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QUANTITATIVE ETHNOMEDICINAL STUDY OF THE CHAKMA COMMUNITY IN BANGLADESH INTEGRATING NETWORK PHARMACOLOGY AND MOLECULAR DOCKING

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Abstract

The present study documents and quantitatively evaluates the ethnomedicinal knowledge of the Chakma community in Rangamati Sadar Upazila, Bangladesh, integrates network pharmacology and molecular docking to explore the molecular mechanisms underlying the therapeutic potential of the most culturally important species. Field investigations were conducted using open-ended and semi-structured interviews with 102 informants. A total of 82 medicinal plant species representing 78 genera and 49 families were recorded. Herbs were the dominant growth form (54.9%) and leaves were the most frequently used plant part (53.2%). Quantitative analysis revealed high Informant Consensus Factor (FIC) values (0.90–1.00) across 13 disease categories, indicating strong agreement among informants. Use Value (UV) analysis identified *Clerodendrum infortunatum* as the most culturally important species. Network pharmacology analysis identified 167 unique targets associated with hepatic fibrosis, and protein-protein interaction network unraveled 10 hub genes, including CASP3, EGFR, ESR1, MMP9, GSK3B, MTOR, ERBB2, MDM2, PIK3CA, and MAPK1. Gene Ontology analysis provided insights into key biological processes, cellular components, and molecular functions. PI3K–AKT signaling pathway have been identified from KEGG that demonstrated prominent role in the progression of hepatic fibrosis. Molecular docking demonstrated strong binding affinities of key phytocompounds, with 4-Carvomenthenol emerging as the most promising for drug design. These findings provide a quantitative baseline of Chakma ethnomedicine and translate traditional knowledge into molecular-level evidence, offering a scientific foundation for future drug discovery and conservation of indigenous medicinal heritage.

Introduction

Ethnobotanical research explores the complex relationship between plants and people, particularly the use of plants for medicinal, cultural, and economic purposes, and their longstanding role as sources of essential goods (Uddin *et al*., 2015). In modern pharmaceutical research, traditional plant-based knowledge contributes far beyond identifying new drug candidates; it also supports the development of healthcare practices that are culturally appropriate and therapeutically effective (Gupta *et al*., 2005). According to the World Health Organization (WHO), over 80% of the global population relies on herbal medicines for their health necessities (WHO, 2000; Kong *et al*., 2009). More than half of the pharmaceuticals used today have roots in

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traditional ethnomedicinal practices (Ahmed *et al.*, 2023). South and Southeast Asia are globally recognized as regions of exceptional medicinal plant diversity, where plant resources form the backbone of many traditional healthcare practices (Shakil *et al*., 2024).

Bangladesh, endowed with rich biodiversity and deeply rooted cultural heritage, represents an important reservoir of medicinal plant resources and indigenous healing practices. Of the approximately 5,000 angiosperm taxa recorded in Bangladesh (Rahman, 2020), nearly 1,000 species are reported to possess medicinal or therapeutic properties (Islam *et al*., 2018). Medicinal plants are deeply embedded in traditional healthcare systems that have evolved over centuries, including Ayurveda, Unani, and folk medicinal practices (Palash *et al*., 2021). Indigenous treatments are widely applied in Bangladesh for common ailments, such as fever, colds, diarrhoea, and dysentery, showing the central role of medicinal plants in the country's healthcare practices (Hossain *et al*., 2024). Ancient practices relied on commonly available plants *Azadirachta indica*, *Ocimum tenuiflorum*, and *Phyllanthus emblica*) for treating a wide range of ailments (Islas *et al*., 2020; Anand *et al*., 2022). However, with the advent of modern allopathic medicine during the colonial era, traditional systems experienced a decline, overshadowed by the dominance of Western medicine. Despite this, traditional healers, known as *Kabiraj* and *Baiddhya*, have continued to practice, preserving valuable ethnobotanical knowledge (Rahman and Rafieian-Kopaei, 2017). This vast repository of ethnomedicinal knowledge is primarily practiced by rural and indigenous communities, where over 80% of the population depends on traditional medicine for primary healthcare (Karunamoorthi and Tsehaye, 2012; Marcelino *et al*., 2023).

Despite this rich heritage, traditional ethnomedicinal plants is rapidly eroding due to deforestation, habitat degradation, overharvesting, market-driven land-use change, and acculturation of younger generations. The Chittagong Hill Tracts (CHT) in south-eastern Bangladesh, comprising a mosaic of forested hills and ethnic minority settlements, are particularly notable for their cultural and biological diversity (Rahmatullah *et al*., 2010). The Chittagong Hill Tracts, consisting of three southeastern districts, are home to twelve indigenous groups (Faruque *et al*., 2018). Among these groups, the Chakma represent one of the largest and most influential communities, with a long-standing tradition of using wild and cultivated plants to treat a wide range of ailments through specialized healers and household practices (Malek *et al*., 2014). In the challenging socio-economic conditions of Rangamati and surrounding regions, the Chakma people continue to rely on traditional knowledge for healthcare. However, younger generations show less interest in traditional medicinal practices, leading to the gradual loss of this valuable knowledge. Although a few ethnomedicinal studies have been conducted on this community, comprehensive quantitative research remains lacking (Roy *et al.*, 2008; Malek *et al.*, 2014).

Quantitative ethnobotany provides a systematic framework for identifying culturally important medicinal plants; however, it often lacks mechanistic insights into how these traditional remedies exert their therapeutic effects. In this context, network pharmacology and molecular docking have emerged as powerful integrative tools that bridge traditional knowledge with modern molecular science (Ahmed *et al.*, 2023). Network pharmacology facilitates the exploration of multi-component, multi-target interactions, reflecting the holistic nature of plant-based therapies, whereas molecular docking predicts the binding affinity and interaction patterns of bioactive compounds with disease-related protein targets (Ugbaja *et al.*, 2026). Together, these integrative approaches enable the validation of ethnomedicinal claims at the molecular level, identify key bioactive constituents and pathways, and support the rational prioritization of medicinal plants for further pharmacological and drug discovery research (Ahmed and Rahman, 2024).

Quantitative ethnomedicinal data for the Chakma community remain scarce, and the molecular mechanisms underlying the therapeutic potential of their culturally important medicinal plants are largely unexplored. Therefore, the present investigation aims to document and quantitatively evaluate Chakma ethnomedicinal knowledge, integrating network pharmacology and molecular docking approaches to identify key bioactive compounds, potential therapeutic targets, and underlying molecular pathways. This integrative and cross-disciplinary framework links traditional ethnomedicinal knowledge with modern biomedical insights, thereby advancing future pharmacological and drug discovery efforts and promoting sustainable healthcare and biodiversity conservation.

Materials and Methods

Ethnobotanical study

Study Area

The present study was conducted in the Rangamati Sadar Upazila of Rangamati district, located in southeastern Bangladesh. Rangamati Sadar Upazila comprises 6 unions (Fig. 1), of which three—Rangamati Pourashava, Saapsori, and Kuduksori were selected for data collection. A total of ten villages, namely Rangapani, Debasish Nagar, TTC Road, Hajasori Purbopara, Kabuksori, Pukursori, Buyoadam, Depposori, Dhormoghor and Dulusori were selected based on geographical location, accessibility, and the availability of medicinal plant diversity and the Chakma community.

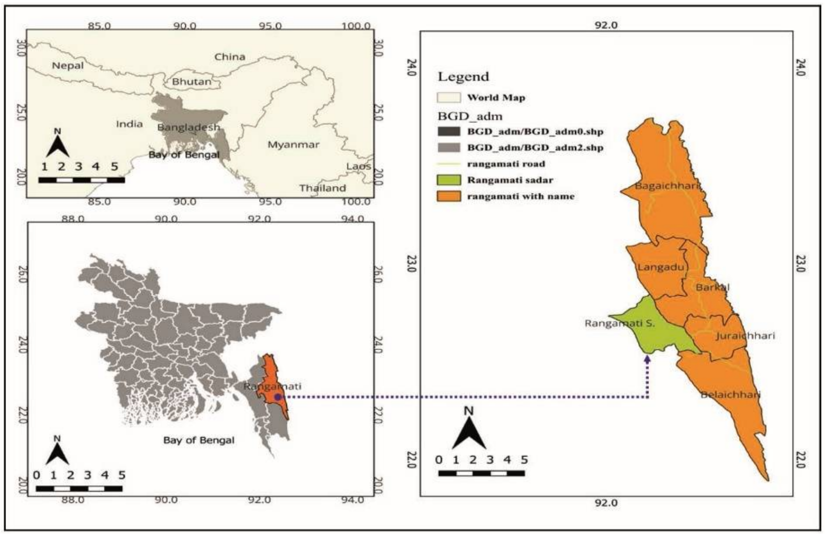

Fig. 1. Geographical location of the study area for ethnobotanical investigation.

