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TOPOLOGICAL INDICES AND QSPR/QSAR ANALYSIS OF SOME DRUGS BEING INVESTIGATED FOR THE TREATMENT OF HEADACHES

Muhammad Shoaib Sardar[1*], Muhammad Asad Ali[2]

[1]*School of Mathematics and Statistics, Gansu Centre for Applied Mathematics, Lanzhou University, Lanzhou, 730000, China; shoaib@lzu.edu.cn*

[2]*School of Mathematics, Minhaj University, Lahore, Pakistan; aliasad5340@gmail.com*

Mohammad Reza Farahani, Mehdi Alaeiyan

Department of Mathematics, Iran University of Science and Technology, Tehran 16844, Iran.
mrfarahani88@gmail.com, alaeiyan@iust.ac.ir

Murat Cancan

Faculty of Education, Van Yuzuncu Yıl University, Zeve Campus, Tuşba, 65080, Van, Turkey
m_cencen@yahoo.com

*Correspondence should be addressed to: shoaib@lzu.edu.cn 0086-15095340456

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Abstract

Students may experience various types of headaches, as well as stress, which can have an impact on their mental and social health as well as their academic performance. Headache is one of the most common aspects of modern life, owing to the rapid changes in human life. Students are subjected to academic stress as a result of academic tests, homework assignments, and other school requirements. Scientists are testing drugs based on medical therapies based on previous research. Many drugs, such as naproxen, flurbiprofen, fenoprofen, ketoprofen, and ibuprofen are listed in the recommendations. Topological index is a molecular descriptor that use to analyze the chemical and physical properties of chemical compounds and can be used in modeling to predict the physicochemical properties and biological activities of molecules in a quantitative structure-property relationship (QSPR) and quantitative structure-activity relationship (QSAR) studies. In this study, M-polynomial methods are used to investigate the several degree-based topological indices for some drugs used for headaches (i.e., naproxen, flurbiprofen, fenoprofen, ketoprofen, and ibuprofen). Furthermore, a QSPR relationship was discovered between the various topological indices and the various physicochemical properties of these antiviral drugs. According to the obtained results, topological indices have a strong correlation with the physicochemical properties of potential drugs.

Keywords: M-polynomial; QSPR/QSAR; Molecular descriptors; Drugs.

Mathematics Subject Classification: 05C07, 05C12, 05C35.

1. Introduction and Preliminaries

Every year, a huge number of novel diseases are discovered as a result of the rapidly evolving viruses. This necessitates the development of additional drugs to treat new diseases. Headache due to tension is one of the most commonly reported problem among adolescents. The pain is frequently minor to moderate and feels like constant pressure is applied to the front portion of face, head, or neck [1]. It may also feel like a belt is tightening around your head. The pain is typically felt both on the head sides. Headache is defined as pain that is not severe, localized or aggravated by activity. There is no significant vomiting and neither photophobia, nor phonophobia or nausea can coexist [2]. Certain drugs that frequently used for relief of

headache has also side effects as in naproxen, ketoprofen, and ibuprofen has side effects like gastrointestinal upset, gastrointestinal bleeding, vomiting and liver damage etc. while in fenoprofen side effects is dizziness, drowsiness, nausea and same as above mentioned side effects present in flurbiprofen [3].The chemical structures are depicted in

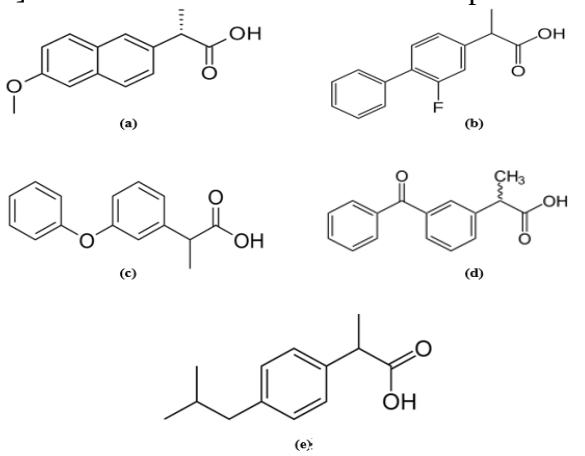

Figure *1*.

The topological index computation technique is being used to evaluate the medicinal properties and biochemical information of new drugs without requiring chemical experimentation, which is greatly appreciated in developing countries [4]. Numerous studies have found a strong obvious link between the chemical properties of chemical compounds and drugs (for example, boiling and melting points) and their molecular structures. Gao, et al., [5] concentrated on a smart polymer family that is widely used in the production of anticancer drugs. Several topological indices are determined using edge dividing methods, and the results compensate for the lack of chemical and medicine trials, providing a theoretical foundation for pharmaceutical engineering. Parveen, et al., [6] used topological indices for the treatment of diabetes and QSPR modeling. QSPR study determined the mathematical relation among the characteristics that under study and different indices associated to the molecular structure of the drugs. For more detailed study about topological indices, we recommend the following articles [7-16, 22-31].

In pharmaceutical sciences, molecular structural properties are critical for the development of a novel products and can be observed through the study of topological indices [17]. In this work, the structure of a drug is expressed as a graph, all graphs are assumed to be simple and linked, where each vertex $V(G)$ expresses an atom and each edge $E(G)$ represents a chemical bond between these atoms. A vertex's degree is determined by the number of edges connected to it. In case of unclear notations and terminologies, please consult the following book [18]. The M-polynomial produces formulas that are sufficiently close to degree-based topological indices. It is the most general polynomial that has been established up till now. M-polynomial is defined as [19]

$$M(G;x,y) = \sum_{s\leq t} m_{st}(G)x^s y^t,$$

where, $m_{st}(G)$ is the number of edges of G, such that $ij \in E(G)$ and $\{d_i, d_j\} = \{s,t\}$.

