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Antimicrobial activity of Palestinian medicinal plants against acne-inducing bacteria

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The antimicrobial activities of 56 Palestinian medicinal plants against etiologic agents of acne vulgaris, mainly *Propionibacterium acnes* and *Staphylococcus aureus* was studied using disc diffusion and broth dilution methods. The results from the disc diffusion method demonstrated that these plants differ significantly in their activity against the studied microorganisms. The most active plants against all bacterial strains were *Rhus coriaria, Ricinus communis,* and *Sarcopoterium spinosum*. Test microorganisms differed significantly in relation to their susceptibility to different plant extracts used. Generally, anaerobic bacteria were more susceptible to plant extracts than aerobic bacteria. Those plants which could inhibit the growth of *P. acnes, R. coriaria, R. communis,* and *S. spinosum* had strong inhibitory effects. 43 plants could inhibit the growth of all aerobic bacteria. Based on a broth dilution method, the *R. coriaria* extract had the greatest antimicrobial effect against *P. acnes* (MIC 6 mg/ml, MBC 6 mg/ml), *S. aureus* (MIC 4 mg/ml, MBC 6 mg/ml)*, E. coli* (MIC 6 mg/ml, MBC 8 mg/ml) and *P. aeruginosa* (4 and 6 mg/ml). Taken together, our data indicate that *R. coriaria*, *R . communis* had a strong inhibitory effect on *P. acnes* and most other test bacteria. Therefore, the two plants would be an interesting topic for further study and possibly for an alternative treatment for acne.

Key words: Acne, *Propionibacterium acnes*, *Staphylococcus aureus*, *Echerichia coli*, *Klebsiella pneumonia*, *Proteus vulgaris*, antimicrobial activity.

INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit, resulting from androgen-induced increased sebum production, inflammation, altered keratinisation, and bacterial collonisation of hair follicles on the face, neck, chest, and back by *Propionibacterium acnes* (Williams et al., 2012). Acne is characterized by comedones, papules, pustules, cysts, nodules and often scars in certain sites of predilection, namely, the face, neck, upper trunk and arms.

As a family of skin disorders, acne is one of the most prevalent dermatologic diseases in the world. It usually affects almost everybody during the life (Scheinfeld, 2007). It affects all most all people aged 15 to 17 years (Rademaker et al., 1989; Law et al., 2010; Yahya, 2009), and is moderate to severe in 15 to 20% (Williams et al., 2012). The pathogenesis of the disease is complex but dependent on several factors including androgen-mediated stimulation of sebaceous gland activity, colonization of the bacterium *P. acnes* (an anaerobic bacterium as a normal constituent of the skin microbial flora), and inflammation (Toyoda and Morohashi, 2001).

The use of natural remedies dates back thousands of years. It is estimated that there are 250,000 to 500,000 species of plants on Earth (Borris, 1996), and 2780

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species of plants in the Palestinian authority territory (Ali-Shtayeh and Jamous, 2002) which offers a great hope in the identification of phytotherapeutic agents and their development into drugs for the treatment of acne vulgaris that affects approximately 80% of the population between the ages of 12 to 25 years (Ghosh et al., 2011).

The interest in beauty is natural, and cosmetics are as ancient as mankind and civilization (Gediya et al., 2011). Therefore, acne vulgaris, which can persist into adulthood, could suppress an individual's self-confidence with regard to physical appearances or even depression that may affect all aspects of life. In view of increasing resistance to existing anti-microbial agents, side effects and sometimes high cost of treatment (Oprika, 2006; Ghosh et al., 2011; Hamburger and Hostettmann, 1991), discovering an effective treatment for acne that is well tolerated by the patients is a challenge.

Singh et al. (2011) reviewed the possible correlation between antimicrobial activities of medicinal plants against the etiologic agents of acne vulgaris. They found that different parts of various medicinal plants belonging to families like Liliaceae, Rutaceae, Zingiberaceae, Myrtaceae, Lamiaceae, etc contain alkaloids, tannins, flavonoids, terpenoids, volatile oil and essential oil which are reported with significant effect against this bacteria.

The development of resistance by a pathogen to many of the commonly used antibiotics provides and impetus for further attempts to search for new antimicrobial agents to combat infections and overcome the problems of resistance and side effects of the currently available antimicrobial agents. Hence, this *in vitro* study was aimed at screening selected Palestinian plants for their antimicrobial activity against *Propionibacterium acnes,* and determine whether their use in folkloric medicine to treat these infections is justified.

MATERIALS AND METHODS

Preparation of plant extracts

Plant parts of 56 plants used in traditional Arabic Palestinian herbal medicine (TAPHM) for the treatment of acnes and other skin disorders were collected from various locations in Palestine (West Bank). Authentification of the plants was done by comparison with plant specimens located at BERC Herbarium and the Biodiversity and Biotechnology Research Unit, BERC, Nablus, Palestine. Voucher specimens of the plants were deposited at BERC Herbarium, Til, Nablus, Palestinian Authority (Table 1).

Microorganisms and media

The microorganisms used included: *P. acnes* (ATCC 6919, ATCC 6921), and eight other strains of this microorganism isolated from different clinical specimens recovered from acne patients and identified using standard procedures. Five medically important bacterial strains were also included (*Staphylococcus aureus* ATCC 25923; *Escherichia coli* ATCC 25922; *Klebsiella pneumonia* ATCC 13883; *Proteus vulgaris* ATCC 13315; and *Pseudomonas aeruginosa* ATCC 27853). All media were purchased from DIFCO (Detroit, MI).

