Phytochemical Screening of *Ficus globosa* Latex (Moraceae) as a Source of Novel Antimicrobial Compounds

Elechi Kelechi Wisdom [1], **Igboaka Chukwuebuka Duke** [2], **Tiamiyu Bashir Bolaji** [3], **Ugbor Mary-Jane Ezinne** [4], **Arthur Clinton** [5], **Faderin Emmanuel Adetunji** [6], **Ezeh Ogochukwu Mercy** [7], **Olowookere Adepeju** [8], **Lawal Olabisi Promise** [9]

[1] *The University of Texas Health, San Antonio*
7703 Floyd Curl Drive, San Antonio, TX 78229, USA

[2] *University of Nigeria, Nsukka*
Nsukka Road, 410001, Nsukka, Enugu State, Nigeria

[3] *University of Ilorin*
P. M. B. 1515, Ilorin, Kwara State, Nigeria

[4] *University of Port Harcourt*
P. M. B. 5323, Choba, Rivers State, Nigeria

[5] *Eastern New Mexico University*
1500 S Ave K, Portales, NM 88130, USA

[6] *Southern Illinois University, Edwardsville*
Campus Box 1015, Edwardsville, Illinois, 62026-1015, USA

[7] *Georgia State University*
P.O. Box 3965, Atlanta, GA 30302-3965, USA

[8] *University of North Carolina at Greensboro*
1400 Spring Garden Street, Greensboro, NC 27412, USA

[9] *University of Benin*
P. M. B. 1154, Ugbowo, Benin City, Edo State, Nigeria

DOI: 10.22178/pos.115-28

LCC Subject Category: RS1-441

Received 26.02.2024
Accepted 24.03.2024
Published online 31.03.2025

Corresponding Author:
Elechi Kelechi Wisdom
kelechiwisdom20@gmail.com

Abstract. The emergence of antimicrobial resistance has necessitated the search for novel therapeutic agents from natural sources. This study evaluated the phytochemical composition of Ficus globosa latex and assessed its antimicrobial activity against selected pathogenic microorganisms. Latex was collected, authenticated, and processed through acetone precipitation followed by drying at 60°C for three weeks. Both fresh and dried latex samples underwent phytochemical screening using standard methods, revealing abundant quantities of resins, steroids, and terpenoids; moderate levels of flavonoids; and trace amounts of fats, oils, and hydrolysable glycosides. Antimicrobial activity was evaluated using the agar well diffusion method against eight pathogenic microorganisms. The dried latex demonstrated significant antimicrobial activity with minimum inhibitory concentrations (MICs) of 3.89 mg/mL against Bacillus subtilis, 14.79 mg/mL against Staphylococcus aureus, and 8.13 mg/mL against Aspergillus niger. In contrast, fresh latex showed activity only against B. subtilis. F. globosa latex exhibits promising antimicrobial activity, particularly against gram-positive bacteria, warranting further investigation for therapeutic applications. The presence of multiple bioactive compounds suggests potential mechanisms for its antimicrobial effects.

Keywords: Ficus globosa; latex; antimicrobial activity; phytochemical screening; minimum inhibitory concentration.

INTRODUCTION

The global healthcare landscape faces an unprecedented crisis in antimicrobial resistance, with traditional antibiotics increasingly failing against common pathogens. Current projections indicate that by 2050, antimicrobial-resistant infections could cause 10 million deaths annually, with associated healthcare costs exceeding $100 trillion globally [1]. This crisis, compounded by a significant decline in new antibiotic development, has created an urgent need to explore novel therapeutic approaches, particularly from natural sources that may offer unique mechanisms of action.

Natural products historically represent the foundation of pharmaceutical discovery, contributing to approximately 60% of currently approved therapeutic agents [2–4]. Their complex molecular architectures, evolved over millions of years, often provide sophisticated mechanisms of action that synthetic compounds rarely achieve. Plant-derived substances, in particular, frequently demonstrate multiple therapeutic effects through diverse biochemical pathways, potentially offering solutions to combat antimicrobial resistance through multi-target approaches.

The genus Ficus, encompassing approximately 800 species and 2000 varieties within the Moraceae family, represents an extensive yet largely untapped reservoir of potential therapeutic compounds [5–7]. These plants have adapted to diverse ecological niches across tropical and subtropical regions, developing unique chemical defences that could translate into novel therapeutic strategies. Traditional medical systems worldwide have utilised various Ficus species for treating conditions ranging from infectious diseases to inflammatory disorders, providing valuable ethnopharmacological data to guide modern drug development efforts [8–10].

