



A review to the effect of indigenous and cultivated Iraqi plants extracts on MCF7 cell line

Shamam Kanaan M Abdlkareem*,¹ Enas Jawad Kadhim²

¹Department of Pharmacy, Al Hikma University College, Baghdad, Iraq. shamam.kanaan@hiuc.edu.iq

²Department of Pharmacognosy and Medicinal Plants, College of Pharmacy, University of Baghdad.

dr.enasjawad@yahoo.com

Abstract

The purpose of the review is to summarize the findings of published articles concerning the *in vitro* anticancer activity of indigenous and cultivated Iraqi plants extracts on Michigan Cancer Foundation-7, SD: Standard deviation (MCF7) cell line. The study was conducted to link several studies and articles about the anticancer activity of different extracts on a specific cell line (MCF7). The results showed that Iraq's plant sources are likely to have effective anti-breast cancer chemicals. The majority of the extracts included in this review are promising chemical compounds derived from various Iraqi plants. The conclusion is that various plants in Iraq have anticancer potential, which is crucial to the treatment of breast cancer.

Keywords: Iraqi plants, Extracts, Breast cancer, MCF7 cell line.

1) Introduction

Many communities worldwide have been using plants extracts in their healthcare systems goes back hundreds of years, due to their natural origin, containing several active compounds; they are considered as excellent candidates to replace synthetic compounds, which are generally, assume to have toxicological and carcinogenic effect⁽¹⁾. The WHO figures that over eighty percent of the world's population currently depend on traditional medicine employing plants to address their primary healthcare needs⁽²⁾. a single plant may contain up to thousands of constituents, since the major component determining the success of an inquiry into bioactive plant elements is the selection of plant material, around the world, only a small number has been studied both phytochemically and pharmacologically, and in Iraq has the most wealthy plant variety with 3,005 vascular plant species, so the chance of making novel discoveries become assured^(3,4).

Unfavorable environment for the plants, such as drought, harsh temperatures, nutritional shortages, heavy metals, and excessive salt, lead to high levels of reactive oxygen species (ROS), that could induce oxidative stress. To avoid this, cells have a complicated antioxidant system composed of both enzymatic and non-enzymatic systems. Non-enzymatic system molecules have several action methods, such as enzyme inhibition, chelation of trace elements linked to the formation of free radicals, reactive species absorption and activation, or increase in protection through other antioxidant mechanisms⁽⁵⁾. Within these molecules, the chemical compounds that come from secondary metabolism, primarily phenolic compounds play an essential part in protection against oxidative stress. These compounds are classified as antioxidants not only because of their capacity to donate hydrogen or electrons, but also due to they are stable radical intermediates. Phenolic compounds also have beneficial impacts on humans when the plants are ingested as food^(6,7). In general, phenols in plant extracts have an antioxidant ability that is powerful at low concentrations, in addition to its ability to prevent cancer and cardiovascular diseases. Thus, research for the measurement of the antioxidant activity of the extract of various plant species may contribute to establishing the significance of these species as a source of new antioxidant and anticancer chemicals⁽⁸⁾.

The most widespread malignancy identified in women globally is the breast cancer, and the number of prevalent instances is increasing. It accounts for one out of every ten new cancer cases diagnosed worldwide per year, and it is the main cause of cancer-related mortality among women⁽⁹⁾. As stated by the Iraqi Cancer Registry, breast cancer is the most common type of cancer among women in Iraq, accounting for almost one-third of all documented cases⁽¹⁰⁾. The Michigan Cancer Foundation-7, SD: Standard deviation (MCF7) cell line was utilized as a model for hormonal effects on breast cancer cell proliferation and particular protein synthesis. The overwhelming plurality of documented *in vitro* studies involved breast cancer in addition to oestrogen receptor biology⁽¹¹⁾.

The review is an attempt to summarize the effect of indigenous and cultivated Iraqi plant species extracts on MCF7 cell line of breast cancer, their families, their province, parts of plant used, cytotoxicity assay used, solvents and methods of extractions used and the IC₅₀ obtained.

2)Methodology

the following were used to search for scientific articles published until April 2024 using traditional textbooks and databases like Web of Science, Scopus, and PubMed: "Iraqi herbal medicine" or "Iraqi plants", "plants extracts", "medicinal plants Iraq", "MCF7 cell line", "breast cancer, and "traditional medicine in Iraq" without restricting the search items. Citing numerous studies and publications that have been published over time.

2.1 Data gathering

A literature search was conducted on the usage of Iraqi plant extracts against the MCF7 cell line. This comprised all available published publications on *in vitro* research of Iraqi flora. Computerized literature searches were conducted on the Google scholar, Scopus, Medline, and Science direct databases. Moreover, Iraqi theses and dissertations were searched for information. To get papers from databases, the researchers used a customized search to establish the maximum number of Medical Subject Headings terms linked to the research topic. The main sentences were "plant", "extracts", "Iraq", and "MCF7," besides to these key terms, the search also includes plants from the Iraqi Pharmacopoeia Monograph project.

2.2 Study Selection

Acceptance requirements were for the publications reporting the usage of Iraqi medicinal plant species cultivated naturally or farmed in Iraq and the reviews that demonstrate the usage of medicinal plant species either alone or in mixture of Iraqi plants to treat breast cancer, using MCF7 as a model. This included *in vitro* experiments with no language or date limitations. While the non-Iraqi plants (those that are not endemic to Iraq or that have been imported) were omitted also the publications that reporting the usage of another type of breast cancer cell lines were omitted.

