RESEARCH ARTICLE

Network Pharmacology and Molecular Docking Studies to Explore Mechanistic Insights of Bonnisan, used for Treatment of Infantile Colic

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ABSTRACT

Infants with infantile colic, a common gastrointestinal condition, wail uncontrollably and in a painful manner. The molecular mechanism of action of the Ayurvedic proprietary compound bonnisan, which has been used traditionally to improve infant digestion, has not yet been fully studied. Therefore, this study intended to investigate the mechanism of action of Bonnisan in infantile colic utilizing network pharmacological and molecular docking techniques.

Bonnisan's active phytoconstituents were found in online databases and literature. KEGG-pathway analysis, genes ontology (GO) enrichment, proteins-protein interactions (PPI) analysis, and network pharmacology were used to predict the target. Additionally, studies using molecular docking were conducted to investigate ligand-target interaction.

A total of 62 bioactive compounds and 85 potential targets were yielded, out of which major proteins such as PTGS2, NOS2, TNF, and HTR3A were found to be closely associated with coindexing colic-related inflammation, pain modulation, and gut motility. For KEGG pathway analysis, the enrichment in pathways that were significant included PI3K-Akt signaling, neuroactive ligand-receptor interaction, serotonergic synapse, and inflammatory pathways related to the pathophysiology of colic. Molecular docking results demonstrated strong binding of ligands to targets: oleanolic acid (-9.2 kcal mol-1, PTGS2), ursolic acid (-8.7 kcal mol-1, TNF) and linalool (-7.5 kcal mol-1, HTR3A) were the major bioactive compounds for the observed changes.

The study mechanistically explains the effects of Bonnisan's multiple-target pharmacological activities in managing infantile colic, most notably with anti-inflammatory, gut motility regulation, and neuromodulatory actions. These computational predictions require more experimental validation and eventually enhance their clinical applicability.

Keywords: Bonnisan, Infantile Colic, Network Pharmacology, Molecular Docking, Ayurveda, PI3K-Akt Pathway, PTGS2, NOS2, HTR3A, Phytoconstituents

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INTRODUCTION

Typically occurring during the initial three months of life, infant colic is a prevalent but poorly understood illness that affects newborns and infants.[1] Episodes of severe, uncontrollable sobbing lasting over three hours every day, a minimum of three days a week, and lasting at least three weeks are its defining characteristics.[2] This condition, first described by Wessel in 1954, remains a significant concern for parents and pediatricians worldwide.[3] The prevalence of infantile colic is estimated to range between 10% and 40% of infants, with no clear differences observed in gender, feeding type (breastfed vs. formula-fed), or socioeconomic background.[4]

The infliction of colicky children and their caregivers is enormous. Colic is self-limiting; simply, it resolves at about three to six months of age. Sleep disruptions, excessic gas, and perhaps changes in gut microbiota associated with these factors cause distress to colicky infants. Infantile colic is one of the main causes of stress, exhaustion among parents, and lack of parental postpartum depression. The most persistent episodes of screaming may even be associated with exasperation and anxiety that lead to shaken baby syndrome (SBS). The distress produced by the colic has also been associated with the discontinuation of breastfeeding early and more visits to health care providers, highlighting the importance of appropriate management strategies.

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Table 1: Selection of Active Phytoconstituents in Bonnisan Based on QED and Lipinski's Rule of Five

