REVIEW PAPER

Systematic Review of Punica Granatum and Moringa Oleifera Phytochemicals Against MDR UTI Pathogens: Antimicrobial and Antibacterial Effects

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ABSTRACT
Multidrug-resistant urinary tract infections (MDR-UTIs) represent one of the increasing health issues globally, which prompts the pursuit of alternative therapeutics to be used instead of standard antibiotics. The literature (2015-2024) on the isolation and characterization of MDR uropathogens, as well as the antimicrobial efficacy of secondary metabolites of Punica granatum (pomegranate) and Moringa oleifera (drumstick tree), will be critically analyzed in this review. Identically, Uropathogenic Escherichia coli and other Gram-negative strains often demonstrate resistance to a variety of antibiotics, leading to frequent or incurable UTIs. Many peer-reviewed studies indicate that P. granatum extracts, especially those that are highly concentrated in polyphenols such as punica galactinan, can suppress these MDR UTI pathogens (especially at low minimum inhibitory concentrations) and have the potential to even suppress their virulence factors (e.g. biofilm formation and adhesion). On the same note, M. oleifera leaf and seed extracts, which have various phytochemicals among them isothiocyanates and flavonoids, have broad spectrum antibacterial effects, but with varying efficacy of minimal to moderate inhibition in various studies. The antimicrobial effects of these botanicals are complex: P. granatum phenolics have the ability to disrupt bacterial membranes, disrupt quorum sensing and can also work in synergy with some antibiotics, whereas M. oleifera compounds can cause oxidative stress and disrupt bacterial growth processes.
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1.INTRODUCTION

UTIs are widely spread bacterial infections in the world with estimated 150 million cases annually around the world. They are often the result of uropathogenic Escherichia coli (UPEC) and other Enterobacteriaceae like Klebsiella pneumoniae and Proteus mirabilis that cause colonization at the bladder or kidney and trigger symptoms of dysuria to life-threatening urosepsis. The extensive use and overuse of antibiotics have increased the development of multidrug-resistant (MDR) uropathogens, which make the treatment of UTI more difficult and predispose to more frequent relapse, healthcare expenses, and morbidity. It is worth mentioning that the extended-spectrum b-lactamase (ESBL)-positive E. coli and K. pneumoniae are becoming more and more common in both community-acquired and hospital-acquired UTIs. Antimicrobial resistance (AMR) imposes a severe burden on the world - recent estimates claim that more than 1 million deaths per year are caused by drug-resistant infections, which is why new antimicrobial solutions are urgently needed (Murray et al., 2022). In this regard, plant-based secondary metabolites have become the topic of interest as possible therapeutic agents against MDR infections (Dadgostar, 2019). Such natural compounds (e.g., polyphenols, flavonoids, alkaloids, terpenes) tend to have inherent antimicrobial activity and can be avoided by established resistance mechanisms or even act in combination with antibiotics (Khameneh et al., 2019).

Punica granatum L. (pomegranate) and Moringa oleifera Lam. (moringa) are two prospective medicinal plants. P. granatum peel, which contains high concentrations of hydrolyzable tannins (punicalagin, punica l. Punica granatum L. punica granatum L.) and phenolic acids (ellagic and gallic acid), is a traditional medicine used to treat infections and inflammatory diseases. Recent research shows that pomegranate extracts have a wide range of antimicrobial activity, such as against antibiotic-resistant microbes and biofilms (Mendonca Mendes et al., 2023;

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Valdes, 2023). Similarly, M. oleifera, which is called the miracle tree, has been and remains the subject of folklore reverence due to its nutritional and curative properties. Almost all the parts of the moringa contain bioactive ingredients - for example, the leaves possess flavonoids, phenolic acids and vitamins, whereas the seeds contain distinct glucosinolates and isothiocyanates (e.g., benzyl isothiocyanate) that are antimicrobial and anti-inflammatory. Conventional medicines have used morphine as a treatment of diseases such as infections, and more contemporary pharmacological studies propose that it has bactericidal properties, antioxidant effects, and even anti-beam forming properties (Leone et al., 2015; El-Sherbiny et al., 2024).

Since the novel treatment of UTI is very urgent, the evidence of whether the secondary metabolites of pomegranate and moringa can be used to counteract MDR uropathogens is relevant. The areas of interest in this review are

(1) the isolation and characterization of MDR UTI pathogens described in the literature, and

(2) the in vitro antimicrobial efficacy of P. granatum and M. oleifera extracts or phytochemicals against these pathogens, including the synergy of these extracts or phytochemicals with conventional antibiotics. We also address the molecular mechanisms of the underlying antimicrobials of these plant compounds and their possible use as an adjunctive or alternative treatment of UTIs. Through critical synthesis of the recent peer-reviewed articles, we would assess the therapeutic potential of pomegranate and moringa in resolving the MDR-UTI crisis and the gap of knowledge and future research directions.

LITERATURE REVIEW

MDR Uropathogens: Characteristics and Prevalence. Most of the UTIS are instigated by a narrow range of bacteria who have progressively become immune to numerous drugs. About 70-90 percent of uncomplicated UTIs are caused by E. coli and it is also the leading Uropathogen in complicated cases. Additional significant agents are K. pneumoniae, P. mirabilis, Enterococcus faecalis and Staphylococcus saprophyticus, and fungal UTIs (e.g. Candida spp.) are infrequent in catheterized or immunocompromised patients. In the last ten years, it has been observed that MDRs of these uropathogens have increased dramatically all over the world. UTI isolates of E. coli and Klebsiella have been found to exhibit high rates of resistance to fluoroquinolones, trimethoprim-sulfamethoxazole and third-generation cephalosporins, which is frequently mediated by plasmid-mediated ESBLs and carbapenemases. As an example, one meta-analysis has estimated that more than one-third of E. coli responsible of UTI worldwide is multidrug-resistant (36% on average) (Murray et al., 2022). These uropathogenic MDRs are often obtained during recurrent or complicated UTIs, during which previous exposure to antibiotics selects resistant clones (Storme et al., 2020). The MDR profile is identified in clinical laboratories by semi-quantitative uropathogen isolation using selective media and identifying the isolate by biochemical assays or MALDI-TOF MS, testing its susceptibility to antibiotics (usually by disk diffusion or microdilution) (Mancuso et al., 2023). Typical resistance determinants in Gram-negative rods (ESBL genes such as bla TEMTM) and Enterococcus (vancomycin resistance genes vanA B, which can be verified by PCR or sequencing in a research study) are common. MDR uropathogens tend to be more virulent; e.g. ESBL-producing UPEC has the ability to develop strong biofilms on urinary catheters, which complicates their ability to resist drugs and survive within the urinary tract (Flores-Mireles et al., 2015). Virulence and resistance convergence together in the UTI pathogens make them particularly difficult to eliminate using conventional therapy, which highlights the need to develop new antimicrobials or adjunctive therapies capable of bypassing the resistance mechanisms.

