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Review Article

MECHANISTIC INSIGHT INTO MEDICINAL PROPERTIES OF INDONESIAN DIVERSE MANGROVE SPECIES: A REVIEW

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ABSTRACT

Mangrove ecosystems in Indonesia harbor a rich diversity of plant species, some of which have been traditionally recognized for their medicinal properties. This study aims to provide mechanistic insights into the medicinal potential of various mangrove species found in Indonesian coastal regions. Through a comprehensive analysis of pharmacological activities and underlying mechanisms, our research seeks to elucidate the therapeutic properties of these diverse mangrove plants. The key terms "Mangrove", "Pharmacological", and "Indonesia" used for searching in three online databases: Science Direct, PubMed, and Google Scholar. The investigation into the pharmacological properties of mangrove species revealed versatile mechanisms of action. Notably, a convergence is observed in their antioxidant mechanisms, as exemplified by Aegiceras corniculatum, Avicennia marina, and Rhizophora mucronata, showcasing robust effects in DPPH, ABTS, and FRAP assays. Additionally, the study highlights significant findings in the realm of anti-inflammatory activities. Mangrove species like Aegialitis rotundifolia, Ceriops decandra, and Rhizophora apiculata demonstrate notable anti-inflammatory effects by inhibiting enzymes like LOX and responding positively to carrageenan induction. A commonality is unveiled in antibacterial effects, with species like Avicennia marina, Ceriops tagal, and Excoecaria agallocha exhibiting potent antibacterial properties in agar diffusion assays. These findings underscore the potential of mangrove species in combating microbial infections through distinct antibacterial mechanisms. Furthermore, understanding the mechanisms behind the medicinal properties of Indonesian mangrove species is crucial for both conservation efforts and the development of novel pharmaceuticals.

Keywords: Mangrove ecosystems, Pharmacological, Diversity, Mangrove species

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INTRODUCTION

Mangrove ecosystems, characterized by a unique interface between terrestrial and marine environments, are renowned reservoirs of biodiversity with ecological and economic significance [1]. Within the Indonesian archipelago, diverse mangrove species thrive along the coastal zones, offering a plethora of ecological services. Beyond their ecological roles, these mangroves have been integral to traditional medicine practices, drawing attention to their potential medicinal properties [2]. The medicinal properties of mangrove plants have been recognized for centuries, with various traditional communities incorporating them into their healthcare practices. Mangroves contribute to human well-being by providing a rich source of bioactive compounds with potential therapeutic applications [3]. These compounds exhibit diverse pharmacological activities, including antioxidant, anti-inflammatory, and antimicrobial properties. Additionally, mangroves have been explored for their potential in treating various health conditions, such as wounds, skin disorders, and respiratory ailments [4]. Further, understanding and harnessing the health benefits of mangroves not only contribute to traditional medicine but also hold promise for future advancements in healthcare and pharmaceutical research.

Indonesia, with its extensive coastline and diverse ecosystems, hosts a rich array of mangrove biodiversity [5]. The mangrove forests, comprising various species such as Rhizophora, Avicennia, and Sonneratia, play a pivotal role in the country's coastal ecosystems [1]. Beyond their ecological significance, Indonesian mangroves have long been intertwined with traditional folk medicine practices. Local communities have recognized and utilized the medicinal properties of mangrove species for generations, relying on them to address various health issues. Different parts of mangrove plants, including leaves, bark, and roots, are employed to create remedies for ailments ranging from skin disorders to respiratory conditions [6]. The diversity of mangrove species in Indonesia offers a multitude of bioactive compounds, contributing to the pharmacological richness of traditional herbal medicine. As custodians of this biodiverse treasure trove, local communities play a vital role in preserving and passing down the knowledge of mangrove-based folk medicine.

