JORDANIAN MEDICINAL PLANTS AS AN ALTERNATIVE SOURCE FOR NEW ANTIMICROBIALS AGAINST MULTI-DRUG RESISTANT: REVIEW

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ABSTRACT: Antibiotic resistance is one of the biggest threats to global health, food security, and development today. Medicinal plants have historically proven their value as a source of molecules with therapeutic potential. The interest in natural product-based drug discovery has revitalized in recent years because synthetic compound libraries and high throughput screening for discovery of new drug leads did not meet the expectations. The aim of this study is to systematically review the use of Jordanian medicinal plants then identify the most attractive plant for the discovery and development of drugs against resistance *Staphylococcus aureus* and *Pseudomonas aeruginosa* based on data collected from previous studies, that investigate the inhibitory effects of methanolic extracts of 8 Jordanian plants and their combinations with three antibiotics, on resistance of *Staphylococcus aureus* and *Pseudomonas aeruginosa* and studies that collected information from local population concerning the use of medicinal plants in Jordan. The results suggested that *Artemisia herba-alba* used in Jordan as traditional medicine has been reported to have a significant effect against the resistance of *Staphylococcus aureus* and *Pseudomonas aeruginosa* when combined with chloramphenicol, gentamycin, and cephalexin. *Artemisia herba-alba* that may help in the discovering of a new antibiotic.

INTRODUCTION: Infectious diseases have been an important cause of morbidity and mortality throughout our history. Primitive people have used plants to cure a variety of human ailments. Even today, many people use higher plants as effective for the treatment of various diseases [1]. Medicinal plants have a historically proven their value as a source of molecules with therapeutic potential, and nowadays still represent a role as a source of inspiration for novel drug compounds (leads) [2, 3].

However, since natural product-based drug discovery is associated with some intrinsic difficulties, the pharmaceutical industry has shifted its main focus toward synthetic compound libraries, and high throughput screening for discovery of new drug leads [4]. The obtained results, however, did not meet the expectations as evident in a declining number of delivering lead compounds in key therapeutic areas [4, 5] as a result of that the interest in natural product-based drug discovery has revitalized in recent years [6, 7].

Natural product research continues to explore a range of lead structures, which may be used as templates for the development of new drugs optimization and provide intermediates that are used in the production of semi-synthetic drugs [8].

Worldwide, hundreds of higher plants are cultivated for substances useful in medicine and pharmacy [9]. The importance of natural products in providing a source of new pharmaceutical compounds cannot be denied [7]. According to the World Health Organization, antibiotic resistance has become a critical global public health issue of this century [10]. Massive overuse of antibiotics drugs has been considering the main cause of resistance development against many antibiotics. So, this has created a serious clinical problem in the treatment of infectious diseases [11]. One of the most problematic drug-resistant pathogens encountered today include methicillin-resistant *Staphylococcus aureus* among the gram-positive bacteria and multidrug-resistant *P. aeruginosa* among the gram-negative bacteria [12].

Since, its discovery in 1880, *Staphylococcus aureus* has been recognized as a versatile micro-organism worldwide [13]. *S. aureus* may found on the face and hands as a part of the normal flora [14]. *S. aureus* is a leading cause of Hospital-Associated (HA) and Community-Associated (CA) bacterial infections in humans, associating with numerous mild skin and soft-tissue infections (SSTIs), as well as endovascular infections, endocarditis, osteomyelitis, septic arthritis, life-threatening pneumonia, bacteremia and toxic shock syndrome [15]. The rising expansion of Meticillin Resistant *S. aureus* (MRSA) and its ability to resist multiple drugs has posted an earnest threat for infection control [16].

