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RESEARCH ARTICLE

In Silico Screening of Triphala Churna against Bacterial Agents

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Abstract

Triphala Churna consisting Triphala and its constituents have been revealed to have antibacterial properties against human pathogens. The phenolic ring of phytochemicals has been confirmed to be toxic against microorganisms and hence responsible for antibacterial effect. It has also been found to possess antimicrobial, anti-inflammatory, anti-oxidant, and other properties. The objective of this project is to investigate which bioactive compounds of Triphala churna have antibacterial action and can protect humans from infection. The majority of the molecules in phytochemical examination were positive for ethanolic and acetone extracts and the physicochemical characteristics were within the acceptable limits. *In silico* data clearly explains that the compounds of Triphala churna follows *Lipinski's rule of five*. The toxicity profile and ADME parameters of the compounds revealed that most of the compounds were nontoxic towards carcinogenicity, mutagenicity, and reproductive effect. Based on the energy type of interaction between these molecules and the study protein, molecular docking revealed that the three compounds from Triphala churna own the highest docking score against InhA protein: Terflavin B (-9.67 Kcal/mol), Ellagic acid (-9.37 Kcal/mol), and Corilagin (-8.57 Kcal/mol).

Keywords: Anti-bacterial Activity, *InhA*, Molecular Docking, Terflavin B, Triphala Churna

1. Introduction

Herbal remedies are among the most ancient medicines in healthcare, and have long been regarded as one of the most potent means of maintaining human health and homeostasis. Traditional herbal medicine has a long history in India[1]. Triphala is a popular and useful medication that is available in Indian medical pharmacopoeia as "Churna," meaning powder. Churna, a finely sieved powder is used as a source of medicinal agent to treat a variety of infections[2]. Throughout the world, infectious diseases continue to be the leading cause of death, and the mortality rate is found to increase day by day. Pneumonia, tuberculosis were the leading causes of death among all infectious diseases. According to recent study, these diseases claim the lives of 50,000 men, women, and children every day. If this trend continues, nearly 44 million people will perish by 2030. Most of the infectious diseases are communicable which is easily transmitted from one person to another. Microorganism causes disease in humans either by disrupting a vital body process or stimulating the immune system to mount a defensive response[3].

Triphala (Sanskrit; tri = three and phala = fruits) is a well-known and revered polyherbal medicine made from the dried fruits of three plant species native to the Indian subcontinent: *Emblica officinalis* (Family Euphorbiaceae), *Terminalia bellerica* (Family Combretaceae), and *Terminalia chebula* (Family Combretaceae). Triphala is known to prolong life and rejuvenate those who consume for an extended period of time, without causing any side effects as it works slowly and gently[4]. It has a variety of potential applications, including free radical scavenging, antioxidant, anti-inflammatory, immunomodulating, appetite stimulation, gastric hyperacidity reduction, dental caries prevention, antipyretic, analgesic,

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antibacterial, antimutagenic, wound healing, anticariogenic, antistress, adaptogenic, hypoglycemic, anticancer, hepatoprotective, chemoprotective, radio protective, and chemo preventive effect[5–13]. *Terminalia bellerica* (TB) containing tannins, flavonoids, and other phenolic compounds are responsible for a variety of biological activities and their fruits acts as an excellent expectorant and a powerful rejuvenator against microbial infections. It has been reported that *Terminalia bellerica* fruit has antimicrobial activity against a wide range of pathogenic bacteria, yeast, and fungi.

Terminalia chebula (TC) was found to have antibacterial activity against a variety of Gram-positive and Gram-negative human pathogenic bacteria. Ellagic acid isolated from TC was found to have a high inhibitory potential against coliforms that form infectious pathogens. *Emblica officinalis* (EO), contains a wide range of active phytochemicals, including flavonoids and its fruit contain anti-microbial phenolic compounds. EO is one of the richest sources of vitamin C, thus possess antioxidant, anti-inflammatory, and antimicrobial activities. The gallic acid and tannic acid, the main phytoconstituents of EO are responsible for strong antimicrobial properties. Also, *In vitro* studies on the leaf and fruit of EO revealed that they possess antibacterial, antiprotozoal, and antifungal activities too. Triphala and its constituents has been traditionally used against a variety of microorganisms as an antimicrobial agent[14]. Various phenolic and nonphenolic compounds present in triphala and their compounds are found to be effective against both pathogenic and non-pathogenic bacterial strain and it is also been demonstrated as broad-spectrum antimicrobial agent against some resistant bacterial isolates[15]. Triphala and its constituents have also been shown to be effective against human pathogenic bacteria[16]. The phenolic ring of phytochemical is shown to be toxic to microorganism. On the basis of evidence that increased hydroxylation results in increased toxicity, the site(s) and number of hydroxyl and phenol groups are thought to be related to their relative toxicity to microorganisms[17]. Furthermore, some researchers discovered that the majority of highly oxidised phenols are inhibitory. Enzyme inhibition by oxidised compounds, possibly through reaction with sulfhydryl groups, or more nonspecific interactions with proteins are thought to be responsible for phenolic toxicity to microorganisms. *Triphala* and its constituents have anti-bacterial properties that can be used as a preventive/remedy for infectious diseases[18].

