

EFFECT OF ANTI-BIOFILM POTENTIAL OF DIFFERENT MEDICINAL PLANTS: REVIEW

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ABSTRACT

Medicinal plant products are the natural products which have been very useful for human to cure various ailments and as an alternative medicine for conventional therapy. However, bacteria in natural environments are mainly exist in biofilm formation and are more susceptible to cause severe infections than the planktonic counterparts. Biofilm is associated with impaired epithelization and granulation tissue formation and also promotes a low-grade inflammatory response that interferes with wound healing. Since the infection caused by biofilm is often very difficult to treat, there is a need to find a new active anti-biofilm agent. In recent past, interest in the therapeutic and nutritional properties of various medicinal plants and its natural phytochemical compounds which have established for their anti-biofilm activities has been increased gradually. In this review, we have described various aerial parts of medicinal plants which have anti-biofilm effect which was evaluated against biofilm producing different bacterial pathogens and antimicrobial agents which are responsible to cure wound healing.

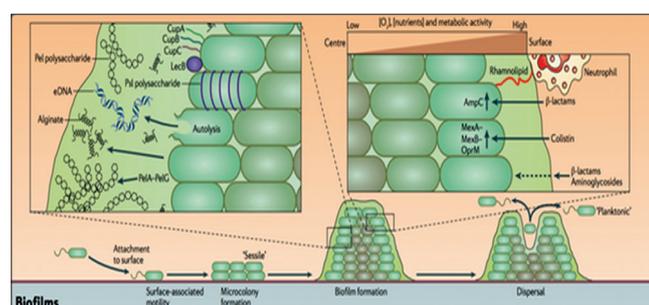
Keywords: Medicinal plants, Phytochemical, Anti-biofilm activity.

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INTRODUCTION

Bacterial biofilm is defined as microbes derived sessile communities of microorganism attached to the living or inert surface and is embedded in the extracellular polymeric substances (EPS) [1]. The role of the biofilm is to attach to the epithelia layer of multicellular organisms, abiotic surfaces, and interfaces between air and water. Some bacterial biofilms have been reported to have useful effects on food chains, sewage treatment of plants, to eliminate petroleum oil or hydrocarbon spillage from the oceans and human chronic bacterial infections. In 1970s, the research on biofilm has been extensive, with significant evidence showing that bacteria exist predominantly as a biofilm phenotype in medical, natural and industrial ecosystem [2]. Today, biofilm is implicated in numerous bacterial infections including those associated with the urinary tract, ear, sinuses, cystic fibrosis, indwelling catheters, chronic wounds, and periodontal disease.

Biofilm is often characterized by surface attachment, structural heterogeneity, genetic diversity, complex community interaction, and an extracellular matrix of polymeric substances. Single celled organisms generally exhibit two different modes of behaviors [3]. Mostly bacterial embedded biofilms arrive in a stationary phase, during these phase physicochemical interactions take place and produced a slime layer, followed by these lower diffusion of active molecules, and then a lesser susceptibility of antimicrobial killing [4]. The bacterial biofilm shows a different metabolic state than planktonic bacteria, mainly during transcription and cell interaction. The mode of biofilm growth results in an increased bacterial resistance against antimicrobial agent and host defense mechanism is now well-documented, and these was highlights the importance of effective biofilm management in chronic infections [3].



LIFE CYCLE OF BIOFILMS

The life cycle of biofilm contains four general stages: First the cells are adhere to a substrate such as polysaccharides or glycoprotein and form microcolonies [5]. As more as cell aggregates, the concentration of chemical signals reaches a point that triggers genetic changes in the cells that cause them to bind tightly to the surface and neighboring cells. These microcolonies produce a thick extracellular matrix composed of exopolysaccharides (EPS), protein, extracellular DNA and other polymer that forms a protective physical barrier around the bacteria, allowing them to grow into a mature biofilm of complex communities that are capable of chemical communication, a process called quorum sensing (QS). QS molecules have been shown to be essential for biofilm formation [6,7].

