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ANTIBACTERIAL ACTIVITY OF PLANT EXTRACTS AND PHYTOCHEMICALS ON ANTIBIOTIC-RESISTANT BACTERIA

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ABSTRACT

The antimicrobial activity of plant extracts and phytochemicals was evaluated with antibiotic susceptible and resistant microorganisms. In addition, the possible synergistic effects when associated with antibiotics were studied. Extracts from the following plants were utilized: *Achillea millifolium* (yarrow), *Caryophyllus aromaticus* (clove), *Melissa offficinalis* (lemon-balm), *Ocimun basilucum* (basil), *Psidium guajava* (guava), *Punica granatum* (pomegranate), *Rosmarinus officinalis* (rosemary), *Salvia officinalis* (sage), *Syzygyum joabolanum* (jambolan) and *Thymus vulgaris* (thyme). The phytochemicals benzoic acid, cinnamic acid, eugenol and farnesol were also utilized. The highest antimicrobial potentials were observed for the extracts of *Caryophyllus aromaticus* and *Syzygyum joabolanum*, which inhibited 64.2 and 57.1% of the tested microorganisms, respectively, with higher activity against antibiotic-resistant bacteria (83.3%). Sage and yarrow extracts did not present any antimicrobial activity. Association of antibiotics and plant extracts showed synergistic antibacterial activity against antibiotic-resistant bacteria. The results obtained with *Pseudomonas aeruginosa* was particularly interesting, since it was inhibited by clove, jambolan, pomegranate and thyme extracts. This inhibition was observed with the individual extracts and when they were used in lower concentrations with ineffective antibiotics.

Key words: plant extracts activity; medicinal plants; antimicrobial activity

INTRODUCTION

Even though pharmacological industries have produced a number of new antibiotics in the last three decades, resistance to these drugs by microorganisms has increased. In general, bacteria have the genetic ability to transmit and acquire resistance to drugs, which are utilized as therapeutic agents (12). Such a fact is cause for concern, because of the number of patients in hospitals who have suppressed immunity, and due to new bacterial strains, which are multi-resistant. Consequently, new infections can occur in hospitals resulting in high mortality.

From 1980 to 1990, Montelli and Levy (27) documented a high incidence of resistant microorganisms in clinical microbiology in Brazil. This fact has also been verified in other clinics around all over world.

The problem of microbial resistance is growing and the outlook for the use of antimicrobial drugs in the future is still uncertain. Therefore, actions must be taken to reduce this problem, for example, to control the use of antibiotic, develop research to better understand the genetic mechanisms of resistance, and to continue studies to develop new drugs, either synthetic or natural. The ultimate goal is to offer appropriate and efficient antimicrobial drugs to the patient.

For a long period of time, plants have been a valuable source of natural products for maintaining human health, especially in the last decade, with more intensive studies for natural therapies. The use of plant compounds for pharmaceutical purposes has gradually increased in Brazil. According to World Health Organization (31) medicinal plants would be the best source to obtain a variety of drugs. About 80% of individuals from

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developed countries use traditional medicine, which has compounds derived from medicinal plants. Therefore, such plants should be investigated to better understand their properties, safety and efficiency (14).

The use of plant extracts and phytochemicals, both with known antimicrobial properties, can be of great significance in therapeutic treatments. In the last few years, a number of studies have been conducted in different countries to prove such efficiency (1,5,18,19,22,35,36)**.** Many plants have been used because of their antimicrobial traits, which are due to compounds synthesized in the secondary metabolism of the plant. These products are known by their active substances, for example, the phenolic compounds which are part of the essential oils (20), as well as in tannin (33).

The antimicrobial properties of plants have been investigated by a number of researchers world wide, especially in Latin America. In Argentina, a research tested 122 known plant species used for therapeutic treatments (4). It was documented that among the compounds extracted from these plants, twelve inhibited the growth of *Staphylococus aureus*, ten inhibited *Escherichia coli*, and four inhibited *Aspergillus niger* and also reported that the most potent compound was one extracted from *Tabebuia impetiginosa*. The antimicrobial properties of compounds obtained from *Parthenum argentatum* against *Candida albicans, Torulopsis, Hansemula, Klebsiella pneumoniae* and *Pseudomonas aeruginosa* was detected (24,25). Work done was observed that the substances extracted from nine known plants in Uruguai did not show any activity against *C. albicans* and *Saccharomyces cerevisiae*, but inhibited the growth of *Bacillus subtilis, E. coli* and *P. aeruginosa* (3).

