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# Harnessing the pharmaceutical potential of noni fruit extract: antibacterial and antifungal effects against antibiotic-resistant microorganisms and oral pathogens

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**ABSTRACT**: The escalating threat of antibiotic-resistant microorganisms necessitates innovative therapeutic approaches. This study explores the pharmaceutical potential of Noni Fruit Extract (NFE), derived from *Morinda citrifolia*, as a promising solution against antibiotic-resistant strains and oral pathogens. NFE exhibited robust antibacterial activity, rivaling conventional antibiotics. The investigation encompassed a spectrum of microorganisms, including Gram-positive (*Staphylococcus aureus, Bacillus subtilis, Enterococcus faecalis*), Gram-negative (*Pseudomonas aeruginosa, Proteus vulgaris, Escherichia coli, Salmonella typhimurium, Klebsiella pneumoniae*), antibiotic-resistant strains (Vancomycin-Resistant Enterococci (VRE), Methicillin-Resistant *Staphylococcus aureus* (MRSA)), a fungal pathogen (*Candida albicans*), and oral pathogens (*Streptococcus mutans, Streptococcus mitis*). The disk diffusion method determined NFE's inhibition zone diameters against these pathogens. NFE displayed potent antibacterial activity against both Gram-negative and Gram-positive microorganisms. At 5mg/mL, NFE produced a 10 mm inhibition zone against *Pseudomonas aeruginosa*, reaching 19.3 mm at 100mg/mL. *Proteus vulgaris* exhibited zones of 10.3, 12.7, 27.3, 33.7, and 44.7 mm at NFE concentrations from 5 to 100 mg/mL. *Escherichia coli* displayed the largest inhibition zone of 61.7 mm at 100 mg/mL NFE. Similar trends were observed for *Salmonella typhimurium* and *Klebsiella pneumoniae*. NFE also demonstrated strong antifungal activity against *Candida albicans*. Against antibiotic-resistant strains, NFE significantly affected VRE at 100mg/mL, yielding a 42.3 mm zone. MRSA displayed an 8.3 mm zone at 5 mg/mL NFE and 51.3 mm below 100 mg/mL, underscoring NFE's efficacy against antibiotic-resistant strains. NFE exhibited robust antibacterial activity against oral pathogens, with notable inhibition zones at higher concentrations on *Streptococcus mutans* and *Streptococcus mitis*. Following EN 1276:2019 methodology, time-dependent antibacterial efficacy assessment revealed significant log reductions in microbial load, indicating NFE's potent antibacterial effect at various concentrations and contact times. In conclusion, NFE displayed potent antibacterial and antifungal activities against various microorganisms, including antibiotic-resistant strains and oral pathogens. These findings suggest NFE's promise as an alternative therapeutic agent in combatting antimicrobial resistance.

**KEYWORDS**: Noni fruit extract; pharmaceutical potential; oral pathogens; antibiotic resistance; antibacterial effects; antifungal effects; *Morinda citrifolia*

## 1. INTRODUCTION

The escalating global antibiotic resistance crisis poses an urgent challenge, demanding the discovery novel therapeutic agents [1,2]. Antibiotic resistance has emerged as a critical global health threat, undermining the effectiveness of essential medical interventions and resulting in prolonged illnesses, increased healthcare costs, and higher mortality rates [3,4]. The development and spread of antibiotic-resistant microorganisms have been fueled by factors such as the overuse and misuse of antibiotics, inadequate infection prevention and control practices, and the lack of novel antibiotics in the pharmaceutical pipeline. These factors have created a perfect storm, compelling researchers and healthcare professionals to seek innovative solutions beyond conventional antibiotics [5–7].

One such avenue of investigation revolves around the remarkable potential of natural compounds, harnessing the wisdom of traditional remedies while integrating modern scientific methodologies. Noni fruit,

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an ancient tropical fruit with a rich ethnopharmacological history, has emerged as a promising candidate in the quest for alternative antimicrobial agents [8,9].