Once the biofilm reaches particular cell density, point of saturation, biofilm turns off the expression of gene producing EPS products and reactivates flagella motility genes to disperse new planktonic cells from disseminating biofilm in search of new environment [8]. The relationship between the host and its microbial communities is carefully balanced, but under certain conditions, it can break down and result in infectious diseases. Microbes of biofilm secrete specific toxins, generate a hypoxic microenvironment, and the host immune system, from all of which may contribute to delayed wound healing [9]. According to a recent publication announcement from the National Institutes of Health, more than 60% of all microbial infections are caused by biofilms [10].

The exploration for alternative therapies is a required and using nowadays, for examples, animal or natural plant products, and/or combination with antibiotics or synthetic compounds seems to be one of the auspicious solutions [11]. Drugs which are derived from natural sources are major interest, and thus they are focused for activity against biofilm producing microorganism. Till now, 80% of human bacterial infections are formed by biofilm-associated, mostly infections are frequently being caused by *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* [12].

Plant-based compounds are widely accepted due to the perception that they are safe, easily available, less expensive, and also have no side effects. Plant-based drugs have greater potential for producing new

drugs and used in traditional medicine to treat the immune booster, chronic and several infectious diseases. The World Health Organization estimated that about 80% of the world populations depends on traditional herbal medicine for their primary healthcare [13]. There are approximately 500,000 plant species occurring worldwide and <1% has been screened for biological active compound [14].

Plant has the ability to synthesize a wide variety of phytochemical compounds as secondary metabolites. Many of the phytochemical have been used to effectively treatment of various ailments for humanity. The different chemical and components extracts of many plants have been proved to be possible sources for new drugs [5]. The plant-derived substances are under research for possible application in pharmaceutical industry includes crude extracts of leaves, stems, barks, root, essential oils, and novel compounds isolated from any of these sources. The effects of plant extracts to prevent biofilm formation and adherence have been shown in earlier studies [8].

Nowadays biofilm is considered major target for pharmacological development of drugs. For example, in future it may be possible to formulate wound care products, such as rinses or dressing, debridement pads, gel, anti-biofilm agent that penetrate through biofilm EPS,

thus exposing the bacteria and increasing their susceptibility to antimicrobials. This review can be contribute to the development of a new approach to prevent and to treat biofilm infections (Table 1).

CONCLUSION

Large group of traditional medicinal plants is used for different medicinal properties, which have a greater potential to cure various diseases. Furthermore, various extracts from different medicinal plant parts such as leaves, flowers, essential oils, root, and barks were also found to possess the anti-biofilm activity. Nowadays, it is known that resistance to antibiotic is often caused by biofilm formation of microbial pathogens. Therefore, the development of effective and safe medicine properties of plant extracts, which have antimicrobial activity have developed in both academic and industrial sectors. In this review, we have described that various aerial parts of traditional medicinal plants were able to inhibit the biofilm formation from various strains, were isolated from different infection sources such as wound, septicemia, urinary tract infections showing its potential value as an alternative to anti-infection agent. Thus, there remaining tremendous scope for a further research study of these traditional medicinal plants to establish their therapeutic efficacy and molecular mechanism of anti-biofilm effect of the bioactive compound.

