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Research article

Network pharmacology study to identify molecular pathways involved in the anti-diabetic activity of *Syzygium cumini* seed constituents

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Abstract: Diabetes is characterized by hyperglycemia and insulin resistance, which significantly increase the risk of morbidity and mortality. *Syzygium cumini* seeds have been used traditionally in the management of diabetes, though the precise molecular mechanisms underlying their effects are not yet fully understood. The present study aimed to elucidate the molecular mechanisms through which *S. cumini* seed extract exerts its beneficial effects in diabetes, employing a network pharmacology approach. The constituents of *S. cumini* seeds were identified from online databases. Eligible constituents were then used to identify target genes through four databases. Genes associated with diabetes were retrieved from two databases. The overlapping genes were selected as the target genes for further analysis. A protein–protein interaction network was constructed using Cytoscape and the STRING database, which helped identify hub genes. This network was then used to perform gene ontology and pathway enrichment analyses. Among the 66 identified constituents, 29 were eligible for inclusion in the analysis. Database screening revealed 986 genes targeted by the selected active constituents, with 392 genes associated with diabetes. Of these, 112 genes overlapped. Following network development, the top 10 hub genes with the highest degree scores were selected for pathway enrichment analysis. The pathway enrichment analysis indicated that *S. cumini* may exert beneficial effects in diabetes by modulating several pathways related to RNA-mediated miRNA transcription, AGE-RAGE signaling, and HIF-1 signaling through multiple genes. The underlying mechanisms may involve enhanced cellular responses to oxidative stress, improved oxidative stress metabolism, and an elevated anti-inflammatory response. The current study provides promising evidence of the beneficial effects of *S. cumini* seed therapy in the management of diabetes. The findings of this study offer a potential direction for future molecular research to confirm the efficacy of *S. cumini* seeds in diabetic

conditions through the pathways described.

Keywords: *Syzygium cumini*; network pharmacology; gene ontology; KEGG; hub genes; diabetes; advanced glycation end products; miRNA

1. Introduction

Diabetes mellitus (DM), a chronic metabolic disorder, is characterized by elevated serum glucose levels, primarily due to reduced insulin production and/or increased insulin resistance. As one of the major metabolic conditions, DM is highly prevalent, affecting millions of individuals worldwide [1]. According to global patient survey data, approximately 537 million adults were living with diabetes in 2021, and with current projections, it is estimated that by 2045, around 783 million adults will have diabetes [2,3]. DM has a significant negative impact on overall health and is a leading cause of serious complications, including cardiovascular issues, renal dysfunction, ophthalmic problems, and nerve damage [3]. In addition to its health consequences, DM is one of the top causes of morbidity worldwide, with an estimated 11.3% of deaths attributed to diabetes or its complications [4,5]. Furthermore, diabetes imposes a substantial economic burden; according to the International Diabetes Federation (IDF), global diabetes-related healthcare expenditures are expected to reach approximately $1.054 trillion by 2045 [3,6].

The management of DM is a complex process that involves both patient-centered pharmacological and non-pharmacological approaches [7]. Current pharmacological treatments include glucose-lowering therapies, injectable insulin, insulin secretagogues, and medications aimed at improving insulin sensitivity. Non-pharmacological interventions, such as exercise, lifestyle modifications, and weight management, are also key components of diabetes management [8,9]. In addition, nutraceuticals, herbal therapies, and dietary supplements are increasingly used alongside the recommended pharmacological and non-pharmacological treatment regimens [10]. Numerous studies have highlighted the beneficial effects of herbal therapies in managing diabetes [3,10].

Syzygium cumini (family Myrtaceae), also known as Indian blackberry, is native to the Indian subcontinent and regions of South Asia, including Bangladesh, Nepal, and Sri Lanka [11]. The fruit, seeds, leaves, and bark of *S. cumini* have been used for centuries to treat various medical conditions, including sore throat, asthma, bronchitis, diarrhea and related ailments, dental issues, psychological conditions, and metabolic disorders [11,12]. The most extensively studied application of *S. cumini* is in the management of diabetes. With over 125 years of research and numerous scientific publications, the use of *S. cumini* has grown exponentially in recent decades for diabetes management [11,13]. However, its use remains under scrutiny due to limited evidence regarding the exact molecular mechanisms behind its anti-diabetic potential.