In 1882, *P. aeruginosa* was successfully isolated in pure culture. *Pseudomonas aeruginosa* is an opportunistic pathogen associated with high morbidity and mortality rates worldwide [12]. *P. aeruginosa* causes urinary tract infections, Respiratory tract infections (*e.g.*, pneumonia), dermatitis, soft tissue infections, bloodstream (*e.g.* bacteremia), bone and joint infections(*e.g.*, osteomyelitis), gastrointestinal infections (*e.g.*, diarrhea, enteritis, enterocolitis), ear infections (*e.g.*, otitis externa and media) and a variety of systemic infections, mostly in patients with severe burns and in cancer and AIDS patients who are immunosuppressed [17]. Therefore, actions must be taken to reduce this problem, according to the World Health Organization medicinal plants would be the best source to obtain a variety of drugs [18]. About 80% of individuals from developed countries use herbal medicinal products as a primary source of healthcare and traditional medical practice, which has compounds derived from medicinal plants [19]. For that reason, using antibiotic resistance inhibitors from plant origin become one of the most successful methods to reduce the resistance to antibiotics. Jordan is a small country but has a great variety of wild plants due to the different geography and weather. About 2500 plant species (of which 2.5% species are listed as endemic) were recorded. The flora Jordan also contains medicinal and herbal species as well as aromatic and spice. Species from these plants, 485 species belonging to 99 different families are categorized as medicinal plants. These species have a broad distribution in the Jordan [20].

In the present work, we correlated 8 Jordanian plants, known to have some antimicrobial effect. Against *Staphylococcus aureus*, *Pseudomonas aeruginosa* for their possible inhibitory effect on resistance to three different antibiotics. Two strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. And then connected these results with collected information concerning the use of medicinal plants from 3 different locals in Jordan. This will help to make more focusing to find plants which could be played as templates for the development of new drugs against antibiotic resistance of *S. aureus* and *P. aeruginosa*.

Literature Review: The use of modern microbiological techniques demonstrates that higher plants frequently exhibit significant potency against human bacterial and fungal pathogens. As seen in [21] they studied the inhibitory effects of methanolic extracts of 19 Jordanian plants and their combinations with seven antibiotics, on the resistance of *Staphylococcus aureus*. Results showed that there are variations in the effect of some combinations used on the resistant and the standard strains probably due to structural changes.

Common results between the two strains showed that combinations of gentamicin and chloramphenicol could be improved by the use of plant materials, whereas nalidixic acid activity cannot be improved when combined with plant materials. Interest in plants as sources of medicines and of novel molecules [22] they studied the inhibitory effects of methanolic extracts of 19

Jordanian plants was combined with seven different antibiotics, on the resistance of *Pseudomonas aeruginosa*. Results showed that there are significant variations in the effects of some combinations used on the resistant and the standard strains probably due to structural changes. Almost all the plant materials used in combination with penicillin G and erythromycin allowed the full growth of the standard strain, while the combination with some plant materials like *Gundelia tournefortii* L. and *Lepidium satium* L. inhibited the growth of the resistant strain. Chloramphenicol, gentamicin, and cephalosporin can be given advantageously with almost all the plant materials used with few exceptions on the resistant strain. The nalidixic acid activity was improved significantly when combined with all plant materials and tested on the standard strain. On the other hand, its activity on the resistant strain was slightly improved using the same combinations.

According to the World Health Organization (WHO), about 4000 million people in developing countries believe in the efficiency of plant remedies and use them regularly [20] gathered information from aboriginal Bedouins in North Badia region of Jordan about used medicinal herbs besides their folk uses. The data were collected from 40 practitioners who utilized medicinal plants and who were regarded as professional. Subsequently, the uses were compared with the reported ones in the literature. The informant consensus factor (Fic) and use value (UV) has been calculated to those herbs and managed illnesses. The data of 73 species were collected; the vast majority of them are safe such as *Achillea falcata*, *Tamarix aphylla,* and *Teucrium polium*. Treatment of inflammation and pain presented the major targeted use of these herbs. Gastrointestinal and respiratory systems, as well as diabetes, depicted the largest Fic values. *Artemisia herba-alba* possessed the highest UV value among the studied herbs.

Medicinal plants are an important element of indigenous systems in Jordan. These resources are usually regarded as part of a culture's traditional knowledge [23]. The aim of the study to collect information from local population concerning the use of medicinal plants of the Mujib region; identify the most important medicinal plants used; determine the relative importance of the species surveyed and calculate the informant consensus factor (Fic) about medicinal plant use. Fifty-eight plants were identified to be still in use in traditional practice in Mujib. The results showed that the highest use values were recorded for the species *Artemisia sieberi* Bess. and *Silybum marianum* (L.) Gaertn. While the highest Fic was cited for digestive problems. Anthropologically.

The study of local knowledge about natural resources is becoming increasingly important in defining strategies and actions for the conservation of medicinal plants [24]. They collected information from local population concerning the use of Ajloun Heights region medicinal plants; identify the most important species used; determine the relative importance of the species surveyed and calculate the Informant Consensus Factor (ICF) about medicinal plant use. The results revealed that 46 plant species grown in the study region are still in use in traditional medicine for the treatment of various diseases.

