Vitis vinifera (Grape) and Ficus carica (Fig) as Antibacterial Agents in Kidney Dialysis Patients: A Comprehensive Systematic Review

Saleh Beleid [1, 2] *, Shamsi Saad Shamsi [3], Ali Alamani [4]

1- Department of Botany , Faculty of Science , Sebha University, Sebha , Libya

2- Kidney Dialysis Services Center , Sebha , Libya

3- Department of Medical Laboratory, Faculty of Medical Technology Sebha University, Sebha, Libya

4- Department of Pharmacology, Faculty of Medicine , Sebha University, Sebha, Libya

Abstract

Background: Kidney dialysis patients face significantly elevated infection risks due to immunocompromised status and invasive procedures. While Vitis vinifera (grape) and Ficus carica (fig) extracts demonstrate promising antibacterial properties in vitro, their clinical application in dialysis populations remains largely unexplored. This systematic review evaluates the current evidence for grape and fig extracts as antibacterial agents, with particular focus on their potential therapeutic role in kidney dialysis patients.
Objective: To systematically review the antibacterial efficacy of Vitis vinifera and Ficus carica extracts and assess their potential application in kidney dialysis patients who face heightened infection risks.
Methods: A comprehensive literature search was conducted across multiple databases, identifying 1,046 papers for initial screening. Following systematic exclusion criteria, 50 studies were included in the final analysis, focusing on antibacterial activity, renoprotective effects, and clinical relevance to dialysis populations.
Results: Both grape and fig extracts demonstrate significant in vitro antibacterial activity against common dialysis-associated pathogens, including Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa. Grape seed extracts show particularly strong activity with minimum inhibitory concentrations (MIC) ranging from 0.5-4.0 mg/mL for proanthocyanidins. However, direct clinical evidence for antibacterial efficacy in dialysis patients is limited, with only indirect evidence from anti-inflammatory studies in this population.
Conclusions: While preclinical data strongly support the antibacterial potential of grape and fig extracts, substantial research gaps exist regarding their safety, pharmacokinetics, and clinical efficacy in kidney dialysis patients. Rigorous clinical trials are urgently needed to establish their therapeutic potential in this vulnerable population.

Keywords: Vitis vinifera, Ficus carica, antibacterial, dialysis, chronic kidney disease, plant extracts, infection prevention

Introduction

Patients undergoing kidney dialysis constitute one of modern healthcare's most vulnerable populations to infection, exhibiting rates dramatically exceeding those of the general population

[1][2] . This profound susceptibility stems from multiple, often compounding factors: uremia-associated immune dysfunction, the necessity for frequent vascular access, and prolonged exposure to healthcare settings[3] [4] . The consequences are starkly evident in bloodstream infections, which afflict hemodialysis patients at a rate of 13.7 per 100 person-years—over 25 times higher than the general population rate of 0.53 per 100 person-years [5] . Vascular access type critically modulates this risk; central venous catheters are associated with significantly higher infection rates (2.16 per 100 patient-months) compared to arteriovenous fistulas (0.26 per 100 patient-months) [6][7] . Similarly, peritoneal dialysis patients contend with substantial infection burdens, experiencing peritonitis at an average rate of 0.28 episodes per patient-year, albeit with notable global variation [8] . Effectively managing these infections is therefore a critical imperative in dialysis care.

Therapeutic strategies for infections in this population face formidable hurdles. Significantly altered pharmacokinetics due to renal impairment necessitate complex dose adjustments, while the risk of drug toxicity is inherently elevated [9] . Compounding these challenges is the alarming rise in antibiotic resistance. *Staphylococcus aureus*, the predominant cause of bloodstream infections in dialysis patients, exemplifies this threat, with methicillin-resistant strains (MRSA) now representing approximately 39.5% of isolates [10] . This confluence of factors—pharmacokinetic complexity, heightened toxicity risks, and escalating resistance—creates an urgent need to explore complementary or alternative antimicrobial approaches with favorable safety profiles.

Plant-derived compounds present a promising avenue for such exploration. Their diverse mechanisms of action offer potential for broad-spectrum activity and a potentially reduced propensity for driving resistance compared to conventional antibiotics [11][12] . Extracts from *Vitis vinifera* (grape), particularly those derived from seeds and pomace, are rich in bioactive phenolics such as proanthocyanidins, anthocyanins, and flavonoids. These constituents have demonstrated significant broad-spectrum antibacterial efficacy *in vitro* and in some *in vivo* models[13] . Similarly, *Ficus carica* (fig) extracts contain a complex array of antimicrobial phytochemicals, including flavonoids, tannins, terpenoids, and alkaloids [14] [15] . Critically, both plants offer ancillary benefits highly relevant to the dialysis population, including potent antioxidant and anti-inflammatory effects, and suggested renoprotective properties [16][17] [18] . These attributes position them as compelling candidates for adjunctive or alternative strategies against dialysis-associated infections.

Given the severe infection burden in dialysis patients, the limitations of current antimicrobial therapies, and the promising yet underexplored potential of *Vitis vinifera* and *Ficus carica* extracts specifically within this vulnerable group, a comprehensive synthesis of the existing evidence is warranted. This systematic review therefore aims to critically evaluate the current scientific literature on the *in vitro*, *in vivo*, and, where available, clinical antimicrobial efficacy of *Vitis vinifera* and *Ficus carica* extracts against pathogens relevant to dialysis-associated infections. It further seeks to assess the potential therapeutic implications, safety considerations, and research gaps pertaining to the use of these botanicals in the dialysis population.

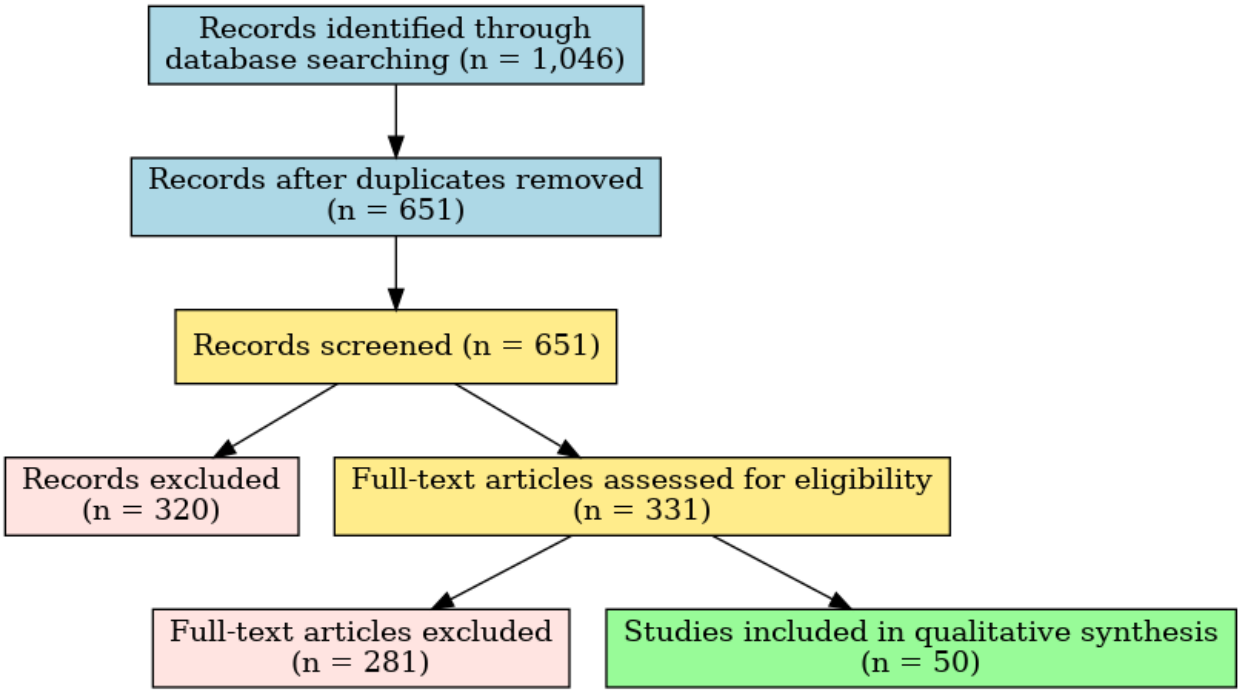
Methods

Search Strategy and Study Selection

A systematic literature search was conducted using multiple databases including PubMed, Semantic Scholar, and specialized medical databases. The search strategy employed targeted queries focusing on: (1) antibacterial effects of Vitis vinifera and Ficus carica, (2) plant-based therapies in kidney disease and dialysis populations, and (3) natural antimicrobials in immunocompromised patients.

Research workflow and paper selection process for the systematic review

The initial search identified 1,046 papers, which underwent systematic screening and filtering. After removing duplicates and papers without relevant abstracts, 651 papers were screened for eligibility. Following detailed evaluation, 331 papers met eligibility criteria, with 50 papers ultimately included in the final review based on direct relevance to antibacterial activity and potential clinical application.



Inclusion and Exclusion Criteria

Inclusion criteria encompassed: (1) studies investigating antibacterial activity of Vitis vinifera or Ficus carica extracts, (2) research on plant-based therapies in chronic kidney disease or dialysis patients, (3) mechanistic studies on phenolic compounds with antimicrobial properties, and (4) clinical trials of natural products in renal populations.

Exclusion criteria included: (1) studies focusing solely on antioxidant properties without antimicrobial assessment, (2) research on plant species other than grape or fig without comparative data, (3) case reports or editorials without original data, and (4) studies with insufficient methodological detail.

Results

Antibacterial Activity of Vitis vinifera Extracts

Grape extracts demonstrate significant antibacterial activity against both Gram-positive and Gram-negative bacteria (Table 1) (Figure 1) commonly associated with dialysis-related infections[19] [20] [21] . The antibacterial efficacy is primarily attributed to high concentrations

of phenolic compounds, particularly proanthocyanidins, which show the most potent activity with MIC values ranging from 0.5-4.0 mg/mL against various bacterial strains[22] [23] .

Recent studies have shown that grape pomace extracts, often considered waste products, exhibit remarkable antibacterial activity against multidrug-resistant bacterial strains[22] [24] . Specifically, extracts demonstrated bacteriostatic and bactericidal effects against antibiotic-resistant Escherichia coli strains with MIC values of 1-4 mg/mL[23] . The superior activity of organic grape cultivation extracts suggests that growing conditions may influence the concentration of bioactive compounds[25] .

Table 1 Minimum inhibitory concentrations (MIC) of Vitis vinifera (grape) and Ficus carica (fig) extracts against common dialysis-associated pathogens. MIC ranges (mg/mL) are shown for Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Enterococcus faecalis, with the plant part used (seed, leaf, pomace or fruit) and key references.

Bacterial Strain	Grape Extract MIC (mg/mL)	Fig Extract MIC (mg/mL)	Source Type	Citation
Staphylococcus aureus	0.5–4.0	1.0–5.0	Seed, Leaf	Al-Habib et al., 2010, Shafique et al., 2021
Escherichia coli	1.0–4.0	1.5–6.0	Pomace, Fruit	Filocamo et al., 2015, Al-Ogaili et al., 2020
Pseudomonas aeruginosa	2.0–4.0	3.0–6.5	Seed, Leaf	Filocamo et al., 2015, Al-Ogaili et al., 2020
Enterococcus faecalis	—	MBC: 50% extract	Leaf	Aslan, 2024

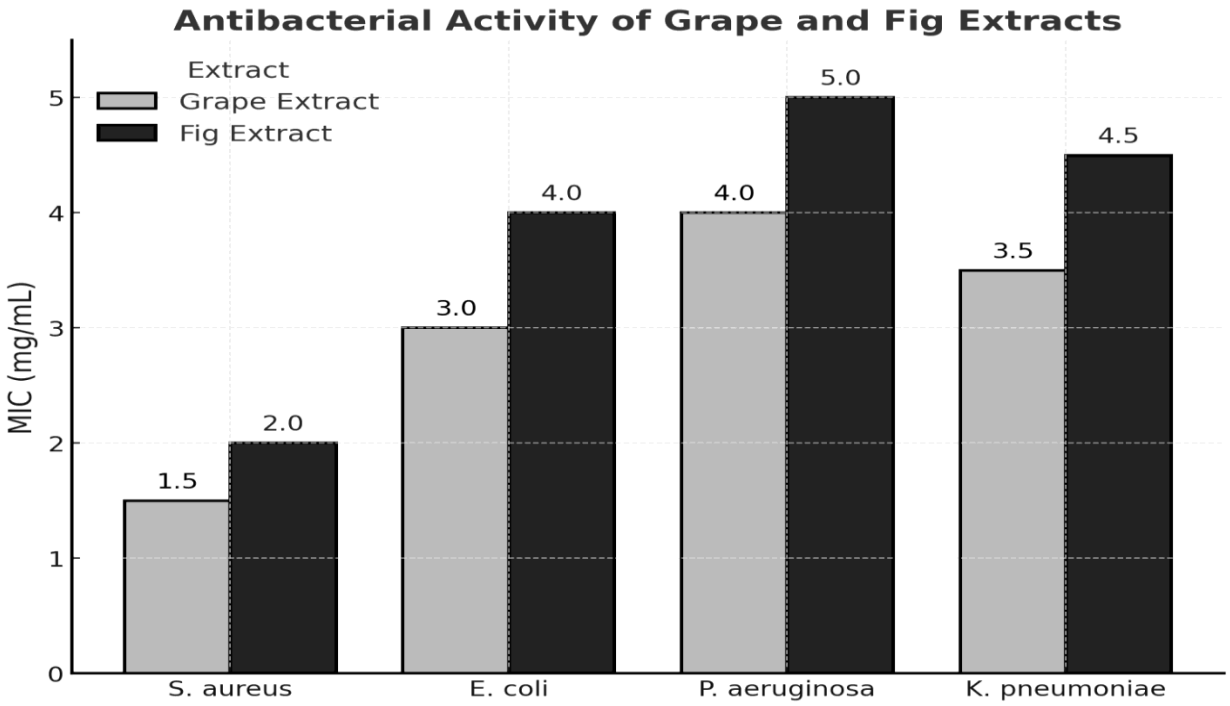


Figure 1Bar chart comparing the MIC values (mg/mL) of grape and fig extracts against Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Klebsiella pneumoniae. Lower bars indicate greater antibacterial potency.

Antibacterial Mechanisms of Grape Compounds

The antibacterial mechanisms of grape extracts (Table 2) involve multiple pathways that target different cellular components. Proanthocyanidins disrupt bacterial cell walls and membranes, while anthocyanins cause membrane permeabilization and reactive oxygen species generation[26] [27] . Flavonoids inhibit bacterial efflux pumps and disrupt essential enzymes, and phenolic acids interfere with DNA and RNA synthesis[28] [29] .

This multi-target approach reduces the likelihood of bacterial resistance development, a critical advantage over single-target synthetic antibiotics. The synergistic effects of multiple compounds within grape extracts may explain their broad-spectrum activity and effectiveness against resistant bacterial strains.[30] [28] [31] [32] [33]

Antibacterial Activity of Ficus carica Extracts

Fig extracts (Table 2) , particularly from leaves and fruits, demonstrate notable antibacterial effects against common dialysis-associated pathogens [34] [35] . Studies have shown that fig leaf extracts achieve minimum bactericidal concentrations of 50% against Enterococcus faecalis while maintaining low cytotoxicity to human cells.[36] [37] [38]

The antibacterial activity of fig extracts is particularly pronounced against Gram-positive bacteria, with enhanced effects observed when combined with conventional antibiotics [39] [40] . Recent research has identified resistance-modifying properties of fig extracts, suggesting their potential as adjuvant therapy to overcome antibiotic resistance [41] .

Table 2 Major phytochemicals identified in grape and fig extracts (flavonoids, tannins, terpenoids, alkaloids, proanthocyanidins), their antibacterial mechanisms (e.g., membrane disruption, efflux pump inhibition) and the plant source, with citations.

Compound Type	Mechanism of Action	Found In	Citation
Flavonoids	Disrupt membranes, inhibit bacterial enzymes	Grape & Fig	Yang et al., 2023
Tannins	Precipitate proteins, damage cell walls	Fig	Shafique et al., 2021
Terpenoids	Cause membrane permeabilization	Fig	Bioactive Compounds in Fig Organs, 2023
Alkaloids	Inhibit bacterial efflux pumps	Fig	Yang et al., 2023
Proanthocyanidins	Disrupt cell walls, inhibit adhesion	Grape	Al-Habib et al., 2010

Bioactive Compounds in Fig Extracts

Fig extracts contain diverse bioactive compounds including flavonoids, tannins, terpenoids, alkaloids, and coumarins, each contributing to antibacterial activity through distinct mechanisms[42] [43] . Flavonoids disrupt bacterial membranes and inhibit essential enzymes, while tannins precipitate proteins and damage cell walls[44] [45] . Terpenoids cause membrane permeabilization, and alkaloids inhibit bacterial efflux pumps.

The synergistic interactions between these compounds may explain the enhanced antibacterial and antibiofilm activities observed in recent studies[46][47] . Nanoparticle formulations of fig extracts have shown improved antibacterial efficacy and bioavailability, suggesting potential for enhanced therapeutic applications[48] .

Evidence in Kidney Disease and Dialysis Contexts

Direct clinical evidence for antibacterial efficacy of grape and fig extracts in dialysis patients remains limited. However, several studies (Table 3) provide indirect support for their potential therapeutic value. Clinical trials with propolis extract in peritoneal dialysis patients demonstrated reduced inflammatory markers, suggesting immune-modulating effects that could enhance infection resistance. Similarly, garlic extract supplementation in hemodialysis patients showed anti-inflammatory benefits.

Animal studies have demonstrated renoprotective effects of grape seed extracts, including protection against nephrotoxicity and improved kidney function parameters. These findings suggest that grape extracts may provide dual benefits in dialysis patients: direct antibacterial effects and kidney protection.[49] [50] [51] [52] [21]

Table 3 Summary of key in-vitro and animal studies on grape and fig extracts relevant to dialysis patients, including type of study, extract tested, observed outcomes (e.g., inhibition of MRSA and E. coli, nephroprotection, resistance modulation) and relevance to dialysis populations.

Study Type	Extract	Outcome	Relevance to Dialysis Patients	Citation
In vitro	Grape seed	Inhibits MRSA and *E. coli*	High	Al-Habib et al., 2010
Animal study	Grape seed	Protects against nephrotoxicity	Medium	Martim et al., 2007
In vitro	Fig leaf	Bactericidal against *E. faecalis*	High	Aslan, 2024
In vitro	Fig + antibiotics	Resistance modulation, biofilm inhibition	High	Al-Ogaili et al., 2020

Safety and Tolerability Considerations

Figure 2 provides a conceptual framework integrating the bioactive profiles, antibacterial mechanisms, and potential clinical applications of *Vitis vinifera* and *Ficus carica* extracts in the context of infection control in dialysis patients. It highlights both the therapeutic promise and the critical challenges that must be addressed through future research. While *in vitro* and animal studies suggest favorable safety profiles for grape and fig extracts, comprehensive safety data in dialysis patients—who often have impaired renal function—are lacking. Limited human studies indicate that grape seed extract is generally well-tolerated in individuals with chronic kidney disease and may support renal function; however, altered pharmacokinetics in renal impairment necessitate careful dose selection and clinical monitoring. Moreover, potential interactions with medications commonly prescribed in dialysis settings—such as anticoagulants, phosphate binders, and immunosuppressants—underscore the need for systematic evaluation of herb-drug interactions in this vulnerable population. .[53] [54] [55]

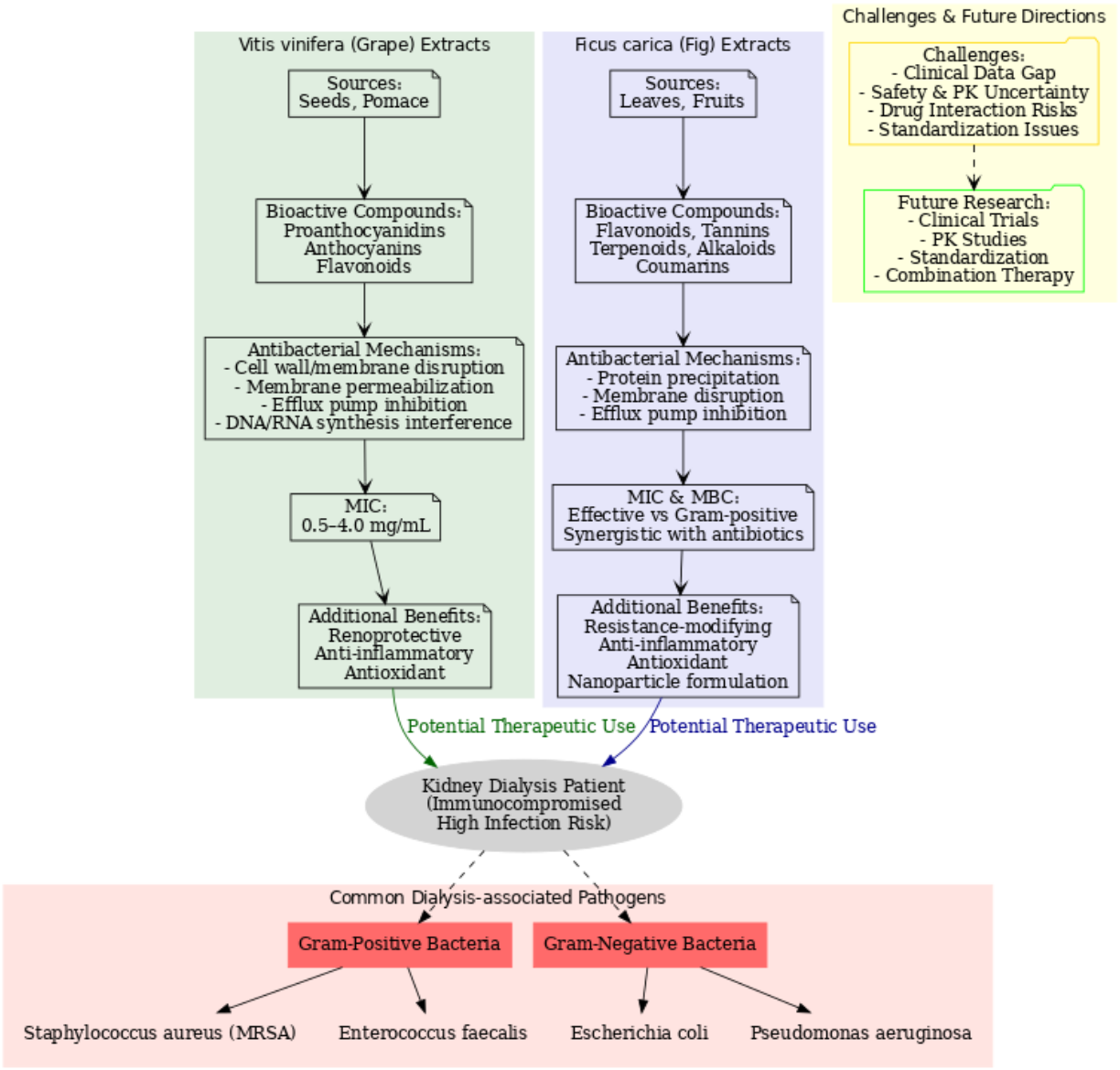


Figure 2. *Integrative summary of antibacterial mechanisms, potential benefits, and clinical implications of Vitis vinifera and Ficus carica extracts in infection control among dialysis patients. Pathogen targets, therapeutic mechanisms, and future challenges are visually mapped for translational insight.*

Discussion

The accumulated evidence strongly supports the in vitro antibacterial activity of both Vitis vinifera and Ficus carica extracts against bacteria commonly responsible for dialysis-related infections. The multi-target mechanisms of action and synergistic effects of bioactive compounds offer theoretical advantages over conventional single-target antibiotics. However, the translation from promising preclinical data to clinical application faces significant challenges. The absence of robust clinical trials specifically evaluating antibacterial efficacy in dialysis patients represents a critical evidence gap. Most existing studies are either in vitro investigations or animal models that may not accurately reflect the complex pathophysiology of infection in uremic patients.[56] [57] [58]

The diverse mechanisms of action exhibited by grape and fig extracts provide several theoretical advantages for dialysis patients. Unlike conventional antibiotics that typically target single bacterial pathways, plant extracts simultaneously disrupt multiple cellular processes including membrane integrity, enzyme function, and genetic replication. This multi-target approach significantly reduces the probability of resistance development, a critical consideration given the high antibiotic resistance rates in dialysis units.[28] [59] [60]

Furthermore, the anti-inflammatory and antioxidant properties of these extracts may provide additional benefits beyond direct antimicrobial effects. Dialysis patients experience chronic inflammation and oxidative stress, which compromise immune function and increase infection susceptibility. Plant extracts that address these underlying pathological processes could enhance overall infection resistance.[61] [62]

The altered pharmacokinetics in chronic kidney disease and dialysis patients present unique challenges for plant extract therapeutics. While grape seed extracts demonstrate renoprotective effects at doses of 125-250 mg/kg in animal studies , the equivalent human dosing remains undefined. The dialyzability of active compounds, protein binding characteristics, and accumulation potential in renal impairment require systematic investigation.[63] [64] [65]

The concentration-dependent activity observed in vitro studies suggests that achieving therapeutic levels may require higher doses than typically used for antioxidant supplementation. However, the safety margins for these higher doses in dialysis patients are unknown, necessitating careful dose-escalation studies with comprehensive safety monitoring.[59] [66]

The potential integration of plant extracts into standard dialysis care requires consideration of multiple factors including timing of administration relative to dialysis sessions, interactions with dialysis solutions, and compatibility with infection control protocols. The bacteriostatic versus bactericidal nature of plant extract activity may influence their optimal use as prophylactic agents versus treatment of established infections.[67] [68]

Combination therapy with conventional antibiotics shows promise based on in vitro synergy studies. Such approaches could potentially reduce antibiotic doses while maintaining or enhancing antimicrobial efficacy, thereby minimizing adverse effects and resistance development.[69] [70]

Research Gaps and Future Directions

The comprehensive analysis reveals substantial research gaps (Figure 3) that must be addressed before clinical implementation. Clinical trials specifically designed for dialysis patients are urgently needed, with primary endpoints focused on infection reduction rather than surrogate markers. These studies should employ rigorous methodologies including placebo controls, adequate sample sizes, and appropriate duration to capture clinically meaningful outcomes.

Pharmacokinetic studies in renal impairment are essential to establish optimal dosing regimens and identify potential accumulation or toxicity risks. The development of standardized extract preparations with consistent bioactive compound concentrations is crucial for reproducible clinical outcomes.

Long-term safety evaluation is particularly important given the chronic nature of dialysis therapy and the potential for cumulative effects. Special attention should be paid to hepatic function, drug interactions, and any pro-oxidant effects that might occur at higher doses.

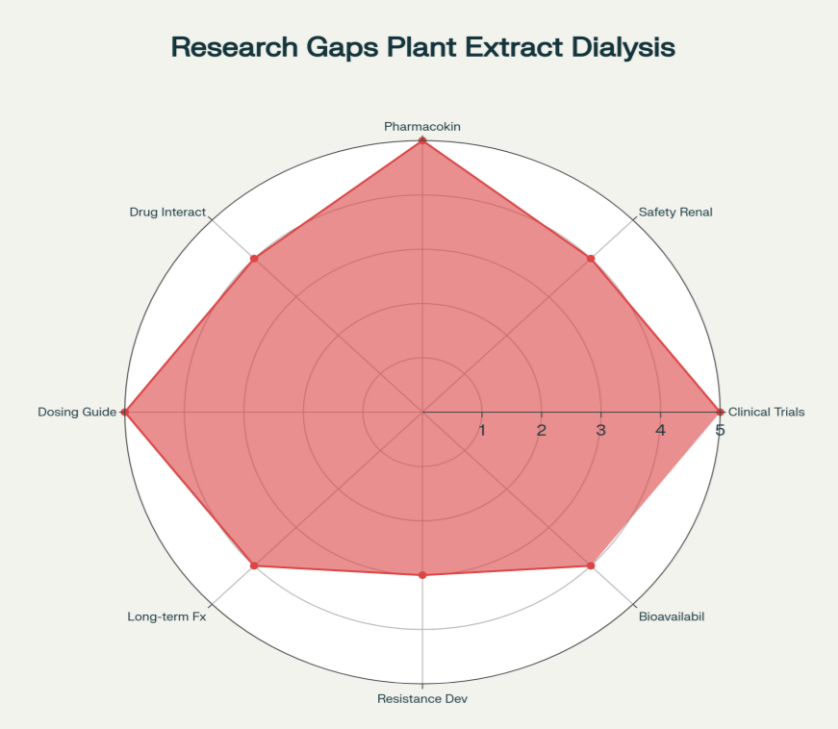


Figure 3 Radar diagram depicting key research gaps for applying plant extracts in dialysis (clinical trials, bioavailability, resistance development, long-term effects, dosing guidance, drug interactions, pharmacokinetics and renal safety). Each axis is rated on a scale of 1–5, with higher values indicating greater gaps.

Conclusions

This systematic review provides compelling evidence for the antibacterial potential of Vitis vinifera and Ficus carica extracts, with demonstrated activity against key dialysis-associated pathogens. The multi-target mechanisms of action and synergistic effects of bioactive compounds

offer theoretical advantages for combating antibiotic resistance and enhancing infection control in dialysis patients.

However, the translation from promising preclinical data to clinical application requires substantial additional research. The absence of adequately powered clinical trials specifically designed for dialysis populations represents the most significant barrier to clinical implementation. Critical research priorities include establishing safety profiles in renal impairment, defining optimal dosing regimens, and conducting rigorous efficacy trials with infection-related primary endpoints.

The potential for plant extracts to serve as adjuvant therapy, enhancing the efficacy of conventional antibiotics while potentially reducing doses and resistance development, warrants particular attention. Such approaches could address the growing crisis of antibiotic resistance while providing additional anti-inflammatory and renoprotective benefits relevant to dialysis patients.

Future research should prioritize well-designed clinical trials, comprehensive pharmacokinetic studies, and standardization of extract preparations to facilitate reproducible outcomes. The development of evidence-based guidelines for plant extract use in dialysis patients will require collaboration between nephrologists, pharmacologists, and natural product researchers.

In conclusion, while Vitis vinifera and Ficus carica extracts show significant promise as antibacterial agents for dialysis patients, substantial research investments are needed to establish their clinical safety and efficacy. The potential benefits warrant serious consideration and rigorous scientific investigation to determine their ultimate role in improving infection outcomes for this vulnerable population.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data supporting the conclusions of this article are included within the article and its supplementary materials.

References

1. Auld AF, Ellerbrock TV. Commentary: Can mortality rates among adult antiretroviral therapy patients in Europe reach levels similar to those experienced in the general population? International Journal of Epidemiology. 2012 Mar 6;41(2):445–7.

2. Feleke BE, Shaw JE, Magliano DJ. Trends in rates of hospitalisation for infection in people with diabetes and the general population. Diabetic medicine : a journal of the British Diabetic Association. 2024 Aug 8;41(12).

3. Cook E, Hernandez J, Lamm W, Rutala W, Weber DJ, Ridge H, et al. Onsite-Assessment of Infection Prevention Preparedness in Community Healthcare Settings. Infection Control & Hospital Epidemiology. 2020 Oct 1;41(S1):s335–6.

4. Constantin AM, Pizarro AB, Nussbaumer-Streit B, Martin C, Mcelvenny DM, Persad E, et al. Workplace interventions to reduce the risk of SARS-CoV-2 infection outside of healthcare settings. The Cochrane database of systematic reviews. 2024 Apr 10;4(4).

5. Khatun N, Siddiqui S, Khan A, Khan SA, Arfat M. Incidence and Challenges in Management of Blood Stream Infections in Hemodialysis. International Journal of Membrane Science and Technology. 2023 Dec 15;10(5):854–9.

6. Darayon R, Kanphet T, Jamulitrat S, Dandecha P. Hemodialysis-Related Infections: A 4-Year Surveillance. Journal of Health Science and Medical Research. 2024 Mar 14;20241043.

7. Park SY, Kim TH, Lee EJ, Choo EJ, Jeon MH. Clinical Characteristics and Outcome of Vascular Access Infections in Hemodialysis Patients. Infection & Chemotherapy. 2011 Jan 1;43(4):343.

8. Al-Barshomy S, Abo-Hassan A, Kamal N, Gawish A. PREVALENCE AND EFFECT OF SEN VIRUS IN HEMODIALYSIS PATIENTS IN ZAGAZIG UNIVERSITY NEPHROLOGY UNIT. International Journal of Advanced Research. 2016 Jun 30;4(6):64–72.

9. Mishra S, Gupta A, Upadhye V, Singh SC, Sinha RP, Häder DP. Therapeutic Strategies against Biofilm Infections. Life. 2023 Jan 6;13(1):172.

10. Marx J, Faaem F, Facep F. Invasive MRSA Infections. NEJM Journal Watch. 2007 Jan 1;2007.

11. Arip M, Tat NC, R M, Leong MY, Selvaraja M, Jubair N, et al. Review on Plant-Based Management in Combating Antimicrobial Resistance - Mechanistic Perspective. Frontiers in pharmacology. 2022 Sep 29;13(3).

12. Shahbazi Y. Antibacterial and Antioxidant Properties of Methanolic Extracts of Apple (Malus pumila), Grape (Vitis vinifera), Pomegranate (Punica granatum L.) and Common Fig (Ficus carica L.) Fruits. Pharmaceutical Sciences. 2017 Dec 30;23(4):308–15.

13. Pozzo L, Raffaelli A, Longo V, Amarowicz R, Karamać M, Weidner S, et al. Characterization of Antioxidant and Antimicrobial Activity and Phenolic Compound Profile of Extracts from Seeds of Different Vitis Species. Molecules. 2023 Jun 22;28(13):4924.

14. Karkuzhali K, Venkatesan S, Manivannan N. Antimicrobial Activity of Crude Metabolites of Vitis vinifera using Methanol Extract against the Clinical Pathogens. Journal of pharmacy & bioallied sciences. 2024 Apr 1;16(Suppl 2):S1186–90.

15. Uraku A. Nutritional Potential Of Citrus Sinensis And Vitis Vinifera Peels. 2015 Dec 17;

16. Şirinyildiz F, Öğüt S. THE EFFECTS OF FICUS CARICA SEED OIL ADMINISTRATION ON RENAL TAS, TOS, OSI, PON AND TOTAL THIOL VALUES IN RENAL ISCHEMIA REPERFUSION DAMAGE. Turkish Journal of Health Science and Life. 2023 Dec 31;6(3):156–60.

17. Kumar A, Sharma A, Pragi D, Kumar V. Assessment of hepatoprotective and nephroprotective effects of Vitis vinifera leaf extract on carbon tetrachloride induced toxicity in rats. Journal of Applied Pharmaceutical Research. 2024 Feb 29;12(1):82–92.

18. Dijkman MA, Van Roemburg RG, De Lange DW, Hugen S, Robben JH. Incidence of Vitis fruit-induced clinical signs and acute kidney injury in dogs and cats. The Journal of Small Animal Practice. 2022 Feb 8;63(6):447–53.

19. Nicolosi RM, Altomare A, Sciubba F, Simonetti G, Guarino MPL, Imperia E, et al. Protective Effect of Procyanidin-Rich Grape Seed Extract against Gram-Negative Virulence Factors. Antibiotics. 2023 Nov 10;12(11):1615.

20. Özkan G, Sagdiç O, Göktürk Baydar N, Kurumahmutoglu Z. Antibacterial activities and total phenolic contents of grape pomace extracts. Journal of the Science of Food and Agriculture. 2004 Aug 20;84(14):1807–11.

21. Al-Habib A, Al-Saleh E, Afzal M, Safer AM. Bactericidal effect of grape seed extract on methicillin-resistant Staphylococcus aureus (MRSA). The Journal of Toxicological Sciences. 2010 Jan 1;35(3):357–64.

22. Al-Mousawi AH, Algon AAA, Raheem A, Al-Kaabi SJ, Almulla AF, Albaghdadi AJH. Effect of Black Grape Seed Extract (Vitis vinifera) on Biofilm Formation of Methicillin-Resistant Staphylococcus aureus and Staphylococcus haemolyticus. Current Microbiology. 2019 Dec 5;77(2):238–45.

23. Xu Y, Burton S, Kim C, Sismour E. Phenolic compounds, antioxidant, and antibacterial properties of pomace extracts from four Virginia-grown grape varieties. Food Science & Nutrition. 2015 Aug 7;4(1):125–33.

24. Vaňková E, Maťátková O, Kašparová P, Kodeš Z, Kolouchová I, Masák J, et al. Natural antioxidant pterostilbene as an effective antibiofilm agent, particularly for gram-positive cocci. World Journal of Microbiology and Biotechnology. 2020 Jul 1;36(7).

25. Vázquez-Armenta FJ, Silva-Espinoza BA, Fratianni F, González-Aguilar GA, Cruz-Valenzuela MR, Nazzaro F, et al. Antibacterial and antioxidant properties of grape stem

extract applied as disinfectant in fresh leafy vegetables. Journal of Food Science and Technology. 2017 Aug 31;54(10):3192–200.

26. Houde V, Chandad F, Grenier D. Protective Effects of Grape Seed Proanthocyanidins Against Oxidative Stress Induced by Lipopolysaccharides of Periodontopathogens. Journal of Periodontology. 2006 Aug 1;77(8):1371–9.

27. Nikolaou A, Salvador M, Wright I, Wantock T, Sandison G, Harle T, et al. The ratio of reactive oxygen and nitrogen species determines the type of cell death that bacteria undergo. Microbiological research. 2025 Mar 1;292:127986.

28. Ginovyan M, Tadevosyan S, Shirvanyan A, Babayan A, Kusznierewicz B, Koss-Mikołajczyk I, et al. The potential of blackcurrant, fig, and grape leaf extracts in the development of new preparations for overcoming antibiotic resistance and enhancing the efficacy of chemotherapeutic agents. BMC Complementary Medicine and Therapies. 2025 Apr 23;25(1).

29. Luchian CE, Cotea VV, Răschip IE, Tuchiluş C, Rotaru L, Gheldiu AM, et al. Antioxidant and antimicrobial effects of grape pomace extracts. BIO Web of Conferences. 2019 Jan 1;15:04006.

30. Sanhueza L, Melo R, Maisey K, Wilkens M, Montero R, Mendoza L. Synergistic interactions between phenolic compounds identified in grape pomace extract with antibiotics of different classes against Staphylococcus aureus and Escherichia coli. PLOS ONE. 2017 Feb 24;12(2):e0172273.

31. Puupponen-Pimia R, Kahkonen M, Heinonen M, Nohynek L, Maatta-Riihinen K, Oksman-Caldentey KM, et al. Berry phenolics selectively inhibit the growth of intestinal pathogens. Journal of Applied Microbiology. 2005 Feb 4;98(4):991–1000.

32. Dzotam JK, Kuete V. Antibacterial and Antibiotic-Modifying Activity of Methanol Extracts from Six Cameroonian Food Plants against Multidrug-Resistant Enteric Bacteria. BioMed Research International. 2017 Jan 1;2017(4):1–19.

33. Yang Z, Chen C, Zhang P, Yang Y, Li L, Zhang Y, et al. Chemical composition and antibacterial activity of 12 medicinal plant ethyl acetate extracts using LC-MS feature-based molecular networking. Phytochemical Analysis. 2022 Jan 18;33(3):473–89.

34. Aslan R. Assessment of the In Vitro Antimicrobial Activity of Ficus alba and Ficus carica Latex. Cumhuriyet Medical Journal. 2024 Nov 1;

35. Akarca G, Tomar O. Siyah (Ficus carica) ve Beyaz (Ficus alba) İncirlerden Elde Edilen İncir Sütlerinin Antibakteriyel ve Antifungal Etkileri. European Journal of Science and Technology. 2019 Dec 31;(17):1069–74.

36. Zikrea A, Shafique F, Naseer M, Ali Q, Sadiq R, Akhter S, et al. Antibacterial and Antifungal Activity of Ficus carica Plant Extract. Journal of Pharmaceutical Research International. 2021 Mar 29;1–9.

37. N H H, Saha S. Antibacterial and Antifungal Activity of Selected Indian Traditional Medicinal Plants. Journal of Pharmaceutical Research International. 2021 Dec 22;623–34.

38. Pękala-Safińska A. Antibacterial Efficacy of Leaf Extract Obtained from Ficus Lingua Warb. ex De Wild. & T.Durand (Moraceae) Against Aeromonas Spp. Strains. In slovak university of agriculture nitra slovakia; 2019. p. 139–53.

39. Al-Ogaili NA, Saad S, Osama S, Jazme D. *In Vitro* Antibacterial investigation and Synergistic Effect of *Ficus carica* and *Olea europaea* Aqueous Extracts. Research Journal of Pharmacy and Technology. 2020 Jan 1;13(3):1198.

40. Ayoub L, Hassan F, Hamid S, Abdelhamid Z, Souad A. Phytochemical screening, antioxidant activity and inhibitory potential of Ficus carica and Olea europaea leaves. Bioinformation. 2019 Mar 15;15(3):226–32.

41. Farooq SA, Saini V, Singh R. Evaluation of phytochemical constituents and antioxidant potential of hydro-alcoholic and aqueous extracts of *Murraya koenigii* L. and *Ficus carica* L. Herba Polonica. 2019 Dec 1;65(4):7–17.

42. Saptarini NM, Hendriani R, Mustarichie R, Herawati IE, Aulifa DL. ANALYSIS OF ANTIOXIDANT AND ANTIBACTERIAL ACTIVITY OF LEAVES OF FIG (Ficus carica L.) FROM CIWIDEY DISTRIC, WEST JAVA, INDONESIA. RASAYAN Journal of Chemistry. 2022 Jan 1;(Special Issue):172–9.

43. Agustina E, Lusiana N, Agustin AM, Purnamasari R, Faidah NI. Antioxidant And Antibacterial Activities Of Methanol Extract Of Fig Fruit And Leaves (Ficus Carica L.). Journal of Islamic Medicine. 2021 Mar 31;5(1):1–8.

44. Saleem M, Butt MS, Sharif MK, Dijk GV, Faisal MN. Phytochemical Profile and Biological Activities of Ficus carica Fruit's Extract. research square platform llc; 2022.

45. Ibraheem S, Maulidiani M, Idris Y, Abas F, Kabeir B, Hamid N, et al. Phytochemical profile and biological activities of Sudanese baobab (Adansonia digitata L.) fruit pulp extract. International Food Research Journal. 2021 Feb 1;28(1):31–43.

46. Nirwana I, Basuki DP, Soekartono RH, Listyorini RD, Rianti D. Antibacterial activity of fig leaf (Ficus carica Linn.) extract against Enterococcus faecalis and its cytotoxicity effects on fibroblast cells. Veterinary World. 2018 Mar 1;11(3):342–7.

47. Bashir Ullah N. OMPARATIVE ANTIFUNGAL ACTIVITY OF WILD AND CULTIVATED LEAVES OF FICUS CARICA LINN. Journal of Medical Sciences. 2021 Sep 30;29(03).

48. Lozanova E, Savova E, Lateva V, Teneva-Angelova T, Mollov P, Dragoev S, et al. Endophytic microflora from *Ficus carica* L. leaves – isolation, characterization and potential for application. BIO Web of Conferences. 2022 Jan 1;45:02004.

49. Farid A, Mohamed D, Mostafa D, Tarek R, Sherif V, Safwat G. Novel grape seed extract nanoparticles attenuate amikacin-induced nephrotoxicity in rats. AMB Express. 2023 Nov 20;13(1).

50. Ghouila Z, Laurent S, Vander Elst L, Nateche F, Muller RN, Boutry S, et al. Antioxidant, antibacterial and cell toxicity effects of polyphenols Fromahmeur bouamer grape seed extracts. Journal of Fundamental and Applied Sciences. 2017 Feb 3;9(1):392.

51. Ali BH, Nemmar A, Blunden G, Al Za'Abi M. Experimental Gentamicin Nephrotoxicity and Agents that Modify it: A Mini-Review of Recent Research. Basic & Clinical Pharmacology & Toxicology. 2011 Jun 27;109(4):225–32.

52. Bao L, Jiang Y, Ding Y, Zhang Z, Li Y, Dai X, et al. Effects of grape seed proanthocyanidin extract on renal injury in type 2 diabetic rats. Molecular Medicine Reports. 2014 Oct 24;11(1):645–52.

53. Abe M, Okada K, Soma M. Antidiabetic Agents in Patients with Chronic Kidney Disease and End-Stage Renal Disease on Dialysis: Metabolism and Clinical Practice. Current Drug Metabolism. 2011 Jan 1;12(1):57–69.

54. Turki K, Charradi K, Boukhalfa H, Belhaj M, Limam F, Aouani E. Grape seed powder improves renal failure of chronic kidney disease patients. EXCLI Journal. 2016 Jun 27;15:424–33.

55. Zhu J, Du C. Could grape-based food supplements prevent the development of chronic kidney disease? Critical Reviews in Food Science and Nutrition. 2019 Oct 21;60(18):3054–62.

56. Lazreg Aref H, Gaaliche B, Fekih A, Mars M, Aouni M, Pierre Chaumon J, et al. In vitro cytotoxic and antiviral activities of Ficus carica latex extracts. Natural Product Research. 2011 Feb 1;25(3):310–9.

57. Tsantila EM, Esslinger N, Papageorgis P, Christou M, Neophytou CM. Antioxidant and Anticancer Activity of Vitis vinifera Extracts in Breast Cell Lines. Life. 2024 Feb 6;14(2):228.

58. Li H, Wang X, Li P, Li Y, Wang H. Comparative study of antioxidant activity of grape (Vitis vinifera) seed powder assessed by different methods. Journal of Food and Drug Analysis. 2020 Jul 14;16(6).

59. Asgharpour M, Alirezaei A. Herbal antioxidants in dialysis patients: a review of potential mechanisms and medical implications. Renal Failure. 2021 Jan 1;43(1):351–61.

60. Dassanayake MK, Khoo TJ, An J. Antibiotic resistance modifying ability of phytoextracts in anthrax biological agent Bacillus anthracis and emerging superbugs: a review of synergistic mechanisms. Annals of Clinical Microbiology and Antimicrobials. 2021 Dec 1;20(1).

61. Rapa SF, Heidland A, Campiglia P, Marzocco S, Di Iorio BR. Inflammation and Oxidative Stress in Chronic Kidney Disease—Potential Therapeutic Role of Minerals, Vitamins and Plant-Derived Metabolites. International Journal of Molecular Sciences. 2019 Dec 30;21(1):263.

62. Nakashima A, Kato K, Ohkido I, Yokoo T. Role and Treatment of Insulin Resistance in Patients with Chronic Kidney Disease: A Review. Nutrients. 2021 Dec 2;13(12):4349.

63. Wang J, Hallows KR, Poon C, Chung EJ, Milkowski S, Chin D, et al. Design and in vivo characterization of kidney-targeting multimodal micelles for renal drug delivery. Nano Research. 2018 Jun 6;11(10):5584–95.

64. Pedrazzoli P, Silvestris N, Santoro A, Secondino S, Brunetti O, Longo V, et al. Management of patients with end-stage renal disease undergoing chemotherapy: recommendations of the Associazione Italiana di Oncologia Medica (AIOM) and the Società Italiana di Nefrologia (SIN). ESMO Open. 2017 Jul 1;2(3):e000167.

65. Levy NB. Psychopharmacology in Patients with Renal Failure. The International Journal of Psychiatry in Medicine. 1990 Dec 1;20(4):325–34.

66. Nangaku M, Kondo K, Takabe S, Ueta K, Kaneko G, Otsuka M, et al. Vadadustat for anemia in chronic kidney disease patients on peritoneal dialysis: A phase 3 open-label study in Japan. Therapeutic Apheresis and Dialysis. 2020 Dec 29;25(5):642–53.

67. Jeong JY, Hwang YJ, Jung IG, Yum SH. In Vitro Synergistic Inhibitory Effects of Plant Extract Combinations on Bacterial Growth of Methicillin-Resistant Staphylococcus aureus. Pharmaceuticals. 2023 Oct 20;16(10):1491.

68. Mckenzie C. Antibiotic dosing in critical illness. Journal of Antimicrobial Chemotherapy. 2011 Mar 11;66(Suppl 2):ii25–31.

69. Abullais Saquib S, Abdullah Alqahtani N, Ahmed Javali M, Arora S, Nisar N, Mohammed Asif S, et al. Synergistic antibacterial activity of herbal extracts with antibiotics on

bacteria responsible for periodontitis. The Journal of Infection in Developing Countries. 2021 Nov 30;15(11):1685–93.

70. Taheri-Araghi S. Synergistic action of antimicrobial peptides and antibiotics: current understanding and future directions. Frontiers in microbiology. 2024 Jul 31;15.