EXPLORING THE POTENTIAL OF *Morindia citrifolia* IN TUBERCULOSIS: A NETWORK PHARMACOLOGICAL APPROACH

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CANDIDATE'S DECLARATION

I Anjali Sharma (2k22/MSCBIO/59) hereby certify that the work which is being presented in the dissertation enlightened "**Exploring the potential of *Morindia citrifolia* in Tuberculosis : A Network Pharmacological Approach**" in partial fulfillment of the requirements for the award of the Degree of Masters in Science, submitted in the Department of Biotechnology, Delhi Technological University is an authentic record of my own work carried out during the period from Aug 2023 to Mar 2024 under the supervision of Dr. Navneeta Bharadvaja.

The matter presented in this dissertation has not been submitted by us for the award of any other degree of this or any other institute.

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CERTIFICATE

This is to certified that Anjali Sharma (2k22/MSCBIO/59) carried out their research work presented in this thesis entitled "**Exploring the potential of *Morindia citrifolia* in Tuberculosis: A Network Pharmacological Approach**" for the award of Master of Science from the Department of Biotechnology, Delhi Technological University, Delhi, under my supervision. The dissertation embodies results of original work, and studies are carried out by the students herself and the contents of the dissertation do not form the basis for the award of any other degree to the candidate or to anybody else from this or any other University/Institution.

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EXPLORING THE POTENTIAL OF *Morindia citrifolia* IN TUBERCULOSIS: A NETWORK PHARMACOLOGICAL APPROACH

ANJALI SHARMA

ABSTRACT

Global mortality rates from tuberculosis (TB) are high, and the disease is still progressive and thriving. *Myobacterium tuberculosis (*Mtb) has developed a resistance to anti- tuberculosis drugs such as rifampin and moxifloxacin. It poses a serious obstacle to it treatment, increasing allelopathic medicines more difficult to administer and resulting in life- threatening health issues. Alternative therapeutic approaches are imperative, especially via investigating phytochemicals from medicinal plant like *Morindia citrifolia* as possible TB inhibitor. Phytochemicals (Nordamnacanthal, Ricinoleic acid, Kaempferol, Octanoic acid, 3-methylbut-2-enyl ester) originating from different parts of plant are recognized for their various advantageous characteristics , such as antibactertial, anti- inflammatory , anti- tuberculosis, and disease- modifying abilities. Because these phytochemicals reduce the virulence of disease and eradicate multi- drug resistance, they have demonstrated promise in the treatment of chronic disease, including TB. An effective method for determining these phytochemicals' capacity to suppress Mycobacterium TB at the early stages of infection is through in silico research. When screening plant phytochemicals, computational techniques are important. This study makes use of a range of computer methods such as network pharmacology and molecular docking to predict the phytochemicals from *Morindia citrifolia* on the molecular processes connected to tuberculosis. The work investigates the main objective for developing precision medicine. The results of the study suggest that *Morindia citrifolia* may be utilized to treat tuberculosis. Natural supplements are reliable and secure substitute for traditional tuberculosis therapies. This study highlights how crucial it is to look into the potential application of natural compunds as a molecular tuberculosis (TB) treatment.

LIST OF PUBLICATIONS

Name of Conference: INTERNATIONAL CONFERENCE on Intelligent Computing and Communication Techniques, JNU, New Delhi

Title of Paper : Exploring potential of Bacopa monnieri's against B19V induced Erythema Infectiosum: An Insilco approach

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LIST OF ABBREVATIONS

TB – Tuberculosis

Mtb – Myobacterium tuberculosis

HIV – Human Immunodeficiency Virus

NAAT – Nucleic acid amplification technique

LPA – Line probe assay

NTM – Non tuberculosis Mycobacteria

PPD – Purified protein derivative

COX - Cyclooxygenase enzyme

ADR - Adverse drug reactions

IMPPAT – Indian Medicinal Plant, Phtytochemistry and Therapeitics

OMIM – Online Mendelian Inheritance

PDB – Protein Data Bank

PPI – Protein – Protein interaction

2D – Two dimensional

3D – Three dimensional

CHAPTER 1

INTRODUCTION

1.1 Background

The major health issues facing the globe worldwide are tuberculosis (TB), next to the Human immunodeficiency virus (HIV). Due to the front-line anti- tuberculosis (Rifampin, rifapentine,) medications' progressive loss of efficacy for TB therapy, the high rates of TB incidence in terms of both morbidity and death have emerged as a major global issue. This disease is communicable which spreads from infected patient to healthy person through sneezing, coughing and the pathogen responsible to this disease is *Myobacterium tuberculosis(*MTB) . The main target site is lung but may spread to other organs like lymph nodes, genitourinary tract &, nervous sytem. Alveolar macrophages form tight structures known as granulomas with the help of neutrophils and other inflammatory cells and these granulomas develop in the lungs to stop M. tuberculosis from growing. M. tuberculosis lives in these granulomas in inactive state for a long period of time by utilizing host lipids and eventually weakens the immune system which leads to reactivation and cause of active disease (Lyadova & Panteleev, 2015). Ninety percent (90%) of those infected experience latent state of infection, in which M.tuberculosis can survive for several years in a non-replicating form without causing illness. In the remaining 10% of those with impaired immune systems, the illness could show up as actively replicating due to HIV- TB co- infection which can cause death (Flynn et al., n.d.).

Even with tremendous attempts to manage the disease, TB is still a large cause of death in underdeveloped nations and is recognized as the world's most common infectious disease. The treatment of this disease has become serious problem because of Myobacterium tuberculosis (Mtb) which is responsible for causing this disease has become resistant to multidrug and also there are adverse side(thrombocytopenia, itching, T- cell destruction) effects because of anti- TB drugs such as rifampin and isoniazid[42]. The inability to protect against TB by BCG vaccine is also main obstacle to eradicate TB from world. T- Cells such as Th1 and Th17 are imperative to protect against *Myobacterium tuberculosis* infection. We need an alternate therapeutic approach which can deal with this deadly pathogen *M.tuberculosis* better and eradicate multi drug resistant. We need new therapeutic drugs that operate on novel targets which have anti-tuberculosis property. Inspite of various efforts to discover effective anti- TB from

medical approach, local plants such as *Morindia citrifolia* can use for the treatment of TB which has less side effects.

The word “Phytochemicals” refers naturally occurring biologically active substances in plants that helps in curing disease. These phytochemicals contains flavonoids, glycosides, anthraquinonenes, carboxylic acids which are used in biomedical therapies. The phytochemicals which are used in treatment of tuberculosis are anthraquinones, glycosides, flavone glycosides, carboxylic acids, and sterols which are present *in Morindia citrifolia*.
There are around 80 species in the genus *Morinda* and family Rubiaceae, which includes the species of *Morinda citrifolia*. With a height of 10 m, *Morinda citrifolia* is a plant with an abundance of large, leaves that are 7-9 cm long and 15-35 cm wide. The tiny white tubular blooms are placed in groups and put onto the peduncle. The corolla is greenish-white, and petiole creates circle-like impressions on stalks. The phytochemicals present in this plants which has anti-tuberculosis property are Nordamnacanthal, Ricinoleic acid, Kaempferol, Octanoic acid, 3-methylbut-2-enyl ester. Although the precise processes behind the antimicrobial activity of plant secondary metabolites remain unclear, several investigations have revealed that noni's phytochemicals are phenolic substance that has the property to harm bacterial cell membranes, inactivate enzymes, & harm bacterial cell walls. It may also function as an antibacterial substance, preventing or even killing *Mycobacterium tuberculosis.*

Several computational software are applied in computational drug design with the help of molecular modeling and docking herein to find out new compounds for selectivity and effectiveness that require further in vitro and in vivo investigation. This technique is significant in the identification of new drugs as well as in drug design since many targets for MTB has been elucidated to involve over 4000 distinct proteins. For this reason, the approach presented here has significant implications for the formulation of new drugs.

In this thesis, I have explored the possibility of *Morindia citrifolia*, a medicinal plant, in treating tuberculosis using a network pharmacological approach. By merging bioinformatics, computational biology, and pharmacological research, I am trying to identify potential targets and pathways impacted by *Morindia citrifolia* and elucidate its mechanisms of action in tuberculosis. This work has the potential to advance our understanding of tuberculosis and uncover novel therapeutic strategies.

1.2. Objectives

1. To analyze *Morindia citrifolia* plant's therapeutic potential for the management of Tuberculosis (TB)

2. To assess the possible synergistic effects of several active phytochemicals and anti-tuberculosis core targets found in *Morindia citrifolia*.