Most of the locals interviewed dealt with well-known safe medicinal plants such as *Achillea falcata*, *Matricaria aurea*, *Majorana syriaca*, *Allium sativum,* and *Allium cepa*. The use of moderately unsafe or toxic plants was noted to be practiced by practitioners and herbalists rather than the locals. These plants include *Ecballium elaterium*, *E. hierosolymitana*, *M. autumnalis,* and *Citrullus colocynthis*. Kidney problems scored the highest ICF while *Crocus hyemalis* was the plant of the highest use value.

The development of new antibiotics from new chemical entities is becoming more and more expensive, time-consuming, and compounded by emerging strains that are drug resistant. Alkaloids are secondary plant metabolites which have been shown to have potent pharmacological activities [25]. They studied the effect of alkaloids from *Callistemon citrinus,* and *Vernonia adoensis* leaves on bacterial growth and efflux pump activity after evaluated on *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The results showed that Callistemon citrinus alkaloids showed antibacterial activity as well as inhibiting ATP-dependent transport of compounds across the cell membrane. These alkaloids may serve as potential courses of

compounds that can act as lead compounds for the development of plant-based antibacterials and their adjunct compounds.

Achillea santolina usually used as antidiabetic, anti-inflammatory and to reduce pain or dryness of the navel and stomach pain [26]. The concentration of the important oil in the dry *Achillea santolina* ranged from 0.11-0.20 % in ten genotypes of this species. It contained 54 volatile components. The main components were fragranyl acetate, terpin-4-ol, and1, 8-cineole, fragranol. *Achillea santolina* also contained flavones, particularly flavonoids and sesquiterpene lactones [27].

Artemisia herba-alba Asso commonly known as the desert wormwood (Arabic name: Sheeh) growing widely in Jordan and in the Middle East [23, 24]. Also, it found in different periods, July (flowering phase), and October and November (vegetative phase) [28]. The essential oils yield ranged between 0.2% and 0.9% (v/d.w.). The main components were camphor, 1,8-cineole, borneol, pinocarvone, camphene, and chrysanthenone [29]. It is used to treat inflammatory disorders (colds, coughing, bronchitis, and diarrhoea), infectious diseases (skin diseases, scabies and syphilis) and others (diabetes, neuralgias). In Jordanian traditional medicine, this plant is used as antiseptic and against skin diseases, scabies, syphilis, fever as well as menstrual and nervous disorders [30].

Cappari spinosa which was commonly used as a medicinal plant contained many biologically active chemical groups including, alkaloids, glycosides, tannins, phenolic, flavonoids, triterpenoids steroids, carbohydrates, saponins and a wide variety of minerals and trace elements. It exerted many pharmacological effects significant as anti-diabetic, antisclerosis, antimicrobial, anti-oxidative, anti-inflammatory, immunomodulatory and antiviral activities providing support to the ancient uses [31, 32].

Hibiscus sabdariffa L. has been used commonly as a food, in herbal drinks, in hot and cold beverages, as a flavoring agent in the food industry and as a herbal medicine [33]. Showed many pharmacological effects significant as antibacterial, anti-oxidant, nephron- and hepato-protective, renal/diuretic effect, effects on lipid metabolism (anti-cholesterol), anti-diabetic and anti-hypertensive

effects among others. This might be linked to strong antioxidant activities. The main constituents of *Hibiscus sabdariffa* Linn. relevant in the context of its pharmacological are organic acids, anthocyanins, polysaccharides and flavonoids [34].

Lepidium sativum L. belongs to family Cruciferae (cabbage family) [35]. The plant is known to contain imidazole, lepidine, semilepidinoside A and B, β-carotenes, ascorbic acid, linoleic acid, oleic acid, palmitic acid, stearic acid [14], sinapic acid and sinapin [36]. *Lepidium sativum* Linn. is widely used in folk medicine for the treatment of hyperactive airways disorders, such as asthma, bronchitis, and cough. Seeds are considered to be a galactagogue, emmenagogue and recommended in inflammation, bronchitis, muscular pain and rheumatism [37].