Network pharmacology is an emerging methodology used to identify and correlate the molecular connections between the active constituents of herbs and the target disease conditions [14,15]. This approach leverages large datasets and machine learning techniques to identify potential multi-targets influenced by biologically active ingredients, offering a significant advantage over the traditional *single molecule–single target* approach in molecular activity studies. *S. cumini* seeds contain a variety of active constituents that may exert a multitude of effects on various targets, contributing to their anti-diabetic potential. Using traditional methods, it can be challenging to fully understand the molecular

mechanisms behind the anti-diabetic activity of *S. cumini* seeds and to identify which specific phytoconstituents are responsible for these effects. While several studies have explored molecular pathways involved in the anti-diabetic activity [11–13], no study has yet evaluated the anti-diabetic potential of *S. cumini* seeds using a network pharmacology approach. Therefore, this study was conducted to elucidate the molecular mechanisms underlying the anti-diabetic effects of *S. cumini* seeds and identify the active constituents responsible for these effects using network pharmacological analysis.

2. Materials and methods

2.1. S. cumini *active constituent identification and selection*

The active constituents in *S. cumini* seeds were identified through an extensive literature search and by screening the IMPPAT (Indian Medicinal Plants, Phytochemistry, and Therapeutics) database (https://cb.imsc.res.in/imppat/) [16]. Briefly, the IMPPAT database was accessed, and the "Basic search" option was selected for database search using "*Syzygium cumini*" as the search term. The search revealed a total of 241 active ingredients, out of which those ingredients specifically present in the seed part were selected for further analysis. The SMILES (Simplified Molecular Input Line Entry System) representation of these constituents was obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) [17]. To select the target active constituents, the compounds were analyzed for their drug-likeness properties using Lipinski's rule, with data sourced from the SwissADME database (http://www.swissadme.ch/) [18]. Compounds that met all of Lipinski's criteria and did not violate any of the properties were selected for further evaluation. Lipinski rule is a set of rules that, based on the molecular structure of the target compound, predicts whether the particular compound of interest will be active in humans following oral consumption. It involves the study of the molecular structure of the target compound in the following parameters: molecular weight higher than 500; more than 5 hydrogen bond donors; more than 10 hydrogen bond acceptors; and calculated log partition coefficient (octanol:water) greater than 5.

2.2. Gene identification, selection, and database construction

The SMILES of the bioactive compounds were used to identify target genes from the Swiss Target Prediction (STP) database (http://www.swisstargetprediction.ch/) [19], SuperPred database (https://prediction.charite.de/) [20], similarity ensemble approach (SEA) database (https://sea.bkslab.org/) [21], and BindingDB database (https://www.bindingdb.org/rwd/bind/index.jsp) [22]. The STP database was screened for potential target genes by entering the molecule SMILES and selecting the target organism *Homo sapiens* from the available options. For BindingDB, the similarity value was set to 1 (indicating 100% similarity to the compound structure). The data of identified genes from these databases were collected in an Excel spreadsheet, and duplicate entries were removed. The UniProt database (https://www.uniprot.org/) was used to gather additional gene-related information, including gene names, UniProt IDs, and accession numbers.

Genes associated with diabetes were identified from the DisGeNet database (https://www.disgenet.com/) [23] and the Comparative Toxicogenomics Database (CTD)

(https://ctdbase.org/) [24]. The terms used to identify target disease genes included "type 2 diabetes" and "type 2 diabetes mellitus". For the CTD search, only genes curated to have disease interactions were selected. The gene data were collected in an Excel spreadsheet, and duplicate entries were removed. Gene-related information was then gathered from the UniProt database.

To identify the genes associated with *S. cumini* bioactive constituents and the disease, the VENNY 2.1 software (https://bioinfogp.cnb.csic.es/tools/venny/) was used. Overlapping genes were identified and selected for further analysis, while non-overlapping genes were excluded from the analysis.

2.3. Protein–protein interaction network construction

The Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database (https://string-db.org/) was used to construct the protein–protein interaction (PPI) network [25]. The names of all the overlapping genes were entered into the database, and after cross-verification, the PPI network was developed. An interaction score of >0.9 (indicating the highest confidence) was applied, and proteins that did not interact within the network were removed. The final PPI network was then developed and used for network construction.

2.4. Network construction, visualization, and hub-gene identification

Using the PPI network from the STRING database, the herb-active-target genes network was constructed and visualized using the Cytoscape desktop application (V 3.10.2) [26, 27]. *S. cumini* was placed at the center of the network, targeting the active ingredients, while the active ingredients were linked to the target genes associated with diabetes. After network construction and visualization, the cytoHubba application was used to analyze the network topology [28]. The genes were evaluated based on their degree value, which represents the number of edges each gene has in the network [29]. Generally, genes with the highest degree values are more likely to be altered by the herb-derived active constituents, thereby providing therapeutic benefits [29]. Therefore, the top 10 genes with the highest degree values were selected, and the network was reconstructed.

