Section A-Research paper
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Utilizing Computational Biology to investigate the anti-viral prospective of *Tinospora cordifolia*

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ABSTRACT:

The viral diseases are the greatest threat to the human health. Although numerous anti-viral agents are available commercially yet they are not potent against the wide continuum of viruses. Thus, it becomes essential to move back to our mother nature for the solution. The common traditional drug – Giloy obtained from *Tinospora cordifolia* so recognized as Guduchi, heart leaved moon seed as well as Gurjo is mentioned in ancient Indian literature which is used against many diseases. It possesses a diversity of phytoconstituents for instance alkaloids, glycosides, steroidal compounds, lactones, terpenoids, polysaccharides which are responsible for the various pharmacological effects viz. antidiabetic, anticancer, antimicrobial, anti-inflammatory, anti-psychiatric, antihypertensive, immunomodulatory, vasorelaxant, and anti-viral action. The anti-viral effect of this plant has piqued the interest of experts in recent years. The current investigation targeted to explore the anti-viral potency of the individual phytoconstituents of Guduchi through *in silico* studies. The PASS online (Prediction of Activity Spectra for Substances) means was used to forecast the anti-viral effect. Even the antiviral potential of each individual phytoconstituent against a variety of viruses was also evaluated. The physicochemical properties, pharmacokinetics, drug-likeliness, medicinal chemistry friendliness and adverse effects of these phytocompounds were also investigated through the *in-silico* techniques. The findings of the study may be used by the upcoming researchers in the streams of phytochemistry, pharmacology and ethnobotany for the purposes of drug discovery. Yet, a more exhaustive exploration at molecular and cellular levels is required. To establish the anti-viral prospective of these phytomolecules, suitable *in vitro* and *in vivo* models need to be established and finally the clinical studies are essential to illuminate the anti-viral potential of the drug.

KEYWORDS: *Tinospora cordifolia*, anti-viral, PASS online, SwissADME, Druglikeness

1 INTRODUCTION

Of all the known pathogens, viruses exhibit a very strong adaptability behavior. They can modify themselves as required. The sufferings of the current scenario are mainly due to the viruses only. Viruses can endure on a variety of animals (e.g., fish, birds, insects) and human beings also. The genomic constitution of viruses may comprise of DNA or RNA and may undergo replication, translation and transcription through numerous means. Although, there is a huge variety of antiviral drugs available commercially yet these are not effective against a broad spectrum of the viral population. Additionally, the enhanced occurrence of mutations in viruses and resistance to antiviral agents has

further reduced their medicinal efficiency[1]. WHO (World Health Organization) has projected that around eighty percent of the world population comes back to the conventional drugs to overcome the pathogenic diseases[2]. Several herbal medical products have demonstrated their effectiveness in the prevention and management of an array of human illnesses.

Tinospora cardifolia (family: Menispermaceae) frequently recognized as Giloe and Guduchi is a very popular drug which has been used since ages for battling against the viral outbreaks due to its potent immunomodulatory and rejuvenating potential. Giloe is also mentioned in Rigveda as the constituent of 'heavenly elixer' or 'soma'. *Tinospora cordifolia* (Wild.) is a big deciduous and perennial climber distributed throughout India, Burma, China and Srilanka thriving in a variety of soils varying from acidic pH to basic pH and fractional to complete sunshine with modest humidity. The plant has fleshy stems, filamentous fleshy aeriform roots, thin grayish bark, heart-shaped airy leaves, unisexual greenish flowers, pea-shaped plumpy glossy fruits and bent pea sized seeds[3]. An array of alkaloids as secondary metabolites are present in stems and roots of Giloe such as Tinosporin, Berberine, Palmetine, Mangoflorine, Choline, Isocolumbin, Tetrahydropalmitine, Tembetarine, Jatrorrhizine, Aporphine alkaloids. These phytoconstituents exhibit hypoglycaemic, cytotoxic, anti-infammatory, anti-psychiatric, anti-viral and immunomodulatory activity[4]. Additionally, the entire Giloe plant shows presence of furanolactone, Cleodrane derivatives [(5R, 10R)-4R-8R-dihydroxy-cleroda-13(16), 14-dieno-17, 12S:18, 1S-dilactone], diterpenoid lactones, columbintinosporides, jateorine and tinosporin. These phytocompounds have displayed the pharmacological activities viz effects on inflammation, hypertension, microorganisms, viruses andvasorelaxant effect[5]. Mainly Sterols (e.g., β-sitosterol, Octacosanol, δ-sitosterol, Heptacosanol, Tetrahydrofuran, Nonacosan-15-ol, Hydroxyecdysone, Giloinsterol, Makisterone A, Ecdysterone) are reported in the shoots of *Tinospora cardifolia*. These are effective in the treatment of osteoporosis induced by glucocorticoids and premature inflammatory arthritis. They persuade arrest of G2/M cell cycle as well as restrain tumor necrosis factor-alpha (TNF-α), interleukin IL-1β, (IL)-6 and COX-2 and c-Myc inhibition also occurs which result into reticence of apoptosis[6]. Glycosides, e.g. 18-norcleodrane glucoside, Tinocordiside, Furanoid diterpene glycoside, Tinocordifolioside, Cordioside, Cordifolioside A-D, Syringiapiosyl glycoside, Syringin, Palmatoside C and P, Cardifoliside A-E are mainly found in stem of Giloe. They exhibited immunomodulatory potential in Parkinson's syndrome, motor and cognitive disorder, dementia, neurological diseases such as ALS. They have also displayed the anti-cancer activity be inhibiting NF-k Band[7]. The dynamic nonaromatic compounds like Heptacosanol, Octacosanol and Nanocosan-15-one dichloromethane have been reported in the entire Giloe plant. They have shown their beneficial effects as anti-inflammatory and anti-nociceptive agents. Moreover, they restrain the binding of TNF-α to DNA and offerdefensein opposition to Parkinson's disease induced by 6-hydroxydopamine in rats[8, 9]. Tinocordifolin and Sesquiterpenoids found in shoots of *T. cordifolia* have displayed its therapeutic potential as an antiseptic. Some active phytocompounds such as Jatrorrhizine, N-trans-feruloyltyramine as diacetate, Giloin, 3, (a, 4-di hydroxy-3-methoxy-benzyl)-4-(4- hydroxy-3-methoxy-benzyl) tetrahydrofuran, Tinosporic acid from the other parts of Giloe plant are reported to show anti-HIV action[10].

