- Review paper

# The Pharmacological Prospects of *Curcuma*: A Review of Its Antimicrobial, Antioxidant, and Anticancer Properties

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**(Received: December 10, 2024; Accepted: May 12, 2025; Published (web): June 25, 2025)**

**ABSTRACT:** Cancer stands as a global threat nowadays, and its impact is becoming worse, affecting millions and causing high mortality rates due to drug resistance, improper treatments, and a lack of early detection. Despite advances in therapy, cancer treatment continues to pose significant challenges, largely due to multidrug resistance, treatment inefficacy, and delayed diagnosis. While oxidative stress (OS) is widely recognized as a key driver of carcinogenesis, the role of microbial dysbiosis in cancer progression remains understudied despite its potential significance. Emerging evidence suggests that targeting microorganisms and OS with antibacterial agents and antioxidants could offer novel therapeutic avenues. Natural resources (fruits, vegetables, and plants), particularly the *Curcuma* genus with over 100 species, have traditionally been used for their antimicrobial, antioxidant, and anticancer properties for many years. This review critically evaluates the therapeutic potential of *Curcuma*'s bioactive compounds as natural anticancer agents, emphasizing the interconnected roles of antimicrobial and antioxidant activities in modulating cancer progression. Our evaluation underscores *Curcuma*'s potential as an emerging alternative in cancer treatment, connecting its antimicrobial and antioxidant effects with its role in inhibiting cancer progression.

**Key words**: Antimicrobial activity, antioxidant activity, anticancer activity, *Curcuma* species.

## INTRODUCTION

Cancer begins when a cell develops out of control and then uses the blood and lymphatic systems to spread uncontrollably throughout the body until it destroys healthy cells and causes death.[1] It is a non-communicable disease that causes nearly 10 million deaths per year worldwide.[2] It's the 2nd worldwide top killer and 6th highest mortality rate in Bangladesh, and more than 8.2 and 9.6 million deaths were recorded in 2012 and 2018, respectively.[3,4] Moreover, around 12.7 and 14.1 million new cases were reported in 2008 and 2012, respectively.[4] The global cancer burden is estimated to rise to 29.5 million new cases, and 16.4 million people will lose their lives to cancer by 2040.[5] There are different modes (surgery, radiotherapy, chemotherapy, gene therapy, stem cell therapy, etc.) of cancer treatment, but the major drawbacks of these therapies are serious toxic effects on both cancer and normal cells.[6] Based on traditional knowledge and several research findings, it is known that herbal or plant-based therapy provides better cancer treatment with fewer side effects.[7] Numerous chemical compounds found in plants, such as tannins, alkaloids, terpenoids, flavonoids, pigments, and others, have vital biological roles, such as anti-inflammation, antioxidant, cancer-fighting, and contraceptive effects.[8] Plants are a great source of substances that can fight cancer and interfere with

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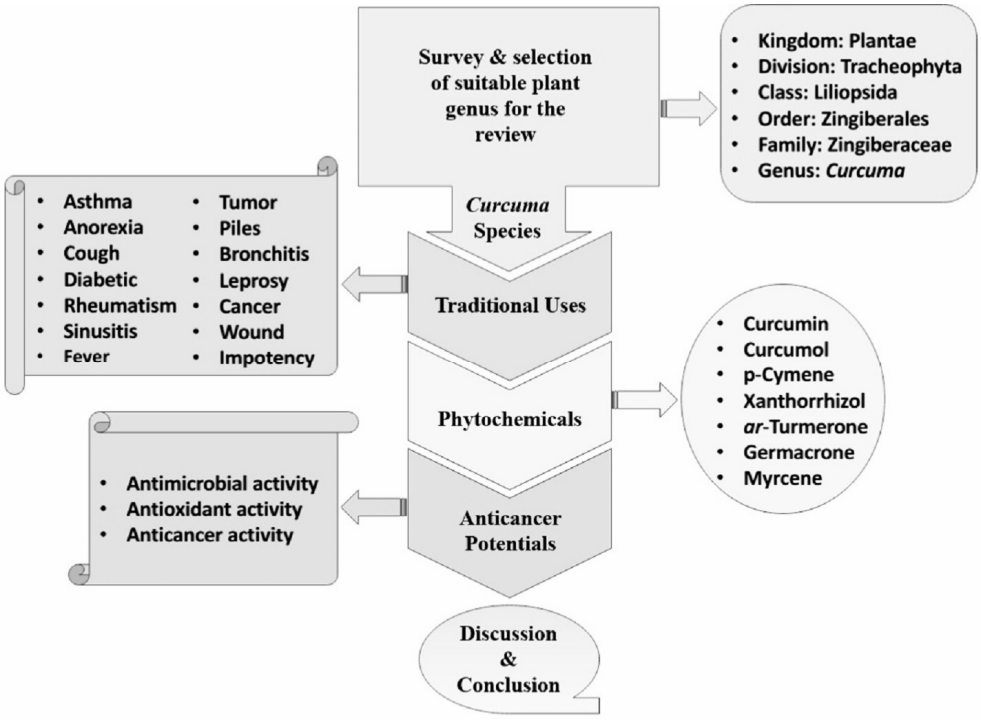
Dhaka Univ. J. Pharm. Sci. **24**(2): 231-249. 2025 (December)
DOI: https://doi.org/10.3329/dujps.v24i2.86375

the specific stage of carcinogenesis.[9] About 35,000 types of plants have been screened for suspected antitumor effects.[10] The diversity of the plant kingdom provides huge opportunities to establish new anticancer drugs.