Antimicrobial susceptibility testing

Disk diffusion method

This experiment was carried out by the method of Hayes and Markovic (2002) with some modifications. *P. acnes* was incubated in liquid Reinforced Clostridium Medium (RCM) for 48 h under anaerobic conditions and adjusted to yield approximately 1.0 x 10^8 CFU/ml. A 1.0 x 10^8 CFU inoculum was spread on blood agar (with sheep blood 5 to 7%) (BASB) medium plates. Discs of 6 mm diameter were prepared from Whatman filter paper No.1, placed in a glass Petri dishes and autoclaved for 15 min. 25 µl of the required extract were added to each sterile disc, and the discs were dried under a laminar flow sterile bench. The final content of each disc was 5 mg of extract. A sterile paper disc impregnated with test material was placed on the agar. Plates were then incubated at 37°C for 72 h under anaerobic conditions (in Gas Pak Jars).

Aerobic bacteria were incubated in Muller–Hinton broth (MHB) for 24 h at 37°C and adjusted to yield approximately 1.0 x 10^8 CFU/ml. The procedures were the same as mentioned above except the plates were incubated at 37°C for 24 h under aerobic conditions.

All disc diffusion tests were performed in three separate experiments and the antibacterial activity was expressed as the mean inhibition zone diameters, IZD (mm) and relative antibacterial activity.

On each plate an appropriate reference antibiotic disc was applied depending on the test microorganism. Ampicillin, Gentamicin, Gentamicin, Ciprofloxacin, Penecillin G, and chloramphenicol served as positive control for *E. coli*, *P. vulgaris*, *P. aeruginosa*, *K. pneumonia*, *S. aureus* and *P. acnes*, respectively.

Determination of minimum inhibitory and bactericidal concentrations

The minimal inhibitory concentration (MIC) values were determined by broth dilution assay (Murray et al., 1995). The cultures were prepared at 24 and 48 h broth cultures of aerobic bacteria, and *P. acnes*, respectively. The MIC was defined as the lowest concentration of the compound to inhibit the growth of microorganisms and the minimum bactericidal concentration (MBC) was defind as the lowest concentration of the compound to kill the microorganisms. A stock solution (200 mg/ml) of plant extract was prepared in 10% DMSO. Several aliquots of the stock solution were prepared (0.2, 0.1, 0.075, 0.05, 0.04, 0.03, and 0.02 ml). The aliquots were made up to 0.2 ml each by adding 0.0, 0.1, 0.125, 0.15, 0.16, 0.17, 0.18 ml DMSO, respectively. For each strain, 10 tubes each with 9.7 ml MHB for aerobic bacteria and 9.7 ml RCM for anaerobic bacteria were prepared and autoclaved. 0.2 ml of each of the above concentrations was added to 7 of the 10 broth tubes to obtain the following dilutions (mg/ml): 40, 20, 15, 10, 8, 6, and 4, respectively. One of the remaining three tubes was used as a positive control by adding 0.2 ml of reference antibiotic solution (100 mg/ml), whereas the other two tubes were used as negative control by adding 0.2 ml of DMSO to one tube and 0.2 ml sterile water to the other. All tubes were inoculated with 0.1 ml of the test suspension (10 CFU/ml). The tubes were then incubated for 24 h at 37°C for the aerobic bacteria and 48 h at 37°C in Gas Pak Jars for the anaerobic bacteria (Murry et al., 1995). After incubation, the MIC of each ingredient was determined by visual inspection of the tubes. The lowest concentration of the active ingredient that inhibited growth of the organism, as detected by lack of visual turbidity (matching the negative growth control) was designated the MIC (Baron et al., 1994).

For minimum bactericidal concentration (MBC), subcultures were made from the visually clear tubes of inoculum with antimicrobial agent (active plants) on MHA plate for aerobic bacteria, and on BASB for anaerobic bacteria. MBC was interpreted to be at a

Table 1. Selected plants used for antibaterial succeptibility testing against *P. acnes* and aerobic bacteria.

Latin name	Family name	English name	Plant part used*	Medicinal uses	References*
Achillea fragrantissima Forssk.	Compositae	Yarrow	AP, FL	Skin, hair, and burns, headache and temperature, cancer, circulatory system, kidney and urinary tract system, weight loss, digestive system, food poisoning, diabetes	1, 2, 3, 9, 10
Ajuga orientaslis L.	Lamiaceae	Eastern Bugle	AP	Skin ailments	2, 3, 6
Allium sativum L.	Liliaceae	Garlic	LF	Weight gain, tooth inflammation, ear diseases, weight loss, skin, hair, and burns, reproductive system, respiratory system, nervous system, skeletal and muscular system, digestive system, cancer, circulatory system, kidney and urinary, tract system, diabetes	1, 2, 3, 6, 9, 11, 12
Arum dioscorides Sibth & Sm	Araceae	Spotted Arum	LF	Circulatory system, diabetes, cancer, digestive system	1, 2, 12, 9
Asparagus aphyllus L.	Liliaceae	Prickly Asparagus	AP	Kidney and urinary tract system, cancer	1, 6, 9, 11
Capparis spinosa L.	Capparidaceae	Caper Bush	FR, FL	Ear diseases, eye diseases, reproductive system, respiratory system, skeletal and muscular system, kidney and urinary tract system	1, 2, 3, 4, 5, 6, 7, 9
Cardaria draba L.) Desv.	Brassicaceae	Heart-Podded Hoary Cress	AP		6
Ceratonia siliqua L.	Caesalpiniaceae	Carob	S	Diabetes, tooth inflammation, weight loss, skin, hair, and burns, respiratory system, digestive system, diabetes, circulatory system, cancer	1, 2, 3, 6, 7, 9, 10, 11, 12
Chrysanthemum coronarium L.	Compositae	Corn Marigold	FL	Respiratory system, digestive system, circulatory system	1, 2, 6
Cicer arietinum L.	Fabaceae	Chick Pea	AP	Kidney and urinary tract system, digestive system, reproductive system, skin, hair, and burns, weight gain, diabetes	9, 1, 10, 12
Clematis cirrhosa L.	Ranunculaceae	Evergreen Virgin's-Power	AP	Skin ailments	1, 2, 3, 4, 5, 6

Table 1. contd.

