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QSPR analysis of anti-hepatitis prescription drugs using degree based topological indices through M-polynomial and NM-polynomial

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Abstract

Chemical graph theory plays a vital role in pharmaceutical research, particularly in the study of antiviral drugs such as those targeting hepatitis. This paper investigates the application of topological descriptors, including M-polynomials and NM-polynomials, to compute degree-based topological indices for eight anti-hepatitis prescription drugs. The study aims to establish correlations between these indices and the physicochemical properties of the drugs, facilitating a deeper understanding of their structural characteristics and potential therapeutic effects. This research uniquely integrates degree-based topological indices and advanced QSPR modelling to elucidate correlations between molecular structures and their therapeutic efficacy. The findings offer significant insights into anti-hepatitis drug design, reducing experimental reliance.

Key findings

- M-polynomial and NM-polynomial frameworks were successfully applied to derive degree-based topological indices for analyzing anti-hepatitis drugs.
- Strong correlations ($r^2 > 0.9$) were observed between specific topological indices and key physicochemical properties, including boiling point and molar refraction.
- The integration of topological indices with QSPR modeling provides an efficient, cost-effective alternative for understanding molecular structures and optimizing drug efficacy.
- The findings demonstrated superior predictive accuracy of degree-based indices, showcasing their potential to reduce experimental reliance in antiviral drug research.
- This study establishes a theoretical foundation for extending topological index-based modeling to other drug classes, such as anti-cancer and anti-viral compounds.

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1. Introduction

Clinical testing of chemical compounds is expensive, which emphasizes the urgent need for cutting-edge facilities and equipment [1]. Chemical graph theory (CGT), which provides a more efficient method, has made this process easier for chemists and pharmacists. The medical profession can produce new and improved hypertension medications more quickly and economically by employing CGT's topological descriptors (indices) tool. The molecular structure of a chemical is represented as a graph in chemical graph theory (CGT), where atoms are the vertices and bonds are the edges. Drug research heavily relies on topological indices, which are numerical descriptors derived from these chemical graphs. Using the QSPR approach [2], the drug property prediction models have been suggested recently. The topological indices are used in chemical structure-based models that forecast the characteristics and actions of pharmaceuticals. The Wiener index, which Wiener invented, is a crucial topological index for characterizing enthalpy of formation and acentric factors in hydrocarbons. It was the first index used to analyze the physical properties of paraffin [3]. There are many different kinds of topological indices: degree-based (D-based), distance-based, and counting-related polynomial and graph indices. In particular, degree-based topological indices are important for chemical graph theory and chemistry research.

Not all topological indices can be computed directly; to get around this problem, researchers frequently employ polynomials. M-polynomial in graph theory was derived by

[4–6] and includes summing pertinent degree-based topological indices as presented by [7]. It was constructed with particular formulas for degree-based topological indices. Additionally, as an expansion of the popular M-polynomial, Mondal et al. [8] presented the NM-polynomial.

In biochemistry, a number of topological indices are used; these are grouped based on the structural characteristics of the graphs they examine. To locate non-incident edges within a graph, Hosoya [9] developed the well-known Hosoya index. Using the graph's spectrum, the Estrada index, first presented in [10], measures structural complexity. Zagreb indices are useful for understanding carbon atom branching and pi-electron energy calculations, according to [11]. Developed by Aftab et al. [12], the ABC-index highlights qualities of molecular structures that are related to thermal properties, such as heat of formation. The values of the first Zagreb connection index were recently predicted in [13] for a variety of chemical structures, such as polyphenyl chains, cyclooctatetraene chains, and chain networks with octagons, hexagons, and pentagons.

According to recent research [14], the hyper Zagreb index (0.786) can effectively predict the molar reactivity of anxiety medications. They also showed that the polarization ability of anxiety drugs is correctly predicted by the harmonic index (0.912). In the meantime, Kirmani et al. [15] investigated degree-based topological indices and polynomials in a particular family of anti-viral medications, emphasizing their essential features. Moreover, Mahboob et al. [16] examined cancer therapy medications using multiplicative degree-related indices. In a different study, Zhang et al. [17] used a linear regression model and degree-related topological indicators to examine the characteristics of anti-malarial medications. According to their findings, there is a significant association (0.961) between the first Zagreb index and boiling temperatures and a useful correlation (0.963) between the harmonic index and molar refraction. According to recent research, topological properties of bioconjugates have been studied extensively. A study examined the topological properties of a Doxorubicin conjugated PEG-PAsp copolymer molecular structure used in cancer treatment [18]. They showed that the ev-degree and ve-degree based topological indices effectively characterize the molecular structure's physicochemical properties. Another investigation focused on the topological study of a Hydroxychloroquine conjugated molecular structure used for treating novel coronavirus (COVID-19) [19]. This study demonstrated the utility of degree-based topological indices in predicting the structural features of antiviral drugs. Additionally, a study explored the topological properties of curcumin and hyaluronic acid conjugated molecular structures, emphasizing their potential as anti-cancer drugs [20]. These findings highlight the critical role of topological indices in understanding the molecular characteristics and applications of bioconjugates in drug delivery and treatment strategies. Graph energies and linear regression models have been effectively applied to predict pharmacological features, facilitating drug discovery and targeted design by linking molecular structures to their characteristics [21]. Another recent work was also focused on distance-dependent entropy measures, developing analytical formulae for Poly Propylene Imine (PPI) and Zinc Porphyrin dendrimers, with patterns visualized through graphical tools [22]. In this study, the neighborhood face index (NFI) was introduced as a novel valency-based descriptor, exhibiting exceptional predictive accuracy with a correlation exceeding 0.9991 for benzenoid hydrocarbons and showcasing its versatility for characterizing properties of carbon nanotubes [23].