Data collection and validation

A total of 102 participants were interviewed, including 17 key informants and 85 general informants. Data were collected using a pre-designed semi-structured questionnaire, with ailments grouped into disease categories for systematic documentation. Key informants were interviewed at locations of their preference, while general informants participated in small group discussions of (8–10 participants) in public settings. All interviews were audio-recorded with prior consent. The survey documented disease categories, plants used, local and Bangla names, plant parts used, preparation methods, and modes of administration. Information was collected in the Chakma language and translated into Bengali. Collected plant specimens were critically examined and identified with the assistance of taxonomic experts, using standard literature (Uddin and Hassan, 2018; Alexiades and Sheldon, 1996), authoritative online databases, herbarium specimens housed at the Dhaka University Salar Khan Herbarium (DUSH), and standard taxonomic keys. Voucher specimens were deposited at DUSH, and photographic records were archived at Chungnam National University, Daejeon, Republic of Korea.

Data analysis

Informant consensus Factor (*FIC*) was calculated to understand how much agreement (consensus) exists among informants about the plants used for treating a particular disease category (Heinrich *et al.*, 1998), using the following equation:

$$F_{ic} = \frac{\mathrm{N_{ur}} - \mathrm{N_t}}{\mathrm{N_{ur}} - 1}$$

where, $\mathrm{N_{ur}}$ is the total number of use reports for a specific disease category, and $\mathrm{N_t}$ is the number of plant species used for that disease category.

The Use Value (*UV*) index was applied to determine the relative importance of individual plant species based on their frequency and diversity of use within the community (Phillips and Gentry, 1993 and Dapar *et al.*, 2020) and it was estimated using the following equation:

$$UV = \frac{\sum \mathrm{U}}{\mathrm{N}}$$

where, U is the total number of uses mentioned for a plant species, and N is the total number of informants who cited the plant.

Fidelity Level (*FL*) was used to identify plant species most consistently used for treating specific ailments, thereby indicating their therapeutic specificity (Friedman *et al.*, 1986). *FL* was calculated using the following equation:

$$FL\,(\%) = \frac{\mathrm{I_p}}{\mathrm{I_u}} \times 100$$

where, $\mathrm{I_p}$ is the number of informants who indicate the use of a species for the same major ailment, and $\mathrm{I_u}$ is the total number of informants who mentioned the same plant for any other use.

Network pharmacology analysis

Identifying key ingredients

Clerodendrum infortunatum was selected for this study based on its highest use value (UV) in the quantitative ethnobotanical survey. Phytochemicals were retrieved from the IMPPAT database (Vivek-Ananth *et al.*, 2023). The pharmacokinetic and toxicity properties of the retrieved compounds were evaluated using the SwissADME and StopTox web servers (Ahmed *et al.*, 2025). Compounds demonstrating favorable drug-likeness and acceptable toxicity profiles were shortlisted, and the three most promising candidates were selected for subsequent target prediction.

Target identification

Hepatic fibrosis–associated genes were sourced from the GeneCards and OMIM databases using “Hepatic Fibrosis” as the search keyword (Yu *et al.*, 2024). Potential target proteins of the selected phytochemicals were predicted using SwissTargetPrediction and STITCH servers (Kuhn *et al.*, 2007; Daina *et al.*, 2019). To identify potential therapeutic targets, the overlapping genes between hepatic fibrosis–associated genes and predicted compound targets were determined using the Venn Diagram Tool.

Protein-protein interaction analysis and hub genes

The intersecting genes were imported into the STRING database to construct a protein–protein interaction (PPI) network (Szklarczyk *et al.*, 2021). The resulting interaction network was exported and visualized in Cytoscape v.3.10.3. Hub genes within the PPI network were identified using the CytoHubba plugin based on topological analysis.

Pathways and interactive analysis of hub genes

Functional enrichment analysis of the hub genes was conducted using the ShinyGO v.0.85 server to assess their biological significance (Ugbaja *et al.*, 2026). Gene Ontology (GO) enrichment was evaluated across the three principal categories—Biological Process (BP), Molecular Function (MF), and Cellular Component (CC), and pathways or terms with a p-value < 0.05 were considered statistically significant. The KEGG (Kyoto Encyclopedia of Genes and Genomes) module of the ShinyGO v.0.85 server was employed to identify biologically significant pathways associated with the hub genes.

Molecular docking analysis

The top five hub genes identified from the protein–protein interaction (PPI) network were selected for molecular docking analysis. The corresponding three-dimensional crystal structures of their encoded proteins were retrieved from the Protein Data Bank using the PDB accession IDs: 2XYG, 9BY4, 1X7R, 5CUH, and 4ACC. Protein and ligand structures were prepared in Schrödinger Maestro (Ahmed *et al.*, 2025). Receptor grids were generated by defining the active site region based on the coordinates of co-crystallized ligand binding residues. Molecular docking simulations were performed using the Glide module in Schrödinger Suite. Molecular interactions were visualized using Biovia Discovery Studio Visualizer (Baroroh *et al.*, 2023).

Results and Discussion

Documentation of medicinal plants in the Chakma community

Distribution of medicinal plant species

The present study documented a total of 82 medicinal plant species belonging to 78 genera and 49 families in the study area. Among those, herbs were the dominant category, accounting for 54.9% (45 species) of the total documented plants. Shrubs were the second most common category, accounting for 23.2% (19 species), followed by trees (18.3%, 15 species), climbers (2.4%, 2 species), and ferns (1.2%, 1 species) (Table 1, Fig. 2A). This distribution pattern indicates that herbaceous species are the most commonly used growth form in traditional Chakma ethnic medicine due to their availability, rapid growth, and ease of processing for medicinal preparations.

In the present study, the number of documented ethnomedicinal plant species was higher than that reported by Malek *et al.* (2014), who recorded 50 medicinal species representing 47 genera and 37 families used by the Chakma community in Khagrachari district. In contrast, Rahman *et al.* (2007) reported a substantially greater diversity, documenting 198 medicinal plant species belonging to 78 families across three districts—Rangamati, Khagrachari, and Bandarban. Roy *et al.* (2008) recorded 90 medicinal plant species from Rangamati district, comparable to the present findings, while Khisha *et al.* (2012) documented approximately 146 plant species used by the Chakma community in the Chittagong Hill Tracts. Beyond Bangladesh, Pandey and Mavinkurve (2014) reported the use of approximately 20 medicinal plant species by the Chakma people in Tripura, India.

Table 1. Ethnomedicinal plants used by the Chakma community of Rangamati Sadar Upazila.

