



Computational analysis of *Salmalia malabarica* (*Bombax ceiba*) for the management of ulcerative colitis

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ABSTRACT

Bombax ceiba leaf petiole is used as an enema in the management of ulcerative colitis, but its molecular mechanisms are yet to be established. The current study employed gene set enrichment, network pharmacology, and molecular docking studies to infer the phytochemicals from *B. ceiba* responsible for the modulation of therapeutic targets of UC. First, data of phytochemicals present in the leaf petiole were retrieved from the literature and public phytochemicals databases and their druggability and toxicity prediction was performed by MolSoft and AdverPred online servers, respectively. Furthermore, phytochemicals probable proteins were predicted by SwissTargetPrediction, and targets of UC were retrieved from the GeneCards database. A set of genes molecular pathways were identified by the STRING, Kyoto Encyclopedia of Genes and Genomics database, and pathways involved in UC were sorted and their network between compounds, targets, and pathways was constructed by the Cytoscape software. Molecular docking of hub-gene and targets was performed by the POAP pipeline. Out of 10 compounds, 7 (showed druggability in which Rutin scored the highest druglikeness score of 0.91. A total of 2830 genes were identified for UC, of which 39 matched with targets of phytochemicals (total of 297). These 39 targets were involved in 125 pathways, of which 14 were associated with UC mainly VEGF, IL-17, Neurotrophin, JAK-STAT, cAMP, TNF, TGF-beta, and NF-kappa B, MAPK, PI3K-Akt signaling pathway. Among the predicted targets, MAPK3, TNF, and PTGS2 were identified as a hub gene. Rutin scored the lowest binding energy of -7.9 kcal/mol and possessed 22 interactions with PTGS2 and Astragaloside and Isoquercitrin were the next lead hit against PTGS2. It has been concluded that the use of *B. ceiba* leaf petiole could be a valuable source against UC.

INTRODUCTION

The term “inflammatory bowel disease” (IBD) refers to a set of idiopathic immune-related gastrointestinal illnesses, in which, ulcerative colitis (UC) and Crohn’s disease (CD) are linked. Different IBD entities and inflammatory phenotypes have different symptoms, which may include diarrhea, rectal bleeding, bowel pain, and weight loss [1,2]. UC is a disease of the colonic mucosa that often begins in the rectum and spreads proximally through all or a portion of the colon [3]. Compared to CD, UC is

more common, and typically manifests in young adults between the ages of 15 and 35 years, although it can occur at any age [4]. Diagnosis of UC is typically made through a combination of clinical evaluation, laboratory tests, imaging studies, and endoscopy with biopsy [5]. UC results from a combination of genetic and environmental factors, while the exact cause of UC is unknown. However, it is thought that it happens in people with genetic susceptibility as a result of an abnormal immunological response to the intestinal microbes. Environmental factors may also play a role in the development of UC, including diet, smoking, and exposure to certain infections [6,7]. There is some evidence to suggest that a Western diet, which is high in fat and low in fiber, may increase the risk of UC [8]. The treatment of UC may involve a variety of medications, including aminosalicylates, corticosteroids, immunomodulators, and biologic agents [9]. Aminosalicylates are the first-line therapy for mild to

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moderate disease and work by reducing inflammation in the colon [10]. Corticosteroids may be used for short-term control of more severe symptoms. Immunomodulators work by suppressing the immune system to reduce inflammation in the colon. Biologic agents are the newer drugs that target specific proteins in the immune system that are involved in inflammation. However, these therapies are associated with a number of side effects such as weight gain, mood swings, acne, skin rash, and allergic reactions. In severe cases of UC, surgery may be necessary to remove the affected portion of the colon [11].

Traditional herbs are a significant source of novel chemicals that are the basis for medications in all major illness areas. According to Parrotta *et al.* [12], the family Bombacaceae includes *Bombax ceiba* Linn. The red cotton tree is also known as the Indian kapok tree in English, semal in Hindi, Shalmali in Sanskrit, shimul in Bengali, kondabrugam in Telugu, and mullilavu in Malayalam [13]. According to Ayurveda, *B. ceiba*, a component in numerous formulations, has shown therapeutic benefits. Menorrhagia, diarrhea, dysentery, and wounds are all treated with it. According to reports, gum or plant petioles are used as enemas in UC [14].

