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Review Article

Dillenia retusa(Godapara) and *Aloe vera*(Komarika) as a Promising Antimicrobial Agent Against Skin Infections: a Mini-Review

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Abstract:

Dillenia retusa (Godapara) is an endemic medicinal plant in Sri Lanka and *Aloe vera* (Komarika) is a succulent plant that probably originated in Northern Africa exhibiting different biological activities. These medicinal plants are an important source of bioactive metabolites in drug development. Skin infection is a global public health issue caused by various microorganisms. Due to the toxic activity and resistance to antimicrobial drugs, the world is focusing to search for effective natural-based antimicrobial drugs to combat microbial diseases. Among the herbal plants, natural bioactive compounds are abundant in *Dillenia retusa* and *Aloe vera* with the potential in the application as active ingredients in drugs. Bioactive compounds present in *Dillenia retusa* such as flavonoids, tannins, and terpenoids are responsible for antimicrobial activity through several mechanisms including the inhibition of microbial metabolism, biofilm formation, membrane function, and extracellular microbial enzyme synthesis. Similarly, bioactive compounds present in *Aloe vera* such as polysaccharides, phenols, and flavonoids have been linked with antimicrobial activity. Therefore, the present review mainly focuses on the bioactive compounds present in *Dillenia retusa* and *Aloe vera* and how these compounds are effective against skin infections.

Keywords- *Dillenia retusa*, *Aloe vera*, Anti-bacterial, Anti-fungal, and Skin infections.

1. Introduction

Infectious diseases are conditions produced by organisms, such as bacteria, viruses, fungi, or parasites. They are the leading causes of death worldwide, especially in economically disadvantaged countries. The development of human civilization has had an impact on the transmission of infectious illnesses, such as airborne viral and bacterial infections, parasitic diseases, and zoonotic diseases [1]. Skin infection is a significant global public health issue. People of various ages, gender, and nations, especially in tropical areas, are affected by the disease. Skin infections can be caused by bacteria, viral, fungi, and parasites [2].

Folliculitis, impetigo, abscesses, cellulitis, toxic epidermal necrolysis, erysipelas, and clostridial gas gangrene can be referred to as common bacterial skin infections. The most common bacterial skin pathogens are *Staphylococcus aureus* (mainly cause) group *A β-hemolytic Streptococci*, *Streptococcus pyogenes*, *Corynebacterium minutissimum*, *Escherichia coli*, *Pseudomonas aeruginosa* [3]. Other than bacteria, fungi also cause skin infections. Some of the skin infections caused by fungi are tinea (Ringworm), cutaneous candidiasis, and oral thrush. The most common fungal skin pathogens are *Trichophyton rubrum*, *Candida Albicans*, *Epidermophyton* [4]. Using worldwide statistics, the yearly number of fungal diseases is projected to be 25,750 [1].

Antibiotics and antifungal drugs are mainly used to treat bacterial and fungal infections respectively. Most antibiotic and antifungal drugs are associated with several side effects including diarrhea, nausea, vomiting, rash allergic reactions etc. [5]. In addition, resistance to antibiotics has been caused due to overuse. Multidrug resistance has been recognized as a strong challenge in the world [6]. Therefore, the world is focusing on finding natural-based products as antimicrobial drugs. It is generally known that medicinal plants have promising antibacterial capabilities, and researchers are still investigating medicinal plants to find novel chemical compounds that have the potential to be effective against infections [7].

Most medicinal plants exhibited anti-microbial activity by altering the metabolic activity of the bacterial cell, regulating gene expression, or interfering with a wide range of molecular targets in the bacterial cell [8]. The life span, distribution, and phytochemical makeup of the world's flora, including medicinal and aromatic plants, are all being significantly impacted by climate change [9]. Climate changes such as wind and temperature have an impact on precipitation, which has an impact on plant architecture, blooming, fruiting, phytochemical composition, and also in competition with other species [10].

Among the available medicinal plants, limited research has been conducted using the medicinal plants *Dillenia retusa* (Godapara) and *Aloe vera*. *Dillenia retusa* (Godapara) is an endemic medicinal plant in Sri Lanka exhibiting a wide

range of pharmacological characteristics, including anti-microbial capabilities that are effective against certain pathogenic bacterial and fungal strains. However, only a few study studies have been conducted on these endemic species. These bio-activities are an important areas of interest and need to be explored [11]. Similarly, *Aloe vera* is a succulent plant used in complementary medicine exhibiting different pharmacological properties such as healing burns and wounds, anti-microbial, anti-inflammatory, anticancer, antioxidant, antidiabetic, and antihyperlipidemic [12]. Therefore, the present review mainly focuses on the bioactive compounds present in *Dillenia retusa* and *Aloe vera* and how these compounds are effective against skin infections.