Moreover, understanding the molecular mechanisms underlying the therapeutic properties of these mangrove plants is of paramount importance. Exploring the molecular intricacies of these bioactive compounds can elucidate the specific pathways through which they exert their medicinal effects [7]. This knowledge not only enhances the efficacy of traditional remedies but also opens avenues for scientific research and pharmaceutical development. Unraveling the molecular mechanisms of mangrove-based folk medicine not only preserves traditional knowledge but also positions these ecosystems as valuable reservoirs for the discovery of novel therapeutic agents. This integration of traditional wisdom with modern scientific understanding reinforces the importance of preserving mangrove biodiversity for the dual benefits of cultural heritage and advancements in healthcare.

Despite this, a comprehensive understanding of the mechanistic insights into the pharmacological activities of Indonesian mangrove species remains limited. Recognizing the critical need for unraveling the medicinal potential of these diverse mangroves, this study delves into the mechanisms governing their pharmacological activities. By employing various assays and methodologies, we aim to elucidate the intricate mechanisms that underscore the medicinal properties of Indonesian mangrove species, with a focus on uncovering their therapeutic potential and contributing to the broader fields of biodiversity conservation and pharmaceutical discovery. This research endeavors to bridge traditional ecological knowledge with modern scientific approaches, shedding light on the multifaceted pharmacological benefits offered by these invaluable mangrove ecosystems.

METHODS

Methods (Style subheading)

In undertaking the review, a methodological framework has been crafted to systematically gather and synthesize existing knowledge on the subject. The process involves the identification and definition of key terms crucial to the scope of the review, namely "Mangrove", "Pharmacological", and "Indonesia". Systematic searches will be conducted across three major online databases—Science Direct, PubMed, and Google Scholar—utilizing these key terms, with stringent inclusion and exclusion criteria applied to filter relevant studies. The retrieved literature will undergo meticulous screening to ensure alignment with the review's objectives, prioritizing studies offering insights into the pharmacological activities, biological properties, and evaluations of mangrove species within the Indonesian context.

Subsequently, relevant information was extracted from selected studies, focusing on mechanistic insights into the medicinal properties of diverse Indonesian mangrove species. This data will be systematically synthesized and organized to construct a coherent narrative, highlighting key mechanistic insights, commonalities, and variations among different mangrove species. A critical analysis of the reviewed literature will be conducted, assessing the strengths and limitations of existing studies and identifying potential avenues for future research. The culmination of these efforts will result in the compilation of a comprehensive review, providing a detailed overview of the mechanistic insights into the medicinal properties of Indonesian mangrove species. Through this methodological approach, the review aims to contribute a nuanced understanding of the subject matter, bridging existing gaps in knowledge and guiding future research endeavors.

RESULTS AND DISCUSSION

Indonesia is one of the countries mega diversity of medicinal plants in the world. Indonesia's tropical forest region has 2nd highest biodiversity in the world after Brazil. There is quite a large diversity of mangroves spread across the Indonesian archipelago [86]. The investigation into the mechanistic insights of medicinal properties of diverse mangrove species in Indonesia, as conducted through a comprehensive review, yielded a substantial volume of publications. A total of 2890 sources were identified through Google Scholar, indicating a rich landscape of scholarly works within this domain. PubMed contributed 17 publications, while Science Direct provided 13 additional sources. After accounting for potential duplications, the final count of unique publications stands at 2860, emphasizing the considerable depth and breadth of existing literature on the subject.

Upon conducting an in-depth analysis to specifically assess the relevance to mangroves, pharmacological activity, and Indonesia, a focused subset of 89 publications was identified (fig. 1). This subset encapsulates the core literature that intricately explores the mechanistic aspects of medicinal properties within Indonesian mangrove species, shedding light on their pharmacological activities. This refined set underscores the concentrated nexus between mangroves, pharmacological exploration, and the unique context of Indonesia within the broader spectrum of existing research.

The analysis of mangrove species distribution in Indonesia reveals the presence of 25 distinct mangrove species across the archipelago, with almost all species spanning across various provinces. Several species exhibit restricted distributions, such as Aegialitis rotundifolia, found exclusively in Java, Bali, Sulawesi, Maluku, and Papua; Avicennia lanata in Kalimantan and Sulawesi; Kandelia candel in Sumatra and Kalimantan; and Rhizophora lamarckii in Sumatra, Maluku, and Papua. The comprehensive distribution map, illustrated in fig. 1, provides an overview of the widespread occurrence of mangrove species throughout Indonesia, emphasizing both their ubiquity and specific regional constraints.