Teucrium polium L. (family Lamiaceae) is a wild-growing flowering plant, found abundantly in South-Western Asia, Europe and North Africa [38]. Traditionally, *Teucrium polium* L. has been used for different pathological conditions such as gastrointestinal disorders, inflammations, diabetes, rheumatism, abdominal pain, indigestion, common cold and Type 2 diabetes [39, 40, 41]. It contained different classes of compounds such as neoclero-dane diterpenoids, the chemotaxonomic markers of the genus, monoterpenes, sesquiterpenes, polyphenols, flavonoids, and fatty acid esters. Up to now, more than 134 active substances with wide structural and chemical diversities have been isolated and characterized from the aerial parts, roots, and seeds of *T. polium* L. subspecies [39, 41].

Fenugreek (*Trigonella foenum-graecum*) is traditional medicinal plant extracts have been evaluated for their potential application in the medicinal purposes. Fenugreek has been used in food as a flavoring agent while ancient times [42]. Fenugreek seed is a good source of calcium, minerals, iron, β-carotene and several vitamins like vitamins A and D. It is a rich source of available carbohydrates and dietary fiber [43]. It is a source of free amino acids; 4-hydroxyisoleucine, histidine, arginine and lysine (25.8%), moisture (11.76%), crude fibre (6.28%), ash content (3.26%) protein (20-30%), fat (6.53%), and energy (394.46 Kcal/100 g seed) [44]. It contains lecithin, choline, minerals, B. complex, phosphates and Para-Amino Benzoic acid (PABA). Also, the main chemical

compounds in fenugreek are saponins, fenugreek in, trigonelline, coumarin, scopoletin, phytic acid and nicotinic acid [42]. *Varthemia iphionoides* Boiss and Blanche are commonly used as a Jordanian folk-medicine for the treatment of gastrointestinal disorders and diabetes mellitus good source of active phytochemical compound Eudesmane sesquiterpene, flavonoids: jaceidine, kumatakenine, xanthomicrol, seven 3-methoxy flavones [45, 46].

METHODOLOGY: English language articles from January 2001 through March 2011 were searched in the electronic databases Pubmed and Science Direct. The Cochrane Library was searched using the following terms as keywords: (Bacterial resistance inhibitors, Methicillin-resistant *Staphylococcus aureus*, *S. aureus*, *Pseudomonas aeruginosa*, plant extracts; antibiotics, ethnopharmacology. Traditional medicine, Medicinal plants, Informant Consensus Factor, Use value, Jordan, Ajloun, Mujib, Northern Badia and Folkloric medicine). No further restrictions were imposed on either search. All articles selected were read to determine whether they met inclusion criteria.

Work Procedures: This study based on two studies concerned about bacterial resistance inhibitors, Methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, plant extracts; antibiotics, ethnopharmacology in Jordan, traditional medicine and medicinal plants [20-24].
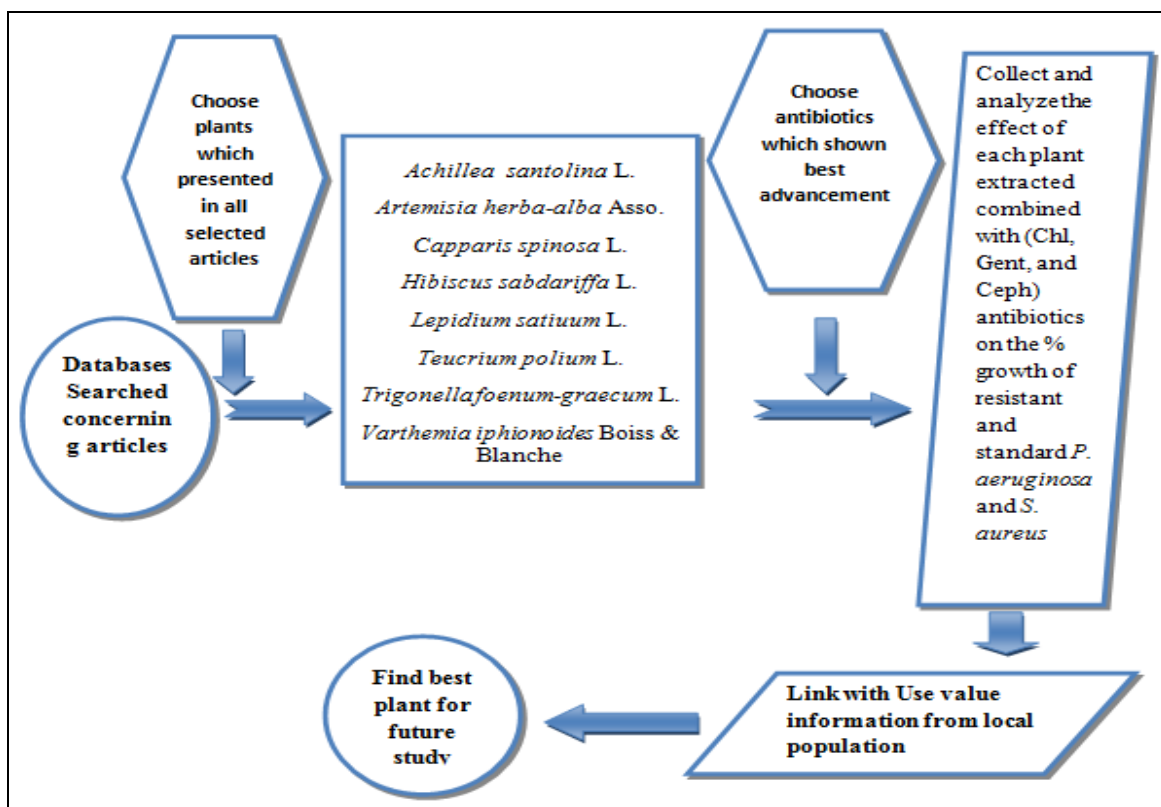
SCHEME 1: WORK PROCEDURES

