**DRF-395**
**[1-5]**

RESEARCH ARTICLE Asian Journal of Dairy and Food Research

# Anti-proliferation Activity of Some Plant Extracts against MCF-7 and Hdfn Cell Lines

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**10.18805/ajdfr.DRF-395**

## ABSTRACT

**Background:** In continuation of the efforts made to find an effective cancer treatment that is relatively safe and with fewer side effects, the current study was developed. Several plants and natural products extracted that are used in folk medicine were used in this study.

**Methods:** The plant extracts were divided into two groups to evaluate their antiproliferation activity against MCF-7 and HdFn cell lines by using an MTT assay.

**Result:** Group A [*Saussurea costus, Linum usitatissimum, Teucrium polium, Artemisia annua, Salvia officinalis* and *Berytephusa cuniclaris (crab)*] gave the best results by decreasing the viability of MCF-7 cancer cell line to 42.98% using 400 µg/ml from the extract, well show no high effect on normal cells. Also, the $IC_{50}$ was calculated for both groups, also group A showed the lower $IC_{50}$ with 65.22 µg/ml. In conclusion, plant extracts and natural products can be effective anticancer drugs with high safety, further studies will establish to confirm the results.

**Key words:** Antiproliferation activity, Cancer, Medical plants, Natural products.

## INTRODUCTION

Cancer continues to be a leading cause of mortality globally, despite the development of numerous treatment approaches as mentioned by Zhang *et al.* (2017), Mishra and Hoque (2021) and Haleem *et al.* (2024). According to Choudhuri *et al.* (2018), cancer is generally defined as a medical disorder marked by uncontrollably growing and reproducing cells as a result of gene accumulating mutations. Conventional ways of treating cancer typically involve radiotherapy, chemotherapy and surgery. However, these treatments' efficiency is diminished by cell resistance to them according to Zhang *et al.* (2017) and Moatasem *et al.* (2023). The number of cancer-related deaths is rising, thus it's important to find effective treatment strategies with fewer side effects and cell toxicity. Natural substances have a variety of health benefits, including the ability to treat cancer. Natural products are made from abundant natural resources, such as plants and are naturally occurring chemicals with biological activity as found by Emaduldeen *et al.* (2022).

According to Hasanpourghadi *et al.* (2017), a large number of medicinal medications in use today are produced from natural substance resources. Natural ingredients have played a significant role in the development of anticancer medications Kalaiselvi *et al.* (2022) and Abutaha *et al.* (2024). Many commonly used anti-cancer medications come from natural sources, including bleomycin from marine sources, actinomycin D and C from bacteria, fencristine, etoposide and paclitaxel from plants. For the foreseeable future, several of these substances which are still the cornerstones of cancer treatment will be essential according to Wall and Wani (1995). In order to continue efforts to find new treatments, our current study includes an influence combination of medical plant extracts known to contain anti-cancer compounds and some natural products. Previous research has proven these plant extracts affect against different types of cancers, these plants are Saussurea costus that was proven to have anti-proliferation against breast, liver, colon prostate, lung and gastric cancers as reported by Shati *et al*. (2020); Tian *et al.* (2017); Hung *et al.* (2010) and Ko *et al*. (2005). Also, Teucrium polium has shown anticancer activity against glioblastoma, colon,

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**How to cite this article:** Emaduldeen, H.A., Alaa, K.J., Dhifaf, J.S., Dhuha, J.M., Mohammed, M.T.A., Moatasem, M.A. and Haniza, H.M.Z. (2025). Anti-proliferation Activity of Some Plant Extracts against MCF-7 and Hdfn Cell Lines. Asian Journal of Dairy and Food Research. 1-5. doi: 10.18805/ajdfr.DRF-395.

**Submitted:** 28-03-2024 **Accepted:** 14-01-2025 **Online:** 08-03-2025

melanoma, lung and breast cancers according to Nematollahi-Mahani *et al.* (2012), Menichini, *et al.* (2009) and Nematollahi-Mahani *et al.* (2007). Moreover, Linum usitatissimum inhibited the growth of prostate, breast, colon and skin cancers reported by Zhou *et al.* (2020), Calado *et al.* (2018), DeLuca *et al.* (2018) and Sharma *et al.* (2014). Furthermore, Artemisia annua shown to be an anticancer against Breast, colon and lung cancers these were founded by Jung *et al.* (2021), Ko *et al*. (2020) and Rassias and Weathers (2019). Also, Zingiber officinale in previous studies was found to work against leukemia, prostate, breast, skin, ovarian, lung, pancreatic and colorectal cancers as mentioned by Wei *et al.* (2005), Salehi *et al.* (2019) and Lee *et al.* (2008). Curcuma longa has anticancer against prostate, colorectal, head and neck, breast, brain, glioblastoma and pancreatic cancers these results proved by Dorai *et al.* (2001), Mudduluru *et al.* (2011) and Chakravarti *et al.* (2006). Allium sativum has also been shown to anticancer on pancreas, lung, breast, prostate, colon, stomach, cervical and liver cancers these mentioned by Gore *et al.* (2021) and Chhabria *et al.* (2015). Additionally, the crap extract was also used in the current study which previously showed antiproliferation against breast and lung cancers reported by Tsukada *et al.* (1990) and Rezakhani *et al.* (2014). Also, Propolis poses anticancer activity against leukemia, breast, pancreas, cervical and oral cancers according to Aso *et al.* (2004), Vatansever *et al.* (2010) and Lapidot *et al.* (2002). For these reasons and others these plants were chosen to evaluate their antiproliferation effects on the cancer cell lines as groups not individual.

