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Deriving M-polynomial Based Topological Descriptors of Oral Antiviral Clinical Drug Nirmatrelvir

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Abstract

The novel human coronavirus known as SARS-CoV-2 poses a serious risk to human health. Regretfully, the US Food and Drug Administration (FDA) has approved very few oral antiviral medications for the treatment of COVID-19 patients. In the current study, we have explored the topological characterization of the orally bio-available SARS M^{pro} inhibitor nirmatrelvir which in combination with ritonavir (under the brand name Paxlovid) is recently approved for emergency use authorization by FDA. Topological indices are a useful tool in chemical graph theory to determine the diverse pharmaceutical, biological and physico-chemical properties of a molecule. In this study, we ascertain several well-known degree-dependent topological indices for the medication nirmatrelvir directly using their common definitions in mathematics and alternatively by utilising M-polynomial after deriving M-polynomial of nirmatrelvir. In addition, we plot the obtained topological indices and the M-polynomial to comprehend the geometric behaviour of them. The outcomes can aid in the investigation of the physical characteristics of the recently created medications utilised to treat COVID-19.

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1 Introduction

Caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome CoronaVirus 2), the Corona Virus Disease 2019 (COVID-19) is a RNA virus that is reported to cause severe pneumonia in serious cases. The catastrophic outbreak of this disease has claimed the life of more than 7 million people globally [51].

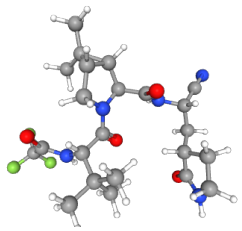
Many strategies have been developed worldwide in unmatched timeline to fight this infectious disease. So far, WHO approved vaccines like COVAXIN®, COVISHIELD™, Moderna: mRNA-1273, Ad26.COV2.S (Janssen COVID-19), BNT162b2 (Tozinameran / Comirnaty) developed by Bharat Biotech International Limited, Oxford University and British-Swedish company AstraZeneca (manufactured by Serum Institute of India Pvt. Limited), Moderna, Johnson & Johnson, Pfizer-BioNTech, respectively, are available as prophylactic measures of COVID-19 [3]. Intravenous therapeutics like remdesivir, sotrovimab, tocilizumab, tixagevimab, etc, were found to be effective to cure the infection brought on by the fatal virus [47]. The need of oral drugs has now become imperative, as it is believed that oral drugs can significantly reduce hospitalization and death. Oral antiviral drugs such as Molnuperavir (RNA dependent RNA polymerase inhibitor), Paxlovid (nirmatrelvir co-packaged with ritonavir) and AT-527 are currently under clinical trials [38, 48].

The current study involves the antiviral medication nirmatrelvir (other familiar names are PF-07321332, UNII-7R9A5P7H32) which is a covalent 3CL protease inhibitor and is developed by Pfizer by modifying Lufotrelvir (PF-07304814) which is another intravenous clinical candidate used for Corona Virus [39]. The SARS-CoV-2 genome encodes four structural proteins and two polyproteins. The polyproteins are cleaved by endopeptidase main protease[5] (M^{pro}) into short non-structural proteins that are important for viral replication. Corona Virus M^{pro} is a cysteine protease having a catalytic dyad of Cys145-His41 in the active site. The presence of Gln residue has been reported to be present in the substrate of M^{pro}. As no human cysteine

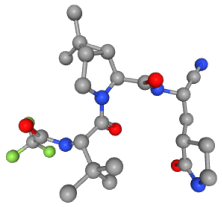
[5]M-pro is also known as 3CL protease.

protease is reported to cleave after Gln, M^{pro} can be used as a potential, selective tractable target for designing drugs against Corona virus. According to the reports, nirmatrelvir inhibits the action of these 3CL proteases, eventually inhibiting the replication of the virus [38].

The molecular formula of nirmatrelvir is $C_{23}H_{32}F_3N_5O_4$. Figures 1(a) and 1(b) depict 3-dimensional images of nirmatrelvir with and without hydrogen, respectively, whereas Figure 2 represents the 2-dimensional chemical structure of nirmatrelvir [37].



(*a*) A 3-D image of nirmatrelvir with hydrogen.



(*b*) A 3-D image of nirmatrelvir without hydrogen.

Figure 1: 3-Dimensional images of Nirmatrelvir / PF-07321332 / Unii-7R9A5P7H32.

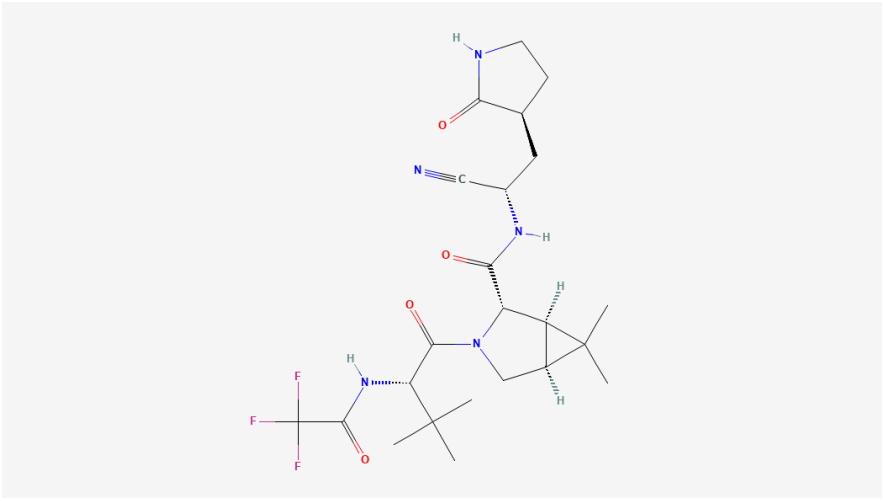


Figure 2: Two-dimensional representations of the chemical structure of nirmatrelvir / PF-07321332 / Unii-7R9A5P7H32.

To comprehend a recently introduced drug's safety profile, effectiveness, and tolerability on the human body, a wide number of research experiments is a common practice. Furthermore, these research experiments essentially require huge time, extensive laboratory experiments, vast financial expenditure and high-tech laboratories, which are exorbitant for economically developing nations. Researchers have shown exceptional interrelations between a large number of chemical molecules' experiments and the chemical graphs that correspond to them to comprehend their pharmaceutical behaviors, biological activities and physico-chemical properties. The above description of the drugs can be substantially predicted in the field of chemical graph theory, which links mathematical chemistry and graph theory, by avoiding the lab experiments [13, 34, 43, 45, 23].

As the topological characterization of nirmatrelvir / PF-07321332 / Unii-7R9A5P7H32 is not investigated so far, our goal is to investigate the different degree-dependent topological indices in order to better understand its related properties and pharmacokinetics. Also, it can open a path to explore further the correlated drugs employed in treating COVID-19 patients.

2 Basics and Survey of Relevant Literature on Topological Indices and M-polynomial

Let $\Lambda = (V, E)$ denotes a connected, simple, unweighted and undirected graph.Its non-empty vertex set and edge set are denoted by $V = V(\Lambda)$ and $E = E(\Lambda)$, respectively. The notation $d(w)$ is used to represent the degree of a vertex $w \in V$. Moreover, we use the notation δ to designate the set $\min\{d(w)|w \in V(\Lambda)\}$, and Δ to designate the set $\max\{d(w)|w \in V(\Lambda)\}$. Usually, a molecular or chemical graph is used to narrate a molecule of a chemical compound. Here, the edges and vertices of the chemical graph are furnished by the atoms and the chemical bonds that connect them, respectively.

A molecular or chemical graph's *topological index* is a real exponent which is a notable and efficient tool during data analysis of the chemical graph and it can reflect different chemical, biological and physical features of that molecular compound. Diverse topological indices are catalogued with reference to several topological behaviors of a chemical molecule. In fact, quantitative structure-activity relationships (QSAR) and quantitative structure-property relationships (QSPR) can actually be found using these individually or combined indices. The researchers are keen to deduce the

topological behavior of the molecular graph by examining the QSPR/QSAR. For detailed discussion, please refer to [13, 34, 43, 45, 23, 31, 32].