Many studies have been conducted in Brazil. The inhibitory activity of *Vatairea macrocarpa* on *Klebsiella spp*. and *S. aureus* was observed (26) and the inhibitory activity of extracts from *Eucaliptus spp*. against soil fungi (9). A more detailed study on antimicrobial compounds was done evaluating extracts from 120 plant species from 28 different families (32). It was documented that 81 extracts obtanained from 58 plants were active against *S. aureus*, and five extracts from four other plants inhibited the growth of *P. aeruginosa*. Another study (23) detected the antibacterial and antifungal (*C. albicans*) activity of essential oils obtained from *Croton triangularis* leaves. Extracts from *Lippia gracilis* and *Xylopia sericea* showed antifungal activity. The investigation of antimicrobial activity as well as cell toxicity of extracts from 30 plant species against five bacteria species and two fungi species was studied (29). It was concluded that ethanol extracts from 70 % of the plants were toxic to cell and only one of the species of *Combretum duarteanum* showed antimicrobial activity. The toxicity of extracts from *Arthemus sativa*, which is known to have antimicrobial activity, was also studied (10). The antimicrobial activity from *Mikania triangularis*, known as “thin leaf guaco”, was tested against five genera of bacteria and three genera of yeast, and showed it had activity against *Bacillus cereus, E. coli, P. aeruginosa, S. aureus* and *S. epidermidis* (13).

Effects of phytochemical were conducted (19, 20) and it was observed the antimicrobial activity of anacardic acid on *S. aureus, Brevibacterium ammoniagenes, Streptococcus mutans* and *Propionibacterium acnes*. Later, it was tested the bactericidal activity of anacardic acid and totarol on methicillin resistant strains of *S. aureus* (MRSA) and the synergistic effect of these compounds associated with methicillin (28).

Hence, more studies pertaining to the use of plants as therapeutic agents should be emphasized, especially those related to the control of antibiotic resistant microbes. The objective of this research was to evaluate the potential of plant extracts and phytochemicals on standard microorganism strains as well as multi-drug resistant bacteria, which were isolated from hospitals. Moreover, we investigated the synergistic effects of extracts with antimicrobial activity in association with antibiotics against drugs resistant bacteria.

MATERIALS AND METHODS

Microbial samples

Fourteen microbial species were analyzed. The bacteria (numbered from 1 to 3) were taken from international collections and are sensitive to the antibiotics listed below. The yeast sample (number 5) and the bacteria (numbers 4 to 14) were isolated from local hospitals for previous studies. 1- *Staphylococcus aureus* ATCC 6538; 2- *Salmonella choleraesuis* ATCC 10708; 3- *Pseudomonas aeruginosa* ATCC 15442; 4- *Bacillus subtilis;* 5- *Candida albicans;* 6- *Proteus* spp.; 7- *Klebsiella pneumoniae* - resistant to AP; 8- *K. pneumoniae* - resistant to AM, AN, AP, CF, CFO, CFR, CO, CR, CTX, NET, NOR, PP, TB and TT; 9- *Shigella* spp. - resistant to AP, CR, CF, CFO, CRO; 10-*Proteus* spp. - resistant to AN, AM, AP, CF, CFO, CO, CR, CRO, CTX, GN, KN, NET, NOR, PP, SFT, TB, TT; 11-*Pseudomonas aeruginosa* - resistant to AN, AM, AP, CF, CFO, CFR, CO, CR, CRO, CTX, GN, KN, NET, NOR, PP, SFT, TB, TT; 12- *Enterobacter aerogenes* - resistant to AN, AM, AP, CF, CFO, CO, CR, CRO, CTX, GN, KN, NET, NOR, PP, SFT, TB, TT; 13- *Escherichia coli* - resistant to AM, AP, CF, CFR, CO, CR, GN, NET, PP, SFT, TB, TT; 14- *Staphylococcus aureus* - resistant to AM, CF, CFO, CFR, CO, EI, GN, KN, MET, NOR, SF, TT.

