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Herbal remedies use by breast cancer patients in the West Bank of Palestine

Nidal Amin Jaradat^{a,*}, Ramzi Shawahna^b, Ahmad Mustafa Eid^a, Rowa Al-Ramahi^a,
Maes Kasem Asma^a, Abdel Naser Zaid^a^a Department of Pharmacy, Faculty of Medicine and Health Sciences, An-Najah National University, P.O. Box 7, Nablus, Palestine^b Physiology, Pharmacology and Toxicology Division, Faculty of Medicine and Health Sciences, An-Najah National University, P.O. Box 7, Nablus, Palestine

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ABSTRACT

Ethnopharmacological relevance: Recent ethnopharmacological surveys showed that herbal remedies are the most preferred modality of complementary and alternative medicine (CAM). In Palestine as in many other countries, herbal remedies are widely used in the treatment of many diseases.

Aim of the study: The aim of this study was to investigate the use of herbal remedies by women living with breast cancer in the West Bank of Palestine.

Methods: This study was a questionnaire based cross-sectional descriptive study on the use of herbal remedies by breast cancer patients in the West Bank. A questionnaire was distributed to 115 patients at outpatient cancer clinics in face to face interviews.

Results: The study had a response rate of 89.6%. Of all respondents, 68% were herbal remedies users. Women with breast cancer used 46 plant species belonging to 32 families. Of these, Brassicaceae and Lamiaceae were the most prevalent. *Ephedra alata* was the most commonly used plant species in the treatment of breast cancer. Leaves and seeds were the most commonly used parts and decoction was the most commonly used method of preparation. Herbal remedies users were more likely to use herbal remedies instead of chemotherapy. The most commonly stated reason for using herbal remedies was the belief in boosting the patient's immune system to fight cancer.

Conclusion: The use of herbal remedies is prevalent in breast cancer patients in Palestine. The use of herbal remedies was associated with educational level, time since diagnosis, type of surgery use, and use of endocrine therapy. It was apparent that the majority of users were satisfied with herbal remedies use. Clinical trials and pharmacological tests are required to be established for the presence of side effects, toxicity and efficacy for these herbal remedies.

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1. Introduction

Cancer is a deadly disease affecting millions of people around the globe. In the United States, one in every four deaths is attributed to cancer (Siegel et al., 2013). According to the statistics of the Palestinian Ministry of Health, the incidence of cancer in the West Bank in 2010 was about 53.7 per 100,000 of the Palestinian population (MoH, 2011). Of these cases, 18.8% were breast cancer (MoH, 2011).

To meet their healthcare needs, patients with cancer often seek therapies within as well as outside the allopathic therapy paradigm (Bauml et al., 2015). The term complementary and alternative medicine (CAM) has evolved to include a variety of

behavioral techniques and clinical approaches including the use of herbal remedies (Burstein et al., 1999). In Palestine as in many other countries, herbal remedies are widely used as CAM in cancer therapy (Ali-Shtayeh et al., 2011). Recent surveys showed that about two-thirds of cancer survivors used CAM (Bauml et al., 2015; Mao et al., 2007, 2011). Prior studies reported even a higher CAM use rates among breast cancer patients, ranging from 67% to 83% (Boon et al., 2000; Richardson et al., 2000). Patients might use CAM in addition to (complementary) or instead of (alternative) allopathic medications (Ali-Shtayeh et al., 2011).

CAM modalities are based heavily on centuries-old traditions. Unfortunately, safety and efficacy of many of these modalities have not been supported by scientific evidence (Bauml et al., 2015). However, recent studies demonstrated evidence for safety and efficacy for some of these modalities (Mao et al., 2014a, 2014b). Today, leading academic cancer centers are setting standards to

* Corresponding author.

E-mail address: nidaljaradat@najah.edu (N.A. Jaradat).

ensure conducting trials using CAM in a scientifically rigorous fashion (Bauml et al., 2015).

Surveys showed that approximately 3000 plant species were utilized as anticancer agents by various traditions around the globe (Cragg and Newman, 2005; Khazir et al., 2014). Accordingly, many dietary supplements and herbal extracts were shown to possess some anticancer activities *in vitro*. These anticancer activities include induction of apoptosis, inhibition of proliferation, inhibition of invasive behavior, induction of cell cycle arrest, and suppression of tumor angiogenesis (Cai et al., 2004; Deepa et al., 2012; Engel et al., 2011; Fang et al., 2013; Gaudet et al., 2004; Mohankumar et al., 2014; Sahpazidou et al., 2014; Shukla and Mehta, 2015; Soares et al., 2011). Probably, the presence of phenols and polyphenols in the plants was the main reason behind their activity against cancer cells. Other compounds with possible anticancer activity include flavonoids, tannins, stilbenes, diarylheptanoids, coumarins, phenolic acids, quinones and lignans (Cai et al., 2004; Deepa et al., 2012; Engel et al., 2011; Fang et al., 2013; Gaudet et al., 2004; Mohankumar et al., 2014; Sahpazidou et al., 2014; Shukla and Mehta, 2015; Soares et al., 2011).

The pattern of CAM use differs from country to country and from culture to another. Previous studies demonstrated that some clinical and sociodemographic factors such as gender, educational level, age, socioeconomic status were predictors of CAM use (Fouladbakhsh et al., 2005; Schernhammer et al., 2009). In Palestine, little is known on the use of CAM by cancer patients, especially women with breast cancer. This study was conducted to evaluate the pattern of CAM use among Palestinian women living with breast cancer, to investigate clinical and sociodemographic predictors of CAM use, and to identify perceived benefits from CAM use.

The study also aims to identify sources of information and the underlying reasons for CAM use. To our knowledge, no previously published study has investigated the pattern of CAM use among Palestinian women living with breast cancer.

2. Methods

This study was conducted in a cross-sectional observational design at outpatient oncology clinics in all governmental hospitals of the West Bank of Palestine. Outpatients attending the oncology clinics between January 2015 and June 2015 were enrolled in this study using a convenience sampling method.

The protocol and ethics of this study were approved by the Institutional Review Board (IRB) of An-Najah National University (protocol #25/Jan/015). All participants gave written informed consents before they took part in the study.

Participants were not offered any incentives and they were able to withdraw from the study at anytime. All data obtained were kept confidential. Participants were assured that refusal to participate in the study would not affect their future healthcare delivery in any way. Two trained research assistants conducted the face to face interviews.

2.1. Structured interview and validation of the questionnaire

Prior to developing and selecting items to be included in the questionnaire, the views of breast cancer patients on medicinal herbs and methods of preparing herbal remedies were explored by interviewing a group of 10 breast cancer patients. Patients were also asked from where they obtained information pertaining to herbal remedies.

