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Unraveling the Efficacy of Traditional Herbal Remedies Against Multi-Drug Resistant Bacterial Infections: A Comprehensive Study of Pathological Impact, Microbial Resistance Mechanisms, Clinical Relevance, and Biochemical Pathways

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ABSTRACT

Background: The increase of multidrug-resistant (MDR) bacterial infections worldwide is a serious health concern that calls for the investigation of other therapeutic modalities. Because of their possible antibacterial qualities, traditional herbal medicines have been used for ages; yet, little is known about how effective they are against MDR infections.

Objective: This study aimed to evaluate the efficacy of various traditional herbal remedies against MDR bacterial infections by assessing their antimicrobial activity, resistance mechanisms, and clinical relevance.

Methodology: A cross-sectional, laboratory-based investigation was conducted from January 2023 to December 2023. involving 230 bacterial isolates from clinical specimens. In addition to phytochemical investigation to discover bioactive components, 10 popular herbal treatments were subjected to the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) tests. The efficacy of these treatments was compared among bacterial strains using chi-square and t-tests.

Results: According to the research, herbal treatments including Adhatoda vasica, Curcuma longa, and Moringa oleifera have strong antibacterial action against MDR pathogens, especially *Klebsiella pneumonia*, *Staphylococcus aureus*, and *Escherichia coli*. Statistically significant differences in their effectiveness were verified by chi-square and t-tests, with p-values < 0.01. Adhatoda vasica had considerable activity against *E. coli* (95%) and *K. Pneumoniae* (85%), whereas Moringa oleifera was most effective against *E. coli* (100%) and *S. aureus* (90%).

Conclusion: Traditional herbal remedies, particularly Moringa oleifera and Curcuma longa, exhibit significant antibacterial potential against MDR pathogens, offering potential alternatives to conventional antibiotics.

Keywords: Multidrug resistance, Herbal remedies, Antibacterial activity, Phytochemicals

Introduction

A major worldwide health concern is the startling increase of multidrug-resistant (MDR) bacterial infections, which compromise the effectiveness of traditional medicines and raise rates of morbidity and death [1,2]. Alternative treatment methods are urgently needed since bacteria including *Klebsiella pneumonia* (*K. Pneumoniae*), *Staphylococcus aureus* (*S. aureus*), and *Escherichia coli* (E. coli) have shown growing resistance to common antibiotics [3]. Antimicrobial resistance is one of the top 10 worldwide public health problems, according to the World Health Organization, which has called for creative ways to deal with this growing issue [4].

In light of this, conventional herbal treatments have become viable options for combating MDR infections [5]. Because medicinal plants contain strong bioactive components such terpenoids, alkaloids, flavonoids, and phenolics, they have been utilized for ages to cure infectious disorders [6]. These substances have a variety of modes of action, including preventing the growth of bacteria, preventing the development of biofilms, and interfering with quorum sensing pathways [7]. Herbal treatments may have a multidimensional mode of action that lowers the risk of developing resistance, in contrast to modern antibiotics [8].

Furthermore, the potential of traditional medicinal herbs to treat infectious disorders is supported by a wealth of ethnobotanical information [9]. Herbal therapies have been used to treat bacterial illnesses by cultures all throughout the world, and many of these treatments are yet unexplored in current drug research initiatives [10]. Researchers have been able

to extract and describe these bioactive compounds thanks to advancements in pharmacology and biochemistry, which have given them important new information on their potential as therapeutics [11].
There are still many obstacles to overcome even with the increased interest in herbal antimicrobials. Thorough scientific research is necessary to address important issues including standardization, toxicity, and the possibility of harmful medication interactions. Furthermore, knowing the resistance mechanisms and biochemical pathways that these treatments target might assist maximize their clinical uses and incorporate them into contemporary therapeutic frameworks.

Research Objective

The study objective was to evaluate the efficacy of traditional herbal remedies against multidrug-resistant bacterial infections by investigating their pathological impact, microbial resistance mechanisms, clinical relevance, and underlying biochemical pathways.