Usually, these standard topological indices of the chemical graphs are categorized into counting related topological indices, spectrum-based topological indices, distance-based topological indices, degree-based topological indices, and degree-distance-based topological indices. Degree-based topological indices are important in the fields of theoretical chemistry, biology, and pharmacology. Some of the standard and citable degree-dependent topological indices and their usual mathematical definitions are summarized in Table 1.

Table 1: Degree-dependent topological indices with their associated derivation formulas via M-polynomial of a graph Λ.

Sl. No.	**Topological Index**	**Proposed around**	**Formula of topological indices**	**f(a,b)**	**Derivation formula over** $(M(\Lambda;x,y))$
a.	First Zagreb Index [20]	1972	$M_1(\Lambda)=\sum_{vw\in E(\Lambda)}(d(v)+d(w))$	$a+b$	$(D_x+D_y)(M(\Lambda;x,y))\|_{x=y=1}$
b.	Second Zagreb Index [20]	1972	$M_2(\Lambda)=\sum_{vw\in E(\Lambda)}(d(v)d(w))$	ab	$(D_xD_y)(M(\Lambda;x,y))\|_{x=y=1}$
c.	Modified Second Zagreb Index [33]	2004	${}^mM_2(\Lambda)=\sum_{vw\in E(\Lambda)}\frac{1}{d(v)d(w)}$	$\frac{1}{ab}$	$(S_xS_y)(M(\Lambda;x,y))\|_{x=y=1}$
d.	General Randić Index [42, 2, 1]	1975, 1998	$R_\alpha(\Lambda)=\sum_{vw\in E(\Lambda)}(d(v)d(w))^\alpha$	$(ab)^\alpha$	$(D_x^\alpha D_y^\alpha)(M(\Lambda;x,y))\|_{x=y=1}$
e.	Inverse Randić Index [42, 2, 1]	1975, 1998	$RR_\alpha(\Lambda)=\sum_{vw\in E(\Lambda)}\frac{1}{(d(v)d(w))^\alpha}$	$\frac{1}{(ab)^\alpha}$	$(S_x^\alpha S_y^\alpha)(M(\Lambda;x,y))\|_{x=y=1}$
f.	Symmetric Division (Deg) Index[49]	2010	$SDD(\Lambda)=\sum_{vw\in E(\Lambda)}\left\{\frac{\min(d(v),d(w))}{\max(d(v),d(w))}+\frac{\max(d(v),d(w))}{\min(d(v),d(w))}\right\}$	$\frac{a^2+b^2}{ab}$	$(D_xS_y+D_yS_x)(M(\Lambda;x,y))\|_{x=y=1}$
g.	Harmonic Index [18]	1993	$H(\Lambda)=\sum_{vw\in E(\Lambda)}\frac{2}{d(v)+d(w)}$	$\frac{2}{a+b}$	$2S_xJ(M(\Lambda;x,y))\|_{x=1}$
h.	Inverse Sum (Indeg) Index [46]	2015	$ISI(\Lambda)=\sum_{vw\in E(\Lambda)}\frac{d(v)d(w)}{d(v)+d(w)}$	$\frac{ab}{a+b}$	$S_xJD_xD_y(M(\Lambda;x,y))\|_{x=1}$
i.	Augmented Zagreb Index [19]	2010	$AZ(\Lambda)=\sum_{vw\in E(\Lambda)}\left\{\frac{d(v)d(w)}{d(v)+d(w)-2}\right\}^3$	$(\frac{ab}{a+b-2})^3$	$S_x^3Q_{-2}JD_x^3D_y^3(M(\Lambda;x,y))\|_{x=1}$

where, $D_y(f(x,y))=y\frac{\partial(f(x,y))}{\partial y}$, $D_x(f(x,y))=x\frac{\partial(f(x,y))}{\partial x}$, $S_y(f(x,y))=\int_0^y\frac{f(x,t)}{t}dt$,

$S_x(f(x,y))=\int_0^x\frac{f(t,y)}{t}dt$, $Q_\alpha(f(x,y))=x^\alpha f(x,y),\ \alpha\neq 0$, $J(f(x,y))=f(x,x)$.

As an alternative for computing the indices of a molecular graph structure using their usual mathematical formulas, a number of graphic polynomials [21] were introduced in the literature. The fundamental concept is to determine a closed-form of an algebraic expression of polynomial of the working molecular graph and hence deduce the values of the indices by employing some particular differentiation or integration operations (or a combination of both) over the algebraic expression of the polynomial.

Some of the well-known polynomials are the matching polynomial [17], the M-polynomial [16, 11, 4, 12], the Tutte polynomial [30], the Schultz polynomial [22], the Hosoya polynomial [24], the Clar covering polynomial (usually known as Zhang-Zhang polynomial) [52], etc. Among them, the M-polynomials plays a significant role in finding the degree dependent topological indices. The concept of M-polynomial was proposed in 2015 by Deutsch and Klavžar [16].

Definition 1 ([16]) *The mathematical expression*

$$M(\Lambda; x, y) = \sum_{\delta \le p \le q \le \Delta} m_{p,q}(\Lambda)\ x^p y^q$$

is commonly known as the M-polynomial of a given graph Λ*, where* $m_{p,q}(\Lambda)$ *denotes the number of edges* $vw \in E(\Lambda)$ *having* $d(v) = p \ge 1$ *and* $d(w) = q \ge 1$.

As justified in [15], any degree-based topological index for a graph $\Lambda = (V, E)$ is symbolized by $D(\Lambda)$, and is expressed as

$$D(\Lambda) = \sum_{uv \in E} f(d(u), d(v)),$$

where the function $f(a, b)$ is catalogued in Table 1 and in fact, it can also be re-written as

$$D(\Lambda) = \sum_{p \le q} m_{p,q}(\Lambda) f(p, q).$$

Moreover, Table 1 summarizes all the algebraic relations between the degree-dependent indices and their corresponding derivation formulas over the M-polynomial of a given graph Λ [16].

To find the M-polynomials and the correlated degree-based topological indices for various molecular graph / network structures, extensive research investigations have been conducted. Some of the such well-known molecular graph / network structures are Coronoid systems [27], Silicon-Carbons [5],

Benzenoid systems [28], Molnupiravir [14], polyhex nanotubes [36], Kagome lattice [25], convex polytopes [44], different Hex-derived networks [29, 6, 7, 8, 40, 10, 9, 41], hyaluronic acid-doxorubicin [26], Remdesivir compound [50], Chloroquine, Remdesivir, Hydroxychloroquine and Theaflavin [35], etc.

3 Methodology

In our current study, we have assessed the molecular structure of the oral antiviral medication nirmatrelvir using standard degree-dependent topological indices. Figure 2 shows the drug's two-dimensional chemical graph structure. we consider the hydrogen suppressed chemical graph of the drug nirmatrelvir, because the vertices corresponding to the hydrogen atoms have no effect on the graph isomorphism. See Figure 3. Let us denote the graph shown in Figure 3 by the symbol $N = (V(N), E(N)) = (V(PF\text{-}07321332), E(PF\text{-}07321332))$.

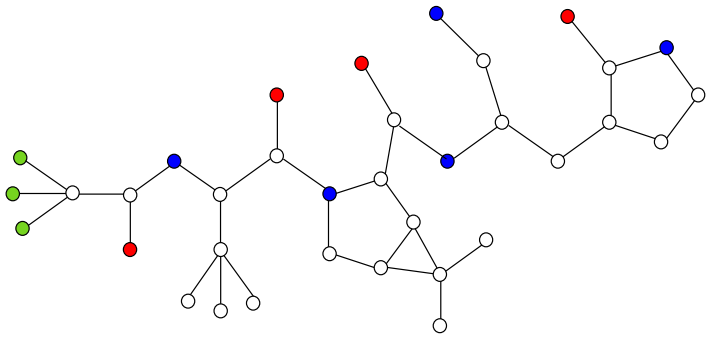


Figure 3: Graphical structure representation of the hydrogen suppressed nirmatrelvir / PF-07321332 / Unii-7R9A5P7H32 with edges and vertices.

