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MINI-REVIEW ARTICLE

An Overview of the Phytochemical Pharmacology and Potential Biomaterials of *Curcuma aeruginosa* Roxb. against COVID-19

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Abstract: Natural materials are gaining popularity in pharmaceuticals and food applications, and they have the potential to alleviate the significant environmental problems generated *via* traditional materials. The *Curcuma* genus, particularly *Curcuma aeruginosa* Roxb., is expanding due to its prominence in culinary and traditional medicinal sectors. *Curcuma* species are esteemed for their rich nutritional value and the discovery of new bioactive compounds exhibiting antioxidative, antimicrobial, anti-inflammatory, and anticancer actions. This study offers a meticulous examination of the traditional uses, ethnopharmacology, phytochemistry, and pharmacological attributes of *C. aeruginosa* (Roxb.). We also delve into the species' bioavailability and health benefits by emphasising the nutritional composition, bioactive components, and biological properties. Given the sparse existing data, this review sought to spotlight the potential of the substances present in this species in functional foods and pharmaceutical arenas. Distinguished by its red flower lobes, greenish-blue rhizome, and other notable features, it has long been employed in traditional medicine for ailments ranging from wounds to asthma, attributable to its disinfectant, expectorant, and tonic properties. Advanced gas chromatography-mass spectrometry (GC-MS) techniques have discerned various phytochemicals from the plant, leading to revelations about its diverse pharmacological potentials, including antioxidative, antimicrobial, anti-inflammatory, and anticancer activities. In the context of the COVID-19 pandemic, *C. aeruginosa* (Roxb.) has stood out as a promising botanical candidate, with ten of its compounds, such as curcumenol and β-pinene, displaying notable efficacy against COVID-19 antigens. Thus, while *C. aeruginosa* Roxb. has already proven its worth in traditional oriental medicine, current findings underscore its potential as a potent therapeutic resource, especially concerning COVID-19, and advocate for intensified research into its pharmaceutical applications.

Keywords: *Curcuma aeruginosa* Roxb., ethnopharmacology, phytochemistry, pharmacological activities, COVID-19, traditional oriental medicine.

1. INTRODUCTION

Plant-based medicines have historically played a crucial role in human health and ecological balance, serving as indispensable resources for nutrition, habitat provision, and overall environmental sustainability [1]. Despite their intrinsic value, significant portions of plant-derived materials, such as leaves, flowers, fruits, and peels, are often discarded as agricultural waste [2]. These by-products, frequently underestimated, are in fact abundant sources of bioactive compounds with notable biochemical and pharmacological potential [3].

Recent advancements in scientific research have highlighted the importance of repurposing plant materials and agricultural by-products to foster sustainable and eco-friendly innovations [4]. This approach aligns with the urgent need for environmentally conscious strategies to address

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global challenges [5]. Plants function as natural biomanufacturers, synthesizing a diverse range of active phytochemicals with profound therapeutic potential (Sidik *et al*., 2024).

These bioactive compounds not only offer extensive medicinal value, but also present novel opportunities for advanced technological applications [3]. For instance, plant-derived compounds can serve as bioreducing agents in the synthesis of nanomaterials, contributing to the development of eco-friendly nanotechnologies. Moreover, their potential as photoactive molecules further expands their utility across various domains, including biomedicine, materials science, and green nanotechnology [2, 3]. By integrating ancestral knowledge with contemporary research, the Zingiberaceae family continues to drive sustainable innovation in medicine and technology, reaffirming its ecological and biomedical significance [6].

The Zingiberaceae family, the largest within the order Zingiberales, exemplifies this dual importance [5, 7]. With over 50 genera and 1,300 species predominantly thriving in tropical and subtropical regions, it is especially diverse in South and Southeast Asia [8, 9]. Genera, such as *Alpinia*, *Zingiber*, and *Curcuma*, are renowned for their bioactive compounds, which have long supported traditional medicine [5]. *Curcuma aeruginosa* Roxb., or Javanese turmeric, is a notable example, widely recognized for its medicinal properties and integration into traditional healthcare [10].

Systematic research into the pharmacological activities of plants, particularly those with antimicrobial and immune-modulating properties, is vital for advancing phytotherapy and addressing pressing global health challenges [11, 12]. The COVID-19 pandemic has highlighted the need for alternative therapeutic strategies, as no specific antiviral drugs are currently available for its treatment [13]. Vaccine limitations further emphasize the necessity of enhancing immunity through adaptive and protective mechanisms. SARS-CoV-2 invades host cells, including macrophages, triggering cytokine responses and inflammatory mediators critical for pathogen elimination [14-16]. Herbal remedies, central to traditional medicine systems, such as Ayurveda, have gained considerable attention for their potential to boost immunity and combat pathogens. During the pandemic, India's Ministry of Ayush issued an advisory advocating the use of herbal formulations to enhance immunity, underscoring the relevance of integrating traditional knowledge with modern research approaches to address contemporary health crises [13].

Herbal and botanical products have historically been fundamental to traditional medicine systems, with East Asia emerging as a particularly vibrant source of therapeutic flora [17]. According to Kamazeri *et al*., these products have played a central role for centuries, offering a repository of potential bioactive compounds [18]. However, the transition of these traditional remedies into pharmaceutical applications requires rigorous analysis, standardization, and validation, to ensure their safety and efficacy [19]. Investments in herbal pharmaceuticals are significant, with some regions allocating up to 40-50% of healthcare expenditures to research and development in this area, driven by the therapeutic potential and minimal adverse effects associated with botanical remedies [20].

Curcuma aeruginosa Roxb., a member of the Zingiberaceae family, exemplifies the dual medicinal and culinary importance of this plant group. Widely recognized as "Temu Hitam", it has been traditionally used to treat respiratory disorders, abdominal conditions, rheumatism, diabetic wounds, and inflammatory diseases [21]. Recent investigations confirm these therapeutic claims, attributing the efficacy of *C. aeruginosa* to its bioactive constituent, curcumin [22]. Curcumin is celebrated for its anti-inflammatory, antioxidant, and immunomodulatory properties, making it a valuable agent in modern medical applications [23]. Despite its promise, the clinical utility of curcumin is constrained by its hydrophobic nature and rapid systemic metabolism, which have spurred interest in biomaterial-based encapsulation techniques to improve its bioavailability and therapeutic efficacy [22, 24].

Curcuma aeruginosa Roxb. is a widely distributed species within the *Curcuma* genus, thriving across tropical and subtropical regions. Its presence has been recorded in Indonesia, Japan, Thailand, Bangladesh, India, Vietnam, Malaysia, Myanmar, Cambodia, and China [7, 9, 25-28], as illustrated in Fig. (**1**). This extensive geographical range highlights the adaptability of *C. aeruginosa* to diverse environmental conditions and under-