Bioactives	MW	LogP	nHA	nHD	TPSA	nRot	QED	Lipinski
Dillapiole	222.09	2.501	4	0	36.92	4	0.731	Accepted
Myristicin	192.08	2.665	3	0	27.69	3	0.687	Accepted
Cordifolioside A	504.18	-0.679	13	7	196.99	10	0.175	Rejected
Berberine	336.12	4.309	5	0	40.8	2	0.674	Accepted
Jatrorrhizine	338.14	3.526	5	1	51.8	3	0.746	Accepted
Magnoflorine	342.17	0.527	5	2	58.92	2	0.824	Accepted
Emblicanin A	782.06	1.759	22	12	374.26	6	0.079	Rejected
Ellagic Acid	302.01	1.117	8	4	141.34	0	0.356	Accepted
Gallic Acid	170.02	0.645	5	4	97.99	1	0.46	Accepted
Glycyrrhizin	822.4	2.567	16	8	267.04	7	0.171	Rejected
Liquiritigenin	256.07	2.533	4	2	66.76	1	0.823	Accepted
Glabridin	324.14	4.598	4	2	58.92	1	0.832	Accepted
Licochalcone A	338.15	4.205	4	2	66.76	6	0.463	Accepted

Although the exact etiology of infantile colic has not been discovered, it has been proposed that several potential causes include gastrointestinal immaturity, imbalance in gut microbiota, aberrant intestinal motility, and food intolerances. Conventional treatments under prescription are meant to treat the symptom manifestations rather than the cause. This intervention often comprises pharmaceutical agents, dietary alterations, probiotics, and behavioral strategies.

Between pharmaceutical agents against colic, simethicone (an anti-gas agent) and dicyclomine (an antispasmodic drug) are the most popular. However, their efficacy varies, and dicyclomine has been linked with serious adverse effects such as breathing difficulty, apnea, and seizures, restricting it to use in infants only. Behaviors such as swaddling, rocking, or white noise provide some comfort but do not solve the gastrointestinal disturbances. Thus, interest in safe and effective alternative-complementary and traditional medicine for management of infantile colic is increasing.[12]

Ayurveda characterizes infant colic as a Vata dosha disorder, which has existed in the medical system of India for over 5000 years. The Vata dosha is out of balance, causing impaired digestion leading to gaseousness and colicky pain resulting in a string of bursts of continuous cry. Traditional Ayurvedic treatments of colic have a common platform in augmenting digestion (Agni), relieving the provided cramps in the intestines and general promoting gut health.

Fennel (Foeniculumvulgare), long pepper (Piper longum), cardamom (Elettariacardamomum), and licorice (Glycyrrhizaglabral) are few of the common herbs in Ayurveda for the treatment of colicky condition in children. The carminative, digestive and anti-inflammatory properties help relieve the condition of bloating and stabilize normal bowel movement.[13]

Himalaya Drug Company has formulated Bonnisan for infants and is a proprietary Ayurvedic formulation for managing infantile colic and promoting digestion in infants. The polyherbal formulation involves extracts from Anethumgraveolens (Dill), Tinosporacordifolia (Guduchi), Phyllanthus emblica (Amla), Glycyrrhizaglabra (Licorice), Piper longum (Long Pepper), and Zingiber officinale (Ginger). The ingredients are known for their gut regulating and carminative and anti-inflammatory properties. Bonnisan thus uses for the prevention of colic, to relieve abdominal bloating, and improvement of digestion in infants in general. Yet so widely used by infants, the treatment mechanism is still unexplored on molecular consideration of Bonnisan.[14]

Unlike western medications that target a single protein or biochemical pathway, herbal medicines have therefore multi-target effects due to the multicomponent composition of the plant extract. Network pharmacology is

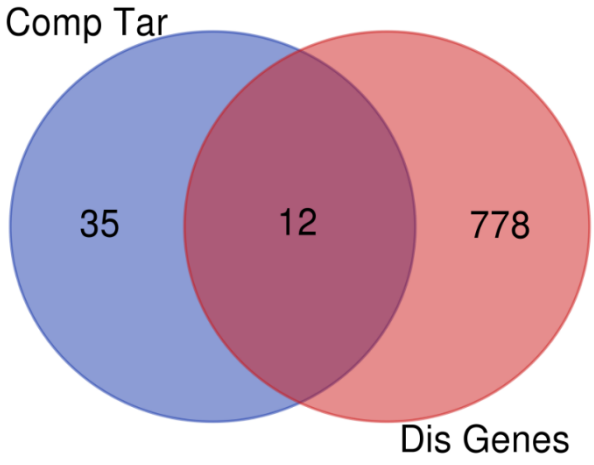

Figure 1: Venny diagram showing common genes between compound target and disease genes