Fig. 1: Distribution patterns of mangrove species in Indonesia. The abbreviation of each species corresponds to its common name as follow: Aegiceras corniculatum (AEC), Aegialitis rotundifolia (AER), Avicennia alba (AVA), Avicennia lanata (AVL), Avicennia marina (AVM), Avicennia officinalis (AVO), Bruguiera cylindrical (BRC), Bruguiera gymnorrhiza (BRG), Bruguiera parviflora (BRP), Bruguiera sexangula (BRS), Ceriops decandra (CED), Ceriops tagal (CET), Excoecaria agallocha (EXA), Heritiera littoralis (HEL), Kandelia candel (KAC), Lumnitzera racemose (LUR), Nypa fruticans (NYF), Rhizophora apiculate (RHA), Rhizophora lamarckii (RHL), Rhizophora mucronata (RHM), Rhizophora stylosa (RHS), Sonneratia alba (SOA), Sonneratia caseolaris (SOC), Xylocarpus granatum (XYG), and Xylocarpus moluccensis (XYM)

Subsequently, we conducted a more in-depth analysis focusing on the pharmacological activities and scientific evidence associated with each mangrove species. This analysis aimed to explore the potential medicinal properties of all Indonesian Mangroves species. The findings of this investigation are presented comprehensively in table 1, which details the observed pharmacological activities and the corresponding scientific evidence supporting each species. The table provides a nuanced overview, allowing for a comprehensive understanding of the diverse therapeutic potentials inherent in these mangrove species.

Table 1: The exploration of pharmacological activities in various mangrove species