The literature was searched and items included in previous studies in addition to the items identified during the interviews with the 10 breast cancer patients were selected and compiled

Table 1
Demographic and clinical characteristics of study population.

| Variables | Breast cancer patients | Prevalence (%) |
|-------------------------------------|------------------------|----------------|
| Age (years) | | |
| 16–29 | 4.00 | 3.90 |
| 30–39 | 10.0 | 9.70 |
| 40–49 | 31.0 | 30.1 |
| 50–59 | 48.0 | 46.6 |
| ≥ 60 | 10.0 | 9.70 |
| Educational level | | |
| Illiterate | 17.0 | 16.5 |
| Primary | 20.0 | 19.4 |
| Secondary | 37.0 | 35.9 |
| University | 29.0 | 28.2 |
| Household income | | |
| Low | 14.0 | 13.6 |
| Medium | 61.0 | 59.2 |
| High | 28.0 | 27.2 |
| Marital status | | |
| Single | 12.0 | 11.7 |
| Married | 74.0 | 71.8 |
| Other | 17.0 | 16.5 |
| Place of residence | | |
| City | 35.0 | 34.0 |
| Village | 58.0 | 56.3 |
| Camp | 10.0 | 9.70 |
| Cancer stage | | |
| Early | 20.0 | 19.4 |
| Intermediate | 33.0 | 32.0 |
| Late | 41.0 | 39.8 |
| Unknown | 9.00 | 8.74 |
| Time since diagnosis (years) | | |
| < 1 year | 47.0 | 45.6 |
| 2–3 years | 35.0 | 34.0 |
| ≥ 3 years | 21.0 | 20.4 |
| Type of surgery | | |
| None | 52.0 | 50.5 |
| Mastectomy | 51.0 | 49.5 |
| Chemotherapy | | |
| Yes | 87.0 | 84.5 |
| No | 16.0 | 15.5 |
| Radiotherapy | | |
| Yes | 68.0 | 66.0 |
| No | 35.0 | 34.0 |
| Endocrine therapy | | |
| Yes | 49.0 | 47.6 |
| No | 54.0 | 52.4 |
| Recurrence/metastasis | | |
| Yes | 17.0 | 16.5 |
| No | 70.0 | 68.0 |
| Unknown | 16.0 | 15.5 |

Table 2
Intentions to use CAM instead of chemotherapy.

| Do you intend to use herbal remedies instead of chemotherapy? | n | % | Current use of herbal remedies | | χ^2 | Odds ratio (95% CI) | P-value |
|---|------|------|--------------------------------|---------|----------|---------------------|----------|
| | | | User | Nonuser | | | |
| Yes | 70.0 | 68.0 | 69.0 | 1.0 | 81.196 | 500 | < 0.0001 |
| No | 33.0 | 32.0 | 4.0 | 29.0 | | (53.58–4670) | |

into a questionnaire. The questionnaire was piloted and revised twice on 12 breast cancer patients. The results obtained from the two pilot trials were not included in the analysis.

Two trained interviewers with experience in interviewing cancer patients administered the questionnaire on the participants of this study.

Data pertaining to sociodemographic information like age, educational level, marital status, place of residence, household income, cancer stage, the period relapsed since the patient was

Table 3
Association of different variables with the use of herbal remedies.

| Variables | n | % | Nonuser | User | χ^2 or Fisher's Exact Test | P- value | Correlation | P- value |
|-------------------------------------|------|------|---------|------|---------------------------------|----------|-------------|----------|
| Age (years) | | | | | | | | |
| 16–29 | 4.0 | 3.9 | 2.0 | 2.0 | 6.9 | 0.123 | 0.11 | |
| 30–39 | 10.0 | 9.7 | 5.0 | 5.0 | | | | |
| 40–49 | 31.0 | 30.1 | 11.0 | 20.0 | | | | |
| 50–59 | 48.0 | 46.6 | 10.0 | 38.0 | | | | |
| ≥ 60 | 10.0 | 9.7 | 5.0 | 5.0 | | | | |
| Educational level | | | | | | | | |
| Illiterate | 17.0 | 16.5 | 8.0 | 9.0 | 8.0 | 0.044 | 0.27 | < 0.01 |
| Primary | 20.0 | 19.4 | 10.0 | 10.0 | | | | |
| Secondary | 37.0 | 35.9 | 10.0 | 27.0 | | | | |
| University | 29.0 | 28.2 | 5.0 | 24.0 | | | | |
| Household income | | | | | | | | |
| Low | 14.0 | 13.6 | 6.0 | 8.0 | 2.4 | 0.298 | 0.15 | |
| Medium | 61.0 | 59.2 | 21.0 | 40.0 | | | | |
| High | 28.0 | 27.2 | 6.0 | 22.0 | | | | |
| Marital status | | | | | | | | |
| Single | 12.0 | 11.7 | 3.0 | 9.0 | 1.0 | 0.593 | 0.03 | |
| Married | 74.0 | 71.8 | 26.0 | 48.0 | | | | |
| Other | 17.0 | 16.5 | 4.0 | 13.0 | | | | |
| Place of residence | | | | | | | | |
| City | 35.0 | 34.0 | 12.0 | 23.0 | 0.664 | 0.780 | 0.06 | |
| Village | 58.0 | 56.3 | 19.0 | 39.0 | | | | |
| Camp | 10.0 | 9.7 | 2.0 | 8.0 | | | | |
| Cancer stage | | | | | | | | |
| Early | 20.0 | 19.4 | 6.0 | 14.0 | 4.4 | 0.214 | –0.16 | |
| Intermediate | 33.0 | 32.0 | 7.0 | 26.0 | | | | |
| Late | 41.0 | 39.8 | 15.0 | 26.0 | | | | |
| Unknown | 9 | 8.74 | 5 | 4 | | | | |
| Time since diagnosis (years) | | | | | | | | |
| < 1 year | 47.0 | 45.6 | 9.0 | 38.0 | 9.5 | 0.009 | –0.30 | < 0.01 |
| 2–3 years | 35.0 | 34.0 | 12.0 | 23.0 | | | | |
| ≥ 3 years | 21.0 | 20.4 | 12.0 | 9.0 | | | | |
| Type of surgery | | | | | | | | |
| None | 52.0 | 50.5 | 11.0 | 42.0 | 6.4 | 0.019 | –0.25 | < 0.05 |
| Mastectomy | 51.0 | 49.5 | 22.0 | 28.0 | | | | |
| Chemotherapy | | | | | | | | |
| Yes | 87.0 | 84.5 | 29.0 | 58.0 | 0.4 | 0.576 | 0.06 | |
| No | 16.0 | 15.5 | 4.0 | 12.0 | | | | |
| Radiotherapy | | | | | | | | |
| Yes | 68.0 | 66.0 | 19.0 | 49.0 | 1.5 | 0.266 | –0.12 | |
| No | 35.0 | 34.0 | 14.0 | 21.0 | | | | |
| Endocrine therapy | | | | | | | | |
| Yes | 49.0 | 47.6 | 11.0 | 38.0 | 3.9 | 0.058 | –0.20 | < 0.05 |
| No | 54.0 | 52.4 | 22.0 | 32.0 | | | | |
| Recurrence/metastasis | | | | | | | | |
| Yes | 17.0 | 16.5 | 7.0 | 13.0 | 4.2 | 0.124 | –0.08 | |
| No | 70.0 | 68.0 | 20.0 | 53.0 | | | | |
| Unknown | 16.0 | 15.5 | 6.0 | 4.0 | | | | |

diagnosed (times since diagnosis) with breast cancer, type of treatments the patient used, if the patient used herbal products or not, the names of herbal remedies used, reasons why the patient used these herbal remedies, who informed the patient about herbals remedies, methods of preparing herbal remedies and the sources of these herbals were collected.