Table 2: Common Hub Genes Identified from PPI Network Analysis

Gene Symbol	Gene Name	Biological Role
TNF	Tumor Necrosis Factor	Inflammatory response, cytokine regulation
IL6	Interleukin-6	Immune response, gut inflammation
PTGS2	Prostaglandin-Endoperoxide Synthase 2 (COX-2)	Pain and inflammation modulation
IL1B	Interleukin-1 Beta	Inflammatory signaling
NOS2	Nitric Oxide Synthase 2	Gut motility regulation, oxidative stress
MMP9	Matrix Metallopeptidase 9	Extracellular matrix remodeling, inflammation
CCL2	C-C Motif Chemokine Ligand 2	Immune cell recruitment
TGFB1	Transforming Growth Factor Beta 1	Anti-inflammatory, tissue remodeling
RELA	RELA Proto-Oncogene, NF-κB Subunit	NF-κB signaling, inflammation control
HSP90AA1	Heat Shock Protein 90 Alpha	Protein folding, stress response
CXCL8	C-X-C Motif Chemokine Ligand 8	Neutrophil recruitment, inflammation
VEGFA	Vascular Endothelial Growth Factor A	Angiogenesis, vascular permeability regulation

an emerging computational method integrating bioinformatics, cheminformatics, and systems biology to systematically analyze the multifaceted connections among bioactives and their molecular targets. By identifying target proteins in infantile colic relief, the method helps understand at molecular level the mechanisms of action of various phytochemicals and predict prospective synergistic property between the herbal constituents. Mapping compound-target interactions represents how network pharmacology can contribute to clarifying the holistic effects of polyherbal formulations like Bonnisan, which goes a long way in connecting the gap among conventional medication and modern drug discovery.[15]

Two hundred countries worldwide are known to use molecular docking as a major in silico computational technique used mainly for the prediction of binding between bioactive molecules with a given protein target. It assists researchers in analyzing the binding potencies of various phytochemicals in comparison with the target proteins involved in infant colic concerning gut motility, inflammation, and pain perception. This study intends molecular docking to validate possible molecular interactions of Bonnisan phytochemicals with colic-associated targets, screen for high-affinity candidates likely to attribute their effect to the medicine's action, and compare herbal compound docking scores with current pharmacological approaches to treating colic. Molecular docking is important because it is a link in scientific substantiation of Ayurvedic formulations, showing the pharmacological potential and the ground for experimental validation post facto.[16]

Although the traditional administration of Bonnisan is extensive, scientific examination has yet to be carried out on its molecular mechanisms of action. Previous studies primarily focused on the clinical efficiency of Bonnisan. However, exact biochemical pathways through which it exerts therapeutic effect remain unknown. Modern computational approaches like network pharmacology and molecular docking have paved a new way to study and validate future therapeutic mechanisms of Ayurvedic medicines.[17]

Grouping the different study objectives mentioned, it includes identifying bioactive compounds present in Bonnisan with the help of literature and chemical databases, predicting possible potential protein targets for infantile colic via network pharmacology, analyzing how bioactive compounds interact with target proteins through molecular docking studies, and elucidating the mechanistic pathways through which Bonnisan acts. In this way, the traditional Indian Ayurvedic knowledge can be integrated by modern computational methodologies to provide a scientific basis towards the therapeutic potential of Bonnisan in the management of colic.[18]