METHODOLOGY

Study Design and Setting

This study was a cross-sectional, laboratory-based investigation and the research spanned 1 years, from January 2023 to December 2023.

Inclusion and Exclusion Criteria

Patients with multidrug-resistant bacterial infections verified by microbial culture and antibiotic sensitivity testing, bacterial isolates from wound, respiratory, urinary, and bloodstream infections, and herbal remedies customarily used in local communities to treat bacterial infections were all included in the study's inclusion criteria. Patients having co-morbid conditions that can affect the course of therapy, such as severe immunosuppression, bacterial isolates showing a vulnerability to first-line antibiotics, and herbal treatments with insufficient evidence on their manufacture and use, were excluded.

Sample Size

A wide variety of multidrug-resistant diseases were represented by the 230 bacterial isolates that were obtained from clinical collections, including blood, urine, sputum, and wound swabs. The effectiveness of ten conventional herbal treatments, which have a long history of antibacterial use, against these resistant bacterial strains was assessed.

Data Collection

Numerous patient samples, such as blood, urine, sputum, and wound swabs, were used to obtain clinical bacterial isolates. To verify multidrug resistance, antibiotic sensitivity testing was carried out using the Kirby-Bauer disk diffusion technique. Traditional methods were followed in the preparation of the herbal treatments, and extracts were subjected to phytochemical screening in order to find bioactive substances such flavonoids, alkaloids, and phenolic compounds that have antibacterial qualities. The effectiveness of the herbal extracts was evaluated using the Minimum Bactericidal Concentration (MBC) and Minimum Inhibitory Concentration (MIC) assays. To support the assessment of the efficacy of these conventional treatments in treating multidrug-resistant infections, information on patient demographics, illness types, and clinical outcomes was gathered from hospital records.

Statistical Analysis

Descriptive statistics, such as means and standard deviations for MIC/MBC values, were used to assess the antibacterial activity of herbal treatments. The efficacy of various treatments across bacterial strains was compared using chi-square and t-tests. Statistical significance was defined as a p-value of less than 0.05. SPSS was used to conduct statistical analysis (version 25.0).

RESULTS

There were 230 patients in the research, most of them were male (60.87%) and between the ages of 18 and 35 (34.78%), with an equal number in the 36–50 and >50 age categories (26.09% each). Wound infections were the most prevalent (34.78%), followed by bloodstream infections (11.04%), respiratory tract infections (30.43%), and urinary tract infections (21.74%). According to clinical results, 65.22% of patients recovered, 21.74% recovered partially, and 13.04% showed no improvement (table 1).

Table 1: Patient Demographics, Infection Types, and Clinical Outcomes

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	140	60.87
	Female	90	39.13
Age Group (years)	<18	30	13.04
	18–35	80	34.78
	36–50	60	26.09
	>50	60	26.09
Infection Type	Wound Infections	80	34.78
	Respiratory Tract Infections	70	30.43
	Urinary Tract Infections	50	21.74

	Bloodstream Infections	30	13.04
Clinical Outcomes	Recovered	150	65.22
	Partial Recovery	50	21.74
	No Improvement	30	13.04

E. coli was the most common (37.39%) among the 230 bacterial isolates from different clinical specimens examined in the research, especially in urine (17.83%) and wound swabs (12.17%). *S. aureus* was often isolated from wound swabs (14.35%) and sputum (16.52%), making up 34.35% of the total (table 2). Sputum (13.91%) and wound swabs (8.26%) included the highest concentration of *K. Pneumoniae*, accounting for 28.25% of isolates. The rates of *K. Pneumoniae* (2.17%), *S. aureus* (3.48%), and *E. coli* (7.39%) were lower in blood samples.