MATERIALS AND METHODS

Retrieval of phytochemicals

Reported phytoconstituents from *S. malabarica* were collated from phytochemistry databases viz., ChEBI, Dr. Dukes DB, PCIDB, and published literature using the keyword “*S. malabarica*, and *Bombax ceiba*.” Each compound’s molecular weight, molecular formula, canonical SMILES, and a number of hydrogen bond donors (HBDs) and acceptors (HBA) were obtained from the PubChem chemical database (<https://pubchem.ncbi.nlm.nih.gov/>) [15].

Drug-likeness and toxicity properties of phytochemicals

The drug-likeness score for each molecule was predicted using MolSoft’s (<https://molsoft.com/>) “Lipinski’s Rule of Five” model. The MolSoft server calculates an overall drug-likeness score of an unknown compound based on the chemical fingerprints. The training set of MolSoft includes 5,000 World Drug Index marketed drugs and 10,000 carefully selected non-drug compounds. [16]. The toxicity profile of each compound was predicted by the AdverPred online server. The AdverPred server mainly predicts six major side effects of the compounds, i.e., arrhythmia, cardiac failure, hepatotoxicity, myocardial infarction, nephrotoxicity, and myocardial infarction. The advantage of the server is that it has data on compounds with “Boxed warning,” “Warnings and Precautions,” and “Adverse reactions” [17]. The druggability and toxicity profile of phytochemicals are shown in Table 1.

Target identification

Genecards®: The Human Gene Database that contains information on all known and predicted human genes, including genomic, proteomic, transcriptomic, genetic, and functional details with respect to specific diseases. We first used this server

to find UC-related targets, and the UniProt protein database was used to gather gene IDs for each protein with a standard reference to the “*Homo sapiens*” species. Canonical phytochemical smiles were submitted to the SwissTargetPrediction system for target identification with probable scores of >0.1%. Compounds targeting only therapeutic targets implicated in UC and associated infections were gathered from the GeneCards after the target prediction.

Compound-gene enrichment

The set of phytochemicals modulating target/protein(s) were queried into the STRING (<https://string-db.org/>) database for protein–protein interaction analysis [18]. Furthermore, molecular pathways modulated by a set of genes were predicted by STRING in-built KEGG pathway database.

Network analysis

Cytoscape is a software program that facilitates the construction of network models to represent interactions and provides functionality for annotating and evaluating connections or relationships within a given dataset. This dataset may include a wide range of entities, including genes, proteins, chemicals, and enzymes. The datasheet of phytochemicals targeting protein molecules and protein molecules’ association with molecular pathways was created from the STRING and KEGG databases. Using these datasheets, the “compound-gene-pathway network” was built by employing Cytoscape ver. 3.6.1. The network was assessed with the “Network Analyzer” command, and the “network was treated as direct.” To express the degree of connections, the edge count and map node size from “low values to small sizes” and map node color from “low values to bright colors” were used between the compound and gene [19].

Docking study

AutoDock Vina was used for the docking study. AutoDock Vina is much faster and more accurate compared to AutoDock 4.0. Each compound’s 3D structures were obtained in the structural data file (*.sdf) format from the PubChem database. Compounds were then converted to pdb format using Discovery Studio Visualizer (DSV) version 2019. From the network analysis, we prioritized the PTGS2 target as a therapeutic target of UC that is potentially associated with inflammation. PTGS2 X-ray crystallographic structure was obtained in pdb format (PDB ID: 5IKT) from the RCSB PDB. The compound “Tolfenamic Acid” is used as a reference compound. The protein was loaded into the PyRx 0.8v software and converted into AutoDock molecules. The grid box was set to the maximum with center_x = 164, y = 186.46, z = 191.95; size_x = 24.04, y = 19.24, size_z = 21.23; and spacing 1 Å and 100 exhaustiveness was set to the system. As a result, nine different docked conformations were obtained, conformation with the least RMSD was selected and the complex was generated. The intermolecular interaction between the ligand and protein with complex was visualized by DSV version 2019 [20–22].