Historically, topological indices were calculated with complex definitions, especially when obtaining several indices in a given category. Numerous algebraic polynomials were created to simplify this process [24–26]. These polynomials allow for differentiation, integration, or composition at defined points, producing a variety of topological indices. M-polynomial stands out among them as a general polynomial that can produce a variety of degree-based topological indices. The creation of new indices is being advanced by ongoing work by different researchers [27–31].

Researchers developed the NM-polynomial to make the computation of these indices easier. NM-polynomial applies the M-polynomial's functionality to neighborhood degree sum-based indices, just as it does for degree-based indices [32]. Kwun et al. [33] examined Vphenylenic nanotubes and nanotori using degree-based topological indices and M-polynomials. M-polynomial based topological descriptors of chemical crystal structures were investigated and their practical applications – discussed in [34]. Furthermore, M-polynomials and topological indices for linear chains of benzene, napthalene, and anthracene were examined in [35].

A separate study [36] used M-polynomials to compute topological indices for silicate networks, and Chaudhry et al. [37] used M-polynomials to derive topological indices for copper (I) oxide molecules.

Shin et al. [38] suggested closed formulas and descriptors for boron triangular nanotubes using M-polynomials, while Liu et al. [39] used them to obtain topological indices for nanotubes.

Furthermore, M-polynomials were utilized in [40, 41] to analyze nanostructures fused with starphene, and Liu et al. [42] looked into topological descriptors for the crystal structure of titanium difluoride (TiF_2). M-polynomial and NM-polynomial for certain anti-COVID-19 compounds were assessed in [43]. Combining these works shows how polynomial-based techniques are useful for defining complex chemical and molecular structures in a variety of contexts. Despite numerous studies on topological indices and QSPR models, this study uniquely emphasizes the degree-based framework for anti-hepatitis drug modelling, filling a critical gap in the literature.

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1.1. Organization of this study

Section 2 of this research discusses the significance of anti-hepatitis medicines and the methods utilized for computations. There are four subsections in Section 3. The drugs under research are partitioned in the first subsection according to the neighborhood degree sum of vertices and the degree of end vertices. Subsection 3.2 contains the description of the M and NM-Polynomials of the structures under study, and Figures 2 and 3 shows graphical representations of these polynomials. Subsection 3.3 describes the calculations and the usage of the regression models to analyze the outcomes of topological indices. Subsection 3.4 gives a comparison of the computed and actual values of the D-Based topological indices. Section 4 is the conclusion.

2. Materials and Methodology

Viral hepatitis is a major global health issue that is frequently caused by factors such as chemical exposure, drug use, certain medical disorders, and excessive alcohol consumption. The types A, B, C, D, E, and G of hepatitis viruses are known to exist. The primary mode of infection for hepatitis A (HAV) and hepatitis E (HEV) is fecal contamination, mostly through the fecal-oral pathway. Hepatitis B (HBV), hepatitis C (HCV), and hepatitis D (HDV) are among the plasma viruses that are frequently transmitted by mucosal or percutaneous contact. Acute viral hepatitis A is a common illness among children worldwide, accounting for 50–60% of pediatric cases [44]. See [45] for a thorough description of hepatitis B, including symptoms, treatment suggestions, and its effects. The most common way that the hepatitis E virus spreads is through feces-contaminated groundwater. See [46] for further information on the origins, development, and course of hepatitis E. Acute hepatitis, which these viruses can cause, can usually be cured in six months for 80 HBV patients and 20 HCV patients.

In advanced countries, HCV is frequently spread through a variety of channels, including intravenous drug use, hemodialysis, dialysis, piercings, needle stick injuries, sexual interaction, and exposure to fetuses. Medical procedures requiring infected needles or syringes and inadequate sanitation of medical equipment in developing nations are common ways for infections such as HIV, hepatitis B, and C to spread.

Recently, an article was released that discussed hepatitis treatment techniques for drug users. Globally, unsafe injection practices and drug usage are estimated to contribute to 8-16 million instances of hepatitis B, 2-5 million cases of hepatitis C, and 80 thousand to 1.5 million cases of HIV [47].

