version of the vertex-PI polynomial, motivates us to define the Additively weighted vertex-PI polynomial of a graphs G is $PI_A(G, x) = \sum_{e=uv\epsilon E(G)} x^{(deg_e^G(u)+deg_e^G(v))(n_e^G(u)+n_e^G(v))}$
and
the Multiplicatively weighted vertex-PI polynomal of a grpah G is
$PI_M(G, x) = \sum_{e=uv\epsilon E(G)} x^{(deg_e^G(u).deg_e^G(v))(n_e^G(u)+n_e^G(v))}$
The computation of topological indices for special molecular drug structures has raised considerable interest among medical and pharmaceutical researchers as it is useful to make up the medicinal and chemical experimental defects. Recently Mondal et al.,[27] several topological indices of COVID-19 based drugs such as remdesivir, chloroquine, hydroxychloroquine and theaflavin have been investigated. In addition, Wang et al., [39] computed topological indices of Hyaluronic Acid, which is thoroughly investigated in cancer therapy because of its excellent physical features. Moreover Ali et al., [1, 40] have theoretically analyzed and obtained several degree-based topological indices and indeg polynomial of Hyaluronic Acid-curcumin

conjugates. Likewise, Zheng et al.,[42] have determined many degree-based topological indices and polynomials for the Hyaluronic Acid-Paclitaxel conjugate, widely used in the therapeutics of cancer.

2. Motivation

Many pharmaceutical enterprises have made great efforts to develop many drugs to treat heart disease one such is Hyaluronic Acid(HA). Hyaluronic Acid is contributes most important to chemical graph multiplication and relocation, which is nontoxic, bio-compatible, biodegradable, and nonimmunogenic. Hyaluronic Acid (HA) is frequently used in anticancer drug delivery, visco-supplementation theraphy, eye surgery, corneal transplantation and even more medical fields.

Since ancient times, curcumin is known to be endowed with remarkable medicinal properties against a range of ailing conditions such as inflammation, cancer, diabetes, neurodegenerative disorders, cardiovascular diseases and asthma, even curcumin very tolerated in human body, due to poor aqueous-solubility of curcumin leads to inadequate bioavailability in biological system. To overcome this conjugates of curcumin with Hyaluronic Acid(HA) has received appreciable attention in recent times not only for increasing bioavailability but also to target tumor cells and tumor metastases for the treatment of numerous cancer. Therefore, conjugates of curcumin with HA is regarded as promising pharmaceutical strategy to improve water solubility, prolong curcumin release at the target site, improve tissue distribution and potentiate therapeutic outcomes[30, 37], computed many degree-based topological indices and polynomials.

Paclitaxel is another compound pharamatical departments which is unique antiproliferative mechanism makes it an efficient anticancer drug [31, 34, 35, 36, 37]. It is an important medication that is prescribed in various forms of cancer in spite of its limitations, such as low solubility and relevant adverse effects. Galer et al.[12, 42, 41, 43, 44] synthesized the HA-Paclitaxel conjugate (HA-PTX), in order to reduce the toxicity of taxanes and improve the antitumor activity. Therefore, different antitumor drugs can be covalently bonded to HA, forming HA-drugs conjugates. Owing to having pharmaceutical to developed of anticancer durgs many topological indices has been studied. For such as molecular structure, from mathematical perspective. Recently many articles has investigates degree based topological indices and its polynomial of HA and HA-based conjugates see [2, 3, 4, 5, 6, 8, 9, 15, 17, 18, 20, 25]. Graph polynomials have many applications and is an important source of structural descriptors see [32]. Since the distance based indices has been shown to have greater predictive ability, the current research on Hyaluronic Acid, Hyaluronic Acid-Curcumin/Paclitaxel conjugates. Computing distance based indices to the family of graph is more complicated then computing degree based indices, in this work we use the edge partition technique to calculate the distance based indices to the Hyaluronic Acid based molecular graphs.

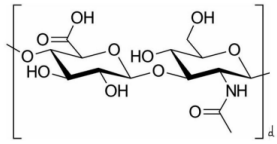

Figure 1. The molecular structure of Hyaluronic Acid HA_d.

Figure 2. The chemical graph of Hyaluronic HA_2.

3. Main Result and Proof

3.1. **Hyaluronic Acid.** In this section, we computing various bond additive topological indices like the Padmakar-Ivan index, Additively Padmakar-Ivan index and Multiplicatively Padmakar-Ivan index and its polynomial of Hyaluronic Acid. Figure 1. illustrate the molecular structure of Hyaluronic Acid. Let H denote the chemical graph of Hyaluronic Acid HA_d with the linear iteration d units. Figure 2. represented the chemical graph of Hyaluronic Acid for $d = 2$ units. For our convenience here we assume $H[H_i]$ be the induced sub graph of H, where H_i is the i^{th} units of H.

In order to obtain the results, let start our discussion with partitioning the edge set of H. By chemical graph structure analysis on the basic of degree of vertices, the edge set of H can be divided into five groups which are summarized as follow:

$E_1(H) = \{e = uv\epsilon E(H) : deg_e^H(u) = 1, deg_e^H(v) = 2\}$, $|E_1(H)| = d$

$E_2(H) = \{e = uv\epsilon E(H) : deg_e^H(u) = 1, deg_e^H(v) = 3\}$, $|E_2(H)| = 7d + 1$

$E_3(H) = \{e = uv\epsilon E(H) : deg_e^H(u) = 2, deg_e^H(v) = 3\}$, $|E_3(H)| = 11d - 2$

$E_4(H) = \{e = uv\epsilon E(H) : deg_e^H(u) = 3, deg_e^H(v) = 3\}$, $|E_4(H)| = 9d - 1$ and

$E_5(H) = \{e = uv\epsilon E(H) : deg_e^H(u) = 2, deg_e^H(v) = 2\}$, $|E_5(H)| = 1$.

So that the order of vertex set and edge set of Hyaluronic Acid is $|V(H)| = 26d$ and $|E(H)| = 28d - 1$. The main results discussed in this section are as follows:

Theorem 3.1. *The Padmakar-Ivan index of Hyaluronic Acid HA_d is given by $PI(HA_d) = (28d - 1)26d$.*

Proof. By graph structure analysis to the Hyaluronic Acid and applying the definition of Padmakar-Ivan index, we get

$$PI(HA_d) = \sum_{e=uv\epsilon E(HA_d)} (n_e^{HA_d}(u) + n_e^{HA_d}(v))$$

$$= \sum_{i=1}^{d} \sum_{e=uv\epsilon E(H_i)} (n_e^H(u) + n_e^H(v)) + \sum_{\substack{i=1 \\ e=xy\epsilon E(H_i \sim H_{i+1})}}^{d-1} (n_e^H(x) + n_e^H(y)),$$

where $H_i \sim H_{i+1}$ is the link of H_i and H_{i+1}

$$= \sum_{i=1}^{d} PI(H_i) + \sum_{i=1}^{d} \sum_{e=uv\epsilon E(H_i)} (|V(H)| - |V(H_i)|) + \sum_{i=1}^{d-1} |V(H)|$$