Companula rapunculus L.	Campanulaceae	Rampion Bellflower	AP	Cancer, diabetes	1
Conium maculatum L.	Apiaceae	Hemlock	LF, FL		6
Convolvulus arvensis L.	Convolvulaceae	Field Bindweed	AP	Digestive system, urinary tract system	1
Coridothymus capitatus (L.) Reichb.	Labiatae	Capitate Thyme	AP	Respiratory system, nervous system, skeletal and muscular system, digestive system, diabetes, cancer	1, 2, 3, 6, 9, 10, 11
Crataegus aronia (L.) Bosc. ex DC.	Rosaceae	Hawthorn, Azarole	LF	Weight loss, skin, hair, and burns, respiratory system, nervous system, skeletal and muscular system, digestive system, headache and temperature, rheumatism and arthritis, diabetes, circulatory system, cancer	1, 2, 3, 4, 6, 7, 9, 10, 12
Daucus carota L.	Apiaceae	Carrot	LF, FL, RT	Kidney and urinary tract system , scurvy, gout, eye diseases, weight loss, skin, hair, and burns, respiratory system, nervous system, digestive system, rheumatism and arthritis, circulatory system, diabetes, cancer	1, 6, 9, 10, 11, 12
Erodium malacoides (L.) L'Hér.	Geraniaceae	Mediterranean stork's bill and oval heron's bill	WP		
Eruca sativa Miller	Brassicaceae	Garden Rocket	WP	Circulatory system, ascites, scurvy, gout, tooth inflammation, skin, hair, and burns, reproductive system, skeletal and muscular system, digestive system, rheumatism and arthritis, diabetes, circulatory system, cancer	1, 2, 3, 6, 9, 10, 11, 12
Foeniculum vulgare Miller	Apiaceae	Fennel	AP	Kidney and urinary tract system, circulatory system, nervous system, respiratory system, weight loss, eye diseases, diabetes, cancer, digestive system	1, 2, 3, 4, 6, 9, 10, 11, 12
Gagea chlorantha (Bieb.) Schult. fil.	Liliaceae	Gagea		Cancer	3, 11
Gundelia tournefortii L.	Compositae	Gundelia	AP	Digestive system, diabetes	6, 9, 10
Lactuca tuberose Jacq.	Compositae	Tuberous Lettuce	AP	Digestive system, circulatory system	1

Table 1. contd.

Linum pubescens Banks & Sol.	Linaceae	Pink Flax	AP, FL	Weight loss, skin, hair, and burns, respiratory system, skeletal and muscular system, digestive system, headache and temperature, kidney and urinary tract system, diabetes, cancer	1, 2, 2, 3, 6, 9, 10, 11
Lupinus pilosus L. (*Lupinus varius* L.)	Papilionaceae	Blue Lupine	AP, S		3
Lycium europaeum L.	Solanaceae	Mediterranean tea tree	AP		6
Majorana syriaca (L.) Rafin.	Labiatae	Wild Thyme, Mother of Thyme	AP	Circulatory system, eye diseases, weight loss, skin, hair, and burns, reproductive system, respiratory system, nervous system, skeletal and muscular system, digestive system, headache and temperature , circulatory system, kidney and urinary tract system, tooth inflammation , diabetes, cancer	1, 2, 6, 9, 10, 11, 12
Mandragora autumnalis Bertol.	Solanaceae	Mandrake	FR		6
Mentha spicata L.	Lamiaceae	Spearmint	AP	Digestive system, respiratory system, weight loss, respiratory system,	1
Notobasis syriaca (L.) Cass.	Compositae	Syrian Thistle	YB	Nervous system	1
Parietaria judiaca L.	Urticaceae	Wall Pellitory	AP	Cancer	3, 4, 5, 6, 11
Paronychia argentea Lam.	Caryophyllaceae	Silvery Whitlow- Wart	AP	Digestive system, weight loss, respiratory system, skeletal and muscular system, digestive system, diabetes, cancer, urinary tract system	1, 2, 3, 5, 6, 9, 10, 11, 12
Petroselinum sativum Hoffm.	Apiaceae	Parsley	WP	Circulatory system, digestive system, diabetes, cancer, reproductive system, reproductive system, kidney and urinary tract system	1, 9, 11, 12
Phagnalon rupestre (L.) DC.	Compositae	African Fleabane, Rock Phagnalon	AP	Weight loss, skin, hair, and burns, skeletal and muscular system, cancer	1, 2, 3, 4, 5, 6, 9, 11, 12
Pinus halepensis Mill.	Pinaceae	Aleppo Pine	LF	Reproductive system, respiratory system, tooth inflammation	1, 2, 3, 5, 6, 7, 9, 12
Pistacia lentiscus L.	Anacardiaceae	Lentisk, Mastic Tree	LF	Reproductive system, respiratory system, skin, hair, and burns, digestive system, headache and temperature, , rheumatism and arthritis, paralysis	1, 2, 7, 9, 12

Table 1. contd.