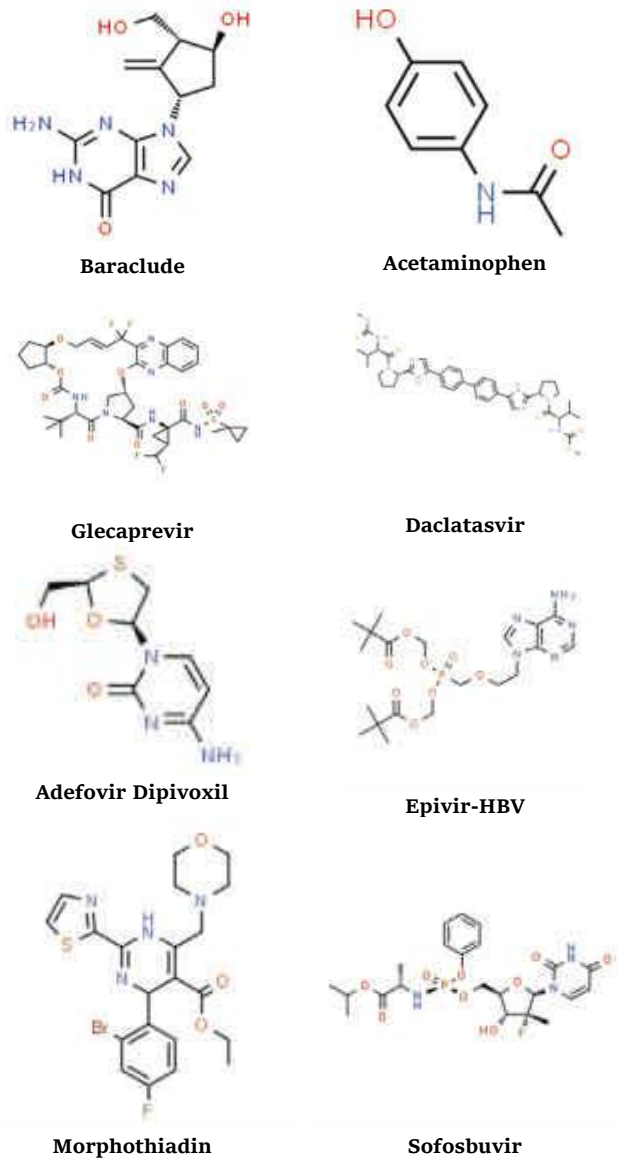

Figure 1 Chemical structures of various drugs.

Table 1 Physicochemical properties of anti-hepatitis drugs.

Drug Name	Boiling Point C	Density Dg/mL	Vapor Pressure mmHg	Enthalpy kJ/mol	Flash Point C	Molar Refraction cm^3 /mol
Baraclude	–	1.8±0.1	–	–	–	67.6±0.5
Acetaminophen	387.8±25	1.3±0.1	0.0±0.9	66.2±3.0	188.4±23.2	42.4±0.3
Glecaprevir	–	1.5±0.1	–	–	–	198.2±0.4
Daclatasvir	1071.2±65	1.3±0.1	0.0±0.3	157.4±3	601.7±34.3	200.8±0.3
Adefovir Dipivoxil	641.0±65	1.4±0.1	0.0±1.9	94.6±3.0	341.5±34.3	121.0±0.5
Epivir-HBV	475.4±55	1.7±0.1	0.0±2.7	85.2±6.0	241.3±31.5	54.1±0.5
Morphothiadin	577.2±60	1.6±0.1	0.0±1.6	86.4±3.0	302.9±32.9	120.9±0.5
Sofosbuvir	–	1.4±0.1	–	–	–	123.5±0.4

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This study describes the use of anti-hepatitis prescription drugs, with their chemical structures depicted in Figure 1. The topological index is a useful analytical tool that uses numerical data to provide information about chemical compounds' properties. There are several types of topological indices, such as energy-based, eccentricity-based, eigenvalue-based, degree-based, and distance-based indices. The most often used of these are degree-based topological indices. A linear regression model is used to evaluate the efficacy of hepatitis drugs. Topological indices are also used to assess and improve the chemical and physical characteristics of drugs. Through a QSPR (Quantitative Structure-Property Relationship) analysis involving 20 topological indices and 8 hepatitis drugs, scientists and pharmacists can better understand how drugs affect the body.

The primary topic of this paper is the examination of several hepatitis drugs. With the use of degree-based technique, eight two-dimensional structures are examined. The features of eight anti-hepatitis drugs are examined using 20 D-Based topological indices that are obtained from M and NM-Polynomial, and their correlation coefficients are observed. The properties of the drug's structure, such as its boiling point, density, vapor pressure, enthalpy, flash point, and molar refraction, must first be understood by a pharmacist before producing any drug. While the focus of this article is on hepatitis drugs, the same approach may be applied to comprehend the characteristics of other medications, including those for blood cancer, heart attacks, breast cancer, asthma, and so on.

The physiochemical properties data such as Boiling Point (BP), Density (D), Vapor Pressure (VP), Enthalpy (P), Flash Point (FP) and Molar Refraction (MR) for eight different anti-hepatitis drugs: Baraclude (A), Acetaminophen (B), Glecaprevir (C), Daclatasvir (D), Adifovir Dipivoxil (E), Epivir-HBV (F), Morphothiadin (G), and Sofosbuvir (H) were obtained from ChemSpider and are presented in Table 1; their chemical structure is shown in Figure 1.