2. Materials and Methods

2.1 Collection and Extraction of Investigational Drug

For this study, Grenera Nutrients private limited's, Triphala churna Powder batch No: OP220002 (manufacturing date Feb 2020) with the batch number and date of preparation was considered. The investigational samples were then extracted with water and organic solvents such as acetone, chloroform and ethanol. For the aqueous extraction, 10 gm of triphala churna powder were combined with 100 ml distilled water, shaken for six hours, and then filtered. Alternatively, acetone, chloroform, and ethanol extracts were collected by mixing 10 gm of powdered samples with 50 ml of each solvent separately for six hours at room temperature by using a mechanical shaker. For phytochemical analysis, the extracts were washed, concentrated, dried, and stored in the refrigerator at 4 °C.

2.2 Phytochemical Screening

The phytochemical analysis was carried out on the isolated extracts from the conventional Siddha formulation (Triphala churna). In both aqueous and organic solvents, the Standard Protocol was performed to validate the presence of phytoconstituents in Triphala churna extract[19].

2.3 Physiochemical Analysis of Triphala Churna

The Standard Protocol has specified in official books released by the World Health Organization, such as IP, CCRAS, and API were followed to examine the foreign organic matter, LOD values, ash values, water and alcohol soluble extracts, heavy metals, and microbial contamination.

2.4 Molecular Property

The chemical constituents of Triphala churna were evaluated for *in silico* studies using MOLINSPIRATION® software to determine the compounds drug-likeness. Log P, polar surface area, molecular weight, and various hydrogen bond and bioactivity scores are all assessed[20].

2.5 ADMET Predictions

The ADMET parameters are being used to calculate the pharmacokinetic properties of ligands, which must be tested in order to determine their function within the body, along with the toxicity. ADMET features of the ligands were investigated using admetSAR[21].

2.6 Toxicity Predictions

The web software Osiris Property Explorer was created by Thomas Sander of Acetelion Pharmaceuticals Ltd, Gewerbestrasse 16, and 4123 Allschwil, Switzerland. Mutagenic, carcinogenicity, irritating, and reproductive impact properties are underlined in red, whereas drug conformation is indicated in green[22].

2.7 Protein Preparation

The x-ray crystal structure of the InhA (Figure 1), PDB id: 2H9I, with a resolution of 2.2Å, was obtained from the Protein Data Bank (www.rcsb.org) and imported into Autodock 1.5.6. The original ligand and water molecules were removed before docking, and hydrogen atoms were added to the protein to correct the ionisation and tautomeric states of the amino acid. Figure 1 represents the crystal structure of *InhA*.

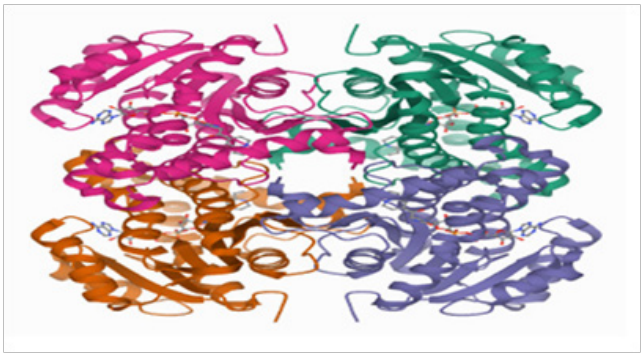


Figure 1. Crystal structure of *InhA*.

2.8 Ligand Preparation

The active phytoconstituents isolated from Triphala churna were drawn in chemdraw Ultra (14.0). Figure 2 illustrate the 2D structures of the active phytoconstitutents. The 2D structures of ligands were imported from chemdraw to obtain 3D structures. The 3D ligands were then exported in pdb format for performing molecular docking against InhA Protein.

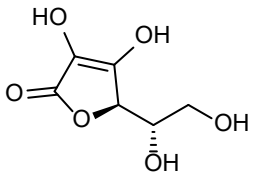
2.9 Molecular Recognition Protein-ligand by Molecular Modelling

To predict the binding affinity and activity of the ligand molecule, molecular docking was performed to determine the scoring function and evaluate protein-ligand interactions. The ligands bioactive binding poses at the active site of the *InhA* were docked using the Autodock® 1.5.6 Program. The binding site was defined using the protein coordinates of 2H9I bound ligand. As a result, the scoring function was generated using the Lamarckian genetic algorithm. The target protein was centered on the grid map for docking calculations. Hydrogen and hydrophobic interactions at the inhibitor site of 2H9I were modelled using Biovia Discovery Studio 2019. Docking interactions were identified by using Pymol