Among these species, *Ficus globosa* stands out as a particularly promising candidate for therapeutic development [11]. This climber or hemi-epiphytic shrub, native to Southeast Asian regions including Myanmar, Thailand, Sumatra, Peninsular Malaysia, Singapore, Borneo, and Java, produces copious white latex with potential therapeutic applications. The species' adaptation to diverse habitats, from lowland forests to mangrove swamps at elevations up to 1,200 meters, suggests the development of unique secondary metabolites that could offer novel solutions to current therapeutic challenges.

Translating traditional botanical knowledge into modern therapeutic agents requires addressing several critical challenges in the drug development pipeline [12]. These include establishing standardised collection and processing methods, identifying and characterising active compounds, developing suitable pharmaceutical formulations, and conducting comprehensive safety and efficacy evaluations. The polymeric nature of fig latex presents additional complexity, requiring innovative approaches to overcome solubility, stability, and bioavailability issues.

Despite its widespread traditional use, systematic investigation of *F. globosa*'s antimicrobial potential has been lacking, representing a significant gap in translational research. The latex's complex physical properties and chemical composition necessitate careful consideration of pharmaceutical development parameters, from initial processing to final formulation strategies. Understanding these characteristics is crucial for developing standardised preparations suitable for clinical applications.

This research adopts a comprehensive translational approach, investigating *F. globosa* latex from initial characterisation through potential therapeutic development. The study specifically addresses key questions in the therapeutic development pipeline: the establishment of standardised collection and processing protocols suitable for pharmaceutical development, comprehensive phytochemical profiling focusing on therapeutically relevant compounds, evaluation of antimicrobial activity against clinically significant pathogens, assessment of concentration-dependent effects relevant to therapeutic dosing, and comparison of fresh versus processed latex preparations to guide formulation development.

These investigations aim to bridge the gap between traditional knowledge and modern therapeutic applications, providing a scientific foundation for developing novel antimicrobial agents from *F. globosa* latex. The findings from this study will contribute to our understanding of natural product-based therapeutics and provide crucial insights for future drug development efforts in addressing the global challenge of antimicrobial resistance.

METHODS

Plant Material Collection and Authentication. Latex samples were collected from *F. globosa*

trees on the University of Nigeria campus during the rainy season (July 2016). Collection occurred between 0600 and 0800 hours to maximise latex flow. The plant species was authenticated by Mr A. Ozioko, a taxonomist at the International Center for Ethnomedicine and Drug Development (INTERCEDD), Nsukka, with voucher specimens deposited in the centre's herbarium.

Latex Processing and Sample Preparation

Fresh Latex Collection: Stem incisions (approximately 5 cm long and 2 mm deep) were made using sterilised stainless steel blades. The exuding latex was collected in sterile borosilicate glass containers, with approximately 100 ml obtained from multiple trees. The collected latex was immediately divided into two portions for phytochemical analysis and antimicrobial studies.

Dried Latex Preparation: The latex designated for drying underwent acetone precipitation using a 1:1.4 ratio of latex to acetone. The precipitated material was separated into small lumps and dried in a temperature-controlled oven at 60 °C for three weeks. This temperature was specifically chosen to preserve thermolabile compounds while achieving the necessary physical properties for subsequent testing.

Phytochemical Analysis. Comprehensive phytochemical screening employed standardised protocols to detect major classes of bioactive compounds. All tests were performed in triplicate to ensure reliability.

Carbohydrate Analysis: Molisch's test was performed using α-naphthol solution in ethanol, with concentrated sulfuric acid carefully added to form a layer. The interface was observed for the characteristic violet ring formation.

Alkaloid Detection: Multiple confirmatory tests were employed using Mayer, Dragendorff, Wagner, and Hager reagents. Samples underwent acid extraction followed by alkalinisation and re-extraction to ensure accurate results.

Glycoside Analysis: A comprehensive glycoside screening protocol included tests for: Reducing sugars (pre- and post-hydrolysis); Cardiac glycosides (Keller-Killiani test); Cyanogenic glycosides (sodium picrate paper method); Anthraquinone glycosides (Borntrager's and modified Bontrager's tests).

Additional Component Analysis. The systematic screening included tests for: Saponins (frothing and hemolysis tests); Tannins (ferric chloride and lead sub-acetate tests); Flavonoids (ammonia and aluminium chloride tests); Resins (precipitation test); Proteins (Millon's and xanthoproteic tests); Steroids (Liebermann-Burchard test); Terpenoids (Salkowski test).

Antimicrobial Studies

Test Microorganisms: Eight pathogenic microorganisms were selected for antimicrobial screening: 1) Gram-positive bacteria: Staphylococcus aureus, Bacillus subtilis; 2) Gram-negative bacteria: Escherichia coli, Pseudomonas aeruginosa, Salmonella typhii, Klebsiella pneumonia; 3) Fungal species: Candida albicans (yeast), Aspergillus niger (mold).

All strains were obtained from the Department of Pharmaceutics and Pharmaceutical Microbiology, University of Nigeria, Nsukka, and maintained through regular subculturing.