2. Therapeutic targets/mechanisms of anti-microbial therapy

The mechanism of the antimicrobial effect allows for the grouping of antimicrobial agents. Agents responsible for disruption of cell wall synthesis, depolarize cell membranes, disruption the synthesis of proteins, disruption of the production of nucleic acids, and the disruption of metabolic processes in bacteria are the primary categories of therapeutic targets [13].

2.1. Disruption of cell wall synthesis

Peptidoglycan is the main component that makes up the bacterial cell wall [14]. N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM) disaccharide subunit glycan chains are the building blocks of peptidoglycan, which are then cross-linked by pentapeptide chains [14]. Antibiotics that impede peptidoglycan formation, such as glycopeptides and β-lactams, make cells more susceptible to osmotic pressure and the process of autolysis [15].

Gram-positive as well as Gram-negative bacteria include peptidoglycan, a crucial element of the bacterial cell wall that produces mechanical assistance. However, the peptidoglycan in Gram-positive bacteria is thick compared to the Gram-negative bacteria [16]. The formation of the peptidoglycan layer is restricted by binding to the D-Ala-D-Ala terminal of the growing peptide chain and also by inhibiting transpeptidase and blocking the cross-linking and extension of the peptidoglycan chain [17][18]. Therefore, natural extracts which can inhibit the synthesis of bacterial cell wall components can be effective for the treatment of bacterial infections.

2.2. Depolarization of bacterial membrane

Bacteria use membranes that have the potential for information processing and signalling. Bacteria can reach a "persister" condition where they become more susceptible to drugs by depolarizing the membrane potential. The “persister membrane potential” (PMF) is maintained by proton pumps, which are reliant on the membrane potential to maintain pH homeostasis. Native protonophores can prevent the division of cells, which needs the potential of the membrane for the appropriate localization of the division site. Finally, intercellular interaction is enabled by the dynamic response of bacterial membrane potential to molecular and electrochemical stimuli [19]. Therefore, the natural extracts which can depolarize cell membranes can be effective for bacterial infections.

2.3. Disruption of protein synthesis

Transcription is the first step in the process of creating messenger RNA (m-RNA) from the information contained in bacterial DNA. Translation is the process by which the macromolecular structure known as the ribosome creates the proteins found in m-RNA. Ribosomes and cytoplasmic factors catalyse protein production. The 30S and 50S subunits of the ribonucleoprotein make up the bacterial 70S ribosome[20]. The 30S or 50S component of the bacterial ribosome is the target of antimicrobials that prevent protein production [21]. Therefore, natural extracts which can interfere with the structure of 30S and 50S ribosomal units can be considered as an effective therapeutic target for bacterial infections.

2.4. Disrupt the production of nucleic acids

The bacterial nucleic acid synthesis can be inhibited via the modification of their conformation and inducing irreversible lesions [22]. Antibiotics prevent DNA gyrase enzyme from nicking DNA that is double-stranded, adding negative supercoils, and subsequently resealing the nicks. When the DNA strands split to allow for transcription or replication, this is required to prevent excessive positive supercoiling. There are two A subunits and two B subunits in the DNA gyrase. The A subunit nicks the DNA, the B subunit adds negative supercoils, and finally, a subunit reseals the strands. The strand-cutting and resealing activity of the A subunit is hampered by the antibiotics via binding to this subunit. Therefore, the natural extracts that can inhibit DNA gyrase enzyme will be considered as an effective antibacterial target for bacterial infections [23].

Further, Topoisomerase IV is an enzyme that cuts and separates the daughter DNA strand following DNA replication. A better effectiveness versus Gram-positive bacteria may be given by a higher affinity to this enzyme. Therefore, the natural extracts which can alter the DNA replication process by inhibiting the action of the Topoisomerase IV enzyme will be another effective way for bacterial infections [20].

2.5. Disrupt metabolic processes

Some of the natural extracts can reduce bacterial infections by acting as anti-metabolites, or competitive inhibitors of bacterial metabolic enzymes. For an example, there are some antibiotics that can inhibit the different stages of the folic acid metabolism pathway that ultimately limits the bacterial cell growth [24]. Dihydrofolate reductase is one of the primary enzymes involved in the conversion of dihydrofolate (DHF) to THF (tetra hydro folic acid) which is necessary for the synthesis of bacterial proteins and nucleic acids and also for the survival of bacteria. Therefore, the natural extracts that can limit the production of THF has bactericidal effects [25].

