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On QSPR Analysis of Clinically Approved NNRTI Antiretroviral Drugs for Treatment of HIV-1 Via Temperature-Based Topological Indies

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Abstract

A potentially life-threatening illness, acquired immune deficiency syndrome affects 39 million individuals worldwide each year. Currently, several antiretroviral medications can help control the disease but cannot treat the human immunodeficiency type 1 virus that causes AIDS. In drug design, topological indices are crucial, aided by quantitative structure-property/activity relationship. In this study, the temperature- based topological indices are calculated using the molecular structure and physicochemical characteristics of non-nucleoside reverse transcriptase inhibitors, such as Nevirapine, Delavirdine, Efavirenz, Etravirine, and Rilpivirine, which are antiretroviral medications. We also examine the pertinent temperature-based topological indices, and it is shown that these indices have a strong correlation and can be used to predict the physicochemical characteristics of HIV-1 treatment medications using quantitative structure-property relationship analysis.

Keywords: HIV-1, NNRTIs Drugs, Temperature-Based Topological Indices, QSPR, Correlation-Regression Analysis.

Introduction

The present study examines the two lentiviruses responsible for AIDS, one of the most severe diseases that might lead to a global pandemic. The simian immunodeficiency virus was repeatedly spread among many animals before HIV-1 and HIV-2 infected humans. Gallo and Luc Montagnier were the first to reveal the isolation of HIV, the primary cause of AIDS, in 1983 [1,2]. However, studies in the 1950s and 1970s showed that HIV was found in both America and Africa and in the years that followed, hundreds of thousands of cases of the illness spread around the world. Two years later, in 1985, it was found that the AIDS epidemic was mainly caused by the human immunodeficiency virus type-2, which also caused a less severe form of immunodeficiency. Data on human immunodeficiency virus type-2 are currently lacking, and only a small number of subtypes have been found [3,4].

According to the International Committee for the Taxonomy of Viruses (ICTV), HIV belongs to the Orthoretrovirinae subfamily, the Reoviridae family, and the Lentivirus genus. The M (major), O (outlier), N (non-M, non-O), and P groups of the human immunodeficiency virus may be distinguished based on different genomic sequences from a distinct transmission event between species. A, B, C, D, F, G, H, J, and K are the nine subtypes of Group M, which is the most widely distributed group. 90% of all AIDS/HIV cases are caused by a Group M infection with the human immunodeficiency virus type-1 [5].

The significant distinctions between Type 1 and Type 2 human immunodeficiency virus shed light on the evolution, tropism, and pathogenesis of viruses. Specifically, compared to the human immunodeficiency virus type-1, type-2 is often less infectious and more difficult to disseminate. Antiretroviral medication therapy has so far been the most successful medical intervention for HIV-1 infection because of its ability to reduce

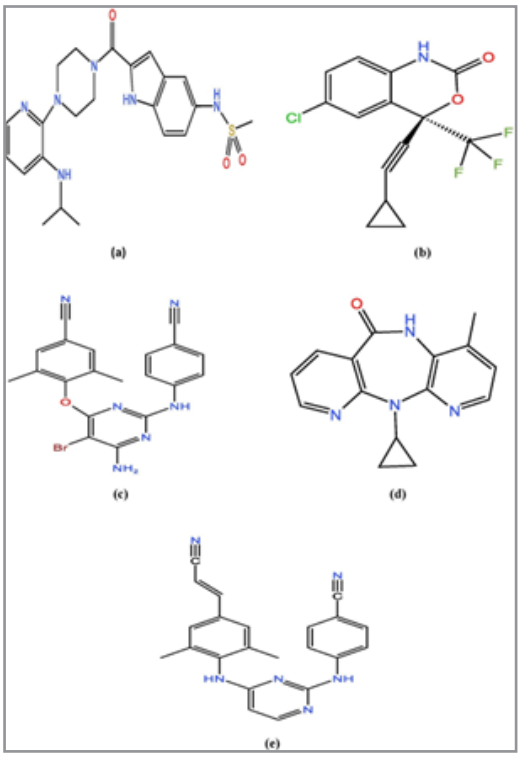

Figure 1: The molecular structure of (a)Delavirdine, (b)Efavirenz, (c)Etravirine, (d)Nevirapine (e)Rilpivirine

HIV-1 replication to undetectable levels. The Food and Drug Administration (FDA)-approved drugs may be used to treat human immunodeficiency virus type-1 infections. The drugs are categorized into six types according to their chemical mechanism and degree of resistance. Integrase inhibitors, protease inhibitors (PIs), fusion inhibitors, coreceptor antagonists, nucleoside reverse transcriptase inhibitors (NRTIs), and non-nucleoside reverse transcriptase inhibitors (NNRTIs) are the counterparts of the first six families of RTIs [6].

Non-nucleoside reverse transcriptase inhibitors are employed in this investigation. The currently advised regimens include an INSTI, a PI enhanced by ritonavir, or two NRTIs with an NNRTI. All of these combi- nations have been demonstrated to raise CD4 cell counts in the great majority of patients and lower HIV RNA levels (B50 copies/mL) after 48 weeks. Non-nucleoside reverse transcriptase inhibitor resistance is more prevalent than protease inhibitor resistance in people who have never taken antiretrovirals. Further- more, it has been demonstrated that patients on non-nucleoside reverse transcriptase inhibitors follow their treatment regimens more often than those taking protease inhibitors. Furthermore, some writers oppose the widespread use of protease inhibitor-based first-line therapy, even if it has more favorable resistance implications than non-nucleoside reverse transcriptase inhibitor-based first-line therapy.

This is due to a shortage of second-line regimens based on various antiretroviral classes for patients who have not responded to an initial antiretroviral treatment, as well as resource limitations in certain countries [7].

One disadvantage of PI-based regimens is the high number of drug interactions linked to them, which can make administering them more difficult for patients who are already on other medications. Compared to regimens based on PIs, drug interactions are less common in regimens using raltegravir, the most commonly used INSTI. However, raltegravir has a low genetic barrier to resistance, similar to non-nucleoside reverse transcriptase inhibitors. The fact that it must be taken twice daily is another disadvantage that relates to treatment adherence. Because of their increased risk of failure due to resistance, non-nucleoside reverse transcriptase inhibitors are frequently not recommended as components of second-line regimens. Conse- quently, antiretroviral drugs that are non-nucleoside reverse transcriptase inhibitors have been discovered. The first generation of non-ribosomal antibiotics (NRTIs) are nevirapine (NVP), delavirdine (DLV), and efavirenz (EFV). Because of their low genetic barrier, resistance can be acquired with a single mutation, and NNRTIs are commonly impacted by cross-resistance. The molecular structure of the five antiretro- viral medications is displayed in Figure 1. As a result, the FDA and the European Union approved Etravirine (ETR) and Rilpivirine (RPV), the first of the second generation of drugs. The next generation is currently in the clinical development stage. Along with current clinical data, this study covers pharma- cokinetics, metabolism, pharmacodynamics, safety, tolerability, and the impact of age, race, and gender variations on the safety and pharmacokinetics of marketed NNRTIs. When it comes to infection RNA resistance and DNA prevention, non-nucleoside reverse transcriptase inhibitor medications function better than other therapies. HIV-1 is treated with these antiretroviral medications, commonly known as non-nucleoside reverse transcriptase inhibitors. Temperature-based topological indices linked to non-nucleoside reverse transcriptase inhibitors may originate from quantitative structure-activity relationship (QSAR) studies, in which various topological characteristics of molecules are connected to their biological activities at various temperatures. Medications for the human immunodeficiency virus type 1. HIV-1 infection is treated with a family of medications called non-nucleoside reverse transcriptase inhibitors [8,9].