To start with, we compute the considered degree-dependent topological indices of the graph N by their respective mathematical formulas stated in Table 1, in Section 4. On the other hand, in Section 5, we obtained a closed-form of an algebraic expression of M-polynomial by partitioning the edge set of the graph N and therefore derived the topological indices by applying the respective mathematical operations (which reported in Table 1) over the M-polynomial. Additionally, in Section 6, we illustrated the obtained M-polynomial and the topological indices (in increasing order) by using Maple-13 software by plotting the surfaces, to view their geometrical nature. In Section 7, we finally come to a conclusion.

4 Definition-based Computation of the Degree-dependent Topological Indices of Nirmatrelvir

We have denoted $N = (V(N), E(N)) = (V(PF\text{-}07321332), E(PF\text{-}07321332))$ to represent the molecular graph of nirmatrelvir / PF-07321332 which is depicted in Figure 3, It follows from Figure 3 that the cardinality of the vertex set $V(N)$ is given by $|V(N)| = 35$ and the cardinality of the edge set $E(N)$ is given by $|E(N)| = 37$. In addition, the minimum degree and maximum degree of a vertex of N are given by $\delta = 1$ and $\Delta = 4$, respectively. Let us now partition $V(N)$ of N into four disjoint sets, on the basis of degree of the vertices, as

$$\begin{aligned} V_1(N) &= \{z \in V(N) : d(z) = 1\}, \\ V_2(N) &= \{z \in V(N) : d(z) = 2\}, \\ V_3(N) &= \{z \in V(N) : d(z) = 3\}, \\ \text{and } V_4(N) &= \{z \in V(N) : d(z) = 4\}, \end{aligned}$$

and their cardinalities are given by $|V_1(N)| = 13,\ |V_2(N)| = 8,\ |V_3(N)| = 11$ and $|V_4(N)| = 3$. Moreover, let us partition $E(N)$ of N into seven disjoint distinct sets based on the degree of the end vertices of all the edges and distinguish them as

$$E_{\{r,s\}} = \{e = v_1v_2 \in E(N) : d(v_1) = r,\ d(v_2) = s\},$$

where $\{r, s\} = \{1, 2\}, \{1, 3\}, \{1, 4\}, \{2, 2\}, \{2, 3\}, \{3, 3\}$ and $\{3, 4\}$, and the cardinalities of them are given by $|E_{\{1,2\}}| = 1,\ |E_{\{1,3\}}| = 4,\ |E_{\{1,4\}}| = 8,$ $|E_{\{2,2\}}| = 2,\ |E_{\{2,3\}}| = 11,\ |E_{\{3,3\}}| = 7$ and $|E_{\{3,4\}}| = 4$.

Let us now compute the degree-dependent topological indices of our considered molecular graph of nirmatrelvir, by their respective mathematical formulas listed in Table 1.

Theorem 2 *Let $N = (V(N), E(N)) = (V(PF\text{-}07321332), E(PF\text{-}07321332))$ be the molecular graph of nirmatrelvir. Then*

(i) $M_1(N) = 192$,

(ii) $M_2(N) = 231$,

(iii) ${}^{m}M_2(N) = \frac{131}{18}$,

(iv) $R_\alpha(N) = 2^\alpha + 4 \times 3^\alpha + 8 \times 4^\alpha + 2 \times 4^\alpha + 11 \times 6^\alpha + 7 \times 9^\alpha + 4 \times 12^\alpha$,

(v) $RR_\alpha(N) = \frac{1}{2^\alpha} + \frac{4}{3^\alpha} + \frac{8}{4^\alpha} + \frac{2}{4^\alpha} + \frac{11}{6^\alpha} + \frac{7}{9^\alpha} + \frac{4}{12^\alpha}$,

(vi) $SDD(N) = 100$,

(vii) $H(N) = \frac{516}{35}$,

(viii) $ISI(N) = \frac{8951}{210}$,

(ix) $AZ(N) = \frac{60370561}{216000}$.

Proof: By using the mathematical definition of the topological indices, their values for graph N are calculated underneath.

(i) **First Zagreb Index:**

$$\begin{aligned} M_1(N) &= \sum_{vw \in E(N)} (d(v) + d(w)) \\ &= 1(1+2) + 4(1+3) + 8(1+4) + 2(2+2) + 11(2+3) \\ &\quad + 7(3+3) + 4(3+4) \\ &= 192. \end{aligned}$$

(ii) **Second Zagreb Index:**

$$\begin{aligned} M_2(N) &= \sum_{vw \in E(N)} (d(v)d(w)) \\ &= 1(1\times 2) + 4(1\times 3) + 8(1\times 4) + 2(2\times 2) + 11(2\times 3) \\ &\quad + 7(3\times 3) + 4(3\times 4) \\ &= 231. \end{aligned}$$

(iii) **Modified Second Zagreb Index:**

$$\begin{aligned} {}^m M_2(N) &= \sum_{vw \in E(N)} \frac{1}{d(v)d(w)} \\ &= \frac{1}{1\times 2} + \frac{4}{1\times 3} + \frac{8}{1\times 4} + \frac{2}{2\times 2} + \frac{11}{2\times 3} + \frac{7}{3\times 3} + \frac{4}{3\times 4} \\ &= \frac{131}{18} \approx 7.2777777. \end{aligned}$$

(iv) **General Randić Index:**

$$\begin{aligned} R_\alpha(N) &= \sum_{vw\in E(N)} (d(v)d(w))^\alpha \\ &= 1(1\times 2)^\alpha + 4(1\times 3)^\alpha + 8(1\times 4)^\alpha + 2(2\times 2)^\alpha + 11(2\times 3)^\alpha \\ &\quad + 7(3\times 3)^\alpha + 4(3\times 4)^\alpha \\ &= 2^\alpha + 4\times 3^\alpha + 8\times 4^\alpha + 2\times 4^\alpha + 11\times 6^\alpha + 7\times 9^\alpha + 4\times 12^\alpha. \end{aligned}$$

(v) **Inverse Randić Index:**

$$\begin{aligned} RR_\alpha(N) &= \sum_{vw\in E(N)} \frac{1}{(d(v)d(w))^\alpha} \\ &= \frac{1}{(1\times 2)^\alpha} + \frac{4}{(1\times 3)^\alpha} + \frac{8}{(1\times 4)^\alpha} + \frac{2}{(2\times 2)^\alpha} + \frac{11}{(2\times 3)^\alpha} \\ &\quad + \frac{7}{(3\times 3)^\alpha} + \frac{4}{(3\times 4)^\alpha} \\ &= \frac{1}{2^\alpha} + \frac{4}{3^\alpha} + \frac{8}{4^\alpha} + \frac{2}{4^\alpha} + \frac{11}{6^\alpha} + \frac{7}{9^\alpha} + \frac{4}{12^\alpha}. \end{aligned}$$

(vi) **Symmetric Division (Deg) Index:**

$$\begin{aligned} SDD(N) &= \sum_{vw\in E(N)} \left\{ \frac{\min(d(v),d(w))}{\max(d(v),d(w))} + \frac{\max(d(v),d(w))}{\min(d(v),d(w))} \right\} \\ &= 1\left\{\frac{1}{2}+\frac{2}{1}\right\} + 4\left\{\frac{1}{3}+\frac{3}{1}\right\} + 8\left\{\frac{1}{4}+\frac{4}{1}\right\} + 2\left\{\frac{2}{2}+\frac{2}{2}\right\} \\ &\quad + 11\left\{\frac{2}{3}+\frac{3}{2}\right\} + 7\left\{\frac{3}{3}+\frac{3}{3}\right\} + 4\left\{\frac{3}{4}+\frac{4}{3}\right\} \\ &= 100. \end{aligned}$$