2.5. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses

The GO and KEGG pathway enrichment analysis was performed using the SRplot database (https://www.bioinformatics.com.cn/srplot) [30], a web-based application for pathway enrichment analysis. The GO analysis evaluates the effects of gene products across three biological components: cellular component (CC), molecular function (MF), and biological process (BP) [31]. The KEGG analysis identifies the biological pathways in which the genes and their products play a direct role, helping to better understand the effects of target genes in various biological pathways [32]. The pathways identified by the GO and KEGG analyses were sorted based on the corrected p-value, and the top 10 pathways were selected. A complete study flowchart is depicted in Figure 1.

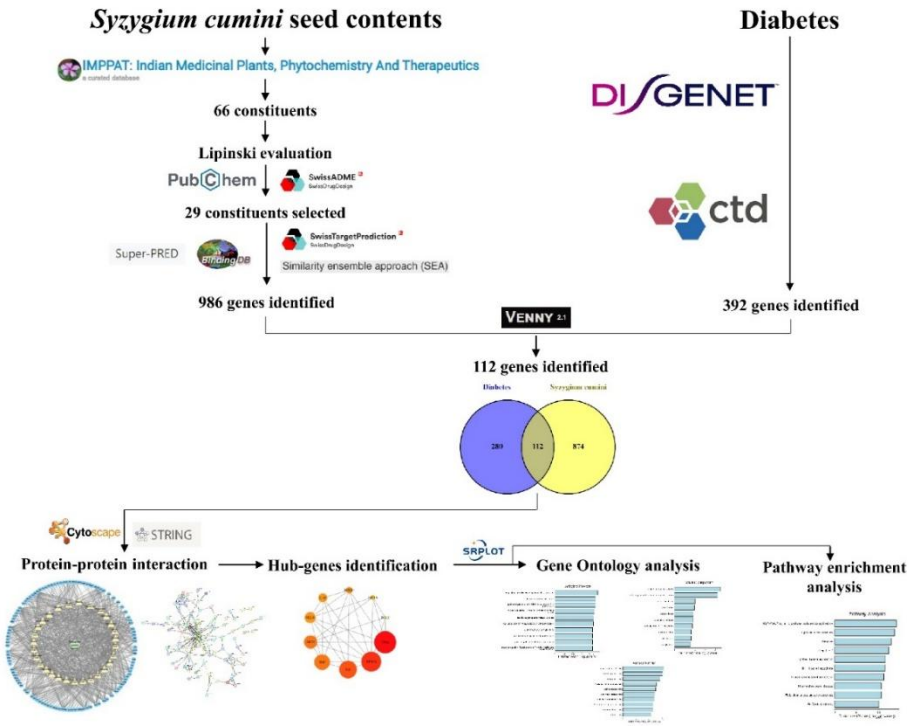

Figure 1. Complete study flowchart.

3. Results

3.1. Active constituent identification and selection

A literature review and search of the online IMPPAT database revealed 66 active constituents in *S. cumini* seed extract. After assessing the drug-likeness of all constituents using the Lipinski criteria, 29 active constituents were selected for further analysis. A complete list of the retrieved and selected active constituents is provided in Table 1, and a detailed description of the active constituents included in the analysis is provided as Table S1 (See Supplementary Material).

3.2. Target gene identification

The SMILES of the selected active constituents were used to identify target genes. After a complete database search and removal of duplicates, a total of 986 genes were identified as targets of the selected active constituents. Similarly, the disease gene search revealed 392 genes after duplicate removal. Using VENNY 2.1, a total of 112 overlapping genes were identified (Figure 2) and selected as the target genes for further analysis.

Table 1. List of all retrieved and included active constituents from *S. cumini* seed extract.