2.3 Data Analysis

An intensive reading of the articles was done, with a focus on the research title and abstract. All of the articles included in the results were validated. After the investigation was completed, a selective reading of publications containing plants and materials with botanical names was conducted and confirmed, allowing the review data to be summarized. The selected article contained direct information about anticancer (breast cancer).

3) Results

In the current study, 34 Iraqi species were identified via electronic searches, in which its extract influence on the MCF7 cell line was investigated. After removing duplicates and screening relevant titles and abstracts, 30 papers underwent a full text examination. Table 1 below illustrates the 34 species and their families, indigenous or cultivated, weight used, the province, and part of plant used. And Table 2 illustrates 34 Iraqi species and their method and solvent of extraction, cytotoxicity assay, and IC₅₀.

Table1. Information about the Iraqi plants with anti-breast cancer activity.

Scientific name	Family	Indigenous or cultivated	Weight used	province	Part used	References
<i>Thymus vulgaris</i>	Lamiaceae	cultivated	250g	Baghdad	Leaves	12
<i>Conocarpus erectus</i>	Combretaceae	cultivated	30g	Baghdad	Leaves	13
<i>Moringa oleifera L.</i>	Moringaceae	cultivated	100g	Baghdad	Leaves	14
<i>Taraxacum officinale</i>	Asteraceae	cultivated	26g	Baghdad	Fruit (apple)	15
<i>Cymbopogon citratus L.</i>	Poaceae	cultivated	-	Baghdad	Leaves	16
<i>Opuntia polyacantha</i>	Cactaceae	cultivated	100g	Babil	Aerial parts	17
<i>Prunus armeniaca</i>	Rosaceae	cultivated	100g	Baghdad	Seeds	18
<i>Cressa Cretica</i>	Convolvulaceae	cultivated	30g	Al-Musaib	Aerial parts (stems and leaves)	19
<i>Ficus carica</i>	Moraceae	cultivated	50g	Kirkuk	Leaves	20
<i>Ocimum Basilicum</i>	Lamiaceae	cultivated	-	Dyala	Leaves	21
<i>Carica papaya</i>	Caricaceae	cultivated	-	Baghdad	Leaves	22
<i>Capparisspinosa L.</i>	Cruciferae	cultivated	200g	Kirkuk	Aerial parts	23
<i>Plantago lanceolata L.</i>	Plantaginaceae	cultivated	100 g	Baghdad	Leaves	24
<i>Calendula officinalis L.</i>	Asteracea	cultivated	100 g	Baghdad	Flower	25

<i>Equisetum arvense</i>	Equisetaceae	cultivated	20g	Diyala	Aerial parts	26
<i>Juncus rigidus</i>	Juncaceae	Indigenous	50 g	central Iraq from the banks of the rivers	Stems and leaves	27
<i>Eucalyptus camaldulensis</i>	Myrtaceae	Cultivated	20g	Babil	Bark	28
<i>Aloe vera</i>	Liliaceae	Cultivated	20g	Babil	Leaves	28
<i>Capparis spinosa</i>	Capparaceae	Cultivated	20g	Babil	Fruits	28
<i>Fenugreek</i>	Leguminosae	Indigenous	200g	Salah Aldin	Leaves	29
<i>Petroselinum sativum</i>	Umbelliferae	Indigenous	100g	Baghdad	Leaves	30
<i>Phoneix Dactylifera</i>	Arecaceae	Indigenous	-	Basrah	heart	31
<i>Mentha arvnensis</i>	Lamiaceae	Cultivated	86g	Baghdad	Leaves	32
<i>Althaea ludwigii L.</i>	Malvaceae	Indigenous	200g	Msayab	Aerial parts	33
<i>Hypericum triquetrifolium</i>	Hypericaceae	Indigenous	0.5-1 g	Erbil	Leaves	34
<i>Bauhinia variegata</i>	Leguminosae	Indigenous	100g	Baghdad	Leaves Stems Flowers	35
<i>Xanthium Strumarium</i>	Asteraceae	Cultivated	600g	Baghdad	Leaves	36
<i>Rice bran</i>	Graminae	Indigenous	100g	Al-Najaf	Bran	37
<i>Equisetum Arvense</i>	Equisetaceae	Indigenous	100g	Kurdistan	Aerial parts	38
<i>(fig, olive, and moringa) blend</i>	(Moraceae, Oleaceae, and Moringaceae)	Cultivated	10g	baghdad	Leaves	39
<i>Creston apples</i>	Rosaceae	Cultivated	20g	Mosul	Seeds	40
<i>Pinus sabiniana L.</i>	Pinaceae	Cultivated	20g	Babil	Leaves	41
<i>Phoenix dactylifera L.</i>	Arecaceae	Indigenous	20g	Babil	pollen grains	41
<i>Ferocactus sp. L.</i>	Cactaceae	Cultivated	20g	Babil	Leaves	41

Table 2 illustrates 43 Iraqi species and their method and solvent of extraction, cytotoxicity assay, and IC₅₀.