**Graphical Abstract**




Microorganisms play important roles in the living body, especially in human health. Generally, the human body contains, on average, 30 trillion cells and 38 trillion bacteria.[11] A growing body of evidence proved that oncogenesis is greatly impacted by bacteria along with various non-virus microorganisms. Microbes can increase cancer risk by changing cellular constituents that maintain the ecosystems of the human body. For instance, *Salmonella typhi* is able to transform bile salts into substances that cause cancer.[12] It may cause hepatobiliary carcinoma,[13] and gallbladder cancer.[14] The synthesis of colibactin allows *Escherichia coli (E. coli)*, as well as *Enterobacteriaceae*, to inflict breaks on both strands of the DNA of host cells.[15] *Porphyromonas gingivalis* has strong antiapoptotic activity and can suppress chemically induced apoptosis.[16] There are microbes that can cause DNA damage by producing free radicals. *B. fragilis* is a microorganism that produces ROS, which can damage the host DNA, leading to the cause of colon cancer.[17,18] *Helicobacter pylori* were determined to promote cell proliferation, and cancerous growths were formed in *Mongolian gerbils.*[19] Many other microorganisms were found to cause oral cancer. These include several species of *Micrococcus, Staphylococcus aureus, Veillonella parvula, Prevotella melaninogenica*, and *Exiguobacterium oxidotolerans*.[20]

When cellular antioxidant defenses are inadequate to neutralize free radicals such as reactive nitrogen species (RNS) and Reactive Oxygen species (ROS), a condition known as oxidative stress (OS) occurs.[21] Free radicals contain unpaired electrons, which are highly reactive and unstable and want to become stable by reacting with large biological molecules like lipids, proteins, and DNA, resulting in abnormal functions of cells. Cancer and other devastating illnesses may have their roots in free radical damage to biological components.[22]

Antioxidants are substances that inhibit a wide variety of physiological functions in the body due to their ability to undergo oxidation at low concentrations.[23] Like free radicals, antioxidants, such as glutathione, alpha lipoic acid, superoxide dismutase, catalase, and coenzyme Q10, are produced endogenously.[24] They are not often good enough to control the free radicals. Consequently, antioxidants like vitamin E, carotenoids, and vitamin C must be supplied from outside sources to the biological system through diets,[25] which can balance free radicals generated within the body during different metabolic processes and play a vital role in order to shield our cells from free radical damage.[26] In the field of cancer treatment, antioxidants have recently gained a lot of attention due to their ability to quench ROS, which are involved in both the initiation and progression of cancer, as well as their role in assisting cancer and precancer cells in surviving after malignant transformation has already taken place.[27] Natural antioxidants can be found in plants.[28]

The use of plants in medicine has not diminished over the years. The World Health Organization estimates that there are 20,000 plants that are utilized for therapeutic purposes. Interest in researching medicinal plants and the powerful compounds they contain has grown in recent years.[29] More than a hundred species make up the genus *Curcuma*, which is in the family Zingiberaceae.[30] Species of *Curcuma* may be found all throughout the northern part of Australia, as well as in Southeast Asia, China, India, and New Guinea. *Curcuma* species are rhizomatous herbs consisting of underground parts, leafy shoots, and leaf blades. *Curcuma* rhizomes possess different colors, such as white, cream, yellow, pale yellow, orange, bluish-green, blue, and black on their inner side.[31] The aerial stems are pseudo-stems formed by leaf-sheaths, and flowers are epigynous, bisexual, and zygomorphic.[32] The rhizomes of *Curcuma* species are the main parts. They have several medical applications.[33] Traditional uses of *Curcuma* species include the treatment of tumors, hemorrhoids, allergies and asthma, inflammation, leprosy, injuries, and many more medical conditions, according to a number of studies.[34] Furthermore, they include several bioactive chemicals that may have significant pharmacological effects, such as antibacterial, antioxidant, neurologically protective, liver-protective, anti-inflammatory, tumor-fighting, and anticancer actions.[35]

**Taxonomical hierarchy** [36]

Kingdom**:** Plantae; Phylum**:** Tracheophyta;
Class: Liliopsida; Order**:** Zingiberales;
Family**:** Zingiberaceae; Genus**:** *Curcuma*

**Traditional uses.** The *Curcuma* species are traditionally important throughout the world. Certain formulations, such as paste, powder, and decoction of different parts (rhizome, leaf, stem, flower, herbaceous material) of the plants of the *Curcuma* genus, have been used to treat several ailments, such as tonsillitis, cough, fever, flu, goiter, rheumatic pains, dysentery, diarrhea, stomachache, malaria, heart disease, tuberculosis, kidney disorders, tumors, cancer, etc.[37] Traditional medicine formulas, including rhizomes, are most commonly used to treat cancer. *Curcuma* species are mostly found in the Asian subcontinent. Table 1 provides a brief explanation of their traditional usage.

**Phytochemicals isolated from *Curcuma* Genus.** *Curcuma* is a medical plant genus that is part of a big family. Numerous chemical phytochemicals have been revealed after extensive phytochemical investigations on *Curcuma* species. The major categories of phytochemicals were found to have flavonoids, tannins, saponins, carbohydrates, proteins, phenols, sterols, and terpenoids.[61] Dried rhizomes were the most common source for the majority of the more than 700 chemicals discovered in *Curcuma* species.[30] Table 2 provides a list of significant chemicals found in *Curcuma* species that have antibacterial, antioxidant, and anticancer properties.