Table 2: Bacterial Isolates from Clinical Specimens

Clinical Specimen	Bacterial Isolate	Frequency (n)	Percentage (n)
Blood	*E. coli*	17	7.39
	S. aureus	8	3.48
	K. Pneumoniae	5	2.17
Urine	*E. coli*	41	17.83
	K. Pneumoniae	9	3.91
Sputum	*S. aureus*	38	16.52
	K. Pneumoniae	32	13.91
Wound Swabs	*S. aureus*	33	14.35
	E. coli	28	12.17
	K. Pneumoniae	19	8.26

E. coli had the greatest sensitivity to gentamicin (70.11%) but the most resistance to amoxicillin (65.52%), according to antimicrobial sensitivity tests, as shown in table 3. *S. aureus* was resistant to erythromycin (55.68%), however it showed great sensitivity to vancomycin (82.28%) and linezolid (88.61%). *K. Pneumoniae* showed significant resistance to ceftriaxone (61.54%), but high susceptibility to imipenem (81.82%) and colistin (80.00%).

Table 3: Antimicrobial Sensitivity Testing Using Kirby-Bauer Method

Bacterial Isolate	Antibiotic	Sensitive (n)	Resistant (n)	Sensitivity (%)	Resistance (%)
E. coli	Ciprofloxacin	50	37	57.47	42.53
	Amoxicillin	30	57	34.48	65.52
	Gentamicin	61	26	70.11	29.89
S. aureus	Vancomycin	65	14	82.28	17.72
	Erythromycin	35	44	44.32	55.68
	Linezolid	70	9	88.61	11.39
K. Pneumoniae	Imipenem	45	10	81.82	18.18
	Ceftriaxone	25	40	38.46	61.54
	Colistin	52	13	80.00	20.00

Herbal treatments' phytochemical analyses showed a variety of bioactive component profiles. The majority of treatments, such as those from Terminalia chebula, Adhatoda vasica, Cassia fistula, and Moringa oleifera, included flavonoids. Moringa oleifera, Adhatoda vasica, and Withania somnifera were discovered to have alkaloids, while Adhatoda vasica, Cassia fistula, Terminalia chebula, and Aloe vera were found to contain phenolics. Zingiber officinale, Syzygium aromaticum, and Curcuma longa were found to contain terpenoids. Allium sativum did not, however, contain measurable amounts of these important substances. various results demonstrate how different biochemical components give various treatments their antibacterial properties (table 4).

Table 4: Bioactive Compound Presence in Herbal Remedies

Herbal Remedy	Flavonoids	Alkaloids	Phenolics	Terpenoids
Moringa oleifera	+	+	-	-
Adhatoda vasica	+	+	+	-
Cassia fistula	+	-	+	-
Terminalia chebula	+	-	+	-
Withania somnifera	-	+	-	-
Syzygium aromaticum	+	-	-	+
Allium sativum	-	-	-	-
Curcuma longa	-	-	-	+
Aloe vera	-	-	+	-
Zingiber officinale	-	-	-	+

The herbal treatments' antibacterial effectiveness varied, according to the results of the MIC and MBC tests. With the lowest MIC/MBC values (16–32 µg/mL and 32–64 µg/mL, respectively), Adhatoda vasica and Curcuma longa shown high efficacy, particularly against *K. Pneumoniae* (85%) and *E. coli* (95% and 90%). With reasonable MIC/MBC ranges, Moringa oleifera and Terminalia chebula also shown good efficacy against *S. aureus* (90 and 85%) and *E. coli* (100% and 90%). Despite requiring higher doses (64–128 µg/mL MIC), remedies such as Cassia fistula and Allium sativum showed substantial effectiveness against *K. Pneumoniae* and *S. aureus*. These results demonstrate these plants' potential as substitute antimicrobials (table 5).

Table 5: MIC and MBC Analysis of Herbal Extracts Against Common Pathogens

Herbal Remedy	**MIC (µg/mL)**	**MBC (µg/mL)**	**Effective Bacterial Strains (%)**
Moringa oleifera	32-64	64-128	*E. coli* (100%), *S. aureus* (90%)
Adhatoda vasica	16-32	32-64	*E. coli* (95%), *K. Pneumoniae* (85%)
Cassia fistula	64-128	128-256	*S. aureus* (88%), *K. Pneumoniae* (78%)
Terminalia chebula	32-64	64-128	*E. coli* (90%), *S. aureus* (85%)
Withania somnifera	16-32	32-64	*E. coli* (80%), *K. Pneumoniae* (75%)
Syzygium aromaticum	32-64	64-128	*E. coli* (85%), *S. aureus* (82%)
Allium sativum	64-128	128-256	*S. aureus* (87%), *K. Pneumoniae* (80%)
Curcuma longa	16-32	32-64	*E. coli* (90%), *S. aureus* (88%)
Aloe vera	64-128	128-256	*E. coli* (78%), *K. Pneumoniae* (85%)
Zingiber officinale	32-64	64-128	*E. coli* (83%), *S. aureus* (80%)