Thus the phytochemistry of *Tinospora cordifolia* displays the presence of diverse secondary metabolites belonging to diverse categories such as alkaloidal, steroidal, glycosidal, nonaromatic phytomolecules, lactones, sesquiterpenoids and long carbohydrates chain. Although these constituents display a number of beneficial pharmacological effects especially the immunmodulatory action, yet there are a very few evidences indicating the antiviral activity of this drug. Thus, the present work intends to investigate the antiviral activity of *Tinospora cardifolia* phytoconstituents and also investigate their physicochemical properties, pharmacokinetics, drug likeliness and adverse effects through *in-silico* techniques.

2 METHODOLOGY

The database PASS ONLINE was explored for investigating the anti-viral potential of the phytocompounds of *Tinospora cardifolia.* SwissADME was utilized to determine the phytomolecules physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry friendliness. The ADVERSE EFFECT GENERATOR was used to study the adverse effects of the phytoconstituents.

2.1 Prediction of antiviral activity

The antiviral activity of the phytochemicals of *Tinospora cordifolia* was envisaged through PASS ONLINE (PREDICTION OF ACTIVITY SPECTRA FOR SUBSTANCES). This is a networked method fabricated for evaluation of wide range of biological activity of an organic compound under investigation. It provides the idea about the expected biological activity of the virtual drug molecule before its isolation, synthesis or testing. It can predict about more than 4000 types of biological actions, together with pharmacological consequences, method of action, side effects and toxicity, interactions with metabolic enzymes as well as transporters, and impact on gene expression etc. This software artifact is accessible commercially. One can very simply approach it through the website link http://www.pharmaexpert.ru/passonline/. To achieve the expected biotic action contour of a particular molecule, merely structural formula is essential; consequently, prediction is achievable even for virtual structureproposed in computer. To avail the PASS Online facility, a previous registration is required. This authorization is free but one ought to give consent for the 'terms and condition' for using this service. Subsequent to registration one can search through the above mentioned link and by creating the smiles of the particular chemical structure with the help of`chem sketch' the broad spectrum of the pharmacological actions of a compound can be predicted.

The PASS (Prediction of Activity Spectra for Substances) provides the approximation of the feasible profiles for biological of the molecules under investigation depending upon their structural methods offered in MOL file or SD file configure. The wide-ranging catalog of expected biological actions comprises of more than four thousand expressions involving pharmacological properties like antidiabetic; metabolism like CYP3A4 inhibition; biochemical mechanism likeCOX-1 inhibitor; toxicity like cancer; transporter-related activities like P-glycoprotein substrate; gene expression regulation like inhibition of VEGF expression. The PASS forecast is due to the structure-activity correlations of an additional 260,000 compounds with known biological actions. For the whole PASS guideline set, the standard accuracy of forecast determined in leave-one-out cross-validation technique is around 95%.

2.2 Evaluation of physicochemical properties, pharmacokinetics and drug likeliness

For a compound to show its pharmacological action, it must approach its destination in adequate concentration and remain there in its active form to display its activity. So it becomes very important to evaluate the ADME (Absorption, Distribution, Metabolism and Excretion) of the medicine before starting the actual experimental work. For this the computer models can provide a very good alternative for evaluating the feasibility of a compound as an active drug molecule. SwissADME is a web tool that helps one to foretell the physicochemical characteristics, pharmacokinetics, drug-likeliness and medicinal chemistry friendliness of a particular drug product. One can freely assess SwissADME through the website http://www.swissadme.ch/. All the actions produced by this software are tabulated on an excel sheet due to which the data storage becomes very expedient. In this, the results can be demonstrated, saved and shared through universal instinctive and interactive charts. In terms of bioavailability, drug-likeness is defined as the likelihood of a molecule becoming an oral medication. Structure or physicochemical analyses of research molecules that had advanced extremely to be considered oral drug molecules were used to determine drug-likeness. Drug similarity characteristics are used to filter chemical libraries in order to avoid compounds with qualities that are most likely discordant with a satisfactory pharmacokinetics outline. This SwissADME area provides admittance to 5 alternative rule-based sifters, each with a different set of attributes within this criterion, the molecule is classified as drug-like. These sifters are frequently derived from investigations conducted by big medicinal corporations in order to enhance the eminence of their exclusive chemical collections. The Lipinski (Pfizer) filter was the first to use the rule-of-five. The procedures of Ghose (Amgen), Veber (GSK), Egan (Pharmacia), and Muegge (Bayer) were adopted and employed. Numerous assessments enable harmony in opinion or the assortment of approaches most suited to the chemical space requirement of the end-user.