Species	Chakma name	Family	Parts used	Mode of use	Ailments
Achyranthes aspera L.	Rangasuloya	Amaranthaceae	Leaf	Extract	Tumor, cancer, skin disease
Adenanthera pavonina L.	Nil Boron gach	Fabaceae	Bark, wood	Decoction	Eye problem, diarrhea
Adiantum lunulatum Houtt.	Goyali lota	Pteridaceae	Root	Decoction	Stomach pain, diarrhea
Aegle marmelos (L.) Corrêa	Bel	Rutaceae	Fruit, leaf	Decoction	Diarrhea, dysentery, stomach disorders
Ageratum conyzoides L.	Monimuizza Kher	Asteraceae	Leaf, stem	Decoction	Skin infections, insect bite, diarrhea, dysentery
Allium sativum L.	Rosun	Amaryllidaceae	Bulb	Extract	Skin disease
Alocassia macrorrhizos (L.) G.Don	Bichuju	Araceae	Rhizome	Raw	Digestive disorder
			Leaf	Extract	Fever
			Rhizome	Paste	Infection, rheumatism, wound healing
Alpinia galanga (L.) Willd.	Khet Hatranga	Zingiberaceae	Rhizome	Extract	Digestive disorders, respiratory problems
A. nigra (Gaertn.) B.L. Burtt	Khetratranga	Zingiberaceae	Rhizome	Extract	Jaundice
			Rhizome	Paste	Fungal infection
Alternanthera dentata Stuchlík *ex* R.E.Fr.	Lal Bisallokoroni	Amaranthaceae	Leaf	Boil	Malaria fever
			Leaf	Extract	Snake bite, Tumor, Infection
Anisomeles indica (L.) Kuntze	Jarbo horin shing	Lamiaceae	Leaf	Extract	Child fever, urine infection, cough
Artocarpus heterophyllus Lam.	Kathal	Moraceae	Leaf	Wilt	Skin diseases
Averrhoa bilimbi L.	Sadi Raich	Oxalidaceae	Fruit, leaf	Raw, Extract	Diabetes, high blood pressure, insect bite
Azadirachta indica A. Juss.	Jat nim	Meliaceae	Bark, leaf	Decoction	Diabetes
			Bark	Extract	Tooth problem
Calotropis gigantea (L.) W.T. Aiton	Akondo pata	Apocynaceae	Leaf	Extract	Helminthiasis
			Leaf	Raw	Inflammation, swelling
Callistemon viminalis (Sol. ex Gaertn.) G.Don	Pra jam	Myrtaceae	Bark, leaf	Decoction	Wounds, skin infections, coughs, bronchitis, respiratory issues
Capsicum annuum L.	Tulse moric	Solanaceae	Leaf	Extract	Cold, fever
			Leaf	Paste	Body pain
Carica papaya L.	Pepe	Caricaceae	Latex, leaf, seed	Extract, paste, crush	Intestinal worms, wounds, fertility problems, malaria, dengue, digestive disorder
Celosia argentea L.	Ranga sumo ful	Amaranthaceae	Leaf, root	Extract, decoction	Irregular menstruation, piles, urine infection
Centella asiatica (L.) Urb.	Minmeni	Apiaceae	Leaf	Paste	Skincare, wound and burn, Blood clotting
			Leaf	Extract	Gastritis, diarrhea
Cinnamomum cassia (L.) D.Don	Courful	Lauraceae	Bark	Decoction	Gastrointestinal disorder, cardiovascular problems
Clerodendrum infortunatum Dennst.	Vatia	Lamiaceae	Leaf	Crush	Liver disease, bone joint pain, skin problem
C. paniculatum L.	Lal vat	Lamiaceae	Leaf	Extract	Blood intoxication
			Leaf	Raw	Rheumatism
Codariocalyx motorius H. Ohashi	Agattergoron ar gach	Fabaceae	Leaf	Extract	Inflammation, mascular pain, asthma, cough
			Root	Extract	Wound healing

Table 1 contd.

Species	Chakma name	Family	Parts used	Mode of use	Ailments
Commelina benghalensis Wall.	Muro baaitty,	Commelinaceae	Leaf	Paste	Snake bite, digestive disorder
Curcuma aromatica Salisb.	Jongli holud	Zingiberaceae	Rhizome	Paste	Skin problem, wound, cut, bruise, inflammation
C. caesia Roxb.	Lal hoilla	Zingiberaceae	Rhizome	Extract	Piles
			Leaf	Extract, paste	Tumor, cancer
Cyanthillium cinereum (L.) H.Rob.	Thanchang phool	Asteraceae	Leaf	Paste, extract	Cough, asthma, fever, diarrhea, dysentery, piles, skin eruptions, boils
Desmodium gangeticum Blanco	Bormajal	Fabaceae	Whole plant	Decoction	Diarrhea, dysentery, piles
Dillenia indica L.	Ululodhe	Dilleniaceae	Fruit	Juice	Diarrhea, dysentery, jaundice
			Flower	Extract	Gynaecological problem
Dioscorea alata L.	Gum	Dioscoreaceae	Tuber, leaf	Cook, extract	Diarrhea, cold, joint pain
Drynaria sparsisora (Desv.) T. Moore	Chad	Polypodiaceae	Leaf	Extract	Skin problem
			Rhizome	Extract	Diarrhea
Eclipta prostrata (L.) L.	Kalahuna	Asteraceae	Leaf, whole plant	Juice, decoction	Hairfall, dandruff problem
Elatostema sessile J.R.Forst & G.Forst	Shilajhar	Urticaceae	Leaf	Paste, extract	Abdominal disorders, body ache, skin problems, boils, pimples
Ficus hispida Roxb. *ex* Wall.	Dhumur gulu	Moraceae	Fruit	Extract	Digestive problems, jaundice, diabetes
Gomphrena globosa L.	Rosna sak.	Amaranthaceae	Leaf, flower	Extract, boil	Urinary issues, diabetes
Gynura nepalensis DC.	Gorbo bay sak	Asteraceae	Leaf	Cook, extract	Dizziness, weakness, diabetes
G. pseudochina Benth.	Kala bay sak	Asteraceae	Leaf	Cook	Diabetes
Hellenia speciosa (J. Koenig) S. R. Dutta	Tok dogi	Costaceae	Rhizome	Paste, extract	Diabetes, respiratory problem, skin disorder, fever
Hibiscus acetosella Welw. *ex*. Hiern.	Amila	Malvaceae	Leaf	Extract, decoction	Stomach pain, jaundice, blood pressure
Hygrophila costata Nees & T.Nees	Jaied	Acanthaceae	Root, leaf	Raw, paste	Piles, cutting, sexual debility
Hymenocallis littoralis (Jacq.) Salisb.	Khobak	Amaryllidaceae	Leaf	Extract	Gastritis, vomiting
Impatiens balsamina L.	Noni ful	Balsaminaceae	Leaf, flower	Paste, extract	Rheumatism, burn, skin inflammations
Jussiaea linifolia Vahl	Puttodana gash	Onagraceae	Leaf	Paste, extract	Piles, cutting, sexual debility
Justicia adhatoda L.	Basok	Acanthaceae	Leaf	Crush	Skin problem, asthma, fever
Kalanchoe pinnata (Lam.) Pers.	Jioch	Crassulaceae	Root	Extract	Immune problem
			Leaf	Extract	Nephrolithiasis
Laportea interrupta (L.) Chew	Gach satta	Urticaceae	Root, leaf	Extract	Asthma, muscular pain, skin problem
Leea macrophylla Roxb. *ex* Hornem.	Ak han dol	Vitaceae	Root, leaf	Extract	Piles, cuts, sexual debility
Lindernia antipoda (L.) Alston	Choto halencha	Linderniaceae	Leaf	Cook, extract	Stomach problems, heat related disorders, boils and wounds

Table 1 contd.