Culture Media Preparation: Nutrient agar (for bacteria) and potato dextrose agar (for fungi) were prepared according to manufacturer specifications. The media were sterilised by autoclaving at 121°C for 15 minutes under 15 psi pressure. Quality control included sterility testing and pH verification.

Standardisation of Microbial Suspensions: Microbial suspensions were standardised using the McFarland 0.5 turbidity standard, approximately equivalent to 1.5 × 108 CFU/ml. Serial dilutions achieved final working concentrations of 104 CFU/ml for testing.

Antimicrobial Activity Assessment

1) Fresh Latex Testing: The agar well diffusion method employed 6 mm diameter wells in seeded agar plates. Fresh latex (0.2 ml) was applied directly to wells, and 15 minutes were allowed for diffusion before incubation. Plates were incubated at 37°C for 24 hours (bacteria) or 25°C for 48 hours (fungi).

2) Dried Latex Testing: Stock solutions (100 mg/ml) were prepared from pulverised dried latex. Serial dilutions produced 50, 25, 12.5, and 6.25 mg/ml concentrations. Activity assessment followed the same well diffusion methodology used for fresh latex.

3) Determination of Minimum Inhibitory Concentration: MIC values were determined through the graphical method, plotting the square of inhibition zone diameters (IZD^2) against the logarithm of concentration. The antilogarithm of the x-intercept provided the MIC value. Confirmatory tests

included extended incubation periods to distinguish between bacteriostatic and bactericidal effects.

4) Statistical Analysis. All experiments were performed in triplicate, with results expressed as mean ± standard deviation. Statistical significance was determined using one-way ANOVA followed by Tukey's post-hoc test, with $p < 0.05$ considered significant.

RESULTS AND DISCUSSION

Phytochemical Analysis. Comprehensive phytochemical screening revealed a distinct profile of secondary metabolites in *F. globosa* latex, as seen in Table 1. This table summarises the phytochemical components detected in *Ficus globosa* latex through a comprehensive screening process.

Table 1 – Phytochemical Profile of *Ficus globosa* Latex Based on Comprehensive Screening

Component	Major (+++)	Moderate (++)	Minor (+)	Absent (-)
Resins	+++			
Steroids	+++			
Terpenoids	+++			
Flavonoids		++		
Fats and oils			+	
Hydrolysable glycosides			+	
Carbohydrates				-
Alkaloids				-
Cardiac glycosides				-
Cyanogenic glycosides				-
Anthracene glycosides				-
Saponins				-
Tannins				-
Proteins				-

The table highlights the presence levels of various secondary metabolites, categorised as major (+++), moderate (++), minor (+), or absent (-). Major components include resins, steroids, and terpenoids, while flavonoids are present at moderate levels, and fats, oils, and hydrolysable glycosides are detected at minor levels. Notably, carbohydrates, alkaloids, cardiac glycosides, and other glycosides are absent. This phytochemical profile provides insights into the bioactive compounds responsible for the latex's observed antimicrobial properties.

Antimicrobial Activity

Fresh Latex Activity Profile: Fresh latex demonstrated selective antimicrobial activity, showing effectiveness only against B. subtilis with an inhibition zone diameter of 10 mm (Figure 1a, b). No activity was observed against other test organisms.

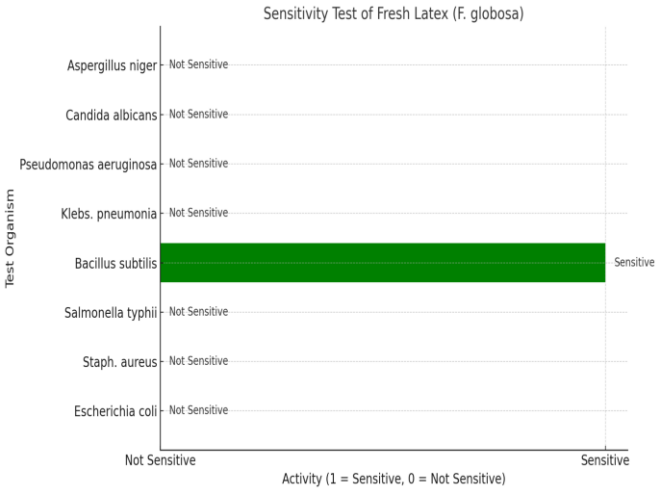

Figure 1a – Antimicrobial Activity of Fresh Latex Against Test Microorganisms

Notes: the sensitivity of fresh *Ficus globosa* latex was evaluated using the agar well diffusion method. The results are presented as 'Sensitive' (green) or 'Not Sensitive' (red) based on the presence or absence of inhibition zones. Among the tested microorganisms, only Bacillus subtilis exhibited sensitivity to the fresh latex, while all others showed no activity).