**Table 1. A list of plants and parts of the plants belongs to the genus *Curcuma* with their locations where they are traditionally used as medicine.**

| Plant Name | Part | Indications | Region | References |
|---|---|---|---|---|
| *C. aeruginosa* Roxb. | Rhizome | Rheumatic disorder | Bangladesh | 38 |
| | Rhizome | White skin, asthma, tumor, piles, lung disease, contusion, soreness in the joints, diarrhea, dysentery, cough | India | 39 |
| | Rhizome | Flatulence, dyspepsia, diarrhea, parasitic infection | Thailand | 40 |
| *C. amada* Roxb. | Root | Impotency | Bangladesh | 41 |
| | Rhizome | Wound, cut, itching, sprain, skin disease | India, Myanmar and Thailand | 42 |
| | Rhizome | Stomachic, carminative, healing, sprain | Manipur, India | 43 |
| *C. angustifolia* Roxb. | Inflorencence | Bacterial and fungal infection, cough, diarrhea | Manipur, India | 43 |
| | Rhizome | Cut, wound, bleeding | Nepal | 44 |
| *C. aromatica* Salisb. | Rhizome and leaf | Indigestion, rheumatism, wound healing, dysentery, helminths infection | India | 45 |
| | Rhizome | Disease with blood stasis, cancer | China | 46 |
| *C. caesia* Roxb. | Tuber | Poisoning, liver pain | Bangladesh | 41 |
| | Rhizome | Asthma, tumor, piles, bronchitis, leprosy, cancer, wound, impotency, fertility, tooth ache, vomiting, allergy | India | 47 |
| *C. glans* K. Larsen and Mood | Rhizome | Headaches, tonsillitis, sore throats, nosebleeds, and herpes simplex virus | Thailand | 40 |
| *C. heyneana* Valeton & Zipj | Rhizome | Skin scrub, wound | Malaysia and Indonesia | 48 |
| *C. inodora* Blatt. | Tuber | Muscular pain | India | 49 |
| *C. leucorrhiza* Roxb. | Rhizome | Cough | India | 50 |
| | Rhizome | Enlarged liver and spleen, stomach ulcer, diabetes and cancer | Manipur | 51 |
| *C. longa* L. | Rhizome | Blood purification | Bangladesh | 52 |
| | Rhizome | Biliary disorder, anorexia, cough, diabetic wound, hepatic disorder, rheumatism, sinusitis | India | 53 |
| | Rhizome | Abdominal pain | China | 53 |
| *C. mangga* Valeton & Zijp | Rhizome | Abdominal illness, chest pain, fever, wound healing | Thailand | 54 |
| *C. montana* Roxb. | Rhizome | Fever | India | 55 |
| *C. parviflora* Wall. | Rhizome | Snakebite | Thailand | 56 |
| *C. phaeocaulis* Valeton. | Rhizome | Gastritis, controlling blood circulation | China | 57 |
| *C. rubescens* Roxb. | Rhizome | Poisoning | Indonesia | 37 |
| *C. thorelii* Gagnep. | Rhizome | Snakebite | Thailand | 56 |
| *C. xanthorrhiza* Roxb. | Rhizome | Skin disease | Thailand | 40 |
| | Rhizome | Illnesses affecting the digestive tract, liver, constipation, diarrhea with blood, dysentery, fever in children, hemorrhoids, high blood pressure, diabetes, cancer | Indonesia | 58,59 |
| *C. zedoaria* (Christm.) Roscoe | Rhizome | Diarrhea | Bangladesh | 52 |
| | Tuber | Cold and infection | India | 60 |
| | Rhizome | Complications such as indigestion, toothache, stagnation of blood, leukoderma, TB, enlarged spleen, common cold, infection, vomiting, and diarrhea | Indonesia | 48 |

**Table 2. List of major compounds isolated from *Curcuma* species having antimicrobial, antioxidant, and anticancer activity with mechanisms.**