2.2. Statistical analysis

Study participants were classified as either herbal remedies users or nonusers according to whether or not they used at least one herbal remedy in the past 6 months. Information on time of since diagnosis, stage of disease, and previous cancer treatments received were abstracted from the patients' medical records. Comparisons between categorical groups were performed using Pearson's Chi-Square (χ^2) or Fisher's Exact Tests, as appropriate. Correlation between categorical data was performed using Spearman's rank correlation. Odds ratios with their 95% confidence intervals (CI) were calculated through binary logistic regression using categorical data. Statistical significance was considered

when the *p*-value was less than 0.05. Data were treated using IBM SPSS for Windows v.21.0 (SPSS Inc., Chicago). All participants, without regard to the number of herbal modalities they used, were weighted equally in the analysis.

3. Results

3.1. Characteristics of participants

In this study, a total of 115 breast cancer patients were approached. Of those, 103 patients accepted to participate in the study and completed the questionnaire, giving a response rate of 89.6%. The demographic and clinical characteristics of the participants are shown in Table 1. The mean age was 48.84 years. Of all participants, 35.0% finished secondary school and 28.2% had high level of education. Most of patients (58.3%) had medium household income and most of them were married (71.8%). Around 50% of the patients received surgery. The majority of the patients received chemotherapy and radiotherapy as shown in Table 1.

Table 4
Most frequently used herbal remedies by breast cancer women in descending order by number of participants in the West Bank.

| Scientific name/English common name/Arabic name/ voucher number | Family | Used part | Method of preparation | Origin | Number of users |
|--|------------------|--------------|-----------------------|----------|-----------------|
| <i>Ephedra alata</i> Decne./Ephedra/Alanda/Pharm-PCT-904 | Ephedraceae | Aerial parts | Decoction | Local | 32 |
| <i>Arum palaestinum</i> Boiss./Cuckoo pint /loof/Pharm-PCT-246 | Araceae | Leaves | Decoction | Local | 26 |
| <i>Nigella arvensis</i> L./Black cumini/Kezha/Pharm-PCT-1640 | Ranunculaceae | Seeds | Decoction | Local | 26 |
| <i>Phoenix dactylifera</i> L./Date/Tamer/Pharm-PCT-1842 | Areaceae | Fruits | Eaten raw | Local | 21 |
| <i>Olea europaea</i> L./Olive/Zaatoon/ Pharm-PCT-1664 | Oleaceae | Fruits | Oil | Local | 21 |
| <i>Annona muricata</i> L./Soursop/Keshta/3289/HNC | Annonaceae | Fruit | Eaten raw | Imported | 17 |
| <i>Linum bienne</i> Mill./Flax/Ketan shaa'/harm-PCT-1431 | Linaceae | Seeds | Decoction | Imported | 14 |
| <i>Trigonella arabica</i> Delile/Fenugreek/Helba mora/Pharm-PCT-2511 | Leguminosae | Seeds | Infusion | Local | 13 |
| <i>Brassica oleracea</i> L./Cauliflower/Zahra/Pharm-PCT-406 | Brassicaceae | Flowers | Eaten raw | Local | 12 |
| <i>Allium albotunicatum</i> O.Schwarz/Garlic/Thom dladi/Pharm-PCT-74 | Amaryllidaceae | Bulb | Juice | Local | 11 |
| <i>Eruca sativa</i> Mill./salad rocket/Jarjer bari/Pharm-PCT-952 | Brassicaceae | Leaves | Eaten raw | Local | 11 |
| <i>Salvia fruticosa</i> Mill./Sage/Maryamya/Pharm-PCT-2117 | Lamiaceae | Aerial parts | Decoction | Local | 11 |
| <i>Camellia sinensis</i> (L.) Kuntze/Green Tea/Shae akhdar/30-s/00280 | Theaceae | Leaves | Decoction | Imported | 11 |
| <i>Crocus sativus</i> L./Saffron/Za'faran/V.N. 2669 | Iridaceae | Flowers | Infusion | Imported | 10 |
| <i>Avena sativa</i> L./Oat/Shofan normandi/Pharm-PCT-346 | Poaceae | Seeds | Infusion | Local | 10 |
| <i>Zingiber officinale</i> Roscoe/Ginger/Zangabil/PARK1003(ANH) | Zingiberaceae | Rhizomes | Infusion | Local | 10 |
| <i>Urtica urens</i> L./Small nettle/Korees harek/Pharm-PCT-2562 | Urticaceae | Aerial parts | Infusion | Local | 9 |
| <i>Taraxacum cyprium</i> H.Lindb./Common dandelion/Hindeba/Pharm-PCT-2395 | Compositae | Leaves | Decoction | Local | 8 |
| <i>Ziziphus spina-christi</i> (Mill.) Georgi/Christ's Jujube/Cedar, Anab/Pharm-PCT-2693 | Rhamnaceae | Flowers | Decoction | Local | 8 |
| <i>Petroselinum crispum</i> (Mill.) Fuss/Parsley/Bokdonas/V.N.126698 | Apiaceae | Fruits | Infusion | Local | 7 |
| <i>Drimys maritima</i> (L.) Stearn/Squill/Basal Alansal/Pharm-PCT-2553 | Asparagaceae | Juice | Infusion | Local | 7 |
| <i>Cinnamomum verum</i> J. Presl/ Cinnamon/Kerfa/BISH0000032747 | Lauraceae | Bark | Infusion | Imported | 7 |
| <i>Brassica oleracea</i> L./Red Cabbage/MLfof/Pharm-PCT-406 | Brassicaceae | Leaves | Juice | Local | 6 |
| <i>Cucurbita pepo</i> L./Pumpkin/Kare'a/080610-09 | Cucurbitaceae | Seeds | Infusion | Local | 6 |
| <i>Malva sylvestris</i> L./Common Malva/Khobeza/Pharm-PCT-1507 | Malvaceae | Leaves | Decoction | Local | 6 |
| <i>Sesamum indicum</i> L./Sesame/ semsem/v.n.109576 | Pedaliaceae | seeds | Eaten raw | Local | 6 |
| <i>Curcuma longa</i> L./Turmeric/Korkom/CL-RM-03-10-22. | Zingiberaceae | Rhizomes | Infusion | Imported | 6 |
| <i>Glycine soja</i> Siebold & Zucc./Soy/Soya/BBCGF20 | Leguminosae | Seeds | Decoction | Imported | 5 |
| <i>Beta vulgaris</i> L./Chard/ Seleq/Pharm-PCT-383 | Amaranthaceae | Leaves | Eaten raw | Local | 4 |
| <i>Matricaria aurea</i> (Loefl.) Sch.Bip./Golden Chamomile/Babonaj thahabi/Pharm-PCT-1519 | Lamiaceae | Flowers | Decoction | Local | 4 |
| <i>Melissa officinalis</i> L./lemon balm/Lewesa/Pharm-PCT-1564 | Lamiaceae | Leaves | Decoction | Local | 4 |
| <i>Rumex vesicarius</i> L./docks/Homeed/Pharm-PCT-2080 | Polygonaceae | Leaves | Eaten raw | Local | 4 |
| <i>Allium cepa</i> L./Onion/Bassal/Pharm-PCT-74 | Amaryllidaceae | Bulb | Eaten raw | Local | 3 |
| <i>Pimpinella anisum</i> L./Anise/Yanson/Pharm-PCT-1859 | Apiaceae | Fruits | Infusion | Local | 3 |
| <i>Capparis spinosa</i> L./Caper bush/Cobar/Pharm-PCT-496 | Capparaceae | Fruits | Infusion | Local | 3 |
| <i>Onopordum cynarocephalum</i> subsp. <i>cynarocephalum</i> /Artichoke Cotton-thistle/kondrees/Pharm-PCT-1692 | Compositae | Flowers | Decoction | Local | 3 |
| <i>Cyclamen persicum</i> Mill./Cyclamen/Za'amatoot/Pharm-PCT-777 | Primulaceae | Roots | Decoction | Local | 3 |
| <i>Sinapis arvensis</i> L./Wild mustard/Khardal/Pharm-PCT-2284 | Brassicaceae | Leaves | Decoction | Local | 2 |
| <i>Silybum marianum</i> (L.) Gaertn./Milk thistle/Khorfeesh/Pharm-PCT-2282 | Compositae | Seeds | Decoction | Local | 2 |
| <i>Aloe vera</i> (L.) Burm.f./Aloe/Sobar/Pharm-PCT-115 | Xanthorrhoeaceae | Juice | Infusion | Local | 2 |
| <i>Rhus coriaria</i> L./Sumac/Somac/Pharm-PCT-2037 | Anacardiaceae | Fruits | Decoction | Local | 1 |
| <i>Foeniculum vulgare</i> Mill./Fennel/Shomar/Pharm-PCT-1041 | Apiaceae | Leaves | Eaten raw | Local | 1 |
| <i>Origanum vulgare</i> L./Thyme/Za'atar/Pharm-PCT-1727 | Lamiaceae | Leaves | Decoction | Local | 1 |
| <i>Psidium guajava</i> L./Guava/Juafa/DPS 0015 | Myrtaceae | Leaves | Decoction | Local | 1 |
| <i>Verbascum sinuatum</i> L./Mullein/A'awarwar/Pharm-PCT-2604 | Scrophulariaceae | Leaves | Decoction | Local | 1 |
| <i>Vitis vinifera</i> L./Grapes/Anab/Pharm-PCT-2665 | Vitaceae | Leaves | Decoction | Local | 1 |