(vii) **Harmonic Index:**

$$\begin{aligned} H(N) &= \sum_{vw\in E(N)} \frac{2}{d(v)+d(w)} \\ &= 1\left\{\frac{2}{1+2}\right\} + 4\left\{\frac{2}{1+3}\right\} + 8\left\{\frac{2}{1+4}\right\} + 2\left\{\frac{2}{2+2}\right\} \end{aligned}$$

$$+11\left\{\frac{2}{2+3}\right\}+7\left\{\frac{2}{3+3}\right\}+4\left\{\frac{2}{3+4}\right\}$$
$$=\frac{1548}{105}$$
$$=\frac{516}{35}\approx 14.7428571.$$

(viii) **Inverse Sum (Indeg) Index:**

$$ISI(N)=\sum_{vw\in E(N)}\frac{d(v)d(w)}{d(v)+d(w)}$$
$$=1\left\{\frac{1\times 2}{1+2}\right\}+4\left\{\frac{1\times 3}{1+3}\right\}+8\left\{\frac{1\times 4}{1+4}\right\}+2\left\{\frac{2\times 2}{2+2}\right\}$$
$$+11\left\{\frac{2\times 3}{2+3}\right\}+7\left\{\frac{3\times 3}{3+3}\right\}+4\left\{\frac{3\times 4}{3+4}\right\}$$
$$=\frac{8951}{210}\approx 42.6238095.$$

(ix) **Augmented Zagreb Index:**

$$AZ(N)=\sum_{vw\in E(N)}\left\{\frac{d(v)d(w)}{d(v)+d(w)-2}\right\}^3$$
$$=1\left\{\frac{1\times 2}{1+2-2}\right\}^3+4\left\{\frac{1\times 3}{1+3-2}\right\}^3+8\left\{\frac{1\times 4}{1+4-2}\right\}^3$$
$$+2\left\{\frac{2\times 2}{2+2-2}\right\}^3+11\left\{\frac{2\times 3}{2+3-2}\right\}^3$$
$$+7\left\{\frac{3\times 3}{3+3-2}\right\}^3+4\left\{\frac{3\times 4}{3+4-2}\right\}^3$$
$$=\frac{60370561}{216000}\approx 279.4933379.$$ □

Remark 3 *From Theorem 2, we see that* $R_\alpha(N)\approx 90.14321042$ *and* $RR_\alpha(N)\approx 15.99527292$ *for* $\alpha=\frac{1}{2}$.

5 M-polynomial of the Graph of Nirmatrelvir / PF-07321332

We now determining a algebraic expression of M-polynomial for the graph structure of nirmatrelvir and subsequently extort the numerical values of the

related topological indices (degree-dependent) by using the listed (Table 1) derivation formulas. Therefore, we will validate the values of the indices calculated in the previous section.

Theorem 4 *Let $N = (V(N), E(N)) = (V(PF\text{-}07321332), E(PF\text{-}07321332))$ be the molecular graph of nirmatrelvir. Then the expression of M-polynomial of the molecular graph is given by*

$$M(N; x, y) = xy^2 + 4xy^3 + 8xy^4 + 2x^2y^2 + 11x^2y^3 + 7x^3y^3 + 4x^3y^4.$$

Proof: We have analysed in the beginning of the previous section that the edge set $E(N)$ has the cardinality 37 and the edge set can be divided into seven discrete subsets based on the degree of the end vertices as

$$E_{\{r,s\}} = \{e = v_1v_2 \in E(N) : d(v_1) = r,\ d(v_2) = s\},$$

where $\{r, s\} = \{1, 2\}, \{1, 3\}, \{1, 4\}, \{2, 2\}, \{2, 3\}, \{3, 3\}$ and $\{3, 4\}$, having frequencies given by $|E_{\{1,2\}}| = 1,\ |E_{\{1,3\}}| = 4,\ |E_{\{1,4\}}| = 8,\ |E_{\{2,2\}}| = 2,$ $|E_{\{2,3\}}| = 11,\ |E_{\{3,3\}}| = 7,$ and $|E_{\{3,4\}}| = 4$. Therefore, for our considered graph N, using the formal definition of the M-polynomial, we have

$$\begin{aligned}
M(N; x, y) &= \sum_{\delta \le p \le q \le \Delta} m_{p,q} x^p y^q, \quad \text{where } p, q \in \{1, 2, 3, 4\} \text{ and } \delta = 1, \Delta = 4 \\
&= m_{1,2}xy^2 + m_{1,3}xy^3 + m_{1,4}xy^4 + m_{2,2}x^2y^2 \\
&\quad + m_{2,3}x^2y^3 + m_{3,3}x^3y^3 + m_{3,4}x^3y^4 \\
&= |E_{\{1,2\}}|\ xy^2 + |E_{\{1,3\}}|\ xy^3 + |E_{\{1,4\}}|\ xy^4 + |E_{\{2,2\}}|\ x^2y^2 \\
&\quad + |E_{\{2,3\}}|\ x^2y^3 + |E_{\{3,3\}}|\ x^3y^3 + |E_{\{3,4\}}|\ x^3y^4 \\
&= xy^2 + 4xy^3 + 8xy^4 + 2x^2y^2 + 11x^2y^3 + 7x^3y^3 + 4x^3y^4. \qquad \square
\end{aligned}$$

The following theorems extract the values the previously discussed topological indices of the graph N from our obtained M-polynomial $M(N; x, y)$. The reader gets to see some of the proofs for the following lemmas.

Lemma 5 *Let N be the graph of nirmatrelvir, then the differential operators $D_x = x\frac{\partial}{\partial x}$, $D_y = y\frac{\partial}{\partial y}$ and D_xD_y over the M-polynomial $M(N; x, y)$ are given by*

$$\begin{aligned}
D_x(M(N; x, y)) &= xy^2 + 4xy^3 + 8xy^4 + 4x^2y^2 + 22x^2y^3 + 21x^3y^3 + 12x^3y^4, \\
D_y(M(N; x, y)) &= 2xy^2 + 12xy^3 + 32xy^4 + 4x^2y^2 + 33x^2y^3 + 21x^3y^3 + 16x^3y^4, \\
D_xD_y(M(N; x, y)) &= 2xy^2 + 12xy^3 + 32xy^4 + 8x^2y^2 + 66x^2y^3 + 63x^3y^3 + 48x^3y^4.
\end{aligned}$$

Theorem 6 *Let N be the graph of nirmatrelvir, then the first and second Zagreb indices of the graph N are given by $M_1(N) = 192$ and $M_2(N) = 231$, respectively.*

Proof: Using Lemma 5 and the main derivation formulas mentioned in Table 1, we have

$$M_1(N) = (D_x + D_y)(M(N; x, y))|_{x=y=1} = 72 + 120 = 192.$$

$$M_2(N) = D_x D_y(M(N; x, y))|_{x=y=1} = 231.$$

□

Lemma 7 *Let N be the graph of nirmatrelvir, then the integral operator $S_x S_y$ over the M-polynomial $M(N; x, y)$ is given by*

$$S_x S_y(M(N; x, y)) = \frac{1}{2}xy^2 + \frac{4}{3}xy^3 + 2xy^4 + \frac{1}{2}x^2y^2 + \frac{11}{6}x^2y^3 + \frac{7}{9}x^3y^3 + \frac{1}{3}x^3y^4.$$

Proof: Let us first impose the integral operator S_y over the M-polynomial $M(N; x, y)$ and then S_x on the obtained result.

$$\begin{aligned}\therefore\ S_y(M(N; x, y)) &= \int_0^y \frac{M(N; x, t)}{t} dt \\ &= \frac{1}{2}xy^2 + \frac{4}{3}xy^3 + 2xy^4 + x^2y^2 + \frac{11}{3}x^2y^3 + \frac{7}{3}x^3y^3 + x^3y^4,\end{aligned}$$

and

$$\begin{aligned}S_x S_y(M(N; x, y)) &= S_x(S_y(M(N; x, y))) \\ &= \frac{1}{2}xy^2 + \frac{4}{3}xy^3 + 2xy^4 + \frac{1}{2}x^2y^2 + \frac{11}{6}x^2y^3 + \frac{7}{9}x^3y^3 + \frac{1}{3}x^3y^4.\end{aligned}$$

