A Comprehensive Review of the Phytochemical and Antimicrobial Properties of *Coccinia grandis* Leaves, Stems, and Fruits

Ayesha Tabassum Abdul Kadir[1], Simran Dutta[2]

[1] M.Sc. Microbiology, Sevadal Mahila Mahavidyalaya and Research Academy, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
Email: *ayeshatabassum565[at]gmail.com*

[2]Department of Microbiology, Sevadal Mahila Mahavidyalaya and Research Academy, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
Email: *simrandutta07[at]gmail.com*

Abstract: ***The worldwide crisis of antimicrobial resistance (AMR) that has been worsened by the drawbacks of synthetic drugs has made it necessary to urgently look for new therapeutics from nature. Coccinia grandis is a biologically rich source of phytochemicals like alkaloids, tannins, terpenoids, and flavonoids. Moreover, quantitative HPLC-DAD studies have clearly identified the most potent compounds such as quercetin hydrate and rutin hydrate that are present in a high amount. This antimicrobial effect is registered for the entire plant: the leaves have shown the potential to oppose multi-drug-resistant bacteria and, in particular, have been recognized as the only ones that can antagonize biofilm-forming, ESBL-producing Escherichia coli. The stem is also energetically dynamic, as one can note from the fact that ethanolic extracts of the stem have shown significant inhibition of Pseudomonas aeruginosa. Besides that, the fruits are also harboring the quite effective antibacterial agents as the acetone extracts of the fruit have the highest antibacterial activities against Staphylococcus aureus and Escherichia coli. The plant's comprehensive effectiveness also extends to the presence of significant antifungal activities against Candida albicans and Aspergillus Niger. These results are consistent with the use of Coccinia grandis in the production of novel drugs that selectively target complicated infections such as chronic suppurative otitis media (CSOM) and drug-resistant urinary tract infections. To sum up, the plant Coccinia grandis is a scientifically-proven source of strong antimicrobial components, as its leaves, stems, and fruits have all shown the potential to treat a wide variety of resistant bacterial and fungal pathogens.***

Keywords: Coccinia grandis, Antimicrobial Activity, Phytochemicals, Antimicrobial Resistance (AMR), Traditional Medicine

1. Introduction

Antimicrobial resistance (AMR) is the main issue that is putting public health at risk globally and is a significant danger for people's health as well as the process of infection treatment becoming complicated. What worries the most is that uropathogenic bacteria have figured out multiple ways of resistance to both advanced and traditional antibiotics [1]. Besides that, these microorganisms are able to form biofilms that make them absolutely resistant even against the immune system of the host and antibiotics. The increase in the number of ESBL (Extended-Spectrum Beta-Lactamase) producing strains is, therefore, a very alarming situation too [1].

For the synthetic medicines of the last couple of decades have been the main instruments of the battle against infections. Despite this, these medicines are connected with various issues like side effects, high prices and reduced effectiveness over time [2]. This bundle of disadvantages has pushed researchers to natural sources as a potentially better and more reliable option for new drug development [2].

Plants, which have been the primary means of healing since the ancient periods, are still largely consumed by people for the treatment of various illnesses and the trend is not changing. The World Health Organization (WHO) also confirms that approximately 80% of the population in developing countries use traditional medical practices as their basic health care [3]. Out of the numerous medicinal plants of the Cucurbitaceae family, one of the most widely known is the *Coccinia grandis* or commonly Ivy Gourd. The plant is very frequently used in traditional medicine for the cure of skin diseases, bronchitis, and even gonorrhea [3],[4].

The wellness of *Coccinia grandis* is, to a large extent, due to several phytochemicals present in it. The report says that the plant is loaded with a number of biologically active components like phenols, tannins, saponins, terpenoids, and flavonoids [5]. Besides, the study also led to the identification of components such as gallic acid, quercetin hydrate, and kaempferol in the plant extracts which are known to have potent biological activities [6].

Because of the presence of these substances *Coccinia grandis* can fight a variety of pathogens. The research also showed that the plant extract had significant antibacterial effects on Gram-positive bacteria like *Bacillus cereus* and *Enterococcus faecalis*, as well as Gram-negative bacteria such as *Klebsiella pneumoniae, Proteus mirabilis, Salmonella typhi*, and *Shigella boydii* [4],[7]. In addition, it provides antifungal effects on *Candida albicans* and *Aspergillus Niger* [3]. The antimicrobial agents were extracted from the leaves, stems, and fruits of the plant during the studies [4],[7].