3. Results and Discussion

3.1 Phytochemical Screening

Phytoconstituents in Triphala Churna contain a wide set of activities that can help fight against chronic infections. In aqueous and organic solvents such as water, acetone, chloroform, and ethanol, the phytochemical constituents of Triphala powdered extract were evaluated and tabulated in Table 1. According to phytochemical analyses of all five extracts, the acetone and ethanol extracts of research samples had positive accuracy for carbohydrates, tannins, steroids, cardiac glycosides, coumarins, flavonoids, proteins, alkaloids, and phenolic compounds. Anti-bacterial, immunomodulatory, anti-fungal, anti-obesity, detoxifiers, and rejuvenators, as well as promoting normal respiratory system function and cleansing the lungs, these components protect the body from bacterial infections.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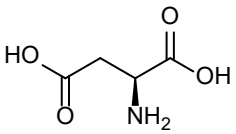
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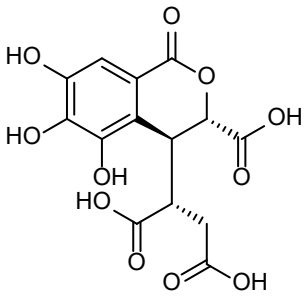
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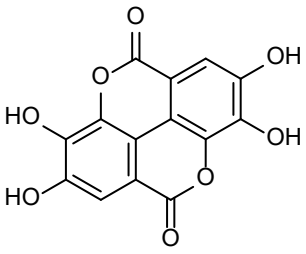
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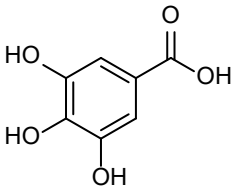
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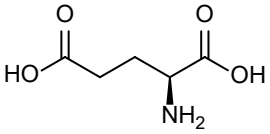
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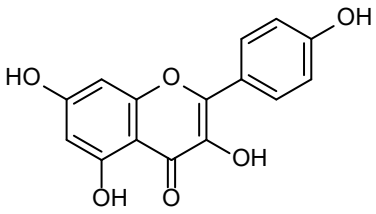
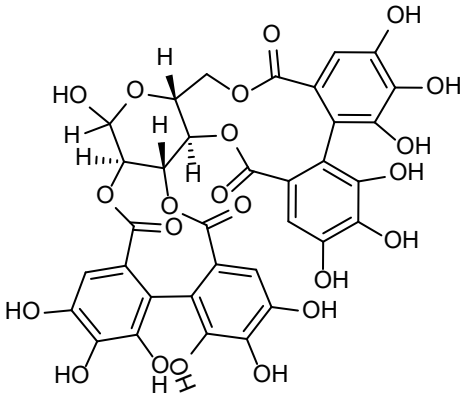

KAEMPFEROL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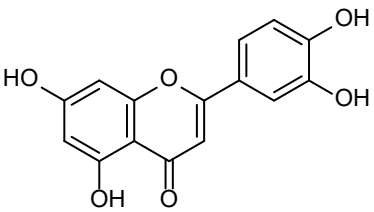
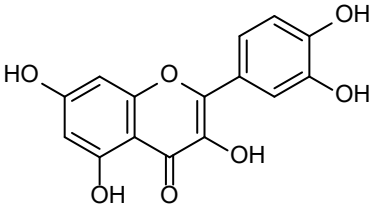

LUTEOLIN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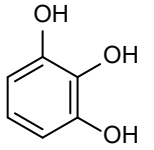
PYROGALLOL