Actives included in the analysis	Actives excluded from the analysis
• Myristic acid • Guaiol • Maslinic acid • Epi-beta-caryophyllene • Quercetin • Betulinic acid • Sterculic acid • Gallic acid • beta-Sitosterol • gamma-Terpineol • Resorcinol • Caryophyllenyl alcohol • alpha-Pinene • Camphene • Ellagic acid • Limonene • Humulene • beta-Pinene • Linoleic acid • p-Cymene • Lauric acid • Caryophyllene oxide • Oleic acid • Myrcene • Guaiacol • Ferulic acid • beta-Copaene • Caffeic acid • epi-Cubenol	• Gamma-Gurjunene • Palmitic acid • Isopropyl-1-methyl-5-methylenecyclodeca-1,6-diene • Delta-Cadinene • Globulol • Pinoresinol 4-O-beta-D-glucopyranoside • Dimethoxybenzene • Alpha-Muurolene • Hexahydroxydiphenoyl-D-glucose • [(Dimethyloxiran-2-yl)methyl]-3-methylfuran • Alpha-Cadinene • Aromadendrene • Malvalic acid • Stearic acid • Epoxyoctadecenoic acid • Tannic acid • Ellagitannin • Isoterpinolene • Humulene epoxide II • Mesitylene • Dihydrodehydrodiconiferyl alcohol • Methylbenzaldehyde • Eucarvone • Corilagin • Gamma-Cadinene • Alpha-Muurolol • Hydroxymethylfurfural • Triacontanol • (2-Hydroxy-4,6-dimethoxy-3-methylphenyl)ethan-1-one • Alpha-Calacorene • Alpha-Copaene • Ethyl benzoate • Hydroxyepicaryophyllene • Allo-Aromadendrene • Dimethoxybenzene • Alpha-Selinene • Hydroxy-caryophyllene

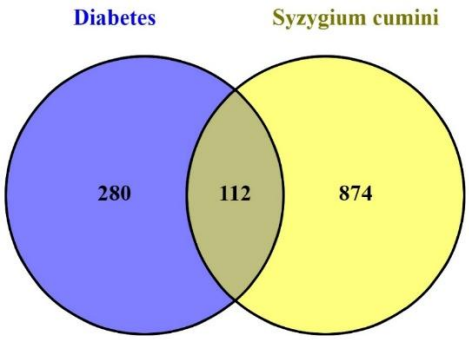

Figure 2. Number of overlapping genes targeted by *S. cumini* seed active constituents and involved in diabetes.

3.3. PPI network and herb-active-disease genes network construction

The 112 genes were entered into the STRING database to construct the PPI network. The network was further refined based on the confidence level and the removal of non-junction proteins, resulting in the final PPI network, as shown in Figure 3. The PPI network was then transferred to the Cytoscape application to construct the herb-active-disease gene network (Figure 3). The network topology was analyzed using cytoHubba to identify the top 10 hub genes (Figure 3). The 10 genes with the highest degree values were BCL2, HIF1A, NFKB1, IL1B, RELA, AKT1, TNF, IL6, STAT3, and TP53 (Table 2).

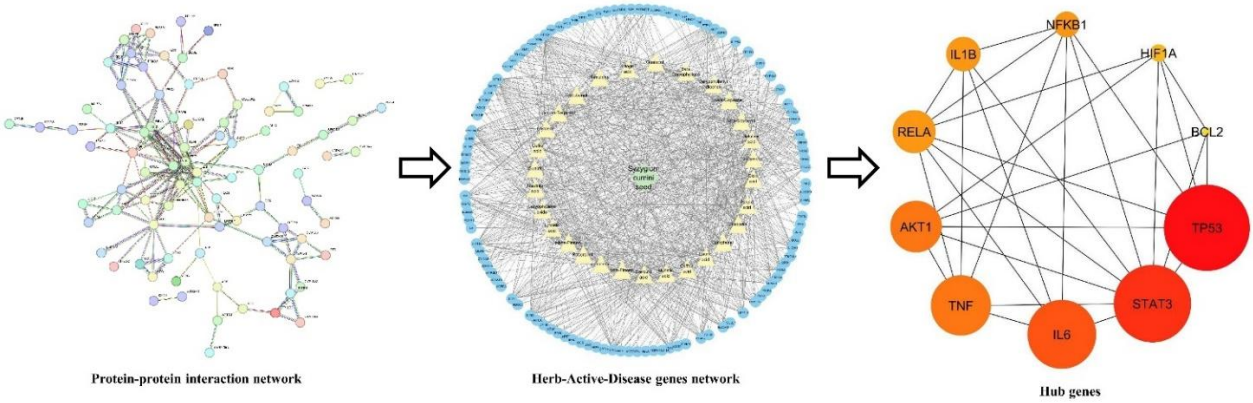

Figure 3. Protein–protein interaction (PPI) network, herb-active-target gene network, and hub genes network.

Table 2. Identified hub genes with rank score.