The fields of computational chemistry and cheminformatics known as Quantitative Structure- Activity/Property Relationship (QSAR) and QSPR aim to create mathematical models that relate the structural features of chemical compounds to their physical, chemical, or biological properties or activities. Chemical graph theory is crucial to QSPR and QSAR studies because it provides a frame- work for representing molecular structures as graphs and obtaining relevant information for predictive modeling. The chemical structure is crucial to drug design, molecular complexity, database selection, and isomer discrimination using QSPR in the study of chemical graph theory [10, 11]. Topological indices are numerical values derived from the graph representation of a molecule. In a molecular graph, atoms are represented by vertices and bonds by edges. Temperature-based topological indices are topological indices that are constructed using notions linked to temperature. The parameters establish a correlation between the temperature-dependent properties of HIV-1 medicines and the molecular structure. These indicators can be used to understand how the structural topology of a molecule influences its behavior concerning temperature. Temperature-Dependent Connectivity Indices and Temperature-Dependent Graph Theoretical Measures [12]. In quantitative structure-activity connection investigations, topological indices are mathe- metical descriptors that forecast a chemical compound's behavior based on its molecular structure. Sample size, slope, correlation coefficient, standard error of estimate, p-value, and other statistical parameters are more frequently used in regression analysis and hypothesis testing, although they can also be pertinent in the context of topological indices [13].

The graph G(V, E) with vertex set V (G) and edge set E(G) is connected if each pair of vertices in G has an edge linking them. In the chemical structure of the drugs that treat HIV-1, we pick a vertex with an atom and attach it to an edge. The graphs used in this research are simple, edge-limited, and loop-free. The number of edges incident to vertex v, denoted by dv, is its degree [14]. To investigate the impact of non-nucleoside reverse transcriptase inhibitor drugs, we use regression and correlation models using temperature-based topological metrics. QSPR models are used to predict the link between a compound's toxicity, property, or activity [15].

The idea of the temperature u of a vertex was first put out by Fajtlowicz in 1988. If G is a connected graph,

$$\mathbf{T(u)} = \frac{\mathbf{d_u}}{n-d}$$

where d(u) is the degree of vertex u and |V (G| = n.

Table 1: Topological indicators of 'G' depending on temperature.

Sum connectivity temperature index	$ST(G) = \sum_{uv \in E(G)} \frac{1}{\sqrt{T(u)+T(v)}}$
Product connectivity temperature index	$ST(G) = \sum_{uv \in E(G)} \frac{1}{\sqrt{T(u) \times T(v)}}$
Symmetric division temperature index	$SDT(G) = \sum_{uv \in E(G)} \left(\frac{T(u)}{T(v)} + \frac{T(v)}{T(u)}\right)$
F-temperature index	$FT(G) = \sum_{uv \in E(G)} (T(u)^2 + T(v)^2)$

A portion of temperature-based topological indicators that Kulli introduced in 2019 are shown in Table

These indicators provide information on certain applications, such as thermal stability, or system dynam- ics, by quantifying the structural characteristics of networks under temperature-dependent conditions. We can calculate the molecular structure of HIV-1 medications using the following temperature indices: F- temperature index, symmetric division temperature index, product connectivity temperature index, and sum connectivity temperature index [16]. The most appropriate temperature-based topological indices and linear regression analyses are obtained to predict the boiling point (BP), enthalpy of vaporization (E), flash point (FP), molar refractivity (MR), polar surface area (PSA), polarizability (P), surface, and molar volume (MV) of these drugs [17].

Methodology and Main Results

The molecular graphs of Nevirapine (N), Delavirdine (D), Efavirenz (Ef), Etravirine (Et), and Rilpivirine (R) shown in Figure 1. have these temperature-based topological indices in this section. These consist of the F-temperature index, symmetric division temperature index, product connectivity temperature index, and temperature-based sum connectivity temperature index [18].

Theorem 1. Let D be the molecular graph of Delavirdine, then
1. **ST(D)** = 84.036.
2. **PT(D)** = 439.747.
3. **SDT(D)** = 84.698.
4. **FT(D)** = 0.5208.

Proof. The molecular graph (D) of Delavirdine is shown, Figure 1(a), which has 32 vertices and 34 edges. we have the following four vertex partitions, $V_1 = \{u \in V(D) | d_u = 1\}$, $V_2 = \{u \in V(D) | d_u = 2\}$, $V_3 = \{u \in V(D) | d_u = 3\}$, $V_4 = \{u \in V(D) | d_u = 4\}$. Therefore, there are 6 edges partitions of D, Which is $E_{13} = \{uv \in E(D) | d_u = 1, dv = 3\}$, $E_{14} = \{uv \in E(D) | d_u = 1, d_v = 4\}$, $E_{22} = \{uv \in E(D) | d_u = 2, d_v = 2\}$, $E_{23} = \{uv \in E(D) | d_u = 2, d_v = 3\}$, $E_{24} = \{uv \in E(D) | d_u = 2, d_v = 4\}$, $E_{33} = \{uv \in E(D) | d_u = 3, d_v = 3\}$.

We can see that $|E_{13}| = 3$, $|E_{14}| = 3$, $|E_{22}| = 6$, $|E_{23}| = 17$, $|E_{24}| = 1$, $|E_{33}| = 4$ from the molecular graph of D.

The Sum Connectivity Temperature Index of D Is

$$ST(D) = \sum_{uv\in E(D)} \left(\frac{1}{\sqrt{T(u)+T(v)}}\right)$$
$$= 3\left(\frac{1}{\sqrt{\frac{1}{32-1}+\frac{3}{32-3}}}\right)+3\left(\frac{1}{\sqrt{\frac{1}{32-1}+\frac{4}{32-4}}}\right)+6\left(\frac{1}{\sqrt{\frac{2}{32-2}+\frac{2}{32-2}}}\right)+17\left(\frac{1}{\sqrt{\frac{2}{32-2}+\frac{3}{32-3}}}\right)$$
$$+ 1\left(\frac{1}{\sqrt{\frac{2}{32-2}+\frac{4}{32-4}}}\right)+4\left(\frac{1}{\sqrt{\frac{3}{32-3}+\frac{3}{32-3}}}\right)$$
$$= 84.036$$

The Product Connectivity Temperature Index of D Is

$$PT(D) = \sum_{uv\in E(D)} \left(\frac{1}{\sqrt{T(u)\times T(v)}}\right)$$
$$= 3\left(\frac{1}{\sqrt{\frac{1}{32-1}\times\frac{3}{32-3}}}\right)+3\left(\frac{1}{\sqrt{\frac{1}{32-1}\times\frac{4}{32-4}}}\right)+6\left(\frac{1}{\sqrt{\frac{2}{32-2}\times\frac{2}{32-2}}}\right)+17\left(\frac{1}{\sqrt{\frac{2}{32-2}\times\frac{3}{32-3}}}\right)$$
$$+ 1\left(\frac{1}{\sqrt{\frac{2}{32-2}\times\frac{4}{32-4}}}\right)+4\left(\frac{1}{\sqrt{\frac{3}{32-3}\times\frac{3}{32-3}}}\right)$$
$$= 439.747.$$

The Symmetric Division Temperature Index of D Is

$$SDT(D) = \sum_{uv\in E(D)} \frac{T(u)^2+T(v)^2}{T(u)\times T(v)}$$
$$= 3\left(\frac{(\frac{1}{32-1})^2+(\frac{3}{32-3})^2}{\frac{1}{32-1}\times\frac{3}{32-3}}\right)+3\left(\frac{(\frac{1}{32-1})^2+(\frac{4}{32-4})^2}{\frac{1}{32-1}\times\frac{4}{32-4}}\right)+6\left(\frac{(\frac{2}{32-2})^2+(\frac{2}{32-2})^2}{\frac{2}{32-2}\times\frac{2}{32-2}}\right)$$
$$+ 17\left(\frac{(\frac{2}{32-2})^2+(\frac{3}{32-3})^2}{\frac{2}{32-2}\times\frac{3}{32-3}}\right)+1\left(\frac{(\frac{2}{32-2})^2+(\frac{4}{32-4})^2}{\frac{2}{32-2}\times\frac{4}{32-4}}\right)+4\left(\frac{(\frac{3}{32-3})^2+(\frac{3}{32-3})^2}{\frac{3}{32-3}\times\frac{3}{32-3}}\right)$$

$$= 84.698.$$

The Forgotten Temperature Index of D Is

$$FT(D) = \sum_{uv\in E(D)} T(u)^2+T(v)^2$$
$$= 3((\frac{1}{32-1})^2+(\frac{3}{32-3})^2)+3((\frac{1}{32-1})^2+(\frac{4}{32-4})^2)+6((\frac{2}{32-2})^2+(\frac{2}{32-2})^2)$$
$$+ 17((\frac{2}{32-2})^2+(\frac{3}{32-3})^2)+1((\frac{2}{32-2})^2+(\frac{4}{32-4})^2)+4((\frac{3}{32-3})^2+(\frac{3}{32-3})^2)$$
$$= 0.5208.$$

Theorem 2. Let Ef be the molecular graph of Efavirenz, then
1. **ST(Ef)** = 42.2455.
2. **PT(Ef)** = 181.5738.
3. **SDT(Ef)** = 61.6563.
4. **FT(Ef)** = 1.07151.