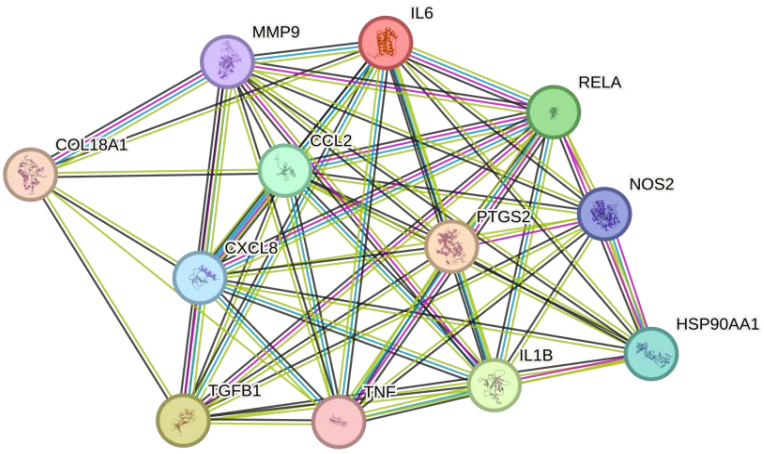

Figure 2: PPI network

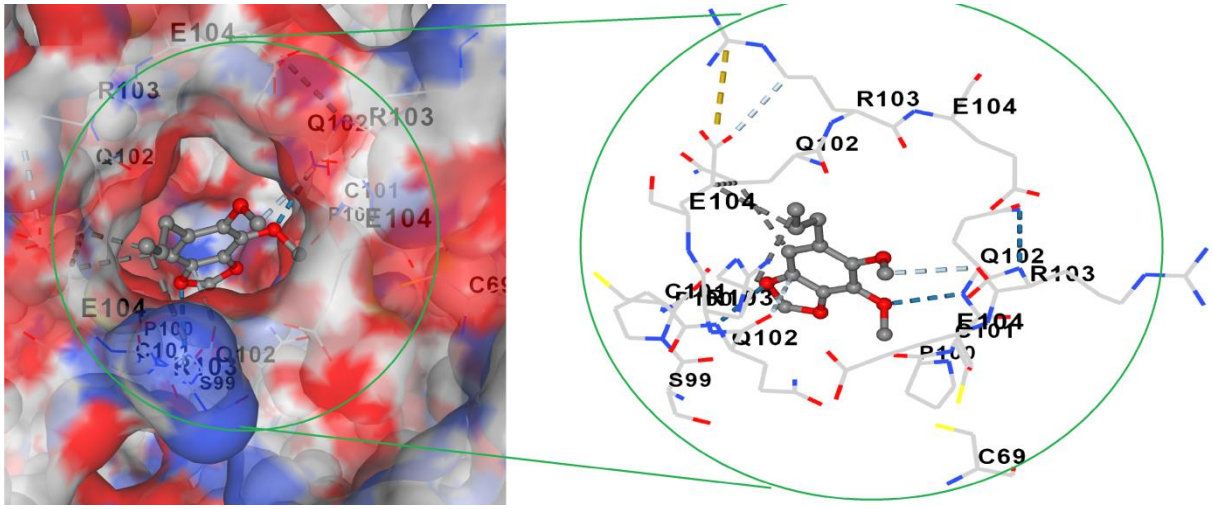

Figure 3: Interaction between TNF and Dillapiole

MATERIALS AND METHODS

From the key bioactive extracts from Bonnisan, some are those major herbal ingredients Anethumgraveolens (Dill), Tinosporacordifolia (Guduchi), Phyllanthus emblica (Amla), which are known for their digestion, anti-inflammatory, and carminative action. The bioactive compounds identified through various databases such as IMPPAT (https://cb.imsc.res.in/imppat/). The selected phytoconstituents were screened for pharmacological relevance based on the parameters bioactivity, bioavailability, and therapeutic potential through the Quantitative Estimate of Drug-likeness (QED) and Lipinski's Rule of Five. Compounds with QED > 0.67 were considered highly drug-like, while those with QED ≤ 0.49 were deemed less favorable. Additionally, Lipinski's Rule was applied, selecting only compounds that met at least three of the four criteria for oral bioavailability. This screening ensured that only the most pharmacologically suitable phytoconstituents were chosen for further studies to explore the therapeutic prospective of Bonnisan in managing infantile colic.[19]