Pyrus syriaca Boiss	Rosaceae	Syrian Pear	LF, FL	Digestive system, food poisoning, kidney and urinary tract system, circulatory system	1, 2, 6, 7, 9
Reseda alba L.	Resedaceae	White mignonette	WP		
Rhus coriaria L.	Anacardiaceae	Sicilian Sumach	AP	Weight loss, tooth inflammation, skin, hair, and burns, digestive system, headache and temperature, diabetes	1, 2, 3, 6, 7, 9
Ricinus communis L.	Euphorbiaceae	Castor Beans	AP	Kidney and urinary tract system, ear diseases, eye diseases, food poisoning, skin, hair, and burns, reproductive system, respiratory system, skeletal and muscular system, digestive system, rheumatism and arthritis, paralysis, bites, stings, cancer	1, 2, 3, 6, 7, 9, 11, 12
Rosa centifolia L.	Rosaceae	Pale Rose	FL	Bites and stings, respiratory system, eye diseases, digestive system, skin, hair, and burns, cancer	1, 9, 11, 12
Rubia tenuifolia D'Urv.	Rubiaceae	Narrow-Leaved Madder	AP	Kidney and urinary tract system	1, 3, 6
Ruta chalepensis L.	Rutaceae	Rue	AP, FL	Ear diseases, skin, hair, and burns, respiratory system, nervous system, skeletal and muscular system, digestive system, headache and temperature, kidney and urinary tract system, paralysis	1, 2, 2, 3, 4, 5, 6, 7, 9, 12
Saccharum ravennae L.	Poaceae	Ravenna grass	FL		
Salvia fruticosa Mill.	Labiatae	White Sage, Common Sage, Garden Sage	LF	Weight loss food poisoning, skin, hair, and burns, reproductive system, respiratory system, nervous system, diabetes, circulatory system, kidney and urinary tract system, headache and temperature, digestive system, tooth inflammation, cancer	1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12
Salvia hierosolymitana Boiss.	Labiatae	Jerusalem Sage	LF	Kidney and urinary tract system, circulatory system, digestive system	1, 6, 9
Sarcopoterium spinosum (L.) Sp.	Rosaceae	Shruppy Barnet	AP	Diabetes, tooth inflammation	1, 2, 3, 4, 6, 7, 9, 12
Satureja thymbra L.	Labiatae	Summer Savory	AP, FL		2, 3, 6

Table 1. contd.

Scabiosa prolifera L.	Dipsacaceae	Carmel daisy	AP		6, 8
Sinapis arvensis L.	Brassicaceae	Mustard/ Wild	WP	Cancer	1, 2, 11
Spinacia oleraceae L.	Chenopodiaceae	Spinach	WP	Kidney and urinary tract system, respiratory system, digestive system, circulatory system	1, 2, 3, 9, 12
Styrax officinalis	Styracaceae	Storax	YB		
Trigonella berythea Boiss. & Blanche (T. foenum- graecum L.)	Fabaceae	Fenugreek Seed,	AP	Kidney and urinary tract system, tooth inflammation, weight loss, skin, hair, and burns, reproductive system, respiratory system, nervous system, skeletal and muscular system, digestive system, rheumatism and arthritis, diabetes, circulatory system, kidney and urinary tract system, cancer	1, 2, 3, 6, 9, 10, 11, 12
Varthemia iphionoides Boiss & Blanche *(Chiliadenus iphionoides* (Boiss. & Blanche) Brullo)	Compositae	Common varthemia	AP	Circulatory system, diabetes, digestive system, respiratory system, weight loss	1, 2, 3, 6, 9, 10, 12
Vicia faba L.	Leguminosae	Broadbean	AP	Kidney and urinary tract system, circulatory system, diabetes, digestive system	1, 2, 3, 6, 9, 10, 12
Viscum cruciatum Sieber & Bioss	Santalaceae	Mistletoe	LF	Cancer, circulatory system	1, 2

References: 1, Ali-Shtayeh and Jamous (2006); 2, Ali-Shtayeh et al. (2000); 3, Ali-Shtayeh et al. (2003a); 4, Ali-Shtayeh et al. (1998); 5, Ali-Shtayeh and Abu-Ghdaib (1999); 6, Khalilia (2001); 7, Ali-Shtayeh et al. (2003b); 8, Crowfoot et al. (1932); 9, Ali-Shtayeh and Jamous (2008); 10, Ali-Shtayeh et al. (2012); 11, Ali-Shtayeh et al. (2011); 12, Yasin (2008).

tube that showed no growth on agar plate (Irobi and Daramala, 1994).

Statistical analysis

Data of the susceptibility test were analysed by three way analysis of variance (ANOVA) with 95% confidence ($P < 0.05$). Determination of relative antimicrobial activity = [(inhibition zone diameter mean of active plant)^2/ (inhibition zone diameter mean of reference antibiotics)^2] × 100%.

RESULTS

Antimicrobial activity of 56 plants

The present study was conducted to evaluate antimicrobial activities of Palestinian medicinal plants against etiologic agents of acne vulgaris, mainly *P. acnes* (Gram-positive). Crude ethanolic extracts of 56 plant species used in folk medicine in Palestine for treatment of several infections and diseases (Table 1) were investigated for their antimicrobial activities against 10 strains of *P. acnes*, and five Gram-negative strains of aerobic bacteria, *E. coli, K. pneumonia, P. vulgaris* and *P. aeruginosa;* and one Gram-positive bacterium *S. aureus*, using two susceptibility tests: the disk diffusion method for measuring the antimicrobial activity, and broth method for the determination of MIC and MBC for the active plant extracts.

Based on the disc diffusion method and related relative antimicrobial activity values (RAA) (Tables 2 and 3), four (7.1%) of the studied plants had high RAA (≥60; IZD range 20.8 to 25.0), and seven (12.5%) had medium (30 to 60; IZD range 11.7 to 15) activity against *P. acnes*. 39 (69.6%) of the plants showed low (RAA < 30; IZD >6 to 10.7) activity and six (10.7%) showed no detectable activity against *P. acnes* (Table 3 and Figure 1). On the other hand, only 1, and 4 of the plants had high activity against only *P. aeruginosa* and *E. coli*, respectively (Tables 2 and 3). Also four, 17, one, and one of the plants had medium activity against *S. aureus*, *E. coli*, *P. aeruginosa*, and *P. vulgaris*, respectively. 20 (35.7%) to 41 (73.2%) plant species showed low activity, and 6 to18 (10.7 to 32.1%) species showed no detectable antimicrobial activity against one or more of the studied aerobic bacterial species (Table 3 and Figure 1).