Table 1: List of medicinal plants which have anti-biofilm activity

Name	Parts used	Types of plant extracts	Medicinal uses of plant	Pathogens used for biofilm	Activities	References
<i>Azadirachta indica</i>	Leaves	Methanol	Various ailments, act as contraceptive and sedative agent	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i>	Antibacterial, anthelmintic and antibiofilm activities	[15,16]
<i>Vitex negundo</i>	Leaves	Methanol, ethyl acetate, petroleum ether, and hexane	Wound, ulcer, asthma, ophthalmic, verminosis, bronchial smooth muscles relaxant, nervine and aphrodisiac	<i>Escherichia coli</i>	Antinociceptive, antimicrobial, anti-inflammatory, antipyretic, anticonvulsant, insecticidal and pesticidal activities	[15]
<i>Tridax procumbens</i>	Leaves	Methanol, ethyl acetate	Bronchial, dysentery, hair growth promotes, and insect repellent	<i>Escherichia coli</i>	Immunomodulatory, wound healing, hepatoprotective, antidiabetic, antiobesity, antimicrobial and anti-inflammatory activities	[15,17]
<i>Ocimum tenuiflorum</i>	Leaves	Methanol	Coughs, colds, vomiting, flatulence, heal peptic ulcers	<i>Escherichia coli</i>	Wound healing effect, radio protective, anti-carcinogenic properties, anti genotoxic, neuroprotective effect, and larvicidal property	[15]
<i>Piper lonum</i> <i>Piper nigrum</i>	Grains	Methanol, petroleum ether, chloroform and ethyl acetate	Malaria, asthma, cough, diabetes and heart problems	<i>Streptococcus pyogens</i>	Anti-biofilm, antibacterial, antioxidant activities	[18]
<i>Pittosporum tetraspermum</i>	Leaves	Ethyl acetate	Chronic bronchitis, rheumatism, skin diseases, cutaneous diseases and leprosy	<i>Escherichia coli</i> , <i>Salmonella typhi</i> , <i>Pseudomonas aeruginosa</i>	Antibacterial, antifungal, anti-biofilm, antioxidant and anticancer activities	[19]
<i>Couroupita guianensis</i>	Fruits	Chloroform	Tumors, pain and hypertension	<i>Pseudomonas aeruginosa</i>	Antimicrobial, antimycobacterial, antifungal, antiseptic, antibiotic, anti-biofilm anti-inflammatory activities.	[20]

(Contd...)

Table 1: (Continued)

Name	Parts used	Types of plant extracts	Medicinal uses of plant	Pathogens used for biofilm	Activities	References
<i>Chamaemelum nobile</i>	Flowers	Aqueous	Malaria, peptic ulcers, wound healing	<i>Pseudomonas aeruginosa</i>	Anti-inflammatory, antimicrobial, antiseptic, anti-swarming activities	[21]
<i>Vinca minor</i>	Leaves	Aquatic, acetone and ethyl acetate	Supporting brain metabolism	<i>Proteus mirabilis</i> , <i>Pseudomonas aeruginosa</i>	Antimicrobial, anti-biofilm activities	[22]
<i>Lavandula angustifolia</i>	Essential oils	Major constituents linalool, alpha terpineol	Cosmetically and therapeutically	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	Anti-biofilm, antibacterial, antifungal activities and antidepressive properties	[23]
<i>Melissa officinalis</i>	Essential oils	Liquid	Gastrointestinal disorders, stress, sleep disorder, spasmolytic, Alzheimer diseases	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	Antibacterial and antifungal	[23,24]
<i>Ficus sansibarica</i>	Fruits, leaves, stem barks	Cold extract methanol, hexane, dichloromethane, ethyl acetate and methanol	Wound healing, tuberculosis, diabetes malaria and HIV	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	Antioxidant, antibacterial, antifungal, antidiabetics, anticancer, anti-inflammatory and antihyperglycemia	[25]
<i>Pongamia pinnata</i>	Leaves	Methanol	Antihelminthic, gonorrhoea, leprosy, inflammation, piles and wound	<i>Streptococcus mutans</i>	Antiplasmodial, anti-inflammatory, antidiarrhoeal, antioxidant, anti-hyperammonemi, antiulcer, antihyperglycaemic and antilipidperoxidative activities	[26]
<i>Zingiber officinale</i>	Root	Ethanol and water	Arthritis, rheumatism, muscular aches, pains, sore throats, dementia, hypertension, and infection diseases	<i>Pseudomonas aeruginosa</i>	Antibiofilm activity, antioxidant, antiemetic, antitumorigenic, and anti-inflammatory activities	[27,28]
<i>Coriandrum sativum</i>	Seed	Ethanol and water	Drug for indigestions, worms, pain in joints and rheumatism	<i>Staphylococcus aureus</i>	Antibiofilm activity	[28]
<i>Leucas aspera</i>	Whole plant	Methanol, ethyl acetate, petroleum ether, and hexane	Scabies, psoriasis, snake bite, laxative, and diaphoretic	<i>Streptococcus pyogenes</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	Antibacterial, anti-inflammatory, antidiarrheal, antioxidant, antibacterial, hepatoprotective, anti-diabetic activities and central nervous system activity	[29]
<i>Artocarpus lakoocha</i>	Bark	Aqueous extracts	Wound, skin lesion, and cosmetic	<i>Candida albicans</i> , <i>Candida tropicalis</i> , <i>Candida dubliniensis</i>	Antiviral, antibiofilm, anticandidal, anti-inflammatory, anticancer activities, anti-HIV properties, anti-skin aging and atherosclerosis	[30,31]
<i>Murraya koenigii</i>	Leaves, essential oil	Ethanol, aqueous	Tonic, chronic wound, stomachic, inflammation, itching, vomiting, cure piles	<i>Pseudomonas aeruginosa</i>	Anti-biofilm, antiulcer, antidiarrhoea, antidiabetics activities, cholesterol reducing property, phagocytic activity, and more useful medicinal properties	[32,33]