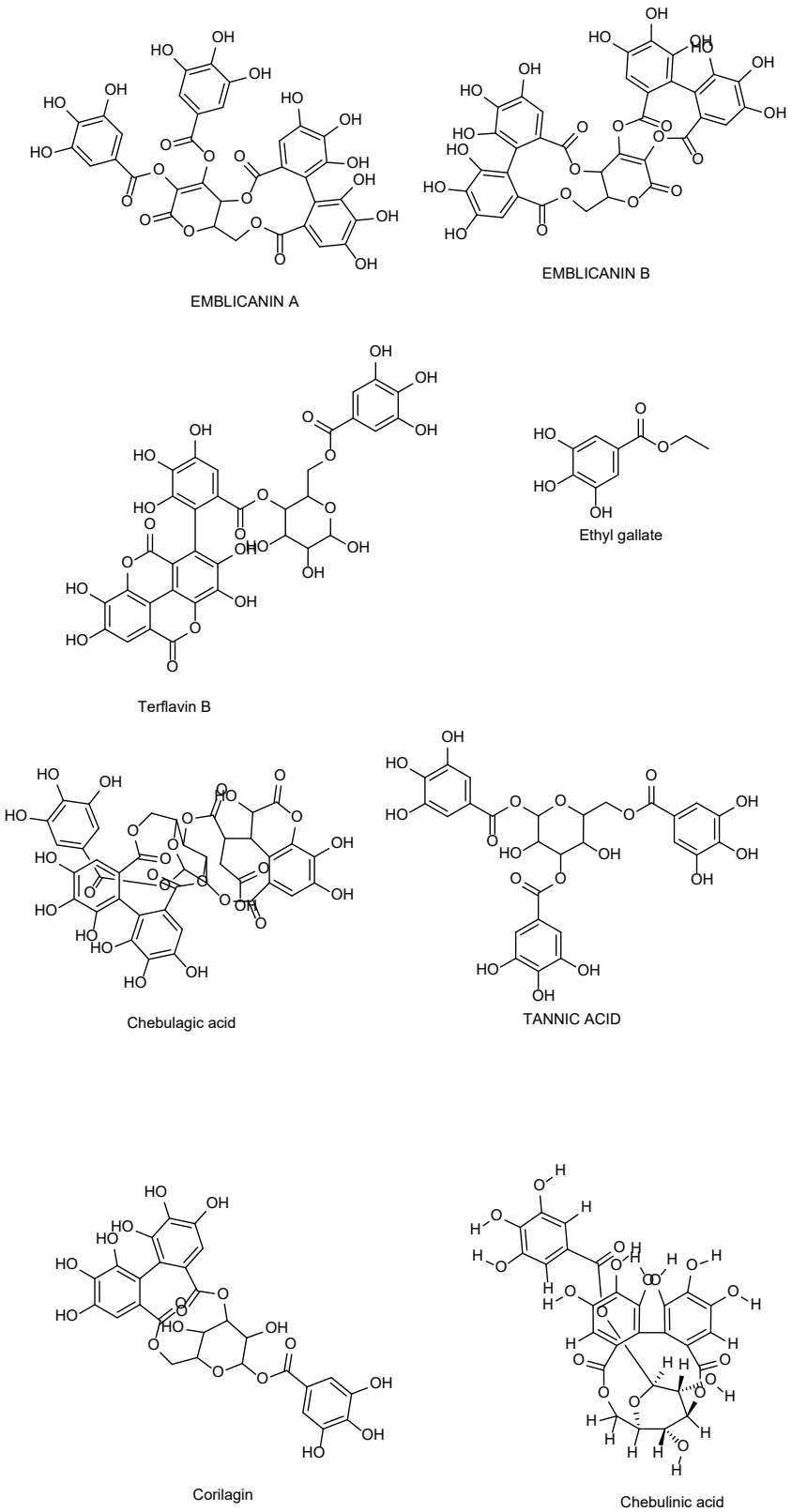

Figure 2. 2D structure of phytoconstituents in Triphala churna.

Table 1. Phytochemical Screening of Triphala Churna

S. No.	Chemical Constituents	Identification Test	Water	Chloroform	Ethanol	Acetone
1.	Alkaloids	Mayer's Test	+	+	+	-
2.	Steroids	Liebermann Test	-	+	+	+
3.	Flavonoids	Hydrochloric acid	+	-	+	+
4.	Saponin	Foam test	+	-	-	+
5.	Phenols	Ferric chloride test	-	-	+	+
6.	Tannins	Ferric chloride test	+	-	+	+
7.	Carbohydrates	Molisch's test	+	-	-	+
8.	Amino acids	Ninhydrin Test	-	-	-	-
9.	Coumarins	Ferric chloride test	+	+	+	+
10.	Cardiac glycosides	Kellers-killani Test	-	-	-	+
11.	Terpenoids	Salkowiski Test	+	+	+	+
12.	Proteins	Xanthoprotein test	-	+	+	+

*(+) - Positive, (-) - Negative

Table 2. Physiochemical Parameter of Triphala Churna

Analysis done	Results of analysis	SPI Specification
Description	Yellowish brown colour fine powder	---------
Loss on Drying at 110 °C	7.56 %	Not more than 12.48 %
Total Ash in %	2.55 %	---------
Acid Insoluble ash %	0.26 %	Not more than 0.61 % w/w
Loss on Ignition	92.44 %	Not more than 94.68 % w/w
Water soluble Extractive	34.49 %	Not more than 50.20 % w/v
Alcohol soluble Extractive	20.64 %	Not more than 33.52 % w/v
Test for Arsenic	BOQ< 0.3 ppm	Not more than 3 ppm
Test for Lead	BOQ < 0.1 ppm	Not more than 10 ppm
Total Microbial Count	1 x 10^4 CFU/g	max 10^5 CFU / gm
Total Fungal Count	Absent	max 10^3 CFU/ gm
E. coli	Absent	Absent
Salmonella sp/g	Absent	Absent
Staphylococcus aureus /g	Absent	Absent
Pseudomonas aeruginosa /g	Absent	Absent
Estimation of Gallic acid	contains 69.38 % of gallic acid	--------