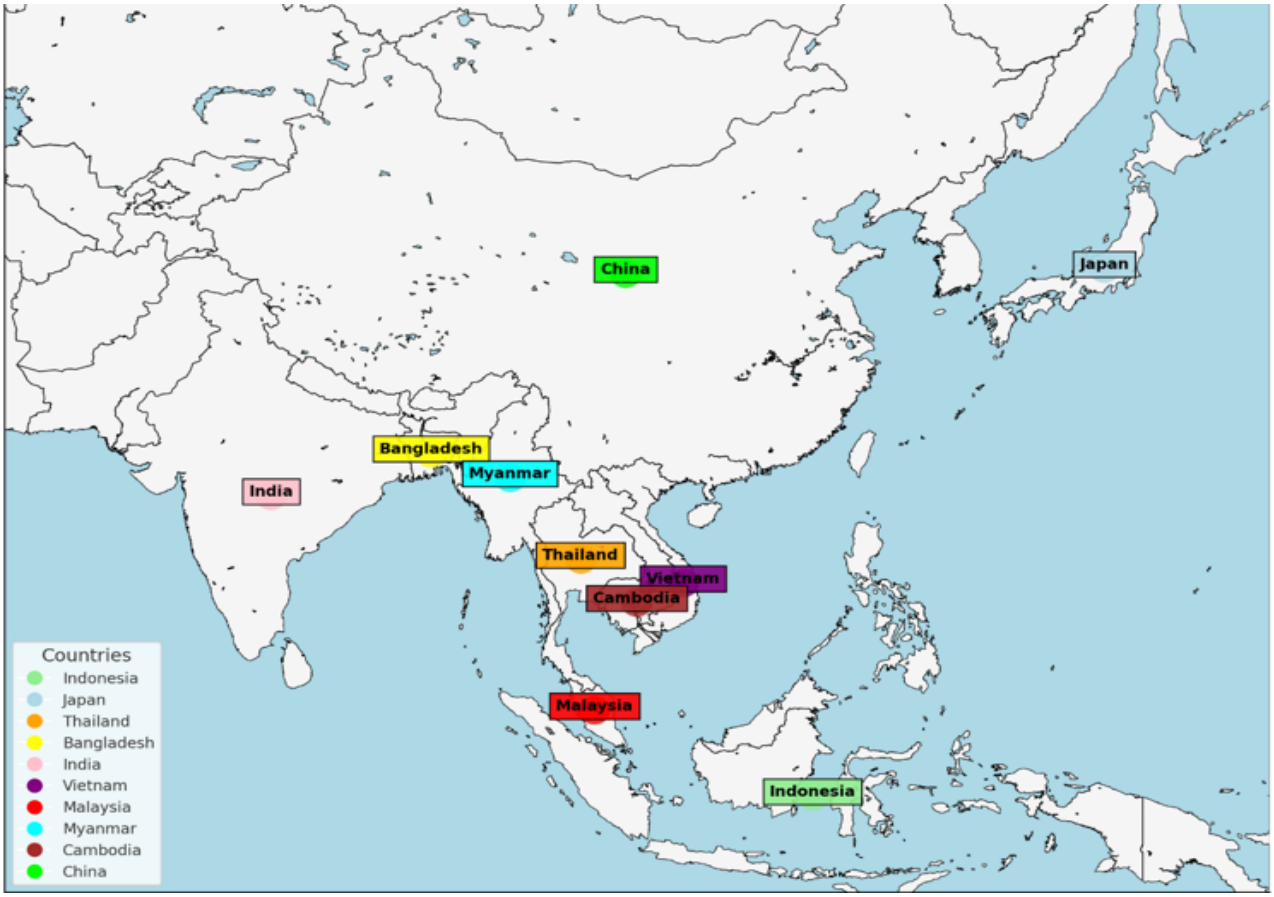

Fig. (1). The distribution of *Curcuma aeruginosa* Roxb. worldwide. *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

scores its ecological and cultural importance across Asia.

According to a study by Lim TK., despite extensive research into the phytochemistry and pharmacology of various *Curcuma* species, there remains a knowledge gap regarding the nutritional, compositional, and health benefits of edible species within the genus [29].

The Zingiberaceae family is characterized by its rhizomatous growth patterns and distinctive sympodial branching. Members of this family exhibit leafy shoots with minimal aerial stems and rhizomes displaying a range of colours, including pale yellow, greenish blue, and pink. These plants' leaves are arranged in a distichous pattern, varying in structure, size, shape, texture, and venation, while protective scale leaves shield the budding rhizomes and axillary buds [30-32]. The unique morphological characteristics of the Zingiberaceae family underscore its adaptability and ecological significance.

The Zingiberaceae family, known for its rich reservoir of bioactive compounds, including ginger and curcumin, has emerged as a pivotal contributor to advanced technological innovations [24, 33]. Curcumin and ginger extracts, for instance, have been effectively utilized in the development of antibacterial biopolymer films, demonstrating significant efficacy in inhibiting bacterial growth and addressing the escalating challenge of antibiotic resistance [22, 34]. Beyond antimicrobial applications, biomaterials derived from this family, such as hydrogels and electrospun fibers, have shown remarkable utility in tissue engineering [35, 36]. These materials, designed to mimic the extracellular matrix (ECM), provide essential scaffolding that supports cellular migration, proliferation, and differentiation. Furthermore, their role as reservoirs for growth factors and signaling molecules highlights their critical contribution to tissue regeneration and the regulation of key cellular processes [21, 37, 38].

This article examines the traditional use of Ayurvedic herbs and their integration into

modern therapeutic applications. The Zingiberaceae family, known for its bioactive diversity, bridges ancient medicinal practices and contemporary healthcare innovations. Among its members, *Curcuma aeruginosa* Roxb. has demonstrated tracheospasmolytic and anti-inflammatory properties, with bioactive compounds showing potential against SARS-CoV-2. Further research is essential to fully realize its antiviral capabilities and therapeutic applications.

2. PLANT MORPHOLOGY OF *CURCUMA AERUGINOSA* ROXB.

Curcuma aeruginosa Roxb., known in Malaysia as "Temu Hitam" or "Temu Ireng", is a rhizomatous plant that can grow up to one and a half meters [39, 40]. Its rhizome, which can be as long as 100 centimetres, is covered in green sheaths and has a pseudo stem reaching 35 centimetres in height [41]. The fragrant plant has sessile tubers with branching structures and succulent roots [42]. Its root tubers are creamy in colour and break smoothly under stress [43]. The rhizome is blue at its centre, turning greyish with age, a colour change noted by Maknoi [44]. *C. aeruginosa* leaves are distichously arranged, measuring 30 to 40 cm in length and 10 to 12 cm in width. They feature a purple or reddish-brown patch on the upper surface that fades as they mature. The plant's lateral inflorescence spans 25 to 30 cm, with a 12 to 18 cm peduncle and a 12 to 15 cm spike. Pink to violet coma bracts, with green streaks below, are large, and the fertile ones, 18 to 20 in number, are green with pink tips and measure about 4.5-5 x 4.4-5 cm [25]. The flowers of *C. aeruginosa* come in groups of 8-10 per bract. They have a 1 cm calyx and a 3-3.3 cm pink corolla tube. Other flower parts include 1.5 x 1.2 cm dorsal lobes, 1.5 x 1 cm lateral lobes, a 7 mm anther with a base spur, 5 mm epigynous glands, and a 5 mm ovary with numerous ovules. The flower's style and stigma characteristics align with the findings of Sari and Supratman [7].

3. VERNACULAR NAMES OF *CURCUMA AERUGINOSA* ROXB.

Curcuma aeruginosa Roxb. is widely distributed across tropical and subtropical areas, especially in Asia. Due to its vast distribution, it is known by various vernacular names. In Malay, it is called "Temu Hitam" [20], and in other regions, names like "Temu Ireng", "Kathali Holud", and "Kha-Min-Dam" [45] are prevalent. Other common names include "Wanmahamek″, "pink and blue ginger" in English, "Mahamek", "black turmeric", "Gajutsu", "Kajeawdang", "kali haldi", Ngo Suk and Ezhu in Chinese, "Karimanjal" in Indian dialects, and "Nghệ Ten Dồng″ in Vietnamese. A comprehensive list of its vernacular names is available in Table **1** and is sourced from previous studies [26-28, 43].

Table 1. Vernacular names of *Curcuma aeruginosa* Roxb.