Species	Pharmacological activity and mechanism	Method	Performance IC50/MC50/IZ/Dosage	Organ	References
AEC	• Anti-oxidant • anti-inflammatory • anticoagulation • Antibacteria	DPPH FRAP Lox inhibitor Prothrombin time test Rema	• 20.49±2.14µg/ml; 33.51±1.59 µg/ml • 72.80±1.20 mg/g AAE; 29.36±0.43 mg/g AAE • 26.79±1.31µg/ml; 59.51±2.45µg/ml • 18.19±0.13µg/ml/min; 10.33±0.14 µg/ml/min • 19.53 g/ml (H37Rv strain)	Bark; Leaf Bark; Leaf Bark; Leaf Bark; Leaf leaf	[8, 9]
AER	• Anti-Inflammatory • Antipyretic • Cytotoxic • Antibacterial	Carrageenan induction *In vitro* Mtt assay Disc diffusion	• 26.75%; 40,13% (indometasin) of 400 mg/kg • N/A • 400 mg/kg • 200 g/ml • 100 µl** ST dan EC	Leaf Leaf Leaf Leaf	[10-12]
AVA	• iCytotoxic • Cytotoxic • Anti diarrheal • Antipyretic • Antidabetic	MTT Assay with widr cells MCF7 and Hela Cells Castor oil induction Yeast induction Inhibition of amylase glucosidase)	• 173.775 µg/ml • 44.68% and 35.89% (500 mg/kgBB) • 200 mg/kgBW • 1.18 and 0.87 mg/ml α-amilase and glukosidase respectively	Leaf Leaf Leaf Leaf	[13-17]
AVL	• Cytotoxic	Widr cells	• 305.928 µg/ml	Leaf	[16, 18-21]
AVM	• Antibacterial • Antimutagenic • Anti-inflammatory • Antiviral • Antioxidants	Agar diffusion MTT assay Mouse model of rheumatoid arthritis *In vitro* DPPH, hydroxyl, superoxide and abts)	• N/A • N/A • N/A • N/A • N/A		
AVO	• Antioxidants • Antimicrobes • Antiulcers • Diuretics Lipschitz • Cytotoxic • Antidiabetic	DPPH; ABTS Disc diffusion Indomethacine induction *In vivo* *In vitro* Inhibition of amylase and glucosidase)	• 4077±3.43µg/ml; 38.8±9.62 µg/ml • 7.8±0.7; 7.0±0.1; and 7.7±0.5E mm to E. coli; S. mutans; and S. Aureus respectively • N/A • 200 mg/kg • 131.2µg/ml • 0.66±0.05 and 0.71±0.1 mg/ml for amylase and glucosidase respectively	Leaf Leaf Leaf Leaf Leaf Leaf	[13, 22-26]
BRC	• Antioxidants • Antidiabetic • Antimicrobials	DPPH STZ-induction Disc diffusion	• 175 µg/ml; 162.5 µg/ml • 5 mg/ml • 14.30 and 13.30 mm for S. aureus and E. Coli respectively	Leaf; Bark Leaf Leaf	[27-34]
BRG	• Antihyperglycemic • Antimicrobial • Anti-inflammatory • Hepatoprotective • Anti-Hemolytic • Antioxidants	STZ-induction *In vitro* COX inhibition test Induction of gain	• 400 mg/kg reduced in day 28^{th} • N/A • 22 dan 23 mm to E. Coli dan S. Aureus respectively • 113.79±0.16(µg/ml • 125 mg/kg	Leaf Leaf Leaf Leaf	
BRP	• Antioxidant	DPPH-*In vitro*	• 105.00 µg/ml	Leaf	[35]
BRS	• Antibacterial	Agar diffusion	• N/A		[36]
CED	• Anti-inflammatory • Antibacterial	Carrageenan induction Agar diffusion	• 400 mg/kg • 2.1±0.28 µg/ml (10 mm)	Leaf Leaf	[37-39]
CET	• Antioxidants • Anti-cancer • Antibacterial and diuretic	DPPH; FRAP *In vitro* Agar diffusion	• 95 µg/ml; 4 mmol AAE/g • 4.18± 0.45 µg/ml and 80.04 ± 0.19 µg/ml to Hela and MDA-MB231respectively • 5,0±0,1 mm to P. aeruginosa and 500 mg/kg (diuresis)	Leaf Leaf Leaf	[40-43]
EXA	• Antioxidants • Anti-inflammatory • Analgesic • Anti cancer • Anti bacterial	Dpph Carrageenan induction Acetic acid induction MTT assay Agar diffusion	• 67.50 µg/µl • 500 mg/kg • 500 mg/kg • 4 and 7 mg/ml for Capan-1 and Miapaca-2 respectively • 10.3±2.7; 6.2±0.8; 8.3±1.2 dan 8.5±0.7 mm for E. Coli, A. tumefaciens, S. mutans, and S. Aureus r	Leaf Leaf Leaf Leaf Leaf	[23, 44-47]
HEL	• Antioxidants • Anti-haemolytic • Anti-bacterial • Anti-inflammatory	DPPH; FRAP Agar diffusion DDS 3% induction	• 121.23±0.32µg/ml and 101.11 ± 0.41 mmol equivalent Fe (II)/gram • 526.90±25.85µg/ml • 16.1±0.17, 15.8±0.44 and 17.6±0.44 mm for E. coli, S. Aureus and S. enterica respectively • Protect againts colitis	Leaf Leaf Leaf Leaf	[48, 49]
KAC	• Anti-Inflammatory • Antioxidant • Antidiabetic	DPPH Inhibition glucosidase	• 1,7±0,1µM • 86.01±0.31% • 206.89 µg/ml	Leaf Leaf Leaf	[50-52]
LUR	• Antioxidant • Cytotoxicity • Hepatoprotective • Antidiabetic • Anticancer	DPPH and ABTS MTT asay on Hep G2 cancer cells Inhibition of amylase and glucosidase MCF7 and hela cells	• 38.89 µg/ml; 44.38 µg/ml • 26.05 µg/ml • 300 mg/kgBB • 3.064±0,022 and 3.01±0,041 µg/ml for amylase and glucosidase respectively • 26.05 and 195.1 µg/ml for MCF7 and HeLa cells respectively	Leaf Leaf Leaf Leaf Leaf	[14, 53-55]
NYF	• Antioxidant • Antidiabetic • Anti-bacterial	DPPH Intraperitoneal glucose tolerance test Disk diffusion	• 2.770±0.012 mg/ml • 56,6% • 6.5±0.4; 7.3±0.5; 6.25±0.3, and 6.8±0.3 mm for E. Coli, A. tumefaciens, S. mutans, and S. Aureus respectively	Leaf Leaf Leaf	[23, 56]