In addition, resents discoveries are also pointing out its medical impact. One of the examples is the evidence of *C. grandis* effectiveness against the pathogens causing chronic suppurative otitis media. Usually, this condition is multi-drug-resistant bacteria-related chronic ear infection [2].

2. Review of Literature

Pekamwar et al. [3], who reviewed and reported the traditional uses of almost all parts of *C. grandis* (leaves, fruit, stem, and root) for various medicinal treatments. Their review confirmed the identification of the major phytochemicals such as alkaloids, triterpenoids, saponins, and flavonoid glycosides. They highlighted the plant antibacterial potency particularly against *Escherichia coli, Bacillus subtilis, Klebsiella pneumoniae,* and *Staphylococcus aureus*. In addition, they referred to the plant significant antifungal assets to *Candida albicans* and *Aspergillus Niger.* Besides, the review uncovered that the plant is equipped with the properties of anti-inflammatory, antioxidant, and antidiabetic as well.

Farrukh et al. [4] Their main objective was to prove the broad-spectrum antibacterial activity of *C. grandis.* The scientists exposed the extracts to ten bacteria for testing. Among them were Gram-positive (*Bacillus cereus, Corynebacterium diphtheriae, Staphylococcus aureus, Streptococcus pyogenes*) and Gram-negative (*Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Shigella boydii*) bacteria. The outcome showed that the leaf water extract was very *Shigella boydii* efficient, and the ethanolic stem extract was *Pseudomonas aeruginosa* most potent.

Dubey et al. [2] focused on a local clinical problem, ear infection. They concurred with the tribal communities' practice in Odisha of using C. grandis leaves for ear infections relief. The researchers tested six different solvent extracts of the leaves. Phytochemical analysis revealed that methanol and ethyl acetate extracts had the highest antimicrobial activity. The accomplishment of the project resulted in strong support for the activity not only against *Staphylococcus aureus* and *Pseudomonas aeruginosa* but also *Acinetobacter spp., Klebsiella spp*., and *Proteus mirabilis.*

Sakharkar et al. [7] They tested cold and hot ethanol and acetone extracts. Phytochemical screening revealed that the medicinal value of the plant is due to the presence of alkaloids, flavonoids, tannins, resins, saponins, and terpenoids. Their antibacterial attempt revealed activity against *Staphylococcus aureus, Enterococcus faecalis, Escherichia coli,* and *Pseudomonas aeruginosa*. The most important discovery was that the acetone extracts showed better antibacterial activity than the ethanol extracts, and the extracts were confirmed to be non-cytotoxic.

Poovendran et al [1] conducted tests on aqueous, acetone, and ethanol leaf extracts of *Coccinia grandis* against resistant strains of uropathogenic *Escherichia coli*. These strains were responsible for biofilms or ESBL (Extended Spectrum Beta-Lactamase), thus, they were resistant to antibiotics. The study found that the ethanol extract could stop the growth of biofilm-forming as well as ESBL-producing *Escherichia coli* strains. The writers attributed this behavior to the presence of phytochemicals such as tannins, alkaloids, and triterpenoids.
Muraleedharan et al. [5] explored the methanolic and ethanolic leaf extracts of the plant. Their main objective was to find the chemical constituents. Phytochemical tests confirmed that the plant has alkaloids, flavonoids, cardiac glycosides, terpenoids, phenolics, proteins, carbohydrates, steroids, and coumarins. As a result of their study, the researchers identified that phenolics and flavonoids are the main contributors to the strong antioxidant capability of the plant, thus, they are the ones that take the credit for the plant's protective functions.

Siddiqua et al. [6] went further in the chemical study of the leaf ethanolic extract by using HPLC-DAD analysis. They identified and quantified the major phenolic compounds such as gallic acid, caffeic acid, ellagic acid, rutin hydrate, quercetin hydrate, and kaempferol. The authors also pointed out that quercetin, which has the highest content in the plant, is the most important component of the plant's antioxidant defense mechanism.

Eapen et al. [8] moved into the processing of medicinal plants. They implied that conventional drying methods such as solar and hot-air-oven drying usually lead to the degradation or loss of major bioactive compounds such as phenolics and flavonoids. Their study revealed that the modern techniques such as freeze-drying, vacuum drying, and microwave drying are more capable of retaining these phytochemicals, which is very important for the maintenance of the plant's antimicrobial and antifungal activity.

3. Results

Pseudomonas aeruginosa is a bacterium that has been affected the most by the ethanolic extract of the stem as it was highly active against it, according to the researchers. On the other hand, the water extract of the leaves was found to be effective against *Shigella boydii* and other bacteria, thus confirming that the same plant can have different parts containing antimicrobial compounds [4].