3. To conduct Network Pharmacology to find out core target genes and important phytochemicals in treating tuberculosis

4. To conduct molecular docking studies to evaluate the affinity of *Morindia citrifolia* active phytochemicals for the main anti-tuberculosis core targets.

CHAPTER 2

REVIEW OF LITERATURE

2.1 Pathogenesis of Tuberculosis

A severe worldwide health, social, and economic burden, tuberculosis (TB) is deadliest and oldest diseases known. It is most prevalent in low- and middle-income nations. Asia has recorded the largest number of tuberculosis cases (44%), followed by Africa (25%). According to the 2019 WHO report, South Africa, Indonesia, China, Pakistan, and India are the top five countries with new TB cases (WHO,2013). Every year, two million people die from tuberculosis (TB); new vaccinations and drugs are needed to stop this disease. Researching the physiology and genetics of Mycobacterium tuberculosis and related mycobacteria is important for the creation of new anti-tubercular medications. M. tuberculosis (Mtb) is the causative agent of tuberculosis (TB) in humans. M. africanum, which only causes TB in certain Africa locations *(*Delogu et al., 2013). Under ideal circumstances, M. tuberculosis (Mtb) can double in 24 hours. One of the main characteristics of Mtb is its different cell wall construction, which plays a important role in virulence and offers an incredibly strong impermeable barrier to harmful substances (Delogu et al., 2013). The mode of transmission of tuberculosis is aerosol. Here's steps of infection and progression of TB [Fig.2.1].

1. **Exposure to TB** – Healthy person inhales Mtb from air or infected person.
2. **Primary Infection** – these bacteria reaches to alveoli of lungs and phagocytized by macrophages present in lungs.
3. **Innate Immune response** – Body's immune system responds and form granulomas (bunch of immune cells that limits the mobility of the pathogens) stops the pathogens from spreading throughout the tissues. But if it fails bacteria survives
4. **Bacterial Multiplication** – Mtb starts to replicate in the alveoli macrophages & diffuse to other cells; organs by blood stream infect lymphatic system.
5. **Cell- Mediated Immune response-** Neutrophils, lymphocytes, and other immune cells migrate to the location of the infection, the adaptive immune starts responding, forming cellular infiltrate and thus bacterial replication is under controlled (Ottenhoff & Kaufmann, 2012)
6. **Latent TB infection -** Non-overt illness signs or symptoms occur in 90–95% of patients (Latent TB). This inactive disease may remain with a person for long period of time with no sign of symptoms (Delogu et al., 2013)

7. **Reactivation**: In a latent state of Mtb , microbes are enclosed in a macrophage and eventually which becomes enclosed in a T- helper cell. 10% of people with the inactive condition have the potential to become active when the granuloma fails to stop the spread of the bacteria and the pathogens (Vynnycky & Fine, 2000) .Therefore, immunosuppression reactivate the bacteria with symptoms and tissue damage.

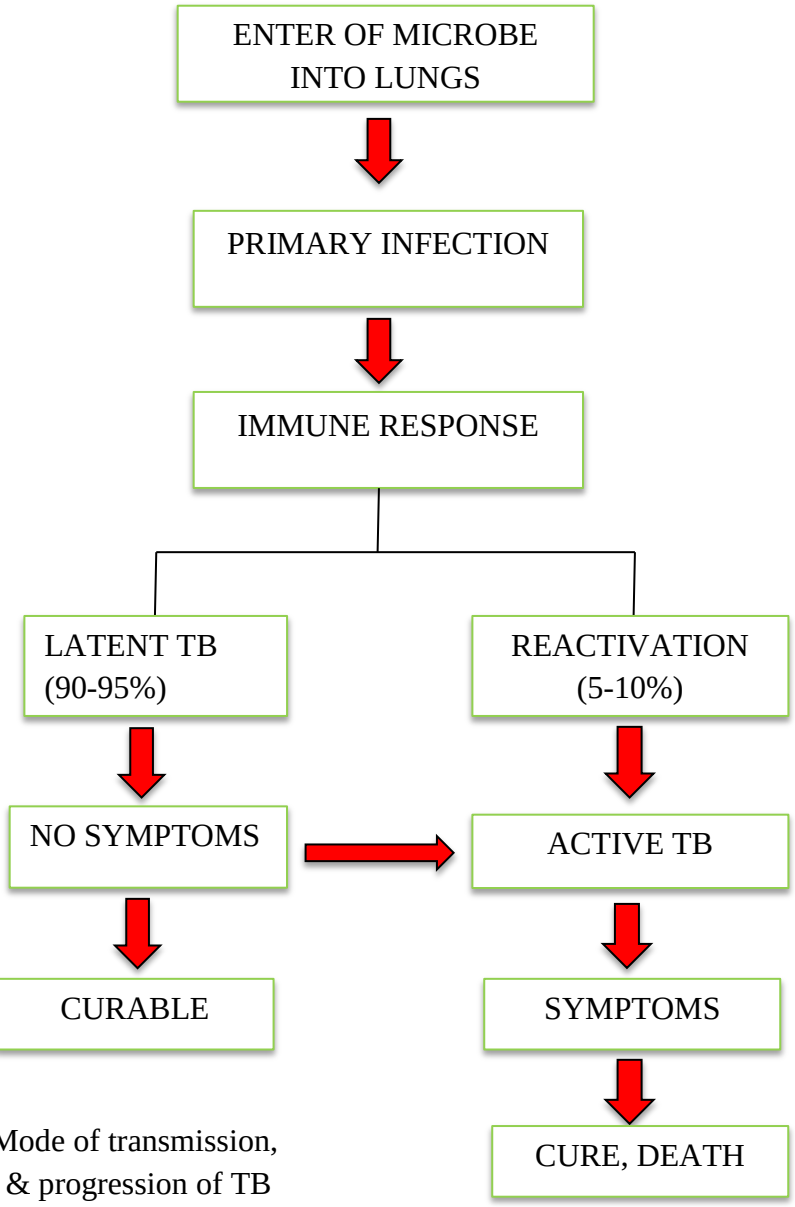


Fig.2.1. Mode of transmission, infection & progression of TB

- **Nucleic acid amplification techniques:** It is most widely used molecular test to diagnose pulmonary tuberculosis. In this sputum and bronchoalveolar lavage fluid is obtained (BAL). Thus, it is possible to quickly confirm a possible diagnosis of TB when AFB is seen on sputum. With very few exceptions, a negative result in this case clearly suggests that the material contains a non-tuberculosis Mycobacteria (NTM) species.

- **Line probe Assays (LPA):** It is a technique that identifies the existence of M. tuberculosis that determine resistant to specific drugs via a process comprising of PCR plus a strip that is lined with oligonucleotide probes. This method involves initially isolating DNA from the sample and then using a technique also known as PCR, to amplify particular sections of genome of the M. tuberculosis bacteria. Further the DNA products are amplified and then incubated with a number of oligonucleotide probes that are stuck to a strip. These probes are artificially made to combine with certain sequences of nucleotides of M. tuberculosis whose linkage may present drug resistance. Detection of Mtb is done through the visual observation of the colored bands that develops on the strip due to hybridization of probes on the membrane[8]. Each band corresponds to a different gene being tested thereby enabling one to identify the bacterium and gains used in identifying the appearance of mutations that make the bacterium resistant to drugs. Commercial products to diagnose TB – Inno- LiPA Rif TB kit (Rossau et al., 1997)

- **Tuberculin Skin Test/ Mantoux test** : Purified protein derivative(PPD) tuberculin is injected intradermal on the arm and after 48-72 hours , injection site is examined (Acharya et al., 2020) . If an induration of a certain size (standard sizes may differ depending on various underlying factors such as HIV, history of contact with TB patient and immunosuppressive therapy) is found then it confirms that the person has had exposure to Mycobacterium tuberculosis and likely harbors LTBI. Nonetheless, positive test results by these non-nucleic acid probes cannot differentiate between the previously mentioned dormant tuberculosis and active forms. No significant induration suggests that person has not been infected with Mtb.