3. Bioactive compound present in *Dillenia retusa* and *Aloe vera*

3.1. Bioactive Compounds present in *Dillenia retusa.*

Figure 1: *Dillenia retusa*, an endemic plant in Sri Lanka

Dillenia retusa belongs to the *Dilleniaceae* family. Plants belonged to the species *Dillenia* are rich in bioactive compounds including flavonoids, triterpenoids, phytosteroids, diterpenes, norisoprenes, ionones, phenolics, anthraquinones, alcohol, and ketones [26]. *Dillenia retusa* is an endemic plant that is mostly found in the moist low country in Sri Lanka. It is rich in bioactive metabolites such as flavonoid, polyphenol (tannins) and triterpenes which exhibit significant biological properties including antidandruff, anti-cancer, anti-fungal, anti-bacterial, anti-nociceptive activity and detoxify snake venoms [11].

Flavonols, dihydroflavonols, a flavan, flavan-3-ols, flavanones, (þ)-Dihydroxykaempferol and (þ)-Dihydroquercetin and chromane are different types of flavonoids present in *Dillenia* species. Although some flavonoids have been identified from the stem bark of *Dillenia* plants, the majority of these flavonoids were isolated from the leaves of these plants [26]. Flavonoids have been reported to exhibit antioxidant, sedative, antidepressant, anticonvulsant, anti-proliferative, anti-inflammatory, anti-microbial, anti-cancer, cardioprotective, antihypertensive, antiulcerogenic, antidiabetic, and hepatoprotective activity [27]. In addition, triterpenes with lupene and oleanene structures are also extracted from the leaves, stem barks, and fruits of *Dillenia* plants and are reported to exhibit numerous biological activities, including antibacterial, antiviral, antitumor, antiosteoclastic differentiation activity, anti-HIV-1, hepatoprotection, antioxidation, antihypertension, and cholesterol reduction [26]. Tannins are a class of bitter and astringent chemical substances that fall under the general category of polyphenols. They are widely distributed in nature and may be found in a variety of leaves, fruits, and the bark of *Dillenia retusa*. Tannins have been reported to exhibit antioxidant and free radical scavenging activity as well as antimicrobial, anti-cancer, anti-nutritional, and cardio-protective properties [28].

According to recent research, in all three extracts (leaves, fruit, bark) substantial quantities of polyphenols and flavonoids were found. The highest polyphenol concentration was found in the bark extract, followed by leaf and fruit extracts. The fruit extract has the highest flavonoid concentration, followed by leaf extract and bark extract. All three extracts had substantially distinct polyphenol and flavonoid contents from one another [11]. *Dillenia retusa* exhibited a significant antibacterial activity via inhibition of cell wall synthesis, nucleic acid and protein synthesis, breakdown the bacterial cell membrane and inhibit the enzymes mainly due to the present of flavonoid and phenolic compounds like tannins.

Similarly, It exhibited a significant antifungal activity via disrupt fungal cell membranes, inhibit specific enzymes and disrupt the metabolic pathways of fungi mainly due to the present of flavonoid, tannins and triterpenes [11].

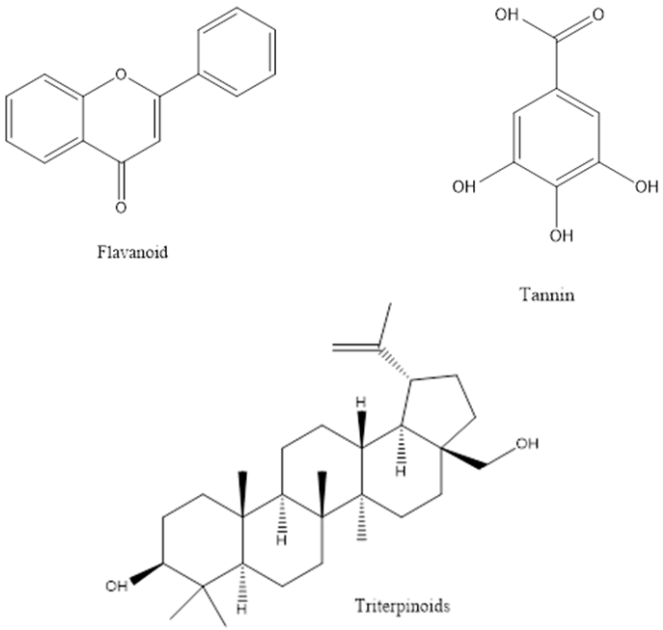
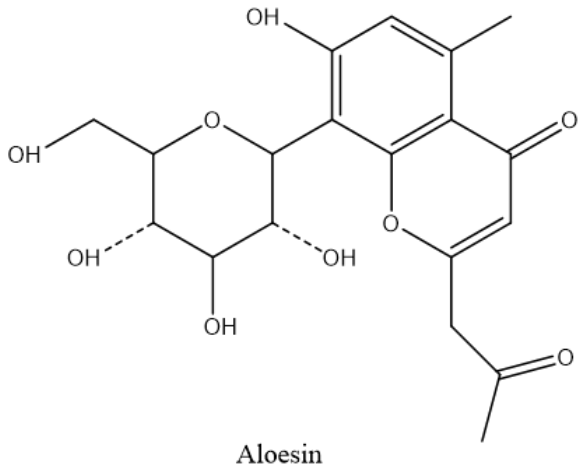