Among participants, 70 patients were herbal remedies users (68.0%), as shown in Table 2. When asked about their intentions to use CAM instead of chemotherapy, current users were more likely to say yes as compared with nonusers, as shown by the χ^2 -test and the calculated odds ratio (Table 2).

Comparing the characteristics of users and nonusers, parameters like educational level, time since diagnosis, type of surgery performed and the use of endocrine therapy were significantly associated, as shown by the χ^2 or Fisher's exact tests and Spearman's correlation coefficients (Table 3). Educational level was positively correlated; whereas, time since diagnosis, type of surgery received and use of endocrine therapy were negatively correlated with herbal therapy use (Table 3).

3.2. Herbal remedies

Sixty-eight percent of the participants reported that they used at least one herbal remedy in the last six months and most of them often used more than one herbal remedies at the same time. The

most commonly used herbal remedy among breast cancer women was *Ephedra alata* (32 patients) followed by *Nigella arvensis* and *Arum palaestinum* each was used by 26 patients while *Phoenix dactylifera* and *Olea europaea* were used by 21 patients each. *Annona muricata* (17 patients), *Linum bienne* (14 patients), and *Trigonella arabica* (13 patients) were also used. Other plants were used by less than 13 patients. Most of the utilized herbals were from local origin, while about 9% of the plants belonged to the Brassicaceae family, the same percentage was reported for Lamiaceae family and about 7% for each of the Apiaceae and Compositae families (Table 4).

Decoction was the most frequently reported method of preparation of herbal remedies used by the participants of this study for the treatment of breast cancer followed by infusion and eating the plants raw as shown in Fig. 1.

The most commonly used parts of the plants in the treatment of breast cancer were leaves. The rest of parts used are shown in Fig. 2.

Participants had wide variety of sources to obtain their herbal

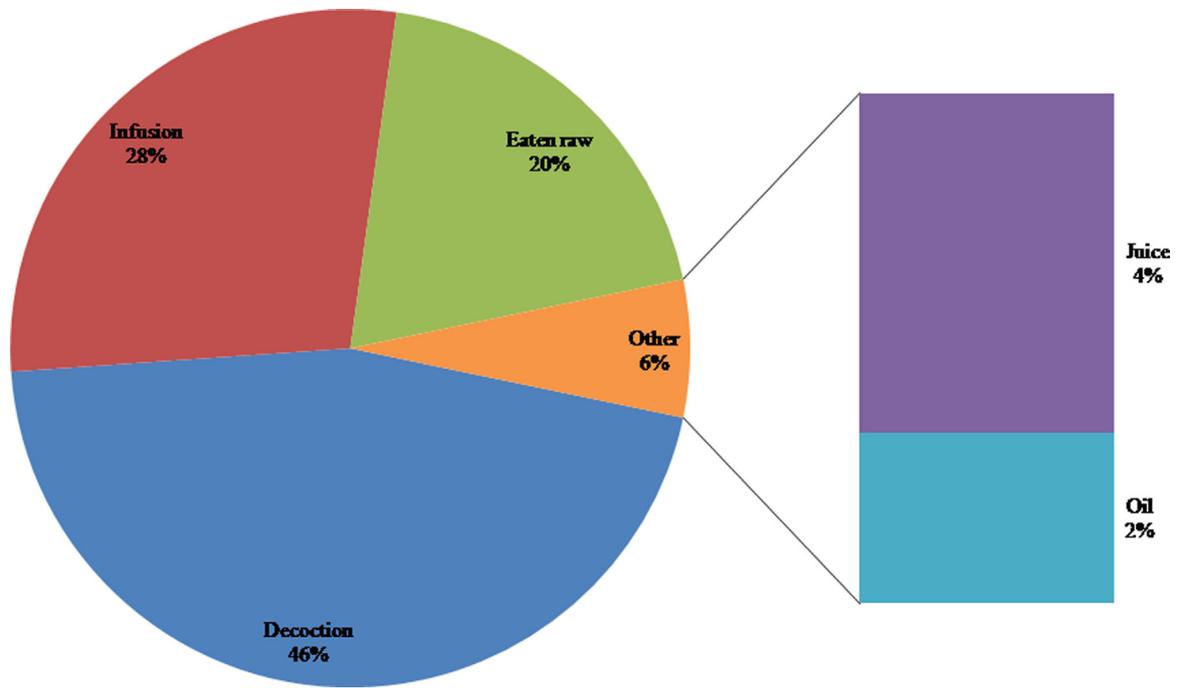


Fig. 1. Frequency of methods of preparation of herbal remedies used by Breast cancer women in this study.