- **Important Biomarkers for TB diagnosis :** CD27+ lymphocytes (blood), intracellular IFN-y(sputm) , IFN-y secreting cells(blood, pleural fluid, cerebrospinal fluid), Lipoarabinomannan (urine) (Acharya et al.,2020)

2.3 Treatment of Tuberculosis

Table I. Drugs used to diagnosis tuberculosis

S.NO	CLASS	DRUGS	REFERENCES
1.	Rifamycins	Rifampin, rifapentine	(Murray et al.,2015)
2.	Fluoroquinolones	Moxifloxacin, gatifloxacin	Murray etal.,2015
3.	Oxazolidinone	Linezolid	(Abou Assi et al., 2017)
4.	Diarylquinoline	Bedaquinline	(Gfeller et al., 2014)
5.	Nitro-dihydro-imidazooxazole	Delamanid	(Murray et al., 2015)
6.	Nitroimidazo-oxazine	Pretomanid	(Murray et al., 2015)

2.4 Limitations of Anti-tuberculosis Drugs

- **Drug Resistance:** Multidrug Resistant TB which are resistant to drugs such as isoniazid . And this resistance is due to the improper use of medication. They can lead to hepatotoxicity, neuropathy and gastrointestinal issues.

- **Bacterial Persistence:** Mycobacterium tuberculosis develops the ability to thrive within the body, remain impervious to the effects of medications, and eventually reactivate.

- **HIV Co-infection:** Treatment of TB often involves using rifampicin, which can interfere with antiretroviral drugs (they are used to manage HIV infection such as protease and integrase inhibitors), which many TB patients take because they are co-infected with HIV.

2.5. *Morinida citrifolia*

Morindia citrifolia which is also known as "noni" belongs to Rubiaceae family is widely used to cure varieties of diseases. It contains phytochemicals which possess antibacterial, antiviral, antifungal, antitumor, anti-inflammatory properites. *Morindia citrifolia* plants and its fruit, leaves and roots contains nutritional and therapeutical values. It is widely distributed all over the world, Tahiti, India, US, Thai and Brazil (Murray et al., 2015).

Anti- tumor activity: It has been shown that the noni juice's ethanol precipitable fraction (ppt), which is a polysaccharide-rich material made up of glucuronic acid, galactose, arabinose, and rhamnose, possesses anti-tumor properties against lung cancer . Noni-ppt seems to increase T-cell, thymocyte, and macrophage production in cell models.

Analgesic activity: Thymus is an imperative immune organ in the human body which produces T- cells and it helps in increasing the T-cell immune response .Noni extract efficacy is strong like morphine with less side effect (Hirazumi et al., 1996)

Anti-inflammatory activity: Noni juice has strong anti- inflammatory activity as compared to drugs such as Celebrex with no side effects as it inhibits cyclooxygenase enzyme (COX-1 and COX-2).

Cardiovascular activity: Noni can be used as a preventive against arteriosclerosis, a condition linked to the oxidation lipoproteins. Using the Cu probe, it was determined that the inhibition percentage of LDL oxidation for methanol and ethyl acetate, respectively, was 81 and 92%, using the TBA-RS technique. This advantageous impact may result from the presence of lignans, dimers of phenylpropanoid compounds.

Antioxidant property: The phytocompounds neutralize free radicals which decrease oxidative stress and inhibit lipid peroxidation.

2.6. Review of existing research on *Morindia citrifolia* and its anti-tuberculosis property

Noni has anti-tuberculosis property as it inhibits and kills *Myobacterium Tuberculosis*. Noni leaves extract kills almost 89 percent of bacteria like Rifampcin drug. Phytochemicals such as anthraquinones , scopoletin possess antibacterial property against *Myobacterium tuberculosis*. Tb caused lung inflammation and its anti-inflammatory property present in phytochemicals such as quercetin reduces

inflammation in the lungs. It also boosts immune system and stimulate immune cells such as macrophages to fight against Mtb. Table 2.2 depicts *Morindia citrifolia* important phytochemicals present in the different parts of plant and their role to diagnose tuberculosis.

Table II. Summary of studies on tuberculosis using *Morindia citrifolia*

Plant part	**Phytochemicals**	**Findings**	**References**
Leaves	Morindin, Urosolic acid b- setosterol	Killed 90% of bacteria in a test tube which is as effective as rifampicin which kills 98%.	
Roots	Rubiadin Soranjidiol Alizarin Anthraquinone Ricinoleic acid	Root extract shows strong antitubular activity with an minimum inhibition concentration(MIC) value of 50 μg/mL	(Sam-Ang et al., 2023)
Fruits	Quercetin Catechin Rutin	Minimum inhibitory dose against Mtb (H37RV) is 40 mg/ml	(Mauliku et al., 2017)
Bark	Morindin	Can be used as adjunct	

2.7. Exploration of the network pharmacology approach and its relevance in studying complex diseases like tuberculosis.

Network pharmacology is an interdisciplinary science that applies network science, system biology, and pharmacology approaches to distinguish the drug-target interactions

and the networks at the systems-level. This strategy has shown to be extremely beneficial in the research of complex illnesses, offering insights about drug targets, treatment methods, and disease mechanisms. The network pharmacology process used for this investigation is conceptualized in the Fig. 2.2.

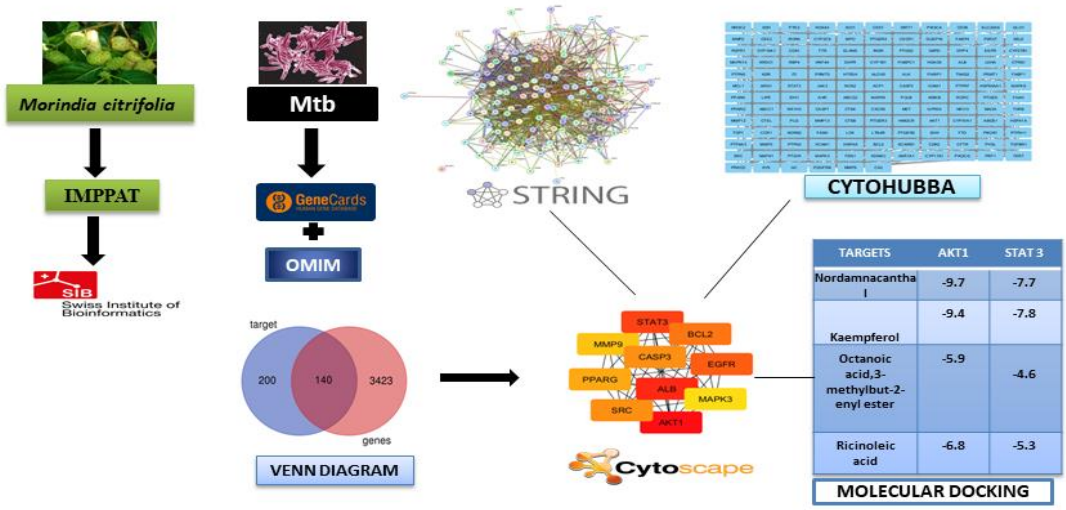


Fig 2.2 Conceptual representation of network pharmacology approach

- **Anticipating negative drug response:** Adverse drug reactions (ADRs) are a major issue in patient safety and drug development. Therefore, the concept of network pharmacology provides an approach to get insights into the network context of drug-target interactions, which is helpful to understand the mechanisms of Adverse Drug Reactions (ADRs) at the systems level. That could also be used to improve and fine-tune dosages or structures for safer drugs.

- **Network pharmacology and personalized medicine**: Systems Biology is considered to be in alignment with Network Pharmacology. Network pharmacology integrates genomics, proteomics, metabolomics, and clinical data to provide a holistic understanding of diseases and drug actions at a systems level. This strategy can thus be used to develop personalized medicine providing individual treatment based on the genetic background and disease network features of each patient

- **Understand disease mechanisms**: Multiple molecular connections and abnormal pathways are shared components in complex diseases. Network pharmacology explores various aspects of disease creation and evaluation, using networks to represent interactions between molecules in diseased states. It provides a holistic knowledge of the disease manifestation through the integration of omics data, drug-target interactions, protein -protein interaction network.

CHAPTER 3

MATERIALS AND METHODOLOGY

3.1 Tools & Softwares

3.1.1 IMPPAT

It is largest database published by Central Council for Research in Ayurvedic Sciences, Government of India. It is manually curated database which contains 1742 Indian Medicinal Plants, 9596 Phytochemicals, and 1124 Therapeutic uses. It also contains 9596 phytochemicals with 2-D and 3-D chemical structures (Mohanraj et al., 2018). One can easily access plant's phytochemicals and in which part of plant they are located and number of plant –part- therapeutic use of association.