$= \sum_{i=1}^{d} PI(H_i) + \sum_{i=1}^{d} |E(H_i)|(|V(H)| - |V(H_i)|) + (d-1)|V(H)|$
Since $PI(H_i) = |E(H_i)||V(H_i)|$ is true for every i, so we have
$PI(HA_d) = \sum_{i=1}^{d} |E(H_i)||V(H_i)| + \sum_{i=1}^{d} |E(H_i)|(|V(H)| - |V(H_i)|) + (d-1)|V(H)|$
$= \sum_{i=1}^{d} |E(H_i)||V(H_i)| + \sum_{i=1}^{d} |E(H_i)||V(H)| - \sum_{i=1}^{d} |E(H_i)||V(H_i)| + (d-1)|V(H)|$
$= \sum_{i=1}^{d} |E(H_i)||V(H)| + (d-1)|V(H)|$, since $\sum_{i=1}^{d} |E(H_i)| = |E(H)| - (d-1)$
$= (|E(H)| - (d-1))|V(H)| + (d-1)|V(H)|$
$= |V(H)||E(H)|$
$= (28d-1)26d$, since $|V(H)| = 26d$
Hence the theorem. □

Theorem 3.2. *The Additively weighted Padmakar-Ivan index of Hyaluronic Acid HA_d is given by $PI_A(HA_d) = (140d-8)26d$.*

Proof. From the graph structure of Hyaluronic Acid and by the definition of Additively weighted Padmakar-Ivan index, we get
$PI_A(HA_d) = \sum_{e=uv \epsilon E(HA_d)} (deg_e^{HA_d}(u) + deg_e^{HA_d}(v))(n_e^{HA_d}(u) + n_e^{HA_d}(v))$
$= (\sum_{e=uv\epsilon E_1(H)} + \sum_{e=uv\epsilon E_2(H)} + \sum_{e=uv\epsilon E_3(H)} + \sum_{e=uv\epsilon E_4(H)} + \sum_{e=uv\epsilon E_5(H)})$
$(deg_e^H(u) + deg_e^H(v))(n_e^H(u) + n_e^H(v))$
$= \sum_{e=uv\epsilon E_1(H)} (1+2)(n_e^H(u) + n_e^H(v)) + \sum_{e=uv\epsilon E_2(H)} (1+3)(n_e^H(u) + n_e^H(v))$
$+ \sum_{e=uv\epsilon E_3(H)} (2+3)(n_e^H(u) + n_e^H(v)) + \sum_{e=uv\epsilon E_4(H)} (3+3)(n_e^H(u) + n_e^H(v))$
$+ \sum_{e=uv\epsilon E_4(H)} (2+2)(n_e^H(u) + n_e^H(v))$
$= d(3)|V(H)| + (7d+1)(4)|V(H)| + (11d-2)(5)|V(H)| + (9d-1)(6)|V(H)| + (1)(4)|V(H)|$
$= 3d|V(H)| + 4(7d+1)|V(H)| + 5(11d-2)|V(H)| + 6(9d-1)|V(H)| + 4|V(H)|$
$= (3d + 28d + 4 + 4 + 55d - 10 + 54d - 6)|V(H)|$, since $|V(H)| = 26d$
$= (140d-8)26d$
Hence the theorem. □

Theorem 3.3. *The Multiplicatively weighted Padmakar-Ivan index of Hyaluronic Acid HA_d is given by $PI_M(HA_d) = (170d-14)26d$.*

Proof. By graph structure analysis to the Hyaluronic Acid and from the definition of Multiplicatively weighted Padmakar-Ivan index, we get
$PI_M(HA_d) = \sum_{e=uv \epsilon E(HA_d)} (deg_u^{HA_d}(u).deg_e^{HA_d}(v))(n_e^{HA_d}(u) + n_e^{HA_d}(v))$
$= (\sum_{e=uv\epsilon E_1(H)} + \sum_{e=uv\epsilon E_2(H)} + \sum_{e=uv\epsilon E_3(H)} + \sum_{e=uv\epsilon E_4(H)}$
$+ \sum_{e=uv\epsilon E_5(H)})(deg_u^H(e).deg_v^H(e))(n_e^H(u) + n_e^H(v))$

$$= \sum_{e=uv\epsilon E_1(H)} (1.2)(n_e^H(u) + n_e^H(v)) + \sum_{e=uv\epsilon E_2(H)} (1.3)(n_e^H(u) + n_e^H(v))$$
$$+ \sum_{e=uv\epsilon E_3(H)} (2.3)(n_e^H(u) + n_e^H(v)) + \sum_{e=uv\epsilon E_4(H)} (3.3)(n_e^H(u) + n_e^H(v))$$
$$+ \sum_{e=uv\epsilon E_5(H)} (2.2)(n_e^H(u) + n_e^H(v))$$
$$= d(2)|V(H)| + (7d+1)(3)|V(H)| + (11d-2)(6)|V(H)| + (9d-1)(9)|V(H)|$$
$$+ (4)|V(H)|$$
$$= (2d + 21d + 3 + 4 + 66d - 12 + 81d - 9)|V(H)|$$
$$= (170d - 14)26d, \text{ since } |V(H)| = 26d$$

Hence the theorem. □

Theorem 3.4. *The Padmakar-Ivan polynomial of Hyaluronic Acid HA_d is given by $PI(HA_d, x) = (28d-1)x^{26d}$.*

Proof. From the graph structure analysis to the Hyaluronic Acid and applying the definition of Padmakar-Ivan ploynomial, we get

$$PI(HA_d, x) = \sum_{e=uv\epsilon E(HA_d)} x^{(n_e^{HA_d}(u) + n_e^{HA_d}(v))}$$
$$= \sum_{i=1}^{d} \sum_{e=uv\epsilon E(H_i)} x^{(n_e^H(u)+n_e^H(v))} + \sum_{\substack{i=1 \\ e=xy\epsilon E(H_i \sim H_{i+1})}}^{d-1} x^{(n_e^H(u)+n_e^H(v))}, \text{ where } H_i \sim H_{i+1}$$

denotes the link of graphs

$$= \sum_{i=1}^{d} |E(H_i)|x^{|V(H)|} + \sum_{i=1}^{d-1} x^{|V(H)|}$$
$$= \sum_{i=1}^{d} 27x^{|V(H)|} + (d-1)x^{|V(H)|}$$
$$= (27d + (d-1))x^{|V(H)|}$$
$$= (28d-1)x^{26d}, \text{ since } |V(H)| = 26d$$

Hence the theorem. □

Theorem 3.5. *The Additively weighted Padmakar-Ivan polynomial Hyaluronic Acid HA_d is given by*
$PI_A(HA_d, x) = dx^{78d} + (7d+2)x^{104d} + (11d-2)x^{130d} + (9d-1)x^{156d}$.