Country	Local Name	References
Malaysia	Temu Hitam, Temu Erang, Temu Ireng	[46]
Indonesia	Konèng Hideung, Temo Erang, Temu Leteng, Temu Koneng, Temu Ireng, Temu Hitam, Temu Lotong, Tamu Hitam	[29, 47]
India	Karimanjal, Neelakua, Mahamek, Jangliadrak	[48, 49]
Thailand	Kamindam, Kajeawdang, Kha Min Dam, Kra-Jeaw, Waan Mahaamek, Phlai	[47, 50, 51]
Vietnam	Nghệ Ten Dồng, Nghê Den, Nghê Xanh, Ngai Tím	[51]
Bangladesh	Kathali Holud, Banada	[28, 49]
China	Ngo Suk, Ezhu	[29, 52]
English	Black ginger, Hidden lily, Pink and blue ginger, Aeruginous turmeric rhizome, Rhizome Zedoariae	[29, 52]
Arabic	Kurkum	[7, 53]

4. TAXONOMY OF *CURCUMA AERUGINOSA* ROXB.

Curcuma aeruginosa Roxb. is a starchy rhizomatous plant from the Zingiberaceae family, also known as the ginger family [51, 54]. Its classification details are provided in Table **2**. The overarching term "ginger" describes various members and species within this family [55]. *C. aeruginosa*, distinguished by its rhizomatous growth and unique fragrance, is part of the Zingiberaceae family and the *Curcuma* genus [33, 44]. The genus "*Curcuma*" is linked to the rhizomatous herb in the Zingiberaceae family and is rooted in the naming conventions set by renowned Swedish botanist Carl Linnaeus [48]. Linnaeus

introduced this generic name in 1753, potentially inspired by the rhizomes' colour [56]. Linnaeus was also pivotal in establishing the binomial nomenclature, a core principle of taxonomy. His contribution, especially in Latin descriptions, is recognised in several botanical works, including those by Choudhury *et al*. and Roxburgh W., (1810) [27, 57]. The name "*C. aeruginosa* Roxburgh" or "*Curcuma aeruginosa* Roxb. " signifies this plant species [7]. The botanical naming convention "Roxburgh" is usually abbreviated to "Roxb." as validated by Erbay Sari and Supratman [7, 56].

Curcuma aeruginosa Roxb. is a stemless, rhizomatous, and aromatic plant belonging to Zingiberaceae family and the genus *Curcuma*. The generic name *Curcuma* was first introduced by the Swedish botanist, zoologist, and physician Carl Linnaeus in 1753, who is widely regarded as the father of taxonomy for formalising the binomial nomenclature system. Most of these early descriptions are presented in Latin.

The botanical name *Curcuma aeruginosa* reflects the Latin naming convention. Additionally, several articles refer to this species as *C. aeruginosa* Roxb. or *C. aeruginosa Roxburgh*, attributing its discovery to William Roxburgh, who identified and described the plant species in 1810. The abbreviation “Roxb.” is a standardised author citation in botanical nomenclature, indicating Roxburgh’s authority in naming the species, as shown in Table **2**

Table 2. The detailed taxonomic classification of *Curcuma aeruginosa* Roxb.

Taxonomic Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Subclass	Zingiberidae
Order	Zingiberales
Family	*Zingiberaceae*
Genus	*Curcuma*
Species	*Aeruginosa*
Scientific name	*Curcuma aeruginosa*

5. TRADITIONAL AND MEDICINAL PROPERTIES OF *CURCUMA AERUGINOSA* ROXB.

Curcuma aeruginosa Roxb. is prevalent across tropical and East Asian territories, with a distinguished botanical footprint in Malaysia [58]. Historically, various plant components, such as its adventitious roots, stems, and leaves, have been utilized by local communities, although their usages have remained relatively specific [59, 60].

Traditional medicinal practices have long recognised the therapeutic potential of this plant, particularly in addressing gastrointestinal ailments, such as colic, indigestion, and stomach ache [59]. Furthermore, a study by Anasamy *et al*. highlighted its significant potential as a rich source of antioxidants [61]. A previous study identified the diverse medicinal efficacy of *Curcuma* species, which is deeply embedded in various traditional medicine doctrines. These remedies address a broad spectrum of conditions, including hypertension, Alzheimer's disease, and malaria-related discomfort and pain. Such claims are further substantiated by research from earlier authors, emphasising its therapeutic potential [62-64]. In Indonesia, where the plant is colloquially termed "Temu ireng", its integration into traditional medical practices is noteworthy [65].

These various studies are strengthened by the evidence that the plant's distinct bitterness enhances appetite and purifies blood post-childbirth. A gamut of maladies, from skin afflictions, like scabies and ulcers, to respiratory and gastrointestinal disorders, has been traditionally addressed using *C. aeruginosa*, as highlighted by the researchers [41, 66].

Referred to as "Temu hitam", *C. aeruginosa* boasts medicinal properties. Extracts and essential oils derived from it demonstrate antibacterial, anti-inflammatory, fever-reducing, and pain-relieving capabilities [39]. Pujimulyani *et al*. conducted a study involving its rhizome, which is associated with many beneficial activities, ranging from antioxidant and antimicrobial properties to promoting hair growth and skin rejuvenation [67]. Furthermore, the rhizome exhibits promise in managing chronic inflammatory conditions, including asthma, cancer, rheumatoid arthritis, and inflammatory bowel diseases, showcasing its anticancer, antioxidant, and antibacterial potential [7].

6. GENERAL HEALTH BENEFITS

Recent scientific investigation provides compelling evidence about the potential benefits of *Curcuma* in resolving a wide range of health-related concerns, including but not limited to acne, inflammation, joint discomfort, asthma, and eczema. Moreover, turmeric demonstrates potential in wound healing, promoting emotional stability, managing blood sugar levels, and modulation of the immune system [18, 68, 69].

7. PHYTOCHEMICAL PROFILE OF *CURCUMA AERUGINOSA* ROXB.

Curcuma aeruginosa Roxb. has garnered considerable scholarly interest in prior study endeavours. Extensive investigations into the phytochemical composition of diverse *Curcuma* species have yielded a wide array of metabolites [70]. Although more than 700 compounds have been found within this genus, a limited number have undergone thorough examination. Significantly, curcumin, derived predominantly from *C. aeruginosa*, has been the focal point of extensive research [26]. These various studies have been further substantiated by the findings of Zohmachhuana *et al*.; extensive studies have identified 34 unique phytochemical compounds exclusively in the rhizomes of *Curcuma aeruginosa* Roxb., with no traces found in the foliage. This distinct chemical profile underscores the rhizome's critical role as a reservoir of bioactive compounds, highlighting its potential for therapeutic applications (Table **3**).

8. VOLATILE CONSTITUENTS OF *CURCUMA AERUGINOSA* ROXB.

Plants are abundant sources of essential oils and volatile constituents, offering significant potential for various applications. These oils are commonly extracted from plant leaves using advanced techniques, including hydrodistillation, steam distillation, and supercritical fluid extraction, with each method tailored to maximise yield and preserve the chemical integrity of the volatile compounds [73]. In the leaves of *C. aeruginosa* Roxb., essential oils, constituting around 0.32% of leaf makeup, have been ascertained [18, 74]. Advanced gas chromatography-mass spectroscopy (GC-MS) examinations have unveiled a broad spectrum of volatile compounds. The distribution encompasses 64.5% terpenoids, 4% steroids, 0.45% phenanthrenes, 0.45% dimethyl hopane, 0.45% thiourea derivatives, 4.5% aromatics, 4.5% alcohols, 2.3% amines, 2.3% sugars, and 16.5% miscellaneous compounds [75]. It is imperative to note that the principal components consist of sesquiterpenes, monoterpenes, esters, and steroids. Table **4** provides a detailed insight into the volatile compounds discerned during extraction.

Table 3. Phytochemicals isolated and identified in the rhizome of *Curcuma aeruginosa* Roxb.

Type	Compounds	Source	References
Flavonoid	Flavone, 3-(5-ethyl-2-methoxy-phenyl)-6-methoxy-chroman-4-one, 3-(3-ethyl-2-methoxy-phenyl)-6-methoxy-chromate-4-one	Rhizome	[7, 39]
-	6-hydroxy-5-methoxy-2-(2-methoxy-phenyl)-chroman-4-one, 8-hydroxy-5-methoxy-3-(2-methoxy-phenyl)-chroman-4-one	-	-
Terpenoid	Difurocumenone, aerugidiol, zedoalactone A, zedoalactone B, zedoarondiol, curzerenone, furanodienone, furanogermenone, zedoarol	Rhizome	[7, 71]
-	Curcumenol, isocurcumenol, aeruginolactone, aeruginone, furanodiene, germacrone, zederone, dehydrocurdione	-	[43]
Terpenoid	Dehydrocurdione, aeruginon, curcumenon, pyrocurzerenone, dehydrochromolaenin, curzeone, linderazulene	Rhizome	[8, 9, 72]
Diarylheptanoid	Curcumin, demethoxycurcumin, bisdemethoxycurcumin	Rhizome	[7]

Table 4. The phytochemicals that have been isolated and identified in *Curcuma aeruginosa* Roxb.