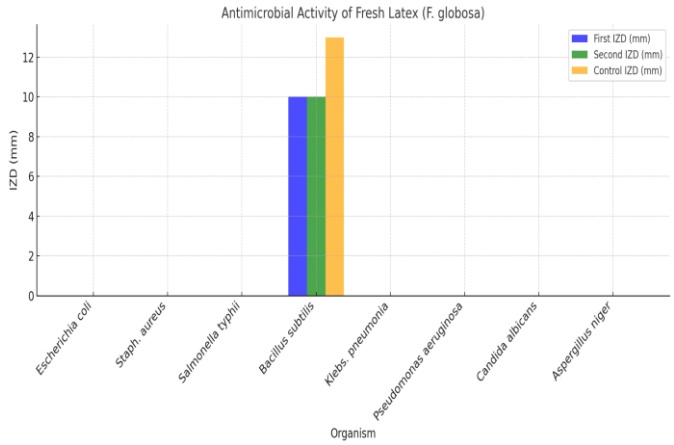

Figure 1b – Antimicrobial Activity of Fresh Latex Against Test Microorganisms

Notes: the antimicrobial activity of fresh *Ficus globosa* latex was evaluated using the agar well diffusion method. The inhibition zone diameters (IZDs) were measured for sensitive microorganisms, compared to the standard control (amoxicillin and clavulanate, 30 µg/ml). Only Bacillus subtilis showed sensitivity to the fresh latex, with inhibition zones recorded for two replicates.

Dried Latex Activity Profile: Table 2 summarises the inhibition zone diameters (IZD), their corresponding squares (IZD^2), and the logarithmic concentrations of dried *Ficus globosa* latex against susceptible microorganisms.

The data highlight the varying sensitivity of microorganisms to the latex, with specific values determined at different concentrations. At 100 mg/ml concentration, the antimicrobial activity of dried *Ficus globosa* latex was evaluated against three microorganisms. The maximum inhibition zone diameters (IZD) and the minimum inhibitory concentrations (MIC) were determined for each organism, as shown in Table 2. The dried latex demonstrated the highest activity against *Bacillus subtilis,* with a maximum IZD of 15 mm and a MIC of 3.89 mg/ml. *Aspergillus niger* showed moderate susceptibility with a maximum IZD of 17 mm and a MIC of 8.13 mg/ml.

In comparison, *Staphylococcus aureus* exhibited an IZD of 13 mm and a MIC of 14.79 mg/ml. The MIC values were determined graphically by plotting IZD^2 against the logarithmic concentration of the dried latex. Figure 2 shows this relationship for the three microorganisms, with x-axis intercepts used to calculate MIC values of 3.89 mg/ml for *B. subtilis*, 8.13 mg/ml for *A. niger*, and 14.79 mg/ml for *S. aureus*.

Table 2 – Antimicrobial Activity of Dried *Ficus globosa* Latex

Microorganisms	Concentration of the latex (mg/ml)	IZD (mm)	Log conc. (mg/ml)	IZD^2 (mm^2)
Staphylococcus aureus	6.25	-	0.796	-
Staphylococcus aureus	12.50	-	1.097	-
Staphylococcus aureus	25.00	7	1.398	49
Staphylococcus aureus	50.00	10	1.699	100
Staphylococcus aureus	100.00	13	2.000	169
Bacillus subtilis	6.25	-	0.796	-
Bacillus subtilis	12.50	7	1.097	49
Bacillus subtilis	25.00	9	1.398	81
Bacillus subtilis	50.00	12	1.699	144
Bacillus subtilis	100.00	15	2.000	225
Aspergillus niger	6.25	8	0.796	64
Aspergillus niger	12.50	9	1.097	81
Aspergillus niger	25.00	11	1.398	121
Aspergillus niger	50.00	13	1.699	169
Aspergillus niger	100.00	17	2.000	289

Notes: Antimicrobial activity of dried *Ficus globosa* latex assessed by inhibition zone diameter (IZD) and logarithmic concentrations for susceptible microorganisms.

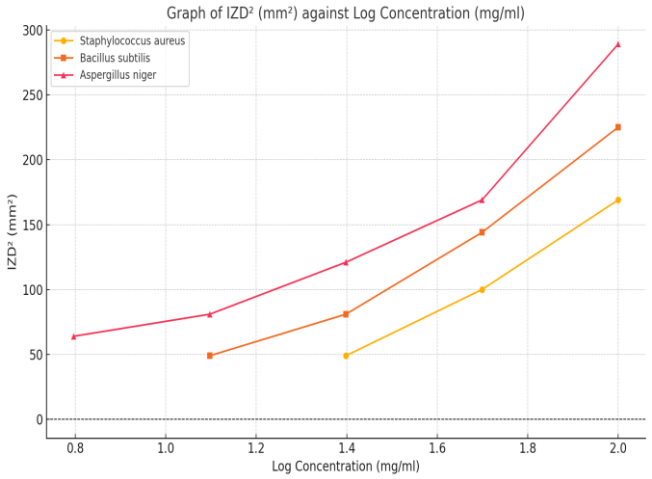

Figure 2 – Graph of IZD² (mm²) against Log Concentration (mg/ml) for Dried *Ficus globosa* Latex