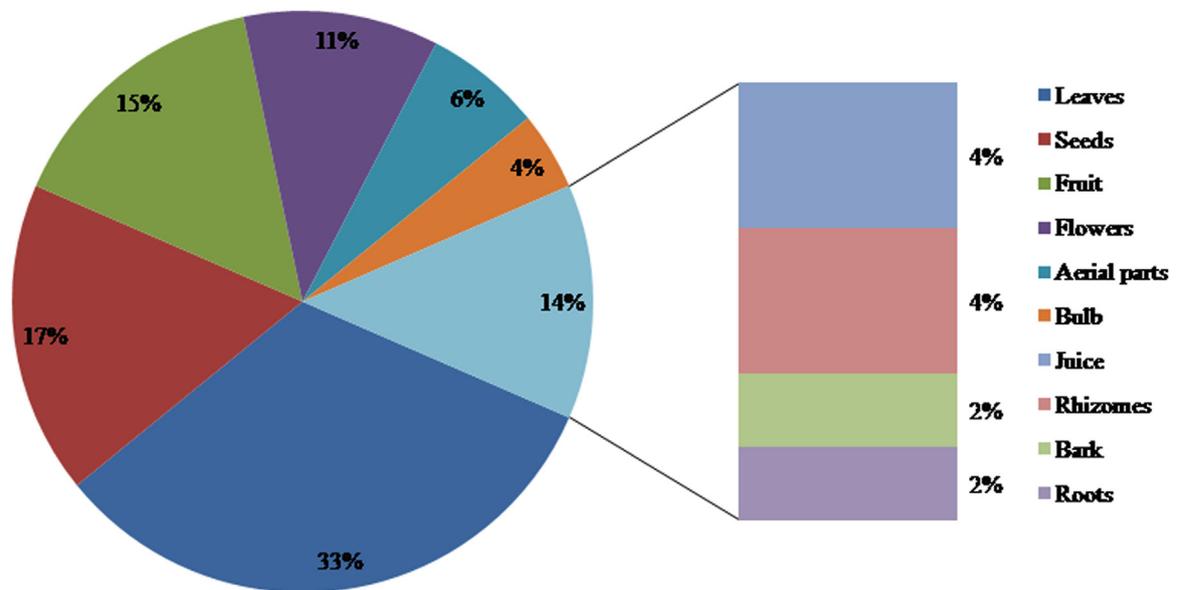


Fig. 2. Frequency of parts from the utilized plants in the treatments of breast cancer in the West Bank.

Table 5
Sources of herbals.

| Source | n | % |
|-------------|----|------|
| Wild life | 35 | 47.9 |
| Herbalists | 15 | 20.5 |
| Friends | 9 | 12.3 |
| Pharmacists | 1 | 1.4 |
| Undeclared | 13 | 17.8 |

remedies; these sources included wild life as a high percentage of the users were villagers (39%), herbal stores (herbalists), friends, pharmacies, and other sources (Table 5).

The sources from where participants obtained knowledge about herbal remedies are shown in Table 6. Many patients

Table 6
Sources of knowledge about herbal remedies.

| Source | n | % |
|----------------|----|------|
| Family friend | 19 | 26 |
| Other patients | 5 | 6.8 |
| Attar | 4 | 5.5 |
| Public media | 3 | 4.1 |
| Pharmacists | 2 | 2.7 |
| Doctors | 1 | 1.4 |
| Internet | 1 | 1.4 |
| Undeclared | 38 | 52.1 |

Table 7
Stated reasons for using herbal remedies.

| Reason | n | % |
|--|----|------|
| Herbal remedies enhance immunity | 30 | 41.1 |
| I was advised to use herbal remedies | 15 | 20.5 |
| Herbal remedies are available and affordable | 9 | 12.3 |
| I don't believe in chemotherapy | 6 | 8.2 |
| Use of herbal remedies is safe | 5 | 6.8 |
| Herbal remedies are effective | 3 | 4.1 |
| I have sufficient experience and information about herbal remedies | 2 | 2.7 |
| Herbal remedies improve chemotherapy and reduces side effects | 2 | 2.7 |
| Herbal remedies reduce pain and fatigue | 1 | 1.4 |

Table 8
Stated reasons for not using herbal remedies.

| Reason | n | % |
|--|----|------|
| I don't have enough information on herbal remedies | 14 | 46.7 |
| I am not convinced that herbal remedies are better than chemotherapy | 13 | 43.3 |
| Herbal remedies might have serious side effects | 3 | 10.0 |

obtained knowledge from family friends and other patients as shown in Table 6.

3.3. The reasons for using herbal remedies

Breast cancer women gave various reasons for the use herbal remedies. When they were asked to provide a primary reason for the particular herbal remedies use, the most commonly reported reason was to enhance the immune system (41.1%). Other reported reasons are shown in Table 7.

When the nonusers were asked why they did not use CAM, 46.7% answered that they do not have enough information about herbal remedies and 43.3% said they do not believe that herbal remedies, as shown in Table 8.

Table 9
Summary of published *in vivo* and *in vitro* activity of the most frequently used plants against cancer.

| Plant species | Reported ethnopharmacological use with reference source | <i>In vivo</i> and <i>in vitro</i> activity against breast cancer with reference source | Side effects and toxicity with reference source |
|----------------------------|---|--|---|
| <i>Ephedra alata</i> | No reference found for ethnopharmacological usage against breast cancer | Evidence for <i>in vitro</i> cytotoxic and cytostatic effects (Kmail et al., 2015) | No reference |
| <i>Arum palaestinum</i> | Reported usage in ethnomedicine in Palestine (Jaradat et al., 2014), Jordan (Oran and Al-Eisawi, 2015) and Turkey (Yesilada, 2008). | Evidence for <i>in vitro</i> apoptotic and antimetabolic (cytostatic) effects (Husein et al., 2014; Diab-Assaf et al., 2012). Evidence for anticancer activity against both breast carcinoma and lymphoblastic leukemia cells (El-Desouky et al., 2007). | Leaves and other plant parts can cause vomiting and swelling in the mouth and throat mucous membranes (Jaradat et al., 2015; Wink, 2010). |
| <i>Nigella arvensis</i> | Reported usage in ethnomedicine in Palestine (Jaradat et al., 2014), Turkey (Everest and Ozturk, 2005) and Ukraine (Mosyakin and Yavorska, 2002). | Thymoquinone and β -elemene were isolated from <i>Nigella</i> seeds oil showed potential anticancer activities (Edris, 2009). | No reference |
| <i>Phoenix dactylifera</i> | Reported usage in ethnomedicine in Morocco (Kabbaj et al., 2012) Pakistan (Manzoor et al., 2012), Iran (Javadi et al., 2015), Saudi Arabia (Al-Musayeb et al., 2012), and Egypt (Aboul-Enein et al., 2012). | Aqueous extract of fruit showed evidence for antimutagenic activity (Ishurd and Kennedy, 2005; Vayalil, 2002) | No reference |
| <i>Olea europaea</i> | Reported usage in folk medicine in Morocco (Kabbaj et al., 2012), Egypt (Aboul-Enein et al., 2012) and Greece (Simopoulos, 2004). | Oil and particularly its phenolic compounds showed a broad spectrum of anti-cancer effects (Cardeno et al., 2013). | No reference |
| <i>Annona muricata</i> | Reported usage in ethnomedicine in Nigeria and Peru (Bussmann and Glenn, 2011; Hutghinson and Dalziel, 1958). | Evidence for <i>in vitro</i> antineoplastic activity of the n-butanolic leaf extract (George et al., 2012) | No reference |
| <i>Linum bienne</i> | Reported usage in ethnomedicine in Palestine (Ali-Shtayeh et al., 2000) | No reference | No reference |
| <i>Trigonella arabica</i> | Reported use in traditional medicine in India (Umasanker and Shruti, 2011), Ethiopia (Abera, 2003) and Pakistan (Saeed et al., 2014). | Evidence for <i>in vitro</i> and <i>in vivo</i> activity against breast cancer (Amin et al., 2005; Khoja et al., 2011). | Seeds may have hypoglycemic effect (Puri et al., 2002). |

4. Discussion

Across different cultures, the use of herbal remedies has evolved as the most preferred CAM modality (Afifi et al., 2010; Akyol and Öz, 2011; Ali-Shtayeh et al., 2011). The current study is the first attempt to qualify and quantify the use of herbal remedies among women living with breast cancer in the West Bank of Palestine.