S. No.	Compounds	Molecular Formula	Plant Part	References
Terpenoids				
1	α-fenchene	-	-	[7]
2	α-fenchol	$C_{10}H_{18}O$	Leaf	[7]
3	α-humulene	$C_{15}H_{24}$	Leaf, rhizome	[76]
4	α-pinene	$C_{10}H_{16}$	Leaf, rhizome	[7]
5	α-selinene	$C_{15}H_{24}$	Leaf	[75]
6	α-thujene	$C_{10}H_{16}$	Leaf	[25, 73]
7	β-caryophyllene	$C_{15}H_{24}$	Leaf	[25]
8	β-cubebene	$C_{15}H_{24}$	Leaf	[73, 77]
9	β-elemene	$C_{15}H_{24}$	Laef, rhizome	[78]
10	β-elemenone	$C_{15}H_{22}O$	Leaf	[25]
11	β-pinene	$C_{10}H_{16}$	Leaf	[73, 78]
12	δ-cadinene	$C_{15}H_{24}$	Leaf	[25]
13	γ-elemene	$C_{15}H_{24}$	Leaf, rhizome	[75, 79]
14	γ-terpinene	$C_{10}H_{16}$	Leaf	[80]
15	(E)-β-famesene	$C_{15}H_{24}$	Leaf	[81]
16	(E)-β-ocimene	$C_{10}H_{16}$	Leaf	[76]
17	(E)-tagetone	$C_{10}H_{16}O$	Leaf	[7]
18	(Z)-β-ocimene	$C_{10}H_{16}$	Leaf	[7]
19	1,8-cineole	$C_{10}H_{18}O$	Leaf, rhizome	[25, 78]
20	Borneol	$C_{10}H_{18}O$	Leaf, rhizome	[25, 78]
21	Camphene	$C_{10}H_{16}$	Leaf, rhizome	[7, 75]
22	Camphor	$C_{10}H_{16}O$	Leaf, rhizome	[7, 75]
23	Carvone	$C_{10}H_{14}O$	Leaf	[80]
24	Caryophyllene	$C_{15}H_{24}$	Rhizome	[73, 79]
25	Caryophyllene oxide	$C_{15}H_{20}O$	Leaf, rhizome	[79]
26	*cis*-carveol	$C_{10}H_{16}O$	Leaf	[7]
27	Curzerenone	$C_{15}H_{18}O_2$	Leaf	[76, 80]
28	Curzerene	$C_{15}H_{20}O_2$	Leaf, rhizome	[76, 80]
29	Epi-curzerenone	$C_{10}H_{18}O_2$	Leaf	[7]
30	Furanodienone	$C_{10}H_{18}O_2$	Rhizome, leaf	[7]
31	Furanogermenone	$C_{15}H_{20}O_2$	Rhizome, leaf	[56]
32	Germacrone	$C_{15}H_{22}O$	Leaf, rhizome	[78]
33	Isoborneol	$C_{10}H_{18}O$	Leaf, rhizome	[80]
34	Isocurcumenol	$C_{15}H_{22}O_2$	Rhizome	[62]

(Table 4) Contd…

35	Isofuranodienone	$C_{10}H_{18}O_2$	Leaf	[7]
36	Linalool	$C_{10}H_{18}O$	Leaf	[7, 62]
37	Myrcene	$C_{10}H_{16}$	Leaf	[78, 80]
38	Myrtenal	$C_{10}H_{14}O$	Leaf	[7]
39	*p*-cymene	$C_{10}H14$	Leaf	[7]
40	Phytol	$C_{20}H_{40}O$	Leaf	[7]
41	Pulegone	$C_{10}H_{16}O$	Leaf	[7]
42	Sabinene	$C_{10}H_{16}$	Leaf	[7]
43	Terpinen-4-ol	$C_{10}H_{18}O$	Leaf, rhizome	[7]
44	*trans*-pinocarveol	$C_{10}H_{16}O$	Leaf	[7]
Alcohols				
45	*trans*-verbenol	$C_{10}H_{16}O$	Leaf	[7]
46	1-hexen-3-ol	$C_6H_{12}O$	Leaf	[7]
47	(E)-2-hexenol	$C_6H_{12}O$	Leaf	[7]
48	(Z)-3-hexenol	$C_6H_{12}O$	Leaf	[7]
49	Hexanol	$C_6H_{14}O$	Leaf	[7]

9. PHARMACOLOGICAL PROPERTIES OF *CURCUMA AERUGINOSA* ROXB.

Curcuma aeruginosa Roxb., a rhizomatous member of the Zingiberaceae family, has garnered significant attention for its diverse pharmacological properties. Its bioactive compounds, including curcuminoids, glycosides, terpenoids, and flavonoids, are associated with notable anti-inflammatory, antioxidant, and anticancer activities, highlighting its therapeutic potential [31, 73, 81]. These attributes underscore its relevance in medicinal and microbiological research, as illustrated in Fig. (**2**).

A previous study conducted by Abdul Aziz *et al*. successfully identified the therapeutic applications of the *Haridra* rhizome, a key component of *C. aeruginosa*. Healthcare professionals have employed this rhizome in managing various health conditions, including diabetes, cholesterol imbalances, inflammation, diarrhoea, liver dysfunction, asthma, and cancer, while demonstrating minimal cytotoxicity toward normal cells. Additionally, the study highlighted the use of *C. aeruginosa* in cosmetic formulations, further emphasising its multifaceted applications [82, 83]. In a study conducted by Sharifi-Rad *et al*., human trials have underscored the efficacy and safety of curcumin, leading to the U.S. Food and Drug Administration designating it as generally considered safe [84].

9.1. Anti-inflammatory Activity

In a previous study, researchers spearheaded an initial investigation into the anti-inflammatory properties of fresh rhizome extracts of *C. aeruginosa* Roxb. This investigation utilized the carrageenan-induced paw edema approach in Wistar rats [85].

The researchers administered diverse extracts (chloroform, methanol, and water) at escalating dosages (ranging from 100 to 800 mg/kg). Concurrently, they orally provided aspirin (200 mg/kg) to the subjects 30 minutes before infusing a 1% (w/v) carrageenan solution into the rats' appendages [86].

In the study performed by Triastuti *et al*., the subsequent data revealed that none of the extracts significantly reduced paw oedema when compared to the benchmark drug aspirin [87].

The *in vivo* anti-inflammatory potential of *C. aeruginosa* Roxb.'s ethanolic extract was assessed by utilizing the croton oil-triggered ear edema method in male BALB/c mice. Test groups were introduced to this extract's varying concentrations (40, 80, and 160 mg/ear). In contrast, the control ensemble received a 1% hydrocortisone solution. Remarkably, post a 24-hour initiation phase, the ethanolic extract, at a concentration of 160 mg/ear, displayed an inhibition rate of 90.35