Figure 2: Some of the bioactive compounds present in *Dillenia retusa*

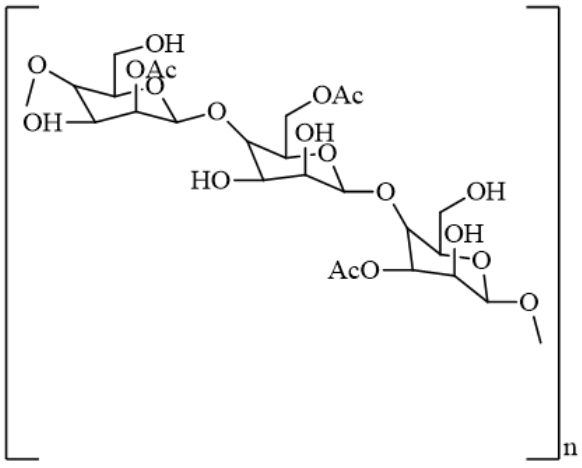
3.2 Bioactive compounds present in *Aloe vera*

Figure 3: *Aloe vera,* a succulent plant species of the genus Aloe.

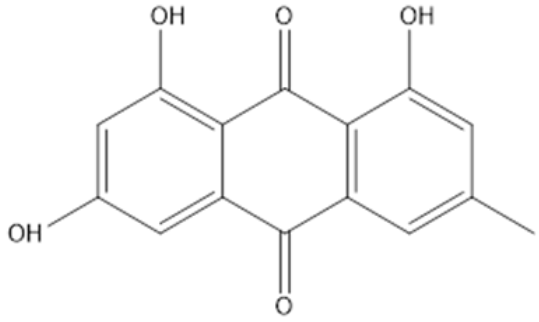
Aloe vera, which belongs to the *Liliaceae* family, has thick, rosette-shaped leaves that are united at the stem. About 98.5%–99.5% of *Aloe vera* gel is made up of water, while the remaining solids comprise more than 200 distinct substances, the majority of which are polysaccharides [29].
The Aloe vera plant is rich in bioactive compounds such as lectins, fatty acids, cholesterol, anthraquinones, flavonoids, terpenoids, chromones, monosaccharides, polysaccharides(acemannan), tannins, sterols, salicylic acid, organic acids, enzymes, saponins, vitamins, minerals, lignins, aloin, anthrone, aloe emodin, aloetinic acid, choline, and complex mucopolysaccharides like hyaluronic acid. [30]. They exhibit significant biological properties including burn and wound healing property, moisturizing and anti- aging effect, immune system restoration, anti-inflammatory action, anti-diabetic effects, anti-oxidant effect, immunomodulatory effect, anti- mutagenic effect and anti-bacterial/ antifungal effects [31].
Polysaccharides and phenolic compounds are considered as primary bioactive compounds of *Aloe vera* that are linked to the treatment of many different diseases [32]. Bioactive polysaccharides, particularly the storage polymer known as acemannan, and various phenolic compounds appear to be the primary elements that clarify the majority of the pharmacological effects including osteogenic, anti-inflammatory, anti-bacteria, antiviral and antitumor activities [29].
The storage polysaccharide found in the protoplast of the parenchymatous cells of *Aloe vera* leaves is acemannan which is made up of a single-chain backbone of partly acetylated mannose units (>60%) and glucose (20%), with side chains produced by galactose (10%) units connected to mannose's C-6 [33]. These acetyl groups, which are the sole non-sugar functional groups in acemannan structurally, appear to be crucial to the physicochemical characteristics and biological activity of *Aloe vera* [33]. Pectins are the most prevalent polysaccharide in *aloe vera* gel, followed by acemannan. As well as pectins are a crucial part of the parenchyma's cell walls, in contrast to the storage acemannan polymer galacturonic acid residues make up a significant portion of *Aloe vera* pectins, typically greater than 95% with less than 5% of neutral sugars. This suggests a structure that consists mostly of lengthy galacturonic acid blocks and has a relatively small number of