Proof. The molecular graph (Ef) of Efavirenz is shown, Figure 1(b), which has 21 vertices and 23 edges. we have the following four vertex partitions, $V_1 = \{u \in V(Ef) | d_u = 1\}$, $V_2 = \{u \in V(Ef) | d_u = 2\}$, $V_3 = \{u \in V(Ef) | d_u = 3\}$, $V_4 = \{u \in V(Ef) | d_u = 4\}$. Therefore, there are 8 edge partitions of Ef, which is $E_{13} = \{uv \in E(Ef) | d_u = 1, d_v = 3\}$, $E_{14} = \{uv \in E(Ef) | d_u = 1, d_v = 4\}$, $E_{22} = \{uv \in E(Ef) | d_u = 2, d_v = 2\}$, $E_{23} = \{uv \in E(Ef) | d_u = 2, d_v = 3\}$, $E_{24} = \{uv \in E(Ef) | d_u = 2, d_v = 4\}$, $E_{33} = \{uv \in E(Ef) | d_u = 3, d_v = 3\}$, $E_{34} = \{uv \in E(Ef) | d_u = 3, d_v = 4\}$, $E_{44} = \{uv \in E(Ef) | d_u = 4, d_v = 4\}$.

We can see that $|E_{13}| = 2$, $|E_{14}| = 3$, $|E_{22}| = 3$, $|E_{23}| = 10$, $|E_{24}| = 2$, $|E_{33}| = 1$, $|E_{34}| = 1$, $|E_{44}| = 1$ from the molecular graph of Ef.

By substituting the values in the temperature-based topological index, we get

The Sum Connectivity Temperature Index of Ef Is

$$ST(Et) = \sum_{uv\in E(Et)} \left(\frac{1}{\sqrt{T(u)+T(v)}}\right)$$
$$= 6\left(\frac{1}{\sqrt{\frac{1}{26-1}+\frac{3}{26-3}}}\right)+2\left(\frac{1}{\sqrt{\frac{2}{26-2}+\frac{2}{26-2}}}\right)+16\left(\frac{1}{\sqrt{\frac{2}{26-2}+\frac{3}{26-3}}}\right)+4\left(\frac{1}{\sqrt{\frac{3}{26-3}+\frac{3}{26-3}}}\right)$$
$$= 59.4203.$$

The Product Connectivity Temperature Index of Ef Is

$$ST(Et) = \sum_{uv\in E(Et)} \left(\frac{1}{\sqrt{T(u)\times T(v)}}\right)$$
$$= 6\left(\frac{1}{\sqrt{\frac{1}{26-1}\times\frac{3}{26-3}}}\right)+2\left(\frac{1}{\sqrt{\frac{2}{26-2}\times\frac{2}{26-2}}}\right)+16\left(\frac{1}{\sqrt{\frac{2}{26-2}\times\frac{3}{26-3}}}\right)+4\left(\frac{1}{\sqrt{\frac{3}{26-3}\times\frac{3}{26-3}}}\right)$$
$$= 273.1995.$$

The Symmetric Division Temperature Index of Ef Is

$$SDT(Et) = \sum_{uv\in E(Et)} \frac{T(u)^2+T(v)^2}{T(u)\times T(v)}$$
$$= 6\left(\frac{(\frac{1}{26-1})^2+(\frac{3}{26-3})^2}{\frac{1}{26-1}\times\frac{3}{26-3}}\right)+2\left(\frac{(\frac{2}{26-2})^2+(\frac{2}{26-2})^2}{\frac{2}{26-2}\times\frac{2}{26-2}}\right)+16\left(\frac{(\frac{2}{26-2})^2+(\frac{3}{26-3})^2}{\frac{2}{26-2}\times\frac{3}{26-3}}\right)$$
$$+ 4\left(\frac{(\frac{3}{26-3})^2+(\frac{3}{26-3})^2}{\frac{3}{26-3}\times\frac{3}{26-3}}\right)$$
$$= 69.0844.$$

The Forgotten Temperature Index of Ef Is

$$FT(Et) = \sum_{uv\in E(Et)} T(u)^2+T(v)^2$$
$$= 6((\frac{1}{26-1})^2+(\frac{3}{26-3})^2)+2((\frac{2}{26-2})^2+(\frac{2}{26-2})^2)+16((\frac{2}{26-2})^2+(\frac{3}{26-3})^2)$$
$$+ 4((\frac{3}{26-3})^2+(\frac{3}{26-3})^2)$$
$$= 0.6579.$$

Theorem 3. Let Et be the molecular graph of Etravirine, then
1. **ST(Et)** = 59.4203.
2. **PT(Et)** = 273.1995.
3. **SDT(Et)** = 69.0844.
4. **FT(Et)** = 0.6579.

Proof. The molecular graph (Et) of etravirine is shown, Figure 1(c), which has 26 vertices and 28 edges. we have the following three vertex partitions, $V_1 = \{u \in V(Et) | d_u = 1\}$, $V_2 = \{u \in V(Et) | d_u = 2\}$, $V_3 = \{u \in V(Et) | d_u = 3\}$. Therefore, there are 4 edge partitions of Et, which is $E_{13} = \{uv \in E(Et) | d_u = 1, d_v = 3\}$, $E_{22} = \{uv \in E(Et) | d_u = 2, d_v = 2\}$, $E_{23} = \{uv \in E(Et) | d_u = 2, d_v = 3\}$, $E_{33} = \{uv \in E(Et) | d_u = 3, d_v = 3\}$. We can see that $|E_{13}| = 6$, $|E_{22}| = 2$, $|E_{23}| = 16$, $|E_{33}| = 4$ from the molecular graph of Et. By substituting the values in the temperature-based topological index, we get

The Sum Connectivity Temperature Index of Et Is

$$ST(N) = \sum_{uv\in E(N)} \left(\frac{1}{\sqrt{T(u)+T(v)}}\right)$$
$$= 2\left(\frac{1}{\sqrt{\frac{1}{20-1}+\frac{3}{20-3}}}\right)+6\left(\frac{1}{\sqrt{\frac{2}{20-2}+\frac{2}{20-2}}}\right)+8\left(\frac{1}{\sqrt{\frac{2}{20-2}+\frac{3}{20-3}}}\right)+7\left(\frac{1}{\sqrt{\frac{3}{20-3}+\frac{3}{20-3}}}\right)$$
$$= 43.6071.$$

The Product Connectivity Temperature Index of Et Is

$$ST(N) = \sum_{uv\in E(N)} \left(\frac{1}{\sqrt{T(u)\times T(v)}}\right)$$
$$= 2\left(\frac{1}{\sqrt{\frac{1}{20-1}\times\frac{3}{20-3}}}\right)+6\left(\frac{1}{\sqrt{\frac{2}{20-2}\times\frac{2}{20-2}}}\right)+8\left(\frac{1}{\sqrt{\frac{2}{20-2}\times\frac{3}{20-3}}}\right)+7\left(\frac{1}{\sqrt{\frac{3}{20-3}\times\frac{3}{20-3}}}\right)$$
$$= 135.5506.$$