Chl, chloramphenicol; Gent, gentamycin; Ceph, cephalexin, P, *Pseudomonas*; S. *Staphylococcus*

Study Hypotheses: In light of the study objectives and models, we derive the following study hypotheses:

H0: the population means are equal: μ1 = μ 2 = μ 3= μ 4 there are no significant differences between % growth of resistant and standard *Pseudomonas aeruginosa* and *Staphylococcus*. H1: the population means are not equal: μ1 ≠ μ 2 ≠ μ 3≠μ 4 there are significant differences between % growth of resistant and standard *Pseudomonas aeruginosa* and *Staphylococcus*.

Statistical Analysis: Our primary statistical analysis investigated the relationship between plant type and the growth of resistant and standard *Pseudomonas aeruginosa* and *Staphylococcus aureus*. We employed a modified intent-to-treat approach whereby, we used the most inclusive sample analyzed in the original publication of each

of the two studies **Table 2**. To investigate the association between plant type and the growth we conducted compared mean (one way ANOVA) that controlled the effect of the study from which the data originated.

RESULTS: By using descriptive analysis, it was determined that the mean of % growth of resistant and standard *Pseudomonas aeruginosa* and *Staphylococcus aureus* as shown in **Table 1**.

TABLE 1: DESCRIPTIVE STATISTICS

	N	Minimum	Maximum	Mean	Std. Deviation
Achillea santolina L.	12	.0	73.9	23.142	32.0361
Artemisia herba-alba Asso.	12	.0	146.5	30.329	46.5894
Capparis spinosa L.	12	.0	121.2	30.075	43.3282
Hibiscus sabdariffa L.	12	.5	95.4	33.267	41.3360
Lepidium satiuum L.	12	.5	95.6	24.933	36.0594
Teucrium polium L.	12	.0	91.3	26.983	37.1719
Trigonella foenum-graecum L.	12	.0	104.0	26.008	41.4546
Varthemia iphionoides Boiss & Blanche	12	.0	86.1	20.350	31.4422
Valid N (list-wise)	12				

TABLE 2: ONE-WAY ANOVA

Plant	1	2	3	4	5	6	7	8
F	8.889	1.624	3.045	5.208	19.463	24.243	114.337	43.093
Sig.	0.006	0.259	0.092	0.028	0	0	0	0

1. *Achillea santolina* L, 2. *Artemisia herba-alba* Asso. 3. *Capparis spinosa* L. 4. *Hibiscus sabdariffa* L. 5. *Lepidium satiuum* L. 6. *Teucrium polium* L.7. *Trigonella foenum-graecum* L8. *Varthemia iphionoides* Boiss & Blanche