Table 1. Druggability of compounds.

Compound	MF	MW(g/mol)	Number of HBA	Number of HBD	LogP	Drug-likeness score
Astragalín	C ₂₁ H ₂₀ O ₁₁	448.10	11 (> 10)	7 (> 5)	-0.12	0.67
Beta-Amyrin	C ₃₀ H ₅₀ O	426.39	1	1	7.95 (> 5)	-0.22
Cellotriose	C ₁₈ H ₃₂ O ₁₆	504.17 (> 500)	16 (> 10)	11 (> 5)	-5.06	0.11
Isoquercitrín	C ₂₁ H ₂₀ O ₁₂	464.10	12 (> 10)	8 (> 5)	-0.54	0.68
Lupeol	C ₃₀ H ₅₀ O	426.39	1	1	8.35	-0.22
Mangiferín	C ₁₉ H ₁₈ O ₁₁	422.08	11	8	-0.13	0.25
Methyl 4-caffeoylquinat	C ₁₇ H ₂₀ O ₉	368.11	9	5	0.19	0.79
Olean-12-en-3-one	C ₃₀ H ₄₈ O	424.37	1	0	8.03 (> 5)	-0.02
Rutin	C ₂₇ H ₃₀ O ₁₆	610.15 (> 500)	16 (> 10)	10 (> 5)	-1.55	0.91
Stigmasterol	C ₂₉ H ₄₈ O	412.37	1	1	7.74 (> 5)	0.62

“MF Molecular Formula; MW Molecular Weight; HBD Hydrogen Bond Donor; HBA Hydrogen Bond Acceptor; LogP; Partition Co-efficient; DLS Druglikeness score”.

Table 2. Toxicity profile of phytochemicals.

Compound	Pa	Pi	Side effect
Astragalín	0.35	0.3	Hepatotoxicity
	0.332	0.127	Nephrotoxicity
beta-Amyrin		Nil	
Cellotriose	0.845	0.008	Nephrotoxicity
	0.351	0.299	Hepatotoxicity
Isoquercitrín	0.369	0.282	Hepatotoxicity
	0.302	0.155	Nephrotoxicity
Lupeol		Nil	
Mangiferín	0.55	0.035	Nephrotoxicity
Methyl 4-caffeoylquinat	0.266	0.206	Cardiac failure
Olean-12-en-3-one			
Rutin	0.384	0.271	Hepatotoxicity
	0.247	0.228	Nephrotoxicity
Stigmasterol		Nil	

Pa Pharmacological activity of compound to produce side effect(s); Pi Pharmacological inactivity of the compound for not to produce side effect(s).

RESULTS

Phytochemicals druggability

10 phytochemicals were reported to be present in the *S. malabarica* / *B. ceiba*. Among 10 bioactives, 7 exhibited positive DLS scores, and Rutin had the highest score of 0.91 (Table 1). Astragalín and Isoquercitrín were also found to be the next best druggable compounds which scored a DLS score of 0.67 and 0.68, respectively. Out of 10 compounds, beta-Amyrin, Lupeol, and Olean-12-en-3-one were found to have no side effects. Cellotriose and Mangiferín were found to have *p*-value of > 0.5 for Nephrotoxicity. Whereas the remaining compounds exhibited *p*-value < 0.5 for side effects (Table 2).

Targets prediction

From the GeneCards, about 2,830 genes were obtained for UC of which 489 were prioritized based on geneCards inferred functionality scores cut-off >50. From the TTD

database, 21 therapeutic targets of UC were collated. Finally, the probable protein targets of 10 compounds were predicted by SwissTargetPrediction. 10 compounds were predicted to hit 297 targets. Out of 297 targets, 39 targets matched with the further peer-interpretation of probable targets with the approved therapeutic targets GeneCards and TTD database UC targets.