2.2.1 Lipinski rule

The Lipinski rule[11] of 5 can be utilized to discriminate among drug-like and non-drug-like compounds. It forecasts a high likelihood of accomplishment or collapse due to drug resemblance for molecules that are able to satisfy atleast 2 of the subsequent criteria's:

- A molecular mass < 500 Dalton is required.
- Extreme lipophilicity (stated as LogP < 5).
- There should be a utmost of five hydrogen bond donors and ten hydrogen bond acceptors.
- Molar refractivity should vary from 40 to 130

2.2.2 Ghose Filter

The Ghose filter calculates physicochemical parameter profiles such as log P, molar refractivity (MR), molecular weight (MW), and atom count to quantify small molecules. The Ghose filter also comprises a qualitative assessment depending on the existence of functional groups and significant substructures. The estimated log P (ClogP) should be amid -0.4 to +5.6 . 160 and 480 flank the qualifying range for MW. In a tiny molecule, the eligible range for MR is stuck between 40 and 130 atoms, while there should be around 20 and 70 atoms[12].

2.2.3 Veber Filter:

Compounds are classified as drug-like if they have Rotatable bonds<= ten, Topological polar surface area (in square kilometres) <= 140 and ≤12 fewer H-bond donors and acceptors, according to the Veber model. The Veber filter is a general-purpose filter for orally active medicines[13].

2.2.4 Egan Rule:

The Egan filter[14] predicts absorption of medication depending on physical progressions concerned with a tiny molecule's membrane permeability. Polar surface area (PSA) and logP are the Egan model's descriptors, with redundant descriptors like MW being omitted. As per this statute, TPSA <= 131.6 and log P <= 5.88.

2.2.5 Muegge Filter*:*

The Muegge replica is a database-sovereign pharmacophore point filter that distinguishes among chemical substances that are drug-like and those that are not. It's based on the idea that non-drug treatments are commonly underutilized. Ketone, hydroxyl, sulfonyl, and amine groups are regarded as significant functional motifs in drug-like compounds. As a result, passing the filter requires a certain number of well-defined pharmacophore points. These purposeful designs enable hydrogen-bonding capacities, which are necessary for certain pharmaceutical interface with their goals. These functional groups can be joined to form pharmacophore points, as defined by the Muegge model. Among the pharmacophore points are amide, amidine, amine, alcohol, carbamate, carboxylic acid, ester, guanidine, ketone, sulfone, sulfonamide and urea functional groups. These pharmacophore sites in tiny compounds may have important interactions with the target protein[15].

2.3 Prediction of the adverse drug reactions

The Adverse effect prediction was carried out through a software utilized for *in–silico* prediction of the expected adverse effects such as Myocardial Infarction, Arrhythmia, Hepatotoxicity, Nephrotoxicity or any other unexpected mold, moderate or severe medical consequence that may arise during the treatment with a particular dug. The most probable Adverse Effects that may be produced by the phytocompounds of *Tinospora cordifolia* were evaluated using the software ADVERSE EFFECT GENERATOR. One can very easily use this software through the link http://www.way2drug.com/adverpred/index.php by simply putting the smiles of the phytocompound. Several

phytoconstituents do not display any of the expected adverse effects, i.e. they are completely safe to be used as a drug and are not detrimental for the individual wellbeing.

3 RESULT AND DISCUSSION

3.1 Prediction of antiviral activity

The results of the predicted antiviral activity of the phytoconstituents of *Tinospora cordifolia* are compiled in **Table 1**. The table displays the expected anti-viral potential of the 38 phytocompounds (along with their chemical structures) of *T. cordifolia*. The possibility of a particular phytocompound to be active as an anti-viral agent is indicated by 'Pa value' while 'Pi value' indicates the inactivity.

3.2 Physicochemical Properties

The physicochemical characteristics of the phytocompounds of *T. cordifolia* are described in **Table 2**. This segment brings together simple molecular and physical constraints such as MW (molecular weight), MR (molecular refractivity), PSA (polar surface area) and count of certain atom kinds. Open Babel, version 2.3.0, was utilized to compute the values. A fragmental strategy called as topological polar surface area (TPSA), which considered P (phosphorus) and S (sulphur) polar atoms estimated the PSA. This has confirmed to be a practical descriptor in a variety of replicas and decrees for swiftly assessing various ADME characteristics, particularly those involving biological barrier passage, such as absorption and brain admittance.

3.3 Pharmacokinetic properties

The Pharmacokinetic properties of phytoconstituents *of T. cordifolia* are exhibited in **Table 3.** Individual ADME behaviours of the chemical under research are evaluated using specialised models, the predictions of which are summarised in the Pharmacokinetics section. A multiple linear regression model, for example, seeks to predict the skin permeability coefficient (Kp). It is based on the work of Potts and Guy, who discovered that Kp is linearly linked to molecule size and lipophilicity (R2 = 0.67). The log Kp (in cm/s) indicates how permeant a molecule is to the skin.

3.4 Drug likeliness

The SwissADME segment provides admittance to 5 alternative rule-based filters, each among a different set of features within which the molecule is classified as drug-like. These filters are frequently derived from scrutiny conducted by big pharmaceutical corporations in order to perk up the worth of their proprietary chemical compilations. The Lipinski (Pfizer) filter was the first rule-of-five filter to be implemented from reference. Adaptations were made to the Egan (Pharmacia), Ghose (Amgen), Muegge (Bayer) and Veber (GSK) techniques. Manifold assessments allow for harmony in opinions or the assortment of techniques most suited to the final-unique consumer's requirements in terms of chemical space or project-related requirements. Any infringement of any of the rules specified here is highlighted in the output panel. The drug likeliness of the phytoconstituents of *T. cordifolia* is compiled in **Table 4**.

3.5 Prediction of Adverse Drug Reactions

The predicted Adverse Effects of the phytoconstituents *of T. cordifolia* are depicted in **Figure 1**.