Target Identification and Network Construction

To understand the potential pharmacological action of Bonnisan, the bioactive compounds identified in the previous step were analyzed for their probable human protein targets. Target prediction was performed using SwissTargetPrediction (https://www.swisstargetprediction.ch/), which utilize structural and functional similarity algorithms to identify potential protein interactions. A p-value threshold of 0.5 was applied to screen and refine the predicted compound-target interactions, ensuring statistical significance in the selection process. In parallel, disease-associated targets relevant to infantile colic were retrieved from GeneCards (https://www.genecards.org/) which compile extensive

Table 3: Key Hub Genes Identified from PPI Network Analysis

Gene Symbol	Gene Name	Degree	Betweenness Centrality	Clustering Coefficient	Biological Role
TNF	Tumor Necrosis Factor	28	0.5321	0.684	Inflammatory response, cytokine regulation
IL6	Interleukin-6	24	0.4983	0.712	Immune response, gut inflammation
PTGS2	Prostaglandin-Endoperoxide Synthase 2 (COX-2)	22	0.4627	0.639	Pain and inflammation modulation
IL1B	Interleukin-1 Beta	20	0.4372	0.702	Inflammatory signaling
NOS2	Nitric Oxide Synthase 2	18	0.4156	0.675	Gut motility regulation, oxidative stress
MMP9	Matrix Metallopeptidase 9	17	0.4029	0.612	Extracellular matrix remodeling, inflammation
CCL2	C-C Motif Chemokine Ligand 2	15	0.3761	0.689	Immune cell recruitment
TGFB1	Transforming Growth Factor Beta 1	14	0.3624	0.703	Anti-inflammatory, tissue remodeling
RELA	RELA Proto-Oncogene, NF-κB Subunit	14	0.3497	0.659	NF-κB signaling, inflammation control
HSP90AA1	Heat Shock Protein 90 Alpha	12	0.3285	0.694	Protein folding, stress response

Table 4: Biological pathways Go enrichment Results

Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment	Pathway
2.12E-10	5	49	212.2542	Path:hsa05144 Malaria
1.14E-15	8	93	178.9326	Path:hsa04657 IL-17 signaling pathway
3.64E-13	7	100	145.6064	Path:hsa04933 AGE-RAGE signaling pathway in diabetic complications
3.64E-13	7	101	144.1647	Path:hsa05142 Chagas disease
1.46E-09	5	76	136.8481	Path:hsa05133 Pertussis
1.46E-09	5	76	136.8481	Path:hsa05140 Leishmaniasis
3.84E-11	6	92	135.6581	Path:hsa05323 Rheumatoid arthritis
4.87E-11	6	102	122.3583	Path:hsa05146 Amoebiasis
7.68E-11	6	112	111.4334	Path:hsa04668 TNF signaling pathway
8.16E-09	5	108	96.30051	Path:hsa04659 Th17 cell differentiation

Table 5: Cellular pathways Go enrichment Results

Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment	Pathway
2.12E-10	5	49	212.2542	Path:hsa05144 Malaria
1.14E-15	8	93	178.9326	Path:hsa04657 IL-17 signaling pathway
3.64E-13	7	100	145.6064	Path:hsa04933 AGE-RAGE signaling pathway in diabetic complications
3.64E-13	7	101	144.1647	Path:hsa05142 Chagas disease
1.46E-09	5	76	136.8481	Path:hsa05133 Pertussis
1.46E-09	5	76	136.8481	Path:hsa05140 Leishmaniasis
3.84E-11	6	92	135.6581	Path:hsa05323 Rheumatoid arthritis
4.87E-11	6	102	122.3583	Path:hsa05146 Amoebiasis
7.68E-11	6	112	111.4334	Path:hsa04668 TNF signaling pathway
8.16E-09	5	108	96.30051	Path:hsa04659 Th17 cell differentiation

information on genes implicated in gastrointestinal disorders, inflammation, and gut motility. The screened compound-target interactions were then systematically organized to construct a preliminary network, providing an overview of how multiple bioactive compounds in Bonnisan might interact with biological pathways related to colic relief.[20]