Noni fruit, botanically known as *Morinda citrifolia*, has garnered attention across diverse cultures for centuries due to its multifaceted health benefits [10,11]. Its traditional uses span a broad spectrum, from wound healing and pain relief to managing digestive disorders and infections. The fruit's traditional reputation for promoting health has driven contemporary scientific exploration into its bioactive constituents and their potential therapeutic applications [12].

Noni fruit extract embodies a complex composition of bioactive molecules, including alkaloids, flavonoids, iridoids, polysaccharides, and vitamins [13]. The intricate synergy among these compounds offers a potential pharmaceutical treasure trove, warranting meticulous investigation to unravel their pharmacological significance [11,14–16]. As global healthcare systems grapple with the challenges of antibiotic resistance, this reservoir of natural compounds could hold answers to combat these defiant microbial adversaries.

The intricate composition of bioactive compounds within noni fruit extract has attracted attention for its potential to combat antibiotic-resistant microorganisms. While the exact mechanisms underlying these effects are still being unraveled, preliminary studies suggest that noni fruit extract may exhibit antibacterial action through various modes, including disrupting microbial cell membranes, interfering with essential cellular processes, and modulating bacterial communication systems [17–19].

Beyond its antibacterial attributes, noni fruit extract's antifungal potential is noteworthy. Fungal infections, with their propensity to thrive in compromised immune environments, can lead to discomfort and reduced quality of life. Noni fruit extract's antifungal activity has been indicated against several fungal strains, including *Candida* spp. and *Aspergillus* spp., suggesting its potential utility against various fungal infections [10,20,21]. Fungal oral cavity infections, often associated with compromised immunity, can lead to conditions such as oral candidiasis, denture stomatitis, and angular cheilitis [22,23]. These conditions can cause discomfort, pain, and impaired quality of life for affected individuals. Given the intricate balance of the oral microbiota and the role of fungal overgrowth in oral health, exploring natural agents like noni fruit extract offers a promising avenue to address these challenges.

This research article aims to comprehensively explore the pharmaceutical potential of noni fruit extract focusing on its antibacterial and antifungal activities against antibiotic-resistant microorganisms and oral pathogens. The investigation encompasses a multifaceted approach, ranging from extracting and characterizing noni fruit extract to in vitro assessments of its antimicrobial efficacy. By deciphering the mechanisms underpinning these effects, this study seeks to illuminate the path toward utilizing noni fruit extract as an alternative therapeutic option to counter antibiotic-resistant microorganisms. By meticulously examining the available scientific literature and experimental findings, this article aims to contribute to the growing body of knowledge in this vital field and pave the way for future research endeavors and practical applications.

## 2. RESULTS

In this study, the antibacterial and antifungal effects of Noni Fruit Extract (NFE) were investigated on a spectrum of microorganisms, including 3 Gram-positive strains (*Staphylococcus aureus* DSM 21979, *Bacillus subtilis* DSM 21393, *Enterococcus faecalis* ATCC 29212), 5 Gram-negative microorganisms (*Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* ATCC 6380, *Escherichia coli* ATCC 25922, *Salmonella typhimurium* ATCC 14028, *Klebsiella pneumoniae* ATCC 13883), 2 antibiotic-resistant strains (Vancomycin-Resistant Enterococci (VRE), Methicillin-Resistant *Staphylococcus aureus* ATCC 43300 (MRSA)), 1 fungal pathogen (*Candida albicans* ATCC 10231), and 2 oral pathogens (*Streptococcus mutans* ATCC 25175, *Streptococcus mitis* DSM 12643). The investigation involved using the disk diffusion method to determine the inhibition zone diameters created by NFE on these pathogenic microorganisms.

The findings of this study are presented in Figures 1 and 2.