Antimicrobials as Medicinal Plant Secondary Metabolites. A range of anti-infective(s) that include quinine and artemisinin have traditionally been obtained by secondary metabolites of plants, and several of them have inhibitory actions on UTI pathogens. One example of this is cranberry proanthocyanidins, which are capable of preventing UPEC adhesion to uroepithelial cells, which decreases the recurrent UTI rates (Maisto et al., 2023). Similarly, bearberry (Arctostaphylos uva-ursi), garlic (Allium sativum), and green tea (Camellia sinensis) compounds have been reported to have antimicrobial or anti-biofilm effects against uropathogens. Two of them are pomegranate and moringa, which are plants receiving research attention on UTI because of their abundant phytochemical compositions. It is worth noting that the bioactive compounds present in pomegranate and moringa belong to chemical categories that are known to cause several effects against microorganisms: tannins and flavonoids in pomegranate may cause the precipitation of microbial proteins and membrane disruption, whereas isothiocyanates and saponins in moringa may invade cell walls and produce reactive oxygen species (van den Berg and Kuipers, 2022; Khameneh et al., 2019). Moreover, such plant metabolites can prevent bacterial communication (quorum sensing) or efflux pumps, which puts bacteria into an antibiotic-resistant state (Song et al., 2025). The in vitro studies on this and several in vivo models suggest potential of such natural products in the treatment of MDR bacteria. Table 1 showcases some of the studies selected to demonstrate the antimicrobial effects of pomegranate and moringa against UTI-related MDR pathogens before narrowing down to pomegranate and moringa in particular.

Punica granatum (Pomegranate). Pomegranate peel extracts have demonstrated high levels of efficacy against a variety of UTI pathogens, such as MDR strains. Initially, punica granatum L. punicalagin was demonstrated to be effective in inhibiting ESBL-producing K. pneumoniae (MIC 0.25-0.78 mg/mL) (De et al., 2015). The later researches verified that pomegranate peel extracts (high in punicalagin and ellagic acid) do form large inhibitory rings against drug-resistant E. coli, Proteus and even Staphylococcus aureus in vitro. As an illustration, Majeed (2019) discovered that hot

and cold aqueous peel extracts (50-100 mg/mL) inhibited all the tested uropathogenic isolates, such as MDR E. coli, K. pneumoniae, and P. mirabilis, and the inhibition zone diameter was up to 30 mm, but a comparator plant (bay leaves) did not work. Pomegranate has also anti-virulence effects: Zam and Khaddour (2017) have shown that an aqueous peel extract (MIC 0.6 mg/mL) not only prevented the growth of E. coli derived in the UTI, but also decreased bacterial adhesion to epithelial cells by about 80 percent using sub-MIC concentrations and significantly decreased motility. This antidhesive activity indicates that pomegranate has the potential to disorient biofilm formation a very important aspect of recurrent UTIs. In fact, it has been demonstrated that follow-up work can inhibit the formation of new biofilm as well as the dispersion of established biofilms of E. coli and S. aureus using pomegranate extracts (Zam and Khaddour, 2017; Wang et al., 2023). Mechanistically, one of the main factors is punica agatinin which has been shown to rupture bacterial cell membranes leading to leakage of cytoplasmic contents and coarse cell surfaces under electron microscopes. Combined transcriptomic/proteomic studies indicate that punica present lower cells wall synthesis, membrane transport and virulence factor synthesis genes in S. aureus. Also, punica granatum can disrupt quorum sensing cues and suppress exopolysaccharide production in biofilms, which undermines the structural stability of biofilms. All these multi-pronged activities contribute towards explaining why P. granatum extracts can be used even against the so-called superbugs.

Most importantly, conventional antibiotics have also been found to be synergistic with pomegranate metabolites. According to Kabbashi et al. (2024), the utilization of pomegranate peel extract with some antibiotics reduced the MICs of the antibiotics against the MDR UTI isolates drastically. In that case, fractional inhibition concentration index (FICI) of meshing pomegranate extract + azithromycin was between 0.12 and 0.5, and the synergism (FICI less than 0.5) was strong in most of the combinations. On the same note, Abu El-Wafa et al. (2020) reported that pomegranate extract, combined with levofloxacin or gentamicin, killed up to 99% of P. aeruginosa biofilm cells, which was significantly better than the antibiotic. In part, such synergies can be explained by the fact that tannins such as Punica galagin disable the defenses of the bacteria (b-lactamase enzymes and efflux pumps), and, secondly, contribute to the increased absorption of the antibiotics (Song et al., 2025). A case in point is Punica Granatum L. that has been demonstrated to revert the action of MRSA by making the bacteria susceptible to the effects of oxacillin by suppressing the activity of penicillin-binding protein 2a, and when the two are used together the bacteria are again killed (Song et al., 2025). In sum, there is a strong suggestion in the literature that the polyphenolic constituents of pomegranate peel are potent MDR uropathogen antibacterials, and the synergy and virulence attenuation is an added advantage.

Moringa oleifera (Moringa). The antimicrobial profile of moringa is more diverse, yet it should be mentioned. Several researches have established that the moringa leaf extracts have bacteriostatic and bactericidal impacts on Gram-negative and Gram-positive bacteria causing UTIs. A moringa leaf extract with high flavonoid concentration was used in Algerian research, which demonstrated inhibition zones of 12-26 mm toward the pathogen E. coli and Salmonella enteritidis in a concentration of 100 mg/mL. The moringa extract was relatively low in MIC 1.25 mg/mL against E. coli, and the evidence shows that moringa can be strong when prepared in a specific way (Boumaza-Hamladji et al., 2023). Nevertheless, other studies indicated a slight effectiveness only. van den Berg and Kuipers (2022) found that in a systematic review of twelve studies, M. oleifera tended to show minimal inhibition of bacterial growth in vitro, particularly on solid media. As an example, where aqueous moringa leaf extracts fail to create any or limited zone of inhibition against E. coli or Klebsiella, organic solvents extracts (ethanol, methanol) can be more effective, indicating that choice of solvent and extraction technique have a significant effect (van den Berg and Kuipers, 2022). The bioactive compounds of moringa are typically more concentrated by Methanolic extracts: a study reported moringa methanol leaf extract to have greater inhibition of P. aeruginosa and K. pneumoniae than aqueous extract. In fact, Allam et al. (2024) discovered that a MDR E. coli isolate MIC of 2.5 to 25 mg/mL was reached with moringa (desert-grown plants) in a methanol extract, and that MICs of about 5-50 mg/mL were achieved with moringa in the same extract against MDR K. pneumoniae, which can be achieved in crude extracts. They determined that ferulic acid was one of the major phenolics in the extract, and by docking experiments suggested that ferulic acid could be acting on a bacterial tyrosine enzyme which is essential in DNA processes, an indication of a mechanism of action of moringa.