Degree-based topological indices used in this paper are First Zagreb index $M_1(G)$, forgotten index $F(G)$, Second Zagreb index $M_2(G)$, redefined third Zagreb index $ReZG_3(G)$ and second modified Zagreb index $mM_2(G)$ and harmonic index $Hr(G)$ [20, 21].

Table *1* shows the formulas and derivation of the above topological indices using the M-Polynomial.

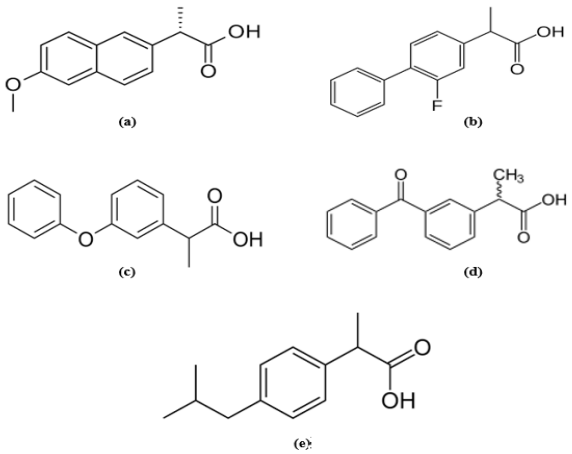

Figure 1: Chemical structure of *(a)* naproxen, *(b)* flurbiprofen, *(c)* fenoprofen, *(d)* ketoprofen and *(e)* ibuprofen.

Table 1: Derivation of Topological indices from M-polynomial.

Topological indices	**Formula**	**Derivation from M-polynomial**
First Zagreb index	$\sum_{ij\in E(G)} (d_i+d_j)$	$(D_x + D_y)f(x,y)\big\vert_{x=y=1}$
Second Zagreb index	$\sum_{ij\in E(G)} (d_i d_j)$	$(D_y D_x)f(x,y)\big\vert_{x=y=1}$
Forgotten index	$\sum_{ij\in E(G)} (d_i^2 + d_j^2)$	$(D_x^2 + D_y^2)f(x,y)\vert_{x=y=1}$
Redefined third Zagreb index	$\sum_{ij\in E(G)} d_i d_j (d_i+d_j)$	$D_x D_y (D_x + D_y)f(x,y)\vert_{x=y=1}$
Second modified Zagreb index	$\sum_{ij\in E(G)} \frac{1}{d_i d_j}$	$S_x S_y f(x,y)\vert_{x=y=1}$
Harmonic index	$\sum_{ij\in E(G)} \frac{2}{d_i + d_j}$	$(2S_x J)f(x,y)\vert_{x=y=1}$

where, $D_x = x\left(\frac{\partial(f(x,y))}{\partial x}\right)$, $D_y = y\left(\frac{\partial(f(x,y))}{\partial y}\right)$, $S_x = \int_0^x \frac{f(t,y)}{t}dt$, $S_y = \int_0^y \frac{f(x,t)}{t}dt$ $J\big(f(x,y)\big) = f(x,x)$.

2. Main Results

In this section, we obtain the expressions for M-polynomials of molecular graphs of naproxen, flurbiprofen, fenoprofen, ketoprofen, and ibuprofen using combinatorial computation, degree counting method based on vertices and edge partition technique.

The molecular graph of naproxen having vertices $V(N) = 17$ and edges$E(N) = 18$.

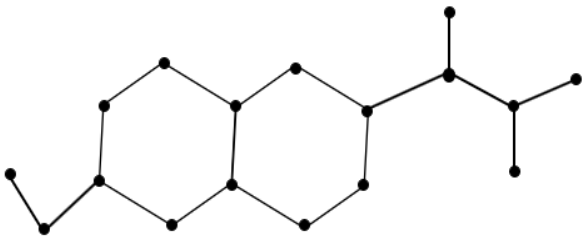

Figure *2* shows the molecular graph of naproxen and graphically representation of naproxen depicted in Figure *3*.

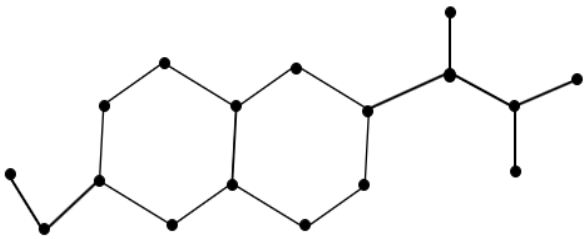

Figure 2: Molecular graph of naproxen.

2.1. Theorem. Let N be the graph of naproxen. Then M-polynomial of N is $M(N;x,y) = xy^2 + 3xy^3 + 2x^2y^2 + 9x^2y^3 + 3x^3y^3$.

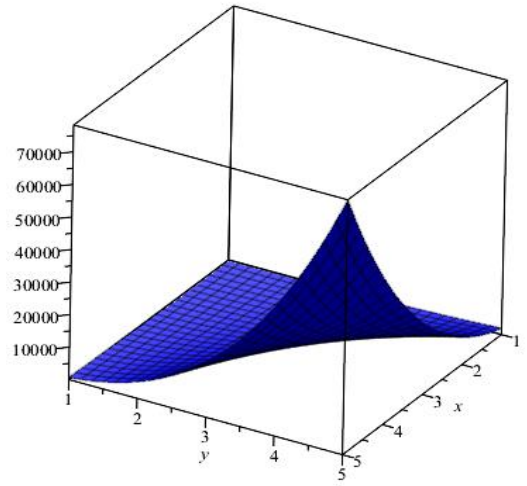

Figure 3: M-polynomial of naproxen.