Proof. From the graph structure by the Hyaluronic Acid and by the definition of Additively weighted Padmakar-Ivan polynomial, we have

$$PI_A(HA_d, x) = \sum_{e=uv\epsilon E(HA_d)} x^{(deg_e^{HA_d}(u) + deg_e^{HA_d}(v))(n_e^{HA_d}(u) + n_e^{HA_d}(v))}$$
$$= \Big(\sum_{e=uv\epsilon E_1(H)} + \sum_{e=uv\epsilon E_2(H)} + \sum_{e=uv\epsilon E_3(H)} + \sum_{e=uv\epsilon E_4(H)} + \sum_{e=uv\epsilon E_5(H)} \Big)$$
$$x^{(deg_e^H(u) + deg_e^H(v))(n_e^H(u) + n_e^H(v))}$$
$$= \sum_{e=uv\epsilon E_1(H)} x^{(1+2)(n_e^H(u)+n_e^H(v))} + \sum_{e=uv\epsilon E_2(H)} x^{(1+3)(n_e^H(u)+n_e^H(v))}$$
$$+ \sum_{e=uv\epsilon E_3(H)} x^{(2+3)(n_e^H(u)+n_e^H(v))} \sum_{e=uv\epsilon E_4(H)} x^{(3+3)(n_e^H(u)+n_e^H(v))}$$
$$+ \sum_{e=uv\epsilon E_5(H)} x^{(2+2)(n_e^H(u)+n_e^H(v))}$$

$= dx^{3|V(H)|} + (7d+1)x^{4|V(H)|} + (11d-2)x^{5|V(H)|} + (9d-1)x^{6|V(H)|} + (1)x^{4|V(H)|}$
$= dx^{3|V(H)|} + (7d+2)x^{4|V(H)|} + (11d-2)x^{5|V(H)|} + (9d-1)x^{6|V(H)|}$
$= dx^{3(26d)} + (7d+2)x^{4(26d)} + (11d-2)x^{5(26d)} + (9d-1)x^{6(26d)}$
$= dx^{78d} + (7d+2)x^{104d} + (11d-2)x^{130d} + (9d-1)x^{156d}$, since $|V(H)| = 26d$
Hence the theorem. □

Theorem 3.6. *The Multiplicatively weighted Padmakar- Ivan polynomial of Hyaluronic Acid HA_d is given by*
$PI_M(HA_d, x) = dx^{52d} + (7d+1)x^{78d} + (11d-2)x^{156d} + (9d-1)x^{234d} + x^{104d}$.

Proof. By graph structure analysis to the Hyaluronic Acid and applying the definition of Multiplicatively weighted Padmakar-Ivan polynomial, we have
$PI_M(HA_d, x) = \sum_{e=uv\epsilon E(HA_d)} x^{(deg_e^{HA_d}(u).deg_e^{HA_d}(v))(n_e^{HA_d}(u)+n_e^{HA_d}(v))}$
$= (\sum_{e=uv\epsilon E_1(H)} + \sum_{e=uv\epsilon E_2(H)} + \sum_{e=uv\epsilon E_3(H)} + \sum_{e=uv\epsilon E_4(H)}$
$+ \sum_{e=uv\epsilon E_5(H)}) x^{(deg_e^H(u).deg_e^H(v))(n_e^H(u)+n_e^H(v))}$
$= \sum_{e=uv\epsilon E_1(H)} x^{(1.2)(n_e^H(u)+n_e^H(v))} + \sum_{e=uv\epsilon E_2(H)} x^{(1.3)(n_e^H(u)+n_e^H(v))}$
$+ \sum_{e=uv\epsilon E_3(H)} x^{(2.3)(n_e^H(u)+n_e^H(v))} + \sum_{e=uv\epsilon E_4(H)} x^{(3.3)(n_e^H(u)+n_e^H(v))}$
$+ \sum_{e=uv\epsilon E_5(H)} x^{(2.2)(n_e^H(u)+n_e^H(v))}$
$= dx^{2|V(H)|} + (7d+1)x^{3|V(H)|} + (11d-2)x^{6|V(H)|} + (9d-1)x^{9|V(H)|} + x^{4|V(H)|}$
$= dx^{2(26d)} + (7d+1)x^{3(26d)} + (11d-2)x^{6(26d)} + (9d-1)x^{9(26d)} + x^{4(26d)}$
$= dx^{52d} + (7d+1)x^{78d} + (11d-2)x^{156d} + (9d-1)x^{234d} + x^{104d}$,since $|V(H)| = 26d$
Hence the theorem. □

Note that similar work had been done for computing spectrum based indices like Estrada indices see[33]. The following corollaries shows the relationship between Padmakar-Ivan index, Additively Padmakar-Ivan index and Multiplicatively Padmakar-Ivan index for Hyaluronic Acid.

Corollary 3.7. $PI_A(H) = 5PI(H) - 3|V(H)|$.

Corollary 3.8. $PI_M(H) = 6PI(H) + (2d-4)|V(H)|$.

Corollary 3.9. $PI(H) < PI_A(H) < PI_M(H)$.

In this connection one may generalize the above corollaries for a families of graphs.

4. Hyaluronic Acid-Curcumin conjugates

In this section, we computing various bond additive topological indices like the Padmakar-Ivan index, Additively Padmakar-Ivan index and Multiplicatively Padmakar-Ivan index and its polynomial of Hyaluronic Acid-Curcumin conjugate.

Figure 3. illustrate the molecular structure of Hyaluronic Acid-Curcumin conjugate. Let J denote the chemical graph of Hyaluronic Acid-Curcumin conjugates HAC_d with the linear iteration d units. Figure 4. represented the chemical graph of Hyaluronic-Acid Curcumin conjugates for $d = 1$ unit. For our convenience here we assume $J[J_i]$ be the induced sub-graph of J, where J_i is the i^{th} units of J. So that the order of vertex set and edge set of Hyaluronic Acid is $|V(H)| = 26d$ and $|E(H)| = 28d - 1$. The main results discussed in this section are as follows:

In order to obtain the results, let start our discussion with partitioning the edge set of J. By chemical graph structure analysis on the basic of degree of vertices the edge sets of J can be divided into five groups which are summarized as follows:
$E_1(J) = \{e = uv \epsilon E(J) : deg_e^J(u) = 1, deg_e^J(v) = 2\}$, $|E_1(J)| = 3d$
$E_2(J) = \{e = uv \epsilon E(J) : deg_e^J(u) = 1, deg_e^J(v) = 3\}$, $|E_2(J)| = 9d + 1$
$E_3(J) = \{e = uv \epsilon E(J) : deg_e^J(u) = 2, deg_e^J(v) = 2\}$, $|E_3(J)| = 4d + 1$
$E_4(J) = \{e = uv \epsilon E(J) : deg_e^J(u) = 2, deg_e^J(v) = 3\}$, $|E_4(J)| = 29d - 2$ and
$E_5(J) = \{e = uv \epsilon E(J) : deg_e^J(u) = 3, deg_e^J(v) = 3\}$, $|E_5(J)| = 11d - 1$.
So that the order of vertex set and edge set of Hyaluronic Acid-Curcumin conjugate is $|V(J)| = 52d$ and $|E(J)| = 56d - 1$. The main results discussed in this section are as follows:

Theorem 4.1. *The Padmakar-Ivan index of Hyaluronic Acid-Curcumin conjugate HAC_d is given by $PI(HAC_d) = (56d - 1)52d$.*