The Symmetric Division Temperature Index of Et Is

$$SD\mathbf{T}(N) = \sum_{uv\in E(N)} \frac{\mathbf{T}(u)^2+\mathbf{T}(v)^2}{\mathbf{T}(u)\times\mathbf{T}(v)}$$
$$= 2(\frac{(\frac{1}{20-1})^2+(\frac{3}{20-3})^2}{\frac{1}{20-1}\times\frac{3}{20-3}} + 6(\frac{(\frac{2}{20-2})^2+(\frac{2}{20-2})^2}{\frac{2}{20-2}\times\frac{2}{20-2}}) + 8(\frac{(\frac{2}{20-2})^2+(\frac{3}{20-3})^2}{\frac{2}{20-2}\times\frac{3}{20-3}})$$
$$+ 7(\frac{(\frac{3}{20-3})^2+(\frac{3}{20-3})^2}{\frac{3}{20-3}\times\frac{3}{20-3}})$$
$$= 51.1095.$$

The Forgotten Temperature Index of Et Is

$$F\mathbf{T}(N) = \sum_{uv\in E(N)} \mathbf{T}(u)^2+\mathbf{T}(v)^2$$
$$= 2((\frac{1}{20-1})^2+(\frac{3}{20-3})^2) + 6((\frac{2}{20-2})^2+(\frac{2}{20-2})^2) + 8((\frac{2}{20-2})^2+(\frac{3}{20-3})^2)$$
$$+ 7((\frac{3}{20-3})^2+(\frac{3}{20-3})^2)$$
$$= 0.99985.$$

Theorem 4. Let N be the molecular graph of Nevirapine, then
1. **ST(N)** = 43.6071.
2. **PT(N)** = 135.5506.
3. **SDT(N)** = 51.1095.
4. **FT(N)** = 0.99985.

Proof. The molecular graph (N) of Nevirapine shows, Figure 1(d), which has 20 vertices and 23 edges. we have the following three vertex partitions, $V_1 = \{u \in V(N)|d_u = 1\}$, $V_2 = \{u \in V(N)|d_u = 2\}$, $V_3 = \{u \in V(N)|d_u = 3\}$. Therefore, there are 4 edge partitions of N, which is $E_{13} = \{uv \in E(N)|d_u = 1, d_v = 3\}$, $E_{22} = \{uv \in E(N)|d_u = 2, d_v = 2\}$, $E_{23} = \{uv \in E(N)|d_u = 2, d_v = 3\}$, $E_{33} = \{uv \in E(N)|d_u = 3, d_v = 3\}$. We can see that $|E_{13}| = 2$, $|E_{22}| = 6$, $|E_{23}| = 8$, $|E_{33}| = 7$ from the molecular graph of N. By substituting the values in the temperature-based topological index, we get

The Sum Connectivity Temperature Index of N Is

$$S\mathbf{T}(N) = \sum_{uv\in E(N)} (\frac{1}{\sqrt{\mathbf{T}(u)+\mathbf{T}(v)}})$$
$$= 2(\frac{1}{\sqrt{\frac{1}{20-1}+\frac{3}{20-3}}}) + 6(\frac{1}{\sqrt{\frac{2}{20-2}+\frac{2}{20-2}}}) + 8(\frac{1}{\sqrt{\frac{2}{20-2}+\frac{3}{20-3}}}) + 7(\frac{1}{\sqrt{\frac{3}{20-3}+\frac{3}{20-3}}})$$
$$= 43.6071.$$

The Product Connectivity Temperature Index of N Is

$$S\mathbf{T}(N) = \sum_{uv\in E(N)} (\frac{1}{\sqrt{\mathbf{T}(u)\times\mathbf{T}(v)}})$$
$$= 2(\frac{1}{\sqrt{\frac{1}{20-1}\times\frac{3}{20-3}}}) + 6(\frac{1}{\sqrt{\frac{2}{20-2}\times\frac{2}{20-2}}}) + 8(\frac{1}{\sqrt{\frac{2}{20-2}\times\frac{3}{20-3}}}) + 7(\frac{1}{\sqrt{\frac{3}{20-3}\times\frac{3}{20-3}}})$$
$$= 135.5506.$$

The Symmetric Division Temperature Index of N Is

$$SD\mathbf{T}(N) = \sum_{uv\in E(N)} \frac{\mathbf{T}(u)^2+\mathbf{T}(v)^2}{\mathbf{T}(u)\times\mathbf{T}(v)}$$
$$= 2(\frac{(\frac{1}{20-1})^2+(\frac{3}{20-3})^2}{\frac{1}{20-1}\times\frac{3}{20-3}} + 6(\frac{(\frac{2}{20-2})^2+(\frac{2}{20-2})^2}{\frac{2}{20-2}\times\frac{2}{20-2}}) + 8(\frac{(\frac{2}{20-2})^2+(\frac{3}{20-3})^2}{\frac{2}{20-2}\times\frac{3}{20-3}})$$
$$+ 7(\frac{(\frac{3}{20-3})^2+(\frac{3}{20-3})^2}{\frac{3}{20-3}\times\frac{3}{20-3}})$$
$$= 51.1095.$$

The Forgotten Temperature Index of N Is

$$F\mathbf{T}(N) = \sum_{uv\in E(N)} \mathbf{T}(u)^2+\mathbf{T}(v)^2$$
$$= 2((\frac{1}{20-1})^2+(\frac{3}{20-3})^2) + 6((\frac{2}{20-2})^2+(\frac{2}{20-2})^2) + 8((\frac{2}{20-2})^2+(\frac{3}{20-3})^2)$$
$$+ 7((\frac{3}{20-3})^2+(\frac{3}{20-3})^2)$$
$$= 0.99985.$$

Theorem 5. Let R be the molecular graph of Rilpivirine, then
1. **ST(R)** = 68.1186.
2. **PT(R)** = 287.4496.
3. **SDT(R)** = 64.7357.
4. **FT(R)** = 0.60916.

Proof. The molecular graph R of Rilpivirine shows n, Figure 1(e), which has 26 vertices and 28 edges. we have the following three vertex partitions, $V_1 = \{u \in V(R)|d_u = 1\}$, $V_2 = \{u \in V(R)|d_u = 2\}$, $V_3 = \{u \in V(R)|d_u = 3\}$. Therefore, there are 5 edge partitions of R, which is $E_{12} = \{uv \in E(R)|d_u = 1, d_v = 2\}$, $E_{13} = \{uv \in E(R)|d_u = 1, d_v = 3\}$, $E_{22} = \{uv \in E(R)|d_u = 2, d_v = 2\}$, $E_{23} = \{uv \in E(R)|d_u = 2, d_v = 3\}$, $E_{33} = \{uv \in E(R)|d_u = 3, d_v = 3\}$. We can see that $|E_{12}| = 1$, $|E_{13}| = 3$, $|E_{22}| = 5$, $|E_{23}| = 17$, $|E_{33}| = 2$ from the molecular graph of R. Again, like theorem 2.1, By substituting the values in temperature-based topological index, we get

The Sum Connectivity Temperature Index of R Is

$$S\mathbf{T}(R) = \sum_{uv\in E(R)} (\frac{1}{\sqrt{\mathbf{T}(u)+\mathbf{T}(v)}})$$
$$= 1(\frac{1}{\sqrt{\frac{1}{26-1}+\frac{2}{26-2}}}) + 3(\frac{1}{\sqrt{\frac{1}{26-1}+\frac{3}{26-3}}}) + 5(\frac{1}{\sqrt{\frac{2}{26-2}+\frac{2}{26-2}}}) + 17(\frac{1}{\sqrt{\frac{2}{26-2}+\frac{3}{26-3}}})$$
$$+ 2(\frac{1}{\sqrt{\frac{3}{26-3}+\frac{3}{26-3}}})$$
$$= 68.1186.$$