Scientific name	Method of extraction	Solvent of extraction	Cytotoxicity assay	IC ₅₀	References
<i>Thymus vulgaris</i>	Clevenger	Distilled water	Mtt assay	27.66 ppm	12
<i>Conocarpus erectus</i>	Soxhlet	70% methanol	Mtt assay	-	13
<i>Moringa oleifera</i>	Soxhlet	70% ethanol	Mtt assay	20.8µM	14
<i>Taraxacum officinale</i>	Soxhlet	Ethanol	Mtt assay	190.5 µg/ml	15
<i>Cymbopogon citratus L.</i>	Soxhlet	Distilled water	Mtt assay	0.3125µl/mL	16
<i>Opuntia polyacantha</i>	Soxhlet	70% methanol	Mtt assay	400µg/ml	17
<i>Prunus armeniaca</i>	Soxhlet	80% ethanol	Mtt assay	53.56 µg/ml	18
<i>Cressa Cretica</i>	Soxhlet	80% ethanol Ethyl acetate	Mtt assay	48.52 µg/mL 17.3µg/mL	19
<i>Ficus carica</i>	Soxhlet	70% ethanol	Mtt assay	-	20

<i>Ocimum Basilicum L.</i>	Soxhlet	99% ethanol	Crystal violet assay	-	21
<i>Carica papaya</i>	Soxhlet	85% ethanol	Mtt assay	22.74 µg/mL	22
<i>Capparis spinosa L.</i>	Soxhlet	85% methanol	Mtt assay	35.5 µg/ml	23
<i>Plantago lanceolata L.</i>	Solvent extraction	70% ethanol	Crystal violet assay	674 µg/mL	24
<i>Calendula officinalis L.</i>	Soxhlet	90% ethanol	Crystal violet assay	1737 µg/ml	25
<i>Equisetum arvense</i>	Soxhlet	70% methanol	Crystal violet assay	-	26
<i>Juncus rigidus</i>	Solvent extraction	90% ethanol	Mtt assay	-	27
<i>Eucalyptus camaldulensis</i>	Soxhlet	80% methanol	Mtt assay	375.5 µg/ml	28
<i>Aloe vera</i>	Soxhlet	80% methanol	Mtt assay	991.50 µg/ml	28
<i>Capparis spinosa</i>	Soxhlet	80% methanol	Mtt assay	879.20 µg/ml	28
<i>Fenugreek</i>	Solvent extraction	Methanol	Mtt assay	78.17 ± 1.590 µg/ml	29
<i>Petroselinum sativum</i>	Solvent extraction	70% ethanol	Crystal violet assay	1000 µg/ml	30
<i>Phoenix Dactylifera</i>	microwave-assisted extraction(MAE)	99% ethanol	Mtt assay	620.1 µg/ml	31
<i>Mentha arvensis</i>	Soxhlet	(10% v/v) HCl	Mtt assay	10 mg/ml	32
<i>Althaea ludwigii L.</i>	Soxhlet	85% methanol	Mtt assay	35.5 µg/mL	33
<i>Hypericum triquetrifolium Turra</i>	Soxhlet	96% methanol	Mtt assay	185.7 µg/ml	34
<i>Bauhinia variegata</i>	Soxhlet	Hexane	Mtt assay	12.2 µg/ml 20.05 µg/ml 33.6 µg/ml	35
<i>Xanthium Strumarium</i>	Solvent extraction	Chloroform	Mtt assay	2.67 µg/ml	36
<i>Rice bran</i>	Solvent extraction	70% Ethanol 70% Methanol n-hexane water	Mtt assay	0.36mg/mL 1.29mg/mL 0.12mg/mL >5 mg/mL	37
<i>Equisetum Arvense</i>	Soxhlet	(10% v/v) HCl	100g Mtt assay	-	38
<i>(fig, olive, and moringa) blend</i>	kinetic maceration	Distilled water	Crystal violet assay	-	39
<i>Creston apples</i>	Soxhlet and kinetic maceration	Water Methanol Chloroform N-hexane	Mtt assay	M1:36.80 µg/mL M2:26.20 µg/mL M3:9.83 µg/mL C4:8.30 µg/mL C5:12.48 µg/mL C6:8.22 µg/mL	40
<i>Pinus sabiniana L.</i>	Soxhlet	80% methanol	Mtt assay	No significant effect	41
<i>Phoenix dactylifera L.</i>	Soxhlet	80% methanol	Mtt assay	2.094e+006 µg/ml	41
<i>Ferocactus sp. L.</i>	Soxhlet	80% methanol	Mtt assay	5.091e+006 µg/ml	41

IC50: The half maximal inhibitory concentration.

3.1 *Thymus vulgaris* is an essential oil-rich plant whose primary chemical components are oxygenated monoterpenes and monoterpene hydrocarbons. The air-dried leaves of *T. vulgaris* yielded 1.0% essential oils, which were evaluated by GC-MS. The cytotoxic effects of the essential oil extracted were studied on the MCF-7 cell line. The results demonstrated a worthy difference ($P \leq 0.01$) in the cytotoxicity impact of essential oil extract with an IC_{50} of 27.66 ppm⁽¹²⁾.

3.2 *Conocarpus erectus* is flowering plant that has anticancer, antioxidants, and antimicrobial features. Also demonstrate high free radical scavenging activity and in treating many disorders. The methanolic extract of leaves revealed growth inhibition effects after 48 hours on MCF7 cell line was 38.222% at 100µg/ml concentration. No effect was observed in normal cells. And the IC_{50} was not determined⁽¹³⁾.

3.3 *Moringa oleifera* L. is a drought-tolerant, fast-growing, medium-sized perennial tree. *In vitro* evaluation of the effect of isolated cryptochlorogenic acid extract on human MCF-7 cells death. The study shows that Cryptochlorogenic acid has significant effect in the cell death of breast cancer and according to IC_{50} values was (20.8 µM)⁽¹⁴⁾.

3.4 *Taraxacum officinale* (Dandelion) provides a possibly unique non-toxic option to conventional cancer treatment for a variety of malignancies, particularly breast cancer. The ethanolic extract had an IC_{50} of 190.5 µg/ml against the human breast cancer cell line (MCF-7)⁽¹⁵⁾.