Gene set enrichment and network analysis

Pathway enrichment study revealed that 10 phytochemicals affected 125 molecular pathways; among which 14 were linked to UC, i.e., “VEGF, IL-17, Neurotrophin, JAK-STAT, cAMP, TNF, TGF-beta, and NF-kappa B, MAPK, PI3K-Akt signaling pathway, Inflammatory bowel disease (IBD), Leukocyte transendothelial migration, Gastric acid secretion, and Apoptosis” (Table 3). The network analysis showed MAPK3, TNF, and PTGS2 protein targets to score the highest edge count. MAPK3 enriched to be involved in VEGF, IL-17, Neurotrophin, cAMP, TNF, TGF-beta, MAPK, PI3K-Akt signaling pathway, and Apoptosis; TNF was enriched to be involved in IL-17, TNF, TGF-beta, NF-kappa B signaling pathways, IBD; whereas, IL-17, TNF, and NF-kappa B signaling pathways (Fig. 1).

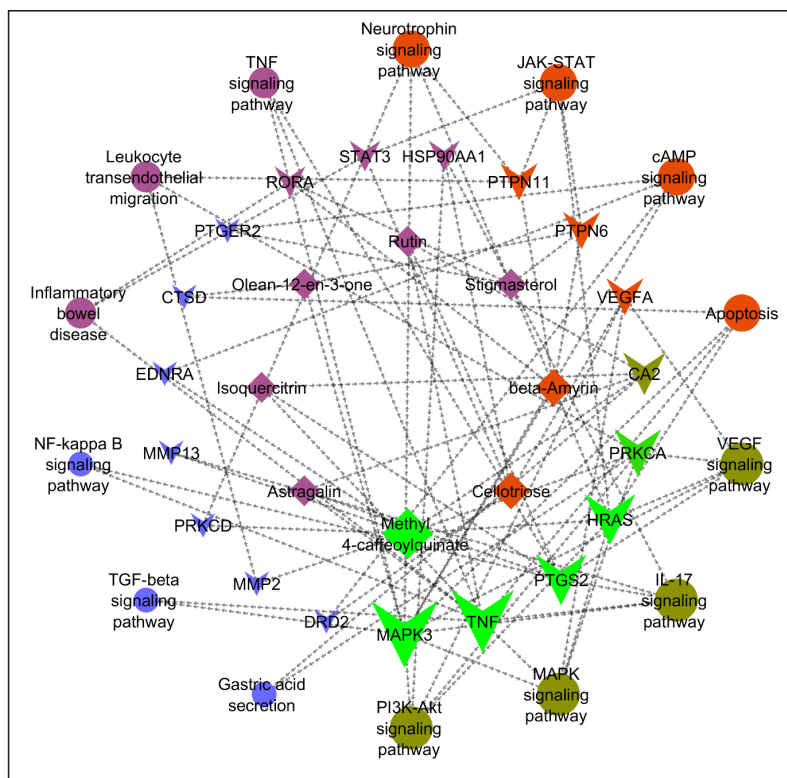
Docking study

From the network analysis, prioritized PTGS2 protein target as a therapeutic target and has a core role in inflammation. Within the network, Astragalín, Isoquercitrín, and Rutin were identified to hit PTGS2. From the docking analysis, it is inferred that Tolfenamic Acid possesses the lowest BE of -9.1 kcal/mol via forming 11 intermolecular interactions. It formed 1 H-bond with Tyr385...O- and 10 non-H-bond interaction with Leu352, Ala527 (3), Val116, Val349 (3), Leu531 (2). All eleven interactions were with active site residues of PTGS2. Among three phytochemicals, Rutin scored the lowest BE of -7.9 kcal/mol via forming 22 intermolecular interactions, i.e., 6 H-Bonds (Ser530...O-, Ser530...OH, Val523...OH, Leu352...OH, His90...O, Tyr385...O-) and 14 non-H-bonds (Phe209, Phe381, Phe210, Phe205, Tyr385, Leu359, Leu531, Ala527 (2), Val349 (2), Ser353 (2), Val523 (2), Ser530). Among 22 interactions, 20 were with active site residues. Interestingly, the other two compounds, Astragalín and Isoquercitrín also formed

Table 3. Pathway enrichment study of protein targets in UC regulated by compounds.