The Product Connectivity Temperature Index of R Is

$$S\mathbf{T}(R) = \sum_{uv\in E(R)} (\frac{1}{\sqrt{\mathbf{T}(u)+\mathbf{T}(v)}})$$
$$= 1(\frac{1}{\sqrt{\frac{1}{26-1}\times\frac{2}{26-2}}}) + 3(\frac{1}{\sqrt{\frac{1}{26-1}\times\frac{3}{26-3}}}) + 5(\frac{1}{\sqrt{\frac{2}{26-2}\times\frac{2}{26-2}}}) + 17(\frac{1}{\sqrt{\frac{2}{26-2}\times\frac{3}{26-3}}})$$
$$+ 2(\frac{1}{\sqrt{\frac{3}{26-3}\times\frac{3}{26-3}}})$$
$$= 287.4496.$$

The Symmetric Division Temperature Index of R Is

$$SD\mathbf{T}(R) = \sum_{uv\in E(R)} \frac{\mathbf{T}(u)^2+\mathbf{T}(v)^2}{\mathbf{T}(u)\times\mathbf{T}(v)}$$
$$= 1(\frac{(\frac{1}{26-1})^2+(\frac{3}{26-3})^2}{\frac{1}{26-1}\times\frac{3}{26-3}} + 3(\frac{(\frac{1}{26-1})^2+(\frac{3}{26-3})^2}{\frac{1}{26-1}\times\frac{3}{26-3}} + 5(\frac{(\frac{2}{26-2})^2+(\frac{2}{26-2})^2}{\frac{2}{26-2}\times\frac{2}{26-2}}) + 17(\frac{(\frac{2}{26-2})^2+(\frac{3}{26-3})^2}{\frac{2}{26-2}\times\frac{3}{26-3}})$$
$$+ 2(\frac{(\frac{3}{26-3})^2+(\frac{3}{26-3})^2}{\frac{3}{26-3}\times\frac{3}{26-3}})$$
$$= 64.7357.$$

The Forgotten Temperature Index of R Is

$$F\mathbf{T}(R) = \sum_{uv\in E(R)} \mathbf{T}(u)^2+\mathbf{T}(v)^2$$
$$= 1((\frac{1}{26-1})^2+(\frac{3}{26-3})^2) + 3((\frac{1}{26-1})^2+(\frac{3}{26-3})^2) + 5((\frac{2}{26-2})^2+(\frac{2}{26-2})^2)$$
$$+ 17((\frac{2}{26-2})^2+(\frac{3}{26-3})^2) + 2((\frac{3}{26-3})^2+(\frac{3}{26-3})^2)$$
$$= 0.60916.$$

Qspr Analysis of Computed Results and Discussion

This section computes the temperature topological indices for the NNRTI drugs used to treat HIV-1. Exam- inning the QSPR analysis of the indicators, it is demonstrated that these indices and the physicochemical properties of the NNRTI drugs used to treat HIV-1 have a substantial link. We collect data on the physico- chemical properties of NNRTI drugs using Chemspider, and we compute regression and correlation models using SPSS software.

The five NNRTI drugs that are clinically used in HIV-1 therapy-nevirapine, delavirdine, efavirenz, etravirine, and rilpivirinewere included in the analysis. The molecular structure of the drugs

is shown in Figure 1. In a graph representation, the bonds are termed its edges, and the atoms are called its vertices [19].

Regression Models

Each of the five drugs' physical properties surface tension, polarizability, polar surface area, enthalpy, flash point, molar refraction, boiling temperatures, and molar volume are analyzed. A linear regression model was used in this study; the model is shown below.

P = A + B[TI]

where TI → is the topological descriptor, A,B → constants, and P → is the drug's physical property. The regression model for the aforementioned topological indices is developed using the linear regression equation discussed.

Using the previously provided linear regression equation, the regression model for the aforementioned topological indices is defined. Physical properties of NNRTI drugs are considered dependent variables, but topological indices for the molecular graphs of five drugs are considered independent factors. To create a linear regression model with SPSS software, the constants A and B in the regression equation are calculated using the training set in Tables 2 and 3. The linear regression equation previously described is used to create the regression model for the topological indices listed above.

Models Of Regression for the Total Connectivity Temperature Index St(G)

- Boiling Point = 11.3921 + 9.0689 [TI]
- Enthalpy = 16.8388 + 1.1265 [TI]
- Flash Point = -39.324 + 5.4849 [TI]
- Molar Refraction = 15.8474 + 1.3445 [TI]
- Polar Surface Area = -20.669 + 1.7998 [TI]
- Polarizability = 6.22066 + 0.5342 [TI]
- Surface Tension = 47.7141 + 0.3685 [TI]
- Molar Volume = 66.3335 + 3.2286 [TI]

Models Of Regression for the Product Connectivity Temperature Index Pt(G)

- Boiling Point = 179.7251 + 1.4243 [TI]
- Enthalpy = 37.6517 + 0.1773 [TI]
- Flash Point = 62.4787 + 0.88614 [TI]
- Molar Refraction = 40.1977 + 0.2134 [TI]
- Polar Surface Area = 9.40178 + 0.2954 [TI]
- Polarizability = 15.8972 + 0.08481 [TI]
- Surface Tension = 53.5503 + 0.0617 [TI]
- Molar Volume = 124.1361 + 0.5152 [TI]

Models Of Regression for the Symmetric Division Temperature Index Sdt(G)

- Boiling Point = -165.3884 + 10.847 [TI]
- Enthalpy = -6.04671 + 1.36144 [TI]
- Flash Point = -146.2633 + 6.561 [TI]
- Molar Refraction = -14.99443 + 1.6782 [TI]
- Polar Surface Area = -60.6605 + 2.2269 [TI]
- Polarizability = -6.0186 + 0.66658 [TI]
- Surface Tension = 45.0936 + 0.37181 [TI]
- Molar Volume = -16.3354 + 4.1602 [TI]

Models Of Regression for the Forgotten Temperature Index Ft(G)

- Boiling Point = 1066.61 - 666.67 [TI]
- Enthalpy = 147.406 - 82.151 [TI]
- Flash Point = 598.883 - 403.21 [TI]
- Molar Refraction = 170.062 - 95.954 [TI]
- Polar Surface Area = 196.691 - 142.59 [TI]
- Polarizability = 67.5031 - 38.136 [TI]
- Surface Tension = 98.8788 - 37.819 [TI]
- Molar Volume = 430.214 - 222.08 [TI]

Temperature-Dependent Topological Index Correlation Coefficients with a Limited Set of Physical and Statistical Factors

Table 2 provides eight physicochemical features of NNRTI antiretroviral drugs included in the study. The data accessibility details for NNRTI antiretroviral drugs with ChemSpider ID references are shown in Table 20. The temperature-based topological indicators are calculated and tabulated in Table 3 according to the methodology section. With possible uses in drug optimization, Table 4 shows the significance of the correlation between temperature-based topological indicators and the physicochemical properties of HIV-1 NNRTI drugs. In addition, it is used to forecast the effects of temperature variations on the drug's stability, solubility, absorption, and overall therapeutic efficacy.

The statistical properties for each of the four topological indices listed above are analyzed for the QSPR investigation: p-value, standard error of estimate, correlation coefficient (R), percentage of the dependent variable (R2), slope (b), constant (A), and sample size (N). A higher p-value indicates that changes in the predictor are unrelated to changes in the responder. Each term's p-value is used to test the null hypothesis.

Table 2: The Pharmacological Properties of HIV-1 (NNRTI) Treatments.

DRUGS	BP	E	FP	MR	PSA	P	T	MV
Delavirdine	732	106.8	396.5	124.3	119	49.3	72.3	328.8
Efavirenz	340.6	58.4	159.8	68.4	38	27.1	51.3	205.3
Etravirine	637.4	94.2	339.3	106.9	121	42.4	86.2	275.7
Nevirapine	415.4	66.8	205	73.7	58	29.2	66.3	197
Rilpivirine	634.1	93.7	337.3	106.6	97	42.3	72.3	287

Table 3: Computed Topological Indicators that are Depending on Temperature for HIV-1 (NNRTI) Drugs.