The efficiency of herbal treatments against bacterial strains was shown to vary significantly, with p-values consistently < 0.01 according to statistical analysis using chi-square and t-tests (table 6). With significant chi-square values (15.8 and 16.7, $p = 0.002$) and t-test values (3.5 and 3.9, $p = 0.006$ and 0.005, respectively) for *E. coli* (100% and 90% effective, respectively), Moringa oleifera and Curcuma longa showed the best effectiveness. With t-test values of 3.6 to 4.2 (p-values between 0.003 and 0.006) and chi-square values ranging from 12.7 to 16.3, Terminalia chebula and Syzygium aromaticum also shown high activity against *E. coli* and *S. aureus*. With chi-square values >10.2 and t-test values >2.8 ($p < 0.012$), remedies such as Adhatoda vasica and Allium sativum shown notable efficacy against *K. Pneumoniae* and *S. aureus*. The statistically significant antibacterial properties of various herbal medicines are shown by these p-values.

Table 6: Chi-square and t-tests Results Comparing the Effectiveness of Herbal Remedies Across Bacterial Strains

Herbal Remedy	**Bacterial Strain**	**Chi-square Value**	**p-value (Significance)**	**t-test Value**	**p-value (Significance)**	**Effective Strain (%)**
Moringa oleifera	E. coli	15.8	0.002	3.5	0.006	100%
	S. aureus	13.2	0.003	3.8	0.004	90%
Adhatoda vasica	E. coli	12.5	0.005	3.4	0.007	95%
	K. Pneumoniae	10.2	0.009	2.8	0.012	85%
Cassia fistula	*S. aureus*	14.8	0.001	4.0	0.003	88%
	K. Pneumoniae	13.0	0.004	3.9	0.005	78%
Terminalia chebula	E. coli	16.3	0.002	3.6	0.006	90%
	S. aureus	13.7	0.003	4.2	0.004	85%
Withania somnifera	E. coli	12.3	0.006	3.2	0.008	80%
	K. Pneumoniae	11.5	0.007	3.1	0.009	75%
Syzygium aromaticum	E. coli	13.5	0.004	3.7	0.005	85%
	S. aureus	12.7	0.005	3.6	0.006	82%
Allium sativum	*S. aureus*	15.2	0.001	4.5	0.002	87%
	K. Pneumoniae	14.0	0.003	4.0	0.004	80%
Curcuma longa	E. coli	16.7	0.002	3.9	0.005	90%
	S. aureus	13.5	0.004	4.1	0.003	88%
Aloe vera	E. coli	12.8	0.005	3.2	0.007	78%
	K. Pneumoniae	11.3	0.008	2.9	0.010	85%
Zingiber officinale	E. coli	14.3	0.003	3.8	0.004	83%
	S. aureus	13.1	0.005	3.6	0.006	80%

DISCUSSION

This research assessed the effectiveness of traditional herbal medicines against types of bacteria known to have significant levels of antibiotic resistance, notably E. coli, *S. aureus*, and *K. Pneumoniae*. With MIC values between 32 and 64 µg/mL and MBC values between 64 and 128 µg/mL against *E. coli* (100% effective) and *S. aureus* (90% effective), the findings showed that Moringa oleifera had the maximum antibacterial activity. These results are in line with earlier research that emphasizes Moringa oleifera's strong antibacterial qualities because of its abundance of bioactive substances, including flavonoids and alkaloids, which have been shown to prevent the development of bacteria and the production of biofilms [12].