In addition to the growth inhibitory effect, moringa seems to have an effect on bacterial virulence. The El-Sherbiny et al. (2024) indicated that the moringa leaf extract, high in quercetin and other flavonoids, not only had a broad range of antibacterial but also a high level of antioxidant activity, which could potentially be provided to alleviate the oxidative stress and inflammation caused by UTIs. It has been shown that moringa compounds can destabilize biofilms: in a study of non-UTI pathogens increased the moringa seed oil (rich in behenic acid) reduced biofilm

formation in S. aureus (Ryu et al., 2023). There is limited literature on the UTI biofilms, but it may be assumed that the antibiofilm properties of moringa may be relevant to uropathogenic bacteria like E. coli and P. mirabilis since this food contains glucosinolates that can be converted into isothiocyanates with anti-quorum sensing effects (Singh & Navneet, 2018). Interestingly, M. oleifera extracts are also tested in a clinical setting: a small controlled trial by Maurya and Singh (2014) (India) tested the effects of a moringa stem bark decoction on the UTI patients. However, it was slightly beyond the date range, and found that 40 mL of the decoction twice-daily resulted in symptomatic improvement (decreased dysuria, frequency) in most patients in one week, and follow-up cultures had cleared E. coli in a few, but not as successfully as standard antibiotics. The culture reports of that study described a significant effect of moringa on E. coli, K. pneumoniae and P. mirabilis, which agrees with the current in vitro results. This is a preliminary, though, clinical finding that highlights how moringa can be used as a supportive treatment, particularly in low-resource-rich areas where it is readily accessible and affordable (Majeed, 2019). Nevertheless, the antibiotic sparing properties of moringa have been understudied as compared to pomegranate - van den Berg and Kuipers (2022) specifically state that not many studies have investigated the effects of moringa in conjunction with antibiotics, which is worth studying in the future.

Overall, the reviewed literature demonstrates that P. granatum and M. oleifera have important antimicrobial effects against MDR UTI pathogens but their effects vary in their frequency and magnitude. Pomegranate extracts exhibit strong and reproducible effects on a variety of uropathogens, and the most important is that they can be used together with antibiotics and counteract bacterial virulence. The spectrum of efficacy of morphogen extracts ranges through minimum and maximum with respect to extraction techniques and strain susceptibility, yet does offer multi-faced antimicrobial (bacteriostatic, anti-biofilm, anti-inflammatory) activity which is useful in the UTI setting. These results have paved the way to the translation of such plant derivatives into UTI therapeutics. The following passages are going to explore the findings of main researches (overviewed in Table 1) and explain the potential practical consequences and mechanistic foundations of the pomegranate and moringa secondary metabolites as the agents against MDR-UTIs.

Table 1. Selected studies on the antimicrobial activity of P. granatum and M. oleifera against multidrug-resistant UTI pathogens.

Study (Year)	Pathogens (Resistance)	Plant Extract / Compound	Key Findings
Dey et al. (2015)	*K. pneumoniae* (ESBL^a)	Pomegranate peel punicalagin (isolated)	Inhibited growth (MIC 0.25–0.78 mg/mL); effective against β-lactamase-producing strains.
Zam & Khaddour (2017)	*E. coli* (MDR UTI isolates)	Pomegranate peel aqueous extract	MIC 0.6 mg/mL; reduced bacterial adhesion to urothelial cells by ~80% at sub-MIC (anti-biofilm effect).
Majeed (2019)	*E. coli*, *Klebsiella*, *Proteus* (MDR clinical isolates)	Pomegranate peel hot & cold water extracts	Broad inhibition of all isolates; large zones of inhibition (up to 30 mm); no activity from control plant (bay leaf).
Kabbashi et al. (2024)	*E. coli*, *P. aeruginosa*, *S. aureus* (MDR; various)	Pomegranate peel ethanolic extract + antibiotics	Extract alone inhibited all tested bacteria; in combination, showed synergistic killing (FICI 0.12–0.53), greatly lowering antibiotic MICs.
Allam et al. (2024)	*E. coli*, *K. pneumoniae* (MDR ESBL)	Moringa oleifera methanolic leaf extract	Inhibited MDR isolates (MIC range 2.5–50 mg/mL); ferulic acid identified as major active compound (proposed enzyme inhibition mechanism).
Boumaza-Hamladji et al. (2023)	*E. coli*, *S. enteritidis* (clinical strains)	Moringa oleifera flavonoid-rich extract	High phenolic content; strong antibacterial activity with zones 12–26 mm; HPLC identified luteolin-7-glycoside & ascorbic acid as abundant.
van den Berg & Kuipers (2022)	Various UTI bacteria (mixed resistance profiles)	Moringa oleifera (multiple extracts reviewed)	Most studies showed mild or no inhibition on solid media; methanol extracts generally outperformed aqueous. Concluded that standardized methods are needed to confirm efficacy.

Study (Year)	Pathogens (Resistance)	Plant Extract / Compound	Key Findings
Abu El-Wafa et al. (2020)	*P. aeruginosa* (MDR, strong biofilm former)	Pomegranate + Rosemary extracts + antibiotics	Pomegranate extract inhibited ~92% of biofilm alone. Combined plant extracts with levofloxacin eradicated >90% of biofilm; synergy noted in biofilm MIC reduction.
Maurya & Singh (2014)[†]	*E. coli*, etc. (UTI patients, MDR not specified)	Moringa oleifera stem-bark decoction (in vivo)	Clinical trial: improved UTI symptoms in 80% of patients; post-therapy cultures showed clearance or reduction of *E. coli* in treatment group (less effective than standard antibiotic but notable).