Proof: Consider the graph of naproxen (N) as depicted in

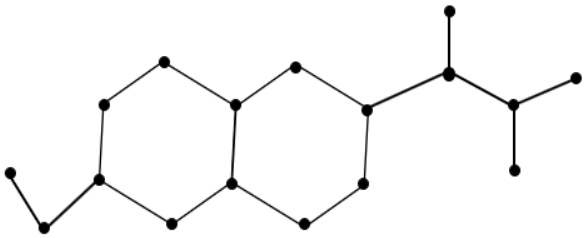

Figure *2*. In N there are five types of edges $E_{(d_i,d_j)}$ where ij is an edge. The first edge separation $E_{1,2}$ contains 1 edge, second edge separation $E_{1,3}$ contains 3 edges, third edge separation $E_{2,2}$ contains 2 edges, fourth edge separation $E_{2,3}$ contains 9 edges and fifth edge separation $E_{3,3}$ contains 3 edges.

$$M(N;x,y) = \sum_{s\leq t} m_{st}(N)x^s y^t.$$

$$M(N;x,y) = \sum_{1\leq 2} m_{12}(N)x^1y^2 + \sum_{1\leq 3} m_{13}(N)x^1y^3 + \sum_{2\leq 2} m_{22}(N)x^2y^2 + \sum_{2\leq 3} m_{23}(N)x^2y^3 + \sum_{3\leq 3} m_{33}(N)x^3y^3.$$

$$= |E_{12}|xy^2 + |E_{13}|xy^3 + |E_{22}|x^2y^2 + |E_{23}|x^2y^3 + |E_{33}|x^3y^3.$$

$$= xy^2 + 3xy^3 + 2x^2y^2 + 9x^2y^3 + 3x^3y^3.$$

Now, by using Theorem 2.1 and Table *1*, we calculate topological indices of the naproxen in proposition 2.1.1.

2.1.1. Proposition: Let N be the graph of naproxen. Then

$$M_1(N) = 86.$$
$$M_2(N) = 100.$$
$$F(N) = 222.$$
$$ReZG_3(N) = 506.$$
$$mM_2(N) = 3.8333$$
$$Hr(N) = 7.7666$$

Proof:

$$M(N;x,y) = f(x,y) = xy^2 + 3xy^3 + 2x^2y^2 + 9x^2y^3 + 3x^3y^3.$$
$$D_x f(x,y) = xy^2 + 3xy^3 + 4x^2y^2 + 18x^2y^3 + 9x^3y^3.$$
$$D_y f(x,y) = 2xy^2 + 9xy^3 + 4x^2y^2 + 27x^2y^3 + 9x^3y^3.$$
$$(D_x + D_y)f(x,y) = 3xy^2 + 12xy^3 + 8x^2y^2 + 45x^2y^3 + 18x^3y^3.$$
$$M_1(N) = (D_x + D_y)f(x,y)\big|_{x=y=1} = 86$$
$$D_y D_x(f(x,y)) = 2xy^2 + 9xy^3 + 8x^2y^2 + 54x^2y^3 + 27x^3y^3.$$
$$M_2(N) = D_y D_x f(x,y)\big|_{x=y=1} = 100$$
$$(D_x^2 + D_y^2)(f(x,y)) = 5xy^2 + 30xy^3 + 16x^2y^2 + 117x^2y^3 + 54x^3y^3.$$
$$F(N) = (D_x^2 + D_y^2)f(x,y)\big|_{x=y=1} = 222$$
$$D_x D_y(D_x + D_y)f(x,y) = 6xy^2 + 36xy^3 + 32x^2y^2 + 270x^2y^3 + 162x^3y^3.$$
$$ReZG_3(N) = D_x D_y(D_x + D_y)f(x,y)\big|_{x=y=1} = 506$$
$$S_x S_y(f(x,y)) = x\frac{y^2}{2} + 3x\frac{y^3}{3} + 2\frac{x^2}{2}\frac{y^2}{2} + 9\frac{x^2}{2}\frac{y^3}{3} + 3\frac{x^3}{3}\frac{y^3}{3}.$$
$$mM_2(N) = S_x S_y f(x,y)\big|_{x=y=1} = 3.8333$$
$$S_x J(f(x,y)) = \frac{x^3}{3} + 5\frac{x^4}{4} + 9\frac{x^5}{5} + 3\frac{x^6}{6}.$$
$$Hr(N) = 2S_x Jf(x,y)|_{x=y=1} = 7.7666$$

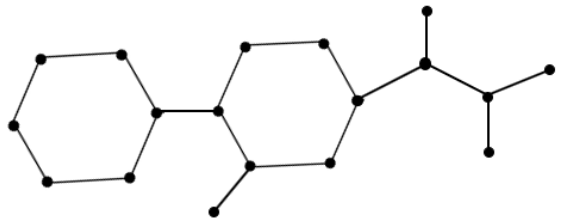

Figure 4: Molecular graph of flurbiprofen.

The molecular graph of flurbiprofen having vertices $V(Fb) = 18$ and edges $E(Fb) = 19$. Figure 4 shows the molecular graph of flurbiprofen and graphically representation of flurbiprofen depicted in Figure 5.

2.2. Theorem

Let Fb be the graph of Flurbiprofen. Then M-polynomial of Fb is

$$M(Fb; x, y) = 4xy^3 + 5x^2y^2 + 6x^2y^3 + 4x^3y^3.$$

Proof: Consider the molecular structure of flurbiprofen (Fb) as shown in Figure 4. In Fb there are four types of edges $E_{(d_i,d_j)}$ where ij is an edge. The first edge separation $E_{1,3}$ contains 4 edges, second edge separation $E_{2,2}$ contains 5 edges, third edge separation $E_{2,3}$ contains 6 edges and fourth edge separation $E_{3,3}$ contains 4 edges.