□

Theorem 8 *Let N be the graph of nirmatrelvir, then the modified second Zagreb index of the graph N is given by ${}^mM_2(N) = \frac{131}{18}$.*

Proof: Using Lemma 7 and the main derivation formula mentioned in Table 1, we have

$${}^mM_2(N) = S_x S_y(M(N; x, y))|_{x=y=1} = \frac{131}{18} \approx 7.2777777.$$

□

Lemma 9 *Let N be the graph of nirmatrelvir, then the differential operator $D_x^\alpha D_y^\alpha$ and the integral operator $S_x^\alpha S_y^\alpha$ over the M-polynomial $M(N;x,y)$ are given by*

$$\begin{aligned}
&D_x^\alpha D_y^\alpha(M(N;x,y))\\
&= 2^\alpha xy^2 + 4\times 3^\alpha xy^3 + 8\times 4^\alpha xy^4 + 2\times 2^\alpha 2^\alpha x^2y^2 + 11\times 2^\alpha 3^\alpha x^2y^3\\
&\quad + 7\times 3^\alpha 3^\alpha x^3y^3 + 4\times 3^\alpha 4^\alpha x^3y^4,\\
&S_xS_y(M(N;x,y))\\
&= \frac{1}{2^\alpha}xy^2 + \frac{4}{3^\alpha}xy^3 + \frac{8}{4^\alpha}xy^4 + \frac{2}{2^\alpha 2^\alpha}x^2y^2 + \frac{11}{2^\alpha 3^\alpha}x^2y^3 + \frac{7}{3^\alpha 3^\alpha}x^3y^3 + \frac{4}{3^\alpha 4^\alpha}x^3y^4.
\end{aligned}$$

Theorem 10 *Let N be the graph of nirmatrelvir, then the general Randić index $R_\alpha(N)$ and inverse Randić index $RR_\alpha(N)$ of the graph N are given by*

$$\begin{aligned}
R_\alpha(N) &= 2^\alpha + 4\times 3^\alpha + 8\times 4^\alpha + 2\times 4^\alpha + 11\times 6^\alpha + 7\times 9^\alpha + 4\times 12^\alpha,\\
\text{and}\quad RR_\alpha(N) &= \frac{1}{2^\alpha} + \frac{4}{3^\alpha} + \frac{8}{4^\alpha} + \frac{2}{4^\alpha} + \frac{11}{6^\alpha} + \frac{7}{9^\alpha} + \frac{4}{12^\alpha}.
\end{aligned}$$

Proof: Using Lemma 9 and the main derivation formulas mentioned in Table 1, we have

$$\begin{aligned}
R_\alpha(N) &= D_x^\alpha D_y^\alpha(M(N;x,y))|_{x=y=1}\\
&= 2^\alpha + 4\times 3^\alpha + 8\times 4^\alpha + 2\times 4^\alpha + 11\times 6^\alpha + 7\times 9^\alpha + 4\times 12^\alpha,\\
\text{and}\quad RR_\alpha(N) &= S_x^\alpha S_y^\alpha(M(N;x,y))|_{x=y=1}\\
&= \frac{1}{2^\alpha} + \frac{4}{3^\alpha} + \frac{8}{4^\alpha} + \frac{2}{4^\alpha} + \frac{11}{6^\alpha} + \frac{7}{9^\alpha} + \frac{4}{12^\alpha}.
\end{aligned}$$

□

Lemma 11 *Let N be the graph of nirmatrelvir, then the operators D_xS_y and D_yS_x over the M-polynomial $M(N;x,y)$ are given by*

$$D_xS_y(M(N;x,y)) = \frac{1}{2}xy^2 + \frac{4}{3}xy^3 + 2xy^4 + 2x^2y^2 + \frac{22}{3}x^2y^3 + 7x^3y^3 + 3x^3y^4,$$

and

$$D_yS_x(M(N;x,y)) = 2xy^2 + 12xy^3 + 32xy^4 + 2x^2y^2 + \frac{33}{2}x^2y^3 + 7x^3y^3 + \frac{16}{3}x^3y^4.$$

Theorem 12 *Let N be the graph of nirmatrelvir, then the symmetric division (deg) index of the graph N is given by $SDD(N) = 100$.*

Proof: Using Lemma 11 and the main derivation formula mentioned in Table 1, we have

$$SDD(N) = (D_xS_y + D_yS_x)(M(N;x,y))|_{x=y=1} = 69 + 31 = 100.$$ □

Lemma 13 *Let N be the graph of nirmatrelvir, then the operator S_xJ over the M-polynomial $M(N;x,y)$ is given by*

$$S_xJ(M(N;x,y)) = \frac{1}{3}x^3 + \frac{3}{2}x^4 + \frac{19}{5}x^5 + \frac{7}{6}x^6 + \frac{4}{7}x^7.$$

Theorem 14 *Let N be the graph of nirmatrelvir, then the harmonic index of the graph N is given by $H(N) = \frac{516}{35}$.*

Proof: Using Lemma 13 and the main derivation formula mentioned in Table 1, the harmonic index of the graph N, derived from the $M(N;x,y)$, is calculated as

$$H(N) = 2S_xJ(M(N;x,y))|_{x=1} = 2\left(\frac{1}{3} + \frac{3}{2} + \frac{19}{5} + \frac{7}{6} + \frac{4}{7}\right)$$

$$= \frac{1548}{105} = \frac{516}{35} \approx 14.7428571.$$

□

Lemma 15 *Let N be the graph of nirmatrelvir, then the operator $S_xJD_xD_y$ over the M-polynomial $M(N;x,y)$ is given by*

$$S_xJD_xD_y(M(N;x,y)) = \frac{2}{3}x^3 + 5x^4 + \frac{98}{5}x^5 + \frac{21}{2}x^6 + \frac{48}{7}x^7.$$

Proof: We know that $J(f(x,y)) = f(x,x)$. Using the computed term $D_xD_y(M(N;x,y))$ in Lemma 5, we have

$$\begin{aligned}
&S_xJD_xD_y(M(N;x,y))\\
&= S_xJ\big(2xy^2 + 12xy^3 + 32xy^4 + 8x^2y^2 + 66x^2y^3 + 63x^3y^3 + 48x^3y^4\big)\\
&= S_x\big(2x^3 + 20x^4 + 98x^5 + 63x^6 + 48x^7\big)\\
&= \frac{2}{3}x^3 + 5x^4 + \frac{98}{5}x^5 + \frac{21}{2}x^6 + \frac{48}{7}x^7.
\end{aligned}$$

□

Theorem 16 *Let N be the graph of nirmatrelvir, then the inverse sum (indeg) index of the graph N is given by $ISI(N) = \frac{8951}{210}$.*

Proof: Using Lemma 15 and the main derivation formula mentioned in Table 1, the inverse sum (indeg) index of the graph N, derived from the $M(N;x,y)$, is calculated as

$$ISI(N) = S_x J D_x D_y (M(N;x,y))|_{x=1}$$

$$= \frac{2}{3} + 5 + \frac{98}{5} + \frac{21}{2} + \frac{48}{7} = \frac{8951}{210} \approx 42.6238095.$$

□

Lemma 17 *Let N be the graph of nirmatrelvir, then the operator $S_x^3 Q_{-2} J D_x^3 D_y^3$ over the M-polynomial $M(N;x,y)$ is given by*

$$\begin{aligned} &S_x^3 Q_{-2} J D_x^3 D_y^3 (M(N;x,y)) \\ &= 2^3 x + \frac{4\times 3^3}{2^3}x^2 + \frac{8\times 4^3}{3^3}x^3 + \frac{2\times 2^3\times 2^3}{2^3}x^2 + \frac{11\times 2^3\times 3^3}{3^3}x^3 \\ &\quad + \frac{7\times 3^3\times 3^3}{4^3}x^4 + \frac{4\times 3^3\times 4^3}{5^3}x^5. \end{aligned}$$