| Isolated Compounds | Pharmacological Activities | Mechanisms | Plant Sources (*Curcuma* species) |
|---|---|---|---|
| β-Caryophyllene (I) | Cytotoxic [62] | Inhibits K562 human erythroleukemic cells [62] | *C. longa* L.[63] |
| 1,8-Cineole (II) | Antioxidant [64] | Suppresses Jurkat cell death induced by $NO_2$ [64] | *C. aeruginosa* Roxb.,[66] *C. amada* Roxb.,[67] *C. aromatica* Salisb.,[63] *C. caesia* Roxb.,[68] *C. harmandii* Gagnep.,[69] *C. longa* L.,[68] *C. zedoaria* (Christm.) Roscoe [63] |
| | Anticarcinogenic [65] | Causes apoptosis in Molt 4B and HL-60 leukemia cells [65] | |
| Curdione (III) | Antibacterial [70] | Disrupts microbial membranes, inhibits key enzymes, and induces oxidative stress through ROS generation [70] | *C. angustifolia* Roxb.,[72] *C. harmandii* Gagnep.,[69] *C. trichosantha* Gagnep.,[73] *C. zedoaria* (Christm.) Roscoe [74] |
| | Antifungal [70] | Increases membrane permeability, leading to leakage of vital intracellular contents and cell lysis [70] | |
| | Anticancer [71] | Increases expression of pro-apoptotic proteins such as cleaved caspase-3 and Bax [71] | |
| Curcumenol (IV) | Antibacterial [75] | Disrupts bacterial cell membranes and inhibit essential metabolic processes [75] | *C. aeruginosa* Roxb.,[68] *C. aromatica* Salisb.,[77] *C. harmandii* Gagnep.,[69] *C. longa* L.[78] |
| | Antitumor [76] | Suppresses Akt-mediated NF-κB activation and inhibits the p38 MAPK signaling pathway [76] | |
| α -Curcumene (V) | Antitumor [79] | Inhibits tumor cell proliferation [79] | *C. xanthorrhiza* Roxb.[79] |
| Curcumin (VI) | Antiviral [80] | Inhibits viral replication and entry [80] | *C. longa* L. [80] |
| | Antioxidant [80] | Scavenges free radical by neutralizing ROS [80] | |
| | Anticancer [80] | Downregulates NF-κB and other pro-survival signaling pathways [80] | |
| Curcumol (VII) | Antitumor [81] | Causes apoptosis in human lung adenocarcinoma ASTC-a-1 cells through a caspase-independent mitochondrial pathway [81] | *C. aromatica* Salisb.,[82] *C. trichosantha* Gagnep.,[73] *C. zedoaria* (Christm.) Roscoe [83] |
| Curzerene (VIII) | Antioxidant [84] | Scavenges free radical like DPPH• by donating hydrogen atom [84] | *C. aeruginosa* Roxb.,[86] *C. aurantiaca* Zijp,[87] *C. phaeocaulis* Valeton,[88] *C. purpurascens* Blume,[89] *C. zedoaria* (Christm.) Roscoe [74] |
| | Antiproliferative [85] | Arrests the cells in the G2/M cell cycle and promoted or induced apoptosis of SPC-A1 cells [85] | |
| Curzerenone (IX) | Anticancer [90] | Induces apoptosis via alteration of apoptosis related proteins (Bax, Bcl-2) and ROS mediated alterations in the MMP [90] | *C. aeruginosa* Roxb.,[66] *C. amada* Roxb.,[91] *C. angustifolia* Roxb.,[92] *C. aromatica* Salisb.,[93] *C. inodora* Blatt.,[94] *C. zedoaria* (Christm.) Roscoe [95] |
| p-Cymene (X) | Antioxidant [96] | Decreases lipid peroxidation and nitrite content, increase SOD and catalase activity [96] | *C. aromatica* Salisb.[63] *C. longa* L.,[98] *C. xanthorrhiza* Roxb.,[40] *C. zedoaria* (Christm.) Roscoe [63] |
| | Antiviral [97] | Impairs the replication of viruses [97] | |
| | Antibacterial [97] | Exhibits broad-spectrum antibacterial properties [97] | |
| | Antifungal [97] | Inhibits mycelial growth and aflatoxin production by down-regulating genes [97] | |
| | Antitumor [97] | Reduces tumor formation by modulating inflammatory factors and promoting beneficial gut microbiota[97] | |

| | | | |
|---|---|---|---|
| 8,9-Dehydro-9-formyl-cycloisolongifolene (XI) | Antioxidant [99] | Scavenges free radicals [99] | *C. aeruginosa* Roxb.,[100] *C. aromatica* Salisb.,[99] *C. phaeocaulis* Valeton [88] |
| | Antitumor [99] | Suppresses cancer cell migration and invasion [99] | |
| β-Elemene (XII) | Antitumor [101] | Inhibits cellular proliferation in cancer cells [101] | *C. aromatica* Salisb.[68] *C. harmandii* Gagnep.,[69] *C. longa* L.,[68] *C. phaeocaulis* Valeton,[88] *C. zedoaria* (Christm.) Roscoe [74] |
| Germacrone (XIII) | Antibacterial [102] | Disrupts bacterial cell membranes [102] | *C. aeruginosa* Roxb.,[105] *C. angustifolia* Roxb.,[106] *C. aromatica* Salisb.,[107] *C. glans* K. Larsen and Mood,[40] *C. harmandii* Gagnep.,[69] *C. inodora* Blatt.,[94] *C. longa* L.,[108] *C. zedoaria* (Christm.) Roscoe [95] |
| | Antioxidant [103] | Scavenges free radical [103] | |
| | Antitumor [104] | Induces G2/M cell cycle arrest and promoting apoptosis [104] | |
| Myrcene (XIV) | Antioxidant [109] | Scavenges free radical [109] | *C. amada* Roxb.,[63] *C. longa* L.,[110] *C. mangga* Valeton and Zijp,[66] |
| α-Phellandrene (XV) | Antioxidant [111] | Scavenges nitric oxide [111] | *C. longa* L.,[112] *C. zedoaria* (Christm.) Roscoe [63] |
| β-Pinene (XVI) | Antimicrobial [113] | Inhibits phospholipase and esterase activities [113] | *C. aeruginosa* Roxb.,[68] *C. glans* K. Larsen and Mood,[40] *C. harmandii* Gagnep.,[69] *C. longa* L.,[115] *C. mangga* Valeton and Zijp,[116] *C. xanthorrhiza* Roxb.[40] |
| | Anticancer [114] | Reduces cell viability [114] | |
| β-Sesquiphellandrene (XVII) | Antioxidant [84] | Scavenges free radical like DPPH• by donating hydrogen atom [84] | *C. aromatica* Salisb.,[99] *C. longa* L.,[118] *C. zedoaria* (Christm.) Roscoe [68] |
| | Anticancer [117] | Suppresses cancer cell colony formation and induce apoptosis [117] | |
| Terpinolene (XVIII) | Antioxidant [119] | Scavenges free radical [119] | *C. longa* L. [120,121] |
| *ar*-Turmerone (XIX) | Antifungal [70] | Increases membrane permeability, leading to leakage of vital intracellular contents and cell lysis [70] | *C. aromatica* Salisb.,[124] *C. caesia* Roxb.,[125] *C. longa* L.,[78] *C. purpurascens* Blume,[89] *C. rubescens* Roxb.[126] |
| | Anticancer [71] | Increases expression of pro-apoptotic proteins such as cleaved caspase-3 and Bax [71] | |
| | Cytotoxic [122] | Induces apoptosis [122] | |
| | Antitumor [79,123] | Inhibits tumor cell proliferation [79] | |
| Xanthorrhizol (XX) | Antimicrobial [127] | Causes leakage of intracellular components and eventual cell death [127] | *C. alismatifolia* Gagnep.,[128] *C. angustifolia* Roxb.,[72] *C. aromatica* Salisb.[129] |
| | Antioxidant [127] | Scavenges free radical [127] | |
| | Anticancer [127] | Induces apoptosis and cell cycle arrest, inhibits NF-κB [127] | |