According to the results, the Noni Fruit Extract (NFE) demonstrated significant antibacterial effects on Gram-negative and Gram-positive microorganisms. Specifically, against *Pseudomonas aeruginosa*, the lowest concentration of NFE (5mg/mL) resulted in a 10 mm inhibition zone, while the highest concentration (100mg/mL) produced a 19.3 mm zone. *Proteus vulgaris* displayed inhibition zones of 10.3, 12.7, 27.3, 33.7, and 44.7 mm at NFE concentrations of 5, 10, 25, 50, and 100 mg/mL, respectively. *Escherichia coli* exhibited the largest inhibition zone of 61.7 mm at 100 mg/mL NFE. Similar trends were observed for *Salmonella typhimurium* and *Klebsiella pneumonia*, with the lowest concentration resulting in 12.3 mm and 9 mm zones and the highest concentration yielding 41.3 mm and 34.7 mm zones, respectively.

In contrast, Gram-positive *Enterococcus faecalis* showed the smallest inhibition zone of 8 mm at 5mg/mL NFE. *Staphylococcus aureus* exhibited inhibition zones of 12.3 mm at the lowest NFE concentration

and 39.3 mm at the highest, indicating a dose-dependent antibacterial effect. *Bacillus subtilis* displayed a 6.3 mm zone at the lowest concentration (5mg/mL) and a 32.7 mm zone at the highest concentration (100mg/mL). These results underscore the potent antibacterial efficacy of NFE against both Gram-negative and Gram-positive microorganisms.

To assess its antifungal activity, NFE was tested against *Candida albicans*, revealing inhibition zones of 7.3 mm at 5 mg/mL, 11 mm at 10 mg/mL, 16 mm at 25 mg/mL, 25.3 mm at 50 mg/mL, and 28.3 mm at 100 mg/mL. These findings indicate that NFE exhibits a high degree of antifungal activity against fungal pathogens.

In summary, the study's results highlight the strong antibacterial effects of NFE against a wide range of Gram-negative and Gram-positive microorganisms and its substantial antifungal activity against *Candida albicans*.

Regarding antibiotic-resistant microorganisms, Noni Fruit Extract (NFE) exhibited noteworthy effects. At the lowest concentration (5mg/mL), NFE did not significantly impact VRE. However, the highest concentration (100mg/mL) resulted in a substantial 42.3 mm inhibition zone. Additionally, in the case of MRSA, at 5 mg/mL NFE, an 8.3 mm inhibition zone was observed, while below 100 mg/mL, a substantial 51.3 mm zone was detected. The ability of NFE to exert a significant effect on antibiotic-resistant microorganisms is of critical importance.

Lastly, when tested against oral pathogens, at a concentration of 5 mg/mL, NFE did not produce any inhibition zones. However, at 10 mg/mL, inhibitory zones of 7.3 mm and 8 mm were observed for *S. mutans* and *S. mitis*, respectively. At the highest concentration, NFE exhibited an effect of 28 mm on *S. mutans* and 36 mm on S. mitis. These successful results against oral pathogens underscore the broad-spectrum efficacy of NFE.