Proof: We know that $J(f(x,y)) = f(x,x)$ and $Q_\alpha(f(x,y)) = x^\alpha f(x,y)$, $\alpha \neq 0$. Let us first apply the differential operator $D_x^3 D_y^3$ on our obtained M-polynomial $M(N;x,y)$ and then impose the remaining operator $S_x^3 Q_{-2} J$ on the attained result:

$$\begin{aligned} &S_x^3 Q_{-2} J D_x^3 D_y^3 (M(N;x,y)) \\ &= S_x^3 Q_{-2} J\big(2^3 xy^2 + 4\times 3^3 xy^3 + 8\times 4^3 xy^4 + 2\times 2^3\times 2^3 x^2y^2 \\ &\qquad + 11\times 2^3\times 3^3 x^2y^3 + 7\times 3^3\times 3^3 x^3y^3 + 4\times 3^3\times 4^3 x^3y^4\big) \\ &= S_x^3 Q_{-2}\big(2^3x^3 + 4\times 3^3x^4 + 8\times 4^3x^5 + 2\times 2^3\times 2^3x^4 + 11\times 2^3\times 3^3x^5 \\ &\qquad + 7\times 3^3\times 3^3x^6 + 4\times 3^3\times 4^3x^7\big) \\ &= S_x^3\big(2^3x + 4\times 3^3x^2 + 8\times 4^3x^3 + 2\times 2^3\times 2^3x^2 + 11\times 2^3\times 3^3x^3 \\ &\qquad + 7\times 3^3\times 3^3x^4 + 4\times 3^3\times 4^3x^5\big) \\ &= 2^3x + \frac{4\times 3^3}{2^3}x^2 + \frac{8\times 4^3}{3^3}x^3 + \frac{2\times 2^3\times 2^3}{2^3}x^2 + \frac{11\times 2^3\times 3^3}{3^3}x^3 \\ &\quad + \frac{7\times 3^3\times 3^3}{4^3}x^4 + \frac{4\times 3^3\times 4^3}{5^3}x^5. \end{aligned}$$

□

Theorem 18 *Let N be the graph of nirmatrelvir, then the augmented Zagreb index of the graph N is given by $AZ(N) = \frac{60370561}{216000}$.*

Proof: Using Lemma 17 and the main derivation formula mentioned in Table 1, the augmented Zagreb index of the graph N, derived from the $M(N;x,y)$, is calculated as

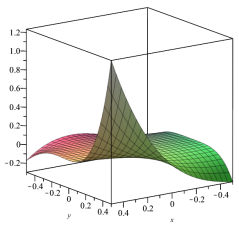
$$\begin{aligned} AZ(N) &= S_x^3 Q_{-2} J D_x^3 D_y^3 (M(N;x,y))|_{x=1} \\ &= 2^3 + 4\left\{\frac{3}{2}\right\}^3 + 8\left\{\frac{4}{3}\right\}^3 + 2\times 2^3 + 11\times 2^3 + 7\left\{\frac{9}{4}\right\}^3 + 4\left\{\frac{12}{5}\right\}^3 \\ &= \frac{60370561}{216000} \approx 279.4933379. \end{aligned}$$

□

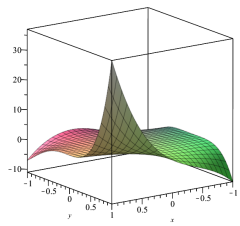
Therefore, we see that with the help of the derivation formulas (as listed in Table 1) over our proposed M-polynomial $M(N;x,y)$ of the graph N, it is an alternative, quick and compact way of finding the standard degree-dependent topological indices.

6 Geometrical Interpretation of the M-polynomial of Nirmatrelvir

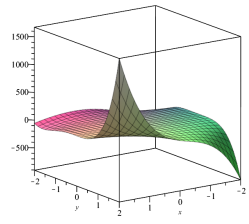
To view the geometrical characteristics of the M-polynomial of nirmatrelvir, we draw the 3-Dimensional surfaces of the M-polynomial of nirmatrelvir by the Maple-20 in numerous domains, such as, $-0.5 \le x, y \le 0.5$ in Figure 4(a), $-1 \le x, y \le 1$ in Figure 4(b), $-2 \le x, y \le 2$ in Figure 4(c), $-3 \le x, y \le 3$ in Figure 4(d), $-4 \le x, y \le 4$ in Figure 4(e) and $-5 \le x, y \le 5$ in Figure 4(f). These surfaces seem to show similar behaviors but in reality, they have different gradients in different regions. Note that, the parameters x and y allow us to regulate the M-polynomial value.



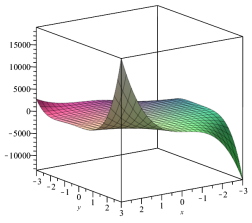
(a) 3-D surface of the M-polynomial of nirmatrelvir in $-0.5 \le x, y \le 0.5$.



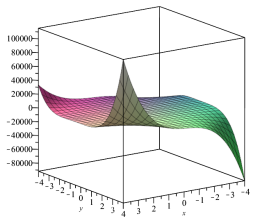
(b) 3-D surface of the M-polynomial of nirmatrelvir in $-1 \le x, y \le 1$.



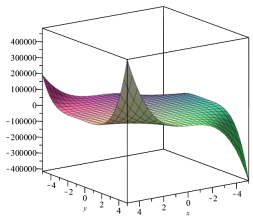
(c) 3-D surface of the M-polynomial of nirmatrelvir in $-2 \le x, y \le 2$.



(*d*) 3-D surface of the M-polynomial of nirmatrelvir in $-3 \leq x, y \leq 3$.



(*e*) 3-D surface of the M-polynomial of nirmatrelvir in $-4 \leq x, y \leq 4$.



(*f*) 3-D surface of the M-polynomial of nirmatrelvir in $-5 \leq x, y \leq 5$.

Figure 4: The 3-Dimensional geometrical illustration of the M-polynomial of nirmatrelvir in numerous regions of x and y.

In order to observe the comparative values, the maximum, minimum and intermediate values of the degree-dependent topological indices of nirmatrelvir, we plot them, in increasing order, in Figure 5.

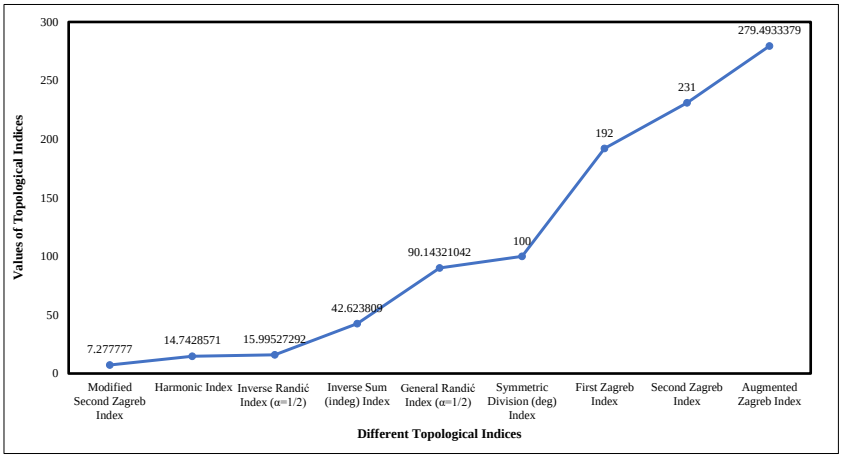


Figure 5: Visualizing the values (in increasing order) of the standard degree-based topological indices of nirmatrelvir.

For the molecular graph $N = (V(N), E(N)) = (V(PF\text{-}07321332), E(PF\text{-}07321332))$ of the drug nirmatrelvir, the degree-dependent topological indices are listed in ascending order as follows: modified second Zagreb index, harmonic index, inverse Randić index ($\alpha = 1/2$) , inverse sum (indeg) index, general Randić index ($\alpha = 1/2$), symmetric division (deg) index, first Zagreb index, second Zagreb index, augmented Zagreb index.