3. Results and Discussions

3.1. Partioning of structures

The structural analysis of graphs can be carried out through edge partitioning, which is a vital technique in graph theory and its applications. This method involves classifying edges into distinct categories based on specific properties of their vertices. In this discussion, we consider two key approaches to edge partitioning. In Degree-Based Edge Partitioning, the edges are grouped according to the degree of their end vertices. For a given edge $e = (u, v)$, the degrees of its end vertices u and v determine its classification. For instance, edges can be categorized as Ei, j, where i and j represent the degrees of the vertices u and v, respectively. In neighborhood degree sum-based edge partitioning, the edges are partitioned based on the sum of the degrees of the neighboring vertices of their endpoints. For the edge $e = (u, v)$, the neighborhood degree sum is calculated as:

$$S(u, v) = \sum_{w \in N(u)} deg(w) + \sum_{x \in N(v)} deg(x), \quad (1)$$

where $N(u)$ and $N(v)$ are the sets of neighbors of vertices u and v, respectively. The process of edge partitioning can be effectively implemented using Python and libraries such as NetworkX. First, the graph must be represented using an appropriate data structure, such as an adjacency list or matrix. The NetworkX library simplifies this process, allowing the creation and manipulation of various types of graphs.

Using Python, the edges can be iterated, and their end vertices' degrees can be extracted using the degree function. The edges can then be classified into categories such as Ei, j.

Similarly, the neighborhood of each vertex can be determined using the neighbors function. The sum of degrees of these neighbors is computed for the endpoints of each edge, and the edges are grouped accordingly. Table 2 shows the portioning of the molecular structures of anti hepatitis drugs.

3.2. M and NM-polynomials

Chemical graph theory is a branch of mathematics that combines graph theory and mathematical modeling of chemical processes. Using topological indices, quantitative structure-property/structure-activity relationship (QSPR/QSAR) analysis is a useful method for predicting a molecule's properties. Researchers' attention has been drawn to neighborhood degree sum-based indices in recent years, which has sparked substantial research on NM-polynomials. Both M-polynomial and NM-polynomial are crucial for developing closed methods for different degree-based topological indices.

For any graph (Γ), M-polynomial is defined as

$$M(\Gamma; x, y) = \sum_{\omega \le i \le j \le \Omega} m_{ij} x^i y^j; \ (d_u, d_v) = (i, j) \quad (2)$$

For any graph (Γ), NM-polynomial is defined as

$$NM(\Gamma; x, y) = \sum_{\omega \le i \le j \le \Omega} m^*{}_{ij} x^i y^j; \ (nd_u, nd_v) = (i, j) \quad (3)$$

where ω and Ω denote the minimum and maximum vertex degrees of Γ, and $u, v \in E(\Gamma)$, $m_{ij}(\Gamma)$ denotes the total number of edges of Γ. Simple connected graphs are employed for each molecular graph Γ in this paper.

The degree-based topological indices shown in Tables 3 and 4 are obtained from the corresponding M- and NM-polynomials, while the list of operators utilized is shown in Table 5. In Table 6, M and NM-Polynomials of anti-hepatitis drugs can be found, and their graphical representation is shown in Figures 2 and 3.

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Table 2 Partitioning of molecular structures of anti-hepatitis drugs.

Drug Name	Edge partitions based on the degree of end vertices	Partioning of edge based on degree of end vertices
Baraclude	$\|E1,3\| = 4$, $\|E2,1\| = 1$, $\|E2,2\| = 1$, $\|E3,3\| = 7$, $\|E3,2\| = 9$	|E2,4| = 1, |E3,5| = 1, |E3,6| = 2, |E3,7| = 1, |E4,8| = 1, |E5,5| = 1,|E5,6| = 2, |E5,8| = 2,|E6,6| = 2, |E6,8| = 4, |E7,8| = 2, |E8,8| = 3
Acetaminophen	|E1,3| = 3, |E2,2| = 2, E2,3| = 6	|E3,4| = 2, |E3,5| = 1, |E4,6| = 1, |E5,5| = 4, |E5,6| = 2, |E6,6| = 1
Glecaprevir	|E1,3| = 6, |E1,4| = 8, |E2,2| = 9, |E2,3| = 22,|E2,4| = 6, |E3,3| = 8, |E3,4| = 4, |E4,4| = 1	|E3,5| = 3, |E3,6| = 1, |E3,7| = 2, |E4,4| = 2, |E4,5| = 5, |E4,6| = 4, |E4,7| = 2, |E4,8| = 2, |E4,9| = 1, |E5,6| = 2, |E5,7| = 5, |E5,9| = 1, |E6,6| = 4, |E6,7| = 7, |E6,8| = 3 |E6,9| = 5 |E7,7| = 3, |E7,8| = 2, |E7,9| = 4, |E7,10| = 3,|E8,8| = 1, |E8,9| = 1, |E9,10| = 1
Daclatasvir	|E1,2| = 2, |E1,3| = 8, |E2,2| = 10, |E2,3| = 26 , |E3,3| = 13	|E2,4| = 2, |E3,5| = 6, |E3,7| = 2, |E4,5| = 6, |E5,5| = 6, |E5,6| = 2, |E5,7| = 12, |E5,8| = 6, |E6,7| = 4, |E6,8| = 2, |E7,7| = 3, |E7,8| = 6, |E8,8| = 2
Adefovir Dipivoxil	|E1,3| = 3, |E1,4| = 7, |E2,2| = 10, |E2,3| = 7 , |E2,4| = 3, |E3,3| = 3 , |E3,4| = 2	|E3,6| = 1, |E3,7| = 2, |E4,4| = 1, |E4,5| = 5, |E4,6| = 9, |E4,7| = 1, |E5,5| = 1, |E5,6| = 1, |E5,7| = 4, |E5,8| = 2, |E6,8| = 1, |E7,8| = 1, |E8,8| = 1
Epivir-HBV	|E1,2| = 1, |E1,3| = 2, |E2,2| = 2, |E2,3| = 9 , |E3,3| = 2	|E2,4| = 1, |E3,5| = 1, |E3,6| = 1, |E4,6| = 1, |E5,5| = 3, |E5,6| = 2, |E5,7| = 1, |E5,8| = 1, |E6,6| = 2, |E6,7| = 1, |E6,8| = 1, |E7,8| = 1
Morphothiadin	|E1,2| = 1, |E1,3| = 3, |E2,2| = 9, |E3,3| = 6,|E2,3| = 15	|E2,3| = 1, |E3,5| = 2, |E3,6| = 2, |E4,4| = 3, |E4,5| = 4, |E5,5| = 2, |E5,6| = 4, |E5,7| = 2,|E5,8| = 1, |E6,6| = 2, |E6,7| = 4, |E6,8| = 2, |E6,9| = 1, |E7,7| = 1, |E7,9| = 1 |E8,8| = 1,|E8,9| = 1
Sofosbuvir	|E1,3| = 7, |E1,4| = 3, |E2,2| = 6, |E2,3| = 13, |E2,4| = 3, |E3,3| = 4, |E3,4| = 2	|E3,4| = 2, |E3,5| = 1, |E3,6| = 3, |E3,8| = 1, |E4,4| = 2, |E4,5| = 2, |E4,6| = 1, |E4,7| = 1 |E4,8| = 2, |E5,5| = 2, |E5,6| = 4, |E5,7| = 1, |E5,8| = 1, |E6,6| = 3, |E6,7| = 4 |E6,8| = 1, |E6,9| = 1, |E7,7| = 2, |E7,8| = 1, |E8,8| = 1, |E8,9| = 2