**Antimicrobial activity of *Curcuma* Species.** When substances have antimicrobial properties, they stop microbes from multiplying, stop them from forming colonies, and eventually kill them.[130] Many different kinds of antimicrobial compounds are available for use in the fight against microbes; they include those that are antimicrobial, antiviral, antifungal, antiprotozoal, etc. Currently, antimicrobial medicines are used to treat cancers linked to viruses along with bacteria. Cancers of the stomach, cervix, hematological system, liver, and brain often require antimicrobial medication treatment. Antimicrobials not only have direct anticancer benefits, but they are also useful when taken in conjunction with other traditional anticancer treatments.[131] For example, anthracycline antibiotics (doxorubicin and daunomycin) and some fluoroquinolones are very effective in cancer treatment.[132,133]

**Antibacterial activity.** Antibacterial activity is the ability to destroy bacteria or suppress their growth or their ability to reproduce.[134,135] Several antibacterial agents have been discovered from different sources through extensive studies over 50 years. It has been reported that several bacterial strains, such as *Bartonella spp.*, *Lawsonia intracellularis*, and *Citrobacterro dentium*, etc. are able to stimulate cell division.[136,137] Besides, *Helicobacter pylori* can cause gastric MALT lymphomas, gastric carcinomas, eye, breast, and lung

cancer.[138] According to the recommendations of the FDA and WHO, the treatment of *Helicobacter pylori* infection involves the use of proton pump inhibitors in conjunction with amoxicillin and clarithromycin.[139] Low-grade MALT lymphomas are currently being treated with these antibiotics as a first line of defense since they are safe, inexpensive, and effective.[140] The rise of MDR-resistant bacteria has rendered antimicrobial medication development insufficient for the provision of adequate healthcare in the modern day.[141] Therefore, identification of new antibacterial agents is very much essential. Antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, and *E. coli* was observed in the water-soluble extracts of *C. longa* rhizome.[142] *C. longa* exhibited antibacterial activity against *Staphylococcus aureus* as well as *Bacillus subtilis* in the form of methanolic extract.[143] Extracts from *C. zedoaria* in petroleum ether, chloroform, and methanol showed antibacterial action against *Escherichia coli* with *Pseudomonas aeruginosa*, *Bacillus cereus*, and *Staphylococcus aureus.*[144] A significant inhibitory effect against *Staphylococcus aureus* as well as *Bacillus cereus* was observed in the essential oil isolated from the rhizome of *C. xanthorrhiza*.[40,145] *C. malabarica* tuber extracts in acetone alongside n-hexane showed antibacterial action against *Staphylococcus aureus*.[60] The tuber extract of *C. leuchorrhiza*, exhibited potent anti-Staphylococcal action.[146] There was antibacterial action against several bacterial strains demonstrated by petroleum ether and chloroform extracts of *C. aromatica* rhizome. These strains included *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Shigella sonnei*, and *Shigella dysenteriae.*[147] The antibacterial activity of the essential oil of *C. phaeocaulis* ranged from mild to high, and it was tested against *Staphylococcus aureus*, *E. coli*, and *Pseudomonas aeruginosa.*[88]