On the basis of RAA values (≥30), the most active plants against test bacteria (19 plants, 33.9%), were *R. coriaria* (RAA 153), *R. communis* (153), *Sarcopoterium spinosum* (120), *Sinapis arvensis* (100), and *Pinus halepensis* (59) against *P. acnes* (Table 4); R. *coriaria* (58), *R. communis* (42), *S. spinosum* (40), and *Viscum cruciatum* (36) against *S. aureus*; *R. coriaria* (215), *V. cruciatum* (149), *R. communis* (144), *Satureja thymbra* (64), *Majorana syriaca* (54), *S. spinosum* (53), *Vicia faba* (44), *Crataegus aronia* (44), *Capparis* (42), *S. arvensis* (42), *Lactuca tuberosa* (42), *Trigonella berythea* (39), *Coridothymus capitatus* (36), *Convolvulus arvensis* (36), *Conium maculatum* (33), *Pyrus syriaca* (33), *Phagnalon rupestre* (31), and *Rosa centifolia* (31) against *E. coli*; *R. coriaria* (77), and *R. communis* (52) against *P. aeruginosa*; *R. coriaria* (30) against *P. vulgaris* (Table 5). However, *R. communis* (21) was the most active plant against *K. pneumonia*.

All plants studied in this work differed significantly in their activity against the test microorganism (F = 51.317, DF = 839, P< 0.05).

Susceptibility of test bacterial strains to plant extracts

Test strains differed significantly in their susceptibility to the different plant extracts used (F = 2.078, DF = 839, P < 0.05). The most sensitive test microorganism was *P. acnes*, followed by *S. aureus*, *E. coli*, *P. aeruginosa*, *P. vulgaris* and *K. pneumonia* with inhibition zone diameter means of 9.8, 9.2, 8.4, 8.4 and 7.8.

Based on the numbers of plants with high and medium activities against the different aerobic bacteria spp, *E. coli* was the most susceptible species, whereas *K. pneumonia* was the least susceptible to the studied plants (Table 3 and Figure 1).

MIC and MBC of the active plant extracts

Based on MIC and MBC results, *P. acnes* (anaerobic bacteria), was shown to be the most susceptible microorganisms with MIC raging from 6 to 29 mg/ml and MBC from 6 to 31.6 mg/ml, and with *R. coriaria* showing the lowest MIC (6 mg/ml) and MBC (6 mg/ml) whereas *V. cruciatum* had the highest MIC (28 mg/ml) and MBC (30 mg/ml) (Table 4).

For aerobic bacteria, the most susceptible microorganism was *S. aureus* with MIC ranging from 4 to 18 mg/ml and MBC from 6 to 21 mg/ml, and the least susceptible microorganism was *K. pneumonia* with MIC ranging from 11 to 25 mg/ml and MBC 15 to 30 mg/ml. *R. coriaria* had the lowest MIC (4 mg/ml), while *L. tuberosa,* and *V. cruiciatums* had the highest MIC (>25 mg/ml) (Table 5).

DISCUSSION

The results of the antimicrbial screening assay of crude extracts of all species of plants showed that the most active plants against all bacterial strains were *R. coriaria, R. communis* and *S. spinosum.* All species of plants included in the present study (except *Arum discorides*, *Ceratonia siliqua*, *Paronychia argentia*) were also found to be active on at least one of the tested bacterial strains. In general, among the tested bacterial strains, *P. acnes* was found to be more sensetive to plant extracts than other aerobic bacteria. On the other hand, *K. pneumonia* was the most insensitive of all the bacteria used in this study.The antimicrobial activity was more pronounced on the Gram-positive bacteria (*P. acnes* and *S. auereus*) than the Gram-negative bacteria (*E. coli* and *Ps. aeruginosa*). In fact, Gram-negative bacteria are frequently reported to have developed multi drug resistance to many of the antibiotics currently available in the market (Alonso et al., 2000; Sader et al., 2002). The reason for the difference in sensitivity between Gram +ve and Gram -ve bacteria might be ascribed to the differences in morphological constitutions between these micoorganisms: Gram –ve bacteria have an outer phospholipidic membrane carrying the structural lipopolysaccharide components. This makes the cell wall impermeable to antimicrobial chemical substances. The Gram +ve bacteria on the other hand are more susceptible having only an outer peptidoglycan layer which is not an effective permeability barrier. Therefore, the cell walls of Gram-negative organisms which are more complex than the Gram-positive ones act as a diffusional barrier and making them less susceptible to the antimicrobial agents than are Gram +ve bacteria (Nostro et al., 2000; Hodges, 2002). In spite of this permeability differences, however, some of the extracts have still exerted some degree of inhibition against Gram -ve organisms as well.

Reports (Arda, 2009) indicate that acne is common among dermatology patients (9 to 12%) in the West Bank (Palestinian Authority territory). Thus, the fact that 50 species of the tested plants (89%) showed activity

Table 2. Relative antimicrobial activity* of plants against *P. acnes* and aerobic bacteria.