Species	Chakma name	Family	Parts used	Mode of use	Ailments
Mangifera indica L.	Aem gach	Anacardiaceae	Leaf, seed	Decoction, extract	Diabetes, bleeding gums, asthma, skin disorders, diarrhea
Manihot esculenta Crantz	Bankye	Euphorbiaceae	Leaf	Raw, extract	High blood pressure
			Bark	Boil	Diabetes
Meyna spinosa Roxb. *ex* Link	Mon hada	Rubiaceae	Fruit, Leaf	Raw, paste	Jaundice, fever, bone fractures
Mimosa pudica L.	Lajuk lota	Fabaceae	Leaf	Extract	Jaundice, fever, bone fractures
Morinda citrifolia L.	Ronigulo	Rubiaceae	Fruit, Leaf	Juice, paste	Immune disorder, joint pain, digestive problems, wounds, swellings, skin infections
Moringa oleifera Lam.	Sajana	Moringaceae	Fruit	Cook	Jaundice
			Bark	Decoction	
Musa balbisiana Colla	Beche Chola	Musaceae	Pseudostem	Extract	Diarrhea
Mussaenda frondosa Roxb.	Shedima	Rubiaceae	Root	Extract	Neurological problem
			Leaf	Extract, Paste	Gastritis, skin problem
Myristica fragrans Houtt.	Jaifol	Myristicaceae	Seed, flower	Extract	Abdominal pain, constipation, anemia, headaches
Ocimum gratissimum Forssk.	Bon Tulse	Lamiaceae	Leaf	Extract	Liver disease
			Leaf	Boil	Jaundice, rheumatic pain
O. tenuiflorum L.	Rohoman	Lamiaceae	Leaf	Extract, paste	Respiratory issues, diabetes, skin problem
Opuntia dillenii Haw.	Laeig gadamana	Cactaceae	Stem	Decoction	Inflammation, fever, impotence
Oroxylum indicum Vent.	Khonangach	Bignoniaceae	Fruit, bark	Raw, decoction	Jaundice
Paederia foetida L.	Lodi pata	Rubiaceae	Leaf	Extract	Dizziness, aesthenia
Pentapetes phoenicea L.	Di bug ga ful	Sterculiaceae	Leaf	Extract	Jaundice, fever
			Bark	Decoction	Muscular pain
Piper longum L.	Vutpan	Piperaceae	Fruit, root	Cook, decoction	Respiratory disorders, digestive problems, jaundice
Psidium guajava L.	Payara	Myrtaceae	Leaf	Decoction	Diarrhea, dysentery, mouth ulcers
Rauvolfia serpentina (L.) Benth. *ex* Kurz	Sur san	Apocynaceae	Root	Decoction, extract	High blood pressure, snakebite
R. tetraphylla L.	Sorpogondha	Apocynaceae	Root, leaf	Powder, extract, decoction	Snake bite, mental disorder, vomiting, menstrual bleeding
Ricinus communis L.	Lalbarol	Euphorbiaceae	Seed	Oil	Wound healing
			Leaf	Extract	Abortion, contraption, tetanus
Scoparia dulcis L.	Hba ganja	Scrophulariaceae	Leaf	Extract	Jaundice
Senna sophera (L.) Roxb.	Sisir nagat	Fabaceae	Bark	Decoctioin	Respiratory disorder
Solanum nigrum L.	Kakmache	Solanaceae	Leaf, fruit	Cook, decoction	Fever, cough, asthma, skin eruptions, ulcers, liver problems

Table 1 contd.

Species	Chakma name	Family	Parts used	Mode of use	Ailments
Sonchus wightianus DC.	Boj molo	Asteraceae	Root, leaf	Extract	Stomach pain, diarrhea
Stephania glabra Miers	Khabukka ludi	Menispermaceae	Leaf	Paste	Snake bite
			Root	Extract	Asthma, fever
Swertia chirayita (Roxb.) H.Karst.	cherota	Gentianaceae	Leaf, stem	Extract, decoction	Fever, cold, malaria, digestive disorders
Synedrella nodiflora (L.) Gaertn.	Pahar ful ghash	Asteraceae	Whole plant, leaf	Extract, decoction	Wounds, boils, skin inflammation
Syzygium cumini (L.) Skeels	Jam	Myrtaceae	Fruit, seed	Raw, crush, extract	Diabetes, urine infection, anemia
Tabernaemontana divaricata G.Don	Hamma	Apocynaceae	Root	Extract	Tooth pain
			Leaf	Extract	Fever
Terminalia arjuna (Roxb. *ex* DC.) Wight & Arn.	Arjun	Combretaceae	Bark	Extract, decoction	High blood presser, immune problem
Tragia involucrata L.	Luddhe satta	Urtiaceae	Leaf, root	Extract	Jaundice
Zingiber officinale Roscoe	Mur adda	Zingiberaceae	Rhizome	Decoction	Cold, gastrointestinal, sore throat
Ziziphus mauritiana Lam.	Boroi	Rhamnaceae	Fruit, bark, leaf	Extract, raw	Digestive problem, immune disorder, gastritis, high blood pressure

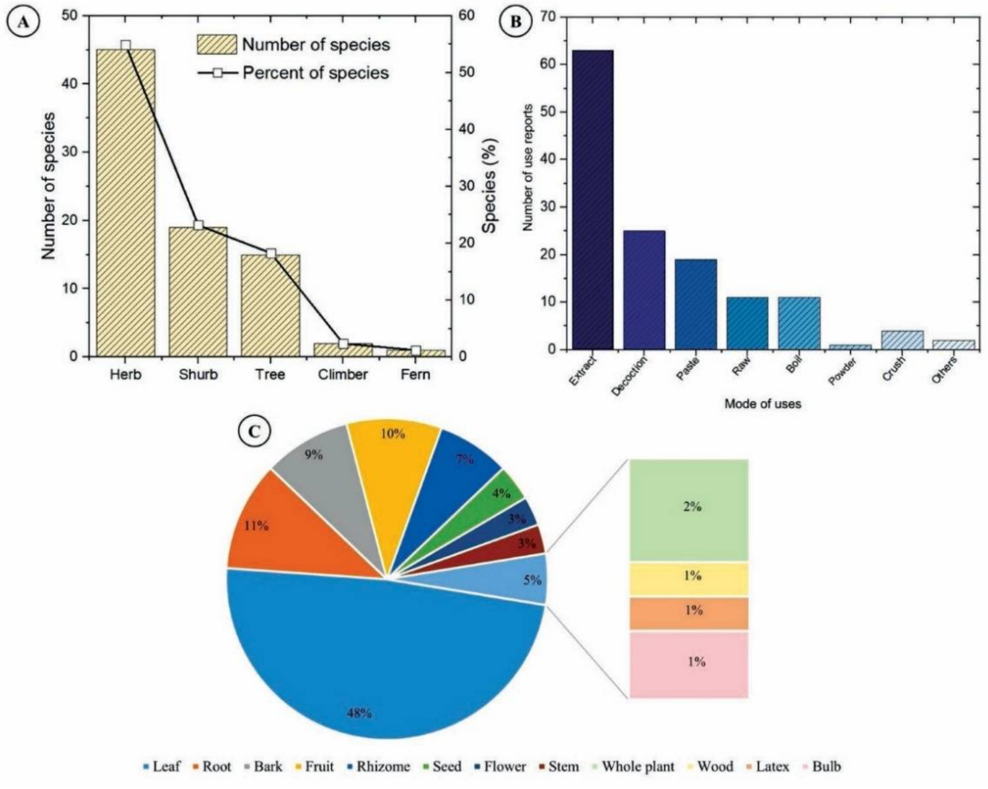

Fig. 2. Ethnomedicinal plant use patterns recorded from the Chakma community of Rangamati Sadar Upazila. A. Habit-wise distribution of the documented ethnomedicinal species, B. Modes of preparation and use practiced by the Chakma community for various formulations, C. Different plant parts utilized in the treatment of various ailments.

Abundance of plant families

Among the 49 recorded families, a relatively small proportion (13 families) accounted for a substantial share of the documented species. Asteraceae was the most dominant family represented by 7 species (8.54%), followed by Fabaceae, Lamiaceae, and Zingiberaceae with 5 species each (6.10% each). Amaranthaceae and Rubiaceae were represented by 4 species each (4.88%), whereas Apocynaceae and Myrtaceae contributed to 3 species each (3.66%). The families Acanthaceae, Amaryllidaceae, Moraceae, Solanaceae, and Urticaceae were represented by 2 species each (2.44%). The remaining 36 families were represented by a single species each, collectively accounting for 43.90% of the total identified species, indicating high taxonomic diversity alongside the dominance of a few key ethnomedicinal families.

Mode of preparation

The traditional medicinal preparation techniques practiced by the Chakma community were categorized into several methods (Fig. 2B). Extract preparation (juice or liquid form) was the most dominant, representing 46.3% (63 use reports). This finding aligns with previous studies in which extracts were identified as the most frequently used preparation method (Sajeeb *et al.*, 2022; Rifat *et al.*, 2022). The second most common method was decoction, accounting for 18.3% (25 uses), followed by paste preparation at 13.9% (19 uses). Boiling and raw consumption were equally reported, each contributing 8.08% (11 uses). Less common methods included crushing, powdering, and other miscellaneous forms, which together constituted less than 10% of the total use reports. The predominance of extract and decoction methods indicates a strong reliance on aqueous, freshly prepared formulations in Chakma traditional.

