

A Systematic Literature Review: The Effect of Date Palms (*Phoenix dactylifera*) toward Breast Cancer MCF-7 Cell Line.

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Abstract

Breast cancer is most significant diagnosed cancer in women that approximately 2.1 millions women were diagnosed with breast cancer and caused 627,000 deaths worldwide in 2018 based on Press Release 2018 from International Agency for Research on Cancer in World Health Organization (WHO) [1]. *Phoenix dactylifera* or in common name, date palm has become one of the choices to avoid breast cancer. The various types of extract methods on difference parts of *P.dactylifera* against breast cancer cell line or known as Michigan Cancer Foundation-7 (MCF-7) were widely discussed in previous research articles. However, it was lack of systematically review on effect of the parts of *P.dactylifera* against breast cancer or MCF-7. PRISMA method was applied on Scopus and Science Direct databases and resulted on six parts of the *P.dactylifera*'s extracts. For future direction, it was encouraged to apply different standard systematic review methods and extra databases.

Keywords: *Breast cancer; MCF-7; Phoenix dactylifera; sunnah food; extract.*

Introduction

Breast cancer is the most frequently diagnosed cancer in women and cause of death in developed countries globally [2]. According to the Press Release 2018 from International Agency for Research on Cancer in World Health Organization (WHO) [1], it was approximately 2.1 millions women were diagnosed with breast cancer and global ranks as the 5th leading cause of death which is 627,000 deaths in the world. Long menstrual history, use of oral contraceptives, no ever having children, lack of physical activity, alcohol consumption, and overweight or obese are risk factors for breast cancer [3]. Rojas and Stuckey [4] were stated that by giving birth and breastfeeding babies could reduce the risk of breast cancer. The consumption of date palm or *Phoenix dactylife* might become one of the choices to prevent breast cancer. The active biochemical compound and pharmacology from date palm towards breast cancer are being focused recently [5]. There was a lot of research papers discussed about date palm that on various effect on cancer. However, it was lack of emphasizing on the systematically review the effect of date palm on breast cancer. Date palm was also defined as the sunnah food used by the Prophet *Rasullulah Shallallahu 'alaihi Wassallam (SAW)* stated inside Holy Qur'an and sunnah books [6]. Most of these foods contain tremendous efficacy, and are taken by Prophet *Rasullulah* as an alternative medicine or maintain health of body [7]. Date palms were mentioned highest number in Holy Quran and sunnah books among other Sunnah foods. Therefore, this paper will review the effect of date palms (*Phoenix dactylife*) on breast cancer systematically.

Towards a systematic review framework on identification of the effect of date palms on breast cancer.

A systematic review is an examination of a clearly formulated question that uses systematic and precised methods to distinguish, select and critically appraise relevant research and to collect and analyse data from studies that are included in the review. Statistical methods may or may not be used to analyse and summarize the results of the included studies [8]. Via a systematic review, researches can be justified, allowing for the identification of gaps and needed directions for future research. Despite abundance of studies on date palm and its effect on health as well as various types of cancers, efforts to systematically review these studies are still lacking. This article attempts to fill the gap in identifies, classifies and characterizes the parts of date palm and their effect on breast cancer. Reports on classification in the peer reviewed literature are used as a proxy of classification, highlighting that this study provides a general and baseline overview of classification. The work fills an important gap in the literature, with most systematic review examining on the male infertility [9,10] or focused on usage of the waste of date palm in industrial areas [11,12,13] or focused on antidiabetic [14]. This study is important as so far there are lacks of identification focused on parts of date palms on breast cancer.

Methodology

In this section the method used to retrieve articles related to identify and classify parts of date palms as well as their effect on breast cancer are discussed. The reviewer used the PRISMA method to include resources (Scopus and Science Direct) in order to run the systematic literature review, eligibility and exclusion criteria, steps of the review process (identification, screening, eligibility) and data abstraction and analysis.

2.1. PRISMA

The review was guided by the PRISMA Statement (Preferred Reporting Items for Systematic reviews and Meta-Analyses). PRISMA is often utilized within the identification and classification areas. According to Shamseer et al. [15], it offers three unique advantages which are 1) to define clear research questions that permits a systematic research, 2) to identify the inclusion and exclusion criteria to reduce duplication of efforts, and 3) to examine large database of scientific literatures in a defined time. The PRISMA Statement allows for rigorous search of terms related to identify and classify parts of date palms as well as their effect on breast cancer. The methodology can be used for determining parts of date palms and their effect on breast cancer.