3.1.2 MolSoft

It is software which is widely used in computational biology for identifying drug-likeness score and molecular property prediction such as molecular formula, molecular weight and Blood-Brain-Barrier score of phytochemicals. Here are some aspects of Molsoft related to network pharmacology

- **Virtual Screening**: Researchers can screen huge libraries of chemicals to find possible therapeutic candidates through MolSoft's virtual screening capabilities.
- **3-D Structure Based Drug Design**: It is used to design new compounds using the target proteins and their three-dimensional structures in structure based drug design. This is essential to design medicines, which can be multifaceted targets within the context of network pharmacology

- **Binding Site Analysis**: This software provides analysis of binding active sites including the identification of potential druggable sites on proteins**.** This on the one hand helps in understanding how drugs may affect multiple targets within a network.

3.1.3 ProTox

It stands for Prediction of Toxicity of Chemicals. The name itself says that it predicts the toxicities such as carcinogenicity, immunogenicity, mutagenicity and cytotoxicity of phytochemicals. This webserver takes canonical smiles or PUBchem- Name as an input and reports overall toxicity radar chart. It has helped computational biology to predict the several toxicity of chemicals. It was published in 2014 (Drwal et al., 2014) and better than software like TOPKAT. One of the novelties of the current webserver is that the

predicted toxicity likelihood can be categorized into different levels of toxicity such as oral toxicity, organ toxicity (e. g. mutagenicity, cytotoxicity and immunotoxicity), toxicological pathways and toxicity targets.

3.1.4 Swiss Target Prediction

It is accessible at: http://www.swisstargetprediction.ch/. It is a server incorporating 2 D and 3 D similarity metrics tailored towards the targets of active compounds, This leads to five separate organisms that might be used to validate predictions and offers opportunities to map predictions based on homology within and across species to match near paralogs and orthologs (Safran et al., 2010).

The Swiss Target Prediction software compares a compound's chemical structure to a database of known ligands and their associated protein targets using a ligand-based technique. Furthermore, a target-based approach is employed to determine likely binding sites and interactions by comparing the substance's chemical properties to those of known protein structures.3.1.5 Gene Card

It was widely used for ~15 years and provides an official, comprehensive set of gene annotations for human genes. Over 73 000 human gene entries have their gene-centric materials automatically mined & integrated from > 80 digital resources to generate this web-based. It has provided concise data of all known and unknown human genes. It has compiled genetic data from extensive data sources such as NCBI. The data for each gene are presented in a ' card ' type format with separate functional components and a various features including text and links to other dedicated and genome-wide databases. Gene Cards Version 3: a renewed platform with new search and support tools. It provides various information of each human gene which includes gene information (gene name, location) , genomic data, protein information , biological pathways , disease pathways and gene ontology.

3.1.6 Omim

Online Mendelian Inheritance in Man was developed to provide a comprehensive, reliable and current data repository for all known human genes and genetic phenotypes as described in the medical literature, and to promote an understanding of genetic heterogeneity, but it is not designed for analysis or diagnosis of disease conditions. The OMIM entry contains numerous cross-references to several genetic databases (Shannon et al., 2003). It helps in difference between disorders and clinical features. One easy and fast way to explore the growing body of knowledge surrounding human genetics is through the site OMIM.

3.1.7 Bioinformatics and Evolutionary Genomics

It is used to draw custom Venn diagrams. Additionally, this tool aims to identify the overlap of certain items from the list. In a text output, which will be generated, only the elements that belong only to a specified list or that have an intersection for each row will be displayed. It will also generate a Venn diagram as a graphical output if there are fewer than seven lists.

3.1.8 Cytoscape

Cytoscape software provides flexibility for network research, extra data import, and visualization. It is a network tool which needs to import its network from external sources. However it can be utilized to any system of molecular components and interactions, utilization is most effective when utilized in harmony with large databases of protein-protein, protein DNA and genetic interactions which are becoming more and more accessible to human and model animal usage. (Chin et al., 2014).

Here, are some functions of Cytoscape :

1. Network Visualisation & Analysis: First of all, Cytoscape is an excellent tool for creating graphics and organizing gorgeous network visualizations. Network data may also be brought in by users and rendered in Edge and Node format. The tool consists of controls of layout and arrangement of the components of the network and also permits one to set and adjust the colour, size and the style for the purpose of isolating or underlining particular properties of the node and the edge respectively. Users may compute network centrality measures in addition to performing clustering, community discovery, network motif identification, and topology analysis.

2. Network Simulation: It includes modules analysis of the dynamics of networks as well as a model of a network's simulation. It must be noted that users can modify dynamic models to better illustrate .This characteristic is useful when examining a biological system or when understanding how a given feature of the network influences biological functionality.

3. Data Visualization: With a tool Cytoscape, users can incorporate network data with other biological data formats, including Gene Expression, Protein annotation, and Functional annotation. The connection enables the visualization of other networks where information such as expression levels, functional annotations routes of the network can be displayed.

3.1.9 Cytoscape- Cytohubba

The Cytoscape plugin, called cytoHubba, uses this particular concept to rate nodes in a network according to their features. CytoHubba has many topological analysis methods which can be used in combination to further analyze complex networks. You can also calculate six shortest paths centralities, Radiality. Another useful tool for retrieving subnetworks from the entire large PPI set is the CytoHubba control panel.

All eleven techniques are computed in a single shopping trip. Additionally, researchers can create a new analytic strategy by combining cytoHubba with other plugins. The greater the interactome coverage, the more powerful the research of protein-protein interactions will be. It is also used to examine the innate immune system, complex

biofilm communities, cancer metabolic network (von Mering et al., 2003). Hub nodes play vital functions in network connection and communication. They are highly coupled nodes that are identified by CytoHubba. Hub nodes are commonly used to represent important proteins or genes in biological systems that have major functional relevance. In addition to centrality-based rankings, CytoHubba provides neighborhood-based techniques (k-core and maximum clique percolated component) and edge-based techniques (edge percolated component and maximal clique centrality). CytoHubba users may customise the analysis by adjusting parameters and settings, such as the number of top-ranked nodes to display, filtering criteria, and choosing the scoring method or collection of techniques. It is widely used in network biology research to identify important nodes, hub proteins, or critical regulatory elements in biological networks. It aids in understanding the network architecture, identifying key nodes, and interpreting the functional and regulatory roles of certain biological system components.

Result Visualisation: CytoHubba is used to visualise the network's top-ranked nodes and their connections. Users may explore and visualise the discovered hub nodes, their connections, and their locations within the network.

3.1.10 String Database

String is funded by Swiss Institute of Bioinformatics. It could assess and compare the relevance of individual predictions. Thus, a unique confidence score is calculated as a combination of scores generated from the STRING over 700 prediction algorithms The framework is centered around benchmarking of different types of associations using a common reference set. It is updated with completely sequenced genomes and 261 033 orthologs. Large-scale investigations encompassing the entire organism as well as targeted studies confined to a small number of proteins or a specific pathway have both made use of STRING.

String provides an unprecedentedly complete and accessible representation of both established and novel interactions with the expected outcome. Interactions in STRING and interactions to protein domains and 3D structures and the respective confidence score are provided using a stable and uniform identifier space which allows integration with other resources and easy access. STRING now has features for an interactive network viewer with full-featured clustering of the network on-the-fly, real-time updated previews of structural data (e.g. homology models), large data updates, and greatly improved connectivity. The only website including hundreds, if not more than 1100, species—from humans to bacteria and archaea—is STRING. It can also perform interaction prediction for thousands of animal species with fully sequenced genomes using the same approach, as it requires large amounts of genome sequence data. The site also reports interaction data between organisms when available, significantly increasing coverage, especially for poorly-studied organisms. It offers analysis of functional enrichment instruments to identify pathways and biological processes that are overrepresented in a group of proteins. This information may be useful in understanding

the functional context of a protein family and how they may be implicated in specific biological processes.

3.1.11 Protein Databank (PDB)

It is a database and stores information on experimentally determined structures of biological macromolecules, such as proteins and nucleic acids (Kim et al., 2016). It tabulates information on primary and secondary structures, references, coordinates, experimental data compiled for crystallographic structures, and pointers to other several scientific databases. Biologists and scientists from all over the world use PDB data and/or deposit their own data into the resource. The shared aim in the community is to provide information that links coordination geometries of macromolecules to their function. It provides major and secondary structure details, atomic coordinates, citations, data of crystallographic structures and links with several scientific databases.. The PDB is used and contributed to by scientists worldwide on a regular basis. This community's integrating focus is the necessity to get data that links the three-dimensional structures of macromolecules to their biological activities. It helps in design of new drugs against diseases.