Recent statistics showed that cancer is the third leading cause of death in Palestine after cardiovascular and cerebrovascular diseases (Ali-Shtayeh et al., 2011; MoH, 2011).

Our findings showed that 68% of the breast cancer patients included in this study used herbal remedies. These results were not surprising and were in line with previous studies in which cancer patients in Palestine believed in the healing effects of medicinal herbs (Ali-Shtayeh and Jamous, 2006; Ali-Shtayeh et al., 2011). These results were concordant with those shown in another study involving cancer patients in which about 61% of the patients indicated that they used herbal remedies (Ali-Shtayeh et al., 2011). Studies in neighboring countries showed that CAM was commonly used and herbal remedies appeared to be the preferred modality in Jordan, Egypt, Lebanon, Syria and Turkey (AbouZid and Mohamed, 2011; Afifi et al., 2010; Akyol and Öz, 2011; Deeb et al., 2013).

Preliminary comparisons with χ^2 or Fisher's exact analyses showed that herbal remedies users and nonusers differed with respect to educational level, time since diagnosis, and type of surgery performed. In line with our findings, Schernhammer et al. demonstrated that patients with more formal education were more likely to believe that CAM was valuable in cancer therapy (Schernhammer et al., 2009). However, users and nonusers did not differ with respect to age, household income, marital status, place of residence, cancer stage, metastasis, use of chemotherapy and radiotherapy. Using nonparametric correlation showed that education positively correlated with herbal remedies use. However, time since diagnosis, type of surgery performed and use of endocrine therapy negatively correlated with herbal remedies use. Contrary to some of our findings, Fouladbakhsh et al. showed that

gender, marital status, cancer stage, cancer treatment, and number of severe symptoms experienced were predictors of CAM use (Fouladbakhsh et al., 2005).

The study showed that 46 plant species were used with various methods of preparation. The most commonly used plants among breast cancer women were *E. alata*, *N. arvensis* and *A. palaestinum*. These findings were not surprising, as *E. alata* was recently publicized and portrayed as effective cancer herbal remedy by the Palestinian public media. Probably, this could be the reason behind its wide use among the study participants. Similarly, *A. palaestinum* is the most famous herb used in the treatment of cancer in Palestine (Ali-Shtayeh and Jamous, 2006; Ali-Shtayeh et al., 2011). Investigations showed that *A. palaestinum* contains antioxidants, that may in part, explain its anticancer activity (Ali-Shtayeh and Jamous, 2006; Ali-Shtayeh et al., 2011). Kmail et al. investigated the activity of *E. alata* in mono and co-cultures of HepG2 and human THP-1 derived macrophages (Kmail et al., 2015). The study concluded that the traditionally promised anticancer activity could be explained, in part, by its cytostatic effects. Interestingly, the plant is not toxic, edible and widely used in the Palestinian folk food and medicine (Ali-Shtayeh and Jamous, 2006; Ali-Shtayeh et al., 2011). *In vitro* investigations using *A. palaestinum* showed that it possessed cytotoxic activity which correlated with its phenolic contents (Husein et al., 2014). In another study El-Desouky et al. isolated a new pyrrole alkaloid *A. palaestinum* which suppressed proliferation of both breast carcinoma and lymphoblastic leukemia cells (El-Desouky et al., 2007). This suppression was shown to be dose-dependent. Investigations conducted in Jordan and Turkey reported similar uses.

Many of the other plants used by participants of this study were previously used for their promised effects against cancer (Abarzua et al., 2007; Asare et al., 2015; Edris, 2009; El-Desouky et al., 2007; Ishurd and Kennedy, 2005; Prabhu and Krishnamoorthy, 2010). Many of these plants are edible and widely used in folk foods. This might suggest that these edible plants might be nontoxic or have low toxicity. However, their safety should not be overestimated as some *T. arabica* species were reported to have hypoglycemic effect (Puri et al., 2002).

In this study, about 9% of the plants used by participants belonged to the Brassicaceae and Lamiaceae families. Not surprisingly, as many plants belonging to these families may possess, at least *in vitro*, anticancer activity (Jahangir et al., 2009; Taborsky et al., 2012). Interestingly, most of the utilized herbals in this study were from local origin as the main source of herbals was from wildlife. In a previous study, Ali-Shtayeh et al. showed that the majority of herbal remedies used by cancer patients in Palestine were of local origin (Ali-Shtayeh et al., 2011).

In this study, decoction was the most commonly used method among patients followed by infusion. These results were concordant with those previously reported in Ali-Shtayeh et al. (2011). Decoction and infusion can exhaustively extract the active ingredients. However, as decoction involves boiling the constituents, the method could be harmful, especially, when the active ingredients are heat labile substances.

In this study, 41.1% of the participants thought that the herbal remedies can boost their immune system to push it to fight cancer. Our results were in line with those shown by Boon et al. in which breast cancer survivors used CAM most often in an attempt to boost the immune system (Boon et al., 2000).

Our study showed that the most commonly used parts of plants were leaves and seeds. These results were concordant with prior studies in the domain. Leaves and seeds of many herbals were previously used by cancer patients in Palestine as shown in Ali-Shtayeh et al. (2011).

4.1. A brief literary review of the most frequently used plants by breast cancer patients in this study

In this study *E. alata*, *A. palaestinum*, *N. arvensis*, *P. dactylifera*, *O. europaea*, *A. muricata*, *L. bienne* and *T. arabica* were the most frequently used plants by breast cancer patients. Table 9 summarizes published *in vivo* and *in vitro* activity of these frequently used plants against cancer.

5. Conclusions

The prevalence of herbal remedies use among breast cancer patients in Palestine was not known. This survey showed that the use of herbal remedies was prevalent in breast cancer patients in Palestine. The use of herbal remedies was associated with educational level, time since diagnosis, type of surgery use, and use of endocrine therapy. It was apparent that the majority of users were satisfied with CAM use. Clinical trials and pharmacological tests are required to be established for the presence of side effects, toxicity and efficacy for these herbal remedies.

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Conflict of interests

Authors declare no conflicts of interests.