Latin name	*P. acnes**	*S. aureus*	*E. coli*	*P. aeruginosa*	*P. vulgaris*	*K. pneumonia*
Achillea fragrantissima Forssk.	14	7	26	6♣	8	4♣
Ajuga orientaslis L.	30	7	26	10	7	4
Allium sativum L.	15	8	33	13	13	8
Arum dioscorides Sibth & Sm	8	4♣	16♣	6	6♣	4
Asparagus aphyllus L.	14	4	16	6	6	4
Capparis spinosa L.	10	29	42	10	14	9
Cardaria draba (L.) Desv.	8	5	28	7	6	5
Ceratonia siliqua L.	8	4	16	6	6	4
Chrysanthemum coronarium L.	15	7	16	12	10	4
Cicer arietinum L.	15	5	16	8	9	7
Clematis cirrhosa L.	26	7	28	10	10	7
Companula rapunculus L.	18	4	16	6	6	4
Conium maculatum L.	11	10	33	6	9	6
Convolvulus arvensis L.	15	8	36	12	10	7
Coridothymus capitatus (L.) Reichb.	15	9	36	12	13	8
Crataegus aronia (L.) Bosc. ex DC.	14	15	44	23	16	11
Daucus carota L.	8	6	22	13	13	5
Erodium malacoides (L.) L'Hér.	21	6	33	14	13	9
Eruca sativa Miller	14	7	28	8	6	4
Foeniculum vulgare Miller	12	6	16	10	9	7
Gagea chlorantha (Bieb.) Schult. fil.	10	4	22	10	10	4
Gundelia tournefortii L.	13	4	16	8	10	7
Lactuca tuberose Jacq.	34	15	42	16	6	4
Linum pubescens Banks & Sol.	18	6	22	10	10	4
Lupinus pilosus L.	15	7	28	11	12	7
Lycium europaeum L.	32	5	16	6	6	4
Majorana syriaca (L.) Rafin.	25	15	54	22	19	18
Mandragora autumnalis Bertol.	11	5	22	6	6	5
Mentha spicata L.	15	7	24	10	9	7
Notobasis syriaca (L.) Cass.	14	7	31	8	6	5
Parietaria judiaca L.	19	7	26	10	9	5
Paronychia argentea Lam.	8♣	4	16	6	6	4
Petroselinum sativum Hoffm.	18	5	18	6	6	4
Phagnalon rupestre (L.) DC.	30	9	31	13	12	9
Pinus halepensis Mill.	50	8	16	14	6	4
Pistacia lentiscus L.	12	8	28	11	10	7
Pyrus syriaca Boiss	18	8	33	14	14	10
Reseda alba L.	10	4	16	6	6	4
Rhus coriaria L.	134	58	215	77	30	19
Ricinus communis L.	117	42	144	52	6	21
Rosa centifolia L.	19	9	31	12	14	10
Rubia tenuifolia D'Urv.	12	9	28	8	12	6
Ruta chalepensis L.	11	4	16	6	10	5
Saccharum ravennae L.	11	7	28	10	6	5
Salvia fruticosa Mill.	33	8	28	10	10	7
Salvia hierosolymitana Boiss.	18	4	16	6	6	4
Sarcopoterium spinosum (L.) Sp.	115	40	53	18	19	16
Satureja thymbra L.	18	14	64	23	23	16

Table 2. contd.

Scabiosa prolifera L	18	4	16	6	8	7
Sinapis arvensis L.	96	13	42	21	14	10
Spinacia oleraceae L.	43	7	28	10	10	5
Styrax officinalis	18	7	28	10	10	5
Trigonella berythea Boiss & Blanche	11	8	39	6	6	4
Varthemia iphionoides Boiss & Blanche	13	7	26	10	9	5
Vicia faba L.	8	12	44	16	15	11
Viscum cruciatum Sieber & Bioss	25	36	149	23	8	9

*Mean values for 10 strains; ♣, no acivity; IZD = 6 mm.

Table 3. Number of plant species (range of inhibition zone diameters in mm)

RAA	*P. acnes*	*S. aureus*	*E. coli*	*P. aeruginosa*	*P. vulgaris*	*K. pneumonia*
No activity	6 (6*)	11(6)	15 (6)	15 (6)	18 (6)	18 (6)
<30(Low activity)	39 (>6-10.8)	41 (7-16.7)	20(6.3 - 8)	39(6.7-12)	37(6.7-12)	38 (6.1-13.9)
30-60(Medium activity)	7(11.7-15.1)	4 (18.7-23.7)	17(8.3-11)	1 (18)	1(13.7)	0
≥60(High activity)	4 (20.8-25.1)	0	4 (12-22)	1 (22)	0	0

*Disc diameter = 6 mm.