1. CONCLUSION:

According to the findings of the preceding investigations, *Tinospora cardiofolia* may offer new sources of anti-viral potential with stable, physiologically active compounds that might provide a technical foundation for the employment of herbs in modern medicine. These projected antiviral properties of plant compounds should be scientifically validated and then effectively communicated. These predicted behaviours can be expanded to include future research into pharmacology, phytochemistry, ethnobotany and other biological actions for drug development. Plants are also being studied by folklorists, pharmacologists, phytochemists, and ethnobotanists for various biological functions.

We found that well-designed bioassay-guided isolation and investigation of these compounds' antiviral properties should be sufficient to fulfil this job. Several research confirming the extract or compounds produced from plant extracts have been reported in the last ten years. These investigations found that extracts include intriguing biopharmaceutical components (anti-viral) that have piqued the curiosity of scientists. To understand anti-viral and other biological actions, more extensive research at the molecular and cellular levels, appropriate animal models, and human clinical investigations are requisite.

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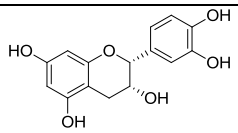
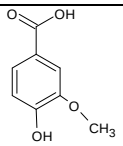
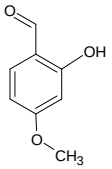
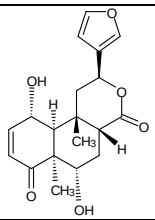
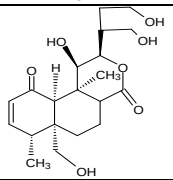
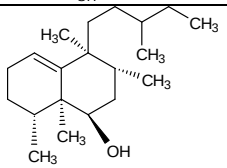
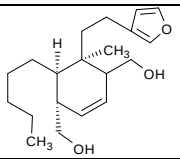
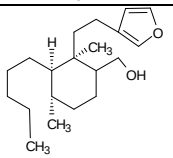
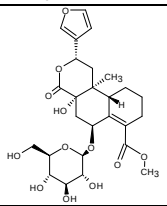
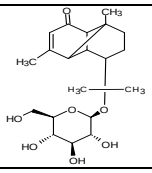
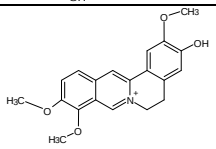
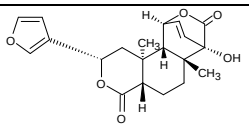
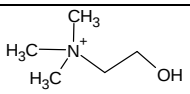
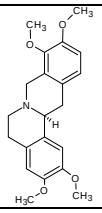
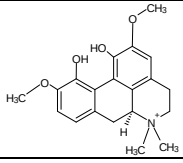
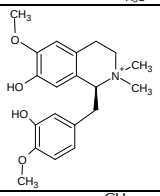
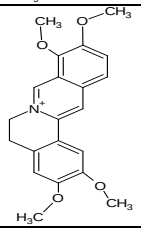
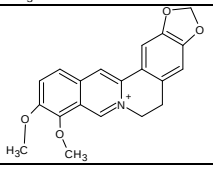
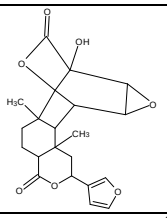
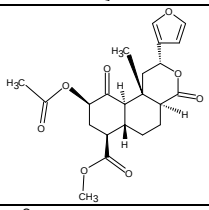
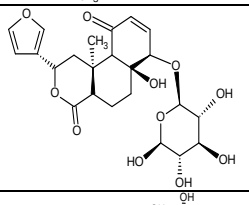
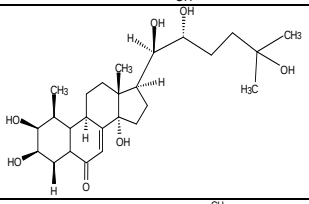
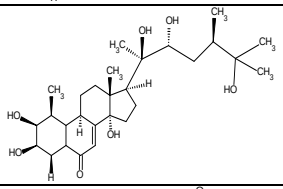
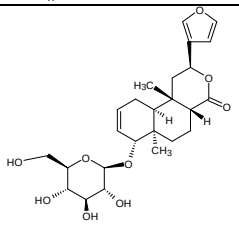
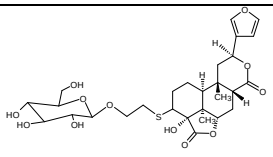
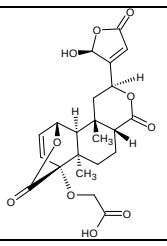
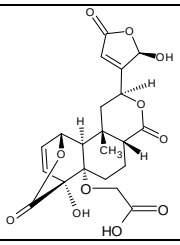
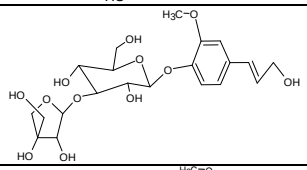
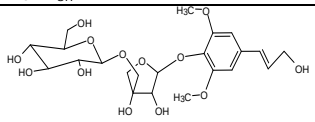
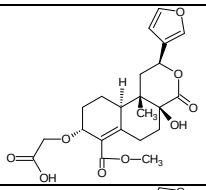
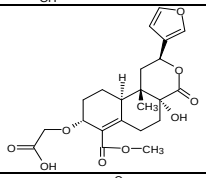
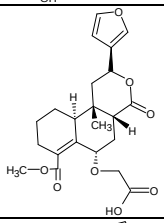
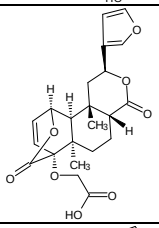
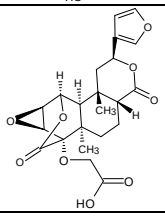
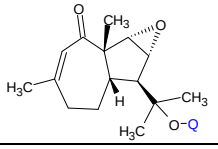
S.NO	NAME	CHEMICAL STRUCTURE	ACTIVITY AND PERCENTAGE Pa Pb Activity
1	Epicatechin		0.692 0.006 Antiviral (Influenza) 0.520 0.018 Antiviral (Rhinovirus) 0.465 0.015 Antiviral (Herpes) 0.378 0.017 Antiviral 0.234 0.130 Antiviral (Influenza A) 0.088 0.087 Antiviral (Hepatitis)
2	4-hydroxy-3-methoxybenzoic acid		0.498 0.051 Antiviral (Picornavirus) 0.207 0.080 Antiviral (Hepatitis B) 0.215 0.137 Antiviral (Poxvirus) 0.108 0.036 Antiviral (Trachoma) 0.124 0.064 Antiviral (Hepatitis) 0.107 0.051 Antiviral (Hepatitis C) 0.130 0.093 Antiviral (HIV) 0.039 0.036 Antiviral (Parainfluenza)
3	2-hydroxy-4-methoxybenzaldehyde		0.367 0.051 Antiviral (Herpes) 0.359 0.149 Antiviral (Picornavirus) 0.174 0.129 Antiviral 0.291 0.273 Antiviral (Rhinovirus)
4	Tinocordin		0.423 0.026 Antiviral (Herpes) 0.340 0.024 Antiviral (Hepatitis B) 0.323 0.192 Antiviral (Picornavirus) 0.102 0.101 Antiviral (Hepatitis)
5	Tinosporaclerodanoid		0.408 0.032 Antiviral (Herpes) 0.397 0.048 Antiviral (Influenza)
6	Tinosporafurandiol		0.445 0.034 Antiviral (Influenza) 0.385 0.042 Antiviral (Herpes) 0.319 0.030 Antiviral (Influenza A) 0.315 0.031 Antiviral 0.134 0.086 Antiviral (HIV)
7	Tinosporaclerodanol		0.426 0.090 Antiviral (Picornavirus) 0.300 0.008 Antiviral (HIV) 0.324 0.076 Antiviral (Herpes) 0.229 0.062 Antiviral (Hepatitis B) 0.253 0.135 Antiviral (Adenovirus)
8	Tinosporafuranol		0.340 0.066 Antiviral (Herpes) 0.282 0.043 Antiviral 0.357 0.147 Antiviral (Rhinovirus) 0.217 0.072 Antiviral (Hepatitis B)
9	Cordioside		0.687 0.006 Antiviral (Influenza) 0.357 0.021 Antiviral (Hepatitis B) 0.119 0.029 Antiviral (Trachoma) 0.136 0.048 Antiviral (Hepatitis) 0.186 0.111 Antiviral