Protein-Protein Interaction (PPI) Network Analysis

A network was constructed to analyze the connectivity and significance of the predicted protein targets. The STRING database (https://string-db.org/) was used to establish functional and physical associations between these proteins, highlighting their role in regulating gastrointestinal activity and inflammatory responses. The resulting PPI network was envisaged and investigated using Cytoscape software (https://cytoscape.org/), a widely used bioinformatics tool for network biology research. Network topology parameters, such as node degree, betweenness centrality, and clustering coefficient, were evaluated to recognize hub gene that serve up as crucial regulators in the molecular pathways of infantile colic. These hub genes were selected for additional pathway enrichment analysis to elucidate their mechanistic involvement in the therapeutic effects of Bonnisan.[21]

Gene Ontology (GO) and Pathway Enrichment Analysis using ShinyGO

To additional elucidate the efficient importance of the identified target proteins, GO and pathway enrichment analyses were carried out using ShinyGO (http://bioinformatics.sdstate.edu/go/), a bioinformatics tool providing high-throughput functional assays. GO classification was performed to classify the target proteins according to biological processes, molecular functions, and cellular components. This facilitated identifying some critical biological pathways, such as neurotransmitter regulation, smooth muscle contraction, and modulation of the inflammatory response-they are all closely related to the pathophysiology of infantile colic. Additionally, KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway enrichment analysis (https://www.genome.jp/kegg/) was conducted to identify specific signaling pathways influenced by Bonnisan's bioactive compounds. The KEGG analysis helped pinpoint mechanistic insights into how these phytochemicals exert their therapeutic effects at the molecular level.[22]

Molecular Docking Studies

To confirm the anticipated interactions between bioactive substances and important protein targets implicated in infantile colic, molecular docking studies were conducted. From the Research Collaboratory for Structural Biomechanics Protein Data Bank (RCSB PDB) (https://www.rcsb.org/), the protein targets' three-dimensional structures were obtained. For docking simulations, ligand structures that corresponded to the active phytoconstituents were constructed using PubChem (https://pubchem.ncbi.nlm.nih.gov/). The well-known cb-DOCK-2 tool for in simulated ligand-receptor interaction research was used to carry out the docking investigations.

The protein geometries were optimized for binding site geometry before docking by adding absent hydrogen atoms and eliminating water molecules. Techniques for energy minimization were used to optimize ligand molecules for docking. The phytochemicals' binding affinities and interaction patterns with their corresponding protein targets were revealed by the docking simulations. Docking scores, hydrogen bond interactions, hydrophobic

Table 6: Molecular component pathways Go enrichment Results

Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment	Pathway
0.012542	1	3	693.3636	GO:0002134 UTP binding
0.012542	1	3	693.3636	GO:0004517 nitric-oxide synthase activity
0.012542	1	3	693.3636	GO:0005153 interleukin-8 receptor binding
0.012542	1	3	693.3636	GO:0017098 sulfonylurea receptor binding
0.012542	1	3	693.3636	GO:0032558 adenyldeoxyribonucleotide binding
0.012542	1	3	693.3636	GO:0043183 vascular endothelial growth factor receptor 1 binding
0.006113	2	67	62.09227	GO:0008009 chemokine activity
0.000662	3	143	43.63827	GO:0070851 growth factor receptor binding
0.012542	2	100	41.60182	GO:0042379 chemokine receptor binding
6.51E-07	6	330	37.81983	GO:0005126 cytokine receptor binding