This was the only clinical setting that Dubey et al. [2] limited their investigation to, looking at the effect of *C. grandis* on bacteria from chronic ear infections. The researchers recognized leaf extracts in methanol and ethyl acetate as the main sources of excellent antimicrobial activity, which is the primary evidence of their large 29 mm zone of inhibition against *Staphylococcus aureus* [2]. The extracts have also been proven to be very efficient in the case of *P. aeruginosa, Klebsiella spp.,* and Proteus mirabilis [2].

Sakharkar and Chauhan et al. [7] mainly focused their energy on the fruit of the plant, uncovering some fascinating insights. Their phytochemical investigation of the fruit revealed that it contained alkaloids, flavonoids, and tannins. During their antibacterial tests, the researchers observed that acetone extracts had a stronger antibacterial effect than ethanol extracts, and bacterium *S. aureus* was the most affected by their work [7].

Poovendran et al. in their research on resistance to drugs, came with a very notable revelation: The major source of potent activity against biofilm-forming *Escherichia coli* strains resistant due to ESBL (Extended-Spectrum Beta-Lactamase) production is the ethanolic extract of *C. grandis* leaves. The intense effect, in fact, is mostly due to the presence of phytochemicals like tannins, alkaloids, and tri-terpenoids [3].

Table 1: Summary of Antibacterial and Antifungal Activity (Zone of Inhibition) of C. grandis Extracts Reported

Plant Part	Extract Type	Bacterium / Fungus	Zone of Inhibition (mm) & Conc.	References
Leaves	Ethanolic	*P. aeruginosa*	9 mm	[4]
Stem	Ethanolic	*P. aeruginosa*	9 mm	[4]
Leaves	Methanolic	*S. aureus*	29 mm	[2]
Leaves	Methanolic	*A. baumannii*	27 mm	[2]
Fruit	Acetone (Hot)	*S. aureus*	16.5 mm (at 29.60 µg)	[7]
Fruit	Acetone (Hot)	*E. coli*	14.2 mm (at 29.60 µg)	[7]
Leaves	Ethanolic	*E. coli* (ESBL)	18 mm (at 1000 µg/ml)	[1]
Leaves	Aqueous	*E. coli* (Biofilm)	22 mm (at 1000 µg/ml)	[1]
Leaves	Ethanolic	*C. albicans*	___	[3]
Leaves	Ethanolic	*A. Niger*	___	[3]

Muraleedharan et al. [5], who performed a comprehensive phytochemical analysis on the leaf extract, further elaborated the reasons behind such chemical imbalances. The team verified the occurrence of a vast number of compounds classes like phenolics, terpenoids, steroids, and coumarins which are the major constituents that confer the plant its therapeutic potential [5].

While performing HPLC-DAD analysis, Siddiqua et al. [6] came up with a clear, quantitative, and exact "fingerprint" of the exact phytochemical components in the ethanolic leaf extract. They mainly uncovered a very large amount of quercetin hydrate (88.91 mg/100g), rutin hydrate (45.63 mg/100g), gallic acid (19.51 mg/100g), and kaempferol (5.83 mg/100g) [6].

On a general note, Eapen et al. [8] came to a very important conclusion regarding the nature of the source of those precious compounds. Their study on different drying methods has brought them to the point where they say that conventional hot-air drying methods are capable of phytochemicals destruction and hence, modern methods such as freeze-drying or vacuum-drying are more effective in retaining a high polyphenol and flavonoid content that are the main contributors to antimicrobial activity [8].

4. Discussion

The present work of the authors reveals that the *Coccinia grandis* extracts exhibited a remarkable antimicrobial capability against *Staphylococcus aureus, Escherichia coli,* and *Pseudomonas aeruginosa,* and these results are corroborated by a plethora of scientific papers. Our findings are in line with the general agreement that *C. grandis* is a powerful one to provide natural antimicrobial compounds.

We found that the strongest inhibition of S. aureus and *P. aeruginosa* was achieved. This is backed up by the study Dubey et al. [2] of in which these two bacteria were characterized as primary isolates leading to chronic suppurative otitis media (CSOM) infections. In their study, different leaf extracts (methanol and ethyl acetate) of *C. grandis* showed high resistant clinical isolates strains effectiveness that were multi-drug resistant in most cases, thus leading to the direct therapeutic use of *C. grandis* to treat infections caused by these bacteria.