3.1.12 Pubchem

It is a public database that contains details about chemicals and their impact on biology.It provides 2-D and 3-D structure of proteins and phytochemicals. One of the greatest repositories of chemical data that is accessible to the public is found on PubChem. It contains information on around 157 million chemical substances, 60 million distinct chemical structures, and one million biological test descriptions from depositors, which together account for over 10,000 distinct protein target sequences. This enormous quantity of data is arranged by PubChem into three interconnected databases: Substance, Compound, and BioAssay. Structure-Data File (SDF) and Comma Separated Values (CSV) are the file formats that are supported for substance deposition.

3.1.13 PyRx

It's a computer methodology that finds leads by screening a lot of database compounds. By focusing on the most promising entries, it saves down on the time and resources needed for experimentally evaluate the database. In order to identify the optimal interacting molecules for experimental testing, it investigates the behavior of small molecules in the binding active site of targets. It works with a variety of operating systems and is easy to use. This utility integrates a number of open-source programmes, including as Open Babel, AutoDock, and AutoDock Vina. In this molecular docking is performed and coordinates are set in the active site and consequently learn about binding energy.

3.1.14 Biovia Discovery Studio

Biovia discovery studio was formely known as Accelrys Discovery Studio. Here are some key feature and fucnctions of Biovia Discovery Studio.

1. Structure-based Drug Design: With Discovery Studio's structure-based drug design tools, researchers may predict binding affinities, perform virtual screening, and examine protein-ligand interactions. Among its characteristics are molecular docking, homology modelling, pharmacophore modelling, and investigation of protein-ligand interactions.

2. Ligand-based Drug Design: The programme allows users to create prediction models, perform ligand similarity searches, and analyse and model ligand structures. The programme provides ligand-based drug discovery tools.

3. Molecular Dynamics Simulations: With the aid of the program's molecular dynamics simulations, users of Discovery Studio may investigate the dynamic behaviour of biomolecules, protein-ligand complexes, and lipid bilayers. Included are tools for system configuration, simulation setup, trajectory analysis, and visualisation of simulation results.

4. Data Analysis and Visualization: Discovery Studio offers a wide range of tools for data analysis and visualization. Users may explore and analyse molecular structures, ligand-protein interactions, chemical properties, and other relevant information. Along with characteristics like scatter plots, histograms, and 2D and 3D visualization, it may be used for data mining.

3.2 Methodology

3.2.1 Screening of phytochemicals of *Morinida citrifolia*

The phytochemicals are acquired from IMPPAT (Indian Medicinal Plants, Phytochemistry and Therapeutics) which is openly accessible at: **https://cb.imsc.res.in/imppat/.** The IMPPAT ID'S were also noted.

3.2.2 Finding likeness as drug and Pharmacokinetic Properties

The Canonical Smiles which are present in phytochemicals are retrieved using PUBCHEM database. MolSoft was accessed to retrieve the data such as Drug likeness score and molecular weight. The conditions for screening were:

- LogP>5
- Molecular weight >500Da
- Less than 5 H-Bond acceptors

The compounds are shortlisted for further. Now, the canonical SMILES were then entered into ProTox to predict toxicity. Only substances with inactive immunogenicity, cytotoxicity, and carcinogenicity were chosen for additional examination from the preceding list.

3.2.3 Identification of target genes of tuberculosis

The potential target genes or disease related genes are acquired from Gene Card and OMIM database using the term 'tuberculosis'. These databases provide genomic data. Select gene symbol from Gene Card and approved symbol from OMIM.

3.2.4 Identifying of intersection gene targets

In an effort to get more unique target genes closely related to disease pathways, the target genes accessed from these databases were compared.. The target genes for *Morindia citrifolia* in TB were mapped using Bioinformatics and evolutionary Genomics which makes Venn diagram to identify putative targets.

3.2.5 Protein- protein intersection analysis

The gene targets were submitted to the STRING database. Tab- separated values (tsv) files containing the PPI analysis results from STRING were then imported into Cytoscape to investigate possible anti- tuberculosis core targets . Targets with a confidence score > o.4 were considered only.

3.2.6 Core Targets identification using CytoHubba

Cytoscape "cytohubba" was used to filter the top 10 targets. The intersection of the achieved goals may be found by applying the four approaches of Degree, Maximum Neighbourhood Component (MNC), Maximal Clique Centrality (MCC), and Closeness. As thus, the main targets were found (Ilievska-Poposka et al., 2018)

3.2.7 Molecular Docking

1. Selection and Preparation of Ligand: Five bioactive compounds (Nordamnacanthal, Ricinoleic acid, Kaempferol, Octanoic acid, 3- methylbut-2-enyl ester) which are selected through network pharmacology are downloaded from PubChem in 3D Sdf format.

2. Selection and Preparation of Target gene: 3D structure of AKT 1(PDB ID: 3O96) and STAT 3(PDB ID: 6njs) were downloaded from RCBS PDB in a PDB format. Using Biovia Discovery Studio, removal of water molecules and addition of polar hydrogen were done to prevent hindrance during ligand binding and saved in a PDBQT format.

3. Docking Analysis: After the target gene and ligand preparation , molecular docking was executed using PyRx. Target gene was loaded and made as a macromolecule and converted in a PDBQT format. Ligands were loaded one by one using Open Bable within PyRx and converted from 3D (three dimensional) structures to PDBQT format. Proteins and phytochemicals that have been uploaded chosen as ligands and macromolecules, respectively, and then stored in the PDBQT format by Vina wizard within PyRx. Then, grid box was created for each ligand in order to docking by making all active sites accessible. Eventually, result was presented in a table displaying different ligands and their binding affinities with target gene.

CHAPTER 4

RESULTS

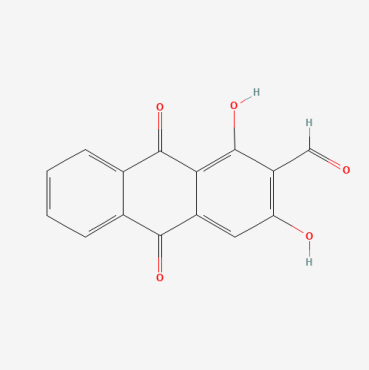
4.1 Screening of *Morinida citrifolia* active phytochemical

The Morindia citrifolia plant produced 98 phytochemicals in total, according to the IMPPAT database. Out of which 10 were shortlisted on the basis of Lipinski's rule (Table 4.1). In essence, 4 drugs were continued for the rest of network pharmacology study as shown in Fig.4.1 (a, b, c,d).

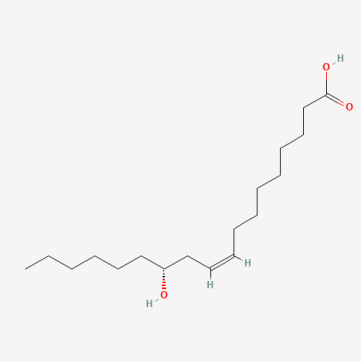
TABLE III. The list of Morindia Citrifolia phytochemicals

PHYTOCHEMICALS	PUBCHEM ID	Molecular weight	Number of HBA	Number of HBD	MolLogS	Drug-likeness model score
Nordamnacanthal	160712	257.11	3	1	-2.84 (in Log(moles/L)) 375.19 (in mg/L)	0.29
Ricinoleic acid	643684	257.11	3	1	-2.84 (in Log(moles/L)) 375.19 (in mg/L)	0.29
Morindin	442756	257.11	3	1	-2.84 (in Log(moles/L)) 375.19 (in mg/L)	0.29
Ursolic acid	64945	456.36	3	2	-5.60 (in Log(moles/L)) 1.15 (in mg/L)	0.66

beta-Sitosterol	222284	414.39	1	1	-6.34 (in Log(mol	0.78
Kaempferol	5280863	286.05	6	4	-2.21 (in Log(moles/L)) 1744.17 (in mg/L)	0.50
Quercetin	5280343	302.04	7	5	-2.19 (in Log(moles/L)) 1952.89 (in mg/L)	0.52
Lycopene	446925	257.11	3	1	-2.84 (in Log(moles/L)) 375.19 (in mg/L)	0.29
3-Methyl-3-butenyl butanoate	6429316	257.11	3	1	-2.84 (in Log(moles/L)) 375.19 (in mg/L)	0.29
Octanoic acid, 3-methylbut-2-enyl ester	531145	257.11	3	1	-2.84 (in Log(moles/L)) 375.19 (in mg/L)	0.29