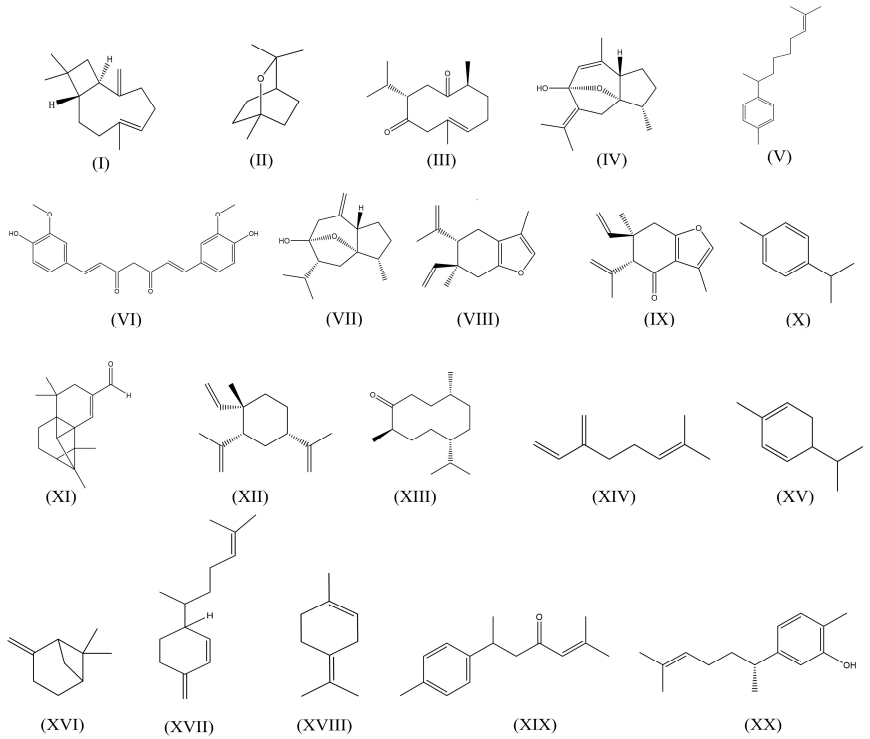



Figure 1. Structure of some phytochemicals found in *Curcuma* species.

**Antiviral activity.** There is a need to find novel chemicals that are effective against viruses since there are currently no treatments that work, because antiviral medication resistance is becoming more

common, and because some antiviral medicines are rather expensive.[148] On the other hand, current antiviral medications may not always have enough antiviral efficacy or be well-tolerated by all patients.[149] An agent that kills a virus or suppresses its ability to replicate is known as an antiviral agent.[150] Multiple investigations have demonstrated that certain antiviral drugs possess anticancer properties.[151] For instance, ribavirin, an antiviral agent, was reported to have beneficial effects in acute myeloid leukemia.[152] Also, another antiviral drug called zidovudine can inhibit telomerase and make glioma cells more radiosensitive, which means it helps fight cancer.[153] For a long time, people have looked to plants for a variety of phytochemicals, which have many biological uses, especially antiviral properties.[154] Antiviral and anti-viremia effects were shown in *C. longa* extract against DENV-2.[155] Several viruses, including HIV, influenza, herpes simplex virus type 1, herpes simplex virus type 2, Coxsackievirus, herpes simplex virus type 3, herpes simplex virus type 4, herpes simplex virus type 5, HTLV-1, and many more, have been shown to be susceptible to curcumin's antiviral effects.[156] Moreover, curcumin exhibited antiviral activity against the Zika and Chikungunya virus.[157] A robust antiviral action against the hepatitis-C virus was observed in the ethanol extracts of *C. domestica*, *C. xanthorrhiza*, and *C. heyneana.*[158]

**Antifungal activity.** Fungi play some important roles in cancer. It can increase the risk of cancer by activating an ancient, first-responder part of the immune system, the complement cascade.[159] Cancer patients undergoing myelotoxic treatment are also at increased risk of developing invasive fungal infections (IFI), which can be fatal.[160] The latest research indicates that *Candida albicans* can promote cancer through many pathways.[161] To have antifungal activity means to be able to kill or slow the growth of fungus while causing little harm to the host.[162] Significant antifungal activity against *Candida albicans* and *Saccharomyces cerevisiae* was demonstrated by the essential oil of *C. phaeocaulis.*[88] There have been reports of *C. longa* having antifungal properties. *Phytophthora infestans*, *Rhizoctonia solani*, and *Erysiphe graminis* were among the fungi that *C. longa* hexane extract inhibited. *Rhizoctonia solani*, *Phytophthora infestans*, *Puccinia recondita*, and *Botrytis cinerea* were all inhibited by the antifungal effects of *C. longa* ethyl acetate extract.[163] Moreover, *C. longa* possessed broad-spectrum antifungal activity against a wide number of pathogenic fungi, including *Aspergillus flavus*,*Fusarium verticillioides*, *Curvularia pallescens*, *Colletotrichum falcatum*, *Aspergillus niger*, *Aspergillus terreus*, *Fusarium oxysporum*, *Fusarium moniliforme*, *Fusarium graminearum*, *Phoma wasabiae*, *Alternaria alternate*, *Botrytis cinerea*, *Chaetomium olivaceum*, *Penicillium pallidum*, *Mycogone perniciosa*, *Verticillium dahlia*, etc.[163] The effects against *Candida albicans* were seen in the essential oil extracted from the rhizome of *C. xanthorrhiza*. Multiple investigations have demonstrated that *C. aromatica* has potent antifungal effects against *Saccharomyces cerevisiae* and *Candida albicans*.[164] Acetone and chloroform fractions of *C. xanthorrhiza* exhibited antifungal activity against *Aspergillus fumigatus*, *Epidermophyton sp.*, *Penicillium sp.*, and *Trichophyton rubrum*. The antifungal activity of *C. soloensis* was found to be weak to moderate.[165] *C. longa*, *C. amada*, *C. xanthorrhiza*, and *C. zedoaria* are just a few of the *C.* species that have been found to have antifungal activity against *Fusarium solani sensu lato*, according to a recent study.[166]