Notes: This graph illustrates the relationship between the logarithmic concentration of dried *Ficus globosa* latex (mg/ml) and the squared inhibition zone diameter (IZD²) for *Staphylococcus aureus*, *Bacillus subtilis*, and *Aspergillus niger*. The intercepts on the x-axis, determined by extrapolating the straight lines to where IZD² equals zero, are used to calculate each microorganism's minimum inhibitory concentration (MIC) values.

Table 3 summarises the intercept values derived from the logarithmic concentration versus IZD^2 (mm^2) plot and their corresponding antilogarithms, which represent the MIC (minimum inhibitory concentration) values of dried *Ficus globosa* latex against *Staphylococcus aureus*, *Aspergillus niger*, and *Bacillus subtilis*. The MIC values, expressed in mg/ml, highlight the sensitivity of each microorganism to the dried latex, with *Bacillus subtilis* showing the highest sensitivity (lowest MIC value).

Table 3 – Minimum Inhibitory Concentration (MIC) of Dried *Ficus globosa* Latex Against Corresponding Susceptible Microorganisms

Microorganism	*Staph. aureus*	*Asper. niger*	*B. subtilis*
Intercept on x-axis	1.17	0.91	0.59
Antilog of intercept = MIC (mg/ml)	14.79	8.13	3.89

As shown in Figure 3a, the antimicrobial activity of dried *Ficus globosa* latex was selective, showing no activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhii*, *Klebsiella pneumonia*, and *Candida albicans*. Also, comparative testing using the standard antibiotic colistin sulphomethate (200 µg/ml) revealed inhibition zone diameters of 23 mm for *Bacillus subtilis*, 18 mm for *Staphylococcus aureus*, and 12 mm for *Aspergillus niger* (Figure 3b). These findings underscore the specificity of *F. globosa* latex in targeting certain pathogens while suggesting its potential role as a selective antimicrobial agent.

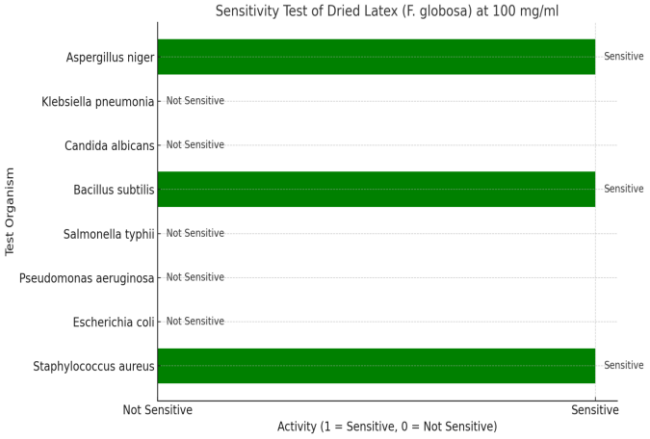

Figure 3A – Minimum Inhibitory Concentration (MIC) of Dried *Ficus globosa* Latex Against Corresponding Susceptible Microorganisms

Notes: This figure represents the sensitivity test of dried *Ficus globosa* latex at a concentration of 100 mg/ml

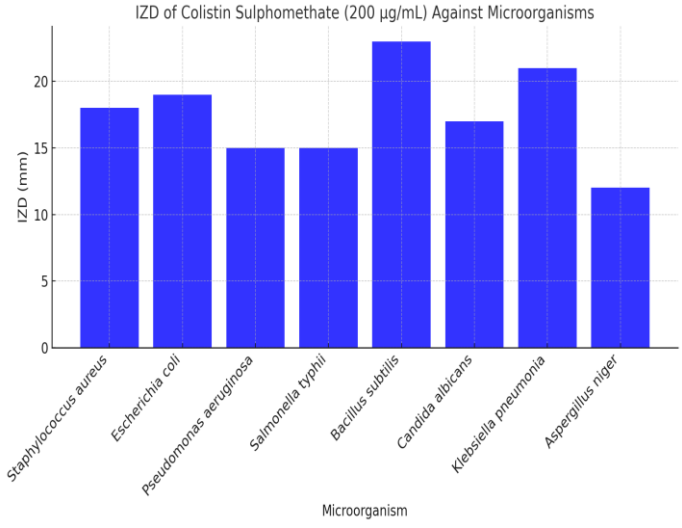

Figure 3b – Minimum Inhibitory Concentration (MIC) of Dried *Ficus globosa* Latex Against Corresponding Susceptible Microorganisms

Notes: This bar graph represents the inhibition zone diameters (IZD) of colistin sulphomethate (200 µg/ml) against various microorganisms. The data highlights the comparative effectiveness of the antimicrobial agent, with Bacillus subtilis showing the largest IZD of 23 mm.