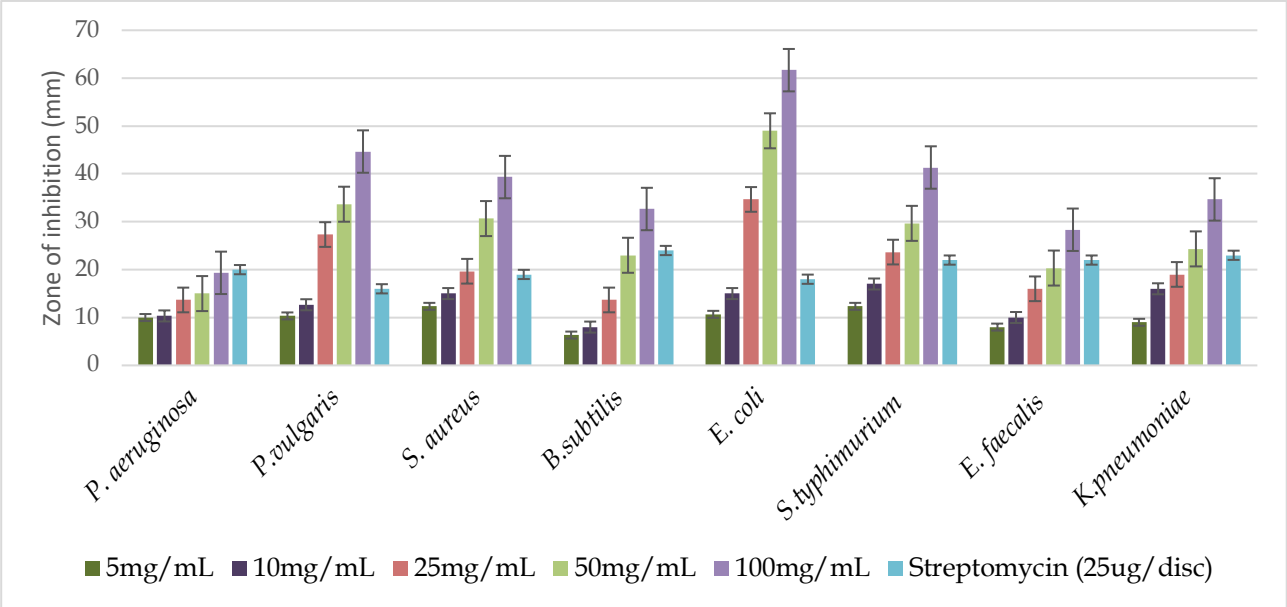


**Figure 1.** Antibacterial activity of noni fruit extract against different pathogens.

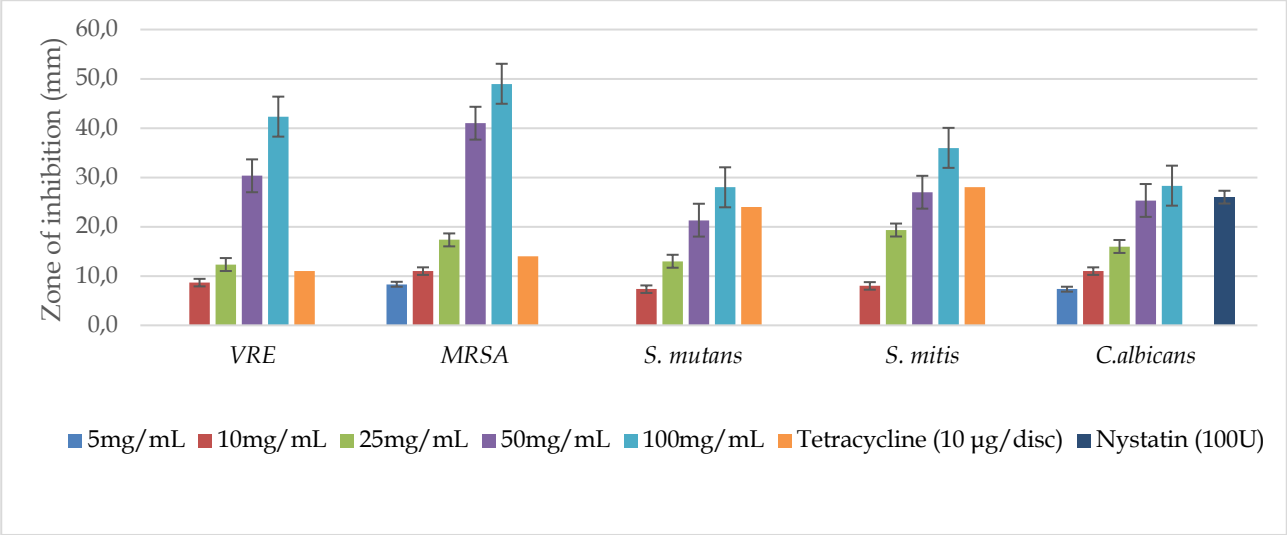


**Figure 2.** Antibacterial activity of noni fruit extract against fungal and oral pathogens.

To assess the time-dependent antibacterial efficacy of Noni Fruit Extract (NFE), the EN 1276:2019 test method was employed. In this method, known quantities of microorganisms are exposed to varying concentrations of NFE for 1 and 5-minute contact periods, and the logarithmic reduction in microbial load is calculated. Achieving a 5-log reduction signifies a 99.999% antimicrobial effectiveness **[24].** The time-dependent efficacy of NFE in solution against different microorganisms is presented in Table 1. The results revealed that at a concentration of 5 mg/mL, NFE achieved a 0.89 log reduction in E. coli after 1 minute and a 1.13 log reduction after 5 minutes. A 5-log reduction in E. coli was observed at 50 mg/mL concentration after only 1 minute of contact. In the case of S. aureus, a 5-log reduction occurred at 25 mg/mL concentration. Against E. faecalis, 5mg/mL NFE resulted in a 0.67 log reduction after 1 minute, while at 25 mg/mL, it caused a reduction of more than 5 logs in microbial load. For *K. pneumoniae*, a concentration of 50 mg/mL NFE yielded a 5-log reduction after 5 minutes of contact. These results highlight the potent antibacterial efficacy of NFE at different concentrations and contact times against these four microorganisms.

**Table 1.** Suspension test results of NFE at different concentrations

| **Concentration of NFE** | **Contact Time** | *Escherichia coli* | *Staphylococcus aureus* | *Enterococcus faecalis* | *Klebsiella pneumoniae* |