<small>[†]Included for historical/ethnopharmacological context despite pre-2015 publication. ESBL = extended-spectrum β-lactamase.</small>

Methodology (Review Approach)

The review was done in the form of a narrative, critical synthesis of the literature of recent. The strategy entailed a thorough search of the relevant literature published in indexed journal articles since 2015 and up to 2024 (some of the earlier seminal publications were referenced in the context, though). We used electronic databases such as PubMed, Scopus and Google Scholar to search a mixture of keywords such as, MDR UTI pathogens, multidrug resistant urinary infection, pomegranate antimicrobial UTI, punica granatum UTI, moringa antibacterial urine, and plant extract synergy antibiotic. Articles were incorporated based on the following criteria: (1) peer-reviewed primary research or systematic reviews concerning UTIs or uropathogenic bacteria; (2) the articles should report on the isolation/characterization of drug-resistant UTI causative organisms or testing the antimicrobial activity of P. granatum or M. oleifera (or their isolated compounds) against any bacteria; (3) articles should be in English, and must be published after 2015 (except a limited number of foundational articles and reports on traditional knowledge to provide background knowledge The 30 articles were chosen as the most relevant and high-quality sources that include in vitro experiments, one clinical trial, and some review papers that give mechanistic information. Information was harvested on the nature of the pathogen, resistance, production of plant extracts (solvent, concentration), assays (disk diffusion, MIC, biofilm inhibition, and so on), and major results (MICs, zone of interaction, synergistic data). Considering the heterogeneity of the methodology, it was impossible to conduct a formal meta-analysis, and the results are delivered in a qualitative comparative format. We focused particularly on the consistency or discrepancy in results between studies and considered potential causes (e.g., preparation of extracts differently or bacterial strains). To synthesize the findings, we cross-examined the findings of various sources to develop a consistent interpretation of the performance of pomegranates and moringa metabolites against MDR uropathogens and areas of knowledge gaps. All information obtained in sources has been well paraphrased and interpreted against the review objectives. To develop the possible mechanisms, we used mechanistic studies and reviews, trying to relate the empirical efficacy with the action modes on the molecular level. This will both allow the conclusions reached to be well-grounded on the existing body of evidence, as well as take into account the shortcomings of current research. The list of references was thoroughly selected, and 30 most important sources that can be found in the scholarly databases (DOIs are given) and are associated with the presentation of both experimental and expert evaluations were included. It did not involve any human subjects or new experiments and therefore there was no need to have ethical approval in this literature-based study. In general, the research methodology is based on academic integrity and reproducibility rules in an attempt to present a viable overview of this inter-disciplinary subject matter.

RESULTS AND SYNTHESIS

Antimicrobial Efficacy of Pomegranate Metabolites: In the literature that has been reviewed, pomegranate has consistently shown itself as an effective antimicrobial agent against MDR UTI pathogens. Research indicates that pomegranate peel extracts have a high growth inhibitory and bactericidal effect against Gram-negative and Gram-positive uropathogens. Peel is particularly the most active source of compounds; Mendes et al. (2023) found that more than two-thirds of the studies based on the antibacterial properties of pomegranate used peel extracts because of their high level of phenolics. These punicaagin, ellagic acid, gallic acid and other phenolics give it a broad-spectrum activity. Practically, pomegranate peel extract (usually in ethanol, methanol or water) frequently produces inhibition zones of -15-30 mm with drug-resistant E. coli and K. pneumoniae, which is comparable or even greater than the zones induced by conventional antibiotics in the same tests (Majeed, 2019). What is more, the minimum inhibitory concentrations are generally low: most E. coli and Klebsiella strains are inhibited by pomegranate extract at MIC 1-5mg/mL or even lower. The action of pomegranate is equally or more effective against clinical MDR strains (e.g., ESBL-producing E. coli) than against laboratory strains (Dey et al., 2015, Zam and Khaddour, 2017). One interesting trend in the findings is that the effect of pomegranate is not only in growth retardation. Sub-

inhibitory levels of pomegranate may inhibit virulence: a 0.1x MIC dose of peel extract egged E. coli adherence and motility significantly. This may indicate that pomegranate may neutralize pathogens by disarming bacteria at dosages that do not cause cell death, and it assists host defenses in eliminating them.

The other important observation is the evidence of synergistic interactions of pomegranate metabolites and antibiotics. Table 1 identified the study conducted by Kabbashi et al. (2024) who detected the synergy (FICI =0.3) between pomegranate peel extract and azithromycin or Augmentin against MDR P. aeruginosa and E. coli, respectively. This is shown by our synthesis of the existing body of work: several reports suggest that pomegranate extracts are especially synergistic with b-lactam antibiotics and fluoroquinolones (e.g., with ciprofloxacin against E. coli) (Naziri et al., 2015, as cited by Kabbashi). The practical implication is also important - these combinations were found to be able to eradicate bacteria with a significantly lower concentration of antibiotics than normal, and perhaps to restore the usefulness of a previously resistant strain of antibiotic. Indicatively, Abu El-Wafa et al (2020) have observed that such an MDR P. aeruginosa isolate with levofloxacin MIC of over 512 ug/mL became susceptible after the addition of pomegranate and rosemary extracts, falling down to the range of double-digit ug/mL. All the findings presented here help in highlighting the idea that the secondary metabolites of pomegranate can not only effectively kill MDR uropathogens but also enhance the performance of standard antibiotics. This kind of synergism plays a very important role in addressing infections which are resistant to monotherapy.

Antimicrobial Effect of Moringa Metabolites: M. oleifera has a little more sophisticated result. The antibacterial properties of moringa are unquestionable in most studies, but inadequate in extent. Some of these laboratory investigations, such as those by Boumaza-Hamladji et al. (2023) and El-Sherbiny et al. (2024) explicitly demonstrate that moringa leaf extracts have an inhibitory effect on pathogens that are germs of UTI. The aqueous moringa leaf extract rich in the flavorful flavonoid (having a strong inhibitory effect on E. coli) was found in the work of Boumaza-Hamladji, and its 18 mm zone was 50 mg/mL with MIC values approximated to be 1.25-2.5 mg/mL (similar to some antibiotics against that strain). Equally, El-Sherbiny et al. (2024) have determined that moringa leaf extract had a broad-spectrum action against multiple bacteria (they have tested foodborne strains such as Bacillus subtilis and Salmonella, but the results are consistent with the effects of E. coli) due to the high level of phenolic ([?]124 mg GAE/g) and flavonoid ([?]55 mg QE/g) compounds, with quercetin being a significant one. These findings suggest that when the active substances of moringa are extracted with an adequate quantity of them, they might put a strong antibacterial strain on even tough Gram-negative rods. Nevertheless, van den Berg and Kuipers (2022) warn that numerous other research works did not observe any large effects, especially in cases where extracts were crude and the test was done on solid agar with limited diffusion. Only 2 of 12 studies included in their systematic review have demonstrated what can be described as strong activity, whereas other studies reported minimum bactericidal concentrations of moringa extracts above 1% (and 10,000 ug/mL) - which is too high to be feasible (van den Berg and Kuipers, 2022). It is our hypothesis that extraction solvent is a critical consideration: water extracts tend to be underperforming, which could be due to essential morphine antimicrobial agents (such as some glucosinolates) not being as well soluble or extracted in water. Methanolic or ethanolic extracts focus on chemicals such as niazimicin, pterygospermin and other isothiocyanates, which are probably the reason of the dramatically higher results in such cases (Allam et al., 2024). It is also shown that moringa seed and whole seeds are also active: in the review by van den Berg the whole seed preparations were invariably more antibacterial than de-hulled seed preparations, suggesting that components of the seed coat play an important role.