10	Tinocordiside		0.456 0.305 0.212 0.164	0.017 0.032 0.186 0.142	Antiviral (Herpes) Antiviral (Hepatitis B) Antiviral (Influenza A) Antiviral
11	Jatrorrhizine		0.448 0.350 0.234 0.164	0.033 0.158 0.130 0.147	Antiviral (Influenza) Antiviral (Rhinovirus) Antiviral (Influenza A) Antiviral (Hepatitis B)
12	Isocolumbin		0.411 0.262 0.275 0.248	0.079 0.045 0.110 0.134	Antiviral (Rhinovirus) Antiviral (Hepatitis B) Antiviral (Herpes) Antiviral (Influenza)
13	Choline		0.450 0.473 0.382 0.294 0.303	0.014 0.063 0.032 0.033 0.089	Antiviral (Adenovirus) Antiviral (Picornavirus) Antiviral (Poxvirus) Antiviral (CMV) Antiviral (Herpes)
14	Tetrahydropalmatine		0.430 0.200	0.063 0.196	Antiviral (Rhinovirus) Antiviral (Influenza)
15	Magnoflorine		0.239 0.299	0.153 0.255	Antiviral (Adenovirus) Antiviral (Rhinovirus)
16	Tembetarine		–		
17	Palmatine		0.357 0.291	0.147 0.243	Antiviral (Rhinovirus) Antiviral (Picornavirus)
18	Berberine		0.368 0.228 0.163	0.057 0.166 0.151	Antiviral (Influenza) Antiviral (Adenovirus) Antiviral (Hepatitis B)

19	Tinosporide		0.401 0.292 0.235	0.090 0.097 0.059	Antiviral (Rhinovirus) Antiviral (Herpes) Antiviral (Hepatitis B)
20	Furanolactone		0.447 0.358 0.218 0.263 0.086	0.050 0.056 0.071 0.118 0062	Antiviral (Rhinovirus) Antiviral (Herpes) Antiviral (Hepatitis B) Antiviral (Influenza) Antiviral (Trachoma)
21	Tinosporaside		0.369 0.400 0.278 0.313 0.097	0.050 0.091 0.040 0.081 0.046	Antiviral (Herpes) Antiviral (Rhinovirus) Antiviral (Hepatitis B) Antiviral (Influenza) Antiviral (Trachoma)
22	Ecdysterone		0.539	0.014	Antiviral (Rhinovirus)
23	Makisterone		0.490	0.028	Antiviral (Rhinovirus)
24	Tinocordioside		0.735 0.585 0.399 0.386 0.253 0.130 0.099 0.079	0.004 0.004 0.015 0.107 0.058 0.054 0.064 0.075	Antiviral (Influenza) Antiviral (Herpes) Antiviral (Hepatitis B) Antiviral (Rhinovirus) Antiviral Antiviral (Hepatitis) Antiviral (Hepatitis C) Antiviral (Trachoma)
25	Cordifolide A		0.352 0.242 0.259 0.162 0.130 0.315	0.022 0.065 0.123 0.027 0.027 0.223	Antiviral (Hepatitis B) Antiviral Antiviral (Influenza) Antiviral (Hepatitis) Antiviral (Hepatitis C) Antiviral (Rhinovirus
26	Cordifolide B		0.413 0.212	0.077 0.075	Antiviral (Rhinovirus) Antiviral (Hepatitis B)