2.2. Resources

This review depends on two main journal databases – Scopus and Science Direct. Scopus is the first database utilized in this review. Scopus is the largest citation and abstract databases of peer-reviewed literature with more than 39,000 journals from more than 11,000 publishers in worldwide. Scopus contains various research subject areas such as life sciences, social sciences, physical sciences and health sciences. Science Direct is used as second database in this review. It is a vigorous database consisting of 4,092 journals and 28,764 books with diverse research domain areas such as physical sciences and engineering, life sciences, health sciences, and social sciences and humanities. Science Direct is managed by the Anglo-Dutch publisher Elsevier and it has 250,000 open access articles. The articles published in open access are mainly peer-reviewed literature research papers.

2.3 Systematic review process

2.3.1 Identification

There were involved four stages in the systematic review process. The review process was performed on 22nd May 2019. The first phase was identified keywords used for the search process. Relying on previous studies and thesaurus as well as encyclopedia keywords similar and related to date palm and breast cancer were used (Table 1). At this stage, after careful screening, 2 duplicated articles were removed.

2.3.2 Screening

In Table 2, several eligibilities and exclusion criterion are determined. First with regard to literature type, only article journals with empirical data are selected which means review article, book series, book, chapter in book and conference proceeding are all excluded. Second, in order to avoid any confusion and difficulty in translating, the searching efforts excluded the non-English publication and focused only on articles published in English. Thirdly, with regard to timeline, a period of 7 years is selected (between 2013 and 2019), an adequate period of time to see the evolution of research and related publications. Lastly, in line with its objective which focused on effect of date palms on breast cancer, only articles related with effect of date palms on breast cancer are selected.

2.3.3 Eligibility

Data Abstraction and Analysis

The remaining articles were assessed and analysed. Efforts were concentrated on specific studies that responded to the formulated questions. The data were extracted by reading through the abstracts first, then, the full articles (in-depth) to identify appropriate studies on *Phoenix dactylifera* and its findings. Qualitative analysis was performed using content analysis to identify effect of *Phoenix dactylifera* on breast cancer. The completed flow diagram of PRISMA is shown in Figure 1.0.

3.0 Results and Discussion

The review resulted in nine studies on *Phoenix dactylifera* mainly focus on six parts of the plant which are pollen [16,17], root [18,19], leaves [20,21], seeds [21,22], fruits [5,21,23] and pits [18] on breast cancer shown in Table 3. They were mainly focused on the effect and concentration of extracted active compounds such as phenolic, flavonoids and alkaloids as antioxidant, antiproliferation and anti-inflammation to inhibit the activity of breast cancer cell line (MCF-7).

3.0.1 Pollen Extract

According to Al-Marzook and Omran [16], the alkaloid content in *Phoenix dactylifera* could reduce the growth of cancer cell, but, it also inhibited on normal cell. The mechanism of alkaloid compounds were preventing the

interaction of free radicals and DNA so that decreasing the damage's level. In short, the type of alkaloid compounds and the concentration level of extract had variable influences toward breast cancer cell and normal cell. In the article of Banu et al. [17], the extract of date palm pollen was used as a biological reducing agent to reduce ionic gold and silver to form the biogenic gold and silver nanoparticles surface. Then, the results were indicated that biogenic gold and silver nanoparticles had a major dose-dependent cytotoxicity after tested on MCF-7 breast cancer cells. However, extract of date palm pollen has no obvious cytotoxicity effect on breast cancer cells, and the authors believe that the anticancer compounds were not transported into the cancer cells. The authors had concluded that low dosages of silver nanoparticles that produced by using non-toxic chemicals are harmless to the human normal cells. The bioflavonoids on the surface of gold and silver nanoparticles could destroy breast cancer cell when transporting them by using gold nanoparticles. Gene expression of the pro-apoptotic protein p53 and anti-apoptotic protein Bcl-2 is the mechanism of breast cancer cell death.

3.0.2 Root Hairs Extract

In the article of Oves et al. [19], silver nanoparticles (AgNPs) was extracted from the root extract of *Phoenix dactylifera* to test their antimicrobial and anti-cancer potential. In this study, to assess the anticancer potential activity of AgNPs, both breast cancer cell lines (MCF-7 cells) and peripheral blood mononuclear cells (PBMCs) were employed as a control. AgNPs were found to decrease the cell viability of MCF-7 cell lines in vitro with IC50 values of 29.6 µg/ml and could act as a controlling agent of human breast cancer. Based on these results, they conclude that biologically synthesized AgNPs exhibited multifunctional properties and could be used against human cancer.

3.0.3 Leaves Extract

In the article of Abutaha et al. [20], ethyl acetate was used to extract leaves of *Phoenix dactylifera*. At the concentration of 126 µg/ml, the cytotoxic activity against MCF-7 breast cancer line was effective. Ethyl acetate fraction had anti-proliferative effects and can be playing a role as potential anticancer treatment for many cancers.