## MATERIALS AND METHODS

### Plants extraction

Groups A and B of plants were used in the current investigation. *Saussurea costus, Teucrium polium, Artemisia annua, Salvia officinalis, Linum usitatissimum* and *Berytephusa cuniclaris* (crab) are among the plants in Group A. *Salvia officinalis, Artemisia annua, Teucrium polium, Linum usitatissimum, Curcuma longa, Ceratonia silique, Zingiber officinale* and *Propolis* were among the plants in group B. All plants and natural materials were purchased in dry, pure circumstances from Baghdad, Iraq and local markets. Each crude plant weighed fifty grams, which were combined with distilled water in a 1:4 ratio (crud plant: water) and allowed to boil for fifteen minutes. According to Handa *et al.* (2008), the concentrated extracts were filtered and allowed to evaporate completely at room temperature. Following that, the dried extract was weighed and seven working concentrations were made.

This study evaluated the anticancer activity of the plant mixture extract using primary dermal fibroblast normal (HdFn) and human breast adenocarcinoma cancer (MCF-7) cell lines. The cells were grown in accordance with Freshney (2015) in 75 $cm^2$ tissue culture flasks with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin (100 U/mL penicillin and 100 μg/mL streptomycin) in a humidified 5% $CO_2$ environment at 37°C in Eagle's Minimum Essential Medium EMEM (ATCC, USA).

Cytotoxicity of plants Group A and B on MCF-7 and HdFn cell lines was assessed using the MTT assay, in which the cell lines from groups A and B were treated for 48 hours at the following concentrations: 400, 200, 100, 50, 25, 12.5 and 6.25 μg/ml. After that, they were incubated with 10μL of MTT at 37°C for two hours. Following the incubation period, each well was filled with 100 μL of DMSO after the media within the cells was aspirated. At 570 nm, the absorbance was measured with a microtiter plate reader.

### Statistical analysis

One-way analysis of variance (ANOVA) was used to evaluate all the data, which were reported as the mean plus or minus three replicates' standard deviation. In addition, the half-maximal inhibitory concentration ($IC_{50}$) values were computed using the regression equation and the best-fit approach. P values were also computed for every group.

## RESULTS AND DISCUSSION

In the current study, the anticancer effects of a number of plants that people use as traditional medicine were assessed collectively against the MCF-7 cancer cell line by comparing it with the effect against the normal HdFn cell line at 48 hours. These plants were gathered in two groups A and B. Group A showed a high antiproliferation effect against MCF-7 cells by using high concentrations (400, 200 and 100 μg/ml) from the extract and the highest was 400 μg/ml where the viability dropped to 42.978% (Table 1). While the control cell has 76.50% viability at the same concentration as shown in Table (1). Also, $IC_{50}$ for group A was calculated and found to be 65.22 μg/ml against the MCF-7 cell line and 338.6 μg/ml on the HdFn cell line. These data showed a promising result where group A extracts were effective on cancer cell lines well it safe on normal cells. The P value was (<0.0001).

Furthermore, group B showed an antiproliferation effect against MCF-7 cells by using a high concentration of 400 μg/ml from the extract where the viability decreased to 62.886%. While the control cell has 74.26% viability at the same concentration as illustrated in Table (2). Also, $IC_{50}$ for group B was calculated and found to be high concentration against the MCF-7 cell line which was 315.1 μg/ml and

**Table 1:** Results of Group A against MCF-7 and HdFn cell line.

| Concentration | Mean viability (%) ± SD | |
|---|---|---|
| μg/ml | MCF-7 | HdFn |
| 400 | 42.98±4.46 | 76.50±4.84 |
| 200 | 51.66±2.9 | 87.92±3.57 |
| 100 | 59.68±1.54 | 92.21±2.7 |
| 50 | 73.95±1.72 | 96.48±1.2 |
| 25 | 86.72±1.30 | 96.95±1.1 |
| 12.5 | 94.71±2.54 | 94.2±2.97 |
| 6.25 | 94.83±1.9 | 94.25±1.62 |

**Table 2:** Results of Group B against MCF-7 and HdFn cell line.

| Concentration | Mean viability (%) ± SD | |
|---|---|---|
| μg mL$^{-}$ | MCF-7 | Hdfn |
| 400 | 62.89±3.7 | 74.26±2.7 |
| 200 | 79.44±1.5 | 88.27±2.6 |
| 100 | 90.39±1.4 | 93.6±2.1 |
| 50 | 93.82±1.29 | 94.17±1.5 |
| 25 | 94.02±2.63 | 95.22±0.82 |
| 12.5 | 95.60±2.02 | 95.56±1.38 |
| 6.25 | 96.29±0.80 | 95.29±1.05 |

804.2 μg/ml against the HdFn cell line. Although $IC_{50}$ of group B on cancer cells is lower than on normal cells it is considered high. The P value was (<0.0001).