Plant parts used for medicine

A variety of plant parts were used in traditional remedies, with leaves being the most frequently cited component, accounting for 53.2% (66 citations) of all reported uses. Other commonly utilized parts included roots (15 uses, 12.1%), bark (12 uses, 9.7%), fruits (11 uses, 8.9%), and rhizomes (10 uses, 8.1%). Less frequently used parts were seeds, flowers, and stems (4 uses each, 3.2%), while whole plants (3 uses) and rarely cited parts such as raw fruit, wood, latex, inner fruit/seed portions, and bulbs (1 use each, <1%) were minimally reported (Fig. 2C). This distribution reflects a strong preference for leaves in the Chakma traditional healthcare system, consistent with findings from other ethnic communities (Uddin *et al.*, 2017; Sajib and Uddin, 2013; Mitu *et al.*, 2022). Leaves are readily available, renewable, easy to harvest and process, and often rich in bioactive compounds, making them suitable for both preventive and curative applications (Ahmed *et al.*, 2023).

Quantitative analysis of the medicinal plants in the Chakma community

Factor of informant consensus (F_{ic}) analysis

The Informant Consensus Factor analysis revealed a high level of agreement among Chakma informants regarding medicinal use across disease categories (Table 2), with values ranging from 0.90 to 1.00, indicating strong homogeneity of traditional knowledge. The highest consensus (*FIC* = 1.0) was observed for nervous system disorders, represented by *Rauvolfia tetraphylla*. This finding was consistent with Mahalakshmi *et al.* (2019) where roots of this species were recorded to treat nervous system disorders. High agreement was also recorded for dental problems and infectious diseases (*Fic*= 0.93), and for pain and inflammation, reproductive disorders, urinary and kidney problems, and liver disorders (*Fic*= 0.92). Respiratory and abdominal disorders showed slightly lower but still strong consensus (*Fic*= 0.90), despite having the highest number of use reports (274 and 304, respectively) and species diversity. Frequently cited key remedies included

Opuntia dillenii, *Manihot esculenta*, *Morinda citrifolia*, *Rauvolfia serpentina*, and *Swertia chirata*. These consistently high *Fic* values suggest well-established, culturally shared ethnomedicinal knowledge within the Chakma community, particularly for common health conditions, aligning with earlier studies (Rifat *et al.*, 2022; Ahmed *et al.*, 2023).

Use Value (UV) analysis

The use value (*UV*) analysis highlights the relative cultural importance and versatility of medicinal plants used by the Chakma community (Table 3). *Clerodendrum infortunatum* ranked highest (UV=1.00), indicating strong cultural prominence, particularly for liver disorders, bone–joint pain and skin diseases. The high use value observed in the present study is consistent with previous ethnomedicinal reports among the Chakma and other ethnic communities in Rangamati (Roy et al., 2008; Islam et al., 2021), supporting its ethnopharmacological significance. Species with comparatively high *UV* values (0.83) including *Elatostema sessile* and *Ageratum conyzoides*, were cited for multiple ailments such as abdominal disorders, wounds, infections, and pain. Moderately important species such as *Alocasia macrorrhizos* and *Carica papaya* (*UV* = 0.75) were mainly associated with digestive and parasitic conditions, while *Ficus hispida* and *Solanum nigrum* (UV = 0.60) were linked to hepatic, metabolic, and respiratory complaints. Species with slightly lower UV values, including *Cyanthillium cinereum*, *Curcuma aromatica*, and *Costus speciosus*, were used for more specific conditions such as skin disorders, inflammation, fever, and diabetes. Overall, higher *UV* values correspond to broader therapeutic applications and frequent citation, reflecting greater cultural prominence within the Chakma ethnomedicinal system.

Table 2. Factor of informant consensus (F_{ic}) analysis of ethnomedicinal plants used in the Chakma community.

Diseases Category	No. of species	Most cited plant	Use reports	F_{ic}
Respiratory disorders (asthma, bronchitis, cold, cough, child fever)	26	*Opuntia dillenii*	274	0.90
Abdominal problems (abdominal pain, constipation, diarrhea, dysentery, gastrointestinal issues)	29	*Manihot esculenta*	304	0.90
Cardiovascular problems (anemia, blood pressure, cardiovascular pain)	10	*Manihot esculenta*	112	0.91
Pain and inflammation (body pain, bone fractures, joint pain, rheumatic pain)	5	*Morinda citrifolia*	53	0.92
Reproductive disorders (menstrual bleeding, postnatal fatigue, abortion, fertility control, irregular menstruation, sexual debility, impotence)	9	*Opuntia dillenii*	103	0.92
Biting and toxication (insect-snake bite, position attack)	8	*Rauvolfia serpentina*	79	0.91
Dental problems (tooth pain, tooth problem)	2	*Tabernaemontana divaricata*	17	0.93
Skin problems (boils, wounds, burns, cuts, eruptions, infections)	20	*Cyanthillium cinereum*	212	0.90
Urinary and kidney problems (diabetes, urinary issues, urine infection, kidney stone)	3	*Celosia argentea*	27	0.92
Nervous system disorders (mental disorder, neurological problem)	1	*Rauvolfia tetraphylla*	12	1
Infectious disease (dengue, malaria fever, tetanus)	4	*Swertia chirayita*	44	0.93
Liver issue (jaundice, liver disease/function/problems, mouth ulcers)	6	*Myristica fragrans*	67	0.92
Common	12	*Meyna spinosa*	117	0.90

Table 3. Use value (UV) index of the top ten medicinal species used in the Chakma community.

Species	Ailments	UV value
Clerodendrum infortunatum	Liver disease, bone joint pain, and skin problems	1
Elatostema sessile	Abdominal disorders, body pain, skin problems	0.83
Ageratum conyzoides	Wounds, skin infections, insect bites, diarrhea, and dysentery	0.83
Alocasia macrorrhizos	Digestive disorder	0.75
Carica papaya	Intestinal worms, wounds, fertility control, malaria, dengue, and digestive disorders	0.75
Ficus hispida	Digestive problems, jaundice, and diabetes	0.60
Solanum nigrum	Fever, cough, asthma, skin eruptions, ulcers, and liver problems	0.60
Cyanthillium cinereum	Cough, asthma, fever, diarrhea, dysentery, piles, skin eruptions, and boils	0.57
Curcuma aromatica	Skin disorders, wounds, cuts, bruises, and inflammation	0.54
Costus speciosus	Diabetes, respiratory and skin problems, and fever	0.44

Fidelity level (FL) analysis

The Fidelity Level (FL) analysis revealed varying degrees of informant agreement regarding the specific therapeutic uses of medicinal plants within the Chakma community (Table 4). FL values ranged from 40% to 81.81%, indicating that some species are strongly associated with particular ailments, while others are used more broadly. The highest FL was recorded for *Ocimum gratissimum* (81.81%) for liver disorders, suggesting a high degree of specificity and cultural validation for this use. Other species with relatively high FL values included *Calotropis gigantea* (69.23%) for muscular pain and swelling, *Kalanchoe pinnata* (64.28%) for immune-related disorders, and *Moringa oleifera* (64.28%) for jaundice. Moderate FL values (50–60%) were observed for several species such as *Azadirachta indica*, *Centella asiatica*, and *Capsicum annuum*, indicating consistent but less exclusive therapeutic use. Species with high FL values represent the most culturally reliable and ailment-specific medicinal plants within Chakma traditional healthcare and may be prioritized for future pharmacological and phytochemical investigations. Similar therapeutic applications of these species have also been documented in previous studies (Hossan *et al.*, 2009; Dutta *et al*., 2021).

Table 4. Fidelity level (FL) analysis of the ethnomedicinal plants used in the Chakma community.