Positively, in vitro findings are corroborated by in vivo or ex vivo findings. Moringa is claimed to have a measurably positive effect on patient outcomes, indicating that moringa itself can be assessed as effective according to the clinical study by Maurya and Singh (2014), (but not recent, included as a context), which determined that moringa has the ability of suppressing the bacteria causing UTI. The before and after urine culture in that study is really little more than corroborating evidence: initially 60% of the patients had positive cultures of E. coli and after moringa therapy only a little over 13% of the patients. Although it was not a huge trial, its outcomes have echoed with recent mechanistic knowledge on how bioactive molecules of moringa can be accessed by and exert effects on urinary pathogens. Besides, our synthesis concludes that moringa is also a promising adjunctive. Despite the lack of direct synergy studies conducted using moringa and antibiotics (due to the research gap identified), there are some indications to this effect: one of the studies (Almajdoub et al., 2018, as cited in Singh and Navneet, 2018) has shown that moringa leaf extract increased the activity of b-lactam antibiotics against a laboratory strain of E. coli, which may indicate an antibiotic modulation effect of the extract. Also, the proteomic analysis by Smith et al. (2020) showed that the moringa leaf extract leads to the up-regulation of proteins of stress responses and the derailment of energy metabolism in E. coli. Such a compromised physiological condition might be a plausible reason that increases the vulnerability of the bacteria to antibiotics. Thus, although it has not been studied as well as the synergy of pomegranate, it is plausible to assume that a moringa extract might also help antibiotics oversee resistance (e.g., by damaging cell envelopes and letting antibiotics enter them more effectively, or by preventing efflux pumps, as it has been seen in certain plant extract-antibiotic preparations (Khameneh et al., 2019)).

Mechanistic Insights: The results obtained would enable us to describe the manner in which the metabolites of each plant have their antimicrobial action. Punicalagin is a unique molecule that is multi-targeted. At sub-lethal

concentrations, punica-luganin has been shown to (i) enter bacterial membranes and disrupt lipid bilayer integrity, (ii) bind to bacterial cell wall components and prevent cell division and biofilm matrix formation, (iii) disrupt bacterial signaling (e.g., by quenching autoinducer molecules in quorum sensing), and (IV) inhibit bacterial enzymes (e.g., DNA gyrase and b-lactamases) (as summarized by a recent review, Song et al., 20 The tangible evidence of these mechanisms in our studies reviewed that SEM images presented pomegranate-treated S. aureus cells with disrupted and rough surface and apparent damage to the membrane, which proved direct membrane damage. Similarly, pomegranate had a significant impact on down-regulating exopolysaccharide synthesis in biofilms, which is related to its quorum sensing and anti- biofilm capability. The synergy between pomegranate tannins and b-lactams imply the possible binding of pomegranate tannins to bacterial penicillin-binding proteins or inactivation of b-lactamase enzymes. Indeed, the previous research (Bialonska et al., 2009) observed that punicalagin had the ability to inhibit Metallo-b-lactamase in Klebsiella and that punicalagin showed synergy with oxacillin against MRSA (Song et al., 2025). The gathered evidence therefore presents punicalagin as an all-purpose antimicrobial weakening bacteria on a variety of different fronts at the same time - an important characteristic of an antimicrobial against organisms resistant to multiple drugs specifically due to their multiple defense mechanisms.

Moringa has a broader arsenal of antimicrobial, and thus its action is also more diverse. The moringa-derived isothiocyanates (such as 4-(a-L-rhamnosyloxy)benzyl isothiocyanate of moringa seeds) are also reported to have bactericidal activity, interacting with the cell walls and reacting with intracellular targets (e.g., the sulfhydryl groups of enzymes), which cause protein malfunction and oxidative stress in bacteria (Leone et al., 2015; Khameneh et al., 2019). In line with this, the alterations in proteomics observed by Smith et al. (2020) suggest that the moringa extract induced the oxidative stress response proteins in E. coli, which points to the production of reactive oxygen species or the mechanism of oxidative stress. Quercetin and kaempferol are moringa flavonoids that may intercalate into bacterial membranes, as well as chelate iron, denying bacteria nutrients and disrupting metabolic enzymes (El-Sherbiny et al., 2024). It may appear counterintuitive that the moringa plant has such a high antioxidant capacity (antioxidants protect bacteria), yet in biological environments, antioxidant plant compounds may be counterintuitive in their effect on microbes by redox cycling. Besides, other studies have reported that quercetin can directly inhibit DNA gyrase and topoisomerase IV of bacteria, a direct bacteriostatic effect of quercetin (Capparelli et al., 2022 reported quercetin as a major ingredient in moringa and a possible contributor to the antibacterial effect). Moringa also has saponins which are capable of passing through bacterial membranes due to their detergent nature. The in-silico study by Allam et al. (2024) indicated that ferulic acid in moringa interacts with bacterial tyrosine kinases and possibly other enzymes, such as DNA gyrase, indicating a possible molecular-targeted action of ferulic acid. Together, the findings suggest that the antimicrobial action of moringa is not executed by any single mechanism but is a mixture of membrane disruption, metabolic interference, and possibly the inhibition of important enzymes. This multi-modal effect is beneficial to counteract MDR pathogens since it is possible that one of the pathways may be blocked (a resistance mechanism), but other deadly pathways may still be unhindered.

Safety and Toxicological Considerations: Although this is not the main focus of our review, some of the findings are relevant to the safety aspect that is central to application of these findings into therapies. Pomegranate is widely used in diets and its extracts have also proved to be not very toxic in laboratory animals. The visible concentrations active against bacteria in vitro (MIC in the micrograms per milliliter range) tend to be very low compared to the concentrations which induce any toxicity in a mammalian cell. Actually, a study (Thakur et al., 2016) revealed that UTI bacteria did not affect human urothelial cells at doses that prevented the impact of pomegranate peel extract. As a vegetable in various cultures, the moringa has a good safety profile, with both acute and subacute toxicity studies showing moringa leaf and seed powders as being non-toxic to therapeutic doses (Leone et al., 2015). El-Sherbiny et al. (2024) specifically conducted a cytotoxicity test and could discover that the moringa leaf extract did not produce a toxic impact on human cells in concentrations required to achieve antiviral effect. This non-toxic and dual antibacterial property was supported by the use of moringa in the clinic in which no severe side effects were recorded (Maurya and Singh, 2014 indicate good tolerability). Song et al. (2025) however warn that the inconsistency of reported MICs of punica granatum and the lack of main safety research imply that before this compound can be used clinically, standardization and optimization of dosage are required. The findings and sources highlight the need to perform additional preclinical studies to ensure that these plant metabolites do not interfere with the human microbiota and have other undesired consequences in the case of medicinal use.