neutral sugar branches [29]. Chromones exist in a variety of isomeric forms in the plant. Aloeresin E, Aloerosin A, and Aloeresin F are a few of them. Several chromones are found in methylated form or are glycosylated in various places. The amounts of chromones would decide whether they would operate as prooxidant or antioxidant agents, despite the fact that they are typically claimed to have antioxidant characteristics [34].
In addition, *Aloe vera* is rich in terpenoids, tannins, flavanoids, alkaoids which exhibit tannins, alkaloids, phenolic chemicals, and flavonoids are essential for plant growth and defense, and are produced in response to microbial diseases [35].
The antioxidants, vitamin A, C, and E are rich in *aloe vera* plants. Thiamine, niacin, riboflavin, vitamin B12, choline, and folic acid are also present. Amylases, lipases, alkaline phophatases, cellulases, catalases, and peroxidases are examples of enzymes in aloe gel that break up carbohydrates and fats to aid in digestion. Lectins have antitumor properties [31]. The aloe plant contains a variety of minerals, including sodium, potassium, calcium, magnesium, selenium, manganese, copper, zinc, chromium, and iron. These minerals are crucial for the proper operation of enzymes that are engaged in different metabolic processes. Further, it contains both polysaccharides (glucomannose and polymannose) and monosaccharides. In addition to D-mannose and D-glucose, which were detected in a 5:4 molar ratio as free monosaccharides, traces of xylose, rhamnose, galactose, and either arabinose or fucose were also present. A significant sugar found in aloevera is mannose-6-phosphate. The polysaccharides modulate the immune system. An excellent moisturizer, glutmannan is utilized in cosmetics. Anthrone-C-glycosides, Barbaloin, aloeemodin-9-anthrone, isobarbaloin, and chromones are some of the anthraquinones found aloe *vera*. They are also effective antimicrobial agents and have potent analgesic effects [30]. Cholesterol, campesterol, -sitosterol, and lupeol are sterols with anti-inflammatory effects. As well lupeol has analgesic and antiseptic qualities. Auxins and gibberellins are hormones with anti-inflammatory and wound-healing properties, while salicylic acid is an aspirin-like substance with anti-inflammatory and antibacterial characteristics [31]. *Aloe vera* gel offers the amino acids necessary for healing and development. It contains seven of the eight essential amino acids and non-essential amino acids. Lignin is an inert chemical that improves the penetration of other substances into the skin when added to topical treatments. Saponins are soap-like compounds with antibacterial and cleaning effects [31].