Rank	Gene name	Rank score
1	*TP53*	16
2	*STAT3*	15
3	*IL6*	13
4	*TNF*	12
5	*AKT1*	12
6	*RELA*	11
7	*IL1B*	11
8	*NFKB1*	11
9	*HIF1A*	9
10	*BCL2*	8

3.4. Pathway enrichment analysis

Using the hub genes, the SRPlot database was employed to conduct pathway enrichment analysis (KEGG and GO). As shown in Figure 4, the active constituents in *S. cumini* seeds may provide beneficial effects in diabetes by targeting pathways involved in the cellular transcription regulator complex, RNA polymerase II transcription regulator complex, nuclear membrane, pore complex, phagocytic cup, glutamatergic synapse, transcription factor TFIID complex, nuclear envelope, myelin sheath, and axonal cytoplasm. The GO analysis revealed that the selected active constituents from *S. cumini* seeds can modulate the binding functions of various macromolecules, including phosphatase, repressive transcription factors, cytokine receptors, ubiquitin protein ligases, DNA-binding transcription factors, histone deacetylases, and proteases.

By interacting with and modulating the aforementioned cellular components and macromolecular activities, the selected constituents can provide beneficial effects in diabetes by modulating the reactive oxygen species metabolic process, cellular response to oxidative stress, intercellular stimuli, and positive regulation of microRNA and DNA transcription factors. As shown in Figure 5, pathway enrichment analysis using the KEGG database revealed that the anti-diabetic potential of *S. cumini* seed extract may be attributed to the effects of its constituents in modulating the AGE-RAGE signaling pathway, lipid metabolism pathways, HIF-1 signaling pathway, and targeting proteins involved in anti-folate resistance.

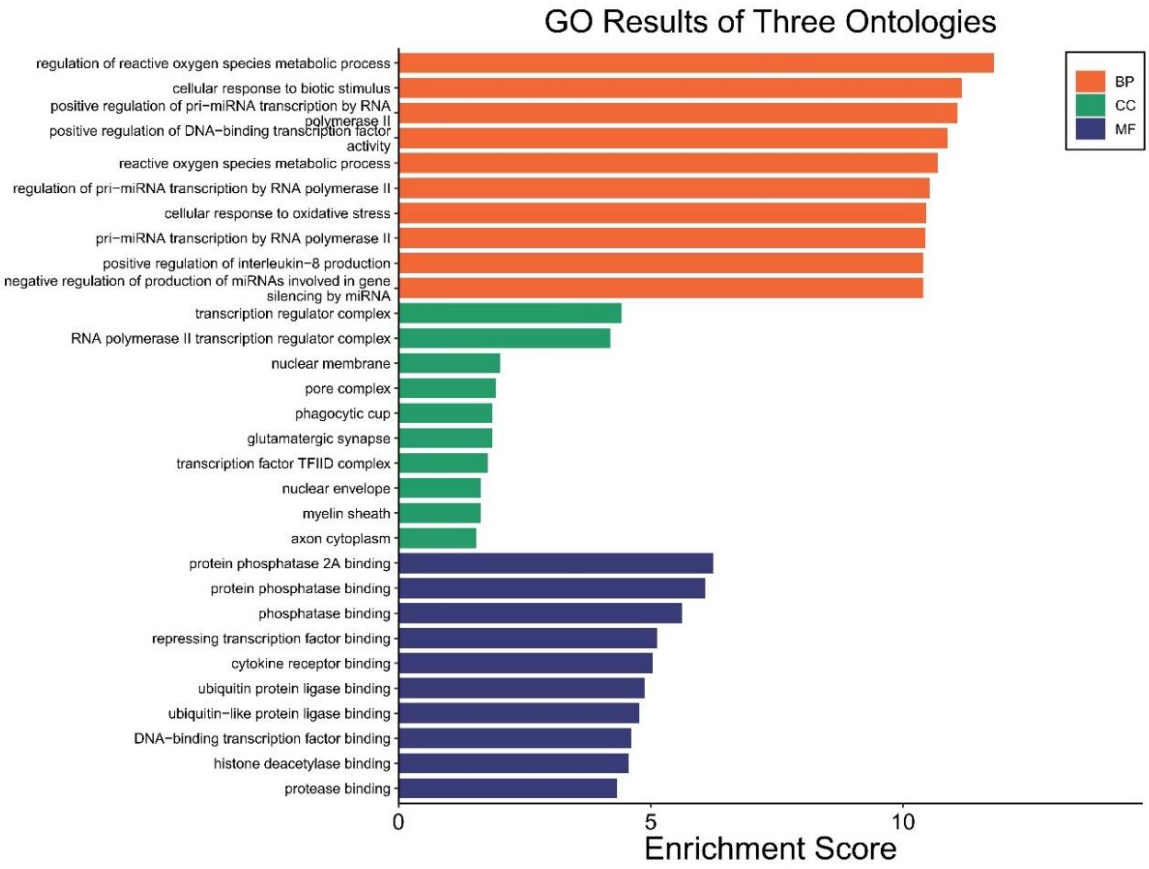

Figure 4. Results of gene ontology (GO) analysis.