Proof. From the graph structure of the Hyaluronic Acid-Curcumin conjugate and by the definition of Padmakar-Ivan index, we have

$$PI(HAC_d) = \sum_{e=uv \epsilon E(HAC_d)} (n_e^{HAC_d}(u) + n_e^{HAC_d}(v))$$

$$= \sum_{i=1}^{d} \sum_{e=uv \epsilon E(J_i)} (n_e^J(u) + n_e^J(v)) + \sum_{\substack{i=1 \\ e=xy \epsilon E(J_i \sim J_{i+1})}}^{d-1} (n_e^J(x) + n_e^J(y)),$$

where $J_i \sim J_{i+1}$ is the link of J_i and J_{i+1}

$$= \sum_{i=1}^{d} PI(J_i) + \sum_{i=1}^{d} \sum_{e \epsilon E(J_i)} (|V(J)| - |V(J_i)|) + (d-1)|V(J)|$$

$$= \sum_{i=1}^{d} PI(J_i) + \sum_{i=1}^{d} |E(J_i)|(|V(J)| - |V(J_i)|) + (d-1)|V(J)|$$

Since $PI(J_i) = |E(J_i)||V(J_i)|$ is true for every i, so we have

$$PI(HAC_d) = \sum_{i=1}^{d} |E(J_i)||V(J_i)| + \sum_{i=1}^{d} |E(J_i)|(|V(J)| - |V(J_i)|) + (d-1)|V(J)|$$

$$= \sum_{i=1}^{d} (|E(J_i)||V(J_i)| + |E(J_i)||V(J)| - |E(J_i)||V(J_i)) + (d-1)|V(J)|$$

$$= (|E(J)| - (d-1))|V(J)| + (d-1)|V(J)|$$

$$= |V(J)||E(J)|$$

$$= (56d - 1)52d$$

Hence the theorem. □

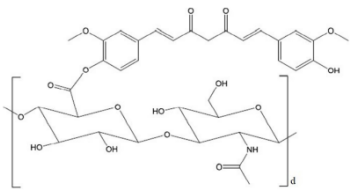

Figure 3. The molecular structure of Hyaluronic Acid-Curcumin conjugates HAC_d.

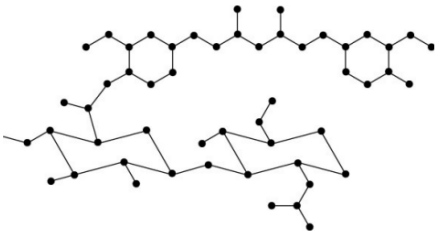

Figure 4. The chemical graph of Hyaluronic Acid-Curcumin conjugates HAC_1.

Theorem 4.2. *The Additively weighted Padmakar-Ivan index of Hyaluronic Acid-Curcumin conjugate HAC_d is given by $PI_A(HAC_d) = (272d - 8)52d$.*

Proof. By graph structure analysis to the Hyaluronic Acid-Curcumin conjugate and applying the definition of Additively weighted Padmakar-Ivan index, we have
$PI_A(HAC_d) = \sum_{e=uv\epsilon E(HAC_d)} (deg_e^{HAC_d}(u) + deg_e^{HAC_d}(v))(n_e^{HAC_d}(u) + n_e^{HAC_d}(v))$.
$= (\sum_{e=uv\epsilon E_1(J)} + \sum_{e=uv\epsilon E_2(J)} + \sum_{e=uv\epsilon E_3(J)} + \sum_{e=uv\epsilon E_4(J)}$
$+ \sum_{e=uv\epsilon E_5(J)})(deg_e^J(u) + deg_e^J(v))(n_e^J(u) + n_e^J(v))$
$= \sum_{e=uv\epsilon E_1(J)} (1+2)(n_e^J(u) + n_e^J(v)) + \sum_{e=uv\epsilon E_2(J)} (1+3)(n_e^J(u) + n_e^J(v))$
$+ \sum_{e=uv\epsilon E_3(J)} (2+2)(n_e^J(u) + n_e^J(v)) + \sum_{e=uv\epsilon E_4(J)} (2+3)(n_e^J(u) + n_e^J(v))$
$+ \sum_{e=uv\epsilon E_5(J)} (3+3)(n_e^J(u) + n_e^J(v))$
$= 3d(3)|V(J)| + (9d+1)(4)|V(J)| + (4d+1)(4)|V(J)| + (29d-2)(5)|V(J)|$
$+ (11d-1)(6)|V(J)|$
$= (9d + 36d + 4 + 16d + 4 + 145d - 10 + 66d - 6)|V(J)|$ as $|V(J)| = 52d$
$= (272d - 8)52d$
Hence the theorem. □

Theorem 4.3. *The Multiplicatively weighted Padmakar-Ivan index of Hyaluronic Acid-Curcumin conjugate HAC_d is given by $PI_M(HAC_d) = (322d - 14)52d$.*

Proof. From the graph structure of Hyaluronic Acid- Curcumin conjugate and from the definition of Multiplicatively weighted Padmakar-Ivan index, we have
$PI_M(HAC_d) = \sum_{e=uv\epsilon E(HAC_d)} (deg_e^{HAC_d}(u).deg_e^{HAC_d}(v))(n_e^{HAC_d}(u) + n_e^{HAC_d}(v))$.
$= (\sum_{e=uv\epsilon E_1(J)} + \sum_{e=uv\epsilon E_2(J)} + \sum_{e=uv\epsilon E_3(J)} + \sum_{e=uv\epsilon E_4(J)}$
$+ \sum_{e=uv\epsilon E_5(J)})(deg_e^J(u)deg_e^J(v))(n_e^J(u) + n_e^J(v))$
$= \sum_{e=uv\epsilon E_1(J)} (1.2)(n_e^J(u) + n_e^J(v)) + \sum_{e=uv\epsilon E_2(J)} (1.3)(n_e^J(u) + n_e^J(v))$

$$+\sum_{e=uv\epsilon E_3(J)}(2.2)(n_e^J(u)+n_e^J(v))+\sum_{e=uv\epsilon E_4(J)}(2.3)(n_e^J(u)+n_e^J(v))$$
$$+\sum_{e=uv\epsilon E_5(J)}(3.3)(n_e^J(u)+n_e^J(v))$$
$$=(3d(2)+(9d+1)(3)+(4d+1)(4)+(29d-2)(6)+(11d-1)(9))\,|V(J)|$$
$$=|V(J)|(6d+27d+3+16d+4+174d-12+99d-9), \text{ since } |V(G)|=52d$$
$$=(322d-14)52d$$

Hence the theorem. □

Theorem 4.4. *The Padmakar-Ivan polynomial of Hyaluronic Acid-Curcumin conjugate (HAC_d) is given by $PI(HAC_d,x)=(56d-1)x^{52d}$*

Proof. By graph structure analysis to the Hyaluronic Acid-Curcumin conjugate and applying the definition of Padmakar-Ivan polynomial, we have

$$PI(HAC_d,x)=\sum_{e=uv\epsilon E(HAC_d)}x^{(n_e^{HAC_d}(u)+n_e^{HAC_d}(v))}$$
$$=\sum_{i=1}^{d}\sum_{e=uv\epsilon E(J_i)}x^{(n_e^J(u)+n_e^J(v))}+\sum_{\substack{i=1\\ e=uv\epsilon E(J_i\sim J_{i+1})}}^{d-1}x^{(n_e^J(u)+n_e^J(v))}, \text{ where } J_i\sim J_{i+1} \text{ de-}$$

noted the link of graphs

$$=\sum_{i=1}^{d}|E(J_i)|x^{|V(J)|}+(d-1)x^{|V(J)|}$$
$$=55dx^{|V(J)|}+(d-1)x^{|V(J)|}$$
$$=(55d+d-1)x^{|V(J)|}, \text{ since } |V(J)|=52d$$
$$=(56d-1)x^{52d}$$

Hence the theorem. □

Theorem 4.5. *The Additively weighted Padmakar-Ivan polynomial of Hyaluronic Acid-Curcumin conjugate, HAC_d is given by*
$PI_A(HAC_d,x)=3dx^{156d}+(13d+2)x^{208d}+(29d-2)x^{260d}+(11d-1)x^{312d}$.