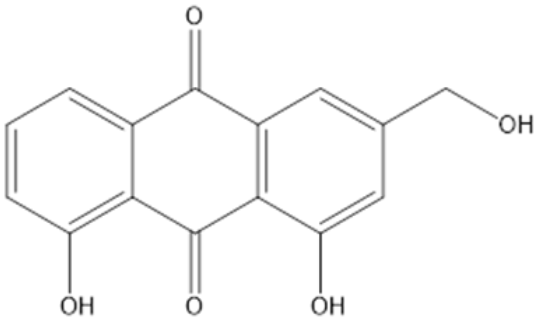
Aloesin



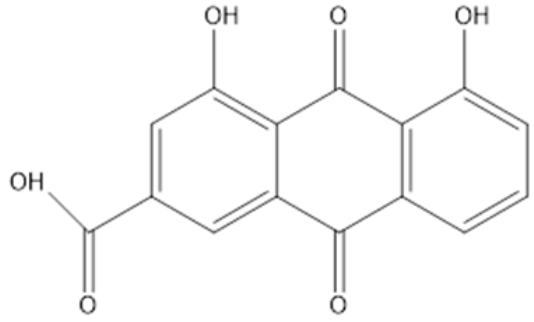
Acemannan



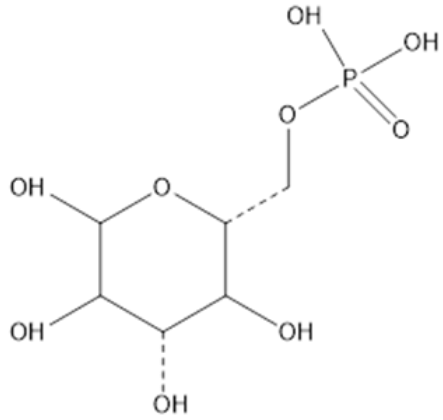
Emoidin



Aloe emoidin



Rhein



Mannose-6-phosphate

Figure 4: Some of the bioactive compounds present in *Aloe vera* plant

4.Antimicrobial potential of *Dillenia retusa* and *Aloe vera*

4.1. Antimicrobial potential of *Dillenia retusa*

In this section, the antimicrobial potential of *Dillenia retusa* has been discussed in three sections as anti-bacterial potential, β- lactamase enzyme inhibitory activity, and anti-fungal potential.

4.1.1. Anti-bacterial potential of *Dillenia retusa*

Due to the existence of an outer and inner membrane barrier and a cell envelope, Gram-negative bacteria are typically more resistant to inhibition than Gram-positive bacteria. This may be because these barriers prevent hydrophilic molecules from passively penetrating the cell envelope and reducing interactions with the cell targets [36]. Additionally, several mechanisms for bacterial resistance are put forth, such as the
inactivation of inhibitors by enzymatic hydrolysis, modification, and alteration of inhibitor targets, and avoiding reaching the target of action via decreased membrane permeability and increased discharge of inhibitors [37].

The *Dillenia retusa* extracts have shown anti-bacterial activities against some Gram-negative resistant bacterial strains and most Gram-positive sensitive bacterial strains. Surprisingly, against two-Gram negative, biofilm-forming bacterial strains, *Pseudomonas aeruginosa* which cause extensive folliculitis and hot tub rash [38] and *Shigella flexneri* which cause sexually transmited skin rashes, rather large inhibitions (> 50%) have been recorded in one research of *Dillenia retusa*, demonstrating the effectiveness of the extracts in inhibiting Gram-negative bacterial growth [11].

According to previous studies, the methanol leaf extract of *D. indica* has been shown to exhibit antibacterial activity against a variety of bacterial species, including *Pseudomonas aerugenosa*, *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi* (MIC: 0.31 - 20 mg/mL) [39]. Additionally, several other *Dillenia* species, such as *Dillenia papuana*, *Dillenia pentagyna*, *Dillenia suffruticosa*, and *Dillenia sumatrana*, have demonstrated antibacterial properties against a variety of bacterial strains, such as *E. coli*, *B. subtilis*, *S. aureus*, *S. flexneri type-1*, and *P. aeruginosa* [40][41][11].

Further, a previous study [11] has proved that the bactericidal activity of the extracts obtained from bark, leaf, and fruit of *Dillenia retusa* was via the inhibition of cell wall synthesis, protein and nucleic acid synthesis, membrane breakdown, and enzyme inhibition bacteria such as *Staphylococcus aureus* which cause eczema, impetigo, folliculitis, furuncles, and primary abscesses [42], *Escherichia coli* which cause skin ulcers [43], and *Salmonella typhi which* cause subcutaneous abscesses and cutaneous ulcers [44] [45] [46]. Therefore, *Dillenia reutusa* has been used as an ingredient in the formulation of topical antibacterial products for skin infections.

Bacteria's resistance mechanisms work through a multi-drug resistant pump system and an outer membrane barrier to inhibit the activity of plant extracts. The phytochemical compounds contained in solvent extracts also directly affect the antibacterial action [47]. According to some research, *Dillenia reutusa* has been used as an ingredient in the formulation of topical antibacterial products.

Triterpenoids and flavonoids are said to be present in the genus *Dillenia* [26]. Polyphenols, flavonoids, and tannins were among the phytochemicals identified by the phytochemical screening. Broad-spectrum anti-bacterial capabilities are said to be present in polyphenols, phenolic acids, and flavonoids. By denying bacteria of iron, hydrogen bonding, or unintended interactions with enzymes and other essential proteins, polyphenolic tannins are known to prevent the growth of bacteria. While flavonoids have been shown to prevent the growth of bacteria by forming complexes with soluble extracellular proteins and the bacterial cell wall [11].

4.1.2.β- Lactamase Enzyme Inhibitory Activity

A bacterial enzyme called β-Lactamase is used to transfer resistance by hydrolyzing the β-lactam ring structure of β-lactam antibiotics [48].