7 Conclusions

In the current study, we have considered a bio-available oral antiviral drug nirmatrelvir (also familiar as PF-07321332, UNII-7R9A5P7H32) which is designed and developed by the scientists of Pfizer. Nirmatrelvir co-packaged with ritonavir tablet is available in the brand name of Paxlovid which is recently granted for emergency use authorization by U.S. FDA to fight against the Corona Virus. Here, we have analyzed some topological attributes of nirmatrelvir which will aid in perceiving the pharmacokinetics and other characteristics of the drug. Some well-known degree-dependent topological indices of nirmatrelvir were calculated by their corresponding mathematical formulas. We also recalculated and validated the indices from the M-polynomial of nirmatrelvir, which is a very swift and precise way to compute the degree-dependent topological indices. The obtained numerical values of the indices and the M-polynomial were assessed graphically to understand their geometrical behavior. This study can serve as new avenue for the investigation of related drugs employed in the treatment of COVID-19 patients.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Author Contribution Statement

Modhuleena Mandal has contributed to the study of literature and discussed the mode of action of nirmatrelvir. She essentially looked into the biological and chemical aspects of the article. Shibsankar Das has contributed in the mathematical and computational part to obtain the indices and M-polynomial of nirmatrelvir and their geometrical behavior. Both the authors contributed in interpreting the results, to write the manuscript with critical analysis and feedback so as to maintain a knowledge base balance in this interdisciplinary work.

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References

[1] Dragan Amić, Drago Bešlo, Bono Lučić, Sonja Nikolić, and Nenad Trinajstić. The vertex-connectivity index revisited. *Journal of Chemical Information and Computer Sciences*, 38(5):819–822, 1998. doi:10.1021/ci980039b.

[2] Béla Bollobás and P. Erdős. Graphs of extremal weights. *Ars Combinatoria*, 50:225–233, 1998.

[3] COVID 19 VACCINE TRACKER. 10 vaccines approved for use by WHO, Retrieved 31 Dec. 2021. URL: https://covid19.trackvaccines.org/agency/who/.

[4] Shibsankar Das and Virendra Kumar. Investigation of closed derivation formula for GQ and QG indices of a graph via M-polynomial. *Iranian Journal of Mathematical Chemistry*, 13(2):129–144, 2022. doi:10.22052/ijmc.2022.246172.1614.

[5] Shibsankar Das and Virendra Kumar. On M-polynomial of the two-dimensional Silicon-Carbons. *Palestine Journal of Mathematics*, 11(Special Issue II):136–157, 2022. URL: https://pjm.ppu.edu/paper/1035-m-polynomial-two-dimensional-silicon-carbons.

[6] Shibsankar Das and Shikha Rai. M-polynomial and related degree-based topological indices of the third type of hex-derived network. *Nanosystems: Physics, Chemistry, Mathematics*, 11(3):267–274, 2020. doi:10.17586/2220-8054-2020-11-3-267-274.

[7] Shibsankar Das and Shikha Rai. M-polynomial and related degree-based topological indices of the third type of chain hex-derived network. *Malaya Journal of Matematik (MJM)*, 8(4):1842–1850, 2020. doi:10.26637/MJM0804/0085.

[8] Shibsankar Das and Shikha Rai. Topological characterization of the third type of triangular hex-derived networks. *Scientific Annals of Computer Science*, 31(2):145–161, 2021. doi:10.7561/SACS.2021.2.145.

[9] Shibsankar Das and Shikha Rai. Degree-based topological descriptors of type 3 rectangular hex-derived networks. *Bulletin of the Institute of Combinatorics and its Applications*, 95:21–37, 2022. URL: http://bica.the-ica.org/Volumes/95//Reprints/BICA2021-26-Reprint.pdf.

[10] Shibsankar Das and Shikha Rai. On M-polynomial and associated topological descriptors of subdivided hex-derived network of type three. *Computational Technologies*, 27(4):84–97, 2022. doi:10.25743/ICT.2022.27.4.007.

[11] Shibsankar Das and Shikha Rai. On closed derivation formulas of Nirmala indices from the M-polynomial of a graph. *Journal of the Indian Chemical Society*, 100(6):101017, 2023. doi:10.1016/j.jics.2023.101017.

[12] Shibsankar Das and Shikha Rai. M-polynomial based mathematical formulation of the (a,b)-Nirmala index and its bounds. *Palestine Journal of Mathematics*, (Article in Press). 2024.

[13] Shibsankar Das, Shikha Rai, and Virendra Kumar. On topological indices of Molnupiravir and its QSPR modelling with some other antiviral drugs to treat COVID-19 patients. *Journal of Mathematical Chemistry*, 62(10):2581–2624, 2024. doi:10.1007/s10910-023-01518-z.

[14] Shibsankar Das, Shikha Rai, and Modhuleena Mandal. M-polynomial and correlated topological indices of antiviral drug Molnupiravir used as a therapy for COVID-19. *Polycyclic Aromatic Compounds*, 43(8):7027–7041, 2023. doi:10.1080/10406638.2022.2131854.

[15] Hanyuan Deng, Jianguang Yang, and Fangli Xia. A general modeling of some vertex-degree based topological indices in benzenoid systems and phenylenes. *Computers & Mathematics with Applications*, 61(10):3017–3023, 2011. doi:10.1016/j.camwa.2011.03.089.

[16] Emeric Deutsch and Sandi Klavžar. M-polynomial and degree-based topological indices. *Iranian Journal of Mathematical Chemistry*, 6(2):93–102, 2015. doi:10.22052/ijmc.2015.10106.

[17] Edward J. Farrell. An introduction to matching polynomials. *Journal of Combinatorial Theory, Series B*, 27(1):75–86, 1979. doi:10.1016/0095-8956(79)90070-4.

[18] Odile Favaron, Maryvonne Mahéo, and J.-F. Saclé. Some eigenvalue properties in graphs (conjectures of Graffiti-II). *Discrete Mathematics*, 111(1-3):197–220, 1993. doi:10.1016/0012-365X(93)90156-N.

[19] Boris Furtula, Ante Graovac, and Damir Vukičević. Augmented Zagreb index. *Journal of Mathematical Chemistry*, 48(2):370–380, 2010. doi:10.1007/s10910-010-9677-3.

[20] I. Gutman and N. Trinajstić. Graph theory and molecular orbitals. total π-electron energy of alternant hydrocarbons. *Chemical Physics Letters*, 17(4):535–538, 1972. doi:10.1016/0009-2614(72)85099-1.

[21] Ivan Gutman. The acyclic polynomial of a graph. *Publications de L'Institut Mathématique*, 22(36):63–69, 1977. URL: http://eudml.org/doc/255036.

[22] Ivan Gutman. Some relations between distance-based polynomials of trees. *Bulletin (Académie serbe des sciences et des arts. Classe des sciences mathématiques et naturelles. Sciences mathématiques)*, 131(30):1–7, 2005. doi:10.2298/BMAT0530001G.

[23] Özge Çolakoğlu Havare. Topological indices and QSPR modeling of some novel drugs used in the cancer treatment. *International Journal of Quantum Chemistry*, 121(24):e26813, 2021. doi:10.1002/qua.26813.

[24] Haruo Hosoya. On some counting polynomials in chemistry. *Discrete Applied Mathematics*, 19(1-3):239–257, 1988. doi:10.1016/0166-218X(88)90017-0.

[25] Zahid Iqbal, Adnan Aslam, Muhammad Ishaq, and Wei Gao. On computations of topological descriptors of kagome lattice. *Polycyclic Aromatic Compounds*, 42(8):4895–4909, 2022. doi:10.1080/10406638.2021.1923537.

[26] Muhammad Ishtiaq, Abdul Rauf, Qammar Rubbab, Muhammad Kamran Siddiqui, and Humaira Ibrahim. Algebraic polynomial based topological properties of anti-tumor drug; hyaluronic acid-doxorubicin (HAD). *Polycyclic Aromatic Compounds*, 42(10):7049–7070, 2022. doi:10.1080/10406638.2021.1995011.