[AM - Amikacin; AP - Ampicillin; CF - Cephalothin CFR - Cefpirome CR - Carbenicillin; CFO - Cefoxitin, CO - Chloramphenicol; CRO - Ceftraxone, CTX - Cefotaxime; EI - Erytromycin, GN - Gentamicin; KN - Kanamycin; LN - Lincomycin, MET - Methicillin; NA - Nalidixic Acid, NET - Netilmicin, NOR - Norfloxacin, NT - Nitrofurantoin, PN - Penicillin, PP - Piperacillin; RF - Rifampicin, SF - Sulfonamide, SFT - Sulfamethoxazole, TB - Tobramycin, TT - Tetracycline; VC - Vancomycin].

Culture media, antibiotics and phytochemical solutions

Brain Heart Infusion (as liquid and solid media) and Mueller-Hinton agar were used. The following antibiotic solutions were prepared prior incorporation into the liquid medium: Chloramphenicol (Carlo Erba) (500 µg/mL); Ampicillin (Honorterápica) (500 µg/mL), and Tetracycline (Bristol) (500 µg/mL). The phytochemical solutions used were: Benzoic Acid (Sigma) dissolved in water, Cinnamic Acid (Fluka), Eugenol (Sigma), and Farnesol (Dragoco) dissolved in ethanol at 10% concentration.

Plant extracts

The methodologies of Harbone (17) and Wagner *et al*. (37) were used to process the ethanolic extracts (1:1) from the ten plants of interest. Seven of them (basil, clove, lemon balm, rosemary, sage, thyme and yarrow) had essential oils as the main active ingredient, while the other three (guava, jambolan and pomegranate) had high contents of tannin. With the exception of clove, all of the plants with essential oils were cultivated from seeds in the Greenhouse of Medicinal Plants at the Methodist University of Piracicaba, SP, Brazil. The seeds were acquired at Semex, SP, Brazil. Clove was obtained from medicinal plants market of São Paulo city. The selected plants with tannins were obtained in the Horticulture Department at the University of Agriculture "Luiz de Queiroz"/USP, Piracicaba, SP, Brazil.

The following lists the plant of interest, plant parts used for extractions, and compounds obtained.

- Thyme (*Thymus vulgaris* L., Lamiaceae) - [stripped and dried leaves and flowers]. Chemical constituents: essential oils (mainly thymol and carvacrol), flavonoids, tannins and triterpenes (8).
- Rosemary (*Rosmarinus officinalis* L., Lamiaceae) - [leaf]. Chemical constituents: flavonoids, phenolic acids (caffeic, chorogenic and rosmarinic) and essencial oils (camphor and cineole) and diterpenes (carnosol) (30)
- Lemon balm (*Melissa officinalis* L., Lamiaceae) - [leaf]. Chemical constituents: essencial oils (containing citral and citronellal monoterpenes), flavonoids and rosmarinic, caffeic and chlorogenic acids (8).
- Sage (*Salvia officinalis* L., Lamiaceae) - [leaf]. Chemical constituents: rosmarinic, caffeic, chlorogenic acids; carnosol, flavonoids, essential oils (mainly thuyone and cineole). (30).
- Basil (*Ocimum basilicum* L., Lamiaceae) - [leaf]. Chemical constituents: essential oils (linalol, estragol and eugenol); tannins and flavonoids (8).
- Yarrow (*Achillea millefolium* L.,Asteraceae) - [flower-heads]. Chemical constituents: flavonoids, tannins, comarins, proazulene. (8,11).
- Clove (*Syzygium aromaticum* (L.) Merr. et Perry = *Caryophyllus aromaticus* L.) - [dried buds]. Chemical constituents: essential oils (eugenol); taninns and flavonoids (8,15).
- Pomegranate (*Punica granatum* L., Punicaceae) - **[**pericarp**].** Chemical constituents: ellagitannins and alkaloids. (36).
- Jambolan (*Syzygium cumini*, Skeels, Myrtaceae) - [leaf]. Chemical constituents: flavonoids and tannins (7).
- Guava (*Psidium guajava* L., Myrtaceae) - [leaf]. Chemical constituents: comarins, essencial oils, flavonoids, triterpenes and ellagitannins. (16).

Screening for the antimicrobial potential of the plant extracts and phytochemicals (6)

The bacteria cultures were grown in Brain Heart Infusion liquid medium at 37 °C. After 6 h of growth, each microorganism, at a concentration of 10^6 cells/mL, was inoculated on the surface of Mueller-Hinton agar plates. Subsequently, filter paper discs (6 mm in diameter) saturated either with extract or phytochemicals (50 µL) were placed on surface of each inoculated plate. To evaluate the efficiency of the methodology, each extract was inserted simultaneously in a hole made (50 µL) in new plates. The plates were incubated at 37 °C for 24 h. After this period, it was possible to observe inhibition zone. Overall, cultured bacteria with halos equal to or greater than 7 mm were considered susceptible to either the tested extract or phytochemical. DMSO and Tween 80 to 2% were used to dissolve the extracts in the culture media when necessary. The controls were the solvents used for each extract and the phytochemicals and they showed no inhibitions in preliminary studies.