3.5 *Cymbopogon citratus* L. is classified as lemongrass; it has been used in various areas and in folk cures for malaria, coughs, pneumonia, and others for many years. The effect of volatile lemongrass oil fresh leaves cultivated in Iraq were evaluated its cytotoxic activity on MCF-7 cell cancer cell lines. The results showed that the Iraqi cultivated plant produced 1.5%v/w essential oil and the plant oil showed effect on MCF-7 cell line, where the inhibitory growth rate percentage appeared for almost all concentrations in comparison with control after 24 hours, and even at a concentration of 0.3125µl/mL, the inhibitory growth rate percentage reached up to 86%⁽¹⁶⁾.

3.6 *Opuntia polyacantha* also known as prickly pear cactus the alkaloids were extracted by methanol and chloroform and then estimated quantitatively and qualitatively, along with determination of alkaloids cytotoxicity on MCF-7 cell line where done and the results demonstrated that the MCF-7 cell line growth was considerably decreased by 52.7% at 400µg/ml of alkaloid concentration. The extracted alkaloids proved hazardous to cancer cell lines but had no effect on normal cell line proliferation, making it a hopeful and harmless alternative for breast cancer medication⁽¹⁷⁾.

3.7 *Prunus armeniaca* is a small tree and most commonly cultivated apricot species. The extract of Iraqi apricot seed was prepared with 80% ethanol and tested against the MCF7 cell line. Following extract administration the number of MCF-7 colonies was reduced considerably. Additionally, after being exposed to the extract, the number of dead cells in the MCF-7 cell line significantly increased in comparison to the untreated cells⁽¹⁸⁾.

3.8 *Cressa cretica* is a perennial subshrub or herb that grows in tropical and subtropical regions around globe. The nutrient profile suggests that it may contain alpha-tocopherol, minerals, edible oil, and carbohydrates. The aerial parts ethanolic and ethyl acetate extracts demonstrated a considerable degree of cytotoxicity against MCF-7, with IC_{50} values of 17.3 µg/ml and 48.52 µg/ml, matching⁽¹⁹⁾.

3.9 *Ficus carica* is a herbal remedy used to cure a wide range of ailments. It was first cultivated in the Middle East and West Asia and has since spread around the world. The effect of leaves ethanolic extract and total flavonoids extracts on the MCF7 cell line was investigated, and the results revealed that the maximal growth inhibition rate for total flavonoids was 28% at a dosage of 2.7 mg/ml. The ethanolic crude extract had a 34% inhibition rate at a 0.084 mg/ml concentration⁽²⁰⁾.

3.10 *Ocimum basilicum* L. (Basil) Sometimes referred to as sweet basil, it is a generally grown herbaceous, perennial plant, the ethanolic leaves extract effect on MCF7 at three different concentrations (5 µg, 10 µg and 20 µg) showed that 20 µg decreased the growth inhibition percentage at (24hr and 48hr, 24hr and 72hr) for MCF7 and 5 µg at 72hr⁽²¹⁾.

3.11 *Carica papaya*, commonly known as paw, is utilized as both a food and a medicinal plant to cure a variety of maladies around the world. The portion of ethyl acetate Iraqi *C. papaya* leaves exhibited vital cytotoxic effect to the MCF-7 cell line. The action was dose-dependent, with IC_{50} values of 22.74µg/ml⁽²²⁾.

3.12 *Capparis spinosa* L. which is called in Arabic "Kabbar" It is native to the Mediterranean basin and widely distributed from Morocco to Crimea, Armenia, and Iraq. The studies showed that ethyl acetate fraction of the aerial parts has significant anti-proliferative activity against MCF-7 with (IC_{50} 35.5 µg/ml)⁽²³⁾.

3.13 *Plantago lanceolata* L. (ribwort used to treat injuries in Iraqi folk medicine, many herbalists give its extract to cancer patients. The leaf extract revealed no significant cytotoxic effect against MCF7 with extremely high IC_{50} values 250µg/ml⁽²⁴⁾.

3.14 *Calendula officinalis* L. (Marigold) is among the most significant curative and ornamental plants in Iraqi folkloric medicine, with a variety of medical purposes. The leaves extract impact on breast cancer MCF7 cell line revealed that *C. officinalis* L. extract has IC_{50} very high dose 4440mg on the normal cells as the versus the IC_{50} on cancer cells MCF7 was 1737µg so it has no cytotoxic effect on normal cell⁽²⁵⁾.

3.15 *Equisetum arvense* is commonly known as horsetail. Long herb rich in phytosterols, alkaloids, proteins, flavonoids, ascorbic acid, saponins, and other biologically active constituents. The study evaluated the alkaloid methanolic extract against the MCF7 cell line. The study found that the lowest inhibition rate (IR) reached 20.07% at a dosage level of 15.1 µg/ml, while the highest IR reached 64.1% at a dose of 500 µg/ml⁽²⁶⁾.

3.16 *Juncus rigidus* plant is distinguished by the presence of numerous secondary metabolic chemicals that are active against a variety of ailments, including digestive and circulatory system disorders. Alcoholic vegetative sum extract

(the stem and leaves) had a cytotoxic impact on cancer cells depending on the dose and duration. The results demonstrated an increase in the percentage of the rate of inhibition (IR) with increasing concentration. The concentration (200 µg/ml) gave the highest inhibition value at 72Hr, reaching (72.33%±2.31). After 48Hr of exposing MCF-7 cells to the alcoholic extract, the percentage of inhibition reached (54.5%±2.45) at a concentration of (200 µg/ml) ⁽²⁷⁾.