**TABLE 3A: MULTIPLE COMPARISONS SCHEFFE OF *ARTEMISIA HERBA-ALBA* ASSO**

Bacterial strain type	Bacterial strain type	Sig.	95% Confidence Interval	
			Lower Bound	Upper Bound
Resistant *Pseudomonas aeruginosa*	Stander *Pseudomonas aeruginosa*	.394	-58.168	187.468
	Resistant *Staphylococcus aureus*	.974	-106.651	138.985
	Stander *Staphylococcus aureus*	.472	-64.285	181.351
Stander *Pseudomonas aeruginosa*	Resistant *Pseudomonas aeruginosa*	.394	-187.468	58.168
	Resistant *Staphylococcus aureus*	.614	-171.301	74.335
	Stander *Staphylococcus aureus*	.998	-128.935	116.701
Resistant *Staphylococcus aureus*	Resistant *Pseudomonas aeruginosa*	.974	-138.985	106.651
	Stander *Pseudomonas aeruginosa*	.614	-74.335	171.301
	Stander *Staphylococcus aureus*	.703	-80.451	165.185
Stander *Staphylococcus aureus*	Resistant *Pseudomonas aeruginosa*	.472	-181.351	64.285
	Stander *Pseudomonas aeruginosa*	.998	-116.701	128.935
	Resistant *Staphylococcus aureus*	.703	-165.185	80.451

*. The mean difference is significant at the 0.05 level.

TABLE 3B: MULTIPLE COMPARISONS SCHEFFE OF *CAPPARIS SPINOSA* L.

Bacterial strain type	Bacterial strain type	Sig.	95% Confidence Interval	
			Lower Bound	Upper Bound
Resistant *Pseudomonas aeruginosa*	Stander *Pseudomonas aeruginosa*	.156	-24.766	173.233
	Resistant *Staphylococcus aureus*	.720	-65.800	132.200
	Stander *Staphylococcus aureus*	.184	-28.466	169.533
Stander *Pseudomonas aeruginosa*	Resistant *Pseudomonas aeruginosa*	.156	-173.233	24.766
	Resistant *Staphylococcus aureus*	.579	-140.033	57.966
	Stander *Staphylococcus aureus*	.999	-102.700	95.300
Resistant *Staphylococcus aureus*	Resistant *Pseudomonas aeruginosa*	.720	-132.200	65.800
	Stander *Pseudomonas aeruginosa*	.579	-57.966	140.033
	Stander *Staphylococcus aureus*	.645	-61.666	136.333
Stander *Staphylococcus aureus*	Resistant *Pseudomonas aeruginosa*	.184	-169.533	28.466
	Stander *Pseudomonas aeruginosa*	.999	-95.300	102.700
	Resistant *Staphylococcus aureus*	.645	-136.333	61.666

*. The mean difference is significant at the 0.05 level.
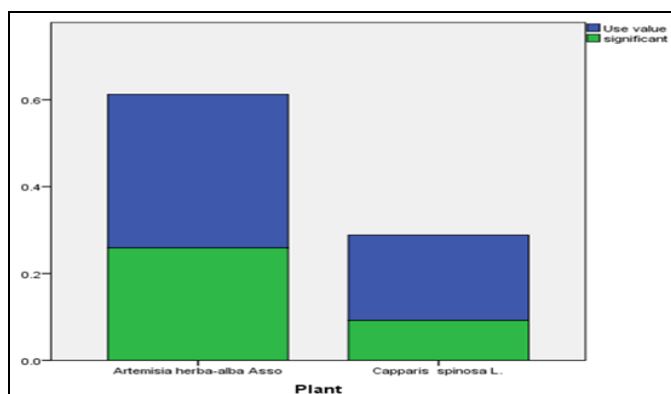
FIG. 1: SHOWN USE VALUE AND ONE-WAY ANOVA SIG. VALUE

DISCUSSION: The results confirm that plant extracted when combined with chloramphenicol, gentamycin and cephalexin antibiotics affect on the % growth of resistant and standard *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The results of *Achillea santolina* L. and *Varthemia iphionoides* Boiss & Blanche., *Hibiscus sabdariffa* L., *Lepidium satiuum* L., *Teucrium polium* L., *Trigonella foenum-graecum* L., shown in **Table 2** showed there was a statistically significant difference in % growth of resistant and standard of *Pseudomonas aeruginosa* and *Staphylococcus aureus* as determined by one-way ANOVA with F(8.889, 5.208, 19.463, 24.243, 114.337 and 43.093) with p-value of (0.006, 0.028, 0.0, 0.0 and 0.0) respectively. Based on these results we rejected the null hypothesis for *Achillea santolina* L. and *Varthemia iphionoides* Boiss & Blanche., *Hibiscus sabdariffa* L., *Lepidium satiuum* L., *Teucrium polium* L., *T. foenum-graecum* L.