Proof. From the graph structure of the Hyaluronic Acid-Curcumin conjugate and by the definition of Additively weighted Padmakar-Ivan polynomial, we have

$$PI_A(HAC_d,x)=\sum_{e=uv\epsilon E(HAC_d)}x^{(deg_e^{HAC_d}(u)+deg_e^{HAC_d}(v))(n_e^{HAC_d}(u)+n_e^{HAC_d}(v))}$$
$$=(\sum_{e=uv\epsilon E_1(J)}+\sum_{e=uv\epsilon E_2(J)}+\sum_{e=uv\epsilon E_3(J)}+\sum_{e=uv\epsilon E_4(J)}$$
$$+\sum_{e=uv\epsilon E_5(J)})x^{(deg_e^J(u)+deg_e^J(v))(n_e^J(u)+n_e^J(v))}$$
$$=\sum_{e=uv\epsilon E_1(J)}x^{(1+2)(n_e^J(u)+n_e^J(v))}+\sum_{e=uv\epsilon E_2(J)}x^{(1+3)(n_e^J(u)+n_e^J(v))}$$
$$+\sum_{e=uv\epsilon E_3(J)}x^{(2+2)(n_e^J(u)+n_e^J(v))}+\sum_{e=uv\epsilon E_4(J)}x^{(2+3)(n_e^J(u)+n_e^J(v))}$$
$$+\sum_{e=uv\epsilon E_5(J)}x^{(3+3)(n_e^J(u)+n_e^J(v))}$$
$$=3dx^{3|V(J)|}+(9d+1)x^{4|V(J)|}+(4d+1)x^{4|V(J)|}+(29d-2)x^{5|V(J)|}+(11d-1)x^{6|V(J)|}$$
$$=3dx^{3(52d)}+(13d+2)x^{4(52d)}+(29d-2)x^{5(52d)}+(11d-1)x^{6(52d)} \text{ since } |V(J)|=52d$$

$= 3dx^{156d} + (13d+2)x^{208d} + (29d-2)x^{260d} + (11d-1)x^{312d}$
Hence the theorem. □

Theorem 4.6. *The Multiplicatively weighted Padmakar-Ivan polynomial of Hyaluronic Acid-Curcumin conjugate HAC_d, is given by $PI_M(HAC_d, x) = 3dx^{104d}$ $+ (9d+1)x^{156d} + (4d+1)x^{208d} + (29d-2)x^{312d} + (11d-1)x^{468d}$.*

Proof. By graph structure analysis to Hyaluronic Acid-Curcumin conjugate and applying the definition of Multiplicatively weighted Padmakar-Ivan index polynomial, we have

$$PI_M(HAC_d, x) = \sum_{e=uv\epsilon E(HAC_d)} x^{(deg_e^{HAC_d}(u).deg_e^{HAC_d}(v))(n_e^{HAC_d}(u)+n_e^{HAC_d}(v))}$$
$$= (\sum_{e=uv\epsilon E_1(J)} + \sum_{e=uv\epsilon E_2(J)} + \sum_{e=uv\epsilon E_3(J)} + \sum_{e=uv\epsilon E_4(J)} + \sum_{e=uv\epsilon E_5(J)})x^{(deg_e^J(u).deg_e^J(v))(n_e^J(u)+n_e^J(v))}$$
$$= \sum_{e=uv\epsilon E_1(J)} x^{(1.2)(n_e^J(u)+n_e^J(v))} + \sum_{e=uv\epsilon E_2(J)} x^{(1.3)(n_e^J(u)+n_e^J(v))} + \sum_{e=uv\epsilon E_3(J)} x^{(2.2)(n_e^J(u)+n_e^J(v))} + \sum_{e=uv\epsilon E_4(J)} x^{(2.3)(n_e^J(u)+n_e^J(v))} + \sum_{e=uv\epsilon E_5(J)} x^{(3.3)(n_e^J(u)+n_e^J(v))}$$
$$= 3dx^{2|V(J)|} + (9d+1)x^{3|V(J)|} + (4d+1)x^{4|V(J)|} + (29d-2)x^{6|V(J)|} + (11d-1)x^{9|V(J)|}$$
$$= 3dx^{2(52d)} + (9d+1)x^{3(52d)} + (4d+1)x^{4(52d)} + (29d-2)x^{6.(52d)} + (11d-1)x^{9(52d)}$$
since $|V(J)| = 52d$
$$= 3dx^{104d} + (9d+1)x^{156d} + (4d+1)x^{208d} + (29d-2)x^{312d} + (11d-1)x^{468d}$$
Hence the theorem. □

The following corollaries shows the relationship between Padmakar-Ivan index, Additively Padmakar-Ivan index and Multiplicatively Padmakar-Ivan index for Hyaluronic Acid-Curcumin conjugate.

Corollary 4.7. $PI_A(J) = 5PI(J) - (8d+3)|V(J)|$.

Corollary 4.8. $PI_M(J) = 5PI(J) - (14d-8)|V(J)|$.

Corollary 4.9. $PI(J) < PI_A(J) < PI_M(J)$.

5. Hyaluronic Acid-Paclitaxel conjugates

In this section, we calculate the exact value of the some bond additive topological indices and its polynomial as discussed in the previous sections for the Hyaluronic Acid-Paclitaxel Conjugates Figure 5. illustrate the molecular structure of Hyaluronic Acid-Paclitaxel conjugates. Let K denote the chemical graph of Hyaluronic Acid-Paclitaxel conjugates HAP_d with the linear iteration d units. Figure 6. represented the chemical graph of Hyaluronic Acid-Paclitaxel conjugates $d = 1$ unit. For our convenience here we assume $K[K_i]$ be the induced sub-graph of K, where K_i is the i^{th} units of K. In order to obtain the results, let start our discussion with partitioning the edge set K. By chemical graph structure analysis

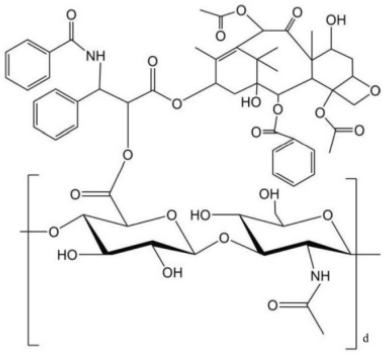

Figure 5. The molecular structure of Hyaluronic Acid-Paclitaxel conjugates $HAP_{d.}$