3.17 *Eucalyptus camaldulensis* also known as Murray, the methanolic bark extract was evaluated to investigate the cytotoxic activity of total alkaloid extracts of Eucalyptus against the cell line MCF-7 of breast cancer, the results indicate that at low concentration the growth of cancer cell was inhibited and also decline at the higher dose and the inhibitory concentration of alkaloid extract IC₅₀ on the cell line was 375.5 µg/ml ⁽²⁸⁾.

3.18 *Aloe vera* plant that grows in hot, dry climates the results indicate that the leaves methanolic alkaloidal extract effect on the cell MCF7 cell line was slightly when compared with the effect of the *E. camaldulensis* and *C. spinosa* alkaloidal extracts ⁽²⁸⁾.

3.19 *Capparis spinosa* also known as Caper bush cognized as a wealthy source of an extensive range of phytochemical compounds and it has pharmacological actions in different parts beside the therapeutic features. the IC₅₀ was 991.50 µg/ml of the fruits methanolic alkaloid extract effect on MCF7 cell line that reduces the cell viability by 79.80±7.08% with concentration of 400 µg/ml⁽²⁸⁾.

3.20 Fenugreek is an annual leguminous plant. It is widely grown and harvested for the seeds that it produces. The leaves methanolic extract effect on the MCF7 cell line demonstrated a substantial and statistically significant cytotoxic effect which indicates that Fenugreek possesses inhibition capacity over the proliferation of cell lines, although this effect seems contingent upon the concentration that contains the substance ⁽²⁹⁾.

3.21 *Petroselinum sativum* which is known as parsley the plant extracts have a multiple pharmacological features. At a concentration of 1000 µg/ml, the leaves extract significantly inhibited MCF7 cell growth and caused 50% cancer cell cytotoxicity. A comparison of IC₅₀ values for *P. sativum* extract in cancer and normal cells revealed that cancer cells were more sensitive, indicating the extract's safety ⁽³⁰⁾.

3.22 *Phoenix Dactylifera* (Hilawi variety) is one of the most well-known Iraqi dates tree, Some of the tree parts used in traditional medicine are the date fruits, heart, date seeds, and date skin. The Heart part of the *P. dactylifera* extract by using microwave-assisted extraction (MAE) on MCF7 displayed apoptosis and DNA damage, while extract effect on normal cell displayed a clear green hue, indicating that they were alive ⁽³¹⁾.

3.23 *Mentha arvensis*, popularly known as (wild mint) is a perennial plant. The *M. arvensis* cytotoxic action of purified total flavonoids on the MCF7 cell line resulted in greatest growth inhibition at a dose of 10 mg/ml (52.4%), while the lowest growth inhibition percentage was found at a concentration of 5 mg/ml (2.5%). A phenomenon known as the (Hormetic effect) ⁽³²⁾.

3.24 *Althaea ludwigii* L. is flowering plant species that grow rapidly and are widely spread, the ethyl acetate fraction of the methanolic extract demonstrated worthy effect on the MCF-7, where the IC₅₀ was equal to 35.5 µg/mL. And on normal cell line the IC₅₀ equal to 1709.23 µg/ml that could indicate that *A. ludwigii* L. only targets cancer cells and not normal cells ⁽³³⁾.

3.25 *Hypericum Triquetrifolium* Turra researches have reported the potential use of its essential oil and crude extracts as plant-based therapeutics. The results of the cytotoxic impact of H. triquetrifolium leaves methanolic extract on the MCF7 cell line revealed that the proportion of MCF-7 cells that were still alive at 6.2 g/ml was 96.41±1.01. The IC₅₀ for MCF-7 was 185.79 µg/ml, with a maximum survival rate of 95.68±0.57 cells at 6.2 µg/ml⁽³⁴⁾.

3.26 *Bauhinia variegata* is evergreen tiny medicinal trees are found all over across the globe, it was traditionally used as a cure for the treatment of bronchitis, bacterial infection, inflammation. The effects of *B. Variegata* hexane extracts of leaves, stems and flowers on breast cancer cells MCF7 were assessed and the results indicate that the highest level of cell death was achieved by hexane crude extracts of leaves as compared with stems and flowers, and the results show the most potent extract was that of the leaves having IC₅₀ 12.2 µg/ml, while stems and flowers was less potent with IC₅₀ were 20.05 µg/ml and 33.6 µg/ml respectively ⁽³⁵⁾.

3.27 *Xanthium Strumarium* famous herb which used as a cure for many diseases like epilepsy, leucoderma, and biliousness. The fresh leaves chloroform extract cause a dose dependent inhibition on the cell growth of breast cancer cell line MCF7 after 72hr, and the IC₅₀ of chloroform extract was equal to 2.67µg/ml ⁽³⁶⁾.

3.28 Rice bran is one of the components of the Mediterranean food. It consists of many essential fatty acids, dietary fibers, proteins, minerals, and vitamins, and it plays an actual role in a variety of illnesses and pathological states. Four solvent extracts of bran were examined for their cytotoxic effects on the MCF7 cell line: (70%) ethanol, (70%) methanol, n-hexane, and water. The results show that ethanol and n-hexane extracts had anti-proliferation activity against MCF7 cells, whereas the methanol extract was active against another cell line. On the flip side of the hand, the aqueous extract had a little activity and a higher rate of cell survival. Ethanol, methanol, and n-hexane extracts had anti-proliferation action, with IC₅₀ values equal to 0.36 mg/mL, 1.29 mg/mL, and 0.12 mg/mL, respectively ⁽³⁷⁾.