Species	Pharmacological activity and mechanism	Method	Performance IC50/MC50/IZ/Dosage	Organ	References
RHA	• Antioxidants • Anti bacterial • Anti Inflammatory • Anti Cancer	DPPH; ABTS Disk diffusion Carrageenan induction MTT asay	• 9.31±1.56; 3.01±0.75 µg/ml • 14 and 9 mm for B. cereus and S. saprophyticus respectively • 0.39± 0.04 mm • 12.06 µg/ml (HepG2)	Leaf Leaf Leaf Leaf	[57-59]
RHLI	• Alzheimer's disease		• N/A		[60]
RHM	• Antioxidants • Anti-inflammatory • Anti-cholinesterase • Antidiabetic • Antidiabetic • Antibacterial • Heptoprotective	DPPH; ABTS Inhibition of cox-1 and COX-2 *In vitro* Aloxane-induced diabetic rats STZ induction Disk diffusion	• 0.38±0.03 mg/ml; 1.25±0.01 mg/ml • 1.42±0.01 COX-1; and 1.38±0.00 mg/ml COX-2 • 59.31 ± 0.35 µg/ml • 60 mg/kg in 30 days • 100 mg/kg • 9.97±0.17, 19.56±0.19, 15.74±0.06, 11.31±0.25, 5.63±0.06, and 16.57±0.22 mm for B. Subtilis, SAureus, S. Faecalis, S. Pyogenes, E. Coli, and P. Aeruginosa respectively • 300 mg/kgbw	Leaf Leaf Leaf Leaf Leaf Leaf Leaf	[54, 61-65]
RHS	• Anti-cholinesterase • Antioxidants • Anti cancer	*In vitro* DPPH MTT asay	• 9.56 µg/ml • 2.69 µg/ml • 51.0 µg/ml	Leaf Leaf Leaf	[59, 66, 67]
SOA	• Anti-bacterial • Antioxidants • Cytotoxic • Antimicrobial • Antidiabetic	Disk diffusion DPPH Disk diffusion In vivo	• 12.5 mm(S. aureus) and 12.5 mm (B. Cereus) • 14.0 µg/ml • 14.94 µg/ml (Hexane) • Bacillus cereus (10 mm), Bacillus subtilis (11 mm), Sarcina lutea (12 mm), Pseudomonas aeruginosa (10 mm) and Shigella dysenteriae (12 mm)	Leaf Bark Leaf Leaf	[68-70]
SOCS	• Antimicrobial • Antioxidants • Anti-cholinesterase • Antidiabetic • Anti-inflation) • Analgesics • Cytotoxic • Anti-diarrhea	Disk diffusion DPPH *In vitro* Inhibition of α-amylase and OGTT Carrageenan induction Acetic acid induction Castor oil induction	• B. subtilis (18.33±0.76 mm), B. coagulans (19.50±0.50 mm) and P. vulgaris (12.67±0.58 mm) • 21.74 µg/ml • 5.87 µg/ml and 37.6 µg/ml • 58.24% at 200 mg/kgbb • 78.23 % at 200 mg/kgbb • 25.0±0.05 µg/ml • 250 mg/kg	Leaf Leaf Leaf Leaf Leaf Leaf Leaf	[71-76]
XYG	• Antimalarials • Antioxidants • Antidiabetic • Antiviral • Anticancer • Antifilarial • Antimicrobial	Plasmodium falciparum DPPH, ABTS, superoxide and hydrogen peroxide scavenging) Inhibition of amylase and glucosidase HIV-1 and IAV A549 Brugia malayi Agar disc diffusion	• 50 µg m/l, and (MIC) 10 µg m/l. • 0.041, 0.039, 0.096, and 0.235 mg/ml • 0.25 and 0.16 mg/ml • HIV-1 15.98 ± 6.87 µM and IAV 14.02 ± 3.54 µM • 10 µM • 0.239 µg/ml	Leaf Leaf Leaf Leaf Leaf Leaf	[17, 26, 40, 77-80]
XYM	• Anti-cancer • Anti-bacterial • Antioxidant • Cytotoxic • Anti-cholinesterase • Anti-cancer • Antidiabetic	(MTT asay against AGS, HT-29 and MDA-MB-435S cells) Disk Diffusion DPPH *In vitro* MTT cell asay hepg2 Inhibition of amylase	• 0.62, 2.5, 1.08 µg/ml • S. Aureus 12.7±1.2 mm and E. Coli 11.9±0.9 mm • 0.000154. • 2.0 x 105 ppm • 21 µg/ml • 25.12µg/ml • 28.4 µg/ml	Leaf Leaf Leaf Leaf Leaf Leaf Leaf	[81-85]