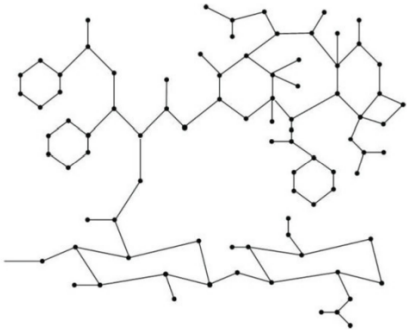

Figure 6. The chemical graph of Hyaluronic Acid-Paclitaxel conjugates HAP_1.

on the basic of degree of vertices the edge set of K can be divided into five groups which are summarized as follows:

$E_1(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 1, deg_e^K(v) = 2\}$, $|E_1(K)| = d$
$E_2(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 1, deg_e^K(v) = 3\}$, $|E_2(K)| = 16d + 1$
$E_3(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 2, deg_e^K(v) = 2\}$, $|E_3(K)| = 13d + 1$
$E_4(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 1, deg_e^K(v) = 4\}$, $|E_4(K)| = 4d$
$E_5(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 2, deg_e^K(v) = 3\}$, $|E_5(K)| = 32d - 2$
$E_6(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 2, deg_e^K(v) = 4\}$, $|E_6(K)| = 3d$
$E_7(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 3, deg_e^K(v) = 3\}$, $|E_7(K)| = 19d - 1$
$E_8(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 3, deg_e^K(v) = 4\}$, $|E_8(K)| = 7d$ and
$E_9(K) = \{e = uv\epsilon E(K) : deg_e^K(u) = 4, deg_e^K(v) = 4\}$, $|E_9(K)| = d$.

So that the order of vertex set and edge set of Hyaluronic Acid-Paclitaxel conjugates is $|V(K)| = 87d$ and $|E(K)| = 96d - 1$. The main results discussion in this section are as follows:

Theorem 5.1. *The Padmakar-Ivan index of Hyaluronic Acid-Paclitaxel conjugate HAP_d is given by $PI(HAP_d) = (96d - 1)87d$.*

Proof. From the graph structure of Hyaluronic Acid-Paclitaxel conjugate and by the definition of Padmakar-Ivan index we get

$$PI(HAP_d) = \sum_{e=uv\epsilon E(HAP_d)} (n_e^{HAP_d}(u) + n_e^{HAP_d}(v))$$

$$= \sum_{i=1}^{d} \sum_{e=uv\epsilon E(K_i)} (n_e^K(u) + n_e^K(v)) + \sum_{\substack{i=1 \\ e=xy\epsilon E(K_i \sim K_{i+1})}}^{d-1} (n_e^K(x) + n_e^K(y)),$$

where $K_i \sim K_{i+1}$ is the link of K_i and K_{i+1}

$$= \sum_{i=1}^{d} PI(K_i) + \sum_{i=1}^{d} \sum_{e=uv\epsilon E(K_i)} (|V(K)| - |V(K_i)|) + (d-1)|V(K)|$$

Since $PI(K_i) = |E(K_i)||V(K_i)|$ is true for every i, so we have

$PI(HAP_d) = \sum_{i=1}^{d} |E(K_i)||V(K_i)| + \sum_{i=1}^{d} |E(K_i)|(|V(K)| - |V(K_i)|) + (d-1)|V(K)|$

$= \sum_{i=1}^{d} (|E(K_i)||V(K_i)| + |E(K_i)||V(K)| - |E(K_i)||V(K_i)|) + (d-1)|V(K)|$

$= \sum_{i=1}^{d} |E(K_i)|(|V(K)|) + (d-1)|V(K)|$

$= (|E(K)| - (d-1))|V(K)| + (d-1)|V(K)|$

$= |V(K)||E(K)|$

$= (96d-1)87d$

Hence the theorem. □

Another interesting degree based descriptor called Sombor index has been investigated for some extremal graphs [11] and the above result may extend for extremal graphs.

Theorem 5.2. *The Additively weighted Padmakar-Ivan index of Hyaluronic Acid-Paclitaxel conjugate (HAP_d) is given by $PI_A(HAP_d) = (488d-8)87d$.*

Proof. By graph structure analysis to the Hyaluronic Acid-Paclitaxel conjugate and from the definition of Additively weighted Padmakar-Ivan index, we have

$PI_A(HAP_d) = \sum_{e=uv\epsilon E(HAP_d)} (deg_e^{HAP_d}(u) + deg_e^{HAP_d}(v))(n_e^{HAP_d}(u) + n_e^{HAP_d}(v))$

$= (\sum_{e=uv\epsilon E_1(K)} + \sum_{e=uv\epsilon E_2(K)} + \sum_{e=uv\epsilon E_3(K)} + \sum_{e=uv\epsilon E_4(K)} + \sum_{e=uv\epsilon E_5(K)} + \sum_{e=uv\epsilon E_6(K)}$

$+ \sum_{e=uv\epsilon E_7(K)} + \sum_{e=uv\epsilon E_8(K)} + \sum_{e=uv\epsilon E_9(K)})(deg_e^K(u) + deg_e^K(v))(n_e^K(u) + n_e^K(v))$

$= \sum_{e=uv\epsilon E_1(K)} (1+2)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_2(K)} (1+3)(n_e^K(u) + n_e^K(v))$

$+ \sum_{e=uv\epsilon E_3(K)} (2+2)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_4(K)} (1+4)(n_e^K(u) + n_e^K(v))$

$+ \sum_{e=uv\epsilon E_5(K)} (2+3)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_6(K)} (2+4)(n_e^K(u) + n_e^K(v))$

$+ \sum_{e=uv\epsilon E_7(K)} (3+3)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_8(K)} (3+4)(n_e^K(u) + n_e^K(v))$

$+ \sum_{e=uv\epsilon E_9(K)} (4+4)(n_e^K(u) + n_e^K(v))$

$= 3d|V(K)| + 4(16d+1)|V(K)| + 4(13d+1)|V(K)| + 5(4d)|V(K)| + 5(32d-2)|V(K)|$

$+ 6(3d)|V(K)| + 6(19d-1)|V(K)| + 7(7d)|V(K)| + 8d|V(K)|$

$= (3d + 64d + 4 + 52d + 4 + 20d + 150d + 10d - 10 + 18d + 114d - 6 + 49d + 8d)|V(K)|$

$= (488d-8)87d$, Since $|V(K)| = 87d$

Hence the theorem. □

Theorem 5.3. *The Multiplicatively weighted Padmakar-Ivan index of the Hyaluronic Acid-Paclitaxel conjugate HAP_d is given by $PI_M(HAP_d) = (605d-14)87d$.*

Proof. By graph structure analysis to the Hyaluronic Acid-Paclitaxel conjugate and applying the definition of Multiplicatively weighted Padmakar-Ivan index, we get

$PI_M(HAP_d) = \sum_{e=uv\epsilon E(HAP_d)} (deg_e^{HAP_d}(u).deg_e^{HAP_d}(v))(n_e^{HAP_d}(u) + n_e^{HAP_d}(v)).$