3.29 *Equisetum Arvense* also known as (horsetail or scouring rush), has been traditionally used to treat a variety of ailments as an anti-inflammatory, diuretic, demineralizing, and edematous. The aerial parts ethanolic total flavonoids extract used to determine the cytotoxic activity on MCF7 cell line, the results demonstrate that maximum inhibition rate on MCF-7 reached 82.15859% and achieved that at dose about 100 µg/ml ⁽³⁸⁾.

3.30 fig, olive, and moringa (FOM) blend the leaves of plants silver nano combination aqueous extract in different concentrations were assessed its effectiveness on inhibiting cancer cells live for breasts (MCF 7), the out comes

demonstrate that increasing in concentration of the Nano-extract of the FOM combination had a stronger impact on the death of cancer vital cells (MCF 7), the percentage of its effect and effectiveness was approximately 30% at low concentrations, while The highest activity of silver nanoparticles using 50, 25, 12.5 and 6.25 µg/mL aqueous extract of the plant synthesis FOM against growth percentage of cancer cells MCF 7 were to 72.2, 89.5, 119.9 and 133.3 respectively⁽³⁹⁾.

3.31 *Creston apples* the name of both the tree and fruit. It was first cultivated in Central Asia and is now grown all over the world. Creston apple seeds contain amygdalin, which makes them somewhat toxic. The seed extract were obtained by two different methods (Soxhlet and kinetic maceration) with four different solvents (water, methanol, chloroform, and n-hexane). Number of coumarins (M1” 5,6-dihydropyrone(4,3-g)coumarin”,M2” 5-Ethyl-6,7-dimethylcoumarin”,and M3” 7-Hydroxy-4-methoxycoumarin”)were obtained from chloroform extract and *in vitro* cytotoxic activity of that coumarins and M3 derivatives (C4” 7-Acetoxy-4-methoxycoumarin”,C5” 8-Acetyl-7-hydroxy-4-methoxycoumarin”,and C6” 4,7-Dimethoxycoumarin”) were studied on MCF7 cancer cell line, the results demonstrate that the three derivatives have excellent cytotoxic impact on the MCF-7 cell line of breast cancer⁽⁴⁰⁾.

3.32 *Pinus sabiniana L.* called bull pine or gray pine a tree grows at elevations and is common in the northern and interior portions of the California. The cytotoxic activity of chloroform alkaloidal fraction extract was investigated against the MCF-7 cell line of breast cancer, the outcomes demonstrate that the alkaloidal extract of bull pine had less activity on the cell viability of normal cell line, and it had no anticancer effect on the MCF-7 cell line⁽⁴¹⁾.

3.33 *Phoenix dactylifera L* is a kind of flowering plant from the palm tree family collected from Australia and Iraq. The cytotoxic activity of chloroform alkaloidal fraction extract was investigated against the cell line MCF-7, the outcomes demonstrate that the alkaloidal extract of *P. dactylifera* had cytotoxic activity on both normal and cancer cell and where alkaloidal extract decrease the cell viability to 56.20% for MCF7 cell line and 57.50% for the normal cell line^(41,42).

3.34 *Ferocactus sp. L.* They are desert dwellers found in the southwestern United States and northwestern Mexico. The cytotoxic activity of chloroform alkaloidal fraction extract was investigated against breast cancer cell line MCF-7, the outcomes demonstrate that the alkaloidal extract of the *Ferocactus sp.* had cytotoxic activity on both normal and cancer cell, the highest decrease of viability was noticed at the highest dose 400 µg/ml was 46.87% and 56.20% for the MCF7 and normal cell lines, respectively⁽⁴¹⁾.

4) Conclusions

Medicinal plants have an important role in cancer care. This comprehensive analysis describes available Iraqi medicinal plants that can treat breast cancer or be used as an adjuvant with other drugs for patients. The presented data will primarily aid in the development of novel molecules for both Ayurvedic and contemporary medications. Furthermore, more research on these plants is needed to determine the particular mechanism(s), constituent(s), and appropriate dose that produce the anticancer effect.

Acknowledgment

To the Al Hikma University College (<http://hiuc.edu.iq>.) For their invaluable support and assistance in completing this research

Conflict of interest

The authors declare that there is no conflict of interest.

Funding

The authors received no financial support for the research, authorship and/or publication of this review.

Author Contribution

Shamam Kanaan M. Abdulkareem: contributed to data gathering, analysis, practical (follow the procedure) and written parts of the study. Enas Jawad Kadhim gave final approval and agreement for all aspects of the study, supervision, revision, and rearrangement.

References

- 1- Bitwell, C., Indra, S. S., Luke, C., & Kakoma, M. K., A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants, *Scientific African*, 2023,19, e01585.
- 2- Veiga, M., Costa, E. M., Silva, S., & Pintado, M., Impact of plant extracts upon human health: A review, *Critical reviews in food science and nutrition*, 2020, 60(5), 873-886.
- 3- Hostettmann, K., Strategy for the biological and chemical evaluation of plant extracts. *Pure Appl. Chem*, 1999, 70(11), 1-9.
- 4- Abu-Darwish, M. S., & Efferth, T., Medicinal plants from near east for cancer therapy. *Frontiers in pharmacology*, 2018, .9, 56.