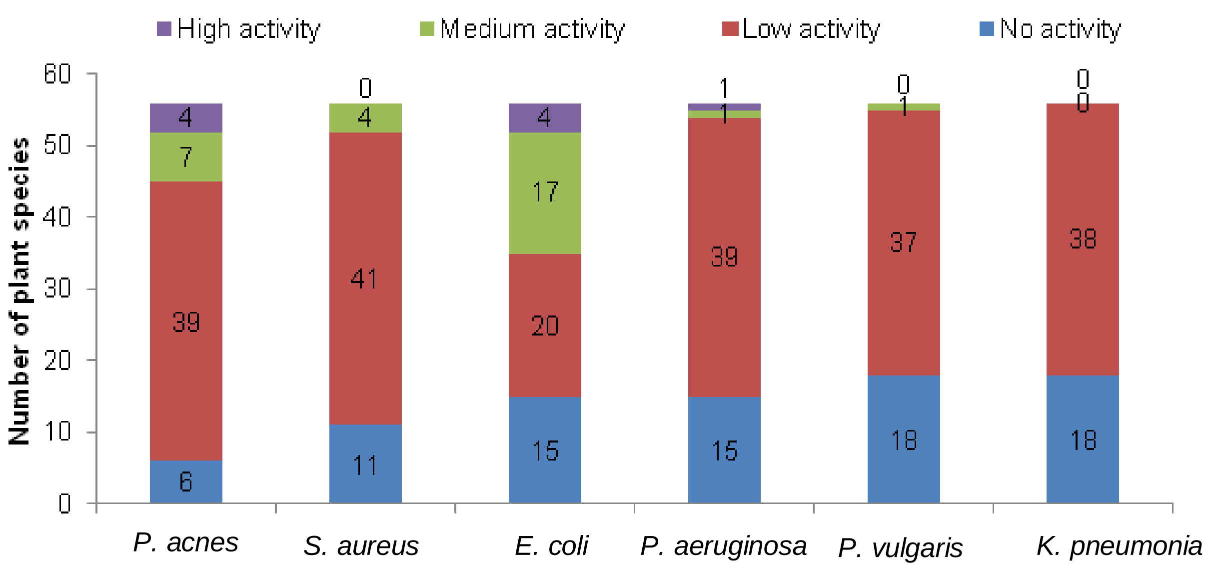

Figure 1. Number of plant spp by catagories of RAA against all test bacteria: no activity; low activity <30; medium, 30 to 60; high, ≥60.

against *P. acnes might* justify the extensive use of these agents for the treatment of skin disorders.

Plants can be efficient in the treatment of acne vulgaris because of four mechanisms including anti-bacterial, anti-inflammatory, anti-oxidant and anti-androgen activities (Azimi et al., 2012). The plants with essential oils (Baser et al., 2006; Peana et al., 1999), flavonoids (Takahashi et al., 2004), alkaloids (Takahashi et al., 2004), and phenolic compounds (Mishra et al., 2011) have antibacterial effects including inhibitory action against acne-inducing bacteria (Takahashi et al., 2004).

Among alkaloids, berberine also gives anti- inflammatory properties (Kumar et al., 2007). Phenolic compounds reveal a dose-dependent anti-oxidant activity that is directly related to the amount of total phenolic contents (Mishra et al., 2011). In addition, a polyphenol-rich extract

Table 4. *Propionibacterium acnes* IZ (mm diam)*, RAA, MIC, and MBC (mg/ml) (mean values for 10 strains) for the most active plants.

Plant	IZ±SE**	RAA±SE	MIC ±SE	MBC±SE
Ajuga orientalis	11.7±0.16	30.1±2.9	20±0	26±0.67
Clematis cirrhosa	10.7±0.1	26±1.26	25±0	28.4±0.27
Lactuca tuberosa	12.4±0.16	34±2.5	20±0	27.4±0.4
Lycium europeum	12±0	32±0.0	20±0	25±0
Majorana syriaca	10.5±0.14	24.8±1.93	29±0.67	31.6±0.27
Phagnalon rupestre	11.7±0.12	30±2	24.8±0.8	24±0.67
Pinus halepensis	15±0.33	50.3±6.5	10±0	15.2±0.53
Rhus coriaria	25±0.21	133.6±13.8	6±0	6±0
Ricinus communis	23±0.33	117±10	6±0	10±0
Salvia fruticosa	12.3±0.28	33.4±4.5	16.2±0.13	10±0
Sarcopoterium spinosum	22.8±0.34	114.5±10.2	6±0	21.6±0.27
Sinapis arvensis	20.8±0.21	96.4±5	10±0	23±0
Sonchus oleraceus	14±0	43±0.0	10±0	16±0
Viscum cruciatum	10.7±0.10	25.2±1.47	25.6±0.4	31.6±0.27
Reference antibiotic♣ (10 mg/disc)	21.3±0.8			

* Disc diameter, 6 (mm); ** standard error (SE); ♣ chloramphenicol.

Table 5. The inhibition zone (mm), RAA, MIC (mg/ml), and MBC (mg/ml) values of most active 10 medicinal plant extracts against 5 aerobic bacterial species. The results are shown as average values from three separate experiments.

Plant	*S. aureus*				*E. coli*				*P. aeruginosa*				*P. vulgaris*				*K. pneumonia*			
	RAA	IZ	MIC	MBC	RAA	IZ	MIC	MBC	RAA	IZ	MIC	MBC	RAA	IZ	MIC	MBC	RAA	IZ	MIC	MBC
Crataegus aronia	15	12±0.3	15±0	18±0	44	10±0	20±0	25±0	23	12±0	20±0.33	25±0.33	16	10±0	20±0.33	25±0	11	10±0	20±0	25±0
Lactuca tuberosa	15	12±0	20±0	20±0	42	9.3±0.3	25±0	30±0	16	10±0	20±0.33	25±0.33	6	6±0	>25	>30	4	6±0	>25	>30
Majorana syriaca	15	12±0	15±	21±0.67	54	11 ±0	14±0.33	21±0.67	22	11.7±0.3	14±0	20±0	19	11±0	12±0	20±0	18	12.7±0.3	15±0.67	20±0.33
Rhus coriaria	58	23.7±0.3	4±0	6±0	215	22 ±0	6±0	8±0	77	22±0	4±0	6±0.33	30	13.7±0.3	15±0	18±0	19	13±0	20±0	25±0
Ricinus communis	42	20 ±0	8±0	10±0	144	18 ±0	14±0.67	16±0	52	18± 0.7	14±0	16±0	6	6±0	>25	>30	21	13.9±0.3	12±0.67	15±0
Sarcopoterium spinosum	40	19.7±0.3	8±0	10±0	53	11 ±0	19±0.67	20±0	18	10.7±0.3	17±0.67	18±0	19	11±0	18±0	20±0	16	12±0	18±0	20±0
Satureja thymbra	14	11.7±0.3	11±0.33	16±0.33	64	12 ±0	12±0	16±0	23	12±0	12±0.67	17±0.67	23	12±0	12±0	16±0	16	12±0	11±0.33	16±0
Sinapis arvensis	13	11.3±0.3	18±0.33	20±0.33	42	9.7 ±0.3	20±0.33	25±0.33	21	11.3±0.3	20±0	25±0	14	9.3±0.7	20±0	25±0	10	9.3±0.3	21±0.33	26±0.67
Vicia faba	12	10.7±0.3	18±0.33	20±0.33	44	10 ±0.6	20±0	25±0	16	10 ±0	20±0	25±0	15	9.7±0.3	20±0	25±0	11	10±0	20±0	25±0
Viscum cruciatum	36	18.7 ±0.3	11±0.67	12±0	149	18.3±0.3	8±0	10±0	23	12 ±0	20±0	25±0	8	7±0	>25	>30	9	9±0	25±0	30±0
Reference antibiotic		31±0.6				15±0				25±0				25±0				30±0		