INDICES	Sum connectivity temperature index	Product connectivity temperature index	Symmetric division temperature index	F-temperature index
DRUGS	ST(G)	PT(G)	SDT(G)	FT(G)
Delavirdine	84.036	439.747	84.698	0.5208
Efavirenz	42.2455	181.5738	61.6563	1.07151
Etravirine	59.4203	273.1995	69.0844	0.6579
Nevirapine	43.6071	135.5506	51.1095	0.99985
Rilpivirine	68.1186	287.4496	64.7357	0.60916

Table 4: The Correlation Coefficient between the Physicochemical Properties of HIV-1 Antiretroviral Medications and the Topological Indicators.

INDICES	BP	E	FP	MR	PSA	P	T	MV
ST(G)	0.9352	0.94211	0.93519	0.95973	0.82761	0.95964	0.49937	0.98033
PT(G)	0.9228	0.93155	0.92279	0.95738	0.85349	0.95723	0.52546	0.98282
SDT(G)	0.7951	0.80936	0.79518	0.85157	0.72793	0.85119	0.35811	0.89794
FT(G)	-0.994	-0.99329	-0.99394	-0.99026	-0.94796	-0.99044	-0.74086	-0.97488

Table 5: Statistical parameters for the QSPR linear regression model for ST(G).

Phy.	N	A	B	R	R2	Standard	p	Indicator
Prop.						error of		
BP	5	11.3921	9.0689	0.93519	0.87458	6.98	0.0009	significant
E	5	16.6388	1.1265	0.94211	0.88757	6.61	0.0008	significant
FP	5	-39.324	5.4849	0.93519	0.87458	6.98	0.0018	significant
MR	5	15.8474	1.3445	0.95973	0.92108	5.54	0.0004	significant
PSA	5	-20.669	1.7998	0.82761	0.68494	11.07	0.036	significant
P	5	6.22066	0.5342	0.95964	0.92091	5.55	0.0022	significant
T	5	47.7141	0.3685	0.49937	0.24937	17.09	0.107	insignificant
MV	5	66.3335	3.2286	0.98033	0.96105	3.89	0.0001	significant

Table 6: Statistical parameters for the QSPR linear regression model for PT(G

Phy.	N	A	B	R	R2	Standard	p	Indicator
Prop.						error of		
						Estimate		
BP	5	179.7251	1.4243	0.92276	0.85148	47.76	0.0005	significant
E	5	37.6517	0.1773	0.93155	0.86778	45.1	0.0055	significant
FP	5	62.4787	0.88614	0.92279	0.85154	47.8	0.11	insignificant
MR	5	40.1977	0.2134	0.95738	0.91658	35.79	0.006	significant
PSA	5	9.40178	0.2954	0.85349	0.72844	64.6	0.0037	significant
P	5	15.8972	0.08481	0.95723	0.91628	35.85	0.003	significant
T	5	53.5503	0.0617	0.52546	0.2761	105.44	0.0066	significant
MV	5	124.1361	0.5152	0.98282	0.96593	22.87	0.45	insignificant

Note that the R-value exceeds 0.6 and the p-value is less than 0.05. Each characteristic has a high value as a result.

The statistical parameters for each of the physical attributes linked to temperature-based indicators are provided in Tables 5, 6, 7, and 8, which have uses in stability analysis and medication optimization. When developing temperature-based indices for NNRTI medications, statistical considerations are crucial in ranking to ensure drug stability, predict pharmacokinetic behavior, and optimize clinical performance across a range of temperature settings.

Regression analysis provides a strong foundation for comprehending and forecasting how temperature affects the physicochemical characteristics of HIV-1 NNRTI medications by comparing computed values

Table 7: Statistical parameters for the QSPR linear regression model for SDT(G)

Phy.	N	A	B	R	R2	Standard	p	Indicator	
Prop.							error of		
							Estimate		
BP	5	-165.3884	10.847	0.79515	0.63226	8.504	0.0011	significant	
E	5	-6.04671	1.36144	0.80936	0.65506	8.235	0.017	significant	
FP	5	-146.2633	6.561	0.79518	0.63231	8.5	0.002	significant	
MR	5	-14.99443	1.6782	0.85157	0.72517	7.35	0.005	significant	
PSA	5	-60.6605	2.2269	0.72793	0.52988	9.61	0.097	insignificant	
P	5	-6.0186	0.66658	0.85119	0.72452	7.35	0.0003	significant	
T	5	45.0936	0.37181	0.35811	0.12824	13.09	0.3	insignificant	
MV	5	-16.3354	4.1602	0.89794	0.80629	6.17	0.0003	significant	

Table 8: Statistical parameters for the QSPR linear regression model for FT(G)

Phy.	N	A	B	R	R2	Standard	p	Indicator	
Prop.									
							error of		
							Estimate		
BP	5	1066.61	-666.67	-0.994	0.98803	0.031	0.0008	significant	
E	5	147.406	-82.151	-0.99329	0.98662	0.03	0.0004	significant	
FP	5	598.883	-403.21	-0.9933	0.98664	0.032	0.0015	significant	
MR	5	170.062	-95.954	-0.99026	0.98061	0.039	0.0004	significant	
PSA	5	196.691	-142.59	-0.94796	0.89862	0.09	0.003	significant	
P	5	67.5031	-38.136	-0.99044	0.98097	0.03	0.0005	significant	
T	5	98.8788	-37.819	-0.74086	0.54887	0.191	0.0001	significant	
MV	5	430.214	-222.08	-0.97488	0.95039	0.063	0.0002	significant	

Table 9: Comparison between physical properties and computed values for boiling point from regression models of TIs.

DRUGS	BOILING POINT FT(G)		ST(G)	PT(G)	SDT(G)
	°C(at 760 mmhg)				
Delavirdine	732±70.0	772.6	764.7	750.7	719.4
Efavirenz	340.6±42.0	406.4	438.3	503.4	353.3
Etravirine	637.4±65.0	550.3	594.4	541	627.9
Nevirapine	415.4±45.0	406.8	372.2	388.9	406.6
Rilpivirine	634.1±65.0	623.2	589	536.8	660.6

Table 10: Comparison between physical properties and computed values for enthalpy from regression models of TIs.

DRUGS	ENTHALPY OF ST(G) FT(G)		PT(G)		SDT(G)
VAPORIZATION					
Kj/mol					
Delavirdine	106.8±3.0	111.3	110.5	108.9	106.3
Efavirenz	58.4±3.0	65.9	69.8	77.9	59.5
Etravirine	94.2±3.0	83.7	89.2	87.4	98.1
Nevirapine	66.8±3.0	65.9	61.6	63.5	66.1
Rilpivirine	93.7±3.0	92.8	88.5	82.1	97.4

Table 11: Comparison between physical properties and computed values for flash point from regression models of TIs.

DRUGS	FLASH POINT ST(G) °C		PT(G)	SDT(G)	FT(G)
Delavirdine	396.5±35.7	421.1	416.3	408.4	397.3
Efavirenz	159.8±27.9	199.6	218.8	258.3	167.4
Etravirine	339.3±34.3	286.5	313.3	304.3	333.5
Nevirapine	205±28.7	199.8	179.2	189.1	199.7
Rilpivirine	337.3±34.3	330.7	310.1	278.5	353.3

from temperature-based topological indices with actual experimental data. The prediction values of HIV- 1 NNRTI drugs, which are used in drug effectiveness, stability analysis, and optimization, are determined using temperature-based topological indices and their physical properties are shown in Tables 9, 10, 11, 12, 13, 14, 15, and 16.

Table 12: Comparison between physical properties and computed values for molar refraction from regression models of TIs.

DRUGS	MOLAR	ST(G)	PT(G)	SDT(G)	FT(G)
			REFRACTIVITY cm3		
Delavirdine	124.3±0.4	128.7	127.8	126.7	122.1
Efavirenz	68.4±0.4	90.1	78.9	88.5	67.4
Etravirine	106.9±0.4	95.7	102.3	100.2	106.9
Nevirapine	73.7±0.3	74.5	69.1	70.7	75.1
Rilpivirine	106.6±0.4	106.5	101.5	93.6	111.6

Table 13: Comparison between physical properties and computed values for polar surface area from regression models of TIs.