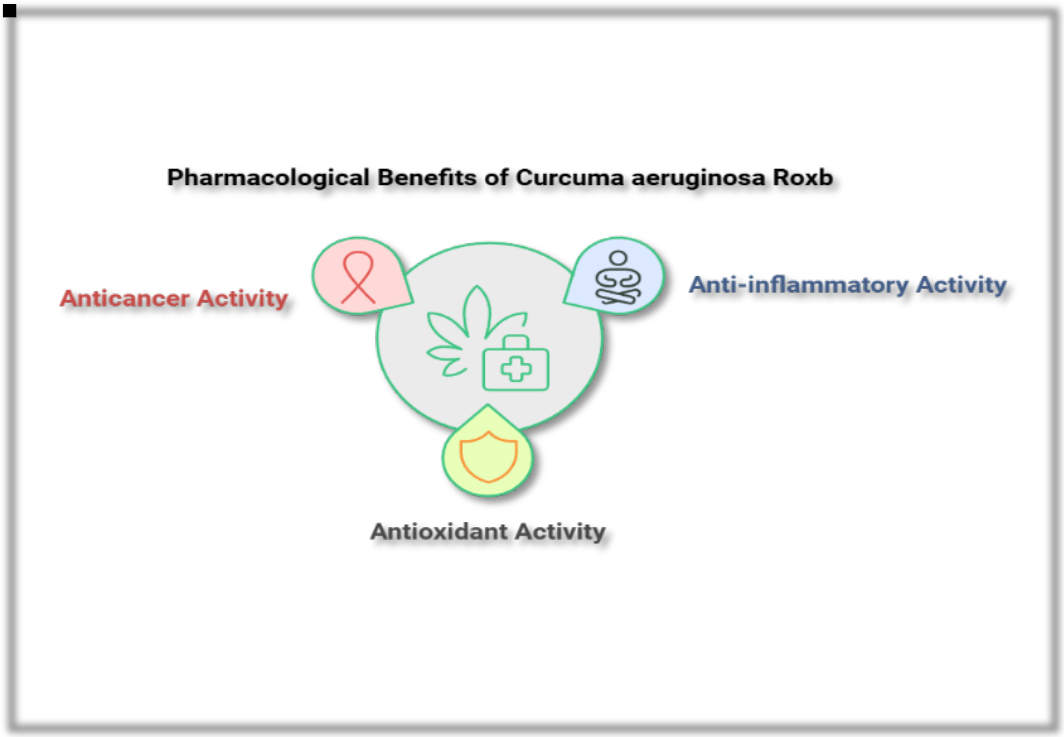

Fig. (2). Pharmacological properties of *Curcuma aeruginosa* Roxb. *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

± 4.22% ($p < 0.05$), outperforming the standard medication [88].

Paramita *et al*. conducted an in-depth evaluation of the ethanolic extract of *C. aeruginosa* Roxb., employing both *in vitro* and *in vivo* methodologies to assess its anti-inflammatory potential. The study utilized an erythrocyte membrane stability assay and a carrageenan-induced paw swelling model. Results indicated a notable EC_{50} value of 47.8 ± 1.6 mg/mL for the extract, surpassing the benchmark drug indomethacin, which recorded an EC_{50} value of 26.4 ± 2.9 mg/mL. The pronounced anti-inflammatory activity was attributed to the synergistic interplay of bioactive compounds, including flavonoids, terpenoids, and steroids, which collectively enhanced membrane stabilization and mitigated inflammatory responses [89].

The extract's anti-inflammatory potency *in vivo* was evident, marking a significant area under the curve (AUC) value at 100 mg/kg. This contrasted with indomethacin's results at 10 mg/kg ($p < 0.05$) [90]. This manifestation indicated the extract's potential to mitigate inflammatory mediator releases, culminating in diminished vascular leakage [28]. Considering these findings, it is evident that further in-depth molecular studies are imperative to unveil the exact mechanism of *C. aeruginosa* extract, coupled with its active compounds, as an anti-inflammatory agent [91].

9.2. Antioxidant Activity

In a meticulous *in vitro* study, George *et al*. explored the antioxidant prowess of the essential oil extracted from *C. aeruginosa* Roxb. With 2,2-diphenyl-1-picrylhydrazyl (DPPH) and nitric oxide scavenging assays, they revealed impressive antioxidant capabilities, with IC_{50} values at 28 µg/mL and 30 µg/mL, respectively [26]. The essential oil showcased a commendable inhibition percentage of 77% at a concentration of 50 µg/mL, slightly lower than the 81% achieved by the reference compound, ascorbic acid, at an identical concentration [27, 92].

Nurcholis *et al*. provided compelling evidence highlighting the significant antioxidant potential of *C. aeruginosa* Roxb. Essential oil analysis, using the phosphomolybdenum assay, revealed an antioxidant activity of 67% at a concentration of 50 µg/mL, closely aligning with the activity of ascorbic acid. Similarly, the reducing power assay reported a value of 2.54% at 50 µg/mL, only mar-

ginally below the 2.67% observed for ascorbic acid. In the nitric oxide (NO) scavenging assay, the essential oil exhibited a 72.3% inhibition rate at 50 μg/mL, slightly lower than ascorbic acid's 76.8%. Further investigations utilizing the DPPH scavenging assay evaluated the antioxidant efficacy of the ethanolic extracts (70% and 96%), underscoring their ability to neutralize free radicals [93]. These findings reinforce *C. aeruginosa* Roxb.'s potential as a potent natural antioxidant, suggesting its suitability for therapeutic and nutraceutical applications [75].

The findings indicated IC_{50} values of 437.07 μg/mL and 681.39 μg/mL for the respective extracts, which were noticeably higher than the 32.91 μg/mL associated with ascorbic acid. The moderate antioxidant activity of the ethanolic extracts underscores the imperative for an intensified probe to discern and catalogue specific antioxidant compounds inherent in *C. aeruginosa* Roxb. [94]. The study by Aryal *et al*. emphasised the formidable antioxidant potential bored by the essential oil obtained from *C. aeruginosa* Roxb. Such revelations indicate potential applications spanning food preservation and addressing oxidative stress-induced complications in various diseases [95].

9.3. Anticancer Activity

Atun *et al*. delved into the cytotoxic potential of *C. aeruginosa* Roxb. extracts, encompassing methanol, n-hexane, and chloroform [8]. The team employed the MTT colorimetric assay to measure the cytotoxic activities on a selection of cell lines, notably MCF-7, Ca Ski, HeLa S3, and T-47D. Both n-hexane and chloroform extracts manifested notable anticancer properties, as indicated by LC50 values of 69.47 ± 2.16 μg/mL and 92.60 ± 4.10 μg/mL for MCF-7 cells and 66.02 ± 0.45 μg/mL for Ca Ski cells, respectively. However, these extracts had limited efficacy against HeLa S3, T-47D, and Vero cell lines, yielding LC_{50} values exceeding 500 μg/mL [75].

Choi *et al*. investigated the antiproliferative properties of *C. aeruginosa* Roxb. essential oil against MCF-7 breast cancer cell lines. The study demonstrated a concentration-dependent inhibition of cancer cell proliferation. At a dosage of 170 μg/mL, the essential oil achieved a 50.2% reduction in MCF-7 cell viability, with an IC_{50} value calculated at 161.0 μg/mL. These findings underscore the potential of *C. aeruginosa* essential oil as a promising natural agent for cancer therapy, warranting further investigation into its molecular mechanisms and therapeutic applications [96].

Additionally, tropolone, an essential oil constituent, has been proposed to inhibit histone deacetylase (HDAC) [97]. Previous findings indicate tropolone's ability to inhibit the growth of various cancer cell lines, such as HCT-116, BXPC-3, and HuT-78, presenting GI_{50} values between 5 and 30 μM. However, a comprehensive assessment of this compound's antiproliferative properties necessitates further investigation [98, 99].

10. EXPLORING POTENTIAL COMPOUNDS FROM *CURCUMA AERUGINOSA* ROXB. AS THERAPEUTIC CANDIDATES AGAINST COVID-19

An in-depth investigation into COVID-19 has highlighted the therapeutic potential of bioactive compounds extracted from *Curcuma aeruginosa* [12]. These findings emphasize the significant role of its phytochemicals in combating SARS-CoV-2, underscoring the necessity for further exploration to unravel their precise mechanisms of action and advance their application in the development of effective antiviral therapies [100].

The therapeutic potential of bioactive compounds in combating SARS-CoV-2 has been substantiated by studies conducted by Liang *et al*. and Walls *et al*. These investigations identified key compounds, including curcumenol, palmitic acid, β-eudesmol, β-pinene, β-sitosterol, succinic acid, 1,8-cineole, α-terpineol, β-caryophyllene, and zingiberene, as outlined in Table **5**. Notably, curcumin, extracted from *Solanum tuberosum*, exhibited superior efficacy to hydroxychloroquine in computational models. Employing molecular docking analyses, the research illuminated interactions between SARS-CoV-2 and critical viral receptors, such as TMPRSS2, PLpro, 3CLpro, RdRp, S protein, and ACE2. These receptors are integral to viral entry, replication, and host-pathogen dynamics, underscoring the therapeutic promise of these bioactive compounds in antiviral strategies [101, 102].