The medical plants that are used in the current study have phytochemical compounds that possess anticancer effects such as the Saussurea costus which contain Sesquiterpene lactones (SLs) according to Lin *et al.* (2016). Furthermore, Teucrium polium is indicated to contain mono and sesquiterpenes, flavonoids, phenolic, saponins terpenoids, alkaloids and terpenoids as reported by Sharifi-Rad *et al.* (2022). Also, Garros *et al.* (2018) found that the Linum usitatissimum used in the current study has phenolic acids, flavonoids and lignin. Artemisia annua is known to contain Artemisinin, coumarins, flavones, flavonols and phenolic acids, sesquiterpenes illustrated by Das (2012). Additionally, Zingiber officinale has Sesquiterpene and gingerols as An *et al.* (2016) mentioned. The well-studied Curcuma longa has many phytochemicals like tannins, alkaloids, saponins, flavonoids, terpenoids, cardiac glycosides and phenolic acids (curcumin) according to Singh and Madan, (2019). Also, Allium sativum is known to contain alliin, allicin, ajoenes, vinyldithiins and flavonoids as Slusarenko *et al.* (2008) found. By influencing the proteins, enzymes and signaling pathways involved in the genesis or progression of malignancies, these phytochemicals-many of which are thought to be pharmaceutically active-have been shown to have potent anticancer properties according to Tariq *et al.* (2017). Phytochemicals are found in trace amounts in the plant extract so using individual plant extracts as anti-cancers requires a huge amount of the same plant, well using multiple plant extracts together provides the required concentrations of the active substance as reported by Lewis and Tollefsbol (2017). So, in the present study, the combination of these plants provided high concentrations of phytochemicals which resulted in duplicated effects against cancer cell lines. Furthermore, a combination of multi-plant extracts or natural products gained more attention in recent years to develop new anticancer drugs or enhance the activity of the exciting ones. In addition, the synergistic effect of plant extracts will show up when multi-plant extracts are used together, which refers to the enhanced or increased effect that is observed when different plant extracts are combined. Many studies have investigated the synergistic effect of plant extracts on various properties, such as antioxidant potential, antimicrobial activity and antifungal activity. The previous study by Saba and colleagues (2017) found that the mixtures of plant extracts exposed higher levels of phenolics, flavonoids and antioxidant activity compared to individual plants which showed more activity than separate plant extracts. For example, the PHY906, Chinese herb medicine contains four plant extracts (Scutellaria baicalensis Georgi, Glycyrrhiza uralensis Fisch., Paeonia lactiflora Pall. and Ziziphus jujube Mill), is a well-known traditional medicine that used for 1800 years. This drug reported to enhance the activity of chemotherapy against gastrointestinal cancer *via* several strategies according to Lam *et al.* (2010), also its work combined with capecitabine to enhance the antitumor activity and decrease the toxicity of capecitabine in HCC (hepatocellular carcinoma) mentioned by Changou *et al.* (2021). There is a hypothesis that suggests the mixture of plant extracts may attack several targets such as receptors, enzymes, signal pathways, *etc.* and all of these result in one goal which destroying the cancer cells as Imming *et al.* (2006) reported. Furthermore, the combination of drugs or natural products may affect the bioavailability in the target site according to Butterweck *et al.* (2000). Furthermore, multidrug therapy in which two or more agents were mixed is a well-known strategy for killing cancer cells and acting the human body immunity or repair mechanisms reported by Doos *et al.* (2014).

## CONCLUSION

Among the results we obtained in our current study is that the combination of plant and natural product extracts in group A gave the best result in the antiproliferation of cancer cells where it reduced the viability at most of the concentrations studied. It also did not affect the normal control cells. These finding prof the anticancer effect of group A extract as well as safety against normal cells. Further studies will be established to evaluate the antioxidant and antiapoptosis ability of the studied extracts on different cancer cell lines. Also, in vivo study will be studied and thus, we will try to find the exact mechanism through which these extracts gave their results.

## ACKNOWLEDGEMENT

The authors express their gratitude to the following institutions and organizations for their invaluable support and scientific assistance: Agriculture College, Al Muthanna University, Environment Research Center, University of Technology- Iraq, Biology Department, Faculty of Science and Mathematics, Sultan Idris Education University.

### Ethical statement

The university of technology in Iraq oversaw the study's completion.

**Conflict of interest**

There is no conflict of interest.

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