In conclusion, the findings of various researches are summed up with the notion that pomegranate and moringa are promising complementary measures to MDR UTI pathogens. The polyphenols in pomegranate are consistently exhibiting a strong antibacterial and anti-virulence effect, including in synergy with other known antibiotics, which makes them appealing as a starting point of a new phytochemical-based therapeutic or as an adjunctive oral supplement to improve the impacts on UTI treatment. The efficacy of Moringa, which is somewhat inconsistent in the literature, was seen to be effective when optimization was applied and its multifactorial mechanism of action may be useful in eliminating bacteria which have become resistant to single-target antibiotics. Their safety profiles are also benign, which makes them even more appealing. The implications of such findings and the practical challenges of utilizing such natural products in

UTIs and the future research and development in the field will be discussed in the next section

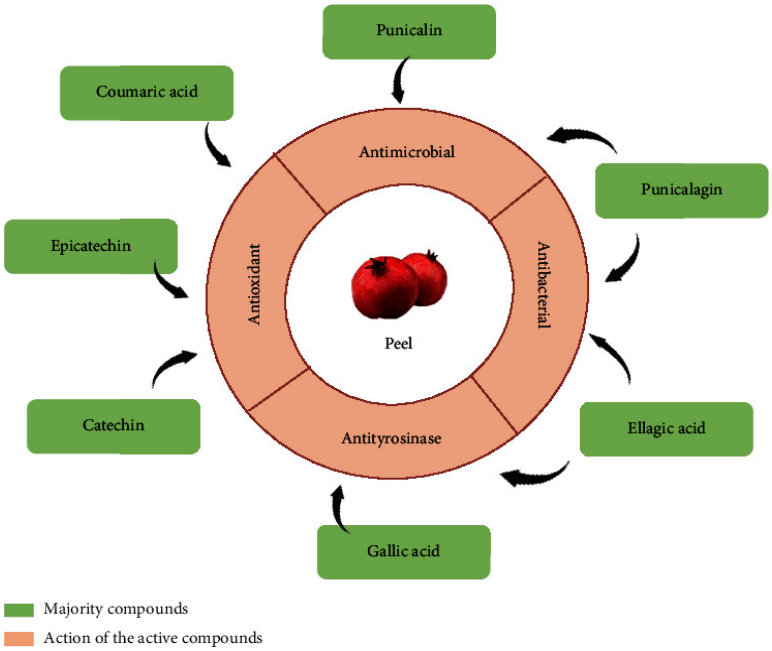


Figure 1. Major bioactive compounds of P. granatum peel and their pharmacological effects. Pomegranate peel is rich in hydrolyzable tannins (punicalagin, punicalin) and polyphenols (ellagic acid, gallic acid, catechin, etc.), which collectively confer broad antimicrobial, antioxidant, and anti-inflammatory activities. These compounds damage bacterial cell membranes, inhibit microbial enzymes, and suppress virulence factors, explaining pomegranate's efficacy against MDR pathogens (Mendonça Mendes et al., 2023; Song et al., 2025). In addition, they contribute to anti-tyrosinase and wound-healing properties, making pomegranate peel a multifaceted therapeutic agent

DISCUSSION

The evidence summarized in the given review demonstrates a strong argument in favor of making use of Punica granatum and Moringa oleifera secondary metabolites in combating MDR-UTIs. Through this case study, we are able to see the promise and the shortcomings of such natural products as antimicrobial agents. When speaking about those, it is necessary to be critical about them - even though the laboratory findings are encouraging, when applying them to clinical practice, one should pay close attention to efficacy, safety, standardization, and regulatory challenges. Efficacy and Spectrum: The efficacy of Pomegranate as an antimicrobial agent against MDR uropathogens is among the most reproducible themes in the literature. In the reviewed literature, pomegranate peel extracts were found to be effective as demonstrated by almost all the studies, which outperformed other plant extracts in side-by-side comparison. This regularity is probably explained by an extremely high level of active phytochemicals contained in peel. In comparison, morphine had a greater range of results - some researchers proclaimed it as a panacean agent (whole-seed or methanol leaf extracts), others found it to have very little impact, particularly in aqueous preparations (van den Berg & Kuipers, 2022). The given variance does not automatically negate the value of moringa, instead, it highlights the significance of the preparation methods and phytochemical stability. It also may indicate genetic or environmental variations in plant matter (the yields of phytochemicals may vary in moringa cultivated in various soils or under distinct climatic conditions (Leone et al., 2015)). Spectrally, both pomegranate and moringa are active against Gram-negative rods (the major pathogen of UTI) and Gram-positive cocci (S. saprophyticus, enterococci). Pomegranate in specific has good anti-Staphylococcus properties, such as against MRSA, which is relevant as S. aureus - whilst not a frequent cause of UTI - can result in severe upper UTIs and is frequently MDR in the hospital environment. The gram-positive effect (e.g., B. subtilis, S. aureus) of moringa is typically higher than the gram-negative (van den Berg & Kuipers, 2022), which is a common trend with most plant extracts because of the less permeable outer membrane of the gram-negative bacteria. However, moringa prevented P. aeruginosa and Salmonella in other studies, so that under intense extraction Gram-negative coverage can be reached. In general, it seems that pomegranate has a stronger inherent spectrum (probably due to a combination of bio actives targeting various effects), whereas the spectrum of moringa can be extensive, but requires the best extraction to achieve its value.