KEGG ID	Signaling pathways	Gene count	FDR	Set of genes within the network
hsa04370	VEGF	5	0.00000597	MAPK3, PTGS2, HRAS, PRKCA, VEGFA
hsa04657	IL-17	5	0.0000283	MMP13, MAPK3, HSP90AA1, PTGS2, TNF
hsa04722	Neurotrophin	4	0.0007	MAPK3, PTPN11, PRKCD, HRAS
hsa05321	IBD	3	0.0016	RORA, STAT3, TNF
hsa04630	JAK-STAT	4	0.0017	STAT3, PTPN11, PTPN6, HRAS
hsa04024	cAMP	4	0.0034	PTGER2, MAPK3, EDNRA, DRD2
hsa04670	Leukocyte transendothelial migration	3	0.0053	MMP2, PTPN11, PRKCA
hsa04668	TNF	3	0.0056	MAPK3, PTGS2, TNF
hsa04971	Gastric acid secretion	2	0.0293	CA2, PRKCA
hsa04350	TGF-beta	2	0.0419	MAPK3, TNF
hsa04064	NF-kappa B	2	0.0484	PTGS2, TNF
hsa04210	Apoptosis	4	0.001	CTSD, MAPK3, TNF, HRAS
hsa04010	MAPK	5	0.0016	MAPK3, TNF, HRAS, PRKCA, VEGFA
hsa04151	PI3K-Akt	5	0.0029	MAPK3, HSP90AA1, HRAS, PRKCA, VEGFA

FDR, False discovery rate.

**Figure 1.** Phytochemical, target protein, and pathway interactions.

interactions with active site residues of PTGS2. Astragalgin formed 14 and Isoquercitrin formed 9 interactions with active site residues of PTGS2. Table 4 and Figure 2 represents the intermolecular interaction of compounds with PTGS2

DISCUSSION

The current study deals with exploring the effect of *B. ceiba* on UC by multiple computational studies viz “target

identification, gene set enrichment analysis, network pharmacology coupled with molecular docking studies.” Identification of potential therapeutic targets is the key to good drug design. Since traditional plants are the starting point for the discovery of new drugs, it stands to reason that a novel treatment strategy, supported by polypharmacology and bioinformatics approaches, could be developed by using multiple compounds found in herbs with a traditional claim against a specific disease with minimal side

Table 4. Binding of compounds with cyclooxygenase 2 protein.

Compound name	PubChem CID	BE (kcal/mol)	H-Bonds	Non-H Bonds	Total no of interactions	No. of interaction with active site
Astragalín	5282102	-6.9	Met522.....OH	Leu359, Leu531, Val349 (2), Ala527(2), Leu352, Ser353(2), Val523(4)	14	14
Isoquercitrín	5280804	-6.9	Met522...OH, Ala527....OH (2)	Ala527 (2), Leu359, Leu531, Val349 (2), Ser353 (2), Val523 (2)	9	9
Rutin	5280805	-7.9	Ser530...O-, Ser530....OH, Val523, Leu352.....OH, His90...O, Tyr385...O-	Phe209, Phe381, Phe210, Phe205, Tyr385, Leu359, Leu531, Ala527 (2), Val349 (2), Ser353 (2), Val523 (2), Ser530	22	20
Tolfenamic Acid	610479	-9.1	Tyr385...O-	Leu352, Ala527 (3), Val116, Val349 (3), Leu531 (2)	11	11

“PDB Protein Data Bank; BE Binding Energy; HBI Hydrogen bond Interaction”.