The extracts and the phytochemicals that showed antimicrobial activity were later tested to determine the Minimal Inhibitory Concentration (MIC) for each bacterial sample. Seven bacterial samples [*P. aeruginosa* (11), *K. pnemoniae* (7, 8), *Shigella* (9), *Proteus* (10), *S. aureus* (14) and *E. aerogenes* (12)] were grown in nutrient broth for 6 h. After, 100 µL of 10^6 cells/mL was inoculated in tubes with nutrient broth supplemented with different concentrations (10 - 500 µL) of the extracts and phytochemicals, respectively. Afterwards 24 h at 37 °C, the MIC of each sample was determined by measuring the optical density in the spectrophotometer (620 nm), comparing the sample readout with the was non inoculated nutrient broth.

Evaluation of the synergistic effect of antibiotics and plant extracts or phytochemicals on resistant bacterial samples

This evaluation was done according to Muroi and Kubo (28). Aliquots of 100 µL of resistant bacterial cultures (10^6 cells/mL) grown in 10 mL of nutrient broth for 6 h were inoculated in nutrient broth supplemented with the respective antibiotics (50 µg/mL) with different concentrations of plant extracts. The concentration for plant extracts/phytochemicals ranged from

10 to 500 µg/mL, based on MIC values, that had previously been evaluated. Only ampicillin and/or chloramphenicol and/or tetracycline were used at the sub-inhibitory concentration (50 µg/mL). The growth conditions were the same as previously mentioned. After 48 h, the optical density of each sample was documented and compared to those of MIC to verify any synergistic effect among the tested compounds.

RESULTS AND DISCUSSION

Evaluation of the antimicrobial potential of plant extracts and phytochemicals

The data pertaining to the antimicrobial potential of the plant extracts and phytochemicals are presented in Tables 1 and 2, and Figs. 1 and 2, respectively.

Table 1. Antimicrobial activity caused by plant extracts (hydro-alcoholic fraction) through agar diffusion method.

microorg.	thyme	rosemary	clove	jambolan	lemonbalm	pomegranate	guava	sage	basil	yarrow
1	-	-	+	+	+	-	+	-	-	-
2	-	-	+	-	+	-	-	-	-	-
3	+	-	+	-	-	+	-	-	+	-
4	-	+	-	-	-	+	-	-	-	-
5	+	+	+	+	-	-	+	-	-	-
6	+	-	-	+	-	-	-	-	-	-
7	-	-	+	+	+	-	-	-	-	-
8	-	-	+	-	-	-	-	-	-	-
9	-	-	+	-	-	-	-	-	-	-
10	-	-	+	+	-	-	-	-	-	-
11	+	-	+	+	-	-	-	-	-	-
12	-	-	-	+	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-	-
14	-	-	-	+	-	-	-	-	-	-

(+) susceptibility (inhibition zone ≥ 7 mm)
(-) absence of susceptibility

(1) *Staphylococcus aureus,* (2) *Salmonella choleraesuis,* (3) *Pseudomonas aeruginosa,* (4) *Bacillus subtilis,* (5) *Candida albicans,* (6) *Proteus* spp, (7) *Klebsiella pneumoniae,* (8) *K. pneumoniae*, (9) *Shigella* spp, (10) *Proteus* spp, (11) *P. aeruginosa,* (12) *Enterobacter aerogenes,* (13) *Escherichia coli,* (14) *S. aureus*.

Table 2. Antimicrobial activity caused by phytochemicals through agar diffusion method.