$$M(Fb; x, y) = \sum_{s \le t} m_{st}(Fb) x^s y^t.$$

$$M(Fb; x, y) = \sum_{1 \le 3} m_{13}(Fb) x^1 y^3 + \sum_{2 \le 2} m_{22}(Fb) x^2 y^2 + \sum_{2 \le 3} m_{23}(Fb) x^2 y^3 + \sum_{3 \le 3} m_{33}(Fb) x^3 y^3.$$

$$= |E_{1,3}| xy^3 + |E_{2,2}| x^2 y^2 + |E_{2,3}| x^2 y^3 + |E_{3,3}| x^3 y^3.$$

$$= 4xy^3 + 5x^2y^2 + 6x^2y^3 + 4x^3y^3.$$

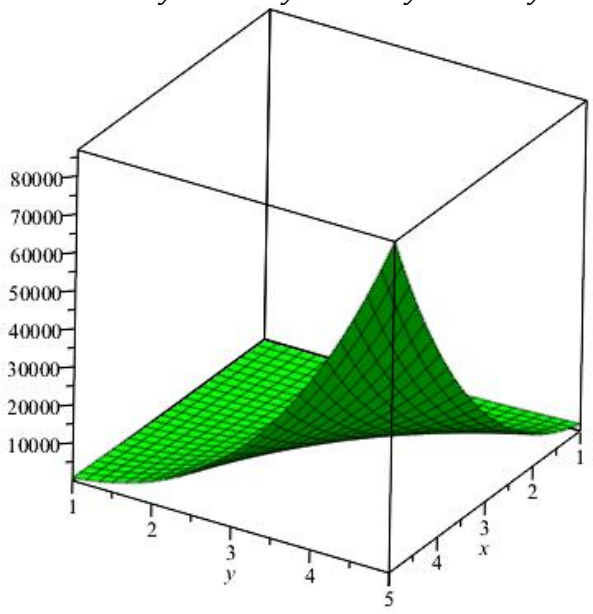

Figure 5: M-polynomial of flurbiprofen.

Now, by using Theorem 2.2 and Table 1, we calculate topological indices of the flurbiprofen in proposition 2.2.1.

2.2.1. Proposition: Let Fb be the graph of Flurbiprofen. Then

$$M_1(Fb) = 90.$$
$$M_2(Fb) = 104.$$
$$F(Fb) = 230.$$
$$ReZG_3(Fb) = 524.$$
$$mM_2(Fb) = 4.0278$$

$$Hr(Fb) = 8.2334$$

Proof:

$$M(Fb; x, y) = f(x, y) = 4xy^3 + 5x^2y^2 + 6x^2y^3 + 4x^3y^3.$$
$$D_x f(x, y) = 4xy^3 + 10x^2y^2 + 12x^2y^3 + 12x^3y^3$$
$$D_y f(x, y) = 12xy^3 + 10x^2y^2 + 18x^2y^3 + 12x^3y^3.$$
$$(D_x + D_y) f(x, y) = 16xy^3 + 20x^2y^2 + 30x^2y^3 + 24x^3y^3.$$
$$M_1(Fb) = (D_x + D_y) f(x, y)\big|_{x=y=1} = 90$$
$$D_y D_x(f(x, y)) = 12xy^3 + 20x^2y^2 + 36x^2y^3 + 36x^3y^3.$$
$$M_2(Fb) = (D_y D_x) f(x, y)\big|_{x=y=1} = 104$$
$$(D_x^2 + D_y^2)(f(x, y)) = 40xy^3 + 40x^2y^2 + 78x^2y^3 + 72x^3y^3.$$
$$F(Fb) = (D_x^2 + D_y^2) f(x, y)\big|_{x=y=1} = 230$$
$$D_x D_y (D_x + D_y) f(x, y) = 48xy^3 + 80x^2y^2 + 180x^2y^3 + 216x^3y^3.$$
$$ReZG_3(Fb) = D_x D_y (D_x + D_y) f(x, y)\big|_{x=y=1} = 524.$$
$$S_x S_y(f(x, y)) = 4x\frac{y^3}{3} + 5\frac{x^2}{2}\frac{y^2}{2} + 6\frac{x^2}{2}\frac{y^3}{3} + 4\frac{x^3}{3}\frac{y^3}{3}.$$
$$mM_2(Fb) = S_x S_y f(x, y)\big|_{x=y=1} = 4.0278$$
$$S_x J(f(x, y)) = 9\frac{x^4}{4} + 6\frac{x^5}{5} + 4\frac{x^6}{6}.$$
$$Hr(Fb) = 2S_x J f(x, y)|_{x=y=1} = 8.2334$$

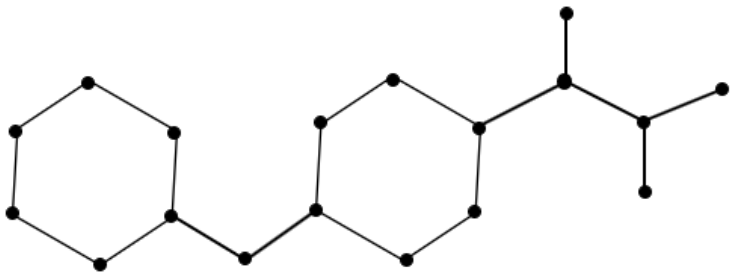

Figure 6: Molecular graph of fenoprofen.

The molecular graph of fenoprofen having vertices $V(H) = 18$ and edges $E(H) = 19$. Figure 6 shows the molecular graph of fenoprofen and graphically representation of fenoprofen depicted in Figure 7.

2.3. Theorem

Let H be the graph of fenoprofen. Then M-polynomial of H is

$$M(H; x, y) = 3xy^3 + 6x^2y^2 + 8x^2y^3 + 2x^3y^3.$$

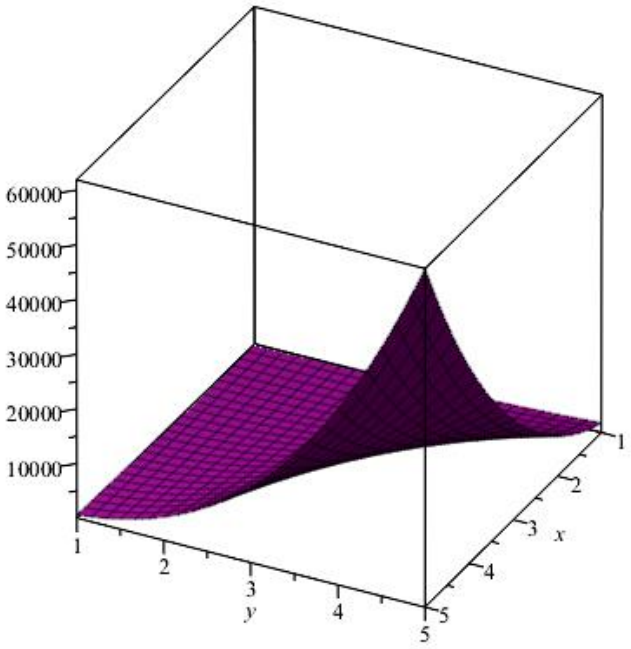

Figure 7: M-polynomial of fenoprofen.