Species	Ailments	I_p	I_u	FL (%)
Alocasia macrorrhizos	Fever	14	35	40
Alpinia nigra	Fungal infection	10	19	52.63
Alternanthera dentata	Tumor	5	10	50
Azadirachta indica	Diabetes	9	15	60
Calatropis gigantea	Muscular pain, swelling	9	13	69.23
Capsicum annuum	Cold	17	31	54.83
Centella asiatica	Gastric	14	24	58.33
Clerodendrum paniculatum	Blood problem	12	21	57.14
Codariocalyx motorius	Wounds	12	24	50
Curcuma caesia	Tumor, cancer	13	26	50
Dillenia indica	Postpartum fatigue	12	24	50

Table 4 contd.

Species	Ailments	I_p	I_u	FL (%)
Drynaria sparsisora	Diarrhea	14	26	53.84
Kalanchoe pinnata	Immune disorder	9	14	64.28
Manihot esculenta	Hypertention	15	30	50
Moringa oleifera	Jaundice	9	14	64.28
Mussaenda frondosa	Gastritis, skin problems	12	20	60
Ocimum gratissimum	Liver problems	9	11	81.81
Pentapetes phoenicea	Masculine pain	13	23	56.52
Ricinus communis	Wounds	12	22	54.54
Stephania glabra	Asthma, fever	12	23	52.17
Tabernaemontana divaricata	Toothache	11	22	50

Network pharmacology analysis

Clerodendrum infortunatum was selected for network pharmacology analysis against hepatic fibrosis due to its highest use value, ethnomedicinal significance, novelty in this therapeutic context, and broad traditional applications. The ADMET screening of 35 phytocompounds of *C. infortunatum* identified three key candidates—Ethyl caffeate, Clerodin, and 4-Carvomenthenol). These compounds showed no violations of Lipinski rule of five and exhibited no severe side effects in the toxicity analysis, indicating their favorable drug-likeness and suitability for target-prediction and subsequent network analysis.

Target analysis

Target prediction identified 167 unique genes as key target of hepatic fibrosis. A total of 943 genes were unraveled as disease associated targets from GeneCards and OMIM databases (Fig. 3A). Comparative analysis revealed that 86 genes were found as common in both compound-target and disease-target datasets which were subsequently used for protein–protein interaction (PPI) network construction. The compound–target network comprised 170 nodes and 191 edges, forming a single connected component, which indicates that all compounds and targets are integrated within one interaction system (Fig. 3B).

The average number of neighbors (2.224) and low network density (0.013) indicate a sparse network structure, reflecting the selective nature of phytochemical–protein interactions rather than indiscriminate binding. The network diameter of 4 and characteristic path length (3.063) suggest that most nodes are connected through only a few intermediate steps, supporting efficient signal propagation. The clustering coefficient reveals the absence of tightly interconnected node clusters, implying that compounds tend to act on distinct targets rather than on highly overlapping protein groups. Furthermore, relatively high network heterogeneity (3.829) and network centralization (0.454) suggest the presence of hub nodes with greater connectivity, which may represent key regulatory targets involved in disease modulation (Yu *et al.*, 2024).

PPI network and hub genes

Protein-protein interaction (PPI) network comprised 75 nodes and 535 edges, forming a single connected component, which indicates strong functional interconnectivity among the identified targets (Fig. 4). The high average number of neighbors (14.267) and network density (0.193) reflect a tightly connected interaction network, suggesting that these proteins participate in closely related biological processes. The short characteristic path length (1.938) and small network

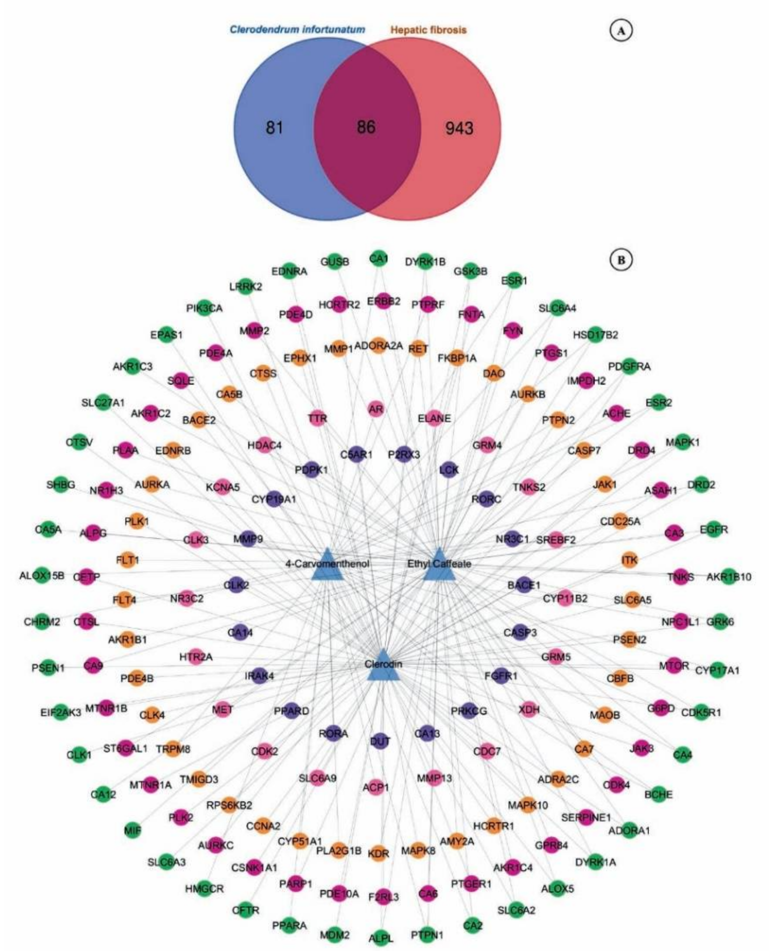

Fig. 3. Target analysis and compound-target network of *C. infortunatum* against hepatic fibrosis. A. Venn diagram showing intersected genes, B. Compound-target network for the three key phytoconstituents.

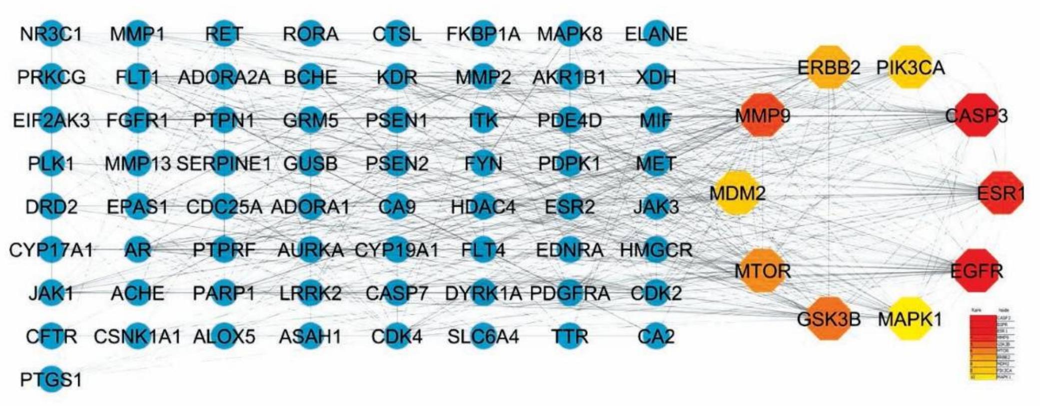

Fig. 4. Protein-protein interaction network analysis showing hub genes against hepatic fibrosis.

diameter (3) indicates efficient communication between nodes, while the relatively high clustering coefficient (0.579) suggests the presence of functionally organized modules. Moderate network centralization (0.524) further supports the existence of key regulatory hub proteins coordinating multiple interactions. Topological analysis identified ten major hub genes associated with hepatic fibrosis: CASP3, EGFR, ESR1, MMP9, GSK3B, MTOR, ERBB2, MDM2, PIK3CA, and MAPK1. These hubs likely play central roles in regulating disease-related pathways and may serve as critical molecular targets underlying the therapeutic effects of the selected phytochemicals (An *et al*., 2021).