**Antioxidant activity of the species of the Genus *Curcuma.*** Unstable chemicals known as free radicals are key players in carcinogenesis because of their ability to destroy DNA within cells. Enzymatic and non-enzymatic processes both contribute to the production of free radicals in the body. In the respiratory chain, phagocytosis, prostaglandin production, and the cytochrome P-450 system, enzyme reactions play an important role; in contrast, non-enzymatic reactions include oxygen's interactions with organic molecules and those started by ionizing processes.[167] Antioxidants are chemicals that halt the oxidation process; they achieve this by locating and destroying free radicals.[168] ROS induces

oxidative carcinogenic damage in DNA. Antioxidants can protect from cancer by scavenging ROS.[169] The free radical scavenging activity was robust due to the curcumin found in both the ethanolic and methanolic extracts of *C.* longa. Antioxidant activity was weak to moderate in the ethanolic *C. aromatica* extracts.[170] *C. purpurascens*, *C. mangga*, *C. phaeocaulis*, *C. heyneana*, and *C. aeruginosa* were among the several *Curcuma* species whose methanolic extracts showed DPPH radical scavenging.[171] Moreover, chloroform extract of *C. heyneana* scavenged DPPH radicals.[172] Ethyl acetate fraction of *C. manga* exerted strong $H_2O_2$-scavenging activity.[173] *C. caesia* extracts in chloroform, benzene, and ethyl acetate were highly effective antioxidants. Chloroform extract outperformed the others in terms of its ability to donate electrons and scavenge free radicals.[174] *C. xanthorrhiza* has been found to possess potent DPPH radical scavenging capabilities in both its ethanolic and aqueous extracts.[175] In addition, *C. angustifolia* exhibited strong antioxidant activity.[176] Different studies have shown that *C. amada*, *C. aromatica*, *C. aurantiaca*, *C. comosa*, *C. latifolia*, *C. longa*, *C. parviflora*, *C. xanthorrhiza*, and *C. zedoaria* were found to have strong antioxidant activity.[171,177]

**Anticancer activity of the species of the Genus *Curcuma*.** The capacity of a substance or agent to combat cancer is known as its anticancer activity.[178] The drug or agent used to combat cancer has the potential to stop, slow, or even reverse the disease's development. Current anticancer medications have their roots in plant sources, accounting for over 80% of the total.[178] It was shown that both the oral and topical administration of *C. longa* extract significantly reduced the risk of N-methyl-N-nitrosourea (MNU)-induced mammary cancer in rats.[179] Ethanol extract of *C. longa* rhizome was cytotoxic to lymphocytes and Dalton's lymphoma, and it inhibited cell proliferation in CHO cells.[180] The n-hexane extract of *C. longa* was found to have cytotoxic effects on the A549 human lung cancer cell line.[181] In addition, several cancer cell lines, including U937, Molt4, A549, and HeLa, were found to have anticancer activity when treated with *C. longa*.[182,183] The anticancer effects of curcumin, a compound derived from the root of the *C. longa*, were shown in a dose- and time-dependent manner when tested on human breast cancer cells (MCF-7).[184] Anticancer activity was demonstrated by several *C. amada* extracts against NCI-H460 and A-549 cells, which are human large-cell lung carcinomas.[185] *C. aromatica* with multiple ingredients was reported to show anticancer property.[186] Human colon carcinoma (LS-174-T) cells were found to be resistant to the anticancer effects of an aqueous *C. aromatica* extract.[187] Further investigation revealed that *C. aromatica* inhibited cell proliferation in Hepa1-6 human hepatocellular carcinoma cells by apoptosis induction.[188] *C. caesia* was reported to show anticancer properties against diethyl nitrosamine (DEN)-induced liver cancer.[189] Mice implanted with Ehrlich's ascites carcinoma (EAC) cells exhibited substantial anticancer activity when treated with an ethanol extract of *C. caesia*.[190] A number of cancer cell lines were shown to have their growth inhibition mechanisms exhibited by extracts of *C. mangga*. These cell lines included MCF-7, HT-29 (human colorectal adenocarcinoma), and PC-3 (human prostate cancer). Furthermore, *C. mangga* exhibited potent cytotoxic effects on Raji cells produced by the Epstein-Barr virus early antigen (EBV-EA).[187] The HT-29 cells were cytotoxically affected by the *C. mangga* n-hexane and ethyl acetate extracts.[191] The oils of *C. phaeocaulis* were highly effective in killing LNCaP and B16 cells.[88] Inducing apoptosis by boosting ROS production, reducing $\Delta\Psi m$, modulating Bcl-2 family protein expression, and activating caspases, several chemicals found in the ethanol extract of *C. phaeocaulis*, including furanodienone, germacrone, and furanodiene, halted the growth of MCF-7 cells.[192] It was shown that *C. purpurascens* exhibited anticancer properties by triggering cell death in HT-29 human cancer cells.[193] The hexane extract of *C. xanthorrhiza* exhibited strong cytotoxic activities.[194] Furthermore, when tumor-bearing mice were administered 7,12-dimethylbenz[α]anthracite and 12-O-tetradecanoylphorbol-13-acetate, the methanol extract of *C. xanthorrhiza* exhibited anticancer

effects.[195] In addition, several types of cancer, including those of the colon, cervix, liver, skin, lungs, tongue, mouth, throat, and ovaries, have demonstrated anticancer effectiveness when treated with *C. xanthorrhiza*.[127] Isopropyl extract of *C. zedoaria* exerted strong anticancer activity against human NCI-H40 cell line,[196] and hexane extract of *C. zedoaria* exerted cytotoxicity against human cervix squamous cell carcinoma (SiHa) and human HepG2.[197] *C. zedoaria* exerted antitumor activity against EAC cell in mice.[198]