27	Cordifolide C		0.413 0.207	0.077 0.080	Antiviral (Rhinovirus) Antiviral (Hepatitis B)
28	Cordifolioside A		0.375 0.268 0.196 0.092	0.055 0.043 0.100 0.053	Antiviral (Influenza) Antiviral (Hepatitis B) Antiviral Antiviral (Trachoma)
29	Cordifolioside B		0.529 0.428 0.352 0.189	0.019 0.024 0.022 0.107	Antiviral (Influenza) Antiviral (Herpes) Antiviral (Hepatitis B) Antiviral
30	Cordifoliside D		0.449 0.400 0.218 0.198 0.108	0.049 0.047 0.070 0.179 0.089	Antiviral (Rhinovirus) Antiviral (Influenza) Antiviral (Hepatitis B) Antiviral (Herpes) Antiviral (Hepatitis)
31	Cordifoliside E		0.449 0.400 0.218 0.198 0.108	0.049 0.047 0.070 0.179 0.089	Antiviral (Rhinovirus) Antiviral (Influenza) Antiviral (Hepatitis B) Antiviral (Herpes) Antiviral (Hepatitis)
32	Cordioside		0.433 0.284 0.113 0.095	0.060 0.103 0.080 0.071	Antiviral (Rhinovirus) Antiviral (Herpes) Antiviral (Hepatitis) Antiviral (Hepatitis C)
33	Palmatoside C		0.249 0.202	0.051 0.174	Antiviral (Hepatitis B) Antiviral (Herpes)
34	Palmatoside F		0.414 0.279 0.226	0.076 0.107 0.065	Antiviral (Rhinovirus) Antiviral (Herpes) Antiviral (Hepatitis B)
35	Tinocordifolioside		0.459 0.326	0.043 0.074	Antiviral (Rhinovirus) Antiviral (Herpes)

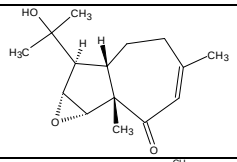
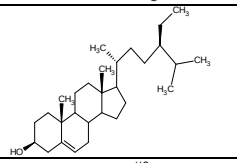
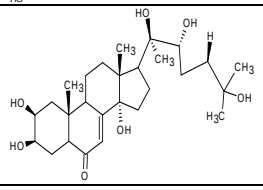
36	Tinocordifolin		0.459 0.326 0.216	0.043 0.074 0.141	Antiviral (Rhinovirus) Antiviral (Herpes) Antiviral (CMV)
37	β- sitosterol		0.686 0.547 0.205	0.006 0.013 0.171	Antiviral (Influenza) Antiviral (Rhinovirus) Antiviral (Herpes)
38	Hydroxyecdysone		0.570 0.245	0.009 0.138	Antiviral (Rhinovirus) Antiviral (Influenza)

Table 1: PASS prediction of Anti-viral activity of Phytoconstituents of *Tinospora cordifolia*

Table 2. Physicochemical Properties of Phytoconstituents of *T. cardifolia*

S.No	Name	Molecular formula	MW	#Heavy atoms	#Aromatic heavy atoms	Fraction Csp3	#Rotatable bonds	#H-bond acceptors	#H-bond donors	MR	TPSA
1	Epicatechin	$C_{15}H_{14}O_6$	290.27	21	12	0.2	1	6	5	74.33	110.38
2	4-hydroxy-3-methoxybenzoic acid	$C_8H_8O_4$	168.15	12	6	0.12	2	4	2	41.92	66.76
3	2-hydroxy-4-methoxybenzaldehyde	$C_8H_8O_3$	152.15	11	6	0.12	2	3	1	40.34	46.53
4	Tinocordin	$C_{19}H_{22}O_6$	346.37	25	5	0.58	1	6	2	87.44	96.97
5	Tinosporaclerodanoid	$C_{20}H_{30}O_7$	382.45	27	0	0.8	5	7	4	97.05	124.29
6	Tinosporafurandiol	$C_{20}H_{36}O$	292.5	21	0	0.9	4	1	1	94.19	20.23
7	Tinosporaclerodanol	$C_{20}H_{32}O_3$	320.47	23	5	0.7	9	3	2	95.25	53.6
8	Tinosporafuranol	$C_{20}H_{34}O_2$	306.48	22	5	0.8	8	2	1	94.57	33.37
9	Cordioside	$C_{26}H_{34}O_{12}$	538.54	38	5	0.69	6	12	5	126.02	185.35
10	Tinocordiside	$C_{20}H_{32}O_7$	384.46	27	0	0.85	3	7	4	98.2	116.45
11	Jatrorrhizine	$C_{20}H_{20}NO_4$	338.38	25	16	0.25	3	4	1	97.33	51.8
12	Isocolumbin	$C_{20}H_{21}O_6$	357.38	26	5	0.6	1	6	1	89.59	85.97
13	Choline	$C_5H_{14}NO$	104.17	7	0	1	2	1	1	29.69	20.23
14	Tetrahydropalmatine	$C_{21}H_{25}NO_4$	355.43	26	12	0.43	4	5	0	103.99	40.16
15	Magnoflorine	$C_{20}H_{24}NO_4$	342.41	25	12	0.4	2	4	2	101.87	58.92
16	Tembetarine	$C_{20}H_{26}NO_4$	344.42	25	12	0.4	4	4	2	102.87	58.92
17	Palmatine	$C_{21}H_{22}NO_4$	352.4	26	16	0.29	4	4	0	101.8	40.8
18	Berberine	$C_{20}H_{18}NO_4$	336.36	25	16		2	4	0	94.87	40.8
19	Tinosporide	$C_{21}H_{22}O_7$	386.4	28	5	0.71	1	7	1	92.27	98.5