GO enrichment analysis

Gene Ontology (GO) enrichment analysis of the identified hub genes revealed several key functional themes relevant to hepatic fibrosis progression (Fig. 5). In the Biological Process category, the strongest enrichment was observed in cellular response to chemical stress, reflecting

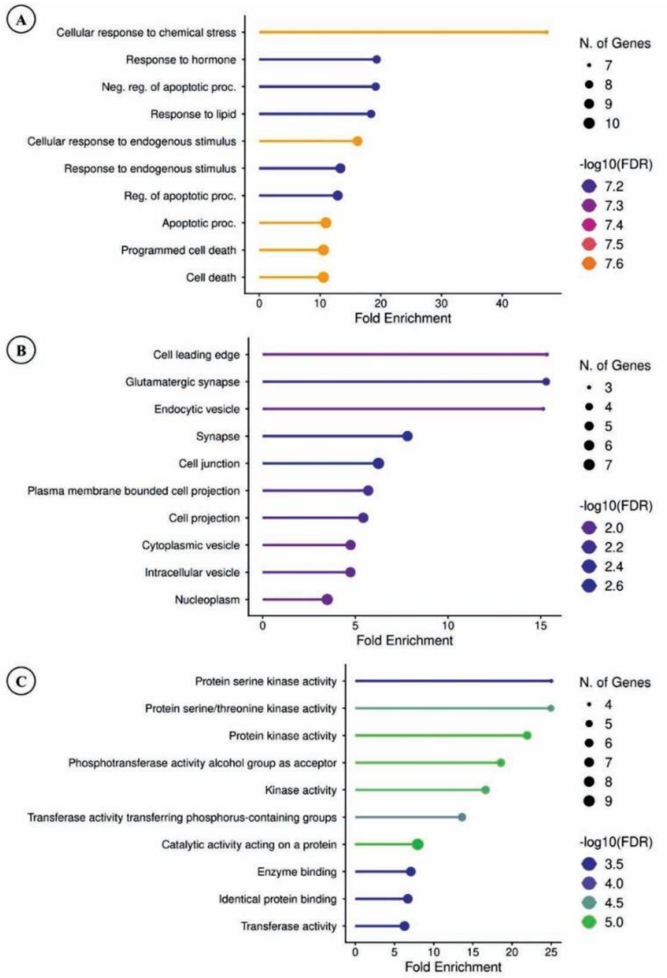

Fig. 5. Gene Ontology enrichment analysis showing the top ten pathways focusing hepatic fibrosis. A. Biological process, B. Cellular component, C. Molecular function.

the well-established role of oxidative stress and toxic injury in activating hepatic stellate cells and promoting fibrotic remodeling. Within the Cellular Component category, enrichment at the cell leading edge suggests involvement in cell migration and tissue remodeling, processes central to fibrogenesis. The appearance of the glutamatergic synapse may indicate signaling-related protein interactions that extend beyond classical neuronal contexts, contributing to intercellular communication. In the Molecular Function category, enrichment of serine/threonine kinase activity underscores the importance of kinase-mediated signaling cascades, including MAPK and PI3K-AKT pathways, which regulate inflammation, cell proliferation, and extracellular matrix deposition during liver fibrosis (An *et al.*, 2021).

Identification of significant signaling pathway from KEGG

KEGG pathway enrichment analysis further indicated that the hub genes were significantly involved in several signaling pathways associated with fibrosis-related cellular processes. Among these, the PI3K-AKT signaling pathway showed prominent enrichment and included multiple hub targets such as MTOR, GSK3B, MDM2, and MAPK1. Mapping these genes onto the KEGG pathway diagram revealed their distribution across key nodes of the signaling cascade, suggesting that the phytocompounds of *Clerodendrum infortunatum* may modulate hepatic fibrosis by regulating PI3K-AKT–mediated pathways involved in cell survival, proliferation, and extracellular matrix remodeling (Fig. 6). Previous studies using network pharmacology have similarly identified the PI3K-AKT pathway as a critical regulator in liver disease progression. For instance, Cheng *et al.* (2022) reported that *Artemisia annua* decoction modulates the inflammation–carcinoma transformation process in chronic liver disease through key targets such as MAPK1 and PIK3CA, primarily via the MAPK and PI3K-AKT signaling pathways. Their findings highlight the importance of these signaling pathways in regulating inflammatory responses and pathological changes in liver tissues. Likewise, Liu *et al*. (2024) demonstrated that *Ixeris sonchifolia* extract induces apoptosis in hepatocellular carcinoma cells by inhibiting the PI3K-AKT signaling pathway, indicating that modulation of this pathway can significantly influence liver cell survival and disease progression.Consistent with these studies, the present findings suggest that the bioactive compounds of *Clerodendrum infortunatum* may exert anti-fibrotic effects by regulating the PI3K–AKT signaling network through multiple molecular targets. The involvement of hub genes such as MTOR, GSK3B, MDM2, and MAPK1 further supports the hypothesis that modulation of this pathway may influence key mechanisms associated with hepatic fibrosis, including cell proliferation, apoptosis, and extracellular matrix accumulation. Therefore, targeting the PI3K–AKT pathway may represent an important molecular mechanism underlying the therapeutic potential of *Clerodendrum infortunatum* in the management of hepatic fibrosis.

Molecular docking analysis

Molecular docking analysis with the top five hub targets demonstrated efficacy of the key constituents of *Clerodendrum infortunatum* (Table 5). The top selected compounds exhibited moderate to strong binding affinities toward multiple fibrosis-related targets, supporting their potential multi-target therapeutic effects. Among the tested compounds, 4-Carvomenthenol showed the most consistent interactions across the hub proteins, with binding affinity ranging from −5.04 to −6.98 kcal/mol and the lowest mean binding affinity (−5.94 kcal/mol), indicating relatively stable ligand-protein interactions. The compound formed both hydrogen bonds and hydrophobic interactions with CASP3, EGFR, ESR1, and GSK3B receptors, whereas its interaction with MMP9 was mediated exclusively through hydrophobic contacts. The hydrogen bond donating and accepting surfaces have been visualized in the Fig. 7. The presence of both hydrogen and hydrophobic interactions is crucial for stable ligand–receptor binding. Hydrogen bonds provide specificity and proper orientation within the active site, while hydrophobic interactions enhance overall binding strength by stabilizing the ligand within nonpolar regions of the binding pocket. Together, these interactions synergistically improve binding affinity and complex stability. A similar interaction profile characterized by the coexistence of hydrogen bonding and hydrophobic interactions has also been reported in the network pharmacology and molecular docking study of *Carthamus tinctorius* for liver fibrosis (Hu *et al*., 2022), where key bioactive compounds, such as quercetin, demonstrated stable binding with hub targets including ESR1. This consistency further underscores the importance of dual interaction modes in achieving effective multi-target modulation in liver fibrosis.

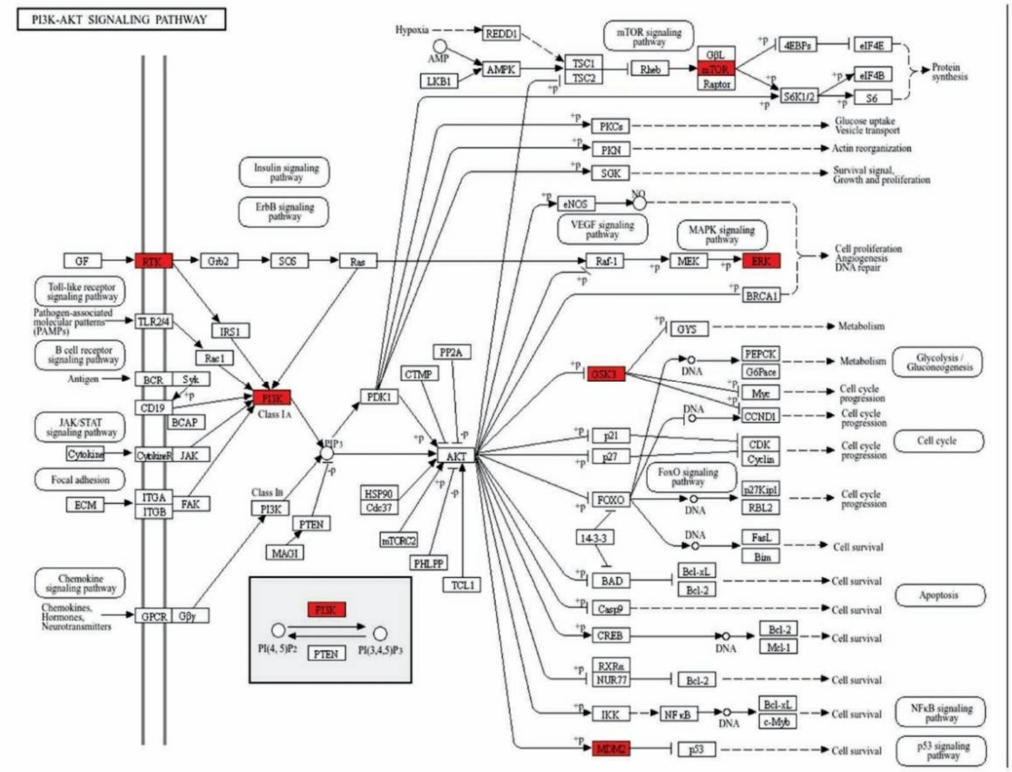

Fig. 6. PI3K–AKT signaling pathway showing the distribution of hub genes identified in the network pharmacology analysis.