Table 3. Analysis of Chemical Constituents in Triphala Churna by Molinspiration

S. No.	Chemical Constituents	Log P	Molecular Weight	TPSA	No. of Rotatable bonds	No. of Hydrogen Donors	No. of Hydrogen Acceptors	Violations
01.	Tannic Acid	7.06	1701.21	777.98	31	25	46	4
02.	Kaempferol	2.17	286.24	111.12	1	4	6	0
03.	Gallic Acid	0.59	170.12	97.98	1	4	5	0
04.	Ellagic Acid	0.94	302.19	141.33	0	4	8	0
05.	Chebulinic Acid	0.40	956.68	447.10	12	13	27	3
06.	Chebulic Acid	-1.14	356.24	198.89	5	6	11	2
07.	Quercetin	1.68	302.24	131.35	1	5	7	0
08.	Luteolin	1.97	286.24	111.12	1	4	6	0
09.	Pyrogallol	0.73	126.11	60.98	0	3	3	0
10.	Citric Acid	-1.98	192.12	132.12	5	4	7	0
11.	Ascorbic Acid	-1.40	176.12	107.22	2	4	6	0
12.	Emblicanin A	2.94	782.53	374.26	6	12	22	3
13.	Emblicanin B	1.57	780.51	382.07	0	12	22	3
14.	Pedunculagin	0.93	784.54	377.42	0	13	22	3
15.	Corilagin	0.31	634.46	310.66	3	11	18	3
16.	Aspartic Acid	-3.52	133.10	100.62	3	4	5	0
17.	Glutamic Acid	-3.25	147.13	100.62	4	4	5	0
18.	Chebulagic Acid	0.07	954.66	447.10	5	13	27	3
19.	Terflavin B	0.25	784.54	385.23	8	13	22	3
20.	Ethyl Gallate	1.23	198.17	86.99	3	3	5	0

3.2 Physiochemical Analysis of Triphala Churna

The investigational product (Triphala churna) shows physicochemical parameter values that are within the limits set out in the I.P and details are tabulated in Table 2.

3.3 Molecular Property

The crystal 3D structure of the following Triphala active compounds was identified from the PubChem database. Molinspiration were used to assess the drug-likeness features of ligands for the active molecules. Lipinski's rule is not followed by some of the natural compounds and the results are tabulated in Table 3.

3.4 ADMET Predictions

The ADMET characteristics of the ligands in the research sample were evaluated using admetSAR. From the results it is clear that none of the chemicals were carcinogenic. Kaempferol, Chebulinic Acid, Quercetin,

Table 4. ADMET Parameters of chemical constituents present in Triphala Churna by admetSAR

S. No.	Chemical Constituents	BBB	P-gpi	Carcinogens	AMES Toxicity	Acute Oral Toxicity	CYP450 Inhibitory
01.	Tannic Acid	-	+	-	-	3.36405253	-
02.	Kaempferol	-	-	-	+	1.73880136	+
03.	Gallic Acid	-	-	-	-	1.55180728	-
04.	Ellagic Acid	-	-	-	-	1.03707826	-
05.	Chebulinic Acid	-	+	-	+	3.23197293	-
06.	Chebulic Acid	-	-	-	-	1.93255258	-
07.	Quercetin	-	-	-	+	2.55876851	+
08.	Luteolin	-	-	-	-	2.52488947	+
09.	Pyrogallol	-	-	-	+	2.66019034	-
10.	Citric Acid	-	-	-	-	2.33229184	-
11.	Ascorbic Acid	+	-	-	-	0.48069346	-
12.	Emblicanin A	-	+	-	-	1.99122572	-
13.	Emblicanin B	-	+	-	-	2.25803328	-
14.	Pedunculagin	-	+	-	+	1.69491005	-
15.	Corilagin	-	+	-	-	2.38526773	-
16.	Aspartic Acid	+	-	-	-	0.68306118	-
17.	Glutamic Acid	+	-	-	-	0.37184775	-
18.	Chebulagic Acid	-	+	-	+	2.98658705	-
19.	Terflavin B	-	+	-	-	1.87034225	-
20.	Ethyl Gallate	+	-	-	-	1.84007943	-

Pyrogallol, Pedunculagin, and Chebulagic Acid were found to be positive in AMES, while others were found to be negative. Table 4 lists the compounds B.B.B., P-gpi, Acute Oral Toxicity, and CYP450 Inhibitory values.

3.5 Toxicity Predictions

Osiris Property Explorer has been used to retrieve the toxicity and biological activity spectra of a number of phytoconstituents, as shown in Table 5. Toxic compounds are represented by red, while dangerous free compounds are represented by green. The non-toxic molecules are then docked by using Autodock.

3.6 Molecular Docking and Interaction

Molecular docking was performed on active constituents obtained from Triphala churna Powder on the binding pocket of enzyme *InhA* in order to identify a potential candidate for treating Bacterial infections (PDB ID: 2H9I). Following the above optimization, all ten compounds were found to be non-toxic, and they were docked against the target enzyme *InhA* and rated based on their docking energies. Compounds with a dock score of 7.0 or even less are thought to be a better representation for bacterial infection control. The table in the supplementary file can be used to perform a detailed assessment. The list of active molecules with