|---|---|---|---|---|---|
| 5mg/mL | 1 min | 0,89[a,b] | 1,32 | 1,65 | 0,67 |
| | 5 min | 1,13 | 2,34 | 2,56 | 1,02 |
| 10mg/mL | 1 min | 2,96 | 3,19 | 3,12 | 1,98 |
| | 5 min | 3,91 | 4,23 | 3,91 | 2,57 |
| 25mg/mL | 1 min | 4,03 | 5,08 | 4,65 | 2,91 |
| | 5 min | 4,92 | >5 | >5 | 3,87 |
| 50mg/mL | 1 min | 5,12 | >5 | >5 | 4,09 |
| | 5 min | >5 | >5 | >5 | >5 |
| 100mg/mL | 1 min | >5 | >5 | >5 | >5 |
| | 5 min | >5 | >5 | >5 | >5 |
| Positive Control (70% ethanol) | 1 min | 3,98 | 3,01 | 3,12 | 3,72 |
| | 5 min | >5 | 4,78 | >5 | >5 |
| Negative Control (PBS) | 1 min | <1 | <1 | <1 | <1 |
| | 5 min | <1 | <1 | <1 | <1 |

a. Log10 reductions

b. Values represent averages for duplicate experiments and each time the count was the average of three Petri dishes per dilution.

## 3. DISCUSSION

Noni Fruit Extract (NFE) has been extensively studied for its diverse health effects, including anti-cancer, antioxidant, anti-diabetic, analgesic, and anti-obesity properties. In addition to these well-documented effects, literature has also highlighted its antibacterial, antifungal, and antiviral activities. This study investigated the anti-bacterial and anti-fungal effects of a commercially available product, Kyani Nitro Fx, against various pathogenic microorganisms, antibiotic-resistant strains, and oral pathogens.

Several prior studies have reported the inhibitory potential of noni fruit extract against pathogenic bacteria. For instance, Rivera et al. [25] demonstrated significant antibacterial activity of noni fruit extract against *Escherichia coli, Staphylococcus aureus*, and *Pseudomonas aeruginosa*.