$PI_M(HAP_d) = (\sum_{e=uv\epsilon E_1(K)} + \sum_{e=uv\epsilon E_2(K)} + \sum_{e=uv\epsilon E_3(K)} + \sum_{e=uv\epsilon E_4(K)} + \sum_{e=uv\epsilon E_5(K)}$
$+ \sum_{e=uv\epsilon E_6(K)} + \sum_{e=uv\epsilon E_7(K)} + \sum_{e=uv\epsilon E_8(K)} + \sum_{e=uv\epsilon E_9(K)})(deg_e^K(u)deg_e^K(v))(n_e^K(u)+n_e^K(v))$
$= \sum_{e=uv\epsilon E_1(K)} (1.2)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_2(K)} (1.3)(n_e^K(u) + n_e^K(v))$
$+ \sum_{e=uv\epsilon E_3(K)} (2.2)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_4(K)} (1.4)(n_e^K(u) + n_e^K(v))$
$+ \sum_{e=uv\epsilon E_5(K)} (2.3)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_6(K)} (2.4)(n_e^K(u) + n_e^K(v))$
$+ \sum_{e=uv\epsilon E_7(K)} (3.3)(n_e^K(u) + n_e^K(v)) + \sum_{e=uv\epsilon E_8(K)} (3.4)(n_e^K(u) + n_e^K(v))$
$+ \sum_{e=uv\epsilon E_9(K)} (4.4)(n_e^K(u) + n_e^K(v))$
$= 2d|V(K)|+3(16d+1)|V(K)|+4(13d+1)|V(K)|+4(4d)|V(K)|+6(32d-2)|V(K)|$
$+ 8(3d)|V(K)| + 9(19d-1)|V(K)| + 12(7d)|V(K)| + 16d|V(K)|$
$= (2d+48d+3+52d+4+16d+180d+12d-12+24d+171d-9+84d+16d)|V(K)|$
$= (605d - 14)87d$, since $|V(K)| = 87d$
Hence the theorem. □

Theorem 5.4. *The Padmakar-Ivan polynomial of Hyaluronic Acid-Paclitaxel conjugate HAP_d is given by $PI(HAP_d, x) = (96d - 1)x^{87d}$*

Proof. From the graph structure analysis to the Hyaluronic Acid-Paclitaxel conjugate and by the definition of Padmakar-Ivan polynomial, we have
$PI(HAP_d, x) = \sum_{e=uv\epsilon E(HAP_d)} x^{(n_e^{HAP_d}(u)+n_e^{HAP_d}(v))}$
$= \sum_{i=1}^{d} \sum_{e=uv\epsilon E(K_i)} x^{(n_e^K(u)+n_e^K(v))} + \sum_{\substack{i=1 \\ e=xy\epsilon E(K_i\sim K_{i+1})}}^{d-1} x^{(n_e^K(u)+n_e^K(v))}$, where $K_i \sim K_{i+1}$ denotes the link of graphs
$= \sum_{i=1}^{d} |E(K_i)|x^{|V(K)|} + (d-1)x^{|V(K)|}$
$= 95dx^{|V(K)|} + (d-1)x^{|V(K)|}$
$= x^{|V(K)|}(95d + d - 1)$, since $|V(K)| = 87d$
$= (96d - 1)x^{87d}$
Hence the theorem. □

Theorem 5.5. *The Additively weighted Padmakar-Ivan polynomial of Hyaluronic Acid-Paclitaxel conjugate HAP_d is given by*
$PI_A(HAP_d, x) = dx^{261d} + (29d + 2)x^{348d} + (36d - 2))x^{435d} + (22d - 1)x^{522d}$
$+ 7dx^{609d} + dx^{696d}$.

Proof. By graph structure analysis to the Hyaluronic Acid-Paclitaxel conjugate and applying the definition of Additively weighted Padmakar-Ivan polynomial, we have

$$PI_A(HAP_d,x)=\sum_{e=uv\epsilon E(HAP_d)} x^{(deg_e^{HAP_d}(u)+deg_e^{HAP_d}(v))(n_e^{HAP_d}(u)+n_e^{HAP_d}(v))}$$
$$=\sum_{\substack{e=uv\epsilon E_i(K)\\ i=1,2,\ldots,9}} x^{(deg_e^K(u)+deg_e^K(v))(n_e^K(u)+n_e^K(v))}$$
$$=\sum_{e=uv\epsilon E_1(K)} x^{(1+2)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_2(K)} x^{(1+3)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_3(K)} x^{(2+2)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_4(K)} x^{(1+4)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_5(K)} x^{(2+3)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_6(K)} x^{(2+4)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_7(K)} x^{(3+3)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_8(K)} x^{(3+4)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_9(K)} x^{(4+4)(n_e^K(u)+n_e^K(v))}$$
$$=dx^{3|V(K)|}+(16d+1)x^{4|V(K)|}+(13d+1)x^{4|V(K)|}+(4d)x^{5|V(K)|}+(32d-2)x^{5|V(K)|}$$
$$+(3d)x^{6|V(K)|}+(19d-1)x^{6|V(K)|}+(7d)x^{7|V(K)|}+dx^{8|V(K)|}, \text{ since } |V(K)|=87d$$
$$=dx^{3(87d)}+(29d+2)x^{4(87d)}+(36d-2))x^{5(87d)}+(22d-1)x^{6(87d)}+7dx^{7(87d)}+dx^{8(87d)}$$
$$=dx^{261d}+(29d+2)x^{348d}+(36d-2)x^{435d}+(22d-1)x^{522d}+7dx^{609d}+dx^{696d}$$

Hence the theorem. □

Theorem 5.6. *The Multiplicatively weighted Padmakar-Ivan polynomial of Hyaluronic Acid-Paclitaxel conjugate HAP_d is given by* $PI_M(HAP_d,x)=dx^{174d}+(16d+1)x^{261d}+(17d+1)x^{348d}+(32d-2)x^{522d}+(3d)x^{696d}+(19d-1)x^{763d}+(7d)x^{1044d}+dx^{1392d}$.

Proof. By graph structure analysis to the Hyaluronic Acid-Paclitaxel conjugate and from the definition of Multiplicatively weighted Padmakar-Ivan polynomial, we have

$$PI_M(HAP_d,x)=\sum_{e=uv\epsilon E(HAP_d)} x^{(deg_e^{HAP_d}(u).deg_e^{HAP_d}(v))(n_e^{HAP_d}(u)+n_e^{HAP_d}(v))}$$
$$=\sum_{\substack{e=uv\epsilon E_i(K)\\ i=1,2,\ldots,9}} x^{(deg_e^K(u).deg_e^K(v))(n_e^K(u)+n_e^K(v))}$$
$$=\sum_{e=uv\epsilon E_1(K)} x^{(1.2)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_2(K)} x^{(1.3)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_3(K)} x^{(2.2)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_4(K)} x^{(1.4)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_5(K)} x^{(2.3)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_6(K)} x^{(2.4)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_7(K)} x^{(3.3)(n_e^K(u)+n_e^K(v))}+\sum_{e=uv\epsilon E_8(K)} x^{(3.4)(n_e^K(u)+n_e^K(v))}$$
$$+\sum_{e=uv\epsilon E_9(K)} x^{(4.4)(n_e^K(u)+n_e^K(v))}$$
$$=dx^{2|V(K)|}+(16d+1)x^{3|V(K)|}+(13d+1)x^{4|V(K)|}+(4d)x^{4|V(K)|}+(32d-2)x^{6|V(K)|}+$$
$$(3d)x^{8|V(K)|}+(19d-1)x^{9|V(K)|}+(7d)x^{12|V(K)|}+dx^{16|V(K)|}$$
$$=dx^{174d}+(16d+1)x^{261d}+(17d+1)x^{348d}+(32d-2)x^{522d}+(3d)x^{696d}+(19d-1)x^{763d}$$