Table 5. Toxicity Profile of Chemical Constituents

S. No.	Chemical Constituents	Mutagenicity	Carcinogenicity	Irritant	Reproductive Effect	Drug likeness
01.	Tannic Acid	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	1.60
02.	Kaempferol	TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	0.90
03.	Gallic Acid	TOXIC	NON TOXIC	NON TOXIC	TOXIC	0.12
04.	Ellagic Acid	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-1.60
05.	Chebulinic Acid	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	1.19
06.	Chebulic Acid	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-1.14
07.	Quercetin	TOXIC	TOXIC	NON TOXIC	NON TOXIC	1.60
08.	Luteolin	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	1.90
09.	Pyrogallol	TOXIC	TOXIC	TOXIC	TOXIC	-3.50
10.	Citric Acid	NON TOXIC	NON TOXIC	TOXIC	NON TOXIC	3.56
11.	Ascorbic Acid	TOXIC	TOXIC	NON TOXIC	TOXIC	0.02
12.	Emblicanin A	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	1.78
13.	Emblicanin B	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-0.04
14.	Pedunculagin	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-0.28
15.	Corilagin	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	1.96
16.	Aspartic Acid	TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-11.99
17.	Glutamic Acid	TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-18.65
18.	Chebulagic Acid	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	1.19
19.	Terflavin B	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	0.36
20.	Ethyl Gallate	NON TOXIC	NON TOXIC	NON TOXIC	NON TOXIC	-3.12

their binding energy and interactions obtained after docking studies are tabulated in Table 6.

Those active molecules with a dock score of 7.0 or less were chosen. Terflavin B (-9.67 Kcal/mol) (Figures 3 and 4), Ellagic acid (-9.37 Kcal/mol) (Figure 5), and Corilagin (-8.57 Kcal/mol) were the three compounds which exhibited highest docking score with *InhA* (2H9I). The rigid docking findings were visualized by Discovery Studio for further evaluation. Terflavin B showed hydrogen bonding interactions with ILE194, MET98, GLY14, SER94 and ILE21, and Ellagic acid showed hydrogen bonding interactions with GLY96, GLY14, VAL65, LEU63, ASP64, in the same way, Corilagin was found to have hydrogen bonding interactions with GLY14, GLY96, VAL65, GLN 66, LYS118. The first level interactions were considered as the most important, the presence of hydrogen bonds interaction in the selected compounds explains that all the three constituents interacted well with the protein (Figure 3).

Table 6. Binding interactions of active constituents with PDB 2H9I

S.No.	Active Constituents	Binding Energy (Kcal/mol)	Binding Interaction
1.	Tannic Acid	-6.54	VAL65,GLY89
2.	Ellagic Acid	-9.37	GLY96,GLY14,VAL65,LEU63,ASP64
3.	Chebulic Acid	-6.12	LEU 46, ARG 43
4.	Luteolin	-7.77	ILE194,TYR1158,ASP150
5.	Citric Acid	-6.69	ARG43, 1LE194
6.	Emblicanin A	-7.61	SER89,ILE65
7.	Emblicanin B	-7.19	GLN 66, LYS 118
8.	Corilagin	-8.57	GLY14,GLY96,VAL65, GLN 66, LYS 118
9.	Terflavin B	-9.67	ILE 194,MET 98,GLY14,SER94,ILE21
10.	Ethyl gallate	-5.76	GLY96,ASP64,VAL65,LEU63
	Isoniazid	-4.8	-4.8GLY 96, ASP 234

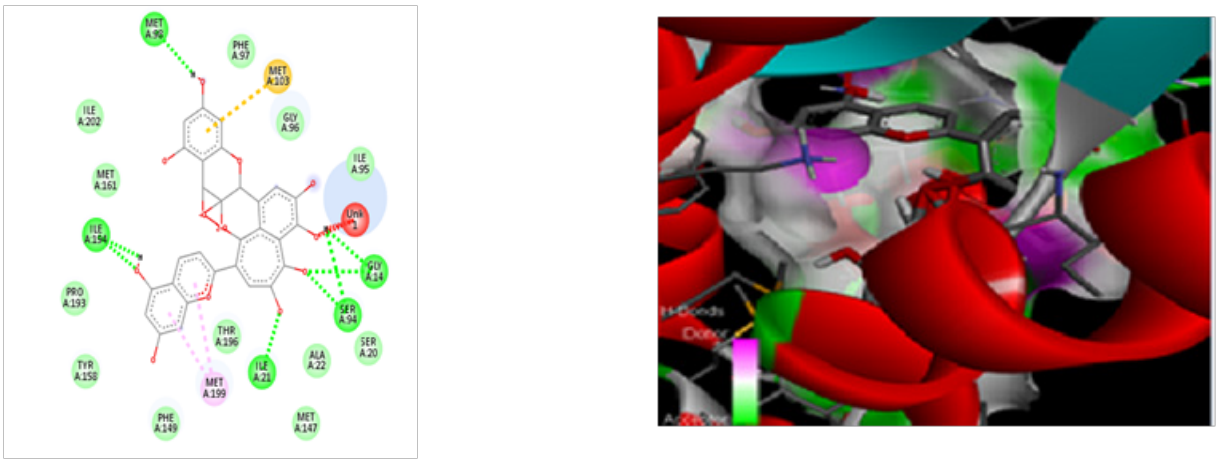

Figure 3. 2D and 3D View of the Binding Conformation of Terflavin B Inhibitor at the active site of *InhA*