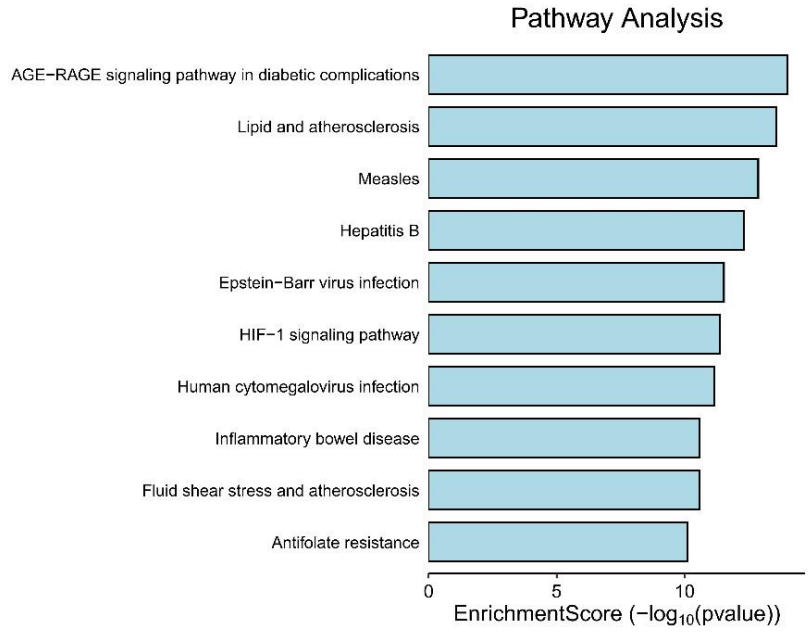

Figure 5. Results of Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis.

4. Discussion

Among the various herbal supplements used in the management of diabetes, *S. cumini* seeds are among the most widely studied and used. Numerous traditional references, along with several clinical studies, have supported the positive effects of *S. cumini* seed extract in diabetes [13,33–35]. While previous studies have successfully identified some molecular mechanisms of action of *S. cumini* seed extract, the exact molecular pathways remain complex. Therefore, the current study aimed to decode the molecular mechanisms underlying the anti-diabetic potential of *S. cumini* seeds using a network pharmacology approach.

Using available literature and online databases, 29 active constituents were identified in *S. cumini* seeds, which have the strongest potential to be orally active and influence diabetes conditions. These active constituents include myristic acid, gamma-terpineol, lauric acid, myrcene, β-copaene, guaiol, quercetin, resorcinol, ellagic acid, p-cymene, sterculic acid, caryophyllenyl alcohol, guaiacol, humulene, oleic acid, ferulic acid, caffeic acid, maslinic acid, betulinic acid, gallic acid, α-pinene, β-pinene, caryophyllene oxide, epicubenol, (E)-2-epi-beta-caryophyllene, β-sitosterol, camphene, limonene, and linoleic acid. Gene identification and analysis revealed that these 29 active constituents can modulate the activity of 112 genes associated with diabetes. Based on these 112 genes, a PPI network was constructed, and network topology analysis revealed ten hub genes: *BCL2*, *HIF1A*, *NFKB1*, *IL1B*, *RELA*, *AKT1*, *TNF*, *IL6*, *STAT3*, and *TP53*. KEGG and GO pathway analysis of these hub genes identified several signaling pathways that may be modulated by the active constituents. The most important signaling pathways included the advanced glycation end-products (AGE)/receptor of AGE (RAGE) signaling pathway, reactive oxygen species (ROS) signaling pathway, RNA-mediated miRNA transcription pathway, and the hypoxia-inducible factor 1 (HIF-1) signaling pathway.