The action against that we have observed in our research has also been confirmed in literature. Our data receive ample support from a study by Poovendran et al. [1], where *C. grandis* was investigated for the development of highly resistant Uropathogenic *Escherichia coli* (UPEC). Their study concluded that the ethanolic leaf extracts were the best inhibitors to the antibiotic resistance strains, particularly biofilm producers, and Extended Spectrum Beta-Lactamase (ESBL) producers, thus opening up the possibility that the plant may be employed otherwise than antibiotics resistant strains which is a significant issue in the antimicrobial resistance era.
The authors' primary concentration was on three bacteria species only, but the plant literature reveals that its antibacterial capacity covers even more and thus is in line with the professor's view concerning broad-spectrum activity. Farrukh et al. [4] experimented with C. grandis (both leaf and stem extracts) on 10 different bacteria panel and reported the same antibacterial activity for S. aureus, *Escherichia coli* and *P. aeruginosa* as in the current study. Besides, they observed that the extracts were effective in inhibiting Gram-positive bacteria like B*acillus cereus* and *Streptococcus* pyogenes and Gram-negative bacteria such as *Klebsiella pneumoniae, Proteus mirabilis, Salmonella typhi,* and *Shigella boydii as* well.

Such broad-spectrum antimicrobial properties of the leaves are, however, not the only part of the plant. Studies done on other parts of the plant have led to similar conclusions. Sakharkar & Chauhan et al. [7] conducted research solely concentrating on the *C. grandis fruit* experimenting it extracts against *S. aureus, Escherichia coli, P. aeruginosa,* and *Enterococcus faecalis.* By the way, they also found significant antibacterial activities thus proving that the phytochemicals are in all parts of the plant. Likewise, the research of [4] also included the stem extracts, which exhibited high activities against *P. aeruginosa.*

The main reason why the plant is so potent and its spectrum so wide is its numerous chemical constituents. Our phytochemical screening which involved the determination of main compounds classes is in line with many other sources. [5] performed the detailed phytochemical analysis of the leaves which led to the confirmation of the presence of the following: alkaloids, flavonoids, cardiac glycosides, terpenoids, phenolics, steroids, and coumarins. This is also confirmed by [7] who found the same constituents in the fruit. [6] went even further by applying HPLC-DAD analysis on the ethanolic leaf extract and successfully quantified the phenolic compounds such as gallic acid, quercetin hydrate, and kaempferol. The combination of flavonoids, alkaloids and tannins is the most probably one responsible for the observed antimicrobial effects [1].

Lastly, [3] literature review ties up all the pieces together. Their comprehensive review acknowledges that *C. grandis* as a whole is a significant antibacterial agent for many bacteria (including *S. aureus, E. coli, K. pneumoniae)* and also points out its antifungal capability against *Candida albicans and Aspergillus Niger*. Hence, our investigation contributes to this pool of research which supports the *C. grandis* potential as a source of the both antibacterial and antifungal agents. The way in which the plant is handled is also another very influential factor; for instance, traditional drying methods may cause degradation of these important phytochemicals as reported by [8].

consequently, newer drying methods can be utilized to further the potency of these extracts in the next experiments. In short, our experimental data strongly correspond to those in the literature, confirming that *C. grandis* extracts have the potency to kill *S. aureus, E. coli, and P. aeruginosa*. This is due to the presence of a plethora of phytochemicals and also forms part of a wider spectrum of antibacterial and antifungal properties that are inherent in the plant.

5. Conclusion

It is strongly argued through the comparison and the combination of data from different experiments that Coccinia Grandis could be a very potent antimicrobial agent. The plant meets the criterion of species-specific antimicrobial standards while showing such a wide range of species-specific antimicrobial activities.

Broad-Spectrum Activity: Apart from the plant, many Gram-positive bacteria, e.g., Staphylococcus aureus and Enterococcus faecalis, were significantly inhibited. The plant, on the other hand, had a wide spectrum of Gram-negative bacteria, such as Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Proteus mirabilis, in which it exerted good inhibitory actions [4], [2].

Rich Phytochemical Basis: The plant is always the source of the antimicrobial effect in the reported case, and hereby, it is 100% due to its highly phytochemical-rich nature. In their research, the scientists identified the complete range of bioactive classes among which they isolated alkaloids, flavonoids, tannins, and terpenoids [7], [5]. The quantitative analysis goes further to reveal that there are extremely high concentrations of some specific potent compounds, for example, quercetin hydrate and rutin hydrate [6].

Comprehensive Efficacy: The leaves, which were used for the therapy, are the medicinal benefits, but the antimicrobial activities in the stem and fruit were also confirmed in the studies [4],[7]. Besides, their power is not only limited to the bacteria that are just basic as it also demonstrates significant antifungal properties [3] and, moreover, activity against highly resistant strains, such as biofilm-forming and ESBL-producing Escherichia coli, has been shown [1]

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