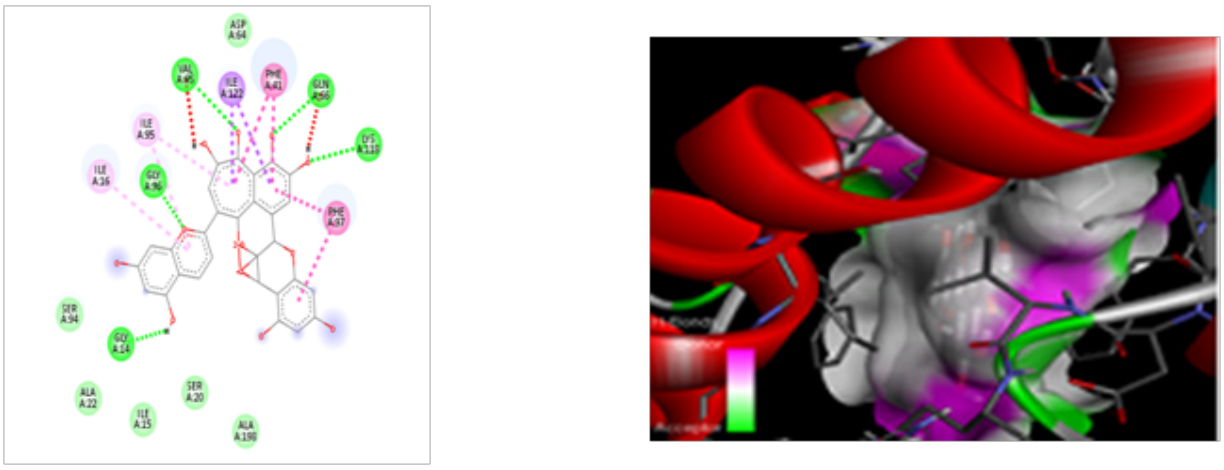

Figure 4. 2D and 3D view of the binding conformations of Terflavin B inhibitor at the active site of *InhA*.

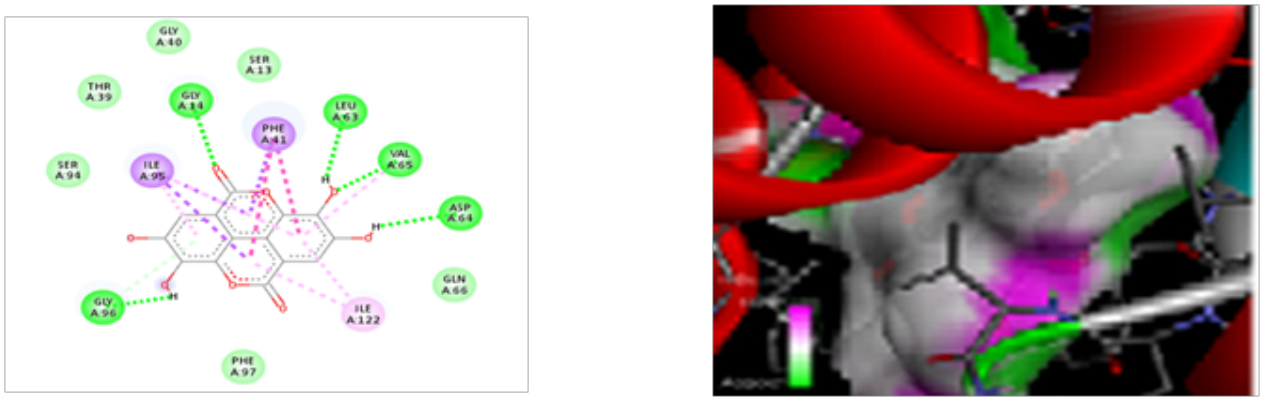

Figure 5. 2D and 3D view of the binding conformation of ellagic acid inhibitor of *InhA*.

4. Conclusion

Owing to the existence of active phytochemical components that are responsible for various pharmacological activities, the medicinal plants are considered as a powerful source of human health. Based on the results, the current study concludes that the test extracts of Triphala powder are high in phytochemical constituents, despite the fact that sample screening revealed variance in phytochemical constituents with the presence and absence of some components. The drug-likeness predicted using Molinspiration, and the physicochemical parameters were within the limits. Docking studies revealed that three molecules (Terflavin B, Corilagin, and Ellagic acid) among top ten that are both chemically and biologically interesting, are proposed as inhibitors against Bacterial agents. This provides a way for the synthesis of these compounds and evaluation of their in vitro and in vivo activity against *InhA* before an enzymatic assay may be considered.