Proof: Consider the molecular structure of fenoprofen (H) as shown in Figure 6. In H there are four types of edges $E_{(d_i,d_j)}$ where ij is an edge. The first edge separation $E_{1,3}$ contains 3 edges, second edge separation $E_{2,2}$ contains 6 edges, third edge separation $E_{2,3}$ contains 8 edges and fourth edge separation $E_{3,3}$ contains 2 edges.

$$M(H;x,y) = \sum_{s\leq t} m_{st}(H)x^s y^t.$$

$$M(H;x,y) = \sum_{1\leq 3} m_{13}(H)x^1y^3 + \sum_{2\leq 2} m_{22}(H)x^2y^2 + \sum_{2\leq 3} m_{23}(H)x^2y^3 + \sum_{3\leq 3} m_{33}(H)x^3y^3.$$

$$= |E_{1,3}|xy^3 + |E_{2,2}|x^2y^2 + |E_{2,3}|x^2y^3 + |E_{3,3}|x^3y^3.$$

$$= 3xy^3 + 6x^2y^2 + 8x^2y^3 + 2x^3y^3.$$

Now, by using Theorem 2.3 and Table 1, we calculate topological indices of the fenoprofen in proposition 2.3.1.

2.3.1. Proposition: Let H be the graph of fenoprofen. Then

$$M_1(H) = 100.$$
$$M_2(H) = 99.$$
$$F(H) = 218.$$
$$ReZG_3(H) = 480.$$
$$mM_2(H) = 4.0556$$
$$Hr(H) = 8.3666$$

Proof:

$$M(H;x,y) = f(x,y) = 3xy^3 + 6x^2y^2 + 8x^2y^3 + 2x^3y^3.$$
$$D_x f(x,y) = 3xy^3 + 12x^2y^2 + 16x^2y^3 + 6x^3y^3.$$
$$D_y f(x,y) = 9xy^3 + 12x^2y^2 + 24x^2y^3 + 6x^3y^3.$$
$$(D_x + D_y)f(x,y) = 12xy^3 + 24x^2y^2 + 40x^2y^3 + 12x^3y^3.$$
$$M_1(H) = (D_x + D_y)f(x,y)\big|_{x=y=1} = 88$$
$$D_y D_x\big(f(x,y)\big) = 9xy^3 + 24x^2y^2 + 48x^2y^3 + 18x^3y^3.$$
$$M_2(H) = D_y D_x f(x,y)\big|_{x=y=1} = 99$$
$$(D_x^2 + D_y^2)\big(f(x,y)\big) = 30xy^3 + 48x^2y^2 + 104x^2y^3 + 36x^3y^3.$$

$$F(H) = \left(D_x^2 + D_y^2\right) f(x,y)\big|_{x=y=1} = 218$$
$$D_x D_y\left(D_x + D_y\right) f(x,y) = 36xy^3 + 96x^2y^2 + 240x^2y^3 + 108x^3y^3.$$
$$ReZG_3(H) = D_x D_y\left(D_x + D_y\right) f(x,y)\big|_{x=y=1} = 480.$$
$$S_x S_y\left(f(x,y)\right) = 3x\frac{y^3}{3} + 6\frac{x^2}{2}\frac{y^2}{2} + 8\frac{x^2}{2}\frac{y^3}{3} + 2\frac{x^3}{3}\frac{y^3}{3}.$$
$$mM_2(H) = S_x S_y f(x,y)\big|_{x=y=1} = 4.0556$$
$$S_x J\left(f(x,y)\right) = 9\frac{x^4}{4} + 8\frac{x^5}{5} + 2\frac{x^6}{6}.$$
$$Hr(H) = 2S_x Jf(x,y)|_{x=y=1} = 8.3666$$

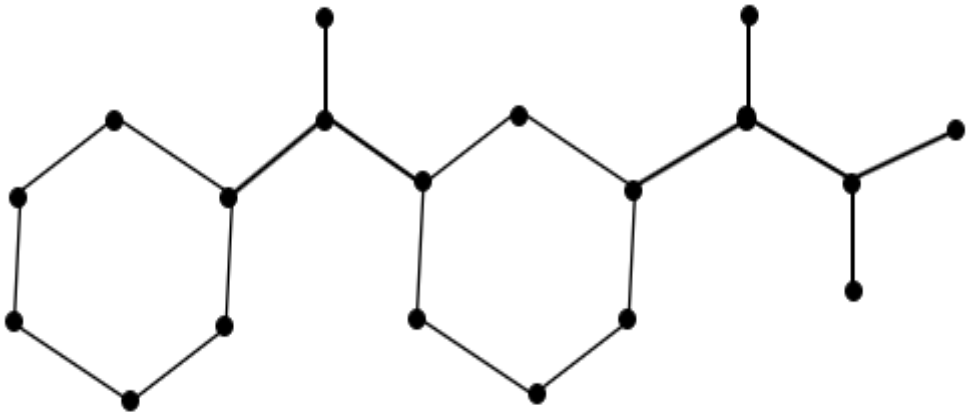

Figure 8: Molecular graph of ketoprofen.

The molecular graph of ketoprofen having vertices $V(K) = 19$ and edges $E(K) = 20$. Figure 8 shows the molecular graph of ketoprofen and graphically representation of ketoprofen depicted in Figure 9.