(a)



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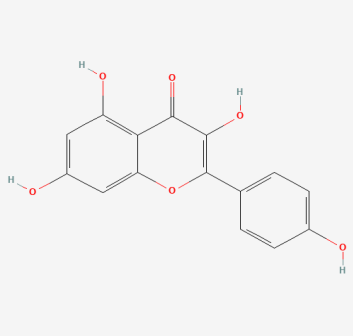

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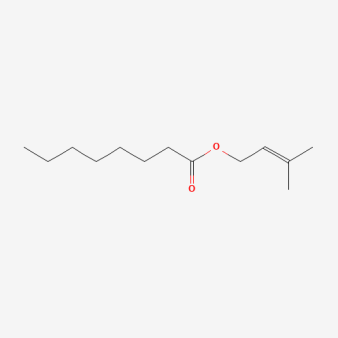

(d)

Fig 4.1 Final compounds selected from network pharmacology for molecular docking (a) Nordamnacanthal. (b) Ricinoleic acid. (c) Kaempferol. (d) Octanoic acid, 3-methylbut-2-enyl ester

4.2 Tuberculosis related gene target

Using OMIM database and Gene Target database, 3423 gene target associated with TB were found.

4.3 Intersection gene target analysis

According to Fig 4.2, Bioinformatics & Evolutionary Genome identified 140 gene targets that were shared by the 200 putative gene targets for the active phytochemicals in *Morindia citrifolia* as well as 3423 gene targets connected to tuberculosis.

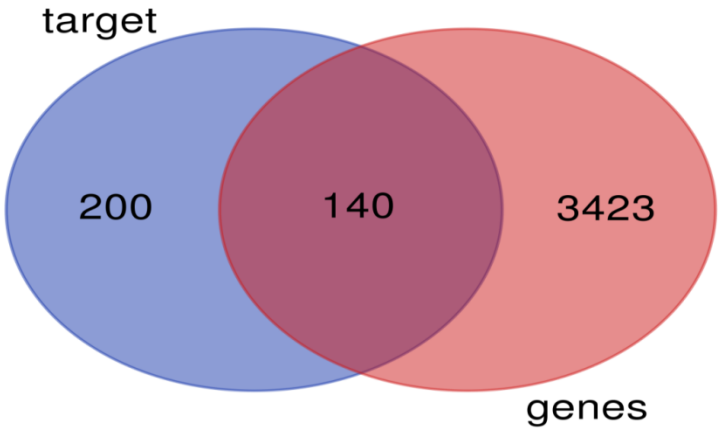

Fig 4.2 Venn diagram showing the commonness between predicted targets and DEGs

4.4 PPI network analysis

A protein – protein interaction (PPI) network was examined by STRING, and it was discovered to have 138 nodes and 1616 edges as shown in Fig 4.3(a). The average local clustering coefficient is 0.567 and the average node degree is 23.420. The following numerical values represent the network's density, diameter, clustering coefficient, and radius: 0.171, 4, 0.567 and 2 respectively. The Cytoscape-formed cluster may be used to investigate the interactions in more detail and identify the main objectives (Fig 4.3 (b)).

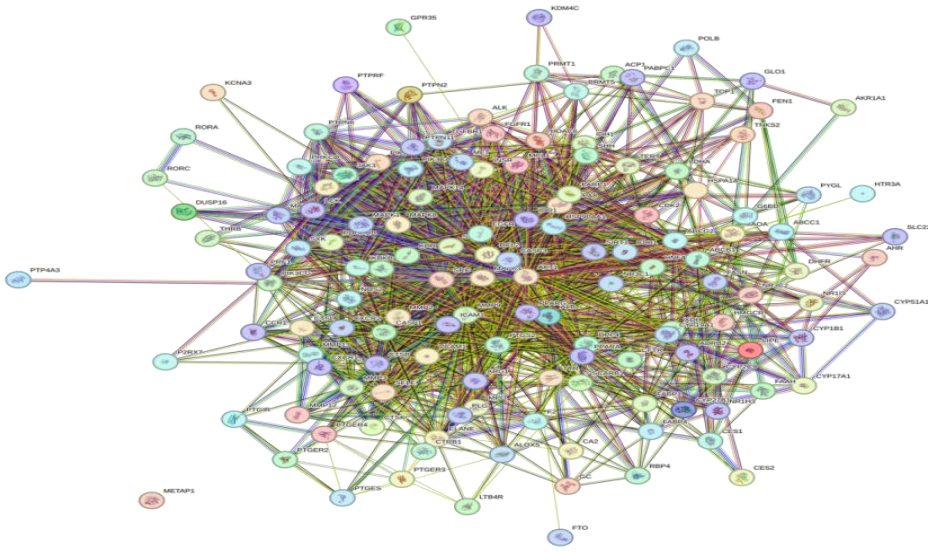

Fig 4.3 (a) PPI interaction formed by STRING

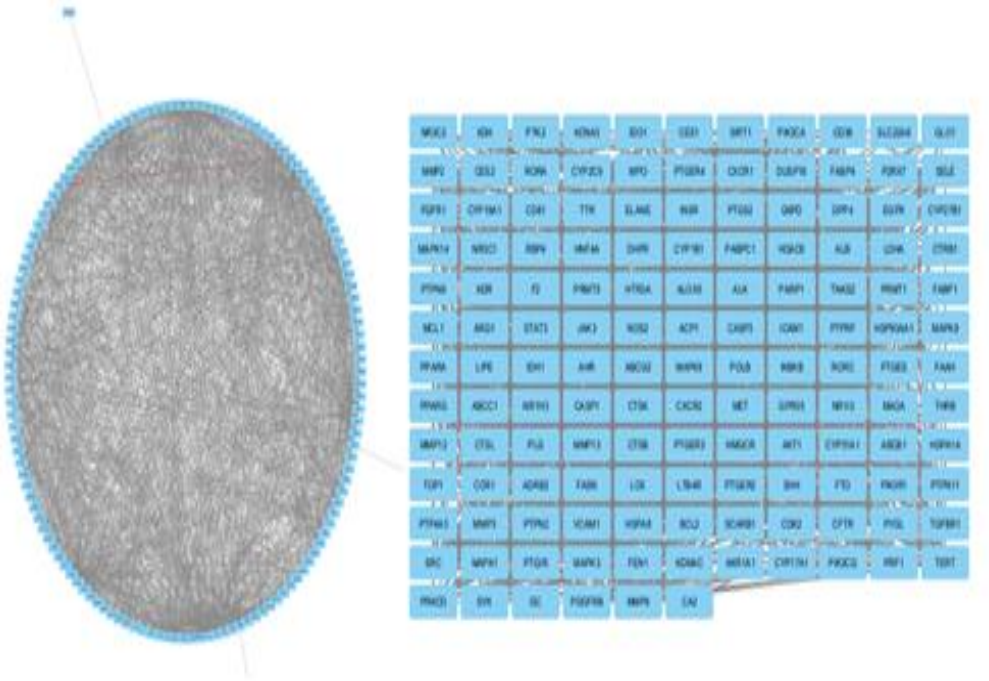

Fig 4.3 (b) Cluster formed by Cytoscape

4.5 Core Target Analysis

Cytoscape cytohubba" was used to filter top 10 targets (Fig. 4.4). The intersection of the achieved goals may be found by applying the four approaches of Degree, Maximum Neighbourhood Component (MNC), Maximal Clique Centrality (MCC), and Closeness. As thus, the main targets were found.