*DPPH: 2,2-diphenyl-1-picrylhydrazyl; FRAP: Ferric Reducing Antioxidant Power; LOX: lipoxygenase; MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; ABTS: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid; DDS: dextran sulfate sodium; COX: Cyclooxygenase; STZ: Streptozotocin; HIV: Human Immunodeficiency Virus; IC: Inhibitor Concentration; MC: Minimal Concentration; IZ: Inhibitor Zone. Aegiceras corniculatum (AEC), Aegialitis rotundifolia (AER), Avicennia alba (AVA), Avicennia lanata (AVL), Avicennia marina (AVM), Avicennia officinalis (AVO), Bruguiera cylindrical (BRC), Bruguiera gymnorrhiza (BRG), Bruguiera parviflora (BRP), Bruguiera sexangula (BRS), Ceriops decandra (CED), Ceriops tagal (CET), Excoecaria agallocha (EXA), Heritiera littoralis (HEL), Kandelia candel (KAC), Lumnitzera racemose (LUR), Nypa fruticans (NYF), Rhizophora apiculate (RHA), Rhizophora lamarckii (RHL), Rhizophora mucronata (RHM), Rhizophora stylosa (RHS), Sonneratia alba (SOA), Sonneratia caseolaris (SOC), Xylocarpus granatum (XYG), and Xylocarpus moluccensis (XYM).

The exploration of pharmacological activities in various mangrove species across Indonesia has uncovered a rich array of bioactive compounds with promising therapeutic applications. From the table above, it can be seen that the Rhizophora family has pharmacological activities, one of which is anti-cancer. This type of mangrove has cytotoxic activity because it contains active chemical compounds, including phenolic compounds, flavonoids, terpenoids and saponins [87]. Among the diverse species studied, a notable convergence is observed in their antioxidant properties. Species like Aegiceras corniculatum, Avicennia marina, and Rhizophora mucronata exhibit potent antioxidant effects, as demonstrated through assays such as DPPH, ABTS, and FRAP (fig. 2). This shared characteristic underscores the potential for collective medicinal benefits, emphasizing the importance of a holistic approach to harnessing the healing potential of mangrove ecosystems.