References

- Abarzua, S., Szewczyk, M., Gailus, S., Richter, D.-U., Ruth, W., Briese, V., Piechulla, B., 2007. Effects of phytoestrogen extracts from *Linum usitatissimum* on the Jeg3 human trophoblast tumour cell line. *Anticancer Res.* 27, 2053–2058.
- Abera, B., 2003. Medicinal plants used in traditional medicine in Jimma Zone, Oromia, Southwest Ethiopia. *Ethiop. J. Health Sci.* 13, 2–8.
- Aboul-Enein, A.M., El-Ela, F.A., Shalaby, E.A., El-Shemy, H.A., 2012. Traditional medicinal plants research in Egypt: studies of antioxidant and anticancer activities. *J. Med. Plant Res.* 6, 689–703.
- AbouZid, S.F., Mohamed, A.A., 2011. Survey on medicinal plants and spices used in Beni-Sueif, Upper Egypt. *J. Ethnobiol. Ethnomed.* 7, 18.
- Afiifi, F.U., Wazaify, M., Jabr, M., Treish, E., 2010. The use of herbal preparations as complementary and alternative medicine (CAM) in a sample of patients with cancer in Jordan. *Complement. Ther. Clin. Pr.* 16, 208–212.
- Akyol, A.D., Öz, B., 2011. The use of complementary and alternative medicine by patients with cancer: in Turkey. *Complement. Ther. Clin. Pract.* 17, 230–234.
- Al-Musayeib, N.M., Mothana, R.A., Al-Massarani, S., Matheussen, A., Cos, P., Maes, L., 2012. Study of the *in vitro* antiplasmodial, antileishmanial and anti-trypansomal activities of medicinal plants from Saudi Arabia. *Molecules* 17, 11379–11390.
- Ali-Shtayeh, M., Jamous, R.M., 2006. Ethnobotany of Palestinian herbal medicine in the northern West Bank and Gaza Strip: review and comprehensive field study. *Biodivers. Environ. Sci. Stud. Ser.* 4, 1–122.
- Ali-Shtayeh, M.S., Jamous, R.M., Jamous, R.M., 2011. Herbal preparation use by patients suffering from cancer in Palestine. *Complement. Ther. Clin. Pract.* 17, 235–240.
- Ali-Shtayeh, M.S., Yaniv, Z., Mahajna, J., 2000. Ethnobotanical survey in the Palestinian area: a classification of the healing potential of medicinal plants. *J. Ethnopharmacol.* 73, 221–232.
- Amin, A., Alkaabi, A., Al-Falasi, S., Daoud, S.A., 2005. Chemopreventive activities of *Trigonella foenum graecum* (Fenugreek) against breast cancer. *Cell Biol. Int.* 29, 687–694.
- Asare, G.A., Afriyie, D., Ngala, R.A., Abutiati, H., Doku, D., Mahmood, S.A., Rahman, H., 2015. Antiproliferative activity of aqueous leaf extract of *Annona muricata* L. on the prostate, BPH-1 cells, and some target genes. *Integr. Cancer Ther.* 14, 65–74.
- Bauml, J.M., Chokshi, S., Schapira, M.M., Im, E.O., Li, S.Q., Langer, C.J., Ibrahim, S.A., Mao, J.J., 2015. Do attitudes and beliefs regarding complementary and