On the other hand, results of *Artemisia herba-alba* Asso. and *Capparis spinosa* L. Shown in **Table 2** indicated that statistically no significant difference in % growth of resistant and standard of *Pseudomonas aeruginosa* and *Staphylococcus aureus* as determined by one-way ANOVA with (F (1.624 and 3.045) with p value of (0.259 and 0.092) respectively. Based on these results we accept the null hypothesis for *Artemisia herba-alba* Asso. and *Capparis spinosa*.

Multiple Comparisons of *Artemisia herba-alba* Asso. and *Capparis spinosa* L. Shown in **Table 3** of Resistant *Pseudomonas aeruginosa* versus Stander *Pseudomonas aeruginosa*, versus Resistant *Staphylococcus aureus* and Stander *Staphylococcus aureus* comparison, the significance level was more

than p 0.05 among them, thus; The results of each group are not significantly different, and all results showed homogeneity with F-test ratio (1.624 and 3.045) for *Artemisia herba-alba* Asso. and *Capparis spinosa* L. respectively, which is not sufficiently large. As a result, we conclude that all means are statistically equal.

The study found that extracts of *Artemisia herba-alba* affect against *Staphylococcus aureus* and *Pseudomonas aeruginosa* which are matching the findings of [47]. The chloroform extracted of *Artemisia herba-alba* has antibacterial activity against *P. aeruginosa* and *Staphylococcus aureus*. Furthermore, [48] studied ethanol and chloroform extracted from different parts of *Capparis spinosa* (flowers, fruits, leaves, and roots) and founded that *Capparis spinosa* L. roots showed good inhibitory effects against tested *Pseudomonas aeruginosa* and *Staphylococcus aureus* compared with standard antibiotics.

We linked previous studies finds with studies that screened *Artemisia herba-alba* and *Capparis spinosa* as traditional medicine used in Jordan (Ajloun, Mujib and Northern Badia). *Artemisia herba-alba* showed higher UV value at (Ajloun, Mujib and Northern Badia) with 0.2, 0.54 and 0.32 respectively, with a mean of 0.355. While, *Capparis spinosa* showed lesser UV value at (Ajloun, Mujib and Northern Badia) with 0.06, 0.23, 0.3 respectively, with a mean of 0.196. As use-value (UV), is a quantitative method that demonstrates the relative importance of species known locally the *Artemisia herba-alba* have higher UV value than *Capparis spinosa*.

Ancient civilizations have used plants to cure a variety of human ailments. Even today, many people use higher plants as effective for the treatment of various diseases, Medicinal plants have proven, historically, their value as a source of molecules with therapeutic potential, and nowadays still represent a role as a source of inspiration for novel drug compounds (leads) [49]. For that reason, using antimicrobial resistance inhibitors from plant origin like *Artemisia herba-alba* could become one of the most successful methods to reduce the resistance to antimicrobials. *Artemisia herba-alba* will be the best choice for future studies of discovery and development for drugs against

resistance *S. aureus* and *Pseudomonas aeruginosa*. Because of its popularity in Jordan (From different locations) in comparison with *Capparis spinosa* and its effectiveness against *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

CONCLUSION: The 21st-century witnesses a major global health care problem which threatens the entire human life as the appearance and prevalence of multi-drug resistant microorganisms. We must understand that the battle against these microorganisms never ends, but we can beat them by changing our strategy by returning to nature, using active ingredients from plants that survived against microbes since millions of years. The results of *Artemisia herba-alba* used in traditional medicine had been reported to have a significant effect against the resistance of *S. aureus* and *Pseudomonas aeruginosa* when combined with chloramphenicol, gentamycin, and cephalexin. Besides, it has good use-value which demonstrates the relative importance of species known in Jordan. Serious interests should be by focusing on extracting drugs from *Artemisia herba-alba*. Hopefully, the area of antimicrobial research based on the medicinal plant might be proving fruitfully.

CONFLICT OF INTEREST: Nil

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