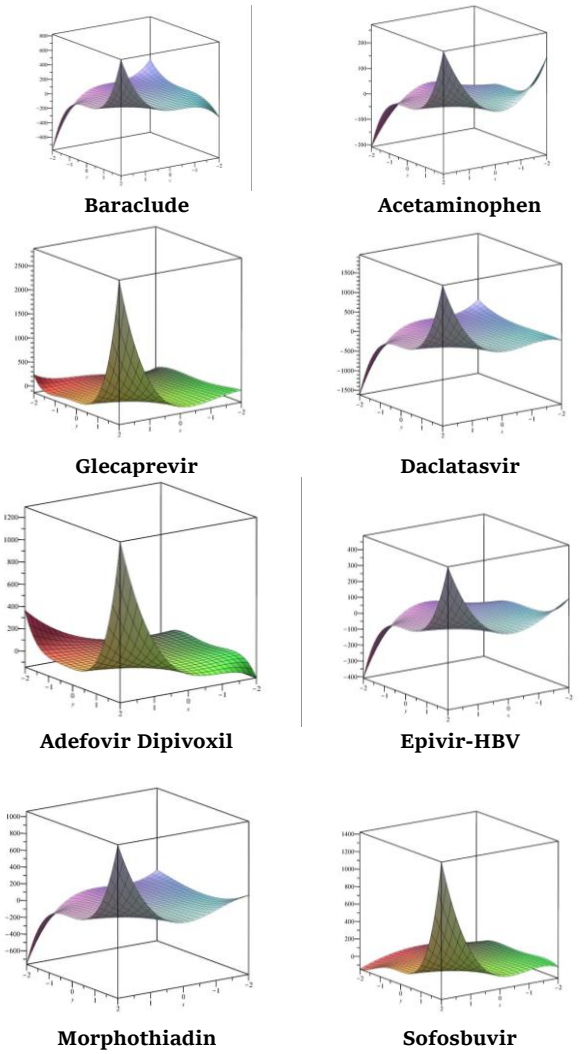

Figure 2 3D Graphical representation of M-Polynomials for anti-hepatitis drugs.