- alternative medicine impact its use among patients with cancer? A cross-sectional survey. *Cancer* 121, 2431–2438.
- Boon, H., Stewart, M., Kennard, M.A., Gray, R., Sawka, C., Brown, J.B., McWilliam, C., Gavin, A., Baron, R.A., Aaron, D., 2000. Use of complementary/alternative medicine by breast cancer survivors in Ontario: prevalence and perceptions. *J. Clin. Oncol.* 18, 2515–2521.
- Burstein, H.J., Gelber, S., Guadagnoli, E., Weeks, J.C., 1999. Use of alternative medicine by women with early-stage breast cancer. *N. Engl. J. Med.* 340, 1733–1739.
- Bussmann, R.W., Glenn, A., 2011. Traditional knowledge for modern ailments—plants used for the treatment of diabetes and cancer in Northern Perú. *J. Med. Plants Res.* 5, 6916–6930.
- Cai, Y., Luo, Q., Sun, M., Corke, H., 2004. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. *Life Sci.* 74, 2157–2184.
- Cardeno, A., Sanchez-Hidalgo, M., Alarcón-De-La-Lastra, C., 2013. An up-date of olive oil phenols in inflammation and cancer: molecular mechanisms and clinical implications. *Curr. Med. Chem.* 20, 4758–4776.
- Cragg, G.M., Newman, D.J., 2005. Plants as a source of anti-cancer agents. *J. Ethnopharmacol.* 100, 72–79.
- Deeb, T., Knio, K., Shinwari, Z.K., Kreydiyyeh, S., Baydoun, E., 2013. Survey of medicinal plants currently used by herbalists in Lebanon. *Pak. J. Bot.* 45, 543–555.
- Deepa, M., Sureshkumar, T., Satheeshkumar, P.K., Priya, S., 2012. Purified mulberry leaf lectin (MLL) induces apoptosis and cell cycle arrest in human breast cancer and colon cancer cells. *Chem. Biol. Interact.* 200, 38–44.
- Diab-Assaf, M., Taleb, R., Shebaby, W., Mansour, A., Moussa, C., Daher, C., Mroueh, M., 2012. Antioxidant and anticancer activities of methanolic, ethyl acetate and chloroform extracts of *Arum palaestinum*. *Planta Med.* 78, 1389–1399.
- Edris, A.E., 2009. Anti-cancer properties of *Nigella* spp. essential oils and their major constituents, thymoquinone and β -elemene. *Curr. Clin. Pharmacol.* 4, 43–46.
- El-Desouky, S., Kim, K.H., Ryu, S.Y., Eweas, A.F., Gamal-Eldeen, A.M., Kim, Y.-K., 2007. A new pyrrole alkaloid isolated from *Arum palaestinum* Boiss. and its biological activities. *Arch. Pharm. Res.* 30, 927–931.
- Engel, N., Oppermann, C., Falodun, A., Kragl, U., 2011. Proliferative effects of five traditional Nigerian medicinal plant extracts on human breast and bone cancer cell lines. *J. Ethnopharmacol.* 137, 1003–1010.
- Everest, A., Ozturk, E., 2005. Focusing on the ethnobotanical uses of plants in Mersin and Adana provinces (Turkey). *J. Ethnobiol. Ethnomed.* 1, 1–6.
- Fang, X.-Y., Chen, W., Fan, J.-T., Song, R., Wang, L., Gu, Y.-H., Zeng, G.-Z., Shen, Y., Wu, X.-F., Tan, N.-H., 2013. Plant cyclopeptide RA-V kills human breast cancer cells by inducing mitochondria-mediated apoptosis through blocking PDK1-AKT interaction. *Toxicol. Appl. Pharmacol.* 267, 95–103.
- Fouladbakhsh, J.M., Stommel, M., Given, B.A., Given, C.W., 2005. Predictors of use of complementary and alternative therapies among patients with cancer. *Oncol. Nurs. Forum* 32, 1115–1122.
- Gaudet, M.M., Britton, J.A., Kabat, G.C., Steck-Scott, S., Eng, S.M., Teitelbaum, S.L., Terry, M.B., Neugut, A.I., Gammon, M.D., 2004. Fruits, vegetables, and micronutrients in relation to breast cancer modified by menopause and hormone receptor status. *Cancer Epidemiol. Biomarkers Prev.* 13, 1485–1494.
- George, V.C., Kumar, D., Rajkumar, V., Suresh, P., Kumar, R.A., 2012. Quantitative assessment of the relative antineoplastic potential of the n-butanolic leaf extract of *Annona muricata* Linn. in normal and immortalized human cell lines. *Asian Pac. J. Cancer Prev.* 13, 699–704.
- Husein, A.I., Ali-Shtayeh, M.S., Jondi, W.J., Zatar, N.A., Abu-Reidah, I.M., Jamous, R.M., 2014. In vitro antioxidant and antitumor activities of six selected plants used in the Traditional Arabic Palestinian herbal medicine. *Pharm. Biol.* 52, 1249–1255.
- Hutghinson, J., Dalziel, J., 1958. *Flora of West Tropical Africa*.
- Ishurd, O., Kennedy, J.F., 2005. The anti-cancer activity of polysaccharide prepared from Libyan dates (*Phoenix dactylifera* L.). *Carbohydr. Polym.* 59, 531–535.
- Jahangir, M., Kim, H.K., Choi, Y.H., Verpoorte, R., 2009. Health-affecting compounds in Brassicaceae. *Compr. Rev. Food Sci. Food Saf.* 8, 31–43.
- Khazir, J., Mir, B.A., Pilcher, L., Riley, D.L., 2014. Role of plants in anticancer drug discovery. *Phytochem. Lett.* 7, 173–181.
- Jaradat, N., Zaid, A.N., Vincieri, F.F., Asmaa, M., 2014. Medicinal herbs and methodologies for their pharmaceutical compounding in the West Bank/Palestine. *Complement. Ther. Clin. Pract.* 20, 280–284.
- Jaradat, N.A., Assali, M., Zaid, A.N., 2015. Variations of exhaustive extraction yields and methods of preparations for (*Arum palaestinum*) Solomon's lily plant in all regions of West Bank/Palestine. *Int. J. Pharmacogn. Phytochem. Res.* 7, 356–360.
- Javadi, B., Iranshahy, M., Emami, S.A., 2015. Anticancer plants in Islamic traditional medicine.
- Kabbaj, F., Meddah, B., Cherrah, Y., Faouzi, E., 2012. Ethnopharmacological profile of traditional plants used in Morocco by cancer patients as herbal therapeutics. *Phytopharmacology* 2, 243–256.
- Khoja, K.K., Shaf, G., Hasan, T.N., Syed, N.A., Al-Khalifa, A.S., Al-Assaf, A.H., Alshatwi, A.A., 2011. Fenugreek, a naturally occurring edible spice, kills MCF-7 human breast cancer cells via an apoptotic pathway. *Asian Pac. J. Cancer Prev.* 12, 3299–3304.
- Kmail, A., Lyoussi, B., Zaid, H., Saad, B., 2015. In vitro assessments of cytotoxic and cytostatic effects of *Asparagus aphyllus*, *Crataegus aronia*, and *Ephedra alata* in monocultures and co-cultures of Hepg2 and THP-1-derived macrophages. *Pharmacog. Comm.* 5, 165–172.
- Manzoor, M., Jan Durrani, M., Jabeen, R., Irfan, S., Ayub, F., Bibi, S., 2012. An ethno botanical study for the treatment of cancer and malaria used by the people of Quetta City. *Int. J. Basic Appl. Sci.* 1, 137–149.
- Mao, J.J., Farrar, J.T., Bruner, D., Zee, J., Bowman, M., Seluzicki, C., DeMichele, A., Xie, S.X., 2014a. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: a randomized trial. *Cancer* 120, 3744–3751.
- Mao, J.J., Farrar, J.T., Xie, S.X., Bowman, M.A., Armstrong, K., 2007. Use of complementary and alternative medicine and prayer among a national sample of cancer survivors compared to other populations without cancer. *Complement. Ther. Med.* 15, 21–29.
- Mao, J.J., Palmer, C.S., Healy, K.E., Desai, K., Amsterdam, J., 2011. Complementary and alternative medicine use among cancer survivors: a population-based study. *J. Cancer Surviv.* 5, 8–17.
- Mao, J.J., Xie, S.X., Farrar, J.T., Stricker, C.T., Bowman, M.A., Bruner, D., DeMichele, A., 2014b. A randomised trial of electro-acupuncture for arthralgia related to aromatase inhibitor use. *Eur. J. Cancer* 50, 267–276.
- MoH, 2011. Palestinian Health Information Center, Ministry of Health. Health Status in Palestine 2010. Ministry of Health, Nablus.
- Mohankumar, K., Pajaniradje, S., Sridharan, S., Singh, V.K., Ronsard, L., Banerjee, A. C., Benson, C.S., Coumar, M.S., Rajagopalan, R., 2014. Mechanism of apoptotic induction in human breast cancer cell, MCF-7, by an analog of curcumin in comparison with curcumin—an in vitro and in silico approach. *Chem. Biol. Interact.* 210, 51–63.
- Mosyakin, S.L., Yavorska, O.G., 2002. The Nonnative Flora of the Kyiv (Kiev) urban area, Ukraine: a checklist and brief analysis. *Urban Habitats* 1, 45–65.
- Oran, S.A., Al-Eisawi, D.M., 2015. Ethnobotanical survey of the medicinal plants in the central mountains (North–South) in Jordan. *J. Biodivers. Environ. Sci.* 6, 381–400.
- Prabhu, A., Krishnamoorthy, M., 2010. Anticancer activity of *Trigonella foenum-graecum* on Ehrlich Ascites carcinoma in *Mus musculus* system. *J. Pharm. Res.* 3, 3.
- Puri, D., Prabhu, K.M., Murthy, P.S., 2002. Mechanism of action of a hypoglycemic principle isolated from fenugreek seeds. *Indian J. Physiol. Pharmacol.* 46, 457–462.
- Richardson, M.A., Sanders, T., Palmer, J.L., Greisinger, A., Singletary, S.E., 2000. Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. *J. Clin. Oncol.* 18, 2505–2514.
- Saeed, H.M.K., Shahzad, Q., Iqbal, I., Nawaz, S., Bano, Q., Irfan, M., Wahid, M., 2014. Check list of ethno pharmacological important plants of Pakistan. *Int. J. Bioassays* 3, 3178–3182.
- Sahpazidou, D., Geromichalos, G.D., Stagos, D., Apostolou, A., Haroutounian, S.A., Tsatsakis, A.M., Tzanakakis, G.N., Hayes, A.W., Kouretas, D., 2014. Anticarcinogenic activity of polyphenolic extracts from grape stems against breast, colon, renal and thyroid cancer cells. *Toxicol. Lett.* 230, 218–224.
- Schernhammer, E.S., Haidinger, G., Waldhor, T., Vutuc, C., 2009. Attitudes about the use of complementary and alternative medicine in cancer treatment. *J. Altern. Complement. Med.* 15, 1115–1120.
- Shukla, S., Mehta, A., 2015. Anticancer potential of medicinal plants and their phytochemicals: a review. *Braz. J. Bot.* 38, 1–12.
- Siegel, R., Naishadham, D., Jemal, A., 2013. Cancer statistics, 2013. *CA Cancer J. Clin.* 63, 11–30.
- Simopoulos, A., 2004. The traditional diet of Greece and cancer. *Eur. J. Cancer Care* 13, 219–230.
- Soares, R., Meireles, M., Rocha, A., Pirraco, A., Obiol, D., Alonso, E., Joos, G., Balogh, G., 2011. Maitake (D fraction) mushroom extract induces apoptosis in breast cancer cells by BAK-1 gene activation. *J. Med. Food* 14, 563–572.
- Taborsky, J., Kunt, M., Kloucek, P., Lachman, J., Zeleny, V., Kokoska, L., 2012. Identification of potential sources of thymoquinone and related compounds in Assteraceae, Cupressaceae, Lamiaceae, and Ranunculaceae families. *Cent. Eur. J. Chem.* 10, 1899–1906.
- Umashanker, M., Shruti, S., 2011. Traditional Indian herbal medicine used as anti-pyretic, antiulcer, anti-diabetic and anticancer: a review. *Int. J. Res. Pharm. Chem.* 1, 1152–1159.
- Vayalil, P.K., 2002. Antioxidant and antimutagenic properties of aqueous extract of date fruit (*Phoenix dactylifera* L. Arecaceae). *J. Agric. Food Chem.* 50, 610–617.
- Wink, M., 2010. Mode of action and toxicology of plant toxins and poisonous plants. *Julius-Kühn-Archiv*, 93–99.
- Yesilada, E., 2008. Novel drug leads from Turkish medicinal plants with diverse pharmacological effects. *Drugs Future* 33, 673–680.