shows anti-androgen effect (Park et al., 2004; Dobrev, 2007). Bisnaphthquinones exhibit remarkable testosterone 5-alpha-reductase inhibitory activity (Gopal and Farahana, 2001).

Xanthohumol and the lupulones have inhibitory activities against acne-inducing bacteria (*P. acnes*, *S. epidermidis* and *S. aureus*), whereas xanthohumol exhibits higher activity in total oxygen radical absorbance capacity as well as single oxygen absorbance capacity (Yamaguchi et al., 2009). The three unsaturated fatty acids (oleic acid, linoleic acid and γ-linolenic acid) inhibit testosterone 5α-reductase action (Norimoto et al., 2010). Hence, combination use of *R. coriaria*, *S. arvensis*, *Pinus halepensis* can be so effective because they include essential oils, flavonoids, alkaloids, phenolic compound, fatty acids, etc, and have significant anti-bacterial, anti-inflammatory, anti-oxidant, and anti-androgen activities.

Studies on cell lines revealed that flavonoid, alkaloid, essential oil, phenol and phenolic compound, tannin, xanthone and xanthone derivative, and the bisnaphthquione derivative are effective in the treatment of acne (Azimi et al., 2012). Animal studies showed that diterpene acid, phenylpropanoid glycosides, acteoside and flavonoids have anti-inflammatory activity.

Literature review on the phytochemical constituents of the active plants in this study revealed that *R. coriaria* contains protocatechuic acid, isoquercitrin, and myricetin-3-0-a-L-rhamnoside (Shabana et al., 2011). Similarly, tannins, saponins, alkaloids, carbohydrates, phenols, flavonoids, sterols and resins are the major components of *R. communis* (Sundarasivarao et al., 1977; Rao et al., 1986; Biswas et al., 2002; Kensa and Yasmin, 2011). The presence of Catechin and epicatechin in *S. spinosum* (Rao et al., 2010), 1-butenyl isoithiocyanate, cubenol, dimethyl trisulfide, dimethyl tetrasulfide, octadecane, 6, 10, 14-tri methyl pentadecane-2-one and indole in *S. arvensis* (Al-Qudah et al., 2011), and caryophyllene oxide, thumbergol, and humulene oxide in *Pinus halepensis* (Abi-Ayad et al., 2011) has been reported.

The essential oil composition of *S. thymbra* comprises the following main constituents: carvacrol, thymol, *p*-cymene, and γ-terpinene, and very rarely α-pinene and sabinene (Giweli et al., 2012).

In addition, recent studies have indicated herbal medicines that are strong antioxidants and have many positive effects in oxidant related diseases (Hasani-Ranjbar et al., 2009). Among these strong antioxidants, Satureja (Momtaz and Abdollahi, 2010), Teucrium (Hasani-Ranjbar et al., 2010) or Urtica (Mehri et al., 2011) species can be numbered as those that remain to be examined in he management of acne vulgaris.

Interestingly, *R. coriaria* extract showed promising antibacterial activities against both *P. acnes* and all aerobic bacteria with the exception of *K. pneumonia*. Also, *R. communis* showed similar activities against all test bacteria except *P. vulgaris*. Our results are in agreement with those of other researches which indicated a strong inhibitory effect of *R. communis* and *R. coriaria* against different microorganisms including *E. coli*, *S. aureus*, and *B. subtilis* (Pesaramelli et al., 2012; Dulger and Gonuz, 2004). Being crude extracts, the overall antimicrobial activity screening results are still indicative of the potential of these herbal drugs as effective medicaments in the treatment of infectious skin disorders.

Based on the initial antimicrobial screening test, the most active plant extracts against bacterial strains were selected for further studies for the determination of MIC and MBC. These values indicate that the extracts of *R. coriaria* were the most potent against *P. acnes, S. aureus*, *E. coli*, *P. aeruginosa*. Similarly, extracts of *Satureja thymbra* was found to be potent against *P. vulgaris* and *K. pneumonia*. The results are in agreement with the initial antimicrobial screening test results.

The lowest MIC value observed was 4 mg/ml (MBC = 6 mg/ml), which was the MIC value of the hydroalcoholic extracts of *R. coriaria* on *S. aureus* and *P. aeruginosa*. On the other hand, the highest MIC value (amongst the most active plant extracts) was registered for *K. pneumoni* (the least sensitive bacterial strain) to the crude extracts of *V. crusiatum.*

In conclusion, all the plants investigated possessed activity against at least one strain of bacteria. The extensive use of these herbal drugs by the local people in treating various types of skin disorders might therefore be justified by their antimicrobial activities against different strains of bacteria, which are known to be responsible for causing various skin infections. The results also indicate that scientific studies carried out on medicinal plants having traditional claims of effectiveness might warrant fruitful results. Further studies aimed at the isolation and identification of active substances could also disclose compounds with better therapeutic value.

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