(Contd...)

Table 1: (Continued)

Name	Parts used	Types of plant extracts	Medicinal uses of plant	Pathogens used for biofilm	Activities	References
<i>Hakea sericea</i>	Aerial parts	Methanol	No medicinal uses	<i>Staphylococcus aureus</i> MRSA	Antioxidant, antibacterial, anti-biofilm and cytotoxicity activities	[34]
<i>Chromolaena odorata</i>	Leave	Chloroform, ethanol	Cough, malaria	<i>Pseudomonas aeruginosa</i>	Antibacterial, antioxidant, anti-biofilm, anti-inflammatory, wound healing	[35]
<i>Terminalia fagifolia</i>	Stem bark	Ethanol	Gastrointestinal disturbances, such as ulcer, gastritis, and diarrhea	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i>	Antibacterial, antibiofilm, antioxidant, gastric antiulcerogenic, and hypokinetics activities. <i>In vitro</i> and <i>in vivo</i> cytotoxicity studies	[36]
<i>Pityrocarpamo moniliformis</i>	Leaves	Aqueous	Healing process	<i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i>	Anti-biofilm, antibacterial activities, antinociceptive, anti-inflammatory agent	[37,38]
<i>Myracrodruon urundeuva</i>	Leaves, branches, and stem bark	Aqueous	Tumors, rheumatism, inflammations, acne, pain, skin problems, allergy, cracks, etc.,	<i>Staphylococcus epidermidis</i>	Anti-biofilm, anti-inflammatory, anti-allergic, and wound healing properties	[39]
<i>Agrimonia eupatoria</i>	Flowers	Ethanol, diethyl ether, water, and acetone	Urinary tract disorders	<i>Pseudomonas aeruginosa</i> , <i>Proteus mirabilis</i>	Anti-inflammatory, neuroprotective, antidiabetics, anticancer, antiobesity properties, antibiofilm, antibacterial, antioxidant activities	[40]
<i>Ibicella lutea</i>	Aerial part	Chloroform	Skin infection	<i>Proteus mirabilis</i>	Biofilm formation, hemagglutination, hemolysis, antibacterial activity	[41]
<i>Myroxylon peruiferum</i>	Leaves, bark-trunk	Hydroalcoholic extracts	Heal new wound, asthma, cold, diarrhea, skin parasites, rheumatism and urinary infection	<i>Staphylococcus epidermidis</i>	Anti-biofilm, antibacterial activities	[42]
<i>Gymnema sylvestre</i>	Leaves	Methanol	Ailments constipation, liver disease, control blood sugar, lipid – lowering agent, ailments constipation, liver disease, control blood sugar, lipid – lowering agent and weight loss	<i>Streptococcus pyogenes</i>	Anti-biofilm, antibacterial activities	[29]
<i>Aerva lanata</i>	Leaves	Methanol, petroleum ether	Headache, uterine tonic, cure kidney stones, jaundice, dyspepsia, pneumonia, typhoid, and skin diseases	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Proteus vulgaris</i>	Anti-diarrhoeal, anti-hyperglycemic, antioxidant, anti-helminthic, anti-inflammatory, diuretic, anti-urolithiatic, analgesic, anti-biofilm activities.	[43,44]

(Contd...)

