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Chemical composition, oxidative stability and antiproliferative activity of *Anethum graveolens* (dill) seed hexane extract

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SUMMARY: This study aimed to evaluate the physicochemical properties, chemical composition, and antiproliferative activity of the hexane extract of *Anethum graveolens* L. (dill) seeds using gas chromatography mass spectrometry (GC-MS). Two fractions, namely the lipid fraction (74%) and volatile fraction (26%), were detected. The extract content of the seeds was about 9.4% and the extract had a pleasant spicy aroma. Oleic acid (52%), *cis*-vaccenic acid (6.2%), linoleic acid (5.5%), and palmitic acid (3.3%) were the key fatty acids in the lipid fraction, while apiol (23%) and d-carvone (2.4%) were the major volatile components. Tocols (tocopherols and tocotrienols) were also detected in the *A. graveolens* extract (155 mg/100 g) and b-tocopherol was identified as the major tocol (71%). Dill extract showed a high oxidative stability (induction time = 45.22 h). Furthermore, dill extract showed antiproliferative activity against breast cancer cell lines.

***KEYWORDS*:** Anethum graveolens*; Antiproliferative activity; Dill seed hexane extract; Oxidative stability; Thermal property; Volatile compounds*

RESUMEN: ***Composición química, estabilidad oxidativa y actividad antiproliferativa del extracto de hexano de semilla de* Anethum graveolens *(eneldo).*** Este estudio tuvo como objetivo evaluar las propiedades fisicoquímicas, la composición química y la actividad antiproliferativa del extracto de hexano de semillas de *Anethum graveolens* L. (eneldo) mediante cromatografía de gases con espectrometría de masas (GC-MS). Se detectaron dos fracciones, la fracción lipídica (74%) y la fracción volátil (26%). El contenido del extracto de las semillas fue de aproximadamente 9,4% y el extracto tenía un agradable aroma picante. Los ácidos oleico (52%), cis-vaccénico (6,2%), linoleico (5,5%) y palmítico (3,3%) fueron los ácidos grasos clave en la fracción lipídica, mientras que el apiol (23%) y la d-carvona (2,4%) fueron los principales componentes volátiles. También se detectaron tocoles (tocoferoles y tocotrienoles) en el extracto de *A. graveolens* (155 mg/100 g) y se identificó el β-tocoferol como el principal tocol (71%). El extracto de eneldo mostró una alta estabilidad oxidativa (tiempo de inducción = 45,22 h). Además, el extracto de eneldo mostró actividad antiproliferativa contra las líneas celulares de cáncer de mama.

PALABRAS CLAVE: *Actividad antiproliferativa;* Anethum graveolens*; Compuestos volátiles; Estabilidad oxidativa; Extracto con hexano de semilla de eneldo; Propiedades térmicas*

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1. INTRODUCTION

Anethum graveolens Linn (*A. graveolens*), also known as dill, is an annual or biennial herb belonging to the Apiaceae family. It is the only species in the genus *Anethum* and is known to originate from Southwest Asia. The plant is cultivated in most parts of the world for its edible leaves and seeds (Shyu *et al*., 2009; Jana and Shekhawat, 2010). It is commonly known as Shibt (Chibt) or ain jaradeh (grasshopper's eye) in the Middle East. *A. graveolens* grows up to 90 cm, with alternate leaves that are exquisitely divided, and exhibits fine empty stems. The flowers are yellow and develop into small umbels. The seeds have a pleasant aromatic odor. In comparison with caraway seeds, dill seeds are flatter, smaller, and lighter (Jana and Shekhawa, 2010). *A. graveolens* seeds and leaves are the most useful parts of the plant. The leaves may be used in meats, eggs, salads, seafoods, and soups, while the seeds are used in soups, bread, and for flavoring pickles (Shyu *et al*., 2009).

A. graveolens seeds have stimulant, carminative, stomachic, and diuretic properties, and are widely used in traditional medicines (Jana and Shekhawat, 2010; He and Huang, 2011). Yang *et al*., (1996) and Lanky *et al*., (1993) found that the consumption of *A. graveolens* leaves may reduce the risk of cholesterolemia and cancer.