2.4. **Theorem.** Let K be the graph of ketoprofen. Then M-polynomial of K is
$$M(K;x,y) = 4xy^3 + 6x^2y^2 + 6x^2y^3 + 4x^3y^3.$$

Proof: Consider the molecular structure of ketoprofen (K) as shown in Figure 8. In K there are four types of edges $E_{(d_i,d_j)}$ where $ij$is an edge. The first edge separation $E_{1,3}$ contains 4 edges, second edge separation $E_{2,2}$ contains 6 edges, third edge separation $E_{2,3}$ contains 6 edges and fourth edge separation $E_{3,3}$ contains 4 edges.

$$M(K;x,y) = \sum_{s\le t} m_{st}(K)x^s y^t.$$
$$M(K;x,y) = \sum_{1\le 3} m_{13}(K)x^1y^3 + \sum_{2\le 2} m_{22}(K)x^2y^2 + \sum_{2\le 3} m_{23}(K)x^2y^3 + \sum_{3\le 3} m_{33}(K)x^3y^3.$$
$$= |E_{13}|xy^3 + |E_{22}|x^2y^2 + |E_{23}|x^2y^3 + |E_{33}|x^3y^3.$$
$$= 4xy^3 + 6x^2y^2 + 6x^2y^3 + 4x^3y^3.$$

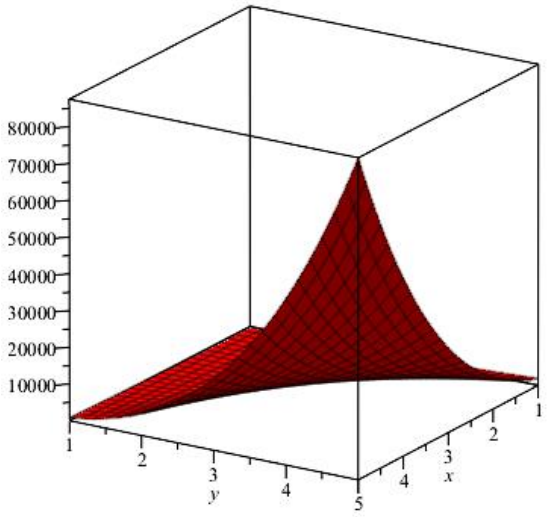

Figure 9: M-polynomial of ketoprofen.

Now, by using Theorem 2.4 and we calculate topological indices of the ketoprofen in proposition 2.4.1.

2.4.1. Proposition: Let K be the graph of ketoprofen. Then

$$M_1(K) = 94.$$
$$M_2(K) = 108.$$
$$F(K) = 238.$$
$$ReZG_3(K) = 540.$$
$$mM_2(K) = 4.2778$$
$$Hr(K) = 8.7334$$

Proof:

$$M(K; x, y) = f(x, y) = 4xy^3 + 6x^2y^2 + 6x^2y^3 + 4x^3y^3.$$
$$D_x f(x, y) = 4xy^3 + 12x^2y^2 + 12x^2y^3 + 12x^3y^3.$$
$$D_y f(x, y) = 12xy^3 + 12x^2y^2 + 18x^2y^3 + 12x^3y^3.$$
$$(D_x + D_y) f(x, y) = 16xy^3 + 24x^2y^2 + 30x^2y^3 + 24x^3y^3.$$
$$M_1(K) = (D_x + D_y) f(x, y)\big|_{x=y=1} = 94$$
$$D_y D_x\big(f(x, y)\big) = 12xy^3 + 24x^2y^2 + 36x^2y^3 + 36x^3y^3.$$
$$M_2(K) = D_y D_x f(x, y)\big|_{x=y=1} = 108$$
$$\big(D_x^2 + D_y^2\big)\big(f(x, y)\big) = 40xy^3 + 48x^2y^2 + 78x^2y^3 + 72x^3y^3.$$
$$F(K) = \big(D_x^2 + D_y^2\big) f(x, y)\big|_{x=y=1} = 238$$
$$D_x D_y\big(D_x + D_y\big) f(x, y) = 48xy^3 + 96x^2y^2 + 180x^2y^3 + 216x^3y^3.$$
$$ReZG_3(K) = D_x D_y\big(D_x + D_y\big) f(x, y)\big|_{x=y=1} = 540.$$
$$S_x S_y\big(f(x, y)\big) = 4x\frac{y^3}{3} + 6\frac{x^2}{2}\frac{y^2}{2} + 6\frac{x^2}{2}\frac{y^3}{3} + 4\frac{x^3}{3}\frac{y^3}{3}.$$
$$mM_2(K) = S_x S_y f(x, y)\big|_{x=y=1} = 4.2778$$
$$S_x J\big(f(x, y)\big) = 10\frac{x^4}{4} + 6\frac{x^5}{5} + 4\frac{x^6}{6}.$$
$$Hr(K) = 2S_x J f(x, y)|_{x=y=1} = 8.7334$$

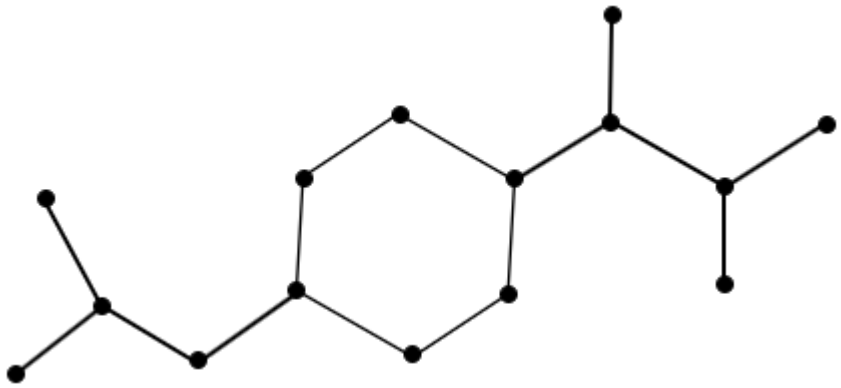

Figure 10: Molecular graph of ibuprofen.