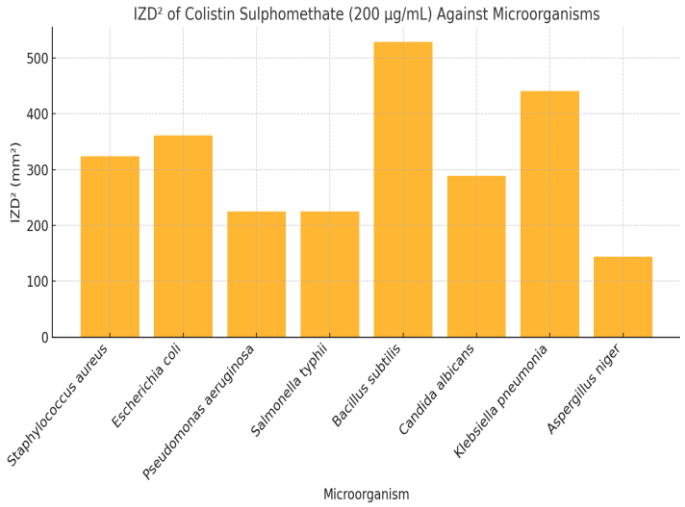

Figure 3c – Minimum Inhibitory Concentration (MIC) of Dried *Ficus globosa* Latex Against Corresponding Susceptible Microorganisms

Notes: This bar graph represents the squared inhibition zone diameters (IZD²) of colistin sulphomethate (200 µg/ml) against the same microorganisms. The IZD² values provide a squared-area representation of antimicrobial activity, with Bacillus subtilis having the largest value of 529 mm².

The comprehensive investigation of *F. globosa* latex reveals significant potential for therapeutic development, particularly in addressing the growing challenge of antimicrobial resistance. The phytochemical analysis demonstrated a complex profile dominated by nonpolar constituents, explaining the observed solubility characteristics and the biological activity patterns.

The abundance of resins, steroids, and terpenoids suggests multiple potential mechanisms of action, a characteristic increasingly valued in modern antimicrobial therapy [13–15]. The moderate presence of flavonoids adds particular interest, as these compounds are known for their antioxidant and anti-inflammatory properties, potentially offering synergistic therapeutic benefits beyond direct antimicrobial activity [16]. The relative absence of polar constituents such as alkaloids, saponins, and tannins distinguishes *F. globosa* latex from other studied Ficus species, suggesting unique evolutionary adaptations that may translate to novel therapeutic applications.

The solubility challenges encountered during this study highlight important considerations for pharmaceutical development. The latex's nonpolar nature necessitated specific processing approaches, including high-temperature drying and careful solvent selection. These findings provide valuable insights for future formulation development, suggesting that lipid-based delivery systems may be particularly suitable for therapeutic applications [17].

The differential activity observed between fresh and dried latex preparations offers intriguing insights into potential activation mechanisms. Fresh latex demonstrated selective activity against B. subtilis, while the dried preparation showed broader antimicrobial effects. This suggests that the drying process may enhance the bioavailability or activation of certain compounds [18, 19], which warrants further investigation to optimise therapeutic preparations.

The MIC values reveal a stronger antimicrobial effect of *F. globosa* latex, particularly against *B. subtilis* (3.89 mg/ml) and *A. niger* (8.13 mg/ml). These values place the latex within a range considered promising for drug development, even as a crude preparation. The observed lower MIC for *B. subtilis* highlights its exceptional susceptibility and underscores the potential of *F. globosa* latex as a targeted therapeutic for gram-positive bacteria.

The antifungal activity against *A. niger* also shows potential for applications in treating fungal infections, particularly in topical formulations, given its intermediate MIC of 8.13 mg/ml. The MIC against *S. aureus* (14.79 mg/ml) further confirms the broad-spectrum potential of the latex, making it a promising candidate for addressing bacterial infections.

These findings support the hypothesis that secondary metabolites, particularly terpenoids and steroids, may interact with unique components of microbial cell walls [20], thereby contributing to the observed selectivity for gram-positive bacteria [13]. This aligns with the broader understanding of terpenoid-rich natural products as potent antimicrobial agents [21, 22].

The MIC values also emphasise the importance of optimising the drying and processing methods to preserve or enhance the bioavailability of active compounds. The enhanced activity seen in dried latex underscores the role of processing in activating or concentrating specific bioactive components [23].