20	Furanolactone	$C_{22}H_{26}O_8$	418.44	30	5	0.64	5	8	0	102.85	109.11
21	Tinosporaside	$C_{23}H_{28}O_{11}$	480.46	34	5	0.65	3	11	5	110.51	176.12
22	Ecdysterone	$C_{26}H_{42}O_7$	466.61	33	0	0.88	5	7	6	125.15	138.45
23	Makisterone	$C_{28}H_{46}O_7$	494.66	35	0	0.89	5	7	6	134.8	138.45
24	Tinocordioside	$C_{25}H_{34}O_9$	478.53	34	5	0.72	4	9	4	118.47	138.82
25	Cordifolide A	$C_{28}H_{38}O_{12}S$	598.66	41	5	0.79	7	12	5	141.32	210.65
26	Cordifolide B	$C_{22}H_{24}O_{10}$	448.42	32	0	0.64	4	10	2	103.74	145.66
27	Cordifolide C	$C_{21}H_{22}O_{11}$	450.39	32	0	0.62	4	11	3	100.39	165.89
28	Cordifolioside A	$C_{21}H_{30}O_{12}$	474.46	33	6	0.62	9	12	7	109.59	187.76
29	Cordifolioside B	$C_{22}H_{32}O_{13}$	504.48	35	6	0.64	10	13	7	116.08	196.99
30	Cordifoliside D	$C_{22}H_{26}O_9$	434.44	31	5	0.59	6	9	2	104.94	132.5
31	Cordifoliside E	$C_{22}H_{26}O_9$	434.44	31	5	0.59	6	9	2	104.94	132.5
32	Cordioside	$C_{22}H_{26}O_8$	418.44	30	5	0.59	6	8	1	103.74	112.27
33	Palmatoside C	$C_{22}H_{24}O_8$	416.42	30	5	0.59	4	8	1	101.41	112.27
34	Palmatoside F	$C_{22}H_{24}O_9$	432.42	31	5	0.68	4	9	1	100.85	124.8
35	Tinocordifolin	$C_{15}H_{22}O_3$	250.33	18	0	0.8	1	3	1	69.63	49.83
36	β- sitosterol	$C_{29}H_{50}O$	414.71	30	0	0.93	6	1	1	133.23	20.23
37	Hydroxyecdysone	$C_{27}H_{44}O_7$	480.63	34	0	0.89	5	7	6	129.74	138.45

Table 3: Pharmacokinetic properties of phytoconstituents *of T. cordifolia*

S.no	Name of constituent	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	GI absorption	BBB permeant	log Kp (cm/s)
1	Epicatechin	High	No	Yes	No	No	No	No	No	-7.82
2	4-hydroxy-3-methoxybenzoic acid	High	No	No	No	No	No	No	No	-6.31
3	2-hydroxy-4-methoxybenzaldehyde	High	Yes	No	No	No	No	No	No	-6.61
4	Tinocordin	High	No	Yes	No	No	No	No	No	-7.82
5	Tinosporaclerodanoid	High	No	Yes	No	No	No	No	No	-8.77
6	Tinosporafurandiol	High	Yes	No	No	No	Yes	Yes	No	-3.5

7	Tinosporaclerodanol	High	Yes	No	No	No	No	Yes	No	-4.87
8	Tinosporafuranol	High	Yes	No	No	No	No	Yes	No	-3.6
9	Cordioside	Low	No	Yes	No	No	No	No	No	-9.92
10	Tinocordiside	High	No	Yes	No	No	No	High	No	-8.26
11	Jatrorrhizine	High	Yes	Yes	Yes	No	No	High	Yes	-5.94
12	Isocolumbin	High	No	Yes	No	No	No	High	No	-6.95
13	Choline	Low	No	No	No	No	No	Low	No	-7.22
14	Tetrahydropalmatine	High	Yes	Yes	No	No	No	High	Yes	-6.17
15	Magnoflorine	High	Yes	Yes	Yes	No	No	High	Yes	-6.44
16	Tembetarine	High	Yes	Yes	No	No	No	High	Yes	-6.25
17	Palmatine	High	Yes	Yes	No	No	No	High	Yes	-5.79
18	Berberine	High	Yes	Yes	Yes	No	No	High	Yes	-5.78
19	Tinosporide	High	No	Yes	No	No	No	Yes	No	-7.83
20	Furanolactone	High	No	No	No	No	No	No	No	-7.35
21	Tinosporaside	Low	No	Yes	No	No	No	No	No	-10.41
22	Ecdysterone	High	No	Yes	No	No	No	No	No	-8.92
23	Makisterone	High	No	Yes	No	No	No	No	No	-8.65
24	Tinocordioside	High	No	Yes	No	No	No	No	No	-8.29
25	Cordifolide A	Low	No	Yes	No	No	No	No	No	-9.7
26	Cordifolide B	Low	No	Yes	No	No	No	No	No	-8.67
27	Cordifolide C	Low	No	Yes	No	No	No	No	No	-9.71
28	Cordifolioside A	Low	No	No	No	No	No	No	No	-10.42
29	Cordifolioside B	Low	No	No	No	No	No	No	No	-11.02
30	Cordifoliside D	High	No	Yes	No	No	No	No	No	-8.32
31	Cordifoliside E	High	No	Yes	No	No	No	No	No	-8.32
32	Cordioside	High	No	Yes	No	No	No	No	No	-7.42
		High	No	Yes	No	No	No	No	No	-7.21