Table 5. Chemical compounds identified in *Curcuma aeruginosa* with potential activity against COVID-19.

S. No.	Name	Molecular Weight	References
1	Curcumenol	$C_{15}H_{22}O_2$	[119, 120]
2	Palmitic acid	$C_{16}H_{32}O_2$	[121, 122]
3	β-eudesmol	$C_{15}H_{26}O$	[30, 123]
4	β-pinene	$C_{10}H_{16}$	[124, 125]
5	β-sitosterol	$C_{29}H_{50}O$	[126 ,127]
6	Succinic acid	$C_4H_6O_4$	[128, 129]
7	1,8-cineole (eucalyptol)	$C_{10}H_{18}O$	[130, 131]
8	α-terpineol	$C_{10}H_{18}O$	[132, 133]
9	β-caryophyllene	$C_{15}H_{24}$	[134, 135]
10	Zingiberene	$C_{15}H_{24}$	[136, 137]

10.1. Curcumenol: A Potential Therapeutic Agent against SARS-CoV-2

Curcumenol, a sesquiterpene compound found in *C. aeruginosa* and related species within the *Curcuma* genus, has demonstrated notable pharmacological properties, including antiviral, anti-inflammatory, and immunomodulatory effects [101, 103]. Recent research has increasingly highlighted curcumenol's potential in addressing SARS-CoV-2, the virus responsible for the COVID-19 pandemic. This review aimed to elucidate the specific mechanisms by which curcumenol exerts its antiviral effects against SARS-CoV-2, offering valuable insights into its potential applications as a therapeutic agent in the battle against COVID-19.

10.2. Mechanisms of Antiviral Action of Curcumenol

Curcumenol, a bioactive compound from *Curcuma* species, exerts its antiviral effects against SARS-CoV-2 through multiple mechanisms, including inhibition of viral entry, disruption of viral replication, and protease activity, along with modulation of the immune response and reduction of oxidative stress [104]. Thimmulappa *et al*. underscored the significant antiviral potential of curcumenol in combating SARS-CoV-2. The compound exhibits a multifaceted mechanism of action, including the inhibition of viral entry, disruption of replication processes, and suppression of critical viral proteases. These findings suggest that curcumenol holds considerable promise as a therapeutic candidate for the development of targeted antiviral strategies against COVID-19, warranting further in-depth investigation [105]. Furthermore, curcumenol's anti-inflammatory, immunoregulatory, and antioxidative properties significantly contribute to regulating the host immune response and minimizing oxidative damage. These characteristics underscore its potential as a therapeutic agent for reducing the severity of COVID-19, as depicted in Fig. (**3**).

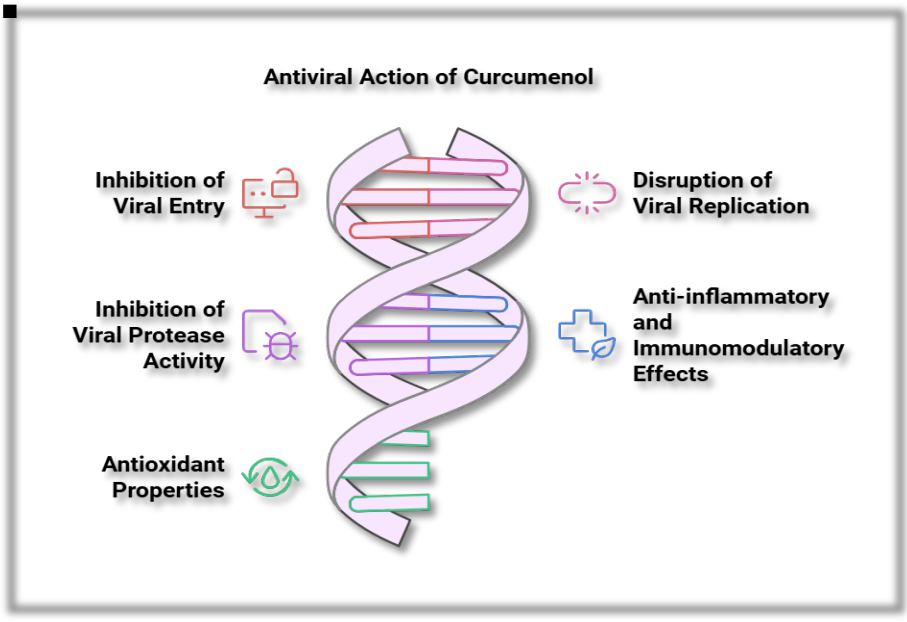

Fig. (3). Mechanisms of the antiviral action of curcumenol. *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

1. Inhibition of Viral Entry: Curcumenol shows promise as an antiviral agent against SARS-CoV-2 by targeting the critical interaction between the spike (S) protein and ACE2 receptor, a key step in viral entry. By disrupting this binding, curcumenol effectively inhibits viral attachment and reduces viral load at the early stages of infection. This early intervention is vital for controlling disease progression, positioning curcumenol as a potential therapeutic candidate for further investigation [106,107].

2. Disruption of Viral Replication: SARS-CoV-2 relies on its RNA-dependent RNA polymerase (RdRp) to facilitate the replication of its RNA genome once inside the host cell. Curcumenol, a bioactive sesquiterpene, has demonstrated potential inhibitory effects on viral RNA polymerases, including RdRp. By targeting and obstructing RdRp activity, curcumenol interferes with viral RNA synthesis, effectively limiting the replication and proliferation of the virus within the host. This mechanism underscores the therapeutic potential of curcumenol as an antiviral agent, warranting further exploration in the development of treatments against SARS-CoV-2 [108]. The research study performed by Das *et al*. suggested that curcumenol's potential to target non-structural proteins (NSPs) is essential for the SARS-CoV-2 replication-transcription complex. By disrupting these proteins, curcumenol may interfere with viral replication at multiple stages, underscoring its promise as a therapeutic candidate against SARS-CoV-2 [109].

3. Inhibition of Viral Protease Activity: Another critical step in the viral life cycle is the cleavage of viral polyproteins by proteases. SARS-CoV-2 relies on two key proteases, the main protease (Mpro) and the papain-like protease (PLpro), for processing its polyproteins into functional viral components. Curcumenol has demonstrated potential inhibitory effects on viral proteases in other viral infections, and it is hypothesized that it could inhibit SARS-CoV-2 Mpro and PLpro as well [110].

4. Anti-inflammatory and Immunomodulatory Activities: Severe cases of COVID-19 are marked by an excessive immune response, often termed a cytokine storm, which results in extensive tissue damage and severe complications, such as acute respiratory distress syndrome (ARDS). Curcumenol has emerged as a potential therapeutic agent due to its potent anti-inflammatory properties, offering a means to modulate the dysregulated immune response observed in these cases (Shao *et al*., 2020). As highlighted by Li *et al*., curcumenol effectively reduces the production of key pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and tumor necrosis factor-alpha (TNF-α). These cytokines are major contributors to the cytokine storm, and their suppression by curcumenol may prevent excessive inflammatory damage to lung tissue and other organs [110]. Additionally, the research work carried out by Perrone *et al*. suggested curcumenol to enhance antiviral immune defenses by promoting the activity of natural killer (NK) cells and cytotoxic T-lymphocytes, which are crucial for eliminating viral infections. By combining anti-inflammatory and immunomodulatory effects, curcumenol offers a promising strategy for mitigating the severe immunopathology associated with COVID-19, warranting further investigation into its therapeutic potential (Perrone *et al*., 2020).

5. Antioxidant Properties and Reduction of Oxidative Stress: Oxidative stress plays a significant role in the pathogenesis of COVID-19, especially in severe cases where there is a high level of reactive oxygen species (ROS) and oxidative damage to lung tissues. Curcumenol possesses strong antioxidant properties, which may help mitigate the oxidative stress associated with SARS-CoV-2 infection [111].