Microorg.	eugenol	farnesol	benzoic acid	cinnamic acid
1	+	-	-	+
2	+	-	-	-
3	-	-	-	-
4	+	-	-	-
5	+	-	-	+
6	-	-	-	-
7	-	-	-	-
8	-	-	+	-
9	-	-	-	-
10	-	-	-	-
11	-	-	-	-
12	-	-	-	+
13	-	-	+	+
14	-	-	-	+

(+) susceptibility (inhibition zone ≥ 7 mm)
(-) absence of susceptibility

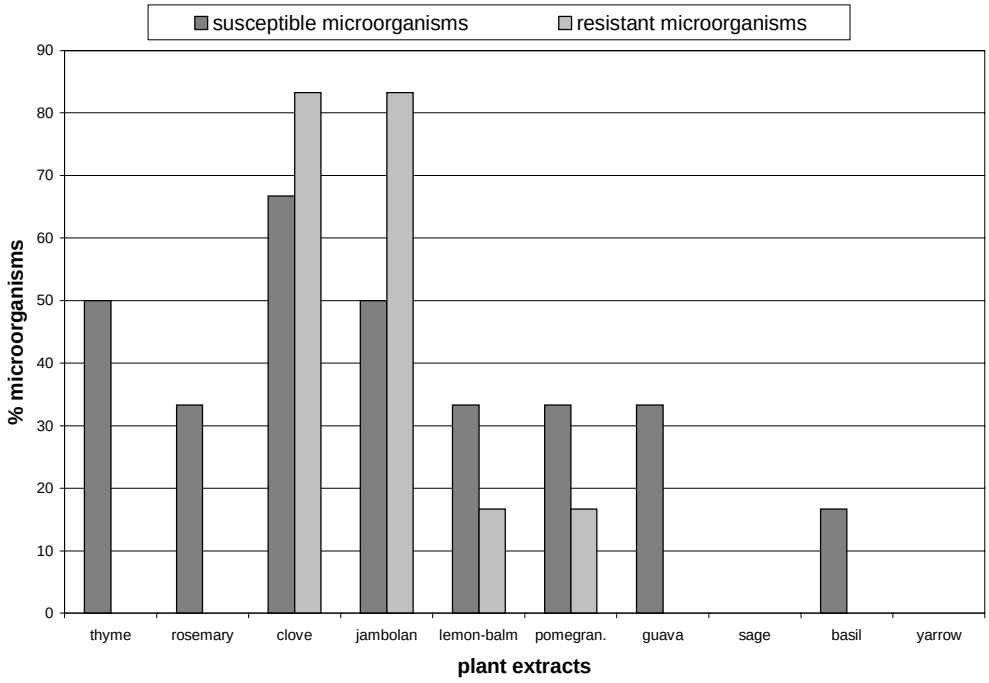

Figure 1 - Antimicrobial activity from plant extracts against susceptible (6) and resistant (8) antibiotic microorganisms

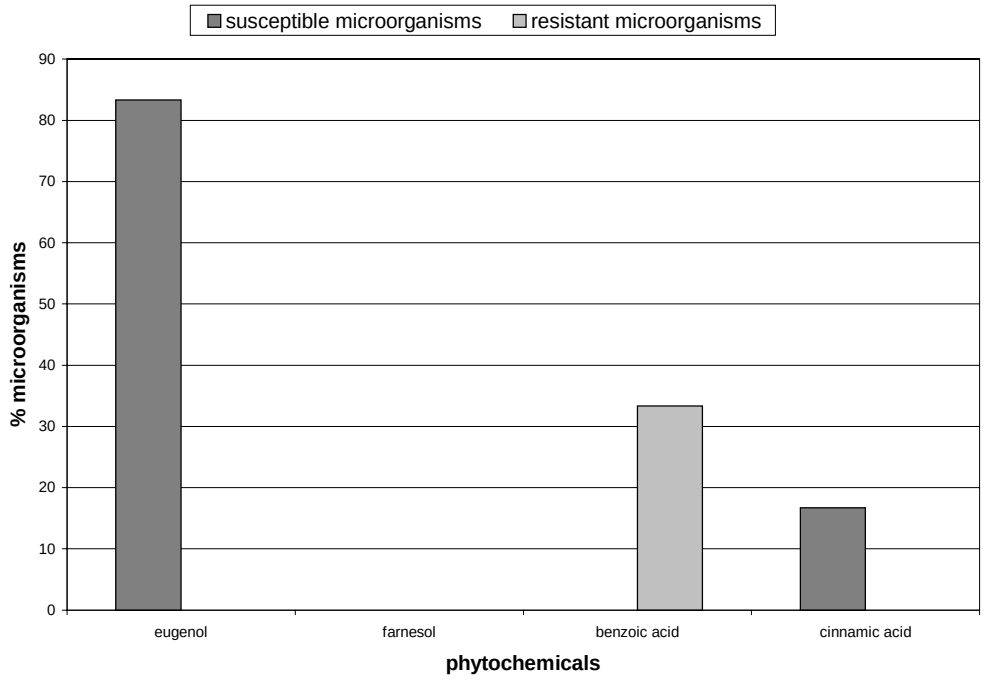

Figure 2 - Antimicrobial activity from phytochemicals against susceptible (6) and resistant (8) antibiotic microorganisms