Extracts from *Dillenia retusa* have been found to contain β-Lactamase enzyme inhibitory activity. The greatest β-lactamase enzyme inhibitory activity was demonstrated by the extract of *Dillenia retusa* leaf, followed by that of *Dillenia retusa* bark. Within the range (100 mcg/ml- 500 mcg/ml) of the tested concentrations, the extract was found to have significant and dose-dependent inhibitory activity [11].

According to earlier research [11], polyphenols, especially flavonoids, may have the ability to operate as β- lactamase inhibitors, affecting the inhibitory activity of the β-lactamase enzyme, primarily found in *Staphylococcus aureus* which cause eczema, impetigo, folliculitis, furuncles, and primary abscesses [42] , *Pseudomonas aeruginosa* which cause extensive folliculitis and hot tub rash [38] and *E. coli* which cause skin ulcers [43][49].

4.1.3. Anti-fungal potential of *Dillenia retusa*

The *Dillenia retusa* extracts containing bioactive compounds such as favanoid, tannin, and triterpenoids have shown anti-fungal activities against *Candida albicans* which cause cutaneous candidiasis, eczema [50] , *Aspergillus niger* which cause eczema, Cutaneous (skin) aspergillosis [51] , and *Candida glabrata* which cause cutaneous candidiasis in HIV/AIDS patients [52] by disrupting fungal cell membranes, inhibiting specific enzymes and disrupting cellular structures or metabolic pathways in fungi [11].

The *Dillenia retusa* leaf (DRL) extract had considerable antifungal activity against *Candida albicans*, *Aspergillus niger*, and *Candida glabrata*, whereas the *Dillenia retusa* fruit (DRF) extract showed moderate antifungal activity against *Candida albicans* and comparably poor antifungal activities against *Aspergillus niger* and *Candida glabrata*. The extract of *Dillenia retusa* bark (DRB) has demonstrated moderate anti-fungal activity against *C. albicans* and demonstrated no anti-fungal activity against any other fungal species such as *A. niger* and *C. glabrata* [11].

The bark and leaf extracts of *Dillenia pentagyna* (3 mg/disc) and *Dillenia suffruticosa* (1 mg/disc) also demonstrated fungal growth inhibitory activities against *A. niger* and *C.*

albicans [40]. Non-polar leaf extracts of *Dillenia indica* have been shown to have the highest fungal growth inhibitory activity against a variety of fungal strains, such as *A. niger* and *C. albicans*. These reported investigations on the anti-fungal activity of other *Dillenia* species found that the action is shown at >0.4 mg, which is also corroborated - with research on *Dillenia retusa* [11].

4.2. Antimicrobial potential of *Aloe vera*

The antimicrobial potential of *Aloe vera* has been widely studied in the last few years due to the presence of numerous bioactive compounds. Among the bioactive compounds present in *Aloe vera*, primary bioactive components including polysaccharides and phenolic compounds have been identified as potential sources for the treatment of many different human diseases. *Aloe vera* plant extracts possess antimicrobial properties that either kill or halt the growth of microorganisms, such as bacteria (antibacterial activity), fungi (antifungal activity), and viruses (antiviral activity).

4.2.1. Antibacterial activity of *Aloe vera*

Previous research has revealed that acetone extracts exhibited the strongest antibacterial and antifungal effects compared to aqueous and ethanol extracts [53]. Further research on *Aloe vera* found that the growth of *Staphylococcus aureus* which cause eczema, impetigo, folliculitis, furuncles, and primary abscesses [42] was suppressed at a high concentration (1/10), but that the growth of *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi* needed intermediate quantities [54]. Another study revealed that the antibacterial activity of *Aloe vera* juice was most efficient against Gram-positive bacteria [54].

Pseudomonas aeruginosa which cause extensive folliculitis and hot tub rash [38] was susceptible to the bactericidal effects of *Aloe vera* gel, and acemannan inhibited it from sticking to human lung epithelial cells in monolayer cultures [55]. It has been demonstrated that glucomannan and acemannan exhibited antibacterial and antiviral properties, activate macrophages, and stimulate immune system [56]. *Aloe vera* gel has been shown to prevent the growth of two bacteria, *Streptococcus pyogenes* which cause infections in the superficial keratin layer (impetigo), the superficial epidermis (erysipelas), the subcutaneous tissue (cellulitis), the fascia (necrotizing fasciitis) [57] and *Streptococcus faecalis* which cause cellulitis [56].The aloe extract has substantial anti-mycobacterial activity against *M. tuberculosis* which cause cutaneous tuberculosis(acute skin infection) in addition to antibacterial activity against *P. aeruginosa*, *E. coli*, *S. aureus*, and *S. typhi*. It was effective against three strains of *Mycobacterium* which cause skin infections (skin ulcers) such as *Mycobacterium fortuitum*, *Mycobacterium smegmatis*, and *Mycobacterium kansasii* [56]. *Aloe vera inner*-leaf gel has been demonstrated to stop the development of *Shigella* and *Streptococcus species in vitro* [58].