By scavenging ROS and reducing oxidative damage, curcumenol can protect lung cells from injury and promote tissue repair. This antioxidant effect is particularly important in reducing the risk of fibrosis and long-term pulmonary damage in patients recovering from COVID-19 [36]. β - eudesmol demonstrated inhibitory activity against the angiotensin-converting enzyme 2 (ACE2) protein and the primary protease of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). According to a study conducted by My *et al*., this finding indicates the possibility of the recommended approach to inhibit the entry of SARS-CoV-2 into human cells. Furthermore, this chemical, which is naturally found in medicinal plants indigenous to Morocco, has been identified as a potential inhibitor of SARS-CoV-2 [102, 112, 113].

Moreover, previous studies utilizing molecular docking techniques have demonstrated β-pinene to exhibit a substantial affinity for the major protease receptor of SARS-CoV-2 (Gu *et al*., 2020; Wang *et al*., 2020). β-sitosterol, a compound that has been involved in the signaling pathway associated with antiviral activity, is hypothesized to exert an influence on the immunological response to the COVID-19 virus. The inhibitory activity of the central protease receptor of SARS-CoV-2 has been demonstrated in molecular tests [114]. β-sitosterol demonstrated notable affinity towards the spike glycoprotein and ACE2, as evidenced by the study conducted by Chowdhury P. [115].

My *et al*. made an additional noteworthy discovery in their research, which involved the isolation of 1,8-cineole (commonly known as eucalyptol) from the plant species *Melaleuca cajuputi*. Molecular evaluations targeting the ACE2 protein and the primary protease of SARS-CoV-2 (PDB6LU7) suggested its potential efficacy in combating COVID-19. The potential therapeutic efficacy of *C. aeruginosa* Roxb. and its constituents in addressing the COVID-19 infection warrants acknowledgment [116]. The compound 1,8-cineole, also known as eucalyptol, has demonstrated potential in terms of both safety and effectiveness against the virus, as indicated earlier [117]. In addition, it has been suggested that α-terpineol may possess inhibitory effects on the ACE2 protein as well as the primary protease of SARS-CoV-2, specifically PDB6LU7, as reported by Colalto and P. In conclusion, recent research indicates zingiberene to exhibit a significant affinity for the ACE2 receptor, suggesting its potential to suppress the SARS-CoV-2 virus [118].

Curcuma aeruginosa Roxb. has garnered attention for its therapeutic potential, primarily attributed to its bioactive constituents, such as curcumenol and curcumin. These compounds exhibit notable antiviral, anti-inflammatory, and antioxidant properties. Comparatively, while *Curcuma longa* (turmeric) is well-recognized for its high curcumin content, *C. aeruginosa* demonstrates equivalent antiviral efficacy. Its mechanisms include the inhibition of viral replication and the modulation of immune responses, underscoring its potential as a therapeutic candidate for various viral infections [138].

Ahmad *et al*. highlighted the therapeutic potential of *C. aeruginosa* in comparison to other traditional medicinal products, such as *Nigella sativa* (black seed) and *Glycyrrhiza glabra* (licorice root). While these traditional remedies exhibit broad-spectrum antiviral and immunomodulatory properties, *C. aeruginosa* distinguishes itself through its specific ability to inhibit viral entry and replication. This targeted mechanism underscores its unique therapeutic potential, particularly in combating viral infections, such as COVID-19 [139].

11. ADVERSE EFFECTS, CONTRAINDICATIONS, PRECAUTIONS, AND SAFETY CONSIDERATIONS OF *C. AERUGINOSA* ROXB.

The health advantages of *Curcuma* are generally acknowledged in academic literature. However, it is essential to exercise caution when using *Curcuma* owing to its potential negative effects and interactions with other substances. It is worth noting that consuming excessive amounts of *Curcuma* may lead to uterine contractions in pregnant women [109]. Fuloria *et al*. emphasized that *C. aeruginosa* may impair iron absorption, necessitating caution in individuals with iron deficiencies to avoid exacerbating related conditions [68].

It is important for individuals, namely men, to be cognizant of research findings that suggest a potential correlation between the use of turmeric and the suppression of testosterone levels, as well as the impairment of sperm motility [60]. The anticoagulant properties associated with *C. aeruginosa* highlight the importance of caution, especially for individuals undergoing surgical procedures. To mitigate the risk of delayed blood clotting, its use should be discontinued at least two weeks prior to any planned surgery. Furthermore, *C. aeruginosa* is contraindicated in individuals with pre-existing gallbladder disorders or bleeding conditions, emphasizing the necessity for thorough medical evaluation and supervision before its use in such populations [84]. A detailed examination of curcumin's safety and toxicity profiles, along with corresponding therapeutic approaches, is illustrated in Fig. (**4**).

The bioavailability of curcumin, the principal active compound in *C. aeruginosa*, is notably limited due to its poor aqueous solubility, rapid metabolic degradation, and swift systemic elimina-

tion. To address these limitations, a range of innovative strategies and advanced formulations have been developed, as illustrated in Fig. (**5**). These approaches aim to enhance curcumin's therapeutic potential by improving its absorption and stability and sustaining its bioactivity.

1. Nano-formulations: Nanoparticles, liposomes, and micelles have been employed to improve curcumin's solubility and stability, leading to enhanced bioavailability. Studies have shown curcumin-loaded nanoparticles to increase cellular uptake and protect the compound from degradation in the gastrointestinal tract, enhancing therapeutic efficacy [140].

2. Phospholipid Complexes (phytosomes): Phytosomes improve curcumin's solubility and absorption. Clinical trials have demonstrated increased bioavailability of curcumin in phytosomal formulations, showing better absorption rates compared to standard extracts [141].

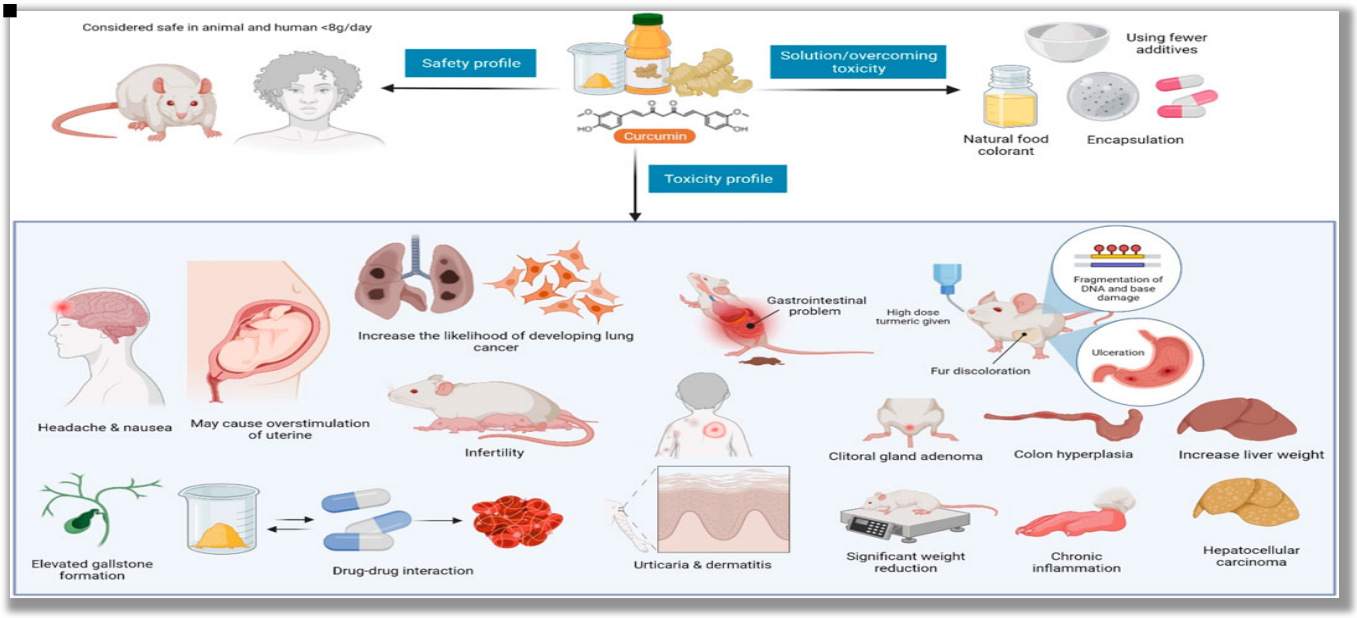

Fig. (4). Safety and toxicity profiles of curcumin and mitigation strategies. Despite its generally acknowledged safety, recent research has revealed uncommon side effects associated with curcumin, such as gastrointestinal discomfort and chronic inflammation. To address these concerns, optimizing curcumin formulations by minimizing the use of additives and exploring tailored curcumin microencapsulation methods is recommended [68]. *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