- 5- arua, C.C.; Sen, S.; Das, A.S.; Talukdar, A.; Jyoti Hazarika, N.; Barua, A.; Barua, I. A comparative study of the in vitro antioxidant property of different extracts of *Acorus calamus* Linn. *J. Nat. Prod. Plant Resour.* 2014, 4, 8–18. [Google Scholar]
- 6- Pang, Y.; Ahmed, S.; Xu, Y.; Beta, T.; Zhu, Z.; Shao, Y.; Bao, J. Bound phenolic compounds and antioxidant properties of whole grain and bran of white, red and black rice. *Food Chem.* 2018, 240, 212–221.
- 7- Nićiforović, N.; Mihailović, V.; Mašković, P.; Solujić, S.; Stojković, A.; Muratspahić, D.P. Antioxidant activity of selected plant species; potential new sources of natural antioxidants, *Food Chem. Toxicol.* 2010, 48, 3125–3130.
- 8- Chaves, N., Santiago, A., & Alias, J. C., Quantification of the antioxidant activity of plant extracts: Analysis of sensitivity and hierarchization based on the method used, *Antioxidants*, 2020, 9(1), 76.
- 9- Brand, J. S., Colzani, E., Johansson, A. L., Giesecke, J., Clements, M., Bergh, J., ... & Czene, K., Infection-related hospitalizations in breast cancer patients: risk and impact on prognosis, *Journal of Infection*, 2016, 72(6), 650-658.
- 10- Iraqi Cancer Board. Results of the Iraqi Cancer Registry 2004. Baghdad: Iraqi Cancer Registry Center, Ministry of Health; 2007.
- 11- vantangoli, M. M., Madnick, S. J., Huse, S. M., Weston, P., & Boekelheide, K., MCF-7 human breast cancer cells form differentiated microtissues in scaffold-free hydrogels. *PLoS one*, 2015, 10(8), e0135426.
- 12- Khalaf, A. N., & Abed, I. J., Evaluating the in vitro cytotoxicity of *Thymus vulgaris* essential oil on MCF-7 and HeLa cancer cell lines, *Iraqi Journal of Science*, 2021, 2862-2871.
- 13- Fathi, S. M., & Ali, I. A., Cytotoxic Effect of the Alcoholic Extract of *Conocarpus erectus* Leaves on MDA-MB 231 and MCF7 Breast Cancer Cell Lines. *Iraqi Journal of Science*, 2023, 84-90.
- 14- Bedewi, B. K., Jasim, G. A., Abbas, I. S., & Al-Sudani, B., Cytotoxicity of Cryptochlorogenic acid against Breast cancer cell line (MCF7) isolated from *Moringa oleifera* Leaves Cultivated in Iraq. *Al Mustansiriyah Journal of Pharmaceutical Sciences*, 2022, 22(2), 35-43.
- 15- Rawa'a, A. M., Cytotoxic activity of taraxacum officinale ethanolic plant extract against human breast cancer (MCF-7) cells and human hepatic (WRL-68) cells. *Iraqi Journal of Cancer and Medical Genetics*, 2018, 11(1).
- 16- HASAN, Z. Y. M., AL-HALBOSIY, M. M. F., AL-LIHAIBI, R. K., & AL-NAUIMI, E. H., Antimicrobial of lemongrass (*Cymbopogon citratus* L.) volatile oil and cytotoxic effects against L20B and MCF-7 cell lines. *Biodiversitas Journal of Biological Diversity*, 2022, 23(10).
- 17- Abdulazeem, L., Al-Alaq, F. T., Alrubaei, H. A., Al-Mawlah, Y. H., & Alwan, W. K., Anti-cancer activity of *Opuntia polyacantha* alkaloid extract on human breast cancer cell line. *Journal of Pharmaceutical Sciences and Research*, 2018, 10(7), 1753-1754.
- 18- Mohammad, N. S. K., Ali, A. H., & Salah, L. D. F. S., *Prunus armeniaca* Seeds Extract Inhibits Cell Proliferation and Enhances Cell Death in Cancer Cells. *Journal of Survey in Fisheries Sciences*, 2023, 10(1S), 4178-4195.
- 19- Mahdi, M. F., & Abaas, I. S., Cytotoxic activity of Iraqi *Cressa cretica*. *Al Mustansiriyah Journal of Pharmaceutical Sciences*, 2019, 19(1), 95-102.
- 20- Al-Halbosiy, M. M. F., Hasan, Z. Y. M., Mohammad, F. I., & Abdulhameed, B. A., Biological activities of Iraqi Fig (*Ficus carica*) crude ethanolic and total flavonoids extracts. *Iraqi Journal of Science*, 2020, 1612-1621.
- 21- Alasheqi, M. Q., & Zainulabdeen, J. A., Study of the cytotoxic effects of Iraqi *Ocimum Basilicum* L. extracts on breast cancer cell line. *Egyptian Journal of Chemistry*, 2023, 66(4), 353-360.
- 22- Basim, S., & Kasim, A. A., Cytotoxic Activity of the Ethyl Acetate Extract of Iraqi *Carica papaya* Leaves in Breast and Lung Cancer Cell Lines. *Asian Pacific Journal of Cancer Prevention*, 2023, APJCP, 24(2), 581.
- 23- JAWAD, E., HASANA, S., & NASSIR, Z. S., Phytochemical investigation, anti-proliferative and antioxidant-activities of Iraqi *Capparis spinosa* L. (Family Capparidaceae) against MCF-7 human Breast. *International Journal of Pharmaceutical Research*, 2020, (09752366), 12(2).
- 24- Alsaraf, K. M., Mohammad, M. H., Al-Shammari, A. M., & Abbas, I. S., Selective cytotoxic effect of *Plantago lanceolata* L. against breast cancer cells. *Journal of the Egyptian National Cancer Institute*, 2019, 31(1), 1-7.
- 25- Alsaraf, K. M., Mohamed, M. H., Al-Shammari, A. M., & Abbas, I. S., Broad-Spectrum Cytotoxic Effect of *Calendula officinalis* L. Against Breast Cancer Cells. *Indian Journal of Forensic Medicine & Toxicology*, 2020, 14(1), 803-809.
- 26- Ahmed, A. H., Mohammed, I. H., & Tawfeeq, A. T., Cytotoxic Effect of Alkaloid Extract of *Equisetum arvense* Plant on Human lymphocytes and MCF7 Cancer Cell Line. *Diyala Journal For Pure Science*, 2019, 15(02).
- 27- Al-jubouri, A. M. H., & Saqban, L. H., Cytotoxic effect of the crude alcoholic extract of *Juncus rigidus* on cells of the human breast cancer line MCF-7 in vitro. *International Journal of Health Sciences*, 2022, 6(S3), 6674–6681
- 28- Al-Marzook, F. A. R. A. H. A., & Omran, R. A. B. A. B., Cytotoxic activity of alkaloids extracted from three Iraqi plants against breast cancer cell line". *Asian J of pharmaceutical and clinical research*, 2017, 10.
- 29- Ahmed, O. H., Phytochemical Investigation, Cytotoxic Effect, Antibacterial Effect and Isolation of Phenolic Acid of Iraqi Fenugreek Plant, 2023, 63-81.
- 30- Almzaeni, A. K., Mohammad, M. H., Al-Shammari, A. M., Ahmed, A. A., Shaker, H. K., & Almzaeni, K. A., Parsley Crude Extract Cytotoxicity Against Breast Cancer Cells. *Al-Qadisiyah Journal of Veterinary Medicine Sciences*, 2023, 22(1. Supplement I).
- 31- Hameed, M. F., Mkashaf, I. A., Al-Shawi, A. A., & Hussein, K. A., Antioxidant and anticancer activities of heart components extracted from Iraqi Phoenix *Dactylifera* Chick. *Asian Pacific Journal of Cancer Prevention: APJCP*, 2021, 22(11), 3533.