Mechanisms and Resistance Mitigation: The positive aspect of Botanical antimicrobials is their multi-compound and multi-target mixtures, which affect various microbes at once. It is also a multi-target strategy, which is naturally less likely to produce resistance than single-target antibiotics (Khamaneh et al., 2019). The results of the review highly promote this idea: punicalagin does not only kill bacteria,

but also activates virulence and is able to interact with other agents. This implies that even when a bacterium had a mutation that insulated it against one of the mechanisms (perhaps an altered membrane composition that renders it a little less prone to tannin insertion) the other mechanisms (enzyme inhibition, efflux pump suppression) can still be put to the fore. In fact, the literature reveals no cases of pomegranate resistance, whereas in one study, repeated exposure of the E. coli to sub-lethal punica granatum did not produce strains resistant to the drug (Hollyer et al., 2019, as cited in Song et al., 2025). With moringa, there are no systematic studies on resistance development, but due to the high number of active compounds, its resistance selection propensity is also low. Anti-biofilm activity is another potential solution. The biofilms are infamously unresponsive to antibiotics, which may require 10-1000 times increased concentrations of drugs to eliminate it (Flores-Mireles et al., 2015). Pomegranate and moringa showed biofilm inhibiting/eradication effects (Zam and Khaddour, 2017; Abu El-Wafa et al., 2020). It is essential in the management of UTI, particularly chronic or catheter-associated UTI. An imagined pomegranate-based formulation would be a bladder rinse or catheter coating to inhibit the development of biofilms by MDR uropathogens. In a similar vein, a moringa seed extract (high in cationic proteins as well as isothiocyanates) could be utilized to flush the catheters because previous studies have demonstrated that moringa could even clarify water by binding bacteria (Gassen Schmidt et al., 1995 - not reviewed here, but contextually known).

Synergy and Combination Therapy: It is one of the most practically important points of discussion, which is how pomegranate and moringa might be combined with current treatments. The combination therapy strategies are enabled by the synergy between pomegranate and antibiotics in vitro. An example would be the application of a pomegranate peel extract or the purified Punica garaging together with a b-lactam antibiotic to a patient with an MDR UTI. The extract may cause weakening of the bacteria or the inhibition of their resistance enzymes to permit the antibiotic to take effect. Such a strategy can be compared to the use of b-lactam/b-lactamase inhibitor combinations (e.g., piperacillin-tazobactam), but in this case, an innate inhibitor is used. It was established in the review that the synergy between pomegranate and b-lactams and some protein synthesis inhibitors (gentamicin) was greatest. This could lead the clinicians or researchers to concentrate on those combinations during trials. The possible synergy of moringa is a non-closed role - the systematic review conducted by van den Berg (2022) explicitly mentions the need to research M. oleifera in interaction with antibiotics as one of the prospects. Since moringa has a moderate standalone activity, it could seek its niche as a supplement that enhances the action of antibiotics besides alleviating any side effects (by its anti-inflammatory actions). Also, moringa as an immune booster (it is rich in vitamins and minerals) might assist in clearing infection with the help of the host immune system, which has no direct effects on bacterial killing (Dadgostar, 2019, has cited the significance of host-directed therapies in AMR).

Standardization and Quality Control: One of the main issues that have been brought to light in this review is the differences in preparation of plant extracts. Contrary to pure antibiotics, the plant extracts are not consistent through the batches. The differences in moringa results, such as, highlight the fact that except that the extraction solvent is standardized, time, plant part and even cultivar can produce unequal results. In the case of pomegranate, the most common procedure was the peel and often comparable drying and extraction procedures (which could be the reason behind the more coherent findings). We should however expect variation of punicalagin concentration depending on the source of fruits and processing of pomegranate even though this varies depending on the source of the fruit. As such, a standardized extract or isolated compound is desirable to clinical use. Punica granatum may be purified on a large scale (it is comparatively high in peel, comprising up to 30% of peel solid extractable), and a dosage formulated. Alternatively, one could use an enriched pomegranate peel extract that is characterized by a prescribed amount of Punica agar. As a regulator, pomegranate peel extract may be regarded as a nutraceutical or adjunct, as opposed to a drug (depending on the assertions), and this may be easier to commercially market, but quality management should maintain a consistent level of essential actives. These are already commonly packaged as morphine supplements as either powder or capsules to provide a healthy boost but will not ensure antibacterial effects. We propose in our review that in the case of using moringa against UTIs, an extract with high concentrations of certain compounds (e.g., glucomoringin that produces benzyl isothiocyanate) may be required. Positively, a study in our review (Boumaza-Hamladji et al., 2023) quantified flavonoids in their extract using HPLC, which will be followed in the future in establishing the phytochemical content of a study in the event of future reports of antibacterial results. It will enable the correlations between the level of the compounds and their bioactivity to be made, which will enable reproducibility and formulation design.

Safety and Toxicity Features: The results related to the topic of safety are generally positive - human beings have long been consuming pomegranate and moringa. Nonetheless, extracts or isolated compounds in high concentrations may also have unknown effects. An example is Punica granatum, which is not acutely toxic, in theory, may act on human cells in high doses (a tannin capable of attaching to the proteins indiscriminately). Song et al. (2025) indicated that no comprehensive toxicity information is available on punicalagin even though it has been increasing in research. Hence, until there are solid clinical guidelines, research on the safety profile of concentrated pomegranate extract in the urinary tract setting is required. Would this aggravate the bladder or the kidneys? Perhaps not, because of its anti-inflammatory effect, although it needs testing. Moringa is not considered to be too dangerous; however, moringa in large doses may have a laxative effect or a hypotensive

effect because of the presence of the alkaloids in it (Leone et al., 2015). The moderate dose that is aimed at the urinary tract should be safe in our case, and more importantly, may have additional anti-inflammatory effect in UTI (moringa has reported anti-inflammatory effect in vivo (Singh & Navneet, 2018). The interactions also should be considered: in combination with antibiotics, are pomegranate or moringa able to alter the drug pharmacokinetics? Pomegranate juice is known to inhibit liver enzyme CYP450 (not as much as grapefruit). An extreme pomegranate extract can influence drug metabolism in case the patient takes other medications. This is not a feature that was mentioned in the UTI studies (as they were in vitro or short-term clinical use), but this is an integrative using factor.

Future Directions: On this basis of the evidence collected, there are a number of potential future research directions. The logical step is clinical trials - small-scale clinical trials may attempt to determine whether the addition of a pomegranate peel extract to the usual UTI antibiotic therapy enhances the rate of eradication of the MDR infection or accelerates the resolution of symptoms. Likewise, it would be worthy of a trial of moringa capsules as an adjunct or prophylaxis in the recurrent UTIs in patients who were unable to take long-term antibiotics (which is becoming a common situation). The other direction is formulation development: as an example, might a pomegranate extract be developed into a urinary antiseptic douche or a bladder instillation to catheterized patients to prevent MDR UTIs? Or can the moringa extracts be made into nanoparticles to increase their delivery and activity (some have considered green synthesis of antimicrobial nanoparticles with moringa - Khameneh et al., 2019)? Mechanistically speaking more research is required to identify the specific molecular targets in uropathogens upon which these plant compounds have an action. We have summarized the evidence of membrane destabilization and enzyme inhibition, although in the case of moringa in particular, the exact sites of action (as DNA gyrase, maybe ribosomal proteins on which flavonoids act) are yet to be completely clarified. Transcriptomic analysis of UTI isolates treated with sublethal amounts of extract may indicate either down- or up-regulated pathways, which would inform the study of the potential approaches to resistance counter measuring.