The *BCL2* gene encodes the B-cell lymphoma-2 (BCL2) protein, a critical regulator of apoptosis. The BCL2 protein inhibits apoptosis and promotes cell survival by binding to and inhibiting the activity of pro-apoptotic proteins in response to extracellular signals such as cytokines and growth factors, as well as intracellular signals including stress and cellular injury [36, 37]. In diabetes, various studies have suggested that *BCL2* gene activity is altered, leading to reduced expression of the BCL2 protein, particularly in pancreatic β cells. This alteration contributes to increased apoptosis of β cells, resulting in reduced insulin production and secretion [36]. Additionally, some studies have highlighted the association between altered *BCL2* expression and insulin resistance in diabetes [38]. Previous research has confirmed that *S. cumini* extract can upregulate *BCL2* gene expression [39,40], which supports the findings of the current study. The *HIF1A* gene encodes the hypoxia-inducible factor 1 alpha (HIF-1α), a major transcription factor involved in cell survival and metabolism under hypoxic conditions [41,42]. The activity of HIF-1α is crucial for maintaining the health of pancreatic β cells and for the expression of glucose transporters in insulin-sensitive tissues [43]. In individuals with diabetes, the activity of HIF-1α is often reduced, which may be associated with the initiation and progression of the disease [43,44]. Although there is promising evidence regarding HIF-1α's role in diabetes, no previous studies have evaluated the effect of *S. cumini* extract on *HIF1A* gene expression. This could be explored in future experimental studies.

The *NFKB1* gene is responsible for the transcription of the p105 protein, a major component of the Nuclear Factor Kappa B (NF-κB) complex [45,46]. Similarly, the *RELA* gene encodes the RelA protein (also known as p65), another key protein in the NF-κB complex [47]. Over-activation of NF-κB leads to a chronic inflammatory state, which has detrimental effects on both insulin secretion and

insulin activity, contributing to increased insulin resistance [48]. While phytoconstituents present in *S. cumini* extract have been shown to inhibit the expression and activity of NF-κB [49], only a few studies have evaluated the anti-diabetic potential of *S. cumini* extract through the NF-κB signaling pathway [50]. These findings support the hypothesis of the current study, which suggests that the anti-diabetic effects of *S. cumini* seed extract may be due to its ability to modulate the NF-κB pathway. The *IL-1B* gene encodes the pro-inflammatory cytokine interleukin-1 beta (IL-1β). In diabetes, prolonged elevated levels of IL-1β are directly associated with reduced glucose utilization and increased insulin resistance [51,52]. Additionally, IL-1β can damage pancreatic β cells, further reducing insulin secretion in response to hyperglycemia [51,52]. The *IL-6* gene encodes cytokine interleukin-6 (IL-6), which is crucial for the body's defense mechanisms [53]. In diabetic individuals, IL-6 levels are elevated, contributing to persistent inflammation that exacerbates insulin resistance [54]. Elevated IL-6 also stimulates the release of other pro-inflammatory cytokines, amplifying the inflammatory response and worsening insulin resistance [55]. Furthermore, IL-6 can damage pancreatic β cells, impairing their function and survival, which further contributes to the decline in insulin secretion, a key factor in the progression of diabetes [56]. Some research also suggests that IL-6 may affect adipose tissue metabolism, promoting lipid accumulation and fostering an inflammatory state that disrupts glucose homeostasis [56]. Similarly, TNF-α levels are significantly elevated in diabetic individuals and are involved in the major complications of diabetes [57,58]. Despite the extensive evidence suggesting the detrimental role of IL-1β, IL-6, and TNF-α in diabetes, the number of studies evaluating the effects of *S. cumini* extract on these cytokines is limited, highlighting the need for more focused mechanistic research.

STAT3 (signal transducer and activator of transcription 3) is a key component of the JAK/STAT signaling pathway, which is activated by various cytokines and growth factors, including IL-6, leptin, and growth hormone. This activation triggers a series of phosphorylation events that regulate the expression of target genes [59]. In diabetes, prolonged STAT3 activation due to a chronic inflammatory state contributes to insulin resistance by promoting the expression of inflammation-related genes [60]. Furthermore, sustained STAT3 signaling can impair pancreatic β-cell function and survival, leading to β-cell dysfunction and apoptosis, which in turn reduces insulin production and exacerbates glucose control in diabetes [61]. While previous molecular docking studies have shown that *S. cumini*–derived constituents can interact with the STAT3 protein [62], the impact of this interaction on diabetes has not yet been explored, presenting a potential pathway for further investigation. The *TP53* gene encodes the p53 protein, a critical tumor suppressor that plays a key role in maintaining genomic stability and regulating the cell cycle [63]. In the context of diabetes, p53 influences glucose metabolism by reducing insulin sensitivity and impairing pancreatic β-cell function. This occurs through the regulation of genes involved in glucose homeostasis, thereby promoting insulin resistance [64]. While previous research has identified the anti-cancer effects of *S. cumini* bark extract through the upregulation of p53 expression, no studies have yet evaluated the anti-diabetic potential of *S. cumini* seed extract in relation to its effect on p53 expression.