Both *A. graveolens* seed and herbage (leaves, stems, and flowers) contain a flavored essential oil, which may alleviate pain, promote digestion, improve appetite, prevent arteriosclerosis, and relieve flatulence (He and Huang, 2011; Stojanov, 1973). Furthermore, *A. graveolens* seed oil is known to eradicate some fungal infections (Lopez *et al*., 2005; Fatope *et al*., 2006).

Cancer is a main health problem with more than 18 million cases and 6 million deaths in 2018 (Bray *et al*., 2018); it causes a great emotional and economic burden (Girgis *et al*., 2018). In Saudi Arabia, a significant increase in breast cancer cases in young women was recorded between 2001 and 2008. Noticeably, the increase was higher in the eastern province of the kingdom indicating the vulnerability of women in this region (Aldosari, 2017). Anticancer drugs are among the main threats in the therapeutic era (Safhi *et al*., 2017). Therefore, there is a need to find new anticancer agents from natural sources to overcome this problem.

There is, however, no thorough report on the antiproliferative activity of *A. graveolens* seed extract. In addition, no sufficient studies on the thermal and oxidative stability of this seed extract have been performed. The physicochemical and thermal properties of this extract were investigated and the tocol and fatty acid compositions were determined. The results obtained may improve our knowledge about the use of *A. graveolens* seed extract in food and other industries.

2. MATERIALS AND METHODS

All measurements were performed in triplicate. The values of the various parameters were expressed as the mean ± standard deviation (SD).

2.1. Plant material and extraction

Mature seeds of *A. graveolens* were collected from the Experimental Research Station Derab, College of Agriculture, King Saud University, Riyadh, Saudi Arabia, during June, 2015. A voucher specimen (KSU no. 24-54-1) was deposited at the Herbarium of the Department of Botany and Microbiology, College of Science, King Saud University, Riyadh 1145, Saudi Arabia. After oven-drying the seeds at 40 °C for 24 h, the dried seeds were milled in a K/IKA-WERKE M20 grinder. A six -place Soxtec 8000 extraction unit (Foss, Suzhou, China) was used to extract the seed oil using hexane as solvent under the following conditions: Boiling temperature of 100 °C, boiling time of 5 min, rinsing time of 20 min, recovery time of 60 min, powder mass of 20 g, and hexane volume of 60 ml. The extract was stored in a refrigerator at −15 °C until analysis. Fatty acid methyl ester standards (FAMEs) were obtained from Sigma-Aldrich Corporation (Steinheim, Germany). Tocopherols and tocotrienols (tocols) were purchased from Sigma Chemical Co. (St. Louis, MO, USA). The chemicals used in this investigation were of analytical grade or chromatographic purity. The sunflower oil used for the thermal analysis was obtained by the same extraction method using seeds purchased from a local market. Sunflower oil was used as standard for comparison purposes.

2.2. Physicochemical properties of *A. graveolens* seed extract

We used International Organization for Standardization (ISO) standards to determine the acidity (ISO 3960) and peroxide value (ISO 660). Carotenoid and chlorophyll contents were determined from the absorption spectra of the extract according to the method described by Nehdi *et al*., (2014a). The spectroscopic properties of *A. graveolens* extract diluted in n-hexane (1, 10%, v/v) were evaluated. The absorbance was measured at 290-400 and 400-800 nm using UV-1800 (Shimadzu, Kyoto, Japan).