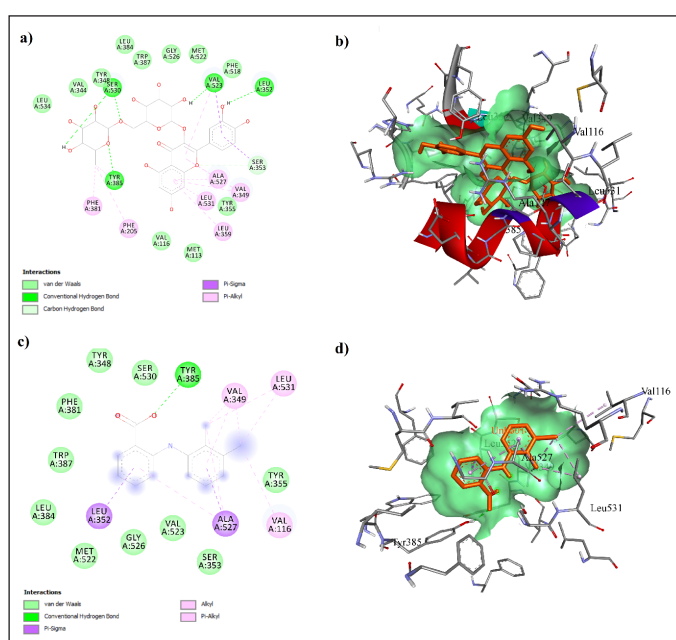


Figure 2. Binding mode of compounds with PTGS2. a) and c) 2D representation of interaction of Rutin and Tolfenamic acid with PTGS2, respectively. b) and d) 3D representation of Rutin and Tolfenamic acid, respectively, within the PTGS2 binding pocket.

effects. The influence of medications on numerous protein targets altering disease pathways is the focus of polypharmacology and bioinformatics. A good therapeutic approach aimed at the potential therapeutic targets will not cause adverse effects by altering the physiological function of the target in healthy tissues. In the current study, initially, we retrieved phytochemicals present in *B. ceiba* using curated herb databases and scientific reports.

We used phytochemicals with drug-like properties to forecast their druggable characteristics. We also used SwissTargetPrediction to identify potential targets for each phytochemical with drug-like properties and selected those compounds that modulated solely therapeutic targets related to UC. The pathways affected by *B. ceiba* phytochemicals were inferred using gene set enrichment and network analysis. To learn more about the molecular mechanism of action and

pharmacological basis of *B. ceiba* with respect to certain proteins and their association with disease-modifying capacity, a network pharmacology study was conducted. This can be scientifically studied by network construction using the Cytoscape tool (topological network) with ease since it can link to external public databases and assures the diverse interpretations

We inferred 8 bioactives of *B. ceiba* to trigger 19 therapeutic protein targets linked with UC, i.e., MAPK3, PTGS2, HRAS, PRKCA, VEGFA, MMP13, HSP90AA1, TNF, PTPN11, PRKCD, RORA, STAT3, PTPN6, PTGER2, EDNRA, DRD2, MMP2, CA2, and CTSD. Furthermore, these 19 targets were linked with 125 molecular pathways, of which 14 were related to UC pathogenesis, i.e., VEGF, IL-17, Neurotrophin, JAK-STAT, cAMP, TNF, TGF-beta, and NF-kappa B, MAPK, PI3K-Akt signaling pathway, IBD, Leukocyte transendothelial migration, Gastric acid secretion, and Apoptosis. The network analysis showed MAPK3, TNF, and PTGS2 protein targets to score the highest edge count. MAPK3 enriched to be involved in VEGF, IL-17, Neurotrophin, cAMP, TNF, TGF-beta, MAPK, PI3K-Akt signaling pathway, and Apoptosis; TNF was enriched to involve in “IL-17, TNF, TGF-beta, NF-kappa B signaling pathways, IBD; whereas, IL-17, TNF, and NF-kappa B signaling pathways.”