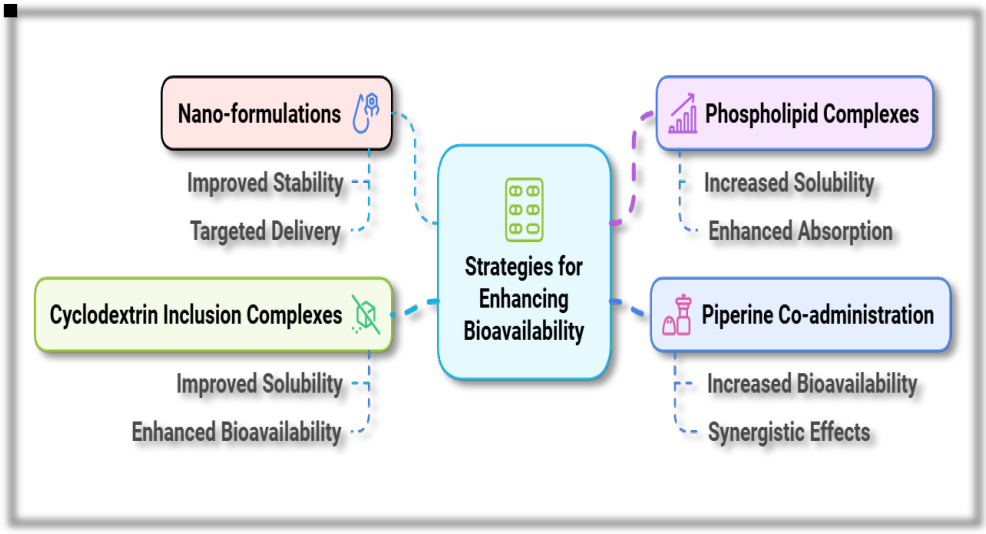

Fig. (5). Strategies for enhancing the bioavailability of curcumin formulations. *(A higher resolution / colour version of this figure is available in the electronic copy of the article).*

3. Piperine Co-administration: Piperine, a natural alkaloid, inhibits the metabolic breakdown of curcumin, improving its absorption [142]. This approach has proven particularly effective in enhancing curcumin's therapeutic outcomes.

4. Cyclodextrin Inclusion Complexes: Cyclodextrins enhance the solubility and stability of curcumin by forming inclusion complexes, further improving its bioavailability and efficacy in clinical applications [110].

11.1. Effectiveness in Practical Applications

Curcuma aeruginosa Roxb., a medicinal herb with potent anti-inflammatory and antioxidant properties, continues to garner attention for its therapeutic potential. Advances, such as nanoformulations and piperine co-administration, have demonstrated improved absorption and enhanced therapeutic efficacy in preclinical and clinical studies. Nevertheless, large-scale human trials are essential to validate these strategies and ensure their long-term safety and efficacy; however, despite its promising potential, the safety profile of *C. aeruginosa* remains a key concern, particularly regarding prolonged use or high dosages [138, 143].

A study conducted by Wilken *et al*. highlighted that the curcuminoid content in *C. aeruginosa* can stimulate bile production, potentially aggravating gastrointestinal conditions, such as gallstones or bile duct obstruction, leading to symptoms, like abdominal pain and indigestion. Furthermore, the use of *C. aeruginosa* is contraindicated in pregnant and breastfeeding women due to a lack of sufficient clinical safety data [143].

High doses or extended use of *C. aeruginosa* have been associated with hepatotoxicity and nephrotoxicity, especially in individuals with preexisting liver or kidney conditions. Furthermore, its interaction with anticoagulant medications may elevate the risk of bleeding due to its potential to enhance the effects of blood thinning agents [144].

In clinical settings, these contraindications necessitate careful patient screening, meticulous dosage management, and regular monitoring of liver and kidney function, particularly in individuals with underlying conditions [145]. Thorough medication reviews are critical to mitigate potential drug interactions before integrating *C. aeruginosa* into therapeutic regimens [146].

Several key research gaps require attention. These include elucidating the molecular mechanisms underlying the bioactivity of its compounds, such as curcuminoids and essential oils, and optimizing strategies to improve bioavailability. While current approaches show promise, long-term studies are necessary to confirm their safety and efficacy in human populations [147, 148].

CONCLUSION

The Zingiberaceae family, particularly *Curcuma aeruginosa* Roxb., offers promising antimicrobial potential and bioactive compounds for therapeutic innovation. Traditionally, the rhizome of *C. aeruginosa* has been used to treat wounds, diarrhea, fever, rheumatism, and asthma, highlighting its broad medicinal value. Its phytochemical profile includes flavonoids, terpenoids, and key constituents, like curzerenone, germacrone, and 1,8-cineole, which exhibit diverse pharmacological activities. Notably, germacrone shows potential in managing androgenic alopecia. Recent studies emphasize *C. aeruginosa*'s antiviral prospects, particularly against SARS-CoV-2. Compounds, such as 1,8-cineole, curcumenol, and zingiberene demonstrate strong binding affinity to ACE2 proteins, suggesting their role in inhibiting viral entry. However, further *in vitro* and *in vivo* studies are necessary to validate these findings. Future research should prioritize elucidating molecular mechanisms, conducting clinical trials, and establishing robust safety profiles to seamlessly integrate *C. aeruginosa* into contemporary pharmaceutical innovations while preserving its rich traditional heritage.

LIST OF ABBREVIATIONS

3CLpro	=	Main protease in coronaviruses (3-chymotrypsin-like protease)
ABTS	=	2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)
ACE2	=	Angiotensin-converting enzyme 2 (a receptor

involved in SARS-CoV-2 entry into cells)

ARDS = Acute respiratory distress syndrome

AUC = Area under the curve (used in pharmacokinetics to describe drug exposure over time)

C. aeruginosa = *Curcuma aeruginosa* Roxb.

COVID-19 = Coronavirus disease 2019

DPPH = 2,2-diphenyl-1-picrylhydrazyl (a common assay for measuring antioxidant activity)

EC_{50} = Half maximal effective concentration (a measure of a drug's potency)

FDA = U.S. Food and Drug Administration

GI_{50} = Growth inhibition 50% (a measure of a compound's ability to inhibit cell growth)

Hydroxychloroquine = A medication evaluated for its potential against SARS-CoV-2

IC_{50} = Half maximal inhibitory concentration (a measure of a substance's effectiveness in inhibiting a specific biological process)

IL-1β = Interleukin-1 beta (a pro-inflammatory cytokine)

IL-6 = Interleukin-6 (a pro-inflammatory cytokine)

Mpro = Main protease of SARS-CoV-2

MTT assay = A colorimetric assay for assessing cell metabolic activity

NK cells = Natural killer cells (type of immune cells involved in viral defense)

NO = Nitric oxide

NSPs = Nonstructural proteins (critical components of the SARS-CoV-2 replication-transcription complex)

PDB6LU7 = Protein Data Bank identifier for the SARS-CoV-2 main protease structure

PLpro = Papain-like protease (a SARS-CoV-2 enzyme)

RdRp = RNA-dependent RNA polymerase (an enzyme critical for SARS-CoV-2 replication)

RNA = Ribonucleic acid

ROS = Reactive oxygen species

SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2

TMPRSS2 = Transmembrane protease serine 2 (a protein critical for SARS-CoV-2 entry into host cells)

TNF-α = Tumor necrosis factor-alpha (a pro-inflammatory cytokine)

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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