Another significant finding emerges in the realm of anti-inflammatory activities. Aegialitis rotundifolia, Ceriops decandra, and Rhizophora apiculata, among others, showcase promising anti-inflammatory effects, inhibiting enzymes like LOX and responding positively to carrageenan induction. This diversity in anti-inflammatory responses across mangrove species opens avenues for targeted therapeutic interventions, highlighting the importance of considering multiple species for their cumulative health benefits. Moreover, the study reveals a commonality in antibacterial effects, as evidenced by species like Avicennia marina, Ceriops tagal, and Excoecaria agallocha, which exhibit potent antibacterial properties in agar diffusion assays (fig. 2). These findings collectively emphasize the potential of mangrove species in combating microbial infections. In conclusion, the shared pharmacological activities observed in diverse mangrove species highlight the need for comprehensive exploration and utilization of these ecosystems in traditional and modern medicine, paving the way for novel drug development and therapeutic interventions.

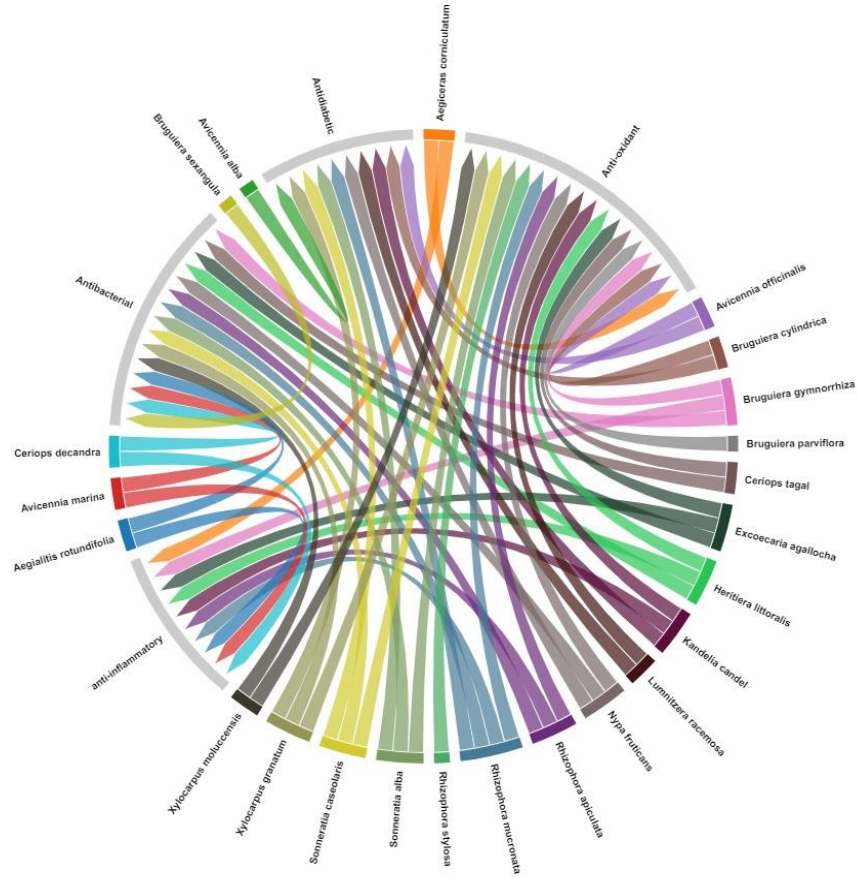

Fig. 2: The representative correlation between pharmacological activity and species in a chord diagram reflects the complex relationship between biological effects and various types of species

CONCLUSION

The investigation into pharmacological activities across diverse mangrove species in Indonesia reveals a notable convergence in antioxidant mechanisms, exemplified by Aegiceras corniculatum, Avicennia marina, and Rhizophora mucronata. Additionally, diverse anti-inflammatory responses are observed in species like Aegialitis rotundifolia, Ceriops decandra, and Rhizophora apiculata, emphasizing opportunities for targeted therapeutic interventions. The commonality in antibacterial effects, seen in Avicennia marina, Ceriops tagal, and Excoecaria agallocha, underscores the potential of mangrove species in combating microbial infections through distinct antibacterial mechanisms. In conclusion, the shared pharmacological activities highlight the need for a comprehensive exploration of mechanisms, offering insights for novel drug development and therapeutic interventions by leveraging the intricate properties of these ecologically crucial ecosystems.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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