Table 5. Molecular docking analysis of the key ingredients using the hub genes derived from protein-protein interaction analysis.

Compounds	Binding affinity of key hub genes (kcal/mol)					Mean Binding Energy (kcal/mol)
	CASP3	EGFR	ESR1	GSK3B	MMP9	
Ethyl caffeate	-4.29	-5.61	-7.61	-6.13	-5.78	-5.88
Clerodin	-2.5	-3.58	ND*	-4.61	-0.31	-2.75
4-Carvomenthenol	-5.17	-5.04	-6.67	-6.98	-5.84	-5.94
Controls	-3.69	-6.65	-9.68	-7.94	-7.36	-7.06

*No valid docking pose generated under selected docking parameters

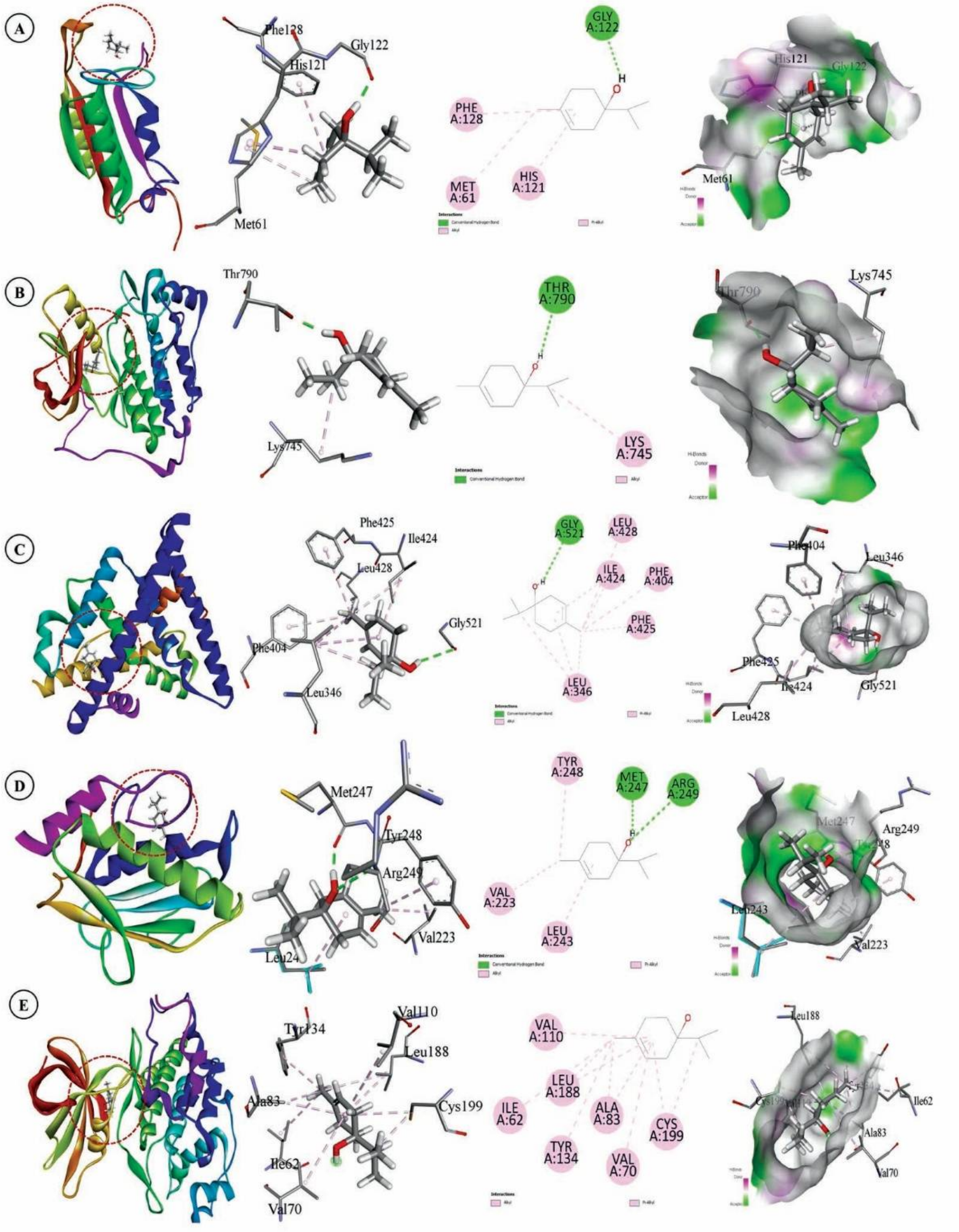

Fig. 7. Docked complexes of 4-Carvomenthenol with three-dimensional interactions, two-dimensional interactions, and hydrogen bond surface view against five key hub proteins. A. CASP3-complex, B. EGFR-complex, C. ESR1-complex, D. GSK3B-complex, and E. MMP9-complex.

Compared to flavonoids reported in *Meconopsis quintuplinervia*, which demonstrated strong binding affinities (−8.5 to −10.1 kcal/mol) toward EGFR, ESR1, GSK3B, and MMP9 (Chen *et al.*, 2026), the key constituents of *C. infortunatum* exhibited moderate binding affinities ranging from −4.29 to −7.61 kcal/mol. Although comparatively lower, these interactions still suggest potential modulatory activity, particularly in apoptosis-related and kinase-mediated pathways relevant to hepatic fibrosis progression. The variation in binding strength may reflect structural differences between flavonoid-rich extract of *M. quintuplinervia* and the terpenoid-phenolic profile of *C. infortunatum*. Ethyl caffeate also demonstrated favorable binding profiles, particularly with ESR1 and GSK3B, with a mean binding affinity of −5.88 kcal/mol. In contrast, Clerodin exhibited comparatively weaker binding affinities and failed to generate a valid docking pose with ESR1 under the selected docking parameters, which may reflect steric or conformational limitations in its interaction with certain targets. As expected, the reference ligands showed stronger binding energies overall; however, the phytocompounds displayed appreciable affinities toward the selected targets, which is noteworthy considering their natural origin and structural diversity (Yu *et al.*, 2024).

This study quantitatively validates the rich ethnomedicinal knowledge of the Chakma community, demonstrating strong informant consensus and culturally structured patterns of plant use. High *Fic, UV,* and *FL* values confirm that several species are consistently and specifically used for major health conditions, with *Clerodendrum infortunatum* identified as the most culturally significant plant. Network pharmacology analysis revealed that key phytochemicals of *C. infortunatum* may exert therapeutic effects against hepatic fibrosis through a multi-target mechanism involving major hub genes, including CASP3, EGFR, ESR1, MMP9, and GSK3B. Functional enrichment analysis highlighted stress response processes and kinase-mediated signaling pathways that are central to fibrogenesis. Molecular docking further supported the multi-target potential of the selected compounds, with 4-Carvomenthenol demonstrating the most stable overall binding interactions. Collectively, these findings bridge traditional Chakma medicinal knowledge with molecular-level evidence, providing a scientific foundation for future pharmacological validation and underscoring the importance of conserving indigenous medicinal heritage as a valuable resource for drug discovery.

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