Future research should focus on isolating and characterising the active compounds responsible for the observed antimicrobial effects. Detailed studies on the mechanisms of action and potential synergistic effects with other antimicrobial agents

will be crucial for advancing *F. globosa* latex toward clinical applications. Furthermore, exploring formulation techniques to improve its bioavailability and stability will be vital for its development as a therapeutic agent.

CONCLUSIONS

This comprehensive study establishes *F. globosa* latex as a promising candidate for therapeutic development, particularly in antimicrobial applications. The research provides several key findings that will guide future development efforts. First, the complex phytochemical profile, dominated by nonpolar constituents, suggests unique mechanisms of action that may help address the challenge of antimicrobial resistance. Second, the demonstrated activity against bacterial and fungal pathogens, with promising effects against gram-positive bacteria, indicates potential systemic and topical therapeutic applications.

The processing challenges encountered and solutions developed provide valuable insights for future pharmaceutical development. Enhancing antimicrobial activity through specific processing methods suggests opportunities for optimising therapeutic preparations. Selective activity against certain pathogens may offer advantages in reduced disruption of normal microbiota and decreased likelihood of resistance development.

Future research directions should focus on several key areas. Isolation and characterisation of specific active compounds will be essential for understanding mechanisms of action and optimising therapeutic effects. Detailed toxicological studies will be needed to establish safety profiles for different routes of administration. The development of standardised formulations suitable for clinical application will require careful consideration of the physical and chemical properties identified in this study. Clinical trials will ultimately be needed to establish efficacy and safety in human populations.

The findings from this study contribute significantly to our understanding of *F. globosa* latex as a potential therapeutic agent and provide a strong foundation for future development efforts. As the global challenge of antimicrobial resistance continues to grow, natural products with novel mechanisms of action, such as those identified here, may play an increasingly important role in therapeutic strategies.

Acknowledgements

The authors thank the Department of Pharmaceutics and Pharmaceutical Microbiology, University of Nigeria, Nsukka, for providing the test organisms and laboratory facilities. Thanks to Mr. A.O Ozioko for his expertise in plant authentication and the International Center for Ethnomedicine and Drug Development (INTERCEDD) for supporting this research.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from public, commercial, or not-for-profit funding agencies.

Ethics Approval

This study did not involve human participants or animals and did not require ethical approval.

Consent to Participate

This study did not involve human participants and did not require consent.

Consent to Publish

This study does not contain data from any person.

Conflict of Interest Disclosure

The authors declare that they have no financial conflict of interest concerning the content of this report. All authors certify that their affiliations with or financial involvement in, within the past 5 years and foreseeable future, any organisation or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed.

REFERENCES

1. O'Neill, Ch. (2016, May). *Tackling Drug-Resistant Infections Globally: Final Report And Recommendations*. Retrieved from https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

2. Atanasov, A. G., Zotchev, S. B., Dirsch, V. M., Orhan, I. E., Banach, M., Rollinger, J. M., Barreca, D., Weckwerth, W., Bauer, R., Bayer, E. A., Majeed, M., Bishayee, A., Bochkov, V., Bonn, G. K., Braidy, N., Bucar, F., Cifuentes, A., D'Onofrio, G., … Supuran, C. T. (2021). Natural products in drug discovery: advances and opportunities. *Nature Reviews Drug Discovery, 20*(3), 200–216. doi: 10.1038/s41573-020-00114-z

3. Dias, D. A., Urban, S., & Roessner, U. (2012). A Historical Overview of Natural Products in Drug Discovery. *Metabolites, 2*(2), 303–336. doi: 10.3390/metabo2020303

4. Cragg, G. M., & Newman, D. J. (2013). Natural products: A continuing source of novel drug leads. *Biochimica et Biophysica Acta (BBA) - General Subjects, 1830*(6), 3670–3695. doi: 10.1016/j.bbagen.2013.02.008

5. Clement, W. L., Bruun-Lund, S., Cohen, A., Kjellberg, F., Weiblen, G. D., & Rønsted, N. (2020). Evolution and classification of figs (Ficus, Moraceae) and their close relatives (Castilleae) united by involucral bracts. *Botanical Journal of the Linnean Society, 193*(3), 316–339. doi: 10.1093/botlinnean/boaa022

6. Boutaj, H. (2024). A Comprehensive Review of Moroccan Medicinal Plants for Diabetes Management. *Diseases, 12*(10), 246. doi: 10.3390/diseases12100246

7. Lansky, E. P., Paavilainen, H. M., Pawlus, A. D., & Newman, R. A. (2008). Ficus spp. (fig): Ethnobotany and potential as anticancer and anti-inflammatory agents. *Journal of Ethnopharmacology, 119*(2), 195–213. doi: 10.1016/j.jep.2008.06.025