Patients with IBD have been found to have elevated levels of expression of MAPKs, which are intracellular serine/threonine-specific kinases that regulate the transcription and stimulation of several transcription factors governing genes involved in IBD in responses to pro-inflammatory cytokines. It has been found that VEGF, a key regulator of angiogenesis in UC, is upregulated in the sera of UC patients and animals with experimental UC. The JAK-STAT signaling plays an essential role in the pathophysiology of UC. Both normal physiological processes and inflammatory responses are mediated by the JAK-STAT pathway. TNF is a proinflammatory mediator that plays an important role in the pathogenesis of IBD. Serum, feces, and mucosal biopsies from IBD patients have been shown to have significantly higher amounts of TNF.

Furthermore, based on the network analysis and well-known therapeutic targets of UC, we chose PTGS2, also known as cyclooxygenase 2 (COX2) from the network. Astragalín, Isoquercitrín, and Rutin were predicted to modulate PTGS2,

and their molecular docking study was carried out using AutoDock vina. The results were compared with the Tolfenamic acid, a known inhibitor of PTGS2. Astragalín, Isoquercitrín, and Rutín formed 14, 9, and 22 interactions with PTGS2, in which 14, 9, and 20 interactions were with active site residues of PTGS2, respectively. While Tolfenamic Acid formed 11 interactions with PTGS2 and all interactions were with active site residues. Tolfenamic Acid scored the lowest BE of -9.1 kcal/mol and Rutín scored -7.9 kcal/mol. However, among three phytochemicals, Rutín BE was found to have the lowest and maximum number of interactions with active site residues. The previous reports also suggest Rutín as a potent inhibitor or down regulator of COX2/PTGS2 [23–25] and could be the better lead molecule against UC along with other molecules present in the *B. ceiba* via multicomponent, multiprotein, and multipathway interaction mechanism.

CONCLUSION

This work reports the molecular mechanisms of phytochemicals reported in the petiole of *B. ceiba* leaves for the management of UC via the use of multiple compounds, multiple proteins, and multiple pathways concept. The identified compounds exhibited druggability with minimal adverse effects when predicted in MolSoft and AdverPred servers. Furthermore, gene set enrichment analysis revealed phytochemicals to modulate key pathways mainly IBD, leukocyte transendothelial migration, gastric acid secretion, and apoptosis. VEGF, IL-17, Neurotrophin, JAK-STAT, cAMP, TNF, TGF- β , and NF- κ B were the signaling pathways that are linked to UC. A molecular docking study validated astragalín, isoquercitrín, and rutin to interact with the active site of PTGS2. Hence, the use of a paste made from the leaf petioles of *B. ceiba* (as described in AYUSH), could be one of the most cost-effective therapeutic natural resources for the management of UC.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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REFERENCES