DRUGS	POLAR SURFACE AREA ˚A2	ST(G)	PT(G)	SDT(G)	FT(G)
Delavirdine	119	130.4	130.7	127.4	122.5
Efavirenz	38	57.7	63	76.6	44.1
Etravirine	121	86.3	95.4	92.3	102.8
Nevirapine	58	57.8	49.4	53.2	55.5
Rilpivirine	97	100.7	94.2	83.5	109.8

Table 14: Comparison between physical properties and computed values for polarizability from regression models of TIs.

DRUGS	POLARIZABILITY		ST(G)		PT(G)
10−24cm3					
Delavirdine	49.3±0.5	51.1	50.8	50.3	48.4
Efavirenz	27.1±0.5	29.5	31.3	35.1	27
Etravirine	42.4±0.5	37.9	40.6	39.7	42.4
Nevirapine	29.2±0.5	29.5	27.4	28	29.7
Rilpivirine	42.3±0.5	42.2	40.2	37.1	44.3

Table 15: Comparison between physical properties and computed values for surface tension from regression models of TIs.

DRUGS	SURFACE TENSION SDT(G) FT(G)		ST(G)		PT(G)
dyne/cm					
Delavirdine	72.3±3.0	78.6	78.8	76.4	79.3
Efavirenz	51.3±5.0	63.7	64.6	68	58.4
Etravirine	86.2±5.0	69.6	71.5	70.6	73.9
Nevirapine	66.3±3.0	63.7	61.9	64.1	61.4
Rilpivirine	72.3±5.0	72.5	71.3	69.2	75.8

Table 16: Comparison between physical properties and computed values for molar volume from regression models of TIs.

DRUGS	MOLAR VOLUME cm3	ST(G)	PT(G)	SDT(G)	FT(G)
Delavirdine	328.8±5.0	337.3	335.7	335	319.2
Efavirenz	205.3±5.0	206.9	217.6	240.2	192.3
Etravirine	275.7±5.0	258.1	274.1	269.3	284.1
Nevirapine	197±5.0	207.1	193.9	196.3	210.4
Rilpivirine	287±5.0	284.1	272.2	252.9	294.9

Comparing Temperature-Based and Degree-Based Topological Indices for the Qspr Analysis of Hiv-1 (Nnrti) Medications.

We have provided some degree-based topological indices (sum-connectivity index, product-connectivity index, symmetric division index, and forgotten index) for the QSPR study of certain HIV-1 drugs (Nevi- rapine, Delavirdine, Efavirenz, Etravirine, and Rilpivirine). To help with drug effectiveness prediction and optimization, Table 17 offers topological indices that are used to compute values for HIV-1 NNRTI medica-tions. The calculated values of temperature-based topological indicators that are employed in regression and correlation models to fore-

cast the physical properties of HIV-1 medications are shown in Table 18. In Table 19, we employ the SPSS software's linear regression model to ascertain the relationship between topological indices and the physicochemical properties of several HIV-1 treatment drugs. It is evident from Tables 4 and 19 that.

Table 17: Degree-based topological indices of G.

Sum connectivity index	$S(G) = \sum_{u,v \in E(G)} \frac{1}{\sqrt{d_u + d_v}}$
Product connectivity index	$P(G) = \sum_{u,v \in E(G)} \frac{1}{\sqrt{d_u \times d_v}}$
Symmetric division index	$SD(G) = \sum_{u,v \in E(G)} (\frac{d_u}{d_v} + \frac{d_v}{d_u})$
Forgotten index	$F(G) = \sum_{u,v \in E(G)} (d_u^2 + d_v^2)$

Table 18: Derived values of degree-based topological indices using various drugs

DRUGS INDICES	Sum connectivity index	Product connectivity index	Symmetric division index	Forgotten index
	SCI(G)	PCI(G)	SDD(G)	F(G)
Delavirdine	15.483	14.859	82.083	442
Efavirenz	10.268	12.985	58.167	340
Etravirine	12.783	12.32	66.67	356
Nevirapine	10.44	9.75	50	298
Rilpivirine	13	12.542	63.33	332

Table 19: correlation between physical properties and degree-based topological indices.

INDICES	BP	E	FP	MR	PSA	P	T	MV
SCI(G)	0.95366	0.96044	0.95365	0.97576	0.8753	0.97556	0.57124	0.98285
PCI(G)	0.56552	0.58341	0.56559	0.64604	0.46239	0.64585	0.04006	0.74606
SDD(G)	0.83495	0.84795	0.83499	0.88535	0.76727	0.885	0.40766	0.92354
F(G)	0.69644	0.71358	0.69646	0.76046	0.62241	0.75985	0.24065	0.8085

• The temperature-based topological indices of PT(G) outperform the degree-based topological indices of P(G) in terms of physicochemical properties.
• The degree-based topological indices of S(G) perform better than the temperature-based topological
indices of ST(G) in terms of physicochemical properties.
• The degree-based topological indices of SD(G) perform better than the temperature-based topological indices of SDT(G) for physicochemical properties.
• In contrast to the degree-based index of physical properties, which shows a little positive connection, the
temperature-based index of physical features for the Forgotten Index shows all negative correlation values.
By contrast, we find that the degree-based topological indices are more connected than the temperature- based index, and we validate this result using the QSPR study of HIV-1 drugs.

Conclusion

This article presents the values of the temperature-based topological indices Nevirapine (N), Delavirdine (D), Efavirenz (Ef), Etravirine (Et), and Rilpivirine (R). The calculated topological indices highly predict the physicochemical characteristics of antiviral drugs used to treat AIDS. The QSPR study looks at the linear regression model. The models are analyzed using eight physicochemical characteristics and four topological indices. The computed temperature-dependent topological indices for HIV-1 (NNRTIs) medications are shown in the 3D model **Figure 2.**

The most effective predictive topological markers when using linear regression models are

1. PT(G) exhibits a good connection (0.983) with molar volume when compared to other physical attributes displayed in Figure 3.
2. According to MR and P, the ST(G) index has the best prediction value (0.959) for the physicochemical characteristics displayed in Figure 4.
3. Similarly, BP, FP, MR, and P predict the temperature-based topological index of ST(G), PT(G), and SDT(G).
4. S(G) exhibits a good connection (0.982) with molar volume when compared to other physical attributes displayed in Figure 5.
5. Figure 6 presents prediction values for the physicochemical properties of HIV-1 drugs. It demonstrates the capability of the S(G) index in drug property forecasting by providing the best prediction (0.975) for MR and P.
6. Similarly, BP, FP, MR, and P predict the temperature-based topological index of S(G), P(G), and SD(G).

The greatest correlation among the temperature and degree-based indicators of HIV-1 medications is plot- ted in Figures 3, 4, 5, and 6. Additionally, we found a substantial correlation between temperature-based

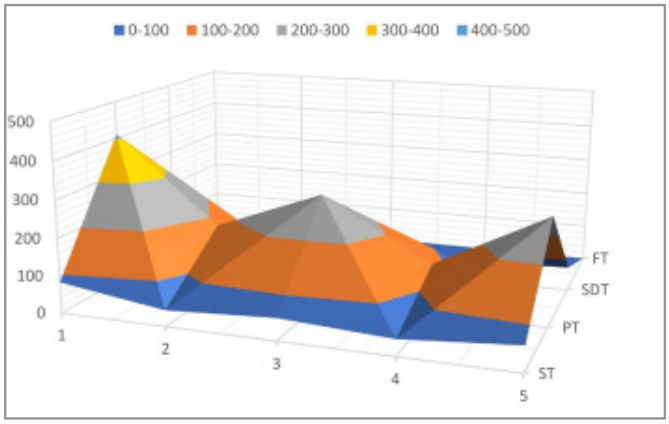

Figure 2: 3D Diagram of Calculated Temperature-Dependent Topological Indices for HIV-1 (NNRTIs) Medication: (1) Delavirdine, (2) Efavirenz, (3) Etravirine, (4) Nevirapine, (5) Rilipirine.