8. Patel, R., Gautam, P. (2014). *Medicinal Potency Of Ficus Bengalensis: A Review*. Retrieved from https://www.researchgate.net/publication/321098074_MEDICINAL_POTENCY_OF_FICUS_BENGALENSIS_A_REVIEW

9. Shi, Y., Mon, A. M., Fu, Y., Zhang, Y., Wang, C., Yang, X., & Wang, Y. (2018). The genus Ficus (Moraceae) used in diet: Its plant diversity, distribution, traditional uses and ethnopharmacological importance. *Journal of Ethnopharmacology, 226*, 185–196. doi: 10.1016/j.jep.2018.07.027

10. Alam, A., & Mazumder, P. M. (2024). The Application of Ficus Species in the Treatment of Neurological Disorders. *Pharmacognosy Magazine, 21*(2), 323–335. doi: 10.1177/09731296241281440

11. Ahmed, S. S., & Rahman, M. O. (2024). From Flora to Pharmaceuticals: 100 new additions to angiosperms of Gafargaon subdistrict in Bangladesh and unraveling antidiabetic drug candidates targeting DPP4 through in silico approach. *PLOS ONE, 19*(3), e0301348. doi: 10.1371/journal.pone.0301348

12. Wachtel-Galor, S., Benzie, I. (2011). *Herbal Medicine: An Introduction to Its History, Usage, Regulation, Current Trends, and Research Needs*. Retrieved from https://pubmed.ncbi.nlm.nih.gov/22593939/

13. Yang, W., Chen, X., Li, Y., Guo, S., Wang, Z., & Yu, X. (2020). Advances in Pharmacological Activities of Terpenoids. *Natural Product Communications, 15*(3). doi: 10.1177/1934578x20903555

14. Adedokun, K. A., Imodoye, S. O., Bello, I. O., Lanihun, A.-A., & Bello, I. O. (2023). Therapeutic potentials of medicinal plants and significance of computational tools in anti-cancer drug discovery. *Phytochemistry, Computational Tools and Databases in Drug Discovery*, 393–455. doi: 10.1016/b978-0-323-90593-0.00017-4

15. Masyita, A., Mustika Sari, R., Dwi Astuti, A., Yasir, B., Rahma Rumata, N., Emran, T. B., Nainu, F., & Simal-Gandara, J. (2022). Terpenes and terpenoids as main bioactive compounds of essential oils,

their roles in human health and potential application as natural food preservatives. *Food Chemistry: X*, 13, 100217. doi: 10.1016/j.fochx.2022.100217

16. Ullah, A., Munir, S., Badshah, S. L., Khan, N., Ghani, L., Poulson, B. G., Emwas, A.-H., & Jaremko, M. (2020). Important Flavonoids and Their Role as a Therapeutic Agent. *Molecules, 25*(22), 5243. doi: 10.3390/molecules25225243

17. Shrestha, H., Bala, R., & Arora, S. (2014). Lipid-Based Drug Delivery Systems. *Journal of Pharmaceutics, 2014*, 1–10. doi: 10.1155/2014/801820

18. Emami, F., Vatanara, A., Park, E. J., & Na, D. H. (2018). Drying Technologies for the Stability and Bioavailability of Biopharmaceuticals. *Pharmaceutics, 10*(3), 131. doi: 10.3390/pharmaceutics10030131

19. Wang, B., Xiang, J., He, B., Tan, S., & Zhou, W. (2023). Enhancing bioavailability of natural extracts for nutritional applications through dry powder inhalers (DPI) spray drying: technological advancements and future directions. *Frontiers in Nutrition, 10*. doi: 10.3389/fnut.2023.1190912

20. Pang, Z., Chen, J., Wang, T., Gao, C., Li, Z., Guo, L., Xu, J., & Cheng, Y. (2021). Linking Plant Secondary Metabolites and Plant Microbiomes: A Review. *Frontiers in Plant Science, 12*. doi: 10.3389/fpls.2021.621276

21. Huang, W., Wang, Y., Tian, W., Cui, X., Tu, P., Li, J., Shi, S., & Liu, X. (2022). Biosynthesis Investigations of Terpenoid, Alkaloid, and Flavonoid Antimicrobial Agents Derived from Medicinal Plants. *Antibiotics, 11*(10), 1380. doi: 10.3390/antibiotics11101380

22. Fotsing Yannick Stephane, F., & Kezetas Jean Jules, B. (2020). Terpenoids as Important Bioactive Constituents of Essential Oils. *Essential Oils - Bioactive Compounds, New Perspectives and Applications*. 10.5772/intechopen.91426

23. Sorrenti, V., Burò, I., Consoli, V., & Vanella, L. (2023). Recent Advances in Health Benefits of Bioactive Compounds from Food Wastes and By-Products: Biochemical Aspects. *International Journal of Molecular Sciences, 24*(3), 2019. doi: 10.3390/ijms24032019