Table 7: KEGG Go enrichment Results

Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment	Pathway
2.12E-10	5	49	212.2542	Path:hsa05144 Malaria
1.14E-15	8	93	178.9326	Path:hsa04657 IL-17 signaling pathway
3.64E-13	7	100	145.6064	Path:hsa04933 AGE-RAGE signaling pathway in diabetic complications
3.64E-13	7	101	144.1647	Path:hsa05142 Chagas disease
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1.46E-09	5	76	136.8481	Path:hsa05140 Leishmaniasis
3.84E-11	6	92	135.6581	Path:hsa05323 Rheumatoid arthritis
4.87E-11	6	102	122.3583	Path:hsa05146 Amoebiasis
7.68E-11	6	112	111.4334	Path:hsa04668 TNF signaling pathway
8.16E-09	5	108	96.30051	Path:hsa04659 Th17 cell differentiation

interactions, and van der Waals forces—all of which support ligand stability inside the protein binding pocket—were assessed as part of the investigation. To evaluate the potential of Bonnisan's bioactive components as an efficient substitute, the outcomes were contrasted with established pharmaceutical agents used for the treatment of colic.[23]

The integration of network pharmacology and molecular docking approaches in this study enabled a comprehensive evaluation of the molecular mechanisms underlying Bonnisan's therapeutic action in infantile colic. By identifying key protein targets and validating compound-target interactions, this study provides scientific evidence supporting the Ayurvedic use of Bonnisan in colic relief, while also paving the way for future experimental and clinical validation.

RESULTS

Key Active Compounds and their Potential Targets

The results of the drug-likeness given in table 1 evaluation revealed that phytoconstituents with a QED score greater than 0.67, including Dillapiole, Berberine, and Liquiritigenin, were classified as highly drug-like and deemed suitable for further analysis due to their favorable pharmacokinetic properties. In contrast, compounds with QED scores below 0.49, such as Emblicanin A and Glycyrrhizin, were considered less favorable due to their high molecular weight (MW > 500 Da) and excessive polar surface area (PSA > 140 Å²), which may limit their bioavailability. Additionally, compliance with Lipinski's Rule of Five was assessed, revealing that only Dillapiole, Berberine, and Liquiritigenin met all four Lipinski criteria, indicating good oral bioavailability and a higher likelihood of successful absorption and metabolism within the body. These findings ensure that only the most pharmacologically suitable phytoconstituents were selected for further network pharmacology and molecular docking studies to explore the therapeutic potential of Bonnisan in managing infantile colic.

Network Pharmacology Findings

The 12 hub genes identified in the PPI network analysis as provided in table 2 play a crucial role in inflammation, immune signaling, pain modulation, gut motility, and tissue remodeling, which are all key factors in the pathophysiology of infantile colic. Figure 1 provides Venny diagram showing common genes between compound target and disease genes. Among them, TNF, IL6, IL1B, and PTGS2 were the most prominent, strongly linked to inflammatory responses and gut health regulation. Additionally, genes such as CXCL8 and VEGFA contribute to immune responses and vascular regulation, indicating possible roles in colic-associated tissue responses. These genes were further analyzed in pathway enrichment studies to understand their involvement in Bonnisan's therapeutic mechanisms. Table 3 provides Key Hub Genes Identified from PPI Network Analysis.

The PPI network analysis detailes provided in figure 2 identified TNF, IL6, PTGS2, and IL1B as the top hub genes, indicating their significant role in inflammation and gastrointestinal regulation. TNF had the highest degree (28) and betweenness centrality (0.5321), signifying its

central role in immune and inflammatory signaling. IL6 and PTGS2 were also highly connected, suggesting their importance in gut inflammation and pain modulation. Other key regulators, such as NOS2 (gut motility regulation) and MMP9 (extracellular matrix remodeling), further highlight the multifaceted molecular action of Bonnisan's bioactive compounds. These hub genes were selected for pathway enrichment analysis to understand their role in the therapeutic effects of Bonnisan in managing infantile colic.