The extracts from basil, clove, guava, jambolan, lemon balm, pomegranate, rosemary and thyme presented antimicrobial activity to at least one of the tested microorganisms. The extracts from clove and jambolan presented the highest activities, i. e., they were able to inhibit 9 (64.2 %) and 8 (57.1 %) types of microorganisms of interest, respectively. Moreover, they also had the highest activity rate against antibiotic resistant bacteria, which was 83.3 % (Fig, 1). On the other hand, the extracts from sage and yarrow did not show any anti-microbial activity.

One of the microorganism that showed susceptibility to these extracts was *C. albicans*. The susceptibility of this yeast to different plant extracts has been documented in the literature (3,23,24,29,33).

Some of the extracts of phytochemicals tested were active against *B. subtilis*. Such results were not totally unexpected since these bacteria form resting spores and are more resistant to environmental conditions than any other tested bacteria.

The microorganism *E.coli*, which is already known to be multi-resistant to drugs, was also resistant to the plant extracts tested. It was susceptible only to benzoic acid and cinnamic acid. On the other hand, *P. aeruginosa* (11), which is also resistant to different antibiotics, had its growth inhibited by the extracts from clove, jambolan, pomegranate and thyme. Such results are very interesting, because this bacterium was isolated from a hospital environment and its control is very difficult by therapeutic means. Studies regarding the mode of action for these compounds in the bacterial cell should be done.

The microorganism susceptibility to different extracts did not correlated with the susceptibility or resistance to a particular antibiotic within the same specie. It was clear that bacteria within the same specie, which are susceptible to drugs, showed the higher susceptibility to extracts than those of resistant species. This fact was evident for *S. aureus* numbers 1 and 14.

Among the phytochemicals, the eugenol, which is extracted from cloves, showed the highest antimicrobial activity. However, when it was associated with cinnamic acid, no activity against resistant bacteria was observed. On the other hand, the benzoic acid, which presented low activity against the investigated bacteria, was the only one that inhibited the resistant ones, while farnesol did not restrain the growth of any tested bacteria.

The data obtained, through the determination of MIC, from the association of antibiotics with extracts or with phytochemicals to observe any synergistic effect are presented in Table 3 and Fig. 3. The results revealed variability in the inhibitory concentrations of each extract for given bacteria. The extracts from jambolan and clove showed activities in the range (concentrations) from 50 to 500 µg/mL, and from 20 to 250 µg/mL, respectively. The lowest variation was observed for eugenol, perhaps due to its purity. Saxena *et al*. (33) documented a MIC varying from 12.5 to 1,000 µg/mL when testing different concentrations of *Rhus glaba* extracts on both, Gram-negative and Gram-positive bacteria.

Evaluation of the synergistic effect of antibiotics and plant extracts or phytochemicals on the resistant bacteria samples

Even though the MIC for seven bacterial samples were determined, only five of them were considered for the synergism experiments (Table 4). This was due to the loss of the resistance for a few antibiotics observed in *S. aureus* (14) and *Shigella* spp (9) bacteria, probably because of the loss of plasmids, where the resistance genes are usually located.

Since the majority of bacteria were resistant to many antibiotics, only ampicillin and/or chloramphenicol and/or tetracycline were used in the synergism assays. This was because the resistance to at least one of these drugs was common in all the bacteria tested.

A synergistic effect was observed for *P. aeruginosa* (11), which is resistant to 19 different antibiotics. This occurred during the association of antibiotics with extracts from clove, jambolan, pomegranate and thyme. The extracts alone from jambolan and thyme in the concentration of 50 µg/mL inhibited the bacterial growth. However, a synergetic effect was observed when 10 µg/mL was combined with each one of the antibiotic

Table 3. Minimal Inhibitory Concentration (MIC) of plant extracts and phytochemicals against antibiotic resistant bacteria.