Hyperglycemia in diabetes leads to the formation of advanced glycation end-products (AGEs), which subsequently activate the AGE receptor of AGE (RAGE) signaling pathway [65]. The activation of the AGE-RAGE pathway triggers a cascade of other signaling events, including the NF-κB pathway, which increases the levels of pro-inflammatory cytokines and oxidative stress. This exacerbates insulin resistance, chronic inflammation, and widespread tissue damage, thereby elevating the risk of diabetes-related complications such as nephropathy and retinopathy [66]. The current analysis suggests that *S.*

cumini seed extract may exert its effects in diabetes by modulating the AGE-RAGE signaling pathway, a hypothesis supported by positive results from previous studies [50], which further strengthens the validity of the current findings. MicroRNAs (miRNAs) are small, non-coding RNA molecules that play a crucial role in regulating protein transcription. Acting as a brake on mRNA transcription, miRNAs interfere with and prevent the excessive translation of target proteins [67,68]. While numerous studies have provided insights into the role of specific miRNAs (such as miR-29a, miR-34a, miR-103, miR-107, miR-126, miR-132, miR-142–3p, miR-144, miR-375, miR-571, miR-661, miR-770–5p, miR-892b, miR-1303, and others) [69–71], the influence of *S. cumini* seed extracts on miRNA activity has not yet been explored. This represents a potential research gap that could be addressed in future studies.

The results of the current study are novel, as no previous research has systematically identified the active constituents in *S. cumini* seed extract based on their structural drug-likeness. Furthermore, this study provides a detailed exploration of the multiple molecular pathways through which the active constituents of *S. cumini* seed extract may exert their anti-diabetic effects. The findings are consistent with those of previous experimental studies, which supports the validity of our results. Additionally, this study has identified several new pathways that have not been explored before, offering promising avenues for future research on the effectiveness of *S. cumini* seed extract in managing diabetes. Also, based on the positive benefits of *S. cumini* seed therapy in complications associated with diabetes, the current study can pave the path for future studies to evaluate the molecular mechanisms of the beneficial effects of *S. cumini* seed constituents on such conditions, utilizing a similar methodological approach. The current study also has potential limitations. The results of the current study are purely experimental, with the absence of experimental validation. It is well known that changes in the amount of active ingredients alter their effect on the molecular mechanism of action of herbal extracts. In the current study, the active constituents were identified from an online database that enlists the presence of active constituents in particular herbal parts based on available scientific evidence. While the presence of a particular set of constituents can be identified, it is putative that herbal extracts are required to be analyzed for the presence of these ingredients in the extract form. While such an analysis was not within the scope of the current study, the observations obtained here can help design future experimental studies to further elucidate the role of individual active constituents in diabetes. Additionally, experimental validation of the study observations is warranted.

5. Conclusions

The current study supports the use of *Syzygium cumini* seed extracts in the management of diabetes. *S. cumini* seeds have a long history of traditional use in various conditions, including diabetes. Several experimental studies have identified specific mechanistic pathways through which *S. cumini* seed extracts are believed to exert their anti-diabetic effects. However, due to the presence of multiple active constituents, each potentially targeting several pathways involved in diabetes, comprehensively identifying all relevant pathways remains a challenging task. In this study, we adopted a network pharmacology approach to uncover the molecular mechanisms underlying the anti-diabetic effects of *Syzygium cumini* seed extracts. The findings are consistent with previous studies and have also identified new pathways that warrant further investigation in future research.

Author contributions

Vishal Dubey was responsible for study conceptualization and ideation, database mining, formal analysis and investigation, writing the original draft, and visualization of the manuscript, along with the final version of manuscript. Jignesh Kansagra was responsible database mining, investigation, and drafting original and final manuscript. Bhargav Kamani was responsible database mining, investigation, and drafting original and final manuscript. Varun Sureja was responsible database mining, investigation, finalizing the manuscript, and supervising the entire study. All authors have read and approved the final version of manuscript.

Use of Generative-AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

The authors declare no conflict of interests in this paper.

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