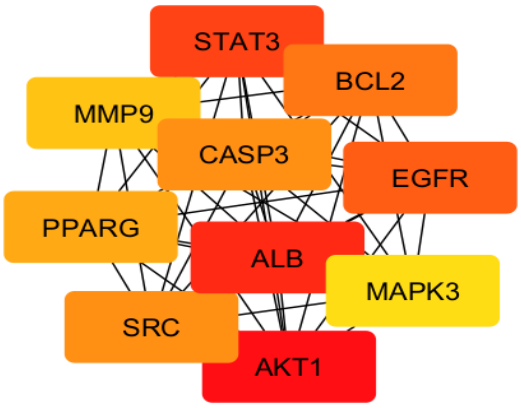

Fig 4.5 Hub genes prediction using CytoHubba

4.6 Molecular Docking Analysis

The top two anti- tuberculosis core targets (AKT 1 & STAT 3) were moleculary docked with the four active phytochemicals from *Morindia citrifolia* (Nordamnacanthal, Ricinoleic acid, Kaempferol, Octanoic acid, 3 - methylbut-2-enyl ester) . The results of molecular docking in terms of binding affinities (kcal/mol) scores are displayed as a heatmap(Table 4.2). 2D and 3D docked complexes formats are depicts in Fig 4.6(a,b). The lower binding affinity demonstrates the stronger binding ability of the targets and phytochemicals. The result demonstrated that all the phytochemicals has good binding affinities. Nordamnacanthal demonstrated excellent binding affinity with both genes AKT1 (-9.7 kcal/mol) and STAT 3 (-7.7 kcal/mol) . Consequently, the molecular docking study's findings provided credibility to the theory that *Morindia citrifolia* may lower tuberculosis by altering these targets' expressions.

Table IV. The heatmap of binding affinities (kcal/mol) for the four phytochemicals found in *Morindia citrifolia* with two anti- tuberculosis core targets

TARGETS	AKT1	STAT 3
Nordamnacanthal	**-9.7**	**-7.7**
Kaempferol	**-9.4**	**-7.8**
Octanoic acid,3-methylbut-2-enyl ester	**-5.9**	**-4.6**
Ricinoleic acid	**-6.8**	**-5.3**

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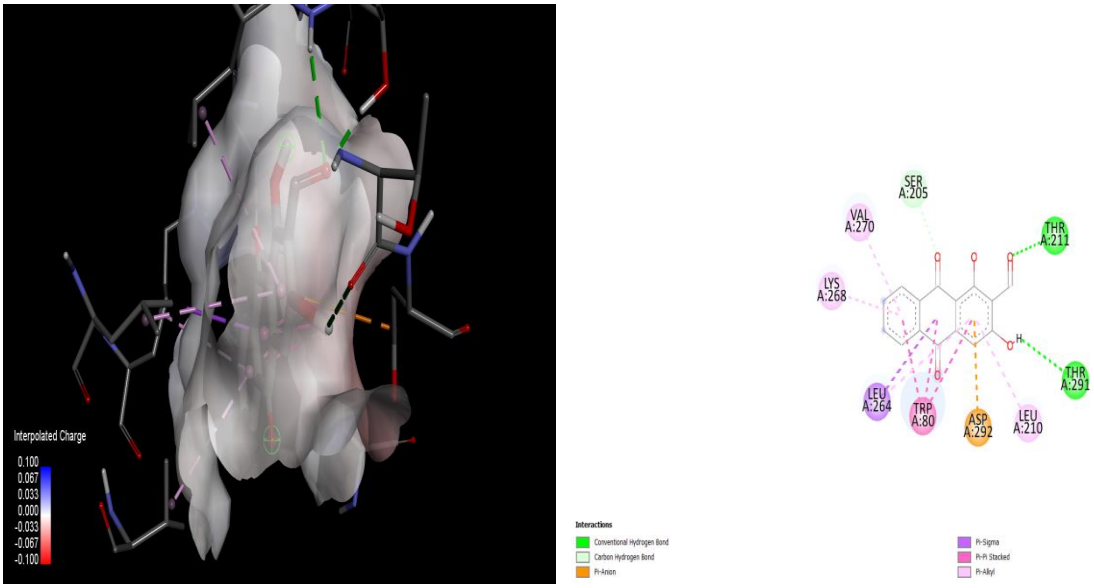
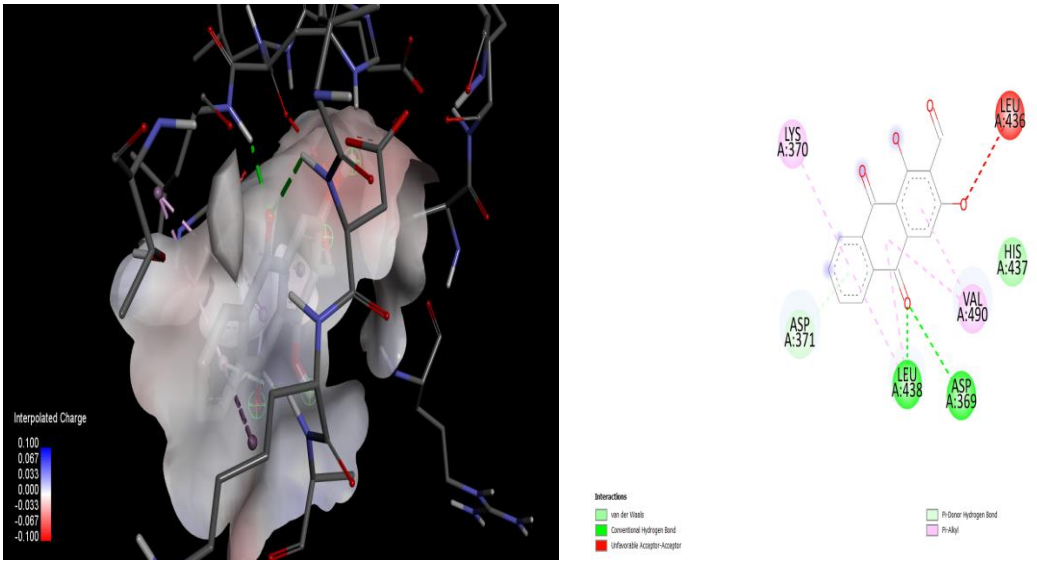


(a)



(b)

Fig 4.6 2D and 3D Molecular docking results. (a) AKT1 binds to all four phytochemicals (b) STAT 3 binds to all four phytochemicals (Nordamnacanthal, Ricinoleic acid, Kaempferol, Octanoic acid,3- methylbut-2-enyl ester)

DISCUSSION

The current study employed a network pharmacological technique to investigate the potential of *Morinida citrifolia*, a medicinal plant, useful in the treatment of Tuberculosis(TB). The work integrates computational biology and pharmacological exploration to identify possible targets and pathways affected by *Morinida citrifolia* and to comprehend its modes of action in tuberculosis. As shown in Table 4.1. ten active phytochemicals which are present different part of *Morindia citrifolia* plant showed anti- tuberculosis properties . The network finding showed that several anti-tuberculosis core targets and active phytochemicals in *Morindia citrifolia* work together synergistically to reduce tuberculosis.

The CytoHubba study included four different approaches to narrow the targets down to the core group. The top 10 core targets were identified based on degree, maximal clique centrality, largest neighbourhood component, and proximity. The critical genes that may be crucial to Morinida citrifolia anti-tuberculosis properties are reflected in these core targets. The network of active phytonutrients in *Morindia citrifolia* and anti-PAAD targets was investigated to have a better understanding of their interactions. Selected gene targets were important for a number of biological functions.

The binding affinity of the active phytochemicals from *Morindia citrifolia* with the main anti-tuberculosis core targets was evaluated by molecular docking studies. The results confirmed the hypothesis that Morindia citrifolia modulates the expression of the targets (AKT1 and STAT3) to exhibit excellent binding affinities between the active phytochemicals and the targets, hence exerting anti-tuberculosis actions. While these phytochemicals are found in several plant sections, the root phytochemical (Nordamnacanthal) had the highest binding affinity (-9.7 and -7.7, respectively) with the genes AKT1 and STAT3. Kampferol , present in fruit has also showed superior binding scores (-9.4 and -7.8 respectively). It was determined that both fruit and roots might be used as drugs to treat the disease.

CHAPTER 5

CONCLUSION

The results of this investigation offer strong and significant evidence that *Morindia citrifolia* has therapeutic promise for tuberculosis. In order to determine their role in the development of tuberculosis, the current study identified the active phytochemicals and elucidated their targets by network pharmacological analysis. These findings showed that *Morindia citrifolia* inhibited tuberculosis by changing important biomolecules and pathways that are known to be involved in the treatment of tuberculosis. This indicates that *Morindia citrifolia*, alongside with other tuberculosis medications, may be used as an adjuvant therapy to enhance patient outcomes. These study further points out the significance of exploring natural product like Morindia citrifolia from molecular stance in the quest for new therapeutic approach for cancer. Natural supplements as described here are safer forms of treatment that may be as effective for patients who have less side effects. The network pharma approach helps in the development of individualised therapy because it supplies the necessary molecular information for Morindia citrifolias anti-tuberculosis activity. Selecting the right formulation and a proper drug delivery system is one of the key strategies to achieving the fullest therapeutic effect. This advancement may increase the tissue selective and bioavailability of Morindia citrifolia drugs thereby increasing their pharmacokinetic and therapeutic values.