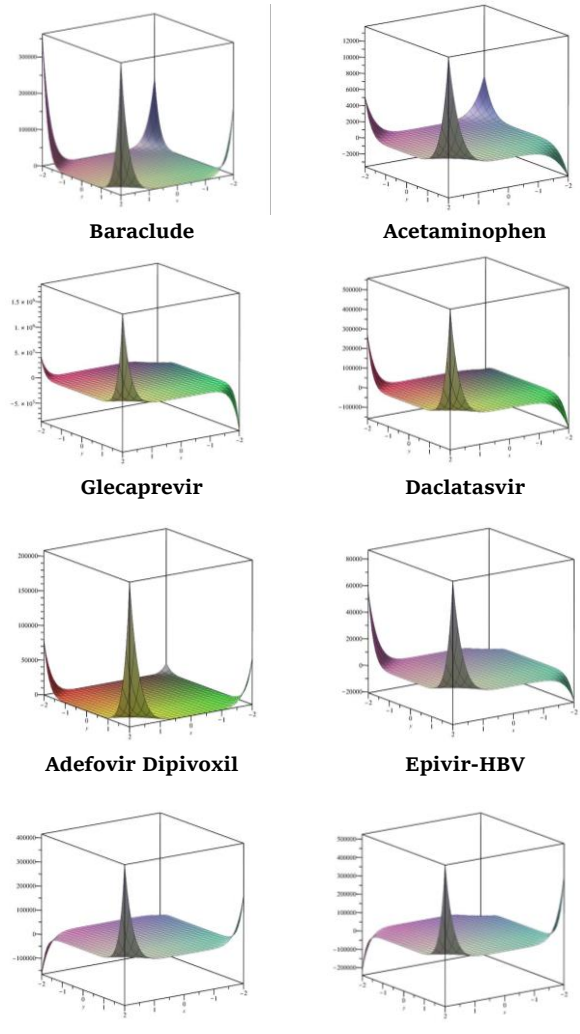

Figure 3 3D Graphical representation of M-Polynomials for anti-hepatitis drugs.

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Table 3 D-Based topological indices derived from M-Polynomial $M(\Gamma; x, y)$.

S.No	Topological indices	$M(\Gamma; x, y)$
1	$M_1(\Gamma)$	$(D_x + D_y)(M(\Gamma; x,y))\|x = y = 1$
2	$M_2(\Gamma)$	$(D_x \cdot D_y)(M(\Gamma; x,y))\|x = y = 1$
3	$M_2^m(\Gamma)$	$(S_x + S_y)(M(\Gamma; x,y))\|x = y = 1$
4	$D_5(\Gamma)$	$(D_x S_y + D_y S_x)(M(\Gamma; x,y))\|x = y = 1$
5	$SDD(\Gamma)$	$(D_x S_x + D_y S_y)(M(\Gamma; x,y))\|x = y = 1$
6	$H(\Gamma)$	$2(S_x)J(M(\Gamma; x,y))\|x = 1$
7	$ISI(\Gamma)$	$S_x J D_x D_y(M(\Gamma; x,y))\|x = y = 1$
8	$ReM_3(\Gamma)$	$D_x D_y(D_x + D_y)(M(\Gamma; x,y))\|x = y = 1$
9	$F(\Gamma)$	$S_x J(D_x + D_y)(M(\Gamma; x,y))\|x = y = 1$
10	$A(\Gamma)$	$(S_x^3 Q_{-2} J D_x^3 D_y^3)(M(\Gamma; x,y))\|x = 1$

Table 4 D-Based topological indices derived from M-Polynomial $M(\Gamma; x, y)$.

S.No	Topological indices	$NM(\Gamma; x, y)$
1	$M_1(\Gamma)$	$(D_x + D_y)(M(\Gamma; x,y))\|x = y = 1$
2	$M_2(\Gamma)$	$(D_x \cdot D_y)(M(\Gamma; x,y))\|x = y = 1$
3	$M_2^m(\Gamma)$	$(S_x + S_y)(M(\Gamma; x,y))\|x = y = 1$
4	$D_5(\Gamma)$	$(D_x S_y + D_y S_x)(M(\Gamma; x,y))\|x = y = 1$
5	$SDD(\Gamma)$	$(D_x S_x + D_y S_y)(M(\Gamma; x,y))\|x = y = 1$
6	$H(\Gamma)$	$2(S_x)J(M(\Gamma; x,y))\|x = 1$
7	$ISI(\Gamma)$	$S_x J D_x D_y(M(\Gamma; x,y))\|x = y = 1$
8	$ReM_3(\Gamma)$	$D_x D_y(D_x + D_y)(M(\Gamma; x,y))\|x = y = 1$
9	$F(\Gamma)$	$S_x J(D_x + D_y)(M(\Gamma; x,y))\|x = y = 1$
10	$A(\Gamma)$	$(S_x^3 Q_{-2} J D_x^3 D_y^3)(M(\Gamma; x,y))\|x = 1$

3.3. Regression model

In this subsection, the physical qualities of several anti-hepatitis drugs, which are also used to treat various diseases with specific topological variables, are compared using the linear regression model, stated as

$$Y = \alpha + \beta(X), \qquad (4)$$

where Y represents the physiochemical property of the drug, α and β are arbitrary constants taken from Table 1 (dependent variables) and Tables 7 and 8 (independent variables also used as coefficients of regression), and X denotes the topological indices.

Statistical parameters such as the regression coefficient β, correlation coefficient r, coefficient of determination r^2, F-statistic, p-value, and sample size n are used in this paper.

The sample size n = 9 was used throughout the paper. These findings provide a robust framework for applying degree-based topological indices to drug modelling, bridging chemical graph theory with practical pharmaceutical research. While indices with r < 0.7 exhibit weaker correlations, they offer insights into unique structural characteristics and can be refined in multi-variable regression models. Future research will extend this methodology to other drug classes, such as anti-cancer and anti-viral compounds, and explore advanced regression models for improved predictive accuracy and broader applicability in drug design.

Table 5 List of operators.

Formula	Derivation
D_x	$x\frac{\partial(f(x,y))}{\partial x}$
D_y	$y\frac{\partial(f(x,y))}{\partial y}$
L_x	$f(x^2, y)$
L_y	$f(x, y^2)$
S_x	$\int_0^x \frac{f(t,y)}{t}\,dt$
S_y	$\int_0^y \frac{f(x,t)}{t}\,dt$
J	$f(x,x)$

Table 6 M and NM-Polynomial of anti-hepatitis drugs.

Drug Name	M-Polynomial	NM-Polynomial
Baraclude	$xy^2 + 4xy^3 + x^2y^2 + 9x^2y^3 + 7x^3y^3$	$x^2y^4 + x^3y^5 + 2x^3y^6 + x^3y^7 + x^4y^8 + x^5y^5 + 2x^5y^6 + 2x^5y^8 + 2x^6y^6 + 4x^6y^8 + 2x^7y^8 + 3x^8y^8$
Acetaminophen	$3xy^3 + 2x^2y^2 + 6x^2y^3$	$2x^3y^4 + x^3y^5 + x^4y^6 + 4x^5y^5 + 2x^5y^6 + x^6y^6$
Glecaprevir	$6xy^3 + 8xy^4 + 9x^2y^2 + 22x^2y^3 + 8x^3y^3 + 4x^3y^4 + x^4y^4 + 6x^2y^4$	$3x^3y^5 + x^3y^6 + 2x^3y^7 + 2x^4y^4 + 5x^4y^5 + 4x^4y^6 + 2x^4y^7 + 2x^4y^8 + x^4y^9 + 2x^5y^6 + 5x^5y^7 + x^5y^9 + 4x^6y^6 + 7x^6y^7 + 3x^6y^8 + 5x^6y^9 + 3x^7y^7 + 2x^7y^8 + 4x^7y^9 + 3x^7y^{10} + x^8y^8 + x^8y^9 + x^9y^{10}$
Daclatasvir	$2xy^2 + 8xy^3 + 10x^2y^2 + 26x^2y^3 + 13x^3y^3$	$2x^2y^4 + 6x^3y^5 + 2x^3y^7 + 6x^4y^5 + 6x^5y^5 + 2x^5y^6 + 12x^5y^7 + 6x^5y^5 + 2x^5y^6 + 12x^5y^7 + 6x^5y^8 + 4x^6y^7 + 2x^6y^8 + 3x^7y^7 + 6x^7y^8 + 2x^8y^8$
Adefovir Dipivoxil	$3xy^3 + 7xy^4 + 10x^2y^2 + 7x^2y^3 + 3x^2y^4 + 3x^3y^3 + 2x^3y^4$	$x^3y^6 + 2x^3y^7 + x^4y^4 + 5x^4y^5 + 9x^4y^6 + x^4y^7 + x^5y^5 + x^5y^6 + 4x^5y^7 + 2x^5y^8 + 5x^6y^7 + x^6y^8 + x^7y^8 + x^8y^8$
Epivir-HBV	$xy^2 + 2xy^3 + 2x^2y^2 + 9x^2y^3 + 2x^3y^3$	$x^2y^4 + x^3y^5 + x^3y^6 + x^4y^6 + 3x^5y^5 + 2x^5y^6 + x^5y^7 + x^5y^8 + 2x^6y^6 + x^6y^7 + x^6y^8 + x^7y^8$
Morphothiadin	$xy^2 + 3xy^3 + 9x^2y^2 + 15x^2y^3 + 6x^3y^3$	$x^2y^3 + 2x^3y^5 + 2x^3y^6 + 3x^4y^4 + 4x^4y^5 + 2x^5y^5 + 4x^5y^6 + 2x^5y^7 + x^5y^8 + 2x^6y^6 + 4x^6y^7 + 2x^6y^8 + x^6y^9 + x^7y^7 + x^7y^9 + x^8y^8 + x^8y^9$
Sofosbuvir	$7xy^3 + 3xy^4 + 6x^2y^2 + 13x^2y^3 + 3x^2y^4 + 4x^3y^3 + 2x^3y^4$	$2x^3y^4 + x^3y^5 + 3x^3y^6 + x^3y^8 + 2x^4y^4 + 2x^4y^5 + x^4y^6 + x^4y^6 + x^4y^7 + 2x^4y^8 + 2x^5y^5 + 4x^5y^6 + x^5y^7 + x^5y^8 + 3x^6y^6 + 4x^6y^7 + x^6y^8 + x^6y^9 + 2x^7y^7 + x^7y^8 + x^8y^8 + 2x^8y^9$

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Linear regression models were implemented using Python, leveraging libraries such as numpy and scipy for statistical calculations. All statistical parameters, including r^2, F-statistic, and p-values, were calculated programmatically, ensuring consistency and reproducibility.

Degree-based topological indices are calculated using the data provided in Tables 2 and 6. Tables 9 and 10 provide the values of these topological indices of the molecular graphs of the drugs under consideration. Supplementary Tables S1 to S20 shows the correlation coefficients that were obtained using a linear regression model between different topological indices and the physiochemical features of (A), (B), (C), (D), (E), (F), (G), and (H).

3.4. Comparison of actual values vs computed values of D-based topological indices

In this subsection we computed the approximate values by using the regression model stated above. Supplementary Tables S21 to S32 represent a comparison (using Python) of the actual and estimated values. These tables offer a comparison between actual values and computed values of various properties of anti-malaria drugs using D-Based topological indices with M-Polynomials or NM-Polynomials. The analysis aims to assess the accuracy of these computational methods in predicting the drug properties. The linear regression models demonstrated that almost all topological indices have strongest correlation coefficient $r > 0.95$ with molar refraction. This indicates its superior predictive capability and relevance for modelling these properties. The results emphasize the utility of the topological indices in QSPR modelling and its potential for guiding drug development efforts effectively. Overall, the comparison reveals that while the computed values generally approximate the actual values, there are discrepancies observed across different drugs and properties. Some drugs show closer agreement between actual and computed values compared to others, indicating variability in the accuracy of the computational models.

These findings underscore the importance of validating computational models used for predicting drug properties. While the computed values offer valuable estimations, further refinement of these computational methods is necessary to enhance their accuracy.

In summary, the analysis highlights both the potential and the limitations of D-Based topological indices with M-Polynomials or NM-Polynomials in predicting drug properties. Continued research and validation efforts are essential to improve the accuracy of these computational models, ultimately benefiting drug development and optimization processes.

4. Limitations

During this research on anti-hepatitis drugs, several difficulties and limitations were identified that can serve as a foundation for future work. One of the key challenges was the limited availability of complete and standardized physicochemical data for all drugs under study, which required cross-referencing multiple databases like ChemSpider to ensure accuracy. Additionally, some topological indices exhibited weaker correlations ($r < 0.7$) with physicochemical properties, highlighting the need for more sophisticated modeling techniques such as multi-variable regression or machine learning to capture non-linear relationships effectively.

Table 7 D-Based topological indices derived from M-Polynomial of anti-hepatitis drugs.

Drug Name	M_1	M_2	M_2^m	D_5	SDD	H	ISI	ReM_3	F	A
Baraclude	110	135	4.36	44	9.10	25.97	718	181.86	22	51.33
Acetaminophen	50	53	2.50	22	4.90	11.45	248	74.12	11	27
Glecaprevir	330	402	11.95	128	25.54	75.16	2220	500.6	64	161
Daclatasvir	286	341	11.94	118	25.07	68.03	1750	479.7	59	134
Adefovir Dip	172	194	7.29	70	14.67	38.18	1020	248.05	35	92.58
Epivir-HBV	76	88	3.39	32	6.93	17.97	440	125.53	16	36.67
Morphothiadin	162	191	6.92	68	14.67	38.92	960	278.16	34	75
Sofosbuvir	188	219	7.73	76	15.80	42.68	1158	279.95	38	95.92

Table 8 D-Based topological indices derived from NM-Polynomial of anti-hepatitis drugs.

Drug Name	NM_1	NM_2	NM_2^m	ND_5	$NSDD$	NH	$NISI$	$NReM_3$	NF	NA
Baraclude	270	845	0.76	44	3814.22	65263.26	11340	1106400456.63	22	47.91
Acetamino	106	259	0.53	22	2.35	26.12	2620	31268.46	11	22.67
Glecaprevir	804	2568	1.96	128	10.70	195.16	35214	23405367749.97	64	137.01
Daclatasvir	682	2013	2.18	118	10.75	165.94	25310	2569917.27	59	125.53
Adefovir Dip	388	1073	1.28	70	6.5	93.88	12644	1316540.65	35	75.26
Epivir-HBV	176	493	0.65	32	3.06	42.99	5842	616206.24	16	33.96
Morphothiadin	382	1118	1.37	68	6.48	93.81	14022	1130173.35	34	70.99
Sofosbuvir	438	1290	1.39	76	6.94	106.50	16376	1668198.67	38	81.54

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Computational complexity in deriving advanced indices, such as the Neighborhood Face Index, also posed a challenge, necessitating the development of automated algorithms for large-scale datasets. Initial graphical representations lacked clarity and required high-resolution replotting for better visualization. To address these limitations, future efforts should focus on establishing centralized and comprehensive databases for drug properties, simplifying computational frameworks for complex indices, integrating advanced regression models to improve predictions, and extending this methodology to other drug classes, including anti-viral and anti-cancer agents, to broaden its application in drug discovery.

5. Conclusions

The treatment of hepatitis remains a significant challenge, necessitating the development of effective and efficient antiviral medications. This study highlights the utility of degree-based topological indices, derived through M-polynomial and NM-polynomial frameworks, in elucidating the structural features and physicochemical properties of eight anti-hepatitis prescription drugs. Statistical analysis revealed robust correlations between specific topological indices and critical physicochemical parameters, underscoring their predictive capability.

These findings provide a theoretical framework that bridges chemical graph theory and pharmaceutical research, offering valuable insights for optimizing existing treatments and guiding the rational design of novel antiviral agents. Furthermore, the incorporation of advanced indices, such as the Neighborhood Face Index, paves the way for improved predictive accuracy. Future work can extend this methodology to other drug classes, including anti-cancer and anti-viral compounds, and explore multi-variable regression models to further enhance QSPR modelling techniques.

Supplementary materials

This manuscript contains supplementary materials, which are available on the corresponding online page.

Data availability statement

No new data is created.

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Conflict of interest

The authors declare no conflict of interest.

Additional information

Website:

University of Alberta, https://www.ualberta.ca/en/index.html.

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