With MIC values of 16–32 µg/mL and MBC values of 32–64 µg/mL against *E. coli* (95% effective) and *K. Pneumoniae* (85% effective), Adhatoda vasica also showed notable activity. This is similar to previous studies that found that Adhatoda vasica's alkaloids and phenolic compounds, which prevent bacterial development, make it an effective treatment for MDR bacteria, particularly *E. coli* and *K. Pneumoniae* [13]. The Cassia fistula findings showed moderate efficacy against *K. Pneumoniae* (78%) and *S. aureus* (88%) with MIC values of 64–128 μg/mL. This result is consistent with earlier research suggesting that the flavonoids and phenolic chemicals found in Cassia fistula, which target bacterial cell walls and membranes, are principally responsible for its antibacterial action [14].

With MIC values of 32–64 μg/mL and MBC values of 64–128 μg/mL against *E. coli* (90%) and *S. aureus* (85%), Terminalia chebula demonstrated strong antibacterial activity. Because of its polyphenolic content, which breaks down bacterial cell membranes and prevents the production of biofilms, Terminalia chebula has been shown to have strong antibacterial qualities [15]. Withania somnifera also demonstrated encouraging outcomes, exhibiting MIC values of 16–32 μg/mL and MBC values of 32–64 μg/mL against *K. Pneumoniae* (75%), and *E. coli* (80%). Because of its alkaloid and flavonoid content, which contribute to its antibacterial qualities, Withania somnifera has been shown in prior studies to be effective against *E. coli* and *K. Pneumoniae* [16].

The results for Syzygium aromaticum, which showed MIC values of 32–64 μg/mL and MBC values of 64–128 μg/mL for *E. coli* (85%) and *S. aureus* (82%), further demonstrated the effectiveness of herbal treatments against MDR bacteria. These findings are consistent with earlier research that shown the antibacterial qualities of Syzygium aromaticum are mostly ascribed to its phenolic components, flavonoids, and essential oils [17]. However, Allium sativum needed higher MIC values (64–128 μg/mL) for both *S. aureus* (87%) and *K. Pneumoniae* (80%), which is in line with earlier research showing that garlic's antibacterial properties stem from its sulfur- and allicin-containing components [18].

The promise of traditional herbal treatments in treating MDR bacterial infections is supported by these findings taken together, providing beneficial substitutes for standard antibiotics. The necessity for more research into the precise mechanisms of action and bioactive chemicals behind the reported antibacterial activity is highlighted by the differences in MIC and MBC values seen across various bacterial strains.

Study Strengths and Limitations

The study's merits include its thorough methodology, which includes evaluating many traditional herbal treatments with established antibacterial qualities and a wide variety of bacterial isolates from clinical specimens. Strong proof of the effectiveness of herbal treatments against MDR bacterial infections was given by the use of both MIC and MBC testing in conjunction with statistical analysis (chi-square and t-tests). Furthermore, the data' validity is increased by the incorporation of phytochemical screening and bioactive molecule identification. However, there are drawbacks, such as the dependence on a specific geographical location (Pakistan), which can restrict the findings' applicability to other areas with different patterns of bacterial resistance. Moreover, the cross-sectional design of the research may not adequately take into consideration long-term clinical results or any differences in the dose and techniques of herbal remedy manufacture. Finally, the research did not thoroughly examine the herbal components' mechanisms of action, which would have shed more light on their effectiveness.

CONCLUSION

This research demonstrates how traditional herbal treatments may effectively treat bacterial infections that are resistant to several drugs, providing viable substitutes for modern antibiotics. Remedies like Moringa oleifera, Curcuma longa, and Adhatoda vasica have shown strong antibacterial activity, which highlights their therapeutic value in treating resistant diseases including *K. Pneumoniae*, *S. aureus*, and E. coli. Even though these results are promising, further investigation is required to confirm their effectiveness in a range of clinical contexts and demographics. In order to include these herbal medicines into clinical practice and combat the rising issue of antibiotic resistance, it will be essential to comprehend the mechanisms of action and optimize dose forms.

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