Bacteria	Plant extracts/phytochemicals (mg/mL)					
	thyme	jambolan	lemon-balm	pomegranate	clove	eugenol
P. aeruginosa (11)	70	50		70	50	
K. pneumoniae (7)			200		100	20
K. pneumoniae **(**8**)**					100	10
Shigella spp (9)					250	10
Proteus spp (10)					20	10
S. aureus (14)		300				
E. aerogenes (12)	70	400				

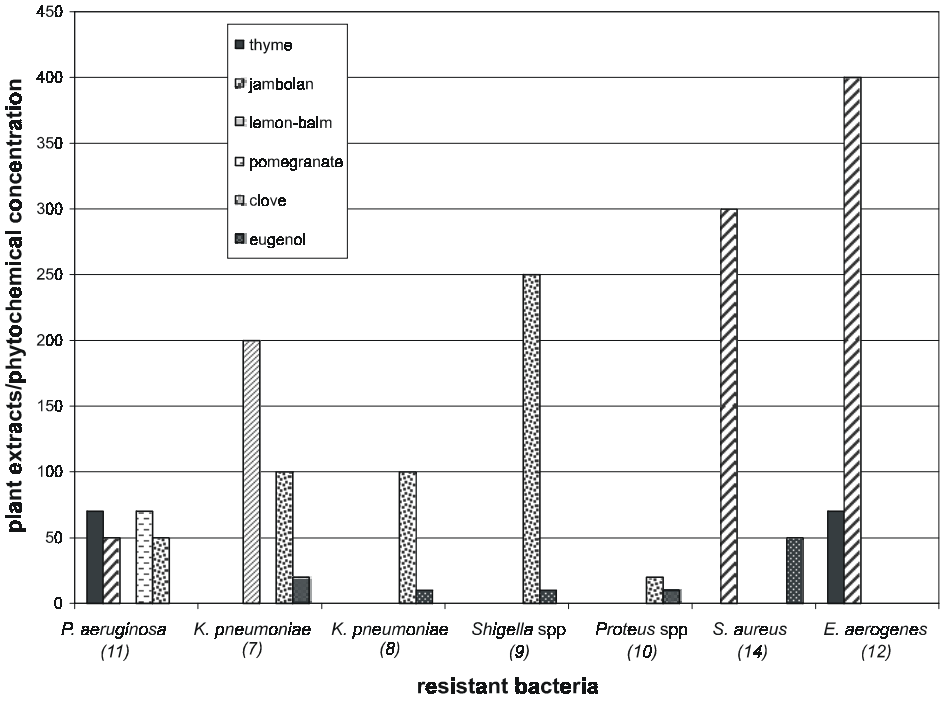

Figure 3 - Minimal Inhibitory Concentration (MIC) of plant extracts/phytochemicals against antibiotic resistant bacteria

tested, even those that did not show any activity by themselves. In the case of pomegranate and clove, the synergetic effect was noted with the extracts in the concentration of 50 and 10 µg/mL, respectively. Moreover, this effect was also observed for *K. pneumoniae* (8) when 20 µg/mL of clove extract was combined to ampicillin. Furthermore, the growth of *Proteus* spp.(10) was inhibited when either clove extract (10 µg/mL) or eugenol (5 µg/mL) was combined to tetracycline. Synergistic effects resulting from the combination of antibiotics with extracts were documented in the literature (28). They studied the association of anacardic acid and totarol with methicillin to inhibit strains of *S. aureus* resistant to methicillin (MRSA).

No synergetic effect was observed when different concentrations of extracts from lemon balm, clove and eugenol were combined with ampicillin to inhibit the growth of *K. pneumoniae* (7) and *E. aerogenes* (12). Only the association of thyme (20 µg/mL) with ampicillin was able to cause such an effect.

The use of plants to heal diseases, including infectious one, has been extensively applied by people. Data from the literature as well as our results reveal the great potential of plants for therapeutic treatment, in spite of the fact that they have not been completely investigated. Therefore, more studies need to be conducted to search for new compounds. Once extracted, and before being used in new therapeutic treatments, they should have their toxicity tested *in vivo*. Bioassays (10, 29) have demonstrated the toxicity of extracts from different plants.

Therefore, our results revealed the importance of plant extracts when associated with antibiotics, to control resistant bacteria, which are becoming a threat to human health. Furthermore, in a few cases, these plant extracts were active against antibiotic resistant bacteria under very low concentration, thus minimizing the possible toxic effects.