2.3. Antiproliferative activity of *A. graveolens* seed extract

2.3.1. Cytotoxicity and cell morphology

The cell lines MCF-7 and MDA-MB-231 were obtained from the DSMZ-German collection of cell cultures and cultivated in Dulbecco's modified

Eagle's medium (DMEM) (Invitrogen, USA) supplemented with 10% fetal bovine serum (FBS; Gibco, USA) in 5% CO_2 and a humidified atmosphere at 37 °C. Cells were plated onto 24-well plates (10^5 cells/mL) and incubated with the extract at increasing concentrations (10, 25, 50, 100 µg/mL) for 48 h. Untreated samples were used as controls. In each well, 100 µL of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) solution (5 mg/mL) were added and the plates were incubated at 37 °C in a 5% CO_2 atmosphere for 2 h. The medium containing the MTT reagent (Invitrogen, USA) was discarded and the formazan product was dissolved with acidified isopropanol (1 mL added to each well). The plates were incubated in a shaker at 200 rpm for 10 min. Optical density was measured at 540 nm wavelength using a plate reader (Biochrom, England) to determine cell viability. The experiments were repeated thrice. The IC_{50} value, or the concentration of *A. graveolens* extract required to inhibit 50% of cell population, was calculated using dose-dependent curves. The morphology of cells exposed to dill extract was observed using a Leica inverse-phase contrast microscope (Leica, Germany).

2.3.2. Lactate dehydrogenase (LDH) release assay

We performed LDH assays to evaluate the LDH release into the media from MDA-MB-231 and MCF-7 cells after 48 h of incubation with dill seed extract at IC_{50} concentration using LDH kit (Sigma, USA). The quantity of LDH released in the media was determined using an enzyme-linked immunosorbent assay (ELISA) reader (Biochrom, England) at 490 nm wavelength.

2.4. Gas chromatography mass spectrometry (GC/MS) analysis

We prepared FAMEs according to the laboratory protocol described by Nehdi *et al*., (2013) and analyzed using a GC-MS (QP2010 Ultra, Shimadzu, Kyoto, Japan). An RT-2560 column (100 m length, 0.25 mm internal diameter, 0.25-µm film thickness) was used for FAME separation. Helium was used as carrier gas at a flow rate of 1.50 mL/min. The oven temperature was increased from 115 °C to 240 °C at a rate of 2 °C/min and held for 15 min. A Shimadzu software (Cat. No. 225-21731-92) was used for the chromatogram analysis. In addition, the NIST analysis software and NIST11 library were used for the interpretation of the mass spectra and identification of each FAME.

2.5. Analysis of tocols (tocopherol and tocotrienol)

The standard ISO 9936 procedure was used to determine the tocol content of *A. graveolens* seed extract. Briefly, a 0.5-g aliquot of the dill extract was dissolved in 25 mL of hexane, and 20 µL of the solution was injected into an LC-20AT high-performance liquid chromatography (HPLC) pump (Shimadzu, Kyoto, Japan). Tocols were separated on a Hypersil silica column (15 cm × 3 mm I.D., 3-µm particle size; Thermo Scientific). An isocratic elution with hexane/2-propanol (99.5:0.5; v/v) at a flow rate of 0.5 mL/min was used for separation. Each tocol was detected by a fluorescence detector set at 330 nm emission wavelength and 295 nm excitation wavelength. Authentic standards were used for the identification of tocols.

2.6. Oxidative stability

The induction time (IT) of each sample was analyzed with a 743 Rancimat analyzer (Metrohm AG, Herisau, Switzerland). Briefly, 3 g of the extract were incubated in the measuring vessel tube and heated up to 110 °C under an air flow rate of 20 L/h to obtain the IT of the extract.

2.7. Thermal analysis

Thermogravimetric (TGA) and first derivate thermogravimetric (DTGA) curves were obtained by a thermogravimetric analyzer TGA-50 (Shimadzu, Kyoto, Japan). A 5-mg sample mass placed in an alumina crucible was heated up to 600 °C at a heating rate of 10 °C/min under a synthetic zero air atmosphere (100 mL/min). The data of three independent measurements were analyzed by Shimadzu TA-60WS (2.20) software.