5. Declaration of Competing Interest

The authors claim no conflict of interest

6. Acknowledgement

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7. References

1. Peterson CT, Denniston K, Chopra D. Therapeutic uses of Triphala in Ayurvedic medicine. J Altern Complement Med. 2017; 23(8):607–14. https://doi.org/10.1089/acm.2017.0083. PMid:28696777. PMCid:PMC5567597
2. Nayak K, Patil A, Vishnuprasad S, Nayak DM. Antibacterial effect of triphala churna against common wound pathogens. Int J Curr Res. 2015; 7(01):12074–7.
3. Singh RK, Gupta R, Dwivedi N. A review on antimicrobial activities of triphala and its constituents. World J Pharm Pharm Sci. 2016; 5(4):535–58.
4. Rao PP. Antioxidant effect of Triphala - Critical review. J Ayurveda Integr Med. 2017; 2(1):213–19. https://doi.org/10.21760/jaims.v2i1.7513
5. Prabu D, Kirubanandan S, Ponnudurai K, Nappinnai M, Jinu A, Renganathan S. Anti-inflammatory and analgesic activities of methanol extract of Triphala - A poly herbal formulation. Orient Pharm Exp Med. 2008; 8(4):423–9. https://doi.org/10.3742/OPEM.2008.8.4.423
6. Chouhan B, Kumawat R, Kotecha M, Ramamurthy A, Nathani S. Triphala: A comprehensive ayurvedic review triphala: A comprehensive ayurvedic review. Int. J. Ayurveda Res. 2013; 4(4):612–17. https://doi.org/10.7897/2277-4343.04433
7. Varma SR, Sivaprakasam TO, Mishra A, et al. Protective effects of Triphala on dermal fibroblasts and human keratinocytes. PLoS One. 2016; 11(1):e0145921. https://doi.org/10.1371/journal.pone.0145921. PMid:26731545 PMCid:PMC4711708
8. Belapurkar P, Goyal P, Tiwari-Barua P. Immunomodulatory effects of triphala and its individual constituents: A review. Indian J Pharm Sci. 2014; 76(6):467–75.
9. Prasad S, Srivastava S. Oxidative stress and cancer: Chemopreventive and therapeutic role of triphala.

Antioxidants. 2020; 9(1):72. https://doi.org/10.3390/antiox9010072. PMid:31941067 PMCid:PMC7022920
10. Murthy M. Anticancer and pro-apoptotic effects of Triphala extract in human breast cancer MCF-7 cells. FASEB J. 2018; 32(S1). https://doi.org/10.1096/fasebj.2018.32.1_supplement.151.2
11. Chainani S, Siddana S, Reddy C, Thippeswamy M, Maurya M, Rudraswamy S. Antimicrobial activity of Triphala on Lactobacilli and Candida albicans: An in vitro study. J Orofac Sci. 2015; 7(2):104. https://doi.org/10.4103/0975-8844.169757
12. Manoraj A, Thevanesam V, Bandara BMR, Ekanayake A, Liyanapathirana V. Synergistic activity between Triphala and selected antibiotics against drug resistant clinical isolates. BMC Complement Altern Med. 2019; 19(1):199. https://doi.org/10.1186/s12906-019-2618-1. PMid:31375093 PMCid:PMC6679468
13. Rao P. Antioxidant effect of Triphala - Critical review. J Ayurveda Integr Med. 2017: 2(1). https://doi.org/10.21760/jaims.v2i1.7513
14. Patil SG, Deshmukh AA, Padol AR, Kale DB. In vitro antimicrobial activity of *Emblica officinalis* fruit by tube dilution method. Toxicol Appl Pharmacol. 2012; 2:49–51
15. Mahalakshmi K, Prabhakar J, Sukumaran VG. Antibacterial activity of Triphala, GTP and curcumin on Enterococci faecalis. Biomedicine. 2006; 26:43–6.
16. Sumathi P, Parvathi A. Antibacterial potential of the three medicinal fruits used in Triphala: An Ayurvedic formulation. J. Med. Plants Res. 2010; 4:1682–5.
17. Zareen N, Jaiganesh R. Antimicrobial effect of Triphala on oral microbes - An in vivo study. Drug Invent Today. 2019; 11(2).
18. Chainani S, Siddana S, Reddy C, Thippeswamy M, Maurya M, Rudraswamy S. Antimicrobial activity of Triphala on *Lactobacilli* and *Candida albicans*: An in vitro study. J Orofac Sci. 2015; 7(2):104. https://doi.org/10.4103/0975-8844.169757
19. Kumar NS, Nair AS, Murali M, Devi PSS. Qualitative phytochemical analysis of triphala extracts. J. Pharmacogn Phytochem. 2017; 6(3):248–51.
20. Duchowicz PR, Talevi A, Bellera C, Bruno-Blanch LE, Castro EA. Application of descriptors based on Lipinski's rules in the QSPR study of aqueous solubilities. Bioorg Med Chem. 2007; 15(11):3711–9. https://doi.org/10.1016/j.bmc.2007.03.044. PMid:17418580
21. Pires DEV, Blundell TL, Ascher DB. PkCSM: Predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. J Med Chem. 2015; 58(9):4066–72. https://doi.org/10.1021/acs.jmedchem.5b00104. PMid:25860834 PMCid:PMC4434528
22. Kumar N, Mishra SS, Sharma CS, Singh HP, Singh H. In silico pharmacokinetic, bioactivity and toxicity evaluation of some selected anti-ulcer agents. Int J Pharm Sci Drug Res. 2017; 9(2). https://doi.org/10.25004/IJPSDR.2017.090205