The molecular graph of ibuprofen having vertices $V(P) = 15$ and edges $E(P) = 15$. Figure 10 shows the molecular graph of ibuprofen and graphically representation of ibuprofen depicted in **Error! Reference source not found.**

2.5. Theorem

Let P be the graph of ibuprofen. Then M-polynomial of P is

$$M(P; x, y) = 5xy^3 + 2x^2y^2 + 6x^2y^3 + 2x^3y^3.$$

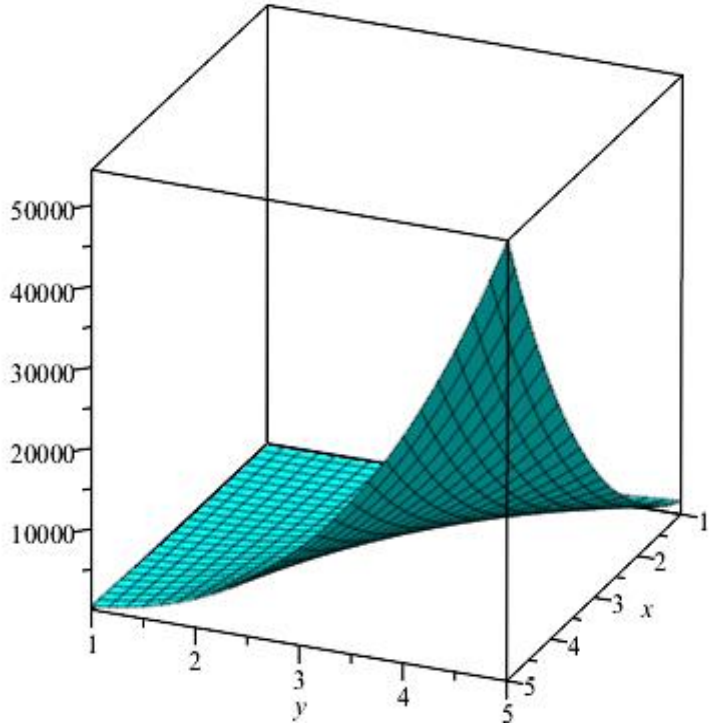

Figure 11: M-polynomial of ibuprofen.

Proof: Consider the molecular structure of ibuprofen (P) as shown in Figure 10. In P there are four types of edges $E_{(d_i,d_j)}$ where ij is an edge. The first edge separation $E_{1,3}$ contains 5 edges, second edge separation $E_{2,2}$ contains 2 edges, third edge separation $E_{2,3}$ contains 6 edges and fourth edge separation $E_{3,3}$ contains 2 edges.

$$M(P; x, y) = \sum_{s \le t} m_{st}(P) x^s y^t.$$

$$M(P; x, y) = \sum_{1 \le 3} m_{13}(P) x^1 y^3 + \sum_{2 \le 2} m_{22}(P) x^2 y^2 + \sum_{2 \le 3} m_{23}(P) x^2 y^3 + \sum_{3 \le 3} m_{33}(P) x^3 y^3.$$

$$= |E_{13}|xy^3 + |E_{22}|x^2y^2 + |E_{23}|x^2y^3 + |E_{33}|x^3y^3.$$
$$= 5xy^3 + 2x^2y^2 + 6x^2y^3 + 2x^3y^3.$$

Now, by using Theorem 2.5 and, we calculate topological indices of the ibuprofen in proposition 2.5.1.

2.5.1. Proposition: Let P be the graph of ibuprofen. Then

$$M_1(P) = 70.$$
$$M_2(P) = 77.$$
$$F(P) = 180.$$
$$ReZG_3(P) = 380.$$
$$mM_2(P) = 3.3892$$
$$Hr(P) = 6.5666$$

Proof:

$$M(P; x, y) = f(x,y) = 5xy^3 + 2x^2y^2 + 6x^2y^3 + 2x^3y^3.$$
$$D_x f(x,y) = 5xy^3 + 4x^2y^2 + 12x^2y^3 + 6x^3y^3.$$
$$D_y f(x,y) = 15xy^3 + 4x^2y^2 + 18x^2y^3 + 6x^3y^3.$$
$$(D_x + D_y)f(x,y) = 20xy^3 + 8x^2y^2 + 30x^2y^3 + 12x^3y^3.$$
$$M_1(P) = (D_x + D_y)f(x,y)\big|_{x=y=1} = 70$$
$$D_y D_x(f(x,y)) = 15xy^3 + 8x^2y^2 + 36x^2y^3 + 18x^3y^3.$$
$$M_2(P) = D_y D_x f(x,y)\big|_{x=y=1} = 77$$
$$(D_x^2 + D_y^2)(f(x,y)) = 50xy^3 + 16x^2y^2 + 78x^2y^3 + 36x^3y^3.$$
$$F(P) = (D_x^2 + D_y^2)f(x,y)\big|_{x=y=1} = 180$$
$$D_x D_y(D_x + D_y)f(x,y) = 60xy^3 + 32x^2y^2 + 180x^2y^3 + 108x^3y^3.$$
$$ReZG_3(P) = D_x D_y(D_x + D_y)f(x,y)\big|_{x=y=1} = 380.$$
$$S_x S_y(f(x,y)) = 5x\frac{y^3}{3} + 2\frac{x^2}{2}\frac{y^2}{2} + 6\frac{x^2}{2}\frac{y^3}{3} + 2\frac{x^3}{3}\frac{y^3}{3}.$$
$$mM_2(P) = S_x S_y f(x,y)\big|_{x=y=1} = 3.3892$$
$$S_x J(f(x,y)) = 7\frac{x^4}{4} + 6\frac{x^5}{5} + 2\frac{x^6}{6}.$$
$$Hr(P) = 2S_x Jf(x,y)|_{x=y=1} = 6.5666$$