33	Palmatoside C									
34	Palmatoside F	High	No	Yes	No	No	No	No	No	-7.9
35	Tinocordifolin	High	Yes	No	No	No	No	No	No	-6.85
36	β- sitosterol	Low	No	No	No	No	No	No	No	-2.2
37	Hydroxyecdysone	High	No	Yes	No	No	No	No	No	-8.91

Table 4. Drug likeliness of the phytoconstituents of *T. cordifolia*

S.No	Name of constituent	TYLipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score
1	Epicatechin	0	0	0	0	0	0.55
2	4-hydroxy-3-methoxybenzoic acid	0	0	0	0	1	0.85
3	2-hydroxy-4-methoxybenzaldehyde	0	2	0	0	1	0.55
4	Tinocordin	0	0	0	0	0	0.55
5	Tinosporaclerodanoid	0	0	0	0	0	0.55
6	Tinosporafurandiol	1	0	0	0	2	0.55
7	Tinosporaclerodanol	0	0	0	0	0	0.55
8	Tinosporafuranol	0	0	0	0	1	0.55
9	Cordioside	2	3	1	1	2	0.17
10	Tinocordiside	0	0	0	0	0	0.55
11	Jatrorrhizine	0	0	0	0	0	0.55
12	Isocolumbin	0	0	0	0	0	0.55
13	Choline	0	2	0	0	1	0.55
14	Tetrahydropalmatine	0	0	0	0	0	0.55
		0	0	0	0	0	0.55

15	Magnoflorine						
16	Tembetarine	0	0	0	0	0	0.55
17	Palmatine	0	0	0	0	0	0.55
18	Berberine	0	0	0	0	0	0.55
19	Tinosporide	0	0	0	0	0	0.55
20	Furanolactone	0	0	0	0	0	0.55
21	Tinosporaside	1	2	1	1	2	0.55
22	Ecdysterone	1	1	0	1	1	0.55
23	Makisterone	1	3	0	1	1	0.55
24	Tinocordioside	0	0	0	1	0	0.55
25	Cordifolide A	2	3	1	1	2	0.17
26	Cordifolide B	0	0	1	1	0	0.56
27	Cordifolide C	1	1	1	1	2	0.11
28	Cordifolioside A	2	1	1	1	3	0.17
29	Cordifolioside B	3	2	1	1	4	0.17
30	Cordifoliside D	0	0	0	1	0	0.56
31	Cordifoliside E	0	0	0	1	0	0.56
32	Cordioside	0	0	0	0	0	0.56
33	Palmatoside C	0	0	0	0	0	0.56
34	Palmatoside F	0	0	0	0	0	0.56
35	Tinocordifolin	0	0	0	0	0	0.55
36	β- sitosterol	1	3	0	1	2	0.55
37	Hydroxyecdysone	1	2	0	1	1	0.55

Figure1. Adverse Drug Reactions of the phytoconstituents *of T. cordifolia*

S.No	Molecule	Cardiac failure		Hepatotoxicity		Myocardial infarction		Arrhythmia		Nephrotoxicity	
		Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi
1	Berberine							0.41	0.177		
2	Palmatine							0.693	0.027		
3	Tembetarine					0.337	0.134	0.557	0.067		
4	Magnoflorine					0.547	0.036	0.608	0.045		
5	Tetrahydropalmatine							0.639	0.036		
6	CHOLINE	0.527	0.044	0.365	0.286	0.613	0.026	0.432	0.162	0.345	0.118
7	Isocolumbin	Adverse effect are not predicted									
8	Jatrorrhizine							0.628	0.039		
9	TINOCORDISIDE									0.477	0.057
10	Cordioside									0.38	0.096
11	Syringin									0.513	0.046
12	Tinosporafuranol									0.359	0.109
13	Tinosporaclerodanol									0.412	0.08
14	TINOSPORAFURANDIOL	Adverse effects are not predicted.									
15	Tinosporaclerodanoid									0.311	0.145
16	Tinocordin	Adverse effects are not predicted.									
17	2-hydroxy-4-methoxybenzaldehyde			0.402	0.257			0.313	0.284		
18	4-hydroxy-3-methoxybenzoic acid	0.272	0.201	0.424	0.241			0.303	0.3	0.329	0.129
19	Epicatechin									0.242	0.236
20	Tinosporide	Adverse effects are not predicted.									
21	Furanolactone	Adverse effects are not predicted.									
22	Tinosporaside									0.289	0.169
23	Ecdysterone	Adverse effects are not predicted.									
24	Makisterone	Adverse effects are not predicted.									
25	Tinocordioside									0.327	0.131
26	Cordifolide A									0.29	0.169
27	Cordifolide B			0.336	0.315						
28	Cordifolide C	Adverse effects are not predicted.									
29	Cordifolioside A									0.535	0.039
30	Cordifolioside B									0.593	0.027
31	Cordifolioside D	Adverse effects are not predicted.									
32	Cordifoliside E	Adverse effects are not predicted.									
33	Cordioside	Adverse effects are not predicted.									
34	Palmatoside C	Adverse effects are not predicted.									
35	Palmatoside F	Adverse effects are not predicted.									
36	Tinocordifolioside	Adverse effects are not predicted.									
37	Tinocordifolin	Adverse effects are not predicted.									
38	beta- sitosterol									0.258	0.205
39	hydroxyecdysone	Adverse effects are not predicted.									