3.0.4 Seeds Extract

In the article of Al-Zubaiday et al. [22], *Phoenix dactylifera* seeds were extracted by using chloroform and it has significant anti-angiogenic activity and significant free radical scavenging activity in MCF-7 breast cancer cell lines. The chloroform P.dactylifera seeds contained antiproliferative compound that reduce the viability of MCF-7 breast cancer cell line. Authors believed that it may be related to the presence of active compounds such as flavonoid, aliphatic alcohols, terpenes, fatty acids and phenolic compounds. These active compounds were proved that contained higher antioxidant activity than Vitamin C, E and carotenoids that inhibited the tumor growth.

3.0.5 Fruits Extract

In the article of Khan et al. [5], the contents of methanolic extract of *Phoenix dactylifera*'s fruits such as flavonoids, aglycones, terpenoids and polyphenolic compounds could result cell death through apoptosis by activating both intrinsic and extrinsic pathways in MCF-7 breast cancer cell line. Zhang et al. [23] had stated that date palm fruits contained mainly sugar, phenolics, triglycerides, triterpenoids, steroids and fatty acids after extracted with water and methanol. Methanolic extracts of date palm fruits indicated that great anti-proliferation against breast cancer cell lines (MCF-7) at the concentration of 100µg/ml.

3.0.6 Pits Extract

In the article of Omran et al. [18], polyphenol compounds of *Phoenix dactylifera* pits extract had cytotoxicity activity against human breast cancer cell line (MCF-7). 7,12-dimethylbenz(a)anthracene (DMBA) can induce vast oxidative damage in breast and cause breast. The concentration of acetone phenolic fraction of *Phoenix dactylifera* at 202 µg/ml had inhibitory activity to prevent the growth of MCF-7 breast cancer cell line.

4.0 Conclusion

PRISMA is a standard guideline for systematic review usually utilized in health science writing [24]. It is suitable for this identification of the effect of date palms (*Phoenix dactylifera*) toward breast cancer. Nevertheless, it was requires more standard systematic review methods for guide research synthesis [25]. Besides, whenever appropriate, extra databases could be utilized such as Web of Sciences and Google Scholar.

Acknowledgement:

We thank our colleagues from Faculty of Applied Science and Technology, Faculty of Chemical Engineering Technology, Department of Research, Publication & Documentation, Institute of Ahli Sunnah wal Jamaah,

Department of Islamic Studies, Center for general Studies and Co-curricular, University Tun Hussein Onn Malaysia, Malaysia who provided insight and expertise that greatly assisted in this systematic review paper.

Funding/support:

This work was supported in part by Vot H459 under Graduate Research Grant or *Geran Penyelidikan Pascasiswazah* (GPPS) founded by Research Management Centre (RMC) University of Tun Hussein Onn Malaysia.

Conflicts of Interest:

All authors have disclosed no conflicts of interest.

Declaration:

This systematic review never been presented, published, or posted online before.

Author contributions:

All authors who contributed to the following items (1) concept or design, (2) acquisition of data, (3) analysis or interpretation of data, (4) drafting of the manuscript, and (5) critical revision for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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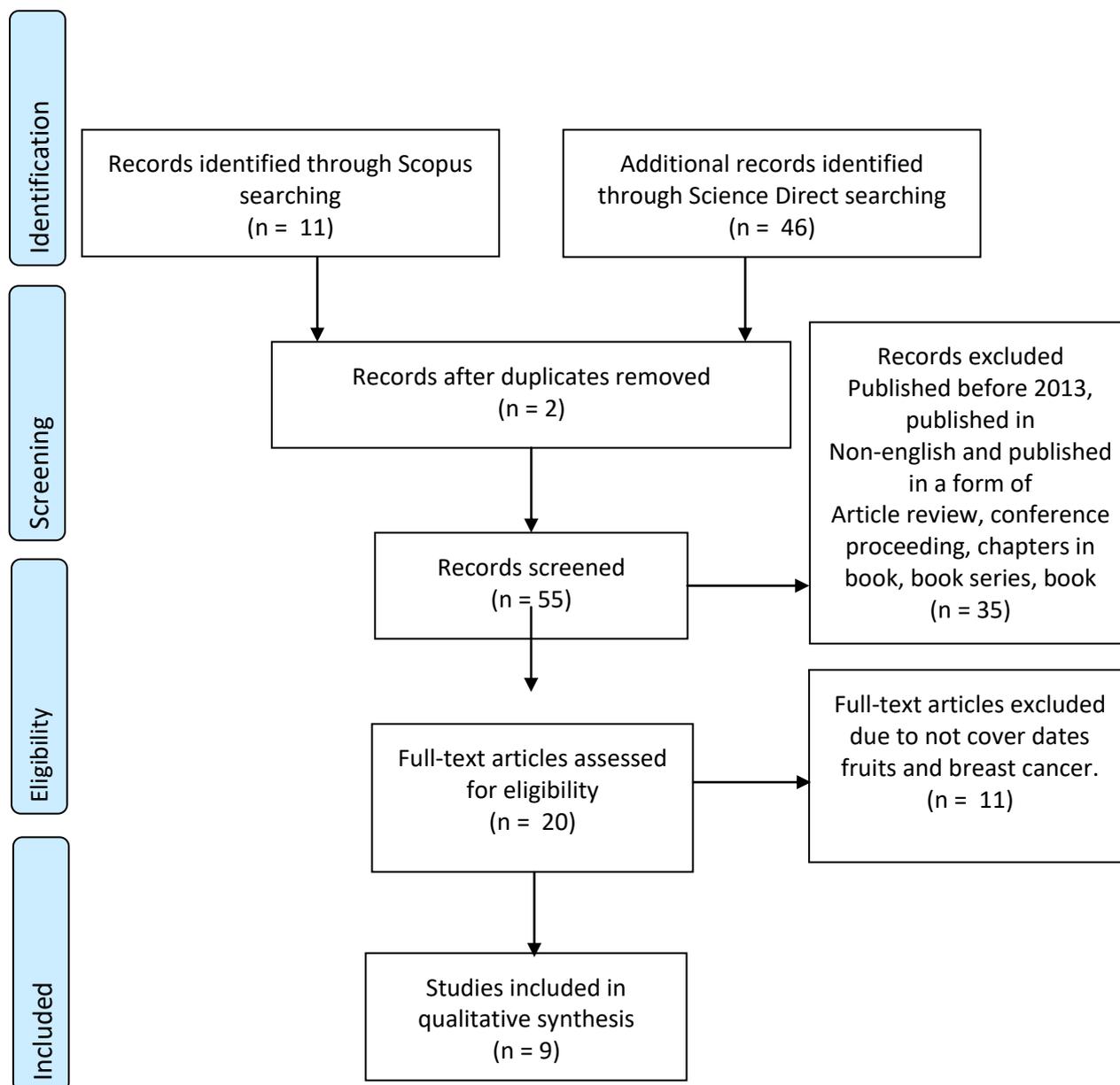


Figure 1.0: Flow diagram of PRISMA

Table 1: Keywords and Searching Information Strategy.

| Database | Search String |
|----------------|--|
| Scopus | TITLE-ABS-KEY(("date fruit*" OR "Phoenix dactylifera") AND ("breast cancer*")) |
| Science Direct | date fruit, Phoenix dactylifera, breast cancer |

Table 2: The Inclusion and Exclusion Criteria

| Criteria | Inclusion | Exclusion |
|----------|-----------|-------------|
| Timeline | 2013-2019 | < 2013 |
| Language | English | Non-english |

| | | |
|-----------------|-----------------------------|---|
| Literature type | Journal (research articles) | Journals (systematic review), conference proceeding, chapters in book, book series, book. |
|-----------------|-----------------------------|---|

Table 3: Studies Analysis

| Authors | Studies on <i>Phoenix dactylifera</i> | Findings |
|----------------------------|--|---|
| Banu et al., 2018 | Pollen extract | Anti-cancerous phytochemical compounds are no remarkable cytotoxicity on the breast cancer cell or Michigan Cancer Foundation-7 (MCF-7) and researcher believed that the compounds not delivered into MCF-7 cell. |
| Oves et al., 2018 | Root hairs extract | Decrease MCF-7 cell's viability in vitro and could play a role as a controlling agent of human breast cancer with its anti-cancer potential effect. |
| Abutaha et al., 2018 | Leaves extract | Has a potential anti-proliferative and anti-inflammatory action in breast cancer cell line (MCF-7) |
| Omran et al., 2017 | Seeds, fruits, leaves and rhizomes extract | High phenolic and flavonoids contents in <i>Phoenix dactylifera</i> and act as antioxidant to scavenge free radicals against MCF-7. |
| Al-Marzook and Omran, 2017 | Pollen grains | Alkaloids compounds in <i>Phoenix dactylifera</i> could reduce the cell viability of MCF-7 and has effect against breast cancer. |
| Omran et al., 2017 | Pits | Phenolic compound in <i>Phoenix dactylifera</i> play a role as antioxidant that inhibit cancer cell line MCF-7 growth. |
| Al-Zubaiday et al., 2016 | Seeds extract | Anti-proliferative activity of <i>Phoenix dactylifera</i> against breast cancer cell line (MCF-7). |
| Khan et al., 2016 | Fruits extract | Date palm inhibited human breast adenocarcinoma (MCF-7) cells in vitro and effect against breast cancer. |
| Zhang et al., 2017 | Fruits extract | Extract inhibit marginal cell proliferation against breast cancer cell line (MCF-7). |