A study was conducted using pathogens Isolated from patients with dental decay and periodontal conditions. The inhibitory activities of *Aloe vera* gel on some cariogenic and periodontopathic pathogens, as well as an advantageous periodontal pathogen, were examined. The findings indicated that *S. mutans* was the species that was the most sensitive with a minimum inhibitory concentration (MIC) of 12.5 g/mL, followed by *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Bacteroides fragilis*. A further investigation indicated that, when used against *Enterococcus bovis* and *Staphylococcus aureus*, the ethanolic extract of *Aloe vera* leaves had a broader zone of growth inhibition with 29–30 mm than did the aqueous extract with 3–4 mm [59]. Further, it was discovered that only the Gram-negative bacteria *Aeromonas hydrophila* and *E. coli* were resistant to the antibacterial effects of *Aloe vera*. Aloe juice has been proven to be bacteriostatic against *Salmonella paratyphi*, *Streptococcus pyogenes*, and *Staphylococcus aureus* in other research [60][61]. A major investigation examined the antimicrobial effects of various aloe preparations, including fresh, preserved, cooling gel, and acne cream, on a variety of microorganisms. It was found that the cooling gel and acne cream had the greatest antibacterial effects on *Staphylococcus aureus*, while the fresh and preserved gel preparations had the greatest antimicrobial effects on *Bacillus subtilis* [62]. The methanol extract has showed the highest antibacterial activity among the solvent extracts in an experiment to test the bactericidal effects of *Aloe vera* extracts, including ethanol, methanol, and distilled water extracts [54].

4.2.2. Antifungal activity of *Aloe vera*

The effects of *Aloe vera* on the mycelium development of *Rhizoctonia solani*, *Fusarium oxysporum*, and *Colletotrichum coccodes* have been investigated. The pulp of *Aloe vera* had an inhibitory effect on *Fusarium oxysporum* at a concentration of 10^4 µl L-1, and the liquid fraction decreased the rate of colony growth at a concentration of 10^5 µl L-1 in *Rhizoctonia* solani, *Fusarium oxysporum*, and *Candida coccodes* [63]. *Aloe vera* inner-leaf gel has demonstrated to stop the development of *Shigella* and *Streptococcus* species *in vitro* [64]. *Trichophyton mentagrophytes* (20.0 mm) which cause Tinea pedis (superficial fungal infection of the epidermis) [65] had their growth inhibited by *Aloe* gel, while *Pseudomonas aeruginosa* and *Candida albicans* are both suppressed by the extract of Aloe leaf [60]. Further, proliferation of *Candida albicans* which cause cutaneous candidiasis, eczema [50] was impeded by a processed *Aloe vera* gel formulation. *Aloe vera* extracts, on the other hand, did not demonstrate antibiotic activity against *Xanthomonas* species [66]. Saponins are another component of *Aloe vera.* These are the soap-like gel components that can clean and have antiseptic qualities. When used against bacteria, viruses, fungi, and yeasts, saponins have potent anti-microbial activity [67].

5. Conclusion

The present review mainly focused on the antibacterial, anti-beta-lactamase enzyme activity, and antifungal activities of *D. retusa* and *Aloe vera*. Bioactive compounds present in *Dillenia retusa* and *Aloe vera* exhibited antimicrobial activity through several mechanisms such as inhibition of microbial metabolism, biofilm formation, membrane function, and extracellular microbial enzyme synthesis.

Therefore, the present mini-review mainly focused on the on the bioactive compounds present in *Dillenia retusa* and *Aloe vera* and how these compounds are effective against skin infections. The findings support the popular usage of *Dillenia retusa* to treat bacterial skin infections such as eczema, impetigo, folliculitis, furuncles, skin abscesses and cutaneous ulcers ,and fungal skin infection such as cutaneous candidiasis, eczema and demonstrate that *Aloe vera* has the potential to create new and highly effective antibiotics that use for the bacterial skin infections such as eczema, impetigo, folliculitis, furuncles, skin abscesses, hot tub rash and fungal infection such as cutaneous candidiasis, eczema and Tinea pedis.

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