[27] K Julietraja and P Venugopal. Computation of degree-based topological descriptors using M-polynomial for coronoid systems. *Polycyclic Aromatic Compounds*, 42(4):1770–1793, 2022. doi:10.1080/10406638.2020.1804415.

[28] K. Julietraja, P. Venugopal, S. Prabhu, and Jia-Bao Liu. M-polynomial and degree-based molecular descriptors of certain classes of benzenoid systems. *Polycyclic Aromatic Compounds*, 42(6):3450–3477, 2022. doi:10.1080/10406638.2020.1867205.

[29] Shin Min Kang, Waqas Nazeer, Manzoor Ahmad Zahid, Abdul Rauf Nizami, Adnan Aslam, and Mobeen Munir. M-polynomials and topological indices of hex-derived networks. *Open Physics*, 16(1):394–403, 2018. doi:10.1515/phys-2018-0054.

[30] Louis H. Kauffman. A Tutte polynomial for signed graphs. *Discrete Applied Mathematics*, 25(1-2):105–127, 1989. doi:10.1016/0166-218X(89)90049-8.

[31] Virendra Kumar and Shibsankar Das. Comparative study of GQ and QG indices as potentially favorable molecular descriptors. *International Journal of Quantum Chemistry*, 124(3):e27334, 2024. doi:10.1002/qua.27334.

[32] Virendra Kumar and Shibsankar Das. On structure sensitivity and chemical applicability of some novel degree-based topological indices. *MATCH Communications in Mathematical and in Computer Chemistry*, 92(1):165–203, 2024. doi:10.46793/match.92-1.165K.

[33] Ante Miličević, Sonja Nikolić, and Nenad Trinajstić. On reformulated Zagreb indices. *Molecular Diversity*, 8:393–399, 2004. doi:10.1016/j.dam.2011.09.021.

[34] Sourav Mondal, Nilanjan De, and Anita Pal. Topological indices of some chemical structures applied for the treatment of COVID-19 patients. *Polycyclic Aromatic Compounds*, 42(4):1220–1234, 2022. doi:10.1080/10406638.2020.1770306.

[35] Sourav Mondal, Muhammad Imran, Nilanjan De, and Anita Pal. Neighborhood M-polynomial of titanium compounds. *Arabian Journal of Chemistry*, 14(8):103244, 2021. doi:10.1016/j.arabjc.2021.103244.

[36] Mobeen Munir, Waqas Nazeer, Shazia Rafique, and Shin Min Kang. M-polynomial and degree-based topological indices of polyhex nanotubes. *Symmetry*, 8(12):149, 2016. doi:10.3390/sym8120149.

[37] National Center for Biotechnology Information. PubChem compound summary for Unii-7R9A5P7H32, Retrieved 31 Dec. 2021. URL: https://pubchem.ncbi.nlm.nih.gov/compound/155903259.

[38] Dafydd R. Owen, Charlotte M. N. Allerton, Annaliesa S. Anderson, Lisa Aschenbrenner, Melissa Avery, Simon Berritt, Britton Boras, Rhonda D. Cardin, Anthony Carlo, Karen J. Coffman, Alyssa Dantonio, Li Di, Heather Eng, RoseAnn Ferre, Ketan S. Gajiwala, Scott A. Gibson, Samantha E. Greasley, Brett L. Hurst, Eugene P. Kadar, Amit S. Kalgutkar, Jack C. Lee, Jisun Lee, Wei Liu, Stephen W. Mason, Stephen Noell, Jonathan J. Novak, R. Scott Obach, Kevin Ogilvie, Nandini C. Patel, Martin Pettersson, Devendra K. Rai, Matthew R. Reese, Matthew F. Sammons, Jean G. Sathish, Ravi Shankar P. Singh, Claire M. Steppan, Al E. Stewart, Jamison B. Tuttle, Lawrence Updyke, Patrick R. Verhoest, Liuqing Wei, Qingyi Yang, and Yuao Zhu. An oral SARS-CoV-2 $M^{p}ro$ inhibitor clinical candidate for the treatment of COVID-19. *Science*, 374(6575):1586–1593, 2021. doi:10.1126/science.abl4784.

[39] Precision Vaccinations. PAXLOVID oral antiviral (PF-07321332), Retrieved 31 Dec. 2021. URL: https://www.precisionvaccinations.com/vaccines/paxlovid-oral-antiviral-pf-07321332.

[40] Shikha Rai and Shibsankar Das. M-polynomial and degree-based topological indices of subdivided chain hex-derived network of type 3. In Isaac Woungang, Sanjay Kumar Dhurandher, Kiran Kumar Pattanaik, Anshul Verma, and Pradeepika Verma, editors, *Advanced Network Technologies and Intelligent Computing*, volume 1534 of *Communications in Computer and Information Science (CCIS) series*, pages 410–424. Springer International Publishing, Cham, 2022. doi:10.1007/978-3-030-96040-7_33.

[41] Shikha Rai and Shibsankar Das. Comparative analysis of M-polynomial based topological indices between poly hex-derived networks and their subdivisions. *Proyecciones (Antofagasta, On line)*, 43(1):69 – 102, 2024. doi:10.22199/issn.0717-6279-5843.

[42] Milan Randić. Characterization of molecular branching. *Journal of the American Chemical Society*, 97(23):6609–6615, 1975. doi:10.1021/ja00856a001.

[43] Abdul Rauf, Muhammad Naeem, and Asia Hanif. Quantitative structure–properties relationship analysis of eigen-value-based indices using COVID-19 drugs structure. *International Journal of Quantum Chemistry*, 123(4):e27030, 2023. doi:10.1002/qua.27030.

[44] Muhammad Riaz, Wei Gao, and A Qudair Baig. M-polynomials and degree-based topological indices of some families of convex polytopes. *Open Journal of Mathematical Sciences*, 2(1):18–28, 2018. doi:10.30538/oms2018.0014.

[45] Maria Singaraj Rosary. Topological study of line graph of remdesivir compound used in the treatment of corona virus. *Polycyclic Aromatic Compounds*, 42(8):5731–5747, 2022. doi:10.1080/10406638.2021.1956552.

[46] Jelena Sedlar, Dragan Stevanović, and Alexander Vasilyev. On the inverse sum indeg index. *Discrete Applied Mathematics*, 184:202–212, 2015. doi:10.1016/j.dam.2014.11.013.

[47] U.S. Centers for Medicare & Medicaid Services. Monoclonal antibody covid-19 infusion, Retrieved 03 Jan. 2022. URL: https://www.cms.gov/medicare/covid-19/monoclonal-antibody-covid-19-infusion.

[48] U.S. Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes first oral antiviral for treatment of COVID-19, Retrieved 03 Jan. 2022. URL: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-oral-antiviral-treatment-covid-19.

[49] Damir Vukičević and Marija Gašperov. Bond additive modeling 1. Adriatic indices. *Croatica Chemica Acta*, 83(3):243–260, 2010. URL: https://hrcak.srce.hr/file/93215.

[50] Jianxin Wei, Murat Cancan, Atiq Ur Rehman, Muhammad Kamran Siddiqui, Muhammad Nasir, Muhammad Tayyab Younas, and Muhammad Farhan Hanif. On topological indices of remdesivir compound used in treatment of corona virus (COVID 19). *Polycyclic Aromatic*

Compounds, 42(7):4300–4316, 2022. doi:10.1080/10406638.2021.1887299.

[51] World Health Organization. WHO coronavirus (COVID-19) dashboard, Accessed 09 Apr. 2024. URL: https://data.who.int/dashboards/covid19/deaths?n=c.

[52] Heping Zhang and Fuji Zhang. The Clar covering polynomial of hexagonal systems I. *Discrete Applied Mathematics*, 69(1-2):147–167, 1996. doi:10.1016/0166-218X(95)00081-2.