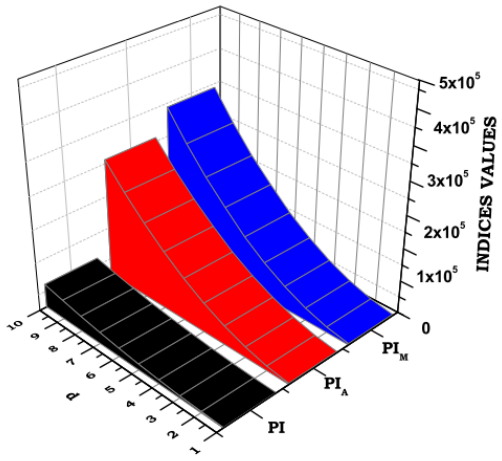

Figure 7. Comparison of PI, PI_A and PI_M indices for Hyaluronic Acid HA_d

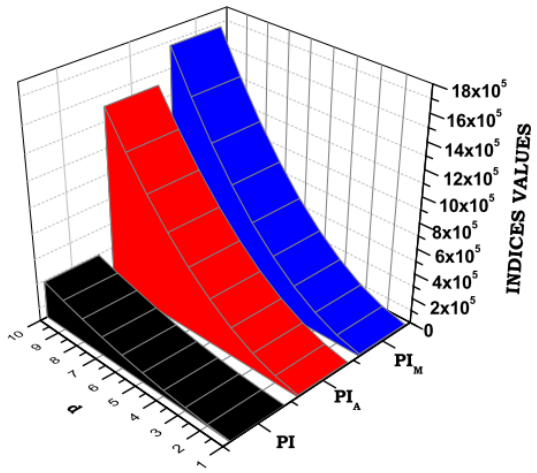

Figure 8. Comparison of PI, PI_A and PI_M indices for Hyaluronic Acid-Curcumin conjugate HAC_d.

$+(7d)x^{1044d} + dx^{1392d}$, Since $|V(K)| = 87d$
Hence the theorem. □

The following corollaries shows the relationship between Padmakar-Ivan index, Additively Padmakar-Ivan index and Multiplicatively Padmakar-Ivan index for Hyaluronic Acid-Paclitaxel conjugate.

Corollary 5.7. $PI_A(K) = 5PI(K) + (8d-3)|V(K)|$

Corollary 5.8. $PI_M(K) = 6PI(K) + (29d-8)|V(K)|$.

Corollary 5.9. $PI(K) < PI_A(K) < PI_M(K)$

6. Comparisons and discussions

The calculation of the molecular invariants of a chemical graphs enables scientists to have a better understanding of the physical chemistry and biological characteristics of drugs. Since drug tests show strong inner relationships between the biomedical and pharmacological characteristics of the drugs and their molecular structure. Hence we studied the exact value of chemical graph PI, PI_A and PI_M for HA_d, HAC_d, HAP_d and compared it. It was found that these indices increases with increasing of d units (see Fig. 7, 8, 9) and from Fig. 10 show that PI index has strong correlation for HAP_d. As these results are helpful in drug discovery as well as chemical science point of view, in this regard, the mathematical properties of Hyaluronic Acid-Curcumin/Paclitaxel conjugate are worth to investigate for future studies.

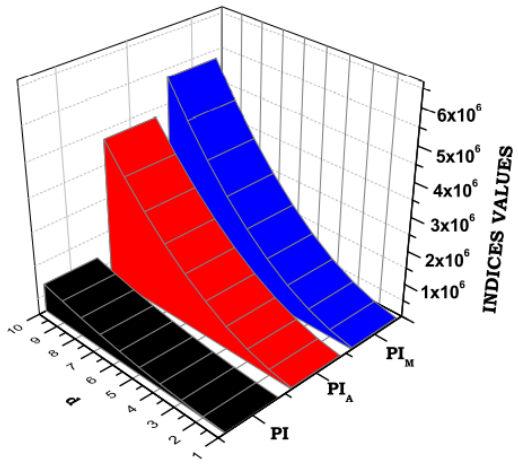

Figure 9. Comparison of PI, PI_A and PI_M indices for Hyaluronic Acid-Paclitaxel conjugate HAP_d.

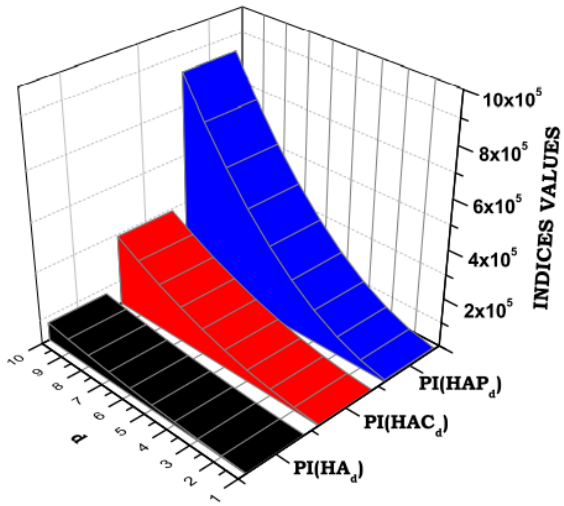

Figure 10. Comparison of PI index for HA_d, HAC_d and HAP_d.

7. Conclusion

Studying the physicochemical properties of the molecular structure is not only time consuming but also a costly process. Therefore, the reearchers in mathematical chemistry shown interest on finding topological indices for various chemical graphs. As the number of vertices of a chemical graph increases, it is difficult to obtain data and make calculations on it. In this case, computational and statistical methods become important for analyzing the behavior of the data. In this way, the desired values can become predictable without time-consuming experiments. Therefore, it has been considered necessary to calculate the molecular invariant called PI related indices and its polynomial for molecular sturcture in order to examine the physicochemical and biological properties of these molecules. Hyaluronic Acid, Hyaluronic Acid Curcumin/Paclitaxel conjugate, are popular lately, especially in drug manufacturing.

In this work, we have calculated some distance, degree-distance based topological indices of Hyaluronic Acid, Hyaluronic Acid-Curcumin/Paclitaxel conjugate such as PI index, weighted Additively PI index, weighted Multiplicatively PI index. In addition, associated polynomials of the above topological indices for Hyaluronic Acid, Hyaluronic Acid-Curcumin/Paclitaxel conjugate were also computed. The results obtained in this study can be incorporated in various QSAR and QSPR models for its applications in the chemical and pharmaceutical science. We extended this work to obtain Szeged and Mostar indices. The computation of

other molecular invariants and polynomial for Hyaluronic Acid, Hyaluronic Acid-Curcumin/Paclitaxel conjugate may be another interesting topic for future studies. Here we pose a problem.

Problem. Characterize the maximal value of PI index, weighted Additively PI index, weighted Multiplicatively PI index among various conjugation to the Hyaluronic Acid.

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