## DISCUSSION

In recent years, significant progress has been made in cancer treatment through diverse therapeutic strategies. However, the emergence of drug resistance in cancer cells has become a major challenge, fueling the search for novel anticancer agents with distinct mechanisms of action. The role of microbes in cancer is increasingly recognized; several studies suggest that certain bacterial strains can contribute to carcinogenesis by promoting malignant transformation within cells. In addition, during cancer, treatment microbial infections may impair the therapeutic efficacy, leading to serious complications.[199] Antibiotics have shown encouraging results in treating a variety of malignancies, and their use in treating infectious infections has led to significant strides in combating a large number of germs. Interestingly, antibiotics not only control infections but have also been reported to exert direct anticancer effects in some malignancies. When it comes to cancer therapy, antioxidants are a crucial component. It reacts with oxidized free radicals and removes them from cells, protecting them from harm.[200,201] Antioxidant supplementation, used by 87% of cancer patients, has been reported to enhance chemotherapy outcomes by improving drug efficacy.[202] Protecting cells against free radicals, which might cause chemotherapy-induced OS, is a crucial function of endogenous antioxidants.[203] Exogenous antioxidants must be consumed through food in order to prevent cell damage caused by free radicals if the body does not produce enough endogenous antioxidants. Dietary sources such as vegetables, fruits, synthetic antioxidants, and supplements serve as important contributors of exogenous antioxidants.[204]

The genus *Curcuma* contains a number of promising medicinal plants having pharmacological activities. Several studies have shown that the *Curcuma* species possess anticancer, antimicrobial, antioxidant, and antitumor activity. In particular, *C. longa* and other *Curcuma* species have demonstrated anticancer potential across various cancer cell lines, including A549, U937, Molt4, MCF-7, and HeLa.[205] When tested on MCF-7 human breast cancer cells, curcumin, a compound from the spice *C. longa*, showed strong anticancer effects. Moreover, furanodienone, germacrone, and furanodiene from *C. phaeocaulis* reduced the proliferation of MCF-7 cells by triggering apoptosis by increasing the generation of ROS, reducing mitochondrial membrane potential ($\Delta\Psi m$), controlling the expression of Bcl-2 family proteins, and activating caspases. Additionally, *C. xanthorrhiza* demonstrated anticancer effects in tumor-bearing mice treated with 7,12-dimethylbenz[α]anthracene and 12-O-tetradecanoylphorbol-13-acetate.[206] Collectively, these findings highlight the therapeutic potential of *Curcuma* species as sources of anticancer, antioxidant, and antimicrobial agents, warranting further investigation into their mechanisms and clinical applicability.

## CONCLUSION

This is a review paper, and all the information has been collected from papers such as indexed Scopus journals, ScienceDirect, and similar sources. In this review, a wide number of the species of the *Curcuma* genus have been discussed to provide a link between their anticancer potentiality and their antimicrobial and antioxidant activities. Many nations, including Bangladesh, employ herbal components from the *Curcuma* genus, which has over 100 species, in traditional medical treatments. Additionally, rural people have long employed *Curcuma* species for the treatment of many maladies,

such as carcinoma, hemorrhoids, allergies and asthma, inflammation, leprosy, wounds, and so on, since ancient times. The traditional medicinal usage of these species is backed by their diverse array of bioactive phytochemicals. In addition, we noticed that the species of the *Curcuma* genus and their phytochemicals were found to show potential anticancer activity in different ways, and it was associated with antioxidant and antimicrobial activities. However, very few species of this genus have been studied so far. Therefore, there is a huge scope for working on the remaining the species to discover new anticancer drugs with the least toxicity.

## ACKNOWLEDGEMENT

The authors are grateful to the Department of Pharmacy, University of Rajshahi, Bangladesh, for providing a desktop facility with an internet connection.

### Funding

The authors declare that they do not have any financial support.

### Conflict of Interest

The authors declare that they do not have any competing interest.

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**List of Abbreviations**

A549: Human lung-cancer cells
CHO: Chinese hamster ovary
DNA: Deoxy ribonucleic acid
ROS: Reactive oxygen species
RNS: Reactive nitrogen species
EAC: Ehrlich's ascites carcinoma
HIV: Human immunodeficiency virus
HSV-1: Herpes simplex virus 1
HSV-2: Herpes simplex virus 2
HCV: Hepatitis C virus
HPV: Human papillomavirus
JEV: Japanese encephalitis virus
HTLV-1: Human T-lymphotropic virus 1
MNU: N-methyl-N-nitrosourea
$IC_{50}$: Half-maximal inhibitory concentration
EBV-EA: Epstein-Barr virus early antigen
HeLa: Human cervical-adenocarcinoma cells
HepG2: Human liver hepatocellular carcinoma cells
HT-29: Human colorectal adenocarcinoma cells
PC-3: Prostate cancer cells
Hepa1-6: Hepatocellular carcinoma
DEN: Diethyl nitrosamine
LS-174-T: Human colon carcinoma cell
NCI-H460: Human large cell lung cancer
MCF-7: Human breast cancer cell
LNCaP: human prostate acedocarcinoma cells
B16: Melanoma cells
DPPH: 2,2-diphenyl-1-picrylhydrazyl
U937: Myeloid leukemia
Molt4: Lymphoblastic leukemia