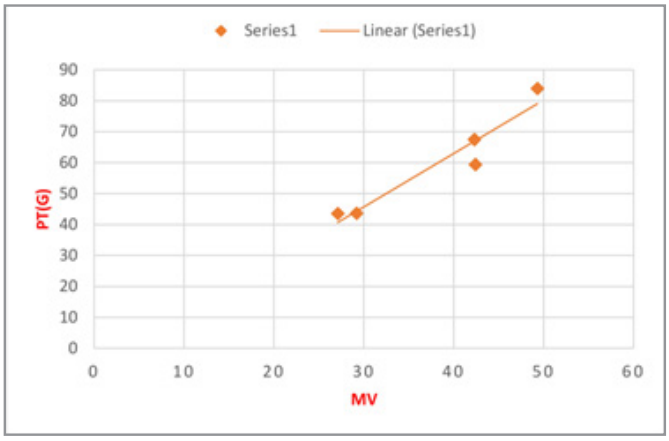

Figure 4: Plots use the sum connectivity temperature index to demonstrate the relationship between polarizability and Molar refraction.

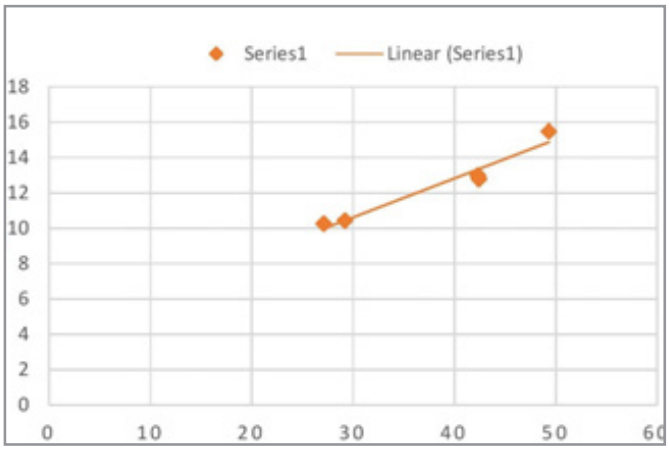

Figure 5: Plots demonstrating the strong correlation between the total connectivity temperature index and molar volume

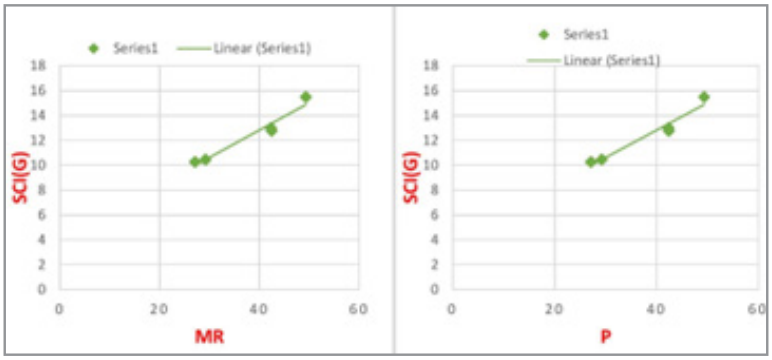

Figure 6: Plots use the sum connectivity temperature index to demonstrate the relationship between polarizability and Molar refraction.

topological indices and degree-based topological indicators, which have strong predictive power. We discovered that the correlation and regression of the given topological indices will assist drug designers in creating novel, inventive medicines by combining pharmaceuticals with positive correlations. Our study may facilitate the development of novel drugs and vaccines to treat AIDS.

Data Availability

These physicochemical properties of HIV-1 NNRTIs medications [Table 2] details were taken from the "Royal Society of Chemistry" (ChemSpider) online website.

Table 20: Chemspider IDs of the HIV-1 NNRTI Drugs.

DRUGS	MOLECULAR FORMULA	CHEMSPIDER ID
Delavirdine	C22H28N6O3S	5423
Efavirenz	C14H9ClF3NO2	57715
Etravirine	C20H15BrN6O	168313
Nevirapine	C15H14N4O	4308
Rilpivirine	C22H18N6	4953643

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All authors contributed equally.

Declaration of Competing Interest

The authors confirm that there are no known conflicts of interest associated with this publication.

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Data Availability

The data used to support the findings of this study are cited at relevant places within the text as references.

References

1. Trinajstic, N. (2018). Chemical graph theory. Routledge, CRC Press.
2. Bondy, J. A., & Murty, U. S. R. Graph theory with applications.
3. Arts, E. J., & Hazuda, D. J. (2012). HIV-1 antiretroviral drug therapy. Cold Spring Harbor Perspectives in Medicine.
4. Vallecillo, G., Sanvisens, A., Martinez, E., Torrens, M., Bolao, F., Tor, J., & Muga, R. (2010). Use of highly active antiretroviral therapy is increasing in HIV-positive severe drug users. Current HIV Research, 8(8), 641–648.
5. Devillers, J., & Balaban, A. T. (Eds.). (1999). Topological indices and related descriptors in QSAR and QSPR. Gordon and Breach.
6. Sahlberg, C., & Zhou, X.-X. (2008). Development of non-nucleoside reverse transcriptase inhibitors for anti-HIV therapy. Anti-Infective Agents in Medicinal Chemistry, 7(2), 101–117.
7. Ahmed, W., Ali, K., Zaman, S., & Raza, A. (2024). Molecular insights into anti-Alzheimer's drugs through predictive modeling using linear regression and QSPR analysis. Modern Physics Letters B.
8. Kulli, V. R. (2019). Computation of some temperature indices of HC5C5p,q nanotubes. Annals of Pure and Applied Mathematics, 20(2).
9. Kansal, N., Garg, P., & Singh, O. (2022). Temperature-based topological indices and QSPR analysis of COVID-19 drugs. Polycyclic Aromatic Compounds.
10. Usach, I., Melis, V., & Peris, J.-E. (2013). Non-nucleoside reverse transcriptase inhibitors: A review on pharmacokinetics, pharmacodynamics, safety, and tolerability. Journal of the International AIDS Society, 16(1), 18567.
11. Tsibris, A. M. N., & Hirsch, M. S. Non-nucleoside reverse transcriptase inhibitors.
12. Singh, O., Garg, P., Kansal, N., & Sharma, G. (2023). On analysis of temperature-based topological indices of anti-cancer drugs. European Chemical Bulletin, 12(10), 9522–9541.
13. Patnin, S., Makarasen, A., Vijitphan, P., Baicharoen, A., Chaiwisutangkun, A., Kuno, M., Sirithana, W., & Techasakul, S. (2023). Design, cross-docking and ONIOM studies of potent antiviral HIV-1 nonnucleoside reverse transcriptase inhibitors. Research Square.
14. Wang, J. (2020). Fast identification of possible drug treatment of coronavirus disease-19 (COVID-19) through computational drug repurposing study. Journal of Chemical Information and Modeling, 60(6), 3277–3286.
15. Arjmand, F., & Shafiei, F. (2018). Prediction of the normal boiling points and enthalpy of vaporization of alcohols and phenols using topological indices. Journal of Structural Chemistry, 59(3), 748–754.
16. Gutman, I. (2013). Degree-based topological indices. Croatica Chemica Acta, 86(4), 351–361.
17. Zhang, X., Reddy, H. G. G., Usha, A., Shanmukha, M. C., Farahani, M. R., & Alaeiyan, M. (2023). A study on anti-malaria drugs using degree-based topological indices through QSPR analysis. ResearchGate, 20(2), 3594–3609.
18. Kirmani, S. A. K., Ali, P., & Azam, F. (2021). Topological indices and QSPR/QSAR analysis of some antiviral drugs being investigated for the treatment of COVID-19 patients. International Journal of Quantum Chemistry.
19. Roy, K., Kar, S., & Das, R. N. (2015). A primer on QSAR/QSPR modeling: Fundamental concepts. Springer.