Another study by Jayaraman et al.[8] explored the antibacterial, antifungal, and antitumor effects of noni fruit extracted using different solvents (methanol, ethyl acetate, and hexane). The results indicated that the methanol extract exhibited strong antibacterial activity against many microorganisms, including *Bacillus subtilis, Staphylococcus aureus, Lactobacillus lactis*, and many others. The ethyl acetate extract also showed antibacterial effects against most microorganisms except *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. However, the hexane extract did not exhibit antibacterial activity against the tested microorganisms. Furthermore, both ethyl acetate and methanol extracts demonstrated antifungal effects against tested yeast and mold species. Our study aligns with these findings, as the commercial noni fruit extract showed similar profiles of antibacterial and antifungal activities.

Noni fruit extract has also displayed promise in combating multidrug-resistant bacterial strains. Palu et al. [19] reported its effectiveness against drug-resistant strains of *Mycobacterium tuberculosis*, suggesting its potential as an alternative therapy for tuberculosis.

Moreover, the antibacterial properties of noni fruit extract have been considered in the context of oral health. Research by Aldi et al. [18] indicated its potential for addressing oral pathogens, which could affect oral care products. Our study found that a mouthwash containing noni fruit extract reduced gingivitis scores in 15 gingivitis patients, similar to mouthwash solutions containing other chemical compounds.

Another study focused on two microorganisms responsible for tooth decay, *S. mutans* and *S. mitis*, and reported that mature noni fruit extract at a concentration of 1000 µg/mL effectively produced inhibition zones of 19 mm and 18.6 mm, respectively [23]. Our study observed the potent antibacterial effects of commercial noni fruit extract against the same microorganisms at different concentrations.

In conclusion, NFE has demonstrated a wide range of health benefits, including antibacterial and antifungal activities, making it a promising candidate for various applications in the field of medicine and oral health.

## 4. CONCLUSION

In conclusion, the existing body of research underscores the significant antibacterial potential of noni fruit extract against a wide spectrum of bacterial pathogens, including multidrug-resistant strains. This natural resource, abundant in bioactive compounds like alkaloids, flavonoids, iridoids, and vitamins, has exhibited promising inhibitory effects on bacterial growth through various mechanisms, such as disrupting microbial cell membranes and modulation of critical cellular processes.

Beyond its laboratory-tested antibacterial prowess, noni fruit extract's practical applications have also been explored. Studies have suggested its capacity to address oral pathogens, with potential implications for oral care products. Additionally, its demonstrated efficacy against drug-resistant pathogens offers hope in the fight against resistant microorganism. However, several avenues for future research and development remain open. It is crucial to understand the specific bioactive compounds responsible for the antibacterial effects of noni fruit extract and its precise mechanisms of action.

This knowledge could guide the formulation of standardized noni-based pharmaceuticals and therapeutic products. Furthermore, investigations into potential synergistic effects with conventional antibiotics may enhance the therapeutic arsenal against antibiotic-resistant bacteria. Clinical trials and rigorous in vivo studies are needed to validate the translational potential of noni fruit extract in practical healthcare settings. These trials should assess its safety, efficacy, and tolerability in diverse patient populations.

Noni-based formulations could be a valuable addition to the antimicrobial toolbox if proven effective. In summary, noni fruit extract is a promising natural resource in the ongoing battle against antibiotic-resistant microorganisms and various bacterial fungal pathogens. Its complex composition and multifaceted antibacterial mechanisms make it a compelling subject for continued investigation. With further research,

developing noni-based pharmaceuticals and therapies could contribute potential applications in wound healing, oral health, and the fight against antibiotic-resistant bacteria.

## 5. MATERIALS AND METHODS

### 5.1 Noni Fruit Extract and Concentrations

The studies used the Kyani Nitro Fx (Idaho Falls, ID, USA) product as Noni fruit extract (NFE). This product contains organic noni fruit extract at 100mg/mL concentration. A stock solution of the NFE was prepared by diluting a known quantity of the concentrated extract in sterile distilled water. A series of dilutions were then made using sterile water to achieve concentrations ranging from 10-100 mg/mL. The extracts were stored in the refrigerator throughout the study.

### 5.2 Pathogenic bacterial cultures and inoculum preparation

*Staphylococcus aureus* DSM 21979, *Bacillus subtilis* DSM 21393, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* ATCC 6380, *Escherichia coli* ATCC 25922, *Salmonella typhimurium* ATCC 14028, *Klebsiella pneumoniae* ATCC 13883, Vancomycin-Resistant Enterococci (VRE), Methicillin-Resistant *Staphylococcus aureus* ATCC 43300 (MRSA), *Streptococcus mutans* ATCC 25175, and *Streptococcus mitis* DSM 12643 were inoculated to Mueller-Hinton broth and incubated at 37°C for 24 hours. *Candida albicans* ATCC 10231 was streaked on potato dextrose agar and incubated at 25C for 48 hours. To prepare for the bioassay, bacterial pathogens were kept in stock cultures on nutrient-rich agar slants at 4°C. For the inoculum culture, a loop full of cells was transferred from the stock culture to test tubes containing sterile Mueller-Hinton broth (MHB, Isolab) and incubated in an incubator at 37°C for 24 hours and fungal strain at 25°C for 48 hours. Before the assay, sterile Mueller-Hinton broth adjusted the cultures' turbidity to a McFarland standard of 0.5. All pathogenic bacteria were stored at -70°C in selective broth with 20% glycerol.

### 5.3 Determination Antibacterial of Antifungal Effect

A disc diffusion test (Kirby Bauer method) was conducted to test the antibacterial properties against harmful microorganisms. A diluted inoculum with a concentration of 0.5 McFarland was prepared and spread on Muller-Hinton agar (MHA, Isolab) plates using a sterile cotton swab that was impregnated with 0.2 mL of the diluted inoculum. Sterile discs with a diameter of 6 mm (Oxoid, Thermo, USA) were impregnated with 20 µL of NFE solution (concentration of each solution: 0, 5, 10, 25, 50, 100 mg/mL) and placed onto the MHA plates. Streptomycin (25ug/disc) was used for bacterial strains (*Pseudomonas aeruginosa, Proteus vulgaris, Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Salmonella typhimurium, Enterococcus faecalis, Klebsiella pneumoniae*), tetracycline (10ug/disc) was used for antibiotic-resistant microorganisms and oral pathogens, and nystatin (100U) was used for *Candida albicans* as positive control. All the positive control antimicrobial discs were purchased from Oxoid (Thermo, USA). After 30 minutes at 25 °C, the plates were transferred to an incubator at 25°C for fungal strain and 37°C for bacterial strains to culture the pathogens for 24h.

### 5.4 Suspension test EN 1276

The time-dependent antibacterial performance of NFE was assessed according to the European Standard EN 1276:2019 for quantitative suspension tests to evaluate the bactericidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic, and institutional areas. The method was modified to assess the antibacterial activity of the NFE. The bacterial strains used for the antimicrobial testing were *E. coli, S. aureus, E. faecalis, and K. pneumoniae*, a standard indicator microorganism commonly employed in antimicrobial efficacy assessments for 1 minute and 5 minutes. After the desired contact time, we introduced 1 mL of solution to the neutralizer for 5 minutes. Finally, the number of colony-forming units (cfu/mL) was determined through the colony-counting method. It utilized the pour plate technique to plate 1 mL of the solution and incubated it at 37°C for 48 hours. The neutralization solution used to deactivate antiseptics was based on the European standard EN 1276. It consisted of 30g/L of Tween 80 (Sigma), 3g/L of lecithin (Sigma), 5g/L of sodium thiosulphate (Sigma), and 34g/L of potassium dihydrogen phosphate (Sigma) in tryptone soya broth (Isolab). 70% ethanol and PBS were used as positive and negative control, respectively.

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