1. Drug Formulation and Delivery methods: Structured medication formulations and delivery systems will enhance the absorptive capacity and effectiveness of drugs. Morinda citrifolia medicines have poor pharmacokinetics and lack tissue specificity; therefore, incorporating nanoparticles, liposomes or designing specific/developed drug delivery systems will enhance drug delivery system.

2.: While the mentioned studies established that Morindia citrifolia contains bioactive compounds with potential anti-tuberculosis activity, it remains imperative to determine the precise molecules that have the desired characteristics. Perhaps a better understanding of the active components can help create new medications and reduce side effects.

LIST OF PUBLICATIONS AND PROOFS

Name of Conference: INTERNATIONAL CONFERENCE on Intelligent Computing and Communication Techniques, JNU, New Delhi
Indexing : Scopus Indexed
Title of Paper : Exploring potential of Bacopa monnieri's against B19V induced Erythema Infectiosum : An Insilco approach
Date of conference: 28th-29th June 2024
Camera Ready Submission : 05th June 2024

Name of Authors: Anjali Sharma, Deeksha Pandey, Navneeta Bhardvaja*

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Conference Paper

Exploring potential of *Bacopa monnieri's* against B19V induced Erythema Infectiosum: An insilico approach

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***Abstract*—Human pathogenic parvovirus B19 (B19V) causes a variety of inflammatory conditions as well as diseases resulting in bone marrow failure. Human erythroid progenitor cells (EPCs) are highly tropism for B19V infection in the bone marrow and fetal liver. The expression of receptor and co-receptor(s) on the cell surface of human EPCs contributes to the exclusive confinement of B19V replication to erythroid lineage cells. It also depends on intracellular components that are necessary for viral replication. Two important processes that encourage B19V replication are the cell cycle arrest at late S-phase and the DNA damage response (DDR) triggered by the B19V infection. Therefore, *Bacopa Monnieri* (Medhya Rasayana) a medicinal herb whose phytocompounds (Cucurbitacin A, Wogonin, Oroxindin, Quercetin, Luteolin, Ursolic acid, Stigmasterol, Beta sitosterol, Rosavin, Dimethoxane, Caryophyllene oxide, 2,4-quinoline diol, Brahmic acid,2 octanol, Loliolide) possess anti-inflammatory, anxiolytic, and antioxidant properties can inhibit this virus from binding to cells and its receptor in the host. In this paper we have used 16 out of all phytochemical that have the potential in inhibiting the activity of the protein (7y56), to prevent the virus from further replication. In essence, while working on this, we are evaluating the phytochemical-protein interactions and their binding affinities. Ursolic acid is found to have the highest binding affinity of -7.6, indicating its strong binding interactions and high potential in modulating the activity of virus by inhibiting its interaction with host.**

***Index Terms*—B19V, 7Y56 protein, *Bacopa monnieri*, Ursolic acid**

I. Introduction

B19 or human parvo virus is a widespread and prevalent infection causing pathogen first identified in 1974. It belongs to the parvoviridae family, particularly the erythrovirus group [1], [2]. Unlike others in this family, B19 only infects humans. The virus consists of a single-stranded DNA genome and a non-enveloped icosahedral capsid, which is made up of two structural proteins, VP-1 and VP-2. The virus measures about 18 to 26 nm in diameter. The prevalence of parvovirus B19 varies depending on age groups. In developed regions, children under five show the lowest infection rate, between 2 to 10 percent, and adults between 20 and 70 have a higher rate at around 40 to 60 percent.The human parvovirus B19 causes Studies show 50 out of 100 adults are at risk [1]. People 70 and older have the highest infection rate, with at least 85 percent exposed [3]. Fetuses with undeveloped immune systems can develop life threatening conditions like anemia or hydropus fetalis from the virus [1], [3]. The virus leads to different illnesses, examples include aplastic crisis in people with anemia. Another issue is acute symmetric polyarthropathy, resembling rheumatoid arthritis. This arthritis form occurs more frequently in women. Respiratory droplets spread the B19 virus. Hand-to-mouth contact transmits it too. Organ transplants are another transmission mode. Infected mothers can pass it to unborn babies [4]. During pregnancy, the virus may go into the womb. It might cause infection and the loss of the unborn child. The virus binds to a protein called P blood antigen receptor, or Gb4Cer (globoside), on cell surfaces. This protein is found in the lungs. The virus sticks to this protein. When the virus binds to this protein, it changes the virus and the cell membrane. The cell membrane becomes weak [4], [5]. After the virus goes into the cell, it multiplies inside the nucleus of the cell. The cell tries to fight the virus. But the virus kills the cell. The virus targets erythroid progenitors, which are cells that make red blood cells. The virus stops new red blood cells from being made. This causes a lack of red blood cells during infection [5]. The virus also binds to other proteins, like Ku80 autoantigen and 51 integrin. These proteins help the virus get into the host cell [4]. Apart from these two, NS1 is also an important protein that is directly related to the replication of B19V, playing a crucial role, as it attaches itself and controls the overall expression of both the genes of the host organism as well as itself [1]. Infection testing typically involves looking for serum anti-B19 IgM antibodies [4]. A positive result indicates that the infection occurred two to four months ago. After a week, the IgG antibody test will become positive. IVIG (intravenous immunoglobulins) is the only antiviral treatment approved by the FDA for B19 in cases of chronic infections or, more rarely, severe acute infections in immunocompromised individuals [6], [7]. Though there are various anti-viral drugs available in the market but none has been proved to be highly

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RESUME

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Knowledgeable about research areas and study procedures. Enthusiastic about setting up and carrying out wide array of studies. Diligent, industrious and efficient in handling minute details with methodical approaches to gain insights into research field.

Work History

Dec 2023 - Mar 2024

Winter Internship

DRDO(Defense Research & Development Organization), Delhi

PROJECT TITLE 1: DEVELOPMENT OF PHOTOLITHOGRAPHY FOR DEVICE FABRICATION
Led a project to develop a high-resolution photolithography process for the fabrication of next-generation nano-devices

Jan 2023 - Jan 2024

Thesis Project

Delhi Technological University

Project 2 - Unveiling the Anti-Tuberculosis Properties of Morinda citrifolia Through Network Pharmacology and Molecular Docking Techniques

Applied network pharmacology & molecular docking approaches to identify potential therapeutic targets of Morindia citrifolia for tuberculosis .
Utilized data from public databases(Biovia Discovery Studio, PyRx, Autodock, Cytoscape, String database, PUBCHEM, Swiss Target Prediction) and in-house datasets to construct interaction networks and performed pathway enrichment analysis.

Software

- PyRx(Autodock)
- Biovia Discovery Studio

Publications

International Conference on Intelligent Computing and Communication Techniques at JNU, New Delhi

· Paper ID 253: Exploring potential of *Bacopa monnieri*'s against B19V induced Erythema Infectiosum: An insilico approach

· Paper ID 252: Unveiling the Potential of Graphene: A Comprehensive Review of Its Role in Biosensing Innovation and Application

Education

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Delhi Technological University - Delhi, India

Jan 2019 - May 2022 **Bachelor of Science in Biotechnology**
Chandigarh University

Jan 2019 - May 2019 **Class XII (CBSCE)**
Army Public School, Pathankot

Jan 2017 - May 2017 **Class X (CBSCE)**
Army Public School, Nasirabad

Certifications

Oct 2022 Secured 3rd Position in Inter-University basketball tournament at IIT KANPUR

Jan 2023 Competed in state-level basketball tournament basketball tournaments

Mar 2023 Secured 2nd position in Inter-University basketball tournament in DTU

Apr 2024 Secured 1st position in Inter-University basketball tournament in DTU

Skills

- Network Pharmacology Analysis
- Photolithography
- Scientific writing
- Molecular Docking
- Chromatography
- Southern and Northern Blotting

- Ultracentrifugation
- Electron Beam Machine

Accomplishments

- Secured 40th Rank in Delhi Technological University Entrance Exam.
- Secured 3rd Rank in Punjab University Entrance Exam.
- Secured 25th Rank in Delhi University Entrance Exam.

Positions Of Responsibility

- Head Girl of school in class 12th.
- Class Representative in Bachelors.
- Captain of basketball team of DTU.