CONCLUSIONS

Our data express:

1. Plant extracts have great potential as antimicrobial compounds against microorganisms. Thus, they can be used in the treatment of infectious diseases caused by resistant microbes.
2. The synergistic effect from the association of antibiotic with plant extracts against resistant bacteria leads to new choices for the treatment of infectious diseases. This effect enables the use of the respective antibiotic when it is no longer effective by itself during therapeutic treatment.

Table 4. Effect of the association of plant extracts/phytochemicals and antibiotics on resistant bacteria. (The concentration of the antibiotics was 50mg/mL).

Bacteria	Association	Extracts /phytochemicals (mg/mL)										
		5	10	20	30	50	70	100	150	200	250	400
P. aeruginosa (11)	J		-		-	+						
	J + TT		+		+	+						
	J + AP		+		+	+						
	J + CO		+		+	+						
	T		-		-	-	+					
	T + TT		+		+	+	+					
	T + AP		+		+	+	+					
	T + CO		+		+	+	+					
	P			-		-	+					
	P + TT			-		+						
	P + AP			-		+						
	P + CO			-		+						
	C		-	-		+						
	C + TT		+	+		+						
	C + AP		+	+		+						
	C + CO		+	+		+						
K. pneumoniae (7)	L					-		-		+		
	L + AP					-		-		+		
	C					-		+				
	C + AP					+		+				
	E		+	+								
	E + AP		+	+								
K. pneumoniae (8)	C			-	-	-		+				
	C + AP			+	+	+		+				
	E	-	+									
	E + AP	-	+									
Proteus (10)	C		-	-								
	C + TT		+	+								
	C + AP		+	+								
	C + CO		+	+								
	E	-	+									
	E + TT	+	+									
	E + AP	+	+									
	E + CO	+	+									
E. aerogenes (12)	J					-		-		-		-
	J + TT					-		-		-		-
	J + AP					-		-		-		-
	T			-		-	+					
	T + TT			-		-	+					
	T + AP			+		+	+					

J - jambolan, T - thyme; P - pomegranate, C - clove, L - lemon-balm, E - eugenol,
TT - tetracycline, AP - ampicillin, CO - cloranfenicol.
(+) susceptibility (-) absence of susceptibility

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RESUMO

Atividade de extratos vegetais e fitofármacos sobre bactérias resistentes a antibióticos

Foi avaliada a atividade antimicrobiana de extratos vegetais e fitofármacos frente a microrganismos sensíveis e resistentes a antibióticos, bem como observado o possível efeito sinérgico da associação entre antibióticos e extratos vegetais. Foram utilizados os extratos de plantas cujo nomes populares são: tomilho, alecrim, cravo-da-Índia, jambolão, erva cidreira, romã, goiaba, sálvia, manjericão e mil-folhas, e ainda os fitofármacos, ácido benzóico, ácido cinâmico, eugenol e farnesol. Na avaliação da atividade antimicrobiana através do método de difusão em agar, foram utilizadas 14 amostras de microrganismos: 1 levedura (*Candida albicans*), 5 bactérias sensíveis **(***Staphylococcus aureus, Salmonella choleraesuis, Pseudomonas aeruginosa, Bacillus subtilis, Proteus* spp) e 8 bactérias resistentes a antibióticos isoladas de ambiente hospitalar (2 amostras diferentes de *Klebsiella pneumoniae, Shigella* spp*, Proteus* spp*, Pseudomonas aeruginosa, Enterobacter aerogenes, Escherichia coli* e *Staphylococcus aureus*. A determinação do CIM e sinergismo foram realizados pela incorporação dos extratos e antibióticos aos meios de culturas liquidos. O maior potencial antimicrobiano foi verificado para os extratos de cravo e jambolão que inibiram, respectivamente, 64,2 e 57,1% dos microrganismos, inclusive com maior atividade sobre os microrganismos resistentes a antibióticos (83,3%). Associação de antibióticos e extratos vegetais ou fitofármacos, sobre bactérias resistentes a antibióticos, mostrou que em alguns casos ocorreu sinergismo, possibilitando que antibióticos já ineficazes apresentassem ação sobre estas bactérias. Os dados obtidos no presente trabalho permitem concluir que estudos mais detalhados sobre o uso terapêutico das plantas devem ser intensificados, principalmente sobre bactérias resistentes a antibióticos, seja na sua ação individual ou em menores concentrações associados com antibióticos.

Palavras-chave: atividade de extratos de plantas; plantas medicinais; atividade antimicrobiana

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