3. Degree-based topological indices and ($QSPR/QSAR$)

The major goal of this section is to create quantitative structure–property/activity relationship ($QSPR/QSAR$) among numerous topological indices and explore several physicochemical properties/activities of drugs such as naproxen, flurbiprofen, fenoprofen, ketoprofen, and ibuprofen in order to determine the effectiveness of the understudy topological indices, the numerical values of understudy topological indices present in Table 2. There are six physicochemical properties investigated such as boiling point (Bp), melting point (Mp), topological polar surface area (TSA), Complexity (C) and molecular weight (Mw). present the values of above-mentioned physicochemical properties of various drugs used for the headache pain relief. These values were attained from PubChem. The values of correlation coefficient (r) of defined degree based topological indices and the physicochemical properties are present in

Table *4*. In the

Table *4* it can be easily observed that modified second Zegreb index (mM_2) shows strong positive correlation that is ($r = 0.996$) with molecular weight (Mw) while, for complexity

(C) forgotten index shows good correlation and for other properties no topological index shows good relation. Graphically representation of correlation among (mM_2) and (Mw) depicted in Figure 12 while, the intercorrelation of computed topological indices shown in Table 5.

Table 2: Numerical values of indices with various headache pain relief drugs.

Drugs	M_1	M_2	F	$ReZG_3$	mM_2	Hr
Naproxen	86	100	222	506	3.8333	7.7666
Flurbiprofen	90	104	230	524	4.0278	8.2334
Fenoprofen	88	99	218	480	4.0556	8.3666
Ketoprofen	94	*108*	*238*	*540*	*4.2778*	*8.7334*
Ibuprofen	*70*	*77*	*180*	*380*	*3.3892*	*6.5666*

Table 3: Headache pain relief drugs with its physicochemical properties.

Drugs	Bp	Mp	TSA	C	Mw
Naproxen	403.9	153	46.5	277	230.26
Flurbiprofen	376.2	111	37.3	286	244.26
Fenoprofen	169	–	46.5	271	242.27
Ketoprofen	431.3	94.7	54.4	331	254.28
Ibuprofen	157	76	37.3	203	206.28

Table 4: Correlation between defined physicochemical properties of headache pain relief drugs and topological indices.

Indices	Bp	Mp	TSA	C	Mw
M_1	0.287316	0.405679	0.593978	0.770137	0.897395
M_2	0.756420	0.474469	0.609637	0.963422	0.957525
F	0.787664	0.458725	0.606447	0.970509	0.952447
$ReZG_3$	0.829147	0.512388	0.573941	0.956872	0.921828
mM_2	0.585431	0.236604	0.690283	0.954815	0.996528
Hr	0.557048	0.293325	0.664299	0.936705	0.993798

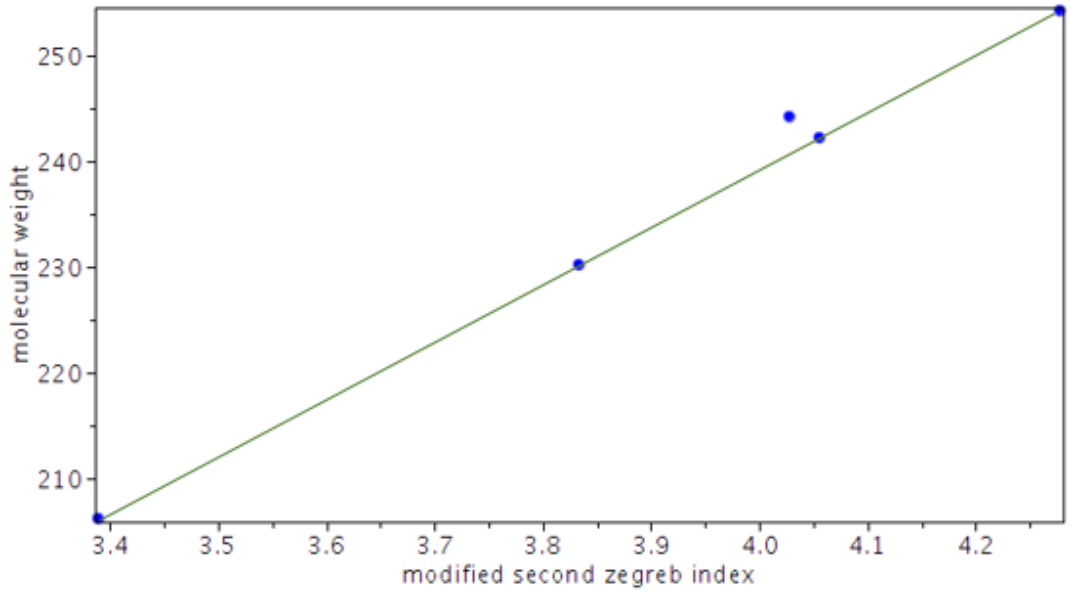

Figure 12: Graph of correlation among modified second Zegreb index and molecular weight.

Table 5: Intercorrelation of the computed topological indices.

Indices	M_1	M_2	F	$ReZG_3$	mM_2	Hr
M_1	1					
M_2	0.8395	1				
F	0.8096	0.9983	1			
$ReZG_3$	0.7664	0.9919	0.9959	1		
mM_2	0.9064	0.9506	0.9443	0.9109	1	
Hr	0.9362	0.9545	0.9440	0.9112	0.9959	1

4. Conclusion

In developing countries, topological indices are introduced to test the medicinal characteristics of drugs. In this study, using drug's structural analysis we compute the several degree-based topological indices such as First Zagreb index $M_1(G)$, Second Zagreb index $M_2(G)$, forgotten index $F(G)$, redefined third Zagreb index $ReZG_3(G)$ and second modified Zagreb index $mM_2(G)$ and harmonic index $Hr(G)$ with the help of M-polynomial for the above defined drugs. Furthermore, we computed intercorrelation of defined topological indices and correlation among these indices and drugs used for headache pain relief. Theoretical findings produced in this article have positive implications for developing novel drug to relieve headache pain.

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