1. Strober W, Fuss I, Mannon P. The fundamental basis of inflammatory bowel disease. *J Clin Invest.* 2007;117(3):514–21.
2. Gracie DJ, Ford AC. IBS-like symptoms in patients with ulcerative colitis. *Clin Exp Gastroenterol.* 2015; 19:101–9.
3. Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel JF, Sandborn WJ, *et al.* Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2013;369(8):699–710.
4. Lockhart-Mummery HE, Morson BC. Crohn's disease (regional enteritis) of the large intestine and its distinction from ulcerative colitis. *Gut.* 1960;1(2):87–105. <http://dx.doi.org/10.1136/gut.1.2.87>
5. Peeters M, Joossens S, Vermeire S, Vlietinck R, Bossuyt X, Rutgeerts P. Diagnostic value of anti-*Saccharomyces cerevisiae* and antineutrophil cytoplasmic autoantibodies in inflammatory bowel disease. *Am J Gastroenterol.* 2001;96(3):730–4.
6. Danese S, Fiorino G, Peyrin-Biroulet L. Positioning therapies in ulcerative colitis. *Clin Gastroenterol Hepatol.* 2020;18(6):1280–90.
7. Loftus Jr EV. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. *Gastroenterology.* 2004;126(6):1504–17.
8. Yang H, McElree C, Roth MP, Shanahan F, Targan SR, Rotter JJ. Familial empirical risks for inflammatory bowel disease: differences between Jews and non-Jews. *Gut.* 1993;34:517–24.
9. Ford AC, Khan KJ, Achkar JP, Moayyedi P. Efficacy of oral vs. topical, or combined oral and topical 5-aminosalicylates, in ulcerative colitis: systematic review and meta-analysis. *Am J Gastroenterol.* 2012;107(2):167–76.
10. Carter MJ, Lobo AJ, Travis SP. Guidelines for the management of inflammatory bowel disease in adults. *Gut.* 2004;53:1–6.
11. Feagan BG, MacDonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochrane Database Syst Rev.* 2012;10:CD000543.
12. Parrotta JA. Healing plants of peninsular India. Wallingford, UK: CABI publishing; 2001.
13. Chaudhary PH, Khadabadi SS. *Bombax ceiba* Linn.: pharmacognosy, ethnobotany and phyto-pharmacology. *Phcog Commun.* 2012;2(3):2–9.
14. Jain A, Katewa SS. Medicinal plant diversity of Sitamata wildlife sanctuary, Rajasthan, India. *J Ethnopharmacol* 2005;102:143–57.
15. Lagunin AS, Ivanov A, Rudik D, Filimonov V, Poroikov G. DIGEP-Pred: web service for *in silico* prediction of drug-induced gene expression profiles based on structural formula. *Bioinformatics.* 2013;29:2062–3. <https://doi.org/10.1093/bioinformatics/btt322>.

16. Lipinski. C.A, Lead- and drug-like compounds: the rule-of-five revolution, *Drug Discov Today Technol.* 2004;1:337–41. <https://doi.org/10.1016/j.ddtec.2004.11.007>.
17. Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Sci Rep.* 2017;7:42717. <https://doi.org/10.1038/srep42717>.
18. Szklarczyk D, Morris JH, Cook H, Kuhn M, Wyder S, Simonovic M, *et al.* The string database in 2017: quality-controlled protein–protein association networks, made broadly accessible. *Nucleic Acids Res.* 2017;45. <https://doi.org/10.1093/nar/gkw937>
19. Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res.* 2003;13:2498–504. <https://doi.org/10.1101/gr.1239303>.
20. Samdani A, Vetrivel U. POAP: A GNU parallel based multithreaded pipeline of open babel and Auto-Dock suite for boosted high throughput virtual screening. *Comput Biol Chem.* 2018 ; 74:39 – 48. <https://doi.org/10.1016/j.compbiolchem.2018.02.012>
21. Biradar P, Patil V, Joshi H, Khanal P, Mallapur S. Experimental validation and network pharmacology evaluation to decipher the mechanism of action of *Erythrina variegata* L. bark against scopolamine-induced memory impairment in rats. *Adv Tradit Med.* 2020;22:1–14.
22. Patil RS, Khatib NA, Patil VS, Suryawanshi SS. Chlorogenic acid may be a potent inhibitor of dimeric SARS-CoV-2 main protease 3CLpro: an *in silico* study. *Tradit Med Res.* 2021;6:20.
23. Enogieru AB, Haylett W, Hiss D, Ekpo O. Inhibition of γ H2AX, COX-2 and regulation of antioxidant enzymes in MPP+-exposed SH-SY5Y cells pre-treated with rutin. *Metab Brain Dis.* 2021;36(7):2119–30.
24. Choi S, Lim TG, Hwang MK, Kim YA, Kim J, Kang NJ, *et al.* Rutin inhibits B[a]PDE-induced cyclooxygenase-2 expression by targeting EGFR kinase activity. *Biochem Pharmacol.* 2013;86(10):1468–75. <https://doi.org/10.1016/j.bcp.2013.08.066>.
25. Moutinho MS, Aragao S, Carmo D, Casaca F, Silva S, Ribeiro J, *et al.* Curcumin and rutin down-regulate cyclooxygenase-2 and reduce tumor-associated inflammation in HPV16-transgenic mice. *Anticancer Res.* 2018;38(3):1461–6.

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