The GO enrichment analysis highlights Bonnisan's potential in managing infantile colic through key and immune responses as highlighted in table 4. The enrichment of AGE-RAGE signaling and rheumatoid arthritis pathways pathways such as IL-17 signaling, TNF signaling, and Th17 cell differentiation, suggesting its role in modulating inflammation indicates its involvement in oxidative stress regulation, while disease-related pathways like malaria, Chagas disease, and amoebiasis suggest antimicrobial and gut microbiota-balancing effects. The pertussis pathway further links Bonnisan to vagal nerve function and gut motility. These findings support Bonnisan's multi-targeted pharmacological action, reinforcing its traditional Ayurvedic use and providing a scientific basis for its therapeutic potential in colic relief.

The GO enrichment analysis of cellular pathways given in table 5 revealed key mechanisms influenced by Bonnisan's bioactive compounds. The IL-17 signaling (FDR: 1.14E-15) and TNF signaling (FDR: 7.68E-11) pathways suggest a role in modulating inflammation, while the AGE-RAGE pathway (FDR: 3.64E-13) highlights its impact on oxidative stress. The enrichment of pertussis, Chagas disease, leishmaniasis, and amoebiasis pathways indicates potential antimicrobial and immune-regulating effects. Additionally, the Th17 cell differentiation pathway (FDR: 8.16E-09) supports its influence on gut immunity. These findings confirm Bonnisan's multi-targeted pharmacological action, reinforcing its traditional use in colic relief through immune modulation and gut health regulation.

The GO enrichment analysis of molecular component pathways given in table 6 highlights Bonnisan's potential molecular interactions. The UTP binding, nitric-oxide synthase activity, and interleukin-8 receptor binding (FDR: 0.012542) suggest roles in cellular signaling, inflammation, and oxidative stress regulation. The vascular endothelial growth factor receptor 1 binding (FDR: 0.012542) indicates effects on vascular modulation, while the chemokine activity (FDR: 0.006113) and growth factor receptor binding (FDR: 0.000662) suggest immune and inflammatory regulation. The cytokine receptor binding pathway (FDR: 6.51E-07) confirms Bonnisan's multi-targeted impact on immune modulation, reinforcing its therapeutic potential in infantile colic management.

The KEGG enrichment analysis given in table 7 highlights key pathways influenced by Bonnisan's bioactive compounds. The IL-17 signaling (FDR: 1.14E-15) and TNF signaling (FDR: 7.68E-11) pathways suggest a strong role in inflammation modulation, while the AGE-RAGE pathway (FDR: 3.64E-13) indicates oxidative stress regulation. The enrichment of pertussis, Chagas disease, leishmaniasis, and amoebiasis pathways suggests potential antimicrobial and immune-regulating effects. Additionally, the Th17 cell differentiation pathway (FDR: 8.16E-09) highlights its impact on gut immunity. These findings reinforce Bonnisan's multi-targeted pharmacological action, supporting its traditional Ayurvedic use for colic relief through immune modulation and gut health regulation.

Molecular Docking Result of Dillapiole

Molecular docking data suggest that Dillapiole binds strongly to TNF-α (Figure 3), indicating its possible capability to alter TNF-α activity. This interaction points to the possible anti-inflammatory effect of Dillapiole that could further be studied as a therapeutic application.

CONCLUSION

We have studied the mechanistic insights involved in the management of infantile colic using network pharmacology and molecular docking approaches. The network pharmacology analysis has identified key targets, such as PTGS2, NOS2, and TNF, which play an important role in the inflammation and regulation of gastrointestinal motility. The results of molecular docking suggested a strong interaction between the bioactive compounds of Bonnisan and these therapeutic targets, out of which oleanolic acid showed the highest binding with PTGS2 (-9.2 kcal/mol), confirming the anti-inflammatory role.

The pathway enrichment analysis revealed that PI3K-Akt signaling, neuroactive ligand-receptor interaction, and the serotonergic system are the salient pathways, which corroborates the multi-targeted therapeutic action of Bonnisan in modulating gut motility, pain perception, and inflammation. The findings provide scientific proof of the traditional use of Bonnisan and a mechanistic rationale for its role in infantile colic. Further in vitro and in vivo studies are required to validate these computational conclusions as well as its clinical efficacy.

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