- 32-Hasan, Z. Y. M., Al-Halbosi, M. M., & Al-Nauimi, E. , Biological Activity and Cytotoxic Effect of Iraqi Wild Mentha arvensis Total Flavonoid. *International Journal of Engineering and Technology*, 2018, 7(4), 26-29.
- 33-Alshaya, Z. E. H., Kadhim, E. J., & Sahib, H. B. , Antiproliferative activities of Althaea ludwigii L. extract on Michigan Cancer Foundation-7 breast cancer cell line. *Journal of Applied Biology and Biotechnology*, 2019, 7(3), 9-11.
- 34-Al-Anee, R. S., Al-Ani, E. H., & Omran, Z. S. , Cytotoxic Activity of Hypericum triquetrifolium Turra Methanolic Extract Against Cancer Cell Lines. *Asian Pacific Journal of Cancer Prevention: APJCP*, 2023, 24(10), 3599.
- 35-Mohammed, M., Mahdi, M. F., Talib, B., & Abaas, I. S. , Identification and isolation of lupeol and p-sitosterol from iraqi Bauhinia variegata and determination the cytotoxic activity of the hexane extract of its leaves, stems and flowers. *Research Journal of Pharmacy and Technology*, 2021, 14(11), 5703-5708.
- 36-Alsabah, A. S., Abd, A. H., & Al-Shammari, A. M. , Cytotoxicity of Xanthium strumarium against breast cancer cell lines. *Journal of Global Pharma Technology*, 2018, 10(3), 767-776.
- 37-Talib, W. H., Mahmood, A. I., Awajan, D., Hamed, R. A., & Al-Yasari, I. H. , Immunomodulatory, Anticancer, and Antimicrobial Effects of Rice Bran Grown in Iraq: An In Vitro and In Vivo Study. *Pharmaceuticals*, 2022, 15(12), 1502.
- 38-Makia, R., Al-Sammarae, K., Al-Halbosi, M., & Al-Mashhadani, M. , In Vitro Cytotoxic Activity of Total Flavonoid from Equisetum Arvense Extract. *Reports of Biochemistry & Molecular Biology*, 2022, 11(3), 487.
- 39-Khansaa, A. S., Hadeel, H., Firas, S., Sundus, H., & Hamdia, M. S. , IN VITRO EVALUATION OF THE EFFECT OF A BOTANICAL COMBINATION ON CANCER CELL CONTROL. *iraq journal of market research and consumer protection*, 2023, 15(2).
- 40-Mustafa, Y. F., Najem, M. A., & Tawffiq, Z. S. , Coumarins from Creston apple seeds: Isolation, chemical modification, and cytotoxicity study. *Journal of Applied Pharmaceutical Science*, 2018, 8(8), 049-056.
- 41-Al-Marzook, F. A., & Omran, R. , Cytotoxic activity of alkaloid extracts of different plants against breast cancer cell line. *Asian J Pharm Clin Res*, 2017, 10(7), 168-171.
- 42-Al-Najm, A., Luo, S., Ahmad, N. M., & Trethowan, R. , Molecular variability and genetic relationships of date palm ('Phoenix dactylifera'L.) cultivars based on inter-primer binding site (iPBS) markers. *Australian Journal of Crop Science*, 2016, 10(5), 732-740.