3. RESULTS AND DISCUSSION

3.1. Fatty acid and volatile compound compositions

The results of GC/MS analysis of *A. graveolens* seed extract (Table 1) revealed that the extract comprised a mixture of fixed oil (74%) and essential oil (26%). The key fatty acids in the fixed oil component were oleic acid (OL) and its isomer *cis*-vaccenic acid (VA), which together represented more than 58% of the total compounds, followed by linoleic acid (LA) (5.5%) and palmitic acid (3.3%). Furthermore, linolenic, stearic, and erucic acids were present at a 4.5% concentration. Olive oil, which is rich in OL, is consumed to reduce the risk of coronary disease (Ruiz-Canela *et al*., 2011). Djoussé *et al*., (2014) observed a correlation between decreased risk of coronary heart disease and high plasma levels of cis-vaccenic acid.

The fatty acid LA has health-promoting effects. Topical application of oil containing LA may prevent skin diseases (acne, inflammation, dryness, and roughness) (Mokbli *et al*., 2018).

The principle volatile compounds were apiol (23%) and d-carvone (2.4%). Furthermore, the

amount of *trans*-dihydrocarvone was only 0.44%. Apiol is a phenylpropanoid compound found in parsley (*Petroselinum crispum*) essential oil extracted from the seed or aerial part (Zhang *et al*., 2006; Farzaei *et al*., 2013). Apiol is the main constituent (90.7%) identified in the hexane extract of *Piper aduncum* leaves. This compound has two symmetrical methoxy groups. The radical-scavenging activity of the benzene ring is improved by the presence of these two methoxy groups, which are strong electron donors. Zhang *et al*., (2006) reported that apiol is the primary contributor to the antioxidant activity of parsley oil.

Elmastaş *et al*., (2006) found that d-carvone is an oxygenated monoterpene with stronger antioxidant activity than α-tocopherol.

TABLE 1. *A. graveolens* seed extract composition (fatty acid and volatile compounds).

Compound	Common name	(%)
Fatty acid		
C8:0	Caprylic	0.10 ± 0.05
C12:0	Lauric acid	0.11 ± 0.01
C14:0	Myristic acid	0.10 ± 0.03
C15:0	Pentadycilic	0.10± 0.01
C16:1(ω7)		0.12± 0.03
C16:1 (ω9)	Palmitoleic acid	0.13± 0.04
C16:1 (ω11)		0.11 ± 0.03
C16:0	Palmitic acid	3.30± 0.12
C17:0	Margaric acid	0.10± 0.02
C17:1(ω7)		0.12 ± 0.02
C18:3(ω3)	Linolenic acid	0.95± 0.04
C18:2(ω6)	Linoleic acid	5.50± 0.33
C18:1(ω9)	Oleic acid	52.00±1.10
C18:1 (ω7)	cis-Vaccenic acid	6.20± 0.54
C18:0	Stearic acid	1.30± 0.04
C20:1(ω9)	Eicosenoic acid	0.52± 0.02
C20:0	Arachidic acid	0.34± 0.04
C22:1(ω9)	Erucic acid	2.30 ± 0.05
C22:0	Behenic acid	0.11± 0.02
C24	Lignoceric	0.12 ± 0.01
C24/1(ω9)		0.23 ± 0.02
Total (%)		74
Volatile compounds		
$C_{10}H_{16}$	d-Limonene	0.33 ± 0.01
$C_6H_{14}O$	3-Hexanol	0.27 ± 0.01
$C_{10}H_{16}O$	*trans*-Dihydrocarvone	0.44 ± 0.02
$C_{10}H_{14}O$	d-Carvone	2.40 ± 0.11
$C_{12}H_{14}O_4$	Apiol	23.00 ± 1.10
Total (%)		26

The % values are the average ± SD of three replicates.

It plays an important role as a free radical-scavenging agent against N(ω)-nitro-L-arginine methyl ester (L-NAME)-induced hypertension, a major factor involved in cardiovascular diseases (Rajeshwari and Raja, 2015).

A. graveolens seed extract is a healthy natural product rich in antioxidant compounds. It can be used in food as a natural preservative and antioxidant to prevent lipid oxidation as well as to retard rancidity (Galanakis *et al*., 2018). Furthermore, it may be used as a pharmaceutical ