INDIAN JOURNAL OF SCIENCE AND TECHNOLOGY

RESEARCH ARTICLE

Temperature Index of Antiviral Drugs Used to Combat Viral Diseases

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OPEN ACCESS

Received: 13-02-2023
Accepted: 11-08-2023
Published: 04-12-2023

Citation: Baby A, Xavier DA, Nair AT, Varghese ES, Akhila S (2023) Temperature Index of Antiviral Drugs Used to Combat Viral Diseases. Indian Journal of Science and Technology 16(SP3): 64-74. https://doi.org/10.17485/IJST/v16iSP3.icrtam271

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Funding: None

Competing Interests: None

Published By Indian Society for Education and Environment (iSee)

ISSN
Print: 0974-6846
Electronic: 0974-5645

Abstract

Objective: To determine the temperature indices for antiviral drugs updated in WHO Disease Outbreak News such as Zika virus, Smallpox and Henipaviruses. Further, applying a regression analysis, the determined results can be used as a property predictive tool. **Method**: The degree counting techniques and edge partition approach is employed for computation of the temperature indices and applying the least square procedure the regression analysis model is extracted. **Findings**: The quantitative values of temperature indices for antiviral drugs used in treatment of few viral diseases are computed and a regression analysis based on the determined values are carried out in order to use as a property prediction tool. **Novelty**: Drug development and design have greatly benefited from the application of chemical graph theory. Temperature indices are pure mathematical descriptions of a molecular structure, which can be used as predictive tool in QSPR/QSAR research. The temperature indices for various chemical structures are being studied by researchers in order to obtain improved property-index correlation compared to that of those obtained through other topological indices.

Keywords: Temperature indices; Zika virus; Smallpox; Henipavirus; Antiviral drugs; Comparative analysis; Regression analysis

1 Introduction

Emergence of chemical graph theory significantly influenced the modern world. Graph theory was combined with chemistry and the concept of chemical graph theory was developed to describe the structures of molecules quantitatively. The idea of topological descriptors was first introduced by H. Wiener in 1947. Eventually, many other topological descriptors were introduced following the pioneering works of Wiener and Randic. Temperature indices are one of many topological descriptors that are important for studying structural properties and have numerous applications in structural chemistry. They are numerical values associated with the chemical structure and are used to correlate the chemical structure with its physical properties, chemical properties or biological activities [(1)].

A flavivirus spread by mosquitoes is the zika virus. In India, reports of the Zika virus have been made in recent years. Acetaminophen, Niclosamide, PHA-690509 and Emricasan are the main repurposed medications used to treat the infection. The variola virus, a member of the orthopoxvirus family, is responsible for smallpox. Tecovirimat, Cidofovir and Brincidofovir are the main antiviral medications used to treat smallpox. Smallpox immunisations, also known as Vaccinia virus vaccines, can prevent smallpox. The Asia-Pacific region is home to zoonotic diseases like henipaviruses. Two henipaviruses that affect people are hendra virus (HeV) and nipah virus (NiV). Additionally, the World Health Organization's Research and Development Blueprint has listed these illnesses as potential epidemic hazards. The repurposing medications used to combat these viruses are ribavirin and chloroquine.

A class of drugs known as analgesics and antipyretics includes acetaminophen. Niclosamide is a member of the anthelmintics drug class, which is used to treat worm diseases. An experimental drug called PHA-690509 inhibits cyclin-dependent kinase. The most effective anti-death substance, a pan-caspase inhibitor called emricasan, was discovered. A high-throughput screen in 2002 led to the discovery of the antiviral medication tecovirimat. It is recommended for use in treating adults and paediatric patients with the condition and is effective against all orthopoxviruses, including vaccinia, cowpox, ectromelia, rabbitpox and monkeypox. Patients who have impaired immune systems may experience less tecovirimat effectiveness. It lessens viremia and aids in stopping viral spread. Brincidofovir is a lipid mimic of cidofovir, and cidofovir is an antiviral drug that is categorized as a nucleotide analogue. Ribavirin belongs to the group of antiviral drugs known as nucleoside analogues. The medication chloroquine belongs to the 4-aminoquinoline pharmacological class and is an antimalarial and amebicide. In regions where malaria is still susceptible to its effects, chloroquine is primarily used to prevent and cure malaria. Rheumatoid arthritis, lupus erythematosus, and amebiasis that develops beyond the intestines are other conditions that may respond to chloroquine treatment. It functions by eradicating the parasites that cause amebiasis and malaria. Muscle issues, appetite loss, diarrhoea, and skin rashes are typical adverse effects. The molecular structures of the antiviral drug compounds are depicted in Figure 1.

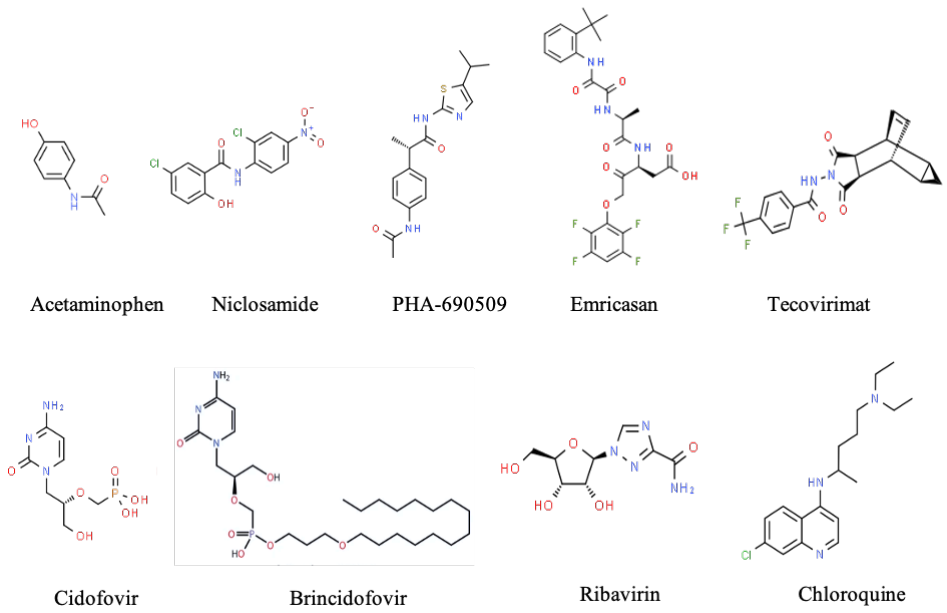

Fig 1. The repurposed medications used to combat Zika virus, Smallpox and Henipaviruses

The temperature indices for various chemical structures are being studied by researchers in order to obtain improved property-indices correlation results compared to that obtained through other topological indices. Studies on temperature indices of chemical networks can be seen in [2–4] and in [5,6], the study of temperature indices on medicinal drugs can be found. In this paper, the temperature indices of the aforementioned pharmacological compounds are examined. Researchers have recently looked at these drugs' distance based and degree based indices [7]. This paper is an extension of existing results on various indices of the drug compounds. Based on the computed results, a regression analysis was carried out and the corresponding outcomes are presented conclusively. The obtained results are further applied in Quantitative Structure - Property Relationship (QSPR) analysis.

2 Methodology

Consider a simple connected graph Φ, with vertex set $V(\Phi)$ and edge set $\Gamma(\Phi)$. The vertex set and edge set's cardinality are denoted as η and ξ respectively. The degree of a vertex $\alpha \in V(\Phi)$, written as d_α, is the number of edges incident to the vertex. The temperature of a vertex, $\alpha \in V(\Phi)$ is defined as

$$t_\alpha = \frac{\delta_\alpha}{\eta - \delta_\alpha} \tag{1}$$

Fajtlowicz defined the idea of vertex's temperature in 1987. The temperature based topological indices were subsequently introduced by V.R. Kulli [8,9] in response to this, and they are described in Table 1.

Table 1. The temperature based topological indices

S. No.	Temperature Index	Mathematical Expression
1	General First Temperature index	$T_1^\gamma(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} (t_\alpha + t_\beta)^\gamma$
2	General Second Temperature index	$T_2^\gamma(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} (t_\alpha \times t_\beta)^\gamma$
3	General Temperature index	$T_\gamma(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} \frac{1}{\sqrt{(t_\alpha)^\gamma + (t_\beta)^\gamma}}$
4	First Hyper Temperature index	$HT_1(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} (t_\alpha + t_\beta)^2$
5	Second Hyper Temperature index	$HT_2(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} (t_\alpha \times t_\beta)^2$
6	Sum Connectivity Temperature index	$ST(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} \frac{1}{\sqrt{t_\alpha + t_\beta}}$
7	Product Connectivity Temperature index	$PT(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} \frac{1}{\sqrt{t_\alpha \times t_\beta}}$
8	Reciprocal Product Connectivity Temperature index	$RPT(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} \sqrt{t_\alpha \times t_\beta}$
9	Forgotten Temperature index	$FT(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} \left((t_\alpha)^2 + (t_\beta)^2\right)$
10	Arithmetic-Geometric Temperature index	$AGT(\Phi) = \sum_{\alpha\beta \in \Gamma(\Phi)} \frac{t_\alpha + t_\beta}{2\sqrt{t_\alpha \times t_\beta}}$

The drug compounds can be redrawn as graph models, which enables the computation of temperature indices. Since the chemical structure's vertices and edges serve as our basis, we employ degree counting techniques and edge partition approach. The temperature indices of the antiviral drugs under consideration are calculated in the upcoming section applying this technique.

3 Results and Discussion

3.1 Theorems on Temperature Indices of Antiviral Medications

Theorem 1: Let A denote the chemical graph of Acetaminophen, then

$T_1^\gamma(A) = 2 \times \left(\frac{4}{9}\right)^\gamma + 3 \times \left(\frac{19}{40}\right)^\gamma + 6 \times \left(\frac{43}{72}\right)^\gamma$

$T_2^\gamma(A) = 2 \times \left(\frac{4}{81}\right)^\gamma + 3 \times \left(\frac{3}{80}\right)^\gamma + 6 \times \left(\frac{1}{12}\right)^\gamma$

$$T_\gamma(A) = \frac{2}{\left(2 \times \left(\frac{2}{9}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{3}{\left(\left(\frac{1}{10}\right)^\gamma + \left(\frac{3}{8}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{6}{\left(\left(\frac{2}{9}\right)^\gamma + \left(\frac{3}{8}\right)^\gamma\right)^{\frac{1}{2}}}$$

$$HT_1(A) = 3.2120, \quad HT_2(A) = 0.0508,$$

$$ST(A) = 15.1168, \quad PT(A) = 45.2765, \quad RPT(A) = 2.7574,$$

$$FT(A) = 1.7895, \quad AGT(A) = 11.8858.$$

Proof: Let A be the chemical graph for acetaminophen. The graph consists of 11 vertices and 11 edges. The vertex degree, d_α, $\alpha \in \Delta(A)$ are 1, 2 and 3. Figure 2**(A)** shows the temperature of each vertex of A as calculated using Equation (1). Based on the vertex temperature, it is seen that there are three edge partitions, $\left(\frac{1}{10}, \frac{3}{8}\right)$; $\left(\frac{2}{9}, \frac{2}{9}\right)$; $\left(\frac{2}{9}, \frac{3}{8}\right)$ and the corresponding edge counts

are 3, 2 and 6 respectively. The following outcomes are achieved by incorporating these data into the mathematical expressions shown in Table 1.

$$1.\ T_1^{\gamma}(A) = \sum_{\alpha\beta \in \Gamma(A)} (t_\alpha + t_\beta)^{\gamma} = 3 \times \left(\frac{1}{10} + \frac{3}{8}\right)^{\gamma} + 2 \times \left(\frac{2}{9} + \frac{2}{9}\right)^{\gamma} + 6 \times \left(\frac{2}{9} + \frac{3}{8}\right)^{\gamma}$$

$$= 2 \times \left(\frac{4}{9}\right)^{\gamma} + 3 \times \left(\frac{19}{40}\right)^{\gamma} + 6 \times \left(\frac{43}{72}\right)^{\gamma}$$

$$2.\ T_2^{\gamma}(A) = \sum_{\alpha\beta \in \Gamma(A)} (t_\alpha \times t_\beta)^{\gamma} = 3 \times \left(\frac{1}{10} \times \frac{3}{8}\right)^{\gamma} + 2 \times \left(\frac{2}{9} \times \frac{2}{9}\right)^{\gamma} + 6 \times \left(\frac{2}{9} \times \frac{3}{8}\right)^{\gamma}$$

$$= 2 \times \left(\frac{4}{81}\right)^{\gamma} + 3 \times \left(\frac{3}{80}\right)^{\gamma} + 6 \times \left(\frac{1}{12}\right)^{\gamma}$$

$$3.\ T_{\gamma}(A) = \sum_{\alpha\beta \in \Gamma(A)} \frac{1}{\sqrt{(t_\alpha)^{\gamma} + (t_\beta)^{\gamma}}} = 3 \times \frac{1}{\sqrt{\left(\frac{1}{10}\right)^{\gamma} + \left(\frac{3}{8}\right)^{\gamma}}} + 2 \times \frac{1}{\sqrt{\left(\frac{2}{9}\right)^{\gamma} + \left(\frac{2}{9}\right)^{\gamma}}} + 6 \times \frac{1}{\sqrt{\left(\frac{2}{9}\right)^{\gamma} + \left(\frac{3}{8}\right)^{\gamma}}}$$

$$= \frac{2}{\left(2 \times \left(\frac{2}{9}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{3}{\left(\left(\frac{1}{10}\right)^{\gamma} + \left(\frac{3}{8}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{6}{\left(\left(\frac{2}{9}\right)^{\gamma} + \left(\frac{3}{8}\right)^{\gamma}\right)^{\frac{1}{2}}}$$

$$4.\ HT_1(A) = \sum_{\alpha\beta \in \Gamma(A)} (t_\alpha + t_\beta)^2 = 3 \times \left(\frac{1}{10} + \frac{3}{8}\right)^2 + 2 \times \left(\frac{2}{9} + \frac{2}{9}\right)^2 + 6 \times \left(\frac{2}{9} + \frac{3}{8}\right)^2 = 3.2120$$

$$5.\ HT_2(A) = \sum_{\alpha\beta \in \Gamma(A)} (t_\alpha \times t_\beta)^2 = 3 \times \left(\frac{1}{10} \times \frac{3}{8}\right)^2 + 2 \times \left(\frac{2}{9} \times \frac{2}{9}\right)^2 + 6 \times \left(\frac{2}{9} \times \frac{3}{8}\right)^2 = 0.0508$$

$$6.\ ST(A) = \sum_{\alpha\beta \in \Gamma(A)} \frac{1}{\sqrt{t_\alpha + t_\beta}} = 3 \times \frac{1}{\sqrt{\frac{1}{10} + \frac{3}{8}}} + 2 \times \frac{1}{\sqrt{\frac{2}{9} + \frac{2}{9}}} + 6 \times \frac{1}{\sqrt{\frac{2}{9} + \frac{3}{8}}} = 15.1168$$

$$7.\ PT(A) = \sum_{\alpha\beta \in \Gamma(A)} \frac{1}{\sqrt{t_\alpha \times t_\beta}} = 3 \times \frac{1}{\sqrt{\frac{1}{10} \times \frac{3}{8}}} + 2 \times \frac{1}{\sqrt{\frac{2}{9} \times \frac{2}{9}}} + 6 \times \frac{1}{\sqrt{\frac{2}{9} \times \frac{3}{8}}} = 45.2765$$

$$8.\ RPT(A) = \sum_{\alpha\beta \in \Gamma(A)} \sqrt{t_\alpha \times t_\beta} = 3 \times \sqrt{\frac{1}{10} \times \frac{3}{8}} + 2 \times \sqrt{\frac{2}{9} \times \frac{2}{9}} + 6 \times \sqrt{\frac{2}{9} \times \frac{3}{8}} = 2.7574$$

$$9.\ FT(A) = \sum_{\alpha\beta \in \Gamma(A)} \left((t_\alpha)^2 + (t_\beta)^2\right) = 3 \times \left(\left(\frac{1}{10}\right)^2 + \left(\frac{3}{8}\right)^2\right) + 2 \times \left(\left(\frac{2}{9}\right)^2 + \left(\frac{2}{9}\right)^2\right) + 6 \times \left(\left(\frac{2}{9}\right)^2 + \left(\frac{3}{8}\right)^2\right) = 1.7895$$

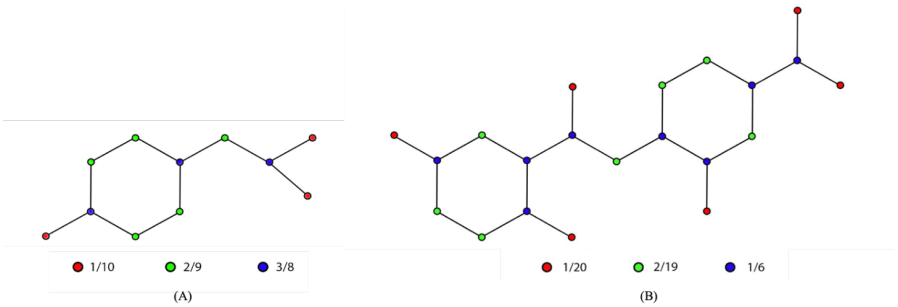

Fig 2. Vertex temperature of vertices in graph A and graph B

$$10.\ AGT(A) = \sum_{\alpha\beta \in \Gamma(A)} \frac{t_\alpha + t_\beta}{2\sqrt{t_\alpha \times t_\beta}} = 3 \times \frac{\frac{1}{10} + \frac{3}{8}}{2\sqrt{\frac{1}{10} \times \frac{3}{8}}} + 3 \times \frac{\frac{2}{9} + \frac{2}{9}}{2\sqrt{\frac{2}{9} \times \frac{2}{9}}} + 3 \times \frac{\frac{2}{9} + \frac{3}{8}}{2\sqrt{\frac{2}{9} \times \frac{3}{8}}}$$

$$= 11.8858$$

Theorem 2: Let B denote the chemical graph of Niclosamide, then
$T_1^\gamma(B) = 2 \times \left(\frac{4}{19}\right)^\gamma + 4 \times \left(\frac{1}{3}\right)^\gamma + 6 \times \left(\frac{13}{60}\right)^\gamma + 10 \times \left(\frac{31}{114}\right)^\gamma$
$T_2^\gamma(B) = 2 \times \left(\frac{4}{361}\right)^\gamma + 4 \times \left(\frac{1}{36}\right)^\gamma + 6 \times \left(\frac{1}{120}\right)^\gamma + 10 \times \left(\frac{1}{57}\right)^\gamma$

$$T_\gamma(B) = \frac{2}{\left(2 \times \left(\frac{2}{19}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{4}{\left(2 \times \left(\frac{1}{6}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{6}{\left(\left(\frac{1}{6}\right)^\gamma + \left(\frac{1}{20}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{10}{\left(\left(\frac{1}{6}\right)^\gamma + \left(\frac{2}{19}\right)^\gamma\right)^{\frac{1}{2}}}$$

$$HT_1(B) = 1.5542,\ HT_2(B) = 0.0068,$$

$$ST(B) = 43.3538,\ PT(B) = 184.2251,\ RPT(B) = 2.7494,$$

$$FT(B) = 0.8368,\ AGT(B) = 23.3855.$$

Proof: The niclosamide compound's chemical graph, designated B, has 21 vertices and 22 edges. Figure 2 **(B)** displays the temperature of each vertex of B as determined by Equation (1). Based on the vertex temperature, four edge partitions $\left(\frac{1}{20}, \frac{1}{6}\right)$; $\left(\frac{2}{19}, \frac{2}{19}\right)$; $\left(\frac{2}{19}, \frac{1}{6}\right)$; $\left(\frac{1}{6}, \frac{1}{6}\right)$ are derived, with respective edge counts of 6, 2, 10, and 4. Further, following the same proving procedure as in Theorem 1, the necessary results are obtained by putting these facts into the mathematical equations provided in Table 1.

Theorem 3: Let C denote the chemical graph of PHA-690509. Then
$T_1^\gamma(C) = 3 \times \left(\frac{3}{10}\right)^\gamma + 3 \times \left(\frac{4}{21}\right)^\gamma + 6 \times \left(\frac{43}{220}\right)^\gamma + 12 \times \left(\frac{103}{420}\right)^\gamma$
$T_2^\gamma(C) = 3 \times \left(\frac{9}{400}\right)^\gamma + 3 \times \left(\frac{4}{441}\right)^\gamma + 6 \times \left(\frac{3}{440}\right)^\gamma + 12 \times \left(\frac{1}{70}\right)^\gamma$

$$T_\gamma(C) = \frac{3}{\left(2 \times \left(\frac{3}{20}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{3}{\left(2 \times \left(\frac{2}{21}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{6}{\left(\left(\frac{1}{22}\right)^\gamma + \left(\frac{3}{20}\right)^\gamma\right)^{\frac{1}{2}}} + \frac{12}{\left(\left(\frac{2}{21}\right)^\gamma + \left(\frac{3}{20}\right)^\gamma\right)^{\frac{1}{2}}}$$

$$HT_1(C) = 1.3298,\ HT_2(C) = 0.0045,$$

$$ST(C) = 50.1545,\ PT(C) = 224.5628,\ RPT(C) = 2.6654,$$
$$FT(C) = 0.7157,\ AGT(C) = 25.4121.$$

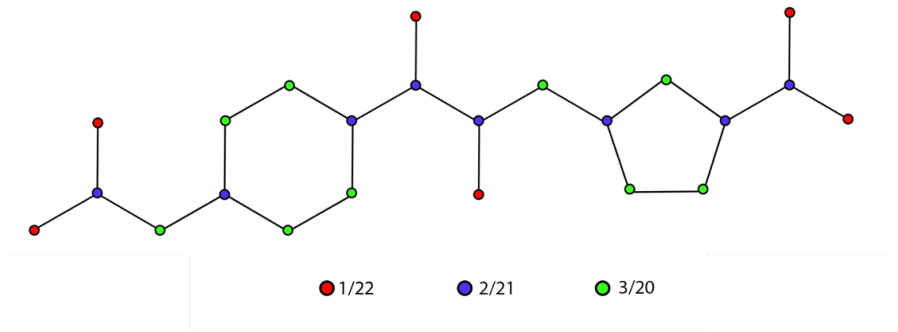

Fig 3. Vertex temperature of vertices in C

Proof: $\Delta(C) = 23$ and $\Gamma(C) = 24$. The temperature of each vertex of C is shown in Figure 3 and C has four edge partitions $\left(\frac{1}{22}, \frac{3}{20}\right)$; $\left(\frac{2}{21}, \frac{2}{21}\right)$; $\left(\frac{2}{21}, \frac{3}{20}\right)$; $\left(\frac{3}{20}, \frac{3}{20}\right)$, with edge count 6, 3, 12 and 3 based on the vertex temperatures, respectively.

The necessary results are attained by plugging these facts into the mathematical equations shown in Table 1 using the same method of proof as in Theorem 1.

Theorem 4: Let D denote the chemical graph of Emricasan. Then

$T_1^{\gamma}(D) = \left(\frac{64}{333}\right)^{\gamma} + 3 \times \left(\frac{16}{117}\right)^{\gamma} + 4 \times \left(\frac{2}{19}\right)^{\gamma} + 8 \times \left(\frac{6}{37}\right)^{\gamma} + 11 \times \left(\frac{154}{1443}\right)^{\gamma} + 14 \times \left(\frac{94}{703}\right)^{\gamma}$

$T_2^{\gamma}(D) = \left(\frac{1}{111}\right)^{\gamma} + 3 \times \left(\frac{1}{351}\right)^{\gamma} + 4 \times \left(\frac{1}{361}\right)^{\gamma} + 8 \times \left(\frac{9}{1369}\right)^{\gamma} + 11 \times \left(\frac{1}{481}\right)^{\gamma} + 14 \times \left(\frac{3}{703}\right)^{\gamma}$

$$T_{\gamma}(D) = \frac{1}{\left(\left(\frac{1}{9}\right)^{\gamma} + \left(\frac{3}{37}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{3}{\left(\left(\frac{1}{9}\right)^{\gamma} + \left(\frac{1}{39}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{4}{\left(2 \times \left(\frac{1}{19}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{8}{\left(2 \times \left(\frac{3}{37}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{11}{\left(\left(\frac{1}{39}\right)^{\gamma} + \left(\frac{3}{37}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{14}{\left(\left(\frac{1}{19}\right)^{\gamma} + \left(\frac{3}{37}\right)^{\gamma}\right)^{\frac{1}{2}}}$$

$$HT_1(D) = 0.7233, \; HT_2(D) = 0.000784,$$

$ST(D) = 114.5465$, $PT(D) = 696.9674$, $RPT(D) = 2.5303$,

$FT(D) = 0.3956$, $AGT(D) = 44.0569$.

Proof: $\Delta(D) = 40$ and $\Gamma(D) = 41$. Figure 4 displays the temperature of each vertex of D and D has six edge partitions $\left(\frac{1}{39}, \frac{3}{37}\right)$; $\left(\frac{1}{39}, \frac{1}{9}\right)$; $\left(\frac{1}{19}, \frac{1}{19}\right)$; $\left(\frac{1}{19}, \frac{3}{37}\right)$; $\left(\frac{3}{37}, \frac{3}{37}\right)$; $\left(\frac{3}{37}, \frac{1}{9}\right)$, with edge count 11, 3, 4, 14, 8 and 1 respectively.

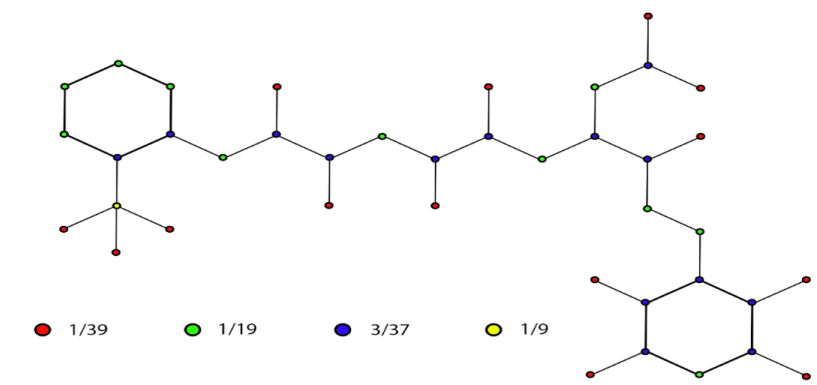

Fig 4. Vertex temperature of vertices in D

Using the same style of proof as in Theorem 1, the necessary outcomes are obtained by entering these facts into the mathematical equations displayed in Table 1.

Theorem 5: Let E denote the chemical graph of Tecovirimat. Then

$T_1^{\gamma}(E) = \left(\frac{55}{184}\right)^{\gamma} + 3 \times \left(\frac{4}{25}\right)^{\gamma} + 3 \times \left(\frac{17}{104}\right)^{\gamma} + 3 \times \left(\frac{127}{598}\right)^{\gamma} + 10 \times \left(\frac{41}{200}\right)^{\gamma} + 11 \times \left(\frac{1}{4}\right)^{\gamma}$

$$T_2^{\gamma}(E) = \left(\tfrac{1}{46}\right)^{\gamma} + 3\times\left(\tfrac{1}{208}\right)^{\gamma} + 3\times\left(\tfrac{2}{299}\right)^{\gamma} + 3\times\left(\tfrac{4}{625}\right)^{\gamma} + 10\times\left(\tfrac{1}{100}\right)^{\gamma} + 11\times\left(\tfrac{1}{64}\right)^{\gamma}$$

$$T_{\gamma}(E) = \frac{1}{\left(\left(\frac{1}{8}\right)^{\gamma}+\left(\frac{4}{23}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{3}{\left(\left(\frac{1}{8}\right)^{\gamma}+\left(\frac{1}{26}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{3}{\left(\left(\frac{1}{26}\right)^{\gamma}+\left(\frac{4}{23}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{3}{\left(2\times\left(\frac{2}{25}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{10}{\left(\left(\frac{1}{8}\right)^{\gamma}+\left(\frac{2}{25}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{11}{\left(2\times\left(\frac{1}{8}\right)^{\gamma}\right)^{\frac{1}{2}}}$$

$$HT_1(E) = 1.4894,\ HT_2(E) = 0.0045,$$

$ST(E) = 67.3454,\ PT(E) = 312.2300,\ RPT(E) = 3.2158,$
$FT(E) = 0.7948,\ AGT(E) = 32.6949.$

Proof: $\Delta(E) = 27$ and $\Gamma(E) = 31$. The temperature of each vertex of E is shown in Figure 5 and E contains six edge partitions $\left(\frac{1}{26},\frac{1}{8}\right)$; $\left(\frac{1}{26},\frac{4}{23}\right)$; $\left(\frac{2}{25},\frac{2}{25}\right)$; $\left(\frac{2}{25},\frac{1}{8}\right)$; $\left(\frac{1}{8},\frac{1}{8}\right)$; $\left(\frac{1}{8},\frac{4}{23}\right)$, with edge counts of 3, 3, 3, 10, 11 and 1 accordingly.

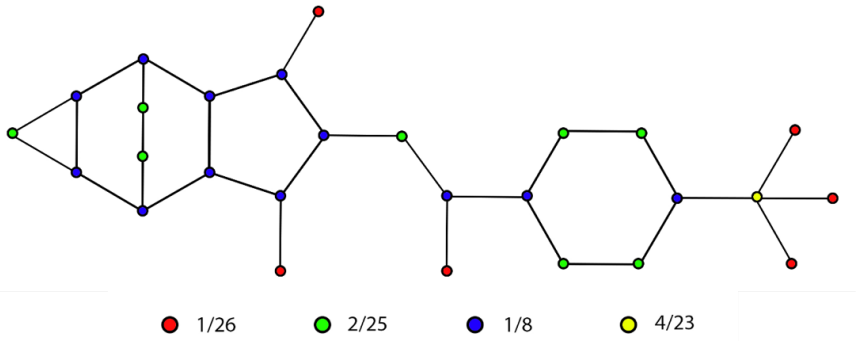

Fig 5. Vertex temperature of vertices in E

The relevant results are achieved by plugging these facts into the mathematical equations shown in Table 1 using the same method of proof as in Theorem 1.

Theorem 6: Let F denote the chemical graph of Cidofovir. Then

$$T_1^{\gamma}(F) = \left(\tfrac{2}{5}\right)^{\gamma} + \left(\tfrac{23}{56}\right)^{\gamma} + \left(\tfrac{25}{136}\right)^{\gamma} + 2\times\left(\tfrac{1}{4}\right)^{\gamma} + 2\times\left(\tfrac{22}{85}\right)^{\gamma} + 3\times\left(\tfrac{41}{119}\right)^{\gamma} + 8\times\left(\tfrac{13}{40}\right)^{\gamma}$$

$$T_2^{\gamma}(F) = \left(\tfrac{1}{25}\right)^{\gamma} + \left(\tfrac{1}{28}\right)^{\gamma} + \left(\tfrac{1}{136}\right)^{\gamma} + 2\times\left(\tfrac{1}{64}\right)^{\gamma} + 2\times\left(\tfrac{1}{85}\right)^{\gamma} + 3\times\left(\tfrac{2}{119}\right)^{\gamma} + 8\times\left(\tfrac{1}{40}\right)^{\gamma}$$

$$T_{\gamma}(F) = \frac{1}{\left(\left(\frac{1}{8}\right)^{\gamma}+\left(\frac{2}{7}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{1}{\left(\left(\frac{1}{8}\right)^{\gamma}+\left(\frac{1}{17}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{1}{\left(2\times\left(\frac{1}{5}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(\left(\frac{1}{5}\right)^{\gamma}+\left(\frac{1}{17}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(2\times\left(\frac{1}{8}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{3}{\left(\left(\frac{2}{7}\right)^{\gamma}+\left(\frac{1}{17}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{8}{\left(\left(\frac{1}{5}\right)^{\gamma}+\left(\frac{1}{8}\right)^{\gamma}\right)^{\frac{1}{2}}}$$

$$HT_1(F) = 1.8226,\ HT_2(F) = 0.0095,$$

$ST(F) = 32.5490,\ PT(F) = 130.1298,\ RPT(F) = 2.5955,$
$FT(F) = 1.0460,\ AGT(F) = 19.7531.$

Proof: $\Delta(F) = \Gamma(F) = 18$. Figure 6 (A) depicts the temperature of each vertex of F and F has seven edge partitions $\left(\frac{1}{17},\frac{1}{8}\right)$; $\left(\frac{1}{17},\frac{1}{5}\right)$; $\left(\frac{1}{17},\frac{2}{7}\right)$; $\left(\frac{1}{8},\frac{1}{8}\right)$; $\left(\frac{1}{8},\frac{1}{5}\right)$; $\left(\frac{1}{8},\frac{2}{7}\right)$; $\left(\frac{1}{5},\frac{1}{5}\right)$, with corresponding edge counts of 1, 2, 3, 2, 8, 1 and 1. Using the same style of proof as in Theorem 1, the required results are obtained by entering these facts into the mathematical equations displayed in Table 1.

Theorem 7: Let G denote the chemical graph of Brincidofovir. Then

$$T_1^{\gamma}(G) = \left(\tfrac{6}{35}\right)^{\gamma} + \left(\tfrac{55}{666}\right)^{\gamma} + 2\left(\left(\tfrac{53}{306}\right)^{\gamma} + \left(\tfrac{91}{629}\right)^{\gamma} + \left(\tfrac{146}{1295}\right)^{\gamma}\right) + 8\times\left(\tfrac{89}{630}\right)^{\gamma} + 22\times\left(\tfrac{1}{9}\right)^{\gamma},$$

$$T_2^{\gamma}(G) = \left(\tfrac{1}{666}\right)^{\gamma} + \left(\tfrac{9}{1225}\right)^{\gamma} + 2\left(\left(\tfrac{1}{153}\right)^{\gamma} + \left(\tfrac{2}{629}\right)^{\gamma} + \left(\tfrac{3}{1295}\right)^{\gamma}\right) + 8\times\left(\tfrac{1}{210}\right)^{\gamma} + 22\times\left(\tfrac{1}{324}\right)^{\gamma},$$

$$T_{\gamma}(G) = \frac{1}{\left(\left(\frac{1}{18}\right)^{\gamma}+\left(\frac{1}{37}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{1}{\left(2\times\left(\frac{3}{35}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(\left(\frac{1}{18}\right)^{\gamma}+\left(\frac{2}{17}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(\left(\frac{2}{17}\right)^{\gamma}+\left(\frac{1}{37}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(\left(\frac{1}{37}\right)^{\gamma}+\left(\frac{3}{35}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{8}{\left(\left(\frac{1}{18}\right)^{\gamma}+\left(\frac{3}{35}\right)^{\gamma}\right)^{\frac{1}{2}}} + \left(2\right.$$

$$HT_1(G) = 0.5948,\ HT_2(G) = 0.0005636,$$

$ST(G) = 109.1999,\ PT(G) = 651.1648,\ RPT(G) = 2.2695,$

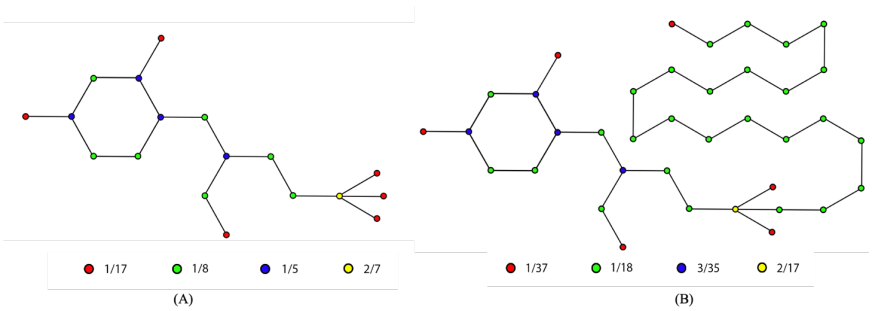

Fig 6. Vertex temperature of vertices in F and G

$FT(G) = 0.3169,\ AGT(G) = 39.3048.$

Proof: $\Delta(G) = \Gamma(G) = 38$. The edge partitions are $\left(\frac{1}{37},\frac{1}{18}\right);\left(\frac{1}{37},\frac{3}{35}\right);\left(\frac{1}{37},\frac{2}{17}\right);\left(\frac{1}{18},\frac{1}{18}\right);\left(\frac{1}{18},\frac{3}{35}\right);\left(\frac{1}{18},\frac{2}{17}\right);\left(\frac{3}{35},\frac{3}{35}\right)$, with edge count 1, 2, 2, 22, 8, 2 and 1 respectively, as in Figure 6 (B). These facts are entered into the mathematical equations shown in Table 1 to produce the necessary results using the same method of proof as in Theorem 1.

Theorem 8: Let H denote the chemical graph of Ribavirin.

$T_1^{\gamma}(H) = \left(\frac{4}{15}\right)^{\gamma} + \left(\frac{47}{240}\right)^{\gamma} + 4\times\left(\frac{31}{112}\right)^{\gamma} + 5\times\left(\frac{3}{7}\right)^{\gamma} + 7\times\left(\frac{73}{210}\right)^{\gamma}$

$T_2^{\gamma}(H) = \left(\frac{1}{120}\right)^{\gamma} + \left(\frac{4}{225}\right)^{\gamma} + 4\times\left(\frac{3}{224}\right)^{\gamma} + 5\times\left(\frac{9}{196}\right)^{\gamma} + 7\times\left(\frac{1}{35}\right)^{\gamma}$

$$T_{\gamma}(H) = \frac{1}{\left(\left(\frac{1}{16}\right)^{\gamma} + \left(\frac{2}{15}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{1}{\left(2\times\left(\frac{2}{15}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{4}{\left(\left(\frac{1}{16}\right)^{\gamma} + \left(\frac{3}{14}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{5}{\left(2\times\left(\frac{3}{14}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{7}{\left(\left(\frac{2}{15}\right)^{\gamma} + \left(\frac{3}{14}\right)^{\gamma}\right)^{\frac{1}{2}}}$$

$$HT_1(H) = 2.1801,\ HT_2(H) = 0.0174,$$

$ST(H) = 31.3095,\ PT(H) = 117.7643,\ RPT(H) = 2.9422,$

$FT(H) = 1.1616,\ AGT(H) = 19.0539.$

Proof: $\Delta(H) = 17$ and $\Gamma(H) = 18$. The temperature of each vertex of H is shown in Figure 7 (A). H includes five edge partitions, $\left(\frac{1}{16},\frac{2}{15}\right);\left(\frac{1}{16},\frac{3}{14}\right);\left(\frac{2}{15},\frac{2}{15}\right);\left(\frac{2}{15},\frac{3}{14}\right);\left(\frac{3}{14},\frac{3}{14}\right)$, with matching edge counts of 1, 4, 1, 7 and 5 respectively. The same method of proof used to prove Theorem 1 is applied to generate the required results using the mathematical expressions provided in Table 1.

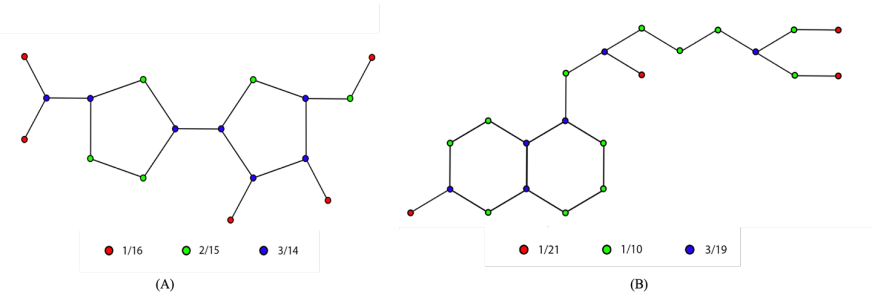

Fig 7. Vertex temperature of vertices in H and I

Theorem 9: Let I denote the chemical graph of Chloroquine. Then

$T_1^{\gamma}(I) = 2\times\left(\frac{6}{19}\right)^{\gamma} + 2\times\left(\frac{31}{210}\right)^{\gamma} + 2\times\left(\frac{82}{399}\right)^{\gamma} + 5\times\left(\frac{1}{5}\right)^{\gamma} + 12\times\left(\frac{49}{190}\right)^{\gamma}$

$T_2^{\gamma}(I) = 2\times\left(\frac{1}{133}\right)^{\gamma} + 2\times\left(\frac{1}{210}\right)^{\gamma} + 2\times\left(\frac{9}{361}\right)^{\gamma} + 5\times\left(\frac{1}{100}\right)^{\gamma} + 12\times\left(\frac{3}{190}\right)^{\gamma}$

$$T_{\gamma}(I) = \frac{2}{\left(\left(\frac{1}{10}\right)^{\gamma} + \left(\frac{1}{21}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(2\times\left(\frac{3}{19}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{2}{\left(\left(\frac{1}{21}\right)^{\gamma} + \left(\frac{3}{19}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{5}{\left(2\times\left(\frac{1}{10}\right)^{\gamma}\right)^{\frac{1}{2}}} + \frac{12}{\left(\left(\frac{1}{10}\right)^{\gamma} + \left(\frac{3}{19}\right)^{\gamma}\right)^{\frac{1}{2}}}$$

$$HT_1(I) = 1.3256,\ HT_2(I) = 0.0049,$$

$ST(I) = 47.9864,\ PT(I) = 210.2132,\ RPT(I) = 2.6351,$
$FT(I) = 0.6978,\ AGT(I) = 23.8236.$

Proof: $\Delta(I) = 22$ and $\Gamma(I) = 23$. With matching edge counts of 2, 2, 5, 12 and 2, I have five edge partitions: $\left(\frac{1}{21}, \frac{1}{10}\right); \left(\frac{1}{21}, \frac{3}{19}\right); \left(\frac{1}{10}, \frac{1}{10}\right); \left(\frac{1}{10}, \frac{3}{19}\right); \left(\frac{3}{19}, \frac{3}{19}\right)$ as depicted in Figure 7 (B). These facts are put through the same process of proof used to prove Theorem 1 in order to produce the necessary results.

3.2 Linear Regression Model for Molecular Weight of Antiviral Medications

Quantitative Structure-Property Relationships (QSPRs) are the eventual outcome of a process that begins with a suitable molecular structure descriptor and ends with some inference, hypothesis, and prediction on the behaviour, properties and characteristics of the molecule. In this section, the linear regression models for molecular weight of the antiviral drugs with their temperature indices are determined using the least square procedure. The following regression model is considered for the analysis.

$Y = a + b\,(X)$where a, b, Y, X stands for y-axis intercept, slope of the line, property of the drug and temperature index of the drug.

The molecular weight of the drugs in this study are given in Table 2 **,** which was taken from PubChem [10–17].

Table 2. The molecular weight of the antiviral medications

Antiviral Drug	Molecular Weight (g/mol)
Acetaminophen	151.16
Niclosamide	327.12
Emricasan	569.5
Tecovirimat	376.3
Cidofovir	279.19
Brincidofovir	561.7

The correlation coefficient, (R) of the temperature indices with the molecular weight of the antiviral medications given in Table 2 were determined with the help of MS Office Excel software analysis tools and the same are presented in Table 3.

Table 3. Correlation coefficient,(R) of temperature indices with molecular weight of drugs

Temperature Index	Correlation coefficient, (R)
First Hyper temperature index	0.9563
Second Hyper temperature index	0.7945
Sum Connectivity temperature index	0.9886
Product Connectivity temperature index	0.9787
Reciprocal Product Connectivity temperature index	0.4563
Forgotten temperature index	0.9563
Arithmetic-Geometric temperature index	0.9784

From the data in Table 3, the Sum Connectivity temperature index has the highest correlation with the molecular weight of the drugs. Hence, the linear regression model of the Sum Connectivity temperature index is best fitted among the temperature indices for the molecular weight and the linear regression equation can be given as,

$$M = 3.9487\,(SC) + 126.02$$

where, M is the molecular weight and SC is the Sum Connectivity temperature index of the drugs.

The scatter diagram of molecular weight with Sum Connectivity temperature index is obtained and is presented in Figure 8.

Using the linear regression model of the Sum Connectivity temperature index for the molecular weight, the molecular weight of ribavirin and chloroquine drugs can be predicted. The actual value and predicted values are given in Table 4.

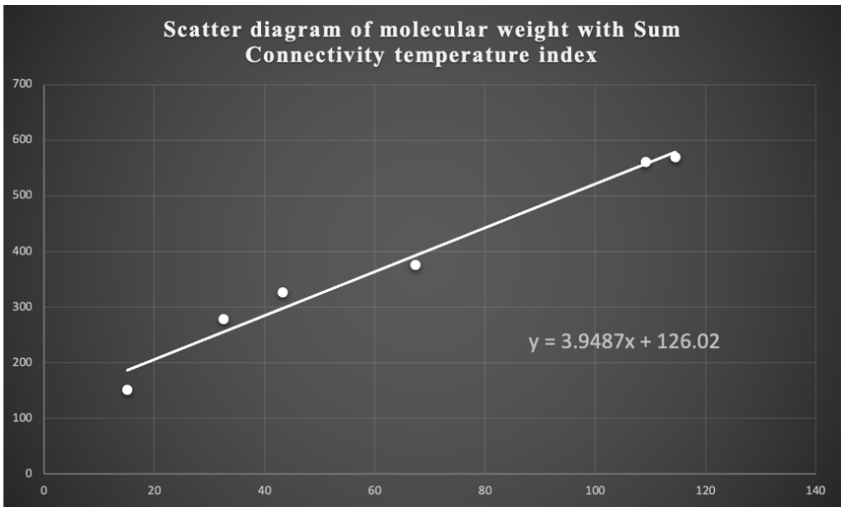

Fig 8. Scatter diagram of molecular weight with Sum Connectivity temperature index

Table 4. Predicted molecular weights of drugs using the linear regression model

Antiviral Drug	Molecular Weight (g/mol)	
	Actual	Predicted
Ribavirin	244.2	249.152
Chloroquine	319.9	315.504

It shows the reliability of topological descriptors in QSPR analysis. Hence, the major application of QSPR analysis is that it can be used to infer the properties, activities and behaviour of a newly designed or untested chemical compound from the molecular structure of similar compounds whose properties, activities and characteristics have already been evaluated.

4 Conclusion

Chemical scientists, medical researchers, and pharmaceutical researchers can employ temperature indices to analyse drug molecule's molecular structures to learn more about the chemical and biological properties of medications. They might be able to analyse the drug compounds in our study more successfully with the aid of our effort, which would also advance the field of medication development. We have determined values of the temperature indices for the drugs and they have undergone a regression analysis with respect to molecular weight and the obtained regression model has efficiently predicted the underlying property of certain other drugs. Hence, temperature indices can be used as a property prediction tool, thus they mark their presence in QSPR analysis. Hopefully, this work will aid in the development of drug design research.

5 Declaration

Presented in "International Conference on Recent Trends in Applied Mathematics (ICRTAM 2023)" during 24th -25th February 2023, organized by Department of Mathematics, Loyola College, Chennai, Tamil Nadu, India. The Organizers claim the peer review responsibility.

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