Table 1: (Continued)

Name	Parts used	Types of plant extracts	Medicinal uses of plant	Pathogens used for biofilm	Activities	References
<i>Anadenanthera colubrina</i>	Stem bark, branches, leaves, fruits	Aqueous	Wounds, inflammation, throat, lung and kidney problems, chest inflammation, allergy, tuberculosis	<i>S. epidermidis</i> , <i>Pseudomonas aeruginosa</i>	Anti-inflammatory, antimicrobial, antiproliferative potential	[39]
<i>Ouratea blanchetiana</i>	Branches, leaves	Aqueous	Gastric distress, astringent, rheumatism, dysentery, diarrhea, sprains, arthritic disorder, inflammation related diseases	<i>Pseudomonas aeruginosa</i>	Anti-tumour, antiviral, antimicrobial activities and other pharmacological activities	[45,46]
<i>Plectranthus amboinicus</i>	Leaf	Methanol extracts	Cold, asthma, constipation, headache, fever and skin diseases	<i>Pseudomonas aeruginosa</i> , <i>Vibrio harveyi</i>	Anti-biofilm, anti-QS, antimicrobial, anti-inflammatory, antitumor, wound healing, anti-epileptic, larvicida, antioxidant and analgesic activities.	[47]
<i>Helichrysum italicum</i>	Leaf	Methanol	Allergies, colds, skin, liver, gallbladder disorder, inflammation, sleeplessness	<i>Pseudomonas aeruginosa</i>	Anti-inflammatory, anti-infection properties, photoprotective anti-erthematosus activities	[48,49]
<i>Vaccinium vitis-idaea</i>	Leaf	Aqueous	Blood clots, cold, kidney cyst, obesity, skin diseases, wounds, mycosis, and anorexia	<i>Escherichia coli</i>	Diuretic, diastolic, diaphoretic, anti-inflammatory effect, antibacterial, antioxidant, anticancer, antiaging activities	[50]
<i>Herniaria glabra</i>	Leaf	Aqueous	Arthritis, respiratory problem, urinary tract infection, rheumatism, and swelling	<i>Escherichia coli</i>	Diuretic, anticonvulsant, astringent, antirheumatic activities	[50]
<i>Euphorbia hirta</i>	Aerial	Methanol	Gastrointestinal, bronchial, parasitosis, amoebic dysentery, and respiratory ailments	<i>Pseudomonas aeruginosa</i>	Antibacterial, anti-biofilm, antioxidant, antihypertensive, anxiolytic, antimalarial, anti-inflammatory, anticancer activities.	[51]
<i>Arctium lappa</i>	Leaf	Ethanol	Diuretic, diaphoretic, blood purifying agent	<i>Staphylococcus aureus</i>	Antibacterial, antioxidant, anti-biofilm, anti-inflammatory activities	[52,53]
<i>Aquilaria crassna</i>	Leaf	Aqueous	Diarrhoea, dysentery, skin diseases, and cardiovascular function enhancer	<i>Staphylococcus epidermidis</i>	Antibacterial, antioxidant, anti-biofilm, antiplasmodic, antidiarrheal activities	[54]
<i>Cymbopogon flexuosus</i>	Essential oil	-	Cosmetics, insecticides, digestive disorder, fever, and antiseptic	<i>Staphylococcus aureus</i>	Antioxidant, anti-inflammatory activities	[55]
<i>Allium sativum</i>	Leaf	Ethanol, methanol	Wound infection, common cold, malaria, lung tuberculosis, hypertension, sexual transmitted, mental disorder, liver diseases, asthma, and diabetes	<i>Escherichia coli</i> , <i>Salmonella typhi</i> , <i>Staphylococcus aureus</i> and <i>Bacillus cereus</i>	Antibacterial, anti-biofilm, antifungal, anti-inflammatory, larvicidal activities	[56]

(Contd...)

Table 1: (Continued)

Name	Parts used	Types of plant extracts	Medicinal uses of plant	Pathogens used for biofilm	Activities	References
<i>Salvia triloba</i>	Leaves, volatile oil	Ethanol	Headaches, toothaches, common cold, digestive problems, oral infection and wound healing	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> and <i>Candida albicans</i>	Anti-biofilm, antiadhesive, anti-MRSA antibacterial activities	[57]
<i>Andrographis paniculata</i>	Leaves	Ethanol, methanol, chloroform, aqueous, and hexane	Fever, dysentery, snakebite, sore throat	<i>Pseudomonas aeruginosa</i>	Antimicrobial, antimalaria, anti-HIV activities	[58]
<i>Hibiscus sabdariffa</i> L.	Leaves	Ethanol	Diuretic, mild laxative, cardiac, nerve diseases	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Klebsiella pneumonia</i> , <i>Proteus mirabilis</i>	Antibacterial, anti-biofilm, antioxidant, antihypertensive, anticancerous activities and cytotoxicity properties	[59,60]
<i>Mentha arvensis</i>	Essential oil from leaf	-	Indigestion, peptic ulcer, skin diseases	<i>Aggregatibacter actinomycetemcomitans</i>	Antibacterial, anti-biofilm activities	[61]
<i>Mentha piperita</i>	Essential oil from leaf	-	Toothpaste digestive tablets, mouthwashes	<i>Aggregatibacter actinomycetemcomitans</i> , <i>Candida albicans</i> , <i>Candida dubliniensis</i>	Antibacterial, antifungal, anti-biofilm, antiviral, antifungal, antioxidant, radioprotective analgesic activities	[61,62]
<i>Lagenaria sicerarita</i>	Fruit	Organic and aqueous	Immunosuppressant, cardio-tonic, cardio protective, diuretic, nutritive agent, purgative, antidote for certain poisons, emetic, bronchodilator, antipyretic, alopecia, and aphrodisiac	<i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> , <i>Streptococcus pyogenes</i>	Antibacterial, antioxidant, anti-biofilm activities	[63]
<i>Buchanania lanzan</i>	Root	Methanol	Digestive, curing blood diseases, cardiotoxic, astringent, glandular swelling, cyclophosphamide induce genotoxicity, oxidative stress. Immunostimulant and astringent properties	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i>	Anti-inflammatory, antibacterial, antioxidant activities	[64]
<i>Calendula officinalis</i>	Flowers	Water	Measles, smallpox, jaundice, costiveness, ointment for wound, ulcer, frostbite, skin damage, scars, and blood purification	<i>Salmonella dysenteriae</i> , <i>Shigella flexneri</i> , <i>Shigella sonnei</i> and <i>Escherichia coli</i>	Antibacterial, anti-biofilm, antiedematous, antiseptic action, antioxidant, antispasmodic activities	[65,66]
<i>Rosa canina</i>	Leaf	Methanol	Cosmetic, food industry, infections, inflammatory diseases, chronic pain, flu and alcoholic beverages	<i>Pseudomonas aeruginosa</i> , <i>Salmonella typhimurium</i>	Antimicrobial, anti-biofilm activities	[67]

(Contd...)

Table 1: (Continued)

Name	Parts used	Types of plant extracts	Medicinal uses of plant	Pathogens used for biofilm	Activities	References
<i>Rhodomyrtus tomentosa</i>	Leaf	Ethanol	Diarrhea, wound healing, urinary test infections	<i>Streptococcus pyogenes</i>	Antioxidant, antibacterial, antibiofilm, cancer-chemopreventive activities	[68]
<i>Humulus lupulus</i> L	Hop cones	Ethanol	Nervous tension, headache, indigestion, sedative, and hypnotic	<i>Staphylococcus aureus</i>	Antiadherent, anti-biofilm, antibacterial, anti-inflammatory, estrogenic activities	[69,70]
<i>Aegle marmelos</i>	Leaves	Ethyl acetate	Sore throats, cold, intestinal ailments, fertility, chest congestion, fish poison, child birth, and intermittent fever	<i>Salmonella typhi</i> , <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i>	Antidiabetic, antiulcer, antimalarial, anti-inflammatory, antiviral, antihyperlipidaemic, antibacterial, antioxidant, anti-biofilm, antifeedant, cytotoxic activities	[71]
<i>Kaempferia rotunda</i>	Rhizome	Ethanol	Heal wounds, cure stomach ailments, post-delivery care, blood clots, jaundice, swelling	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	Antitumor, antiulcer, anti-inflammatory, antiaging activities	[72]

MRSA: Methicillin-resistant *Staphylococcus aureus*

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