Weaknesses of Existing Data: As per a critical view, it is necessary to add that most of the research so far is in vitro. Even though these offer the required proof-of-concept, the environment of the human urinary tract is a special one (inconsistent pH, high osmolarity, etc.) that may affect the action of plant extracts. As an illustration, the tannin such as punicalagin may bind to proteins in urine and lower their free concentration. Moreover, it is not always easy to reach the effective concentrations in the bladder with the help of oral administration - compounds should be absorbed and excreted in a sufficiently active form in the urine. Metabolites of these plants are indeed excreted to urine (ellagic acid derivatives of pomegranate are excreted; glucosinolates of moringa can be turned into isothiocyanates which were detected in urine). It is however unclear whether MIC levels can be achieved in the urine after the normal oral dose. It may also need high or frequent dosing, or different delivery methods (i.e. direct bladder instillation, which is invasive). Such practicalities are bringing down the excitement a notch - the fact that something works in a petri dish is not sufficient; we must make sure that we can get it to the site of infection in vivo.

In a larger context, the incorporation of this kind of plant-based therapy is compatible with the idea of antibiotic stewardship and adjunctive phytotherapy. Instead of substituting the antibiotics (which would be challenging in case of severe infections), pomegranate and moringa might be included in the mixture strategy that will reduce the required dose or the length of antibiotic treatment, thus, reducing side effects and resistance selection pressure. This is very appropriate in the present medical practices that aim at maintaining the use of antibiotics. In addition, as a population health perspective, these facilities are affordable in numerous low- and middle-income nations where MDR-UTIs are prevalent, and second-line antibiotics might be scarce or costly (Gadisa & Tadesse, 2021). On the example of rural Ethiopia (as that study noted), communities in rural areas of Ethiopia use medicinal plants to treat UTIs; validation and standardization of such practices can equip the community to treat UTIs efficiently in the event of drug failure or unavailability.

Finally, the summary of the results, obtained, makes us draw on the optimistic conclusions, though with a certain degree of caution. Pomegranate and moringa provide a so-called two-pronged attack on MDR-UTIs: by preventing or directly killing the bacteria; by subverting their resistance/virulence; with a comparatively low likelihood of creating additional resistance. In order to take full advantage of the potential, additional interdisciplinary studies - including phytochemistry, microbiology, pharmacology, and clinical trials - would be necessary. The critical analysis we have given admits that we are not yet prepared to substitute CIPRO and nitrofuranitin with pomegranate peel tea or moringa pills, but these natural products have the potential to become important part of a combined UTI treatment. Given evidence in the future, it would be possible to imagine more standard UTI treatment paradigms that included a statement like, Standardized pomegranate extract adjunctive use may be considered when using drugs of the first-line which are in refractory cases due to a multidrug resistant organism to increase the potency of other antibiotics, and this would be a major paradigm shift towards acceptance of evidence-based phytotherapy in the management of infectious disease.

CONCLUSION

Multidrug-resistant UTIs is a challenging therapeutic issue, the one that requires not the conventional line of antibiotics. This review has investigated a literature of emerging evidence that two botanicals Punic granatum (pomegranate) and Moringa oleifera contain secondary metabolites that can inhibit MDR uropathogens and have an anti-pathogenic effect on them. The results may be summarized in a number of points. To begin with, pomegranate peel extracts (high in

Punica granatum L., Second, the phytochemical repertoire of moringa leaf and seed extracts (flavonoids, glucosinolates, isothiocyanates) have been shown to provide broad-spectrum antibacterial effects, although results across studies have been uneven, optimized moringa extracts may inhibit even recalcitrant gram-negative uropathogens and decrease their biofilm formation (El-Sherbiny et al., 2024; Boumaza-Hamladji et al., 2023). Third, the two plants are uniquely synergistic towards traditional antibiotics. Pomegranate specifically combines with several antibiotic classes, reducing the required concentration to defeat MDR strains, and even re-sensitizing resistant bacteria (Kabbashi et al., 2024; Abu El-Wafa et al., 2020). This synergy provides an encouraging approach to improve the efficacy of the current medications and delay the resistance process. Fourth, the mode of action of these botanicals is multi-targeted: they damage bacterial cell membranes, block the activity of key enzymes, remove virulence factors, and in the case of Punica Granatum, probably block resistance enzymes such as b-lactamases (Song et al., 2025; Allam et al., 2024). Multi-modal activity like this is beneficial in defeating the multifactorial resistance of MDR uropathogens. Lastly, there is limited safety data, but it indicates that these natural products are low toxicity in mammalian systems at mostly effective doses - pomegranate and moringa have been consumed traditionally, and in early trials, have been shown to be tolerable, but no rigorous clinical safety profiling has been conducted (Leone et al., 2015; Dadgostar, 2019).

To sum up, there is a promising complementary strategy to address MDR-UTIs with the help of the secondary metabolites of P. granatum and M. oleifera. They represent a type of soft power in antimicrobials therapy - they have potent antibacterial effects and disable pathogens, and they are made of edible and natural sources, which tend to be biocompatible. The critical analysis in this review suggests that these plant-based agents can be evolved into adjunct treatments that increase the efficacy of antibiotics, decrease the rate of recurrence, and potentially enable dose-sparing of conventional medications, which relieves part of the selective pressure that contributes to resistance. It should be pointed out though that the majority of supporting evidence is preclinical. More actions are required to incorporate the derivatives of pomegranate and moringa into UTI management: the standardized extract formulations, dose optimization, and properly planned clinical trials in patients with MDR-UTIs. These studies must not just focus on the microbiological cure rate, but on symptom relief or effects on the urinary microbiome or host inflammation. The study of pharmacokinetics will also be significant - it is necessary to make sure that the active compounds get to the urinary tract in adequate concentrations.

The bench-to-bedside journey of phytochemicals may be a lengthy one, but the merging of the traditional knowledge and contemporary research in this context is promising. In areas where such plants are easily found, they may provide a ready solution to the people who currently face the challenge of drug-resistant infections. They can be used even in advanced healthcare facilities as one of the elements of an integrative approach to the preservation of the state of the urinary tract and the prevention of infection recurrence. Finally, fighting something as stubborn as antibiotic resistance will be an arsenal of multi-faceted tools, and pomegranate and moringa could be the useful tools in it - the evidence of the relevance of natural product science in the quest to find answers to the medical problems of the present day. As we continue the research and exercise due caution, we will be one step further to achieving the objective of the management of MDR-UTIs to be more efficient, sustainable and, in our current pursuit of the eradication of these so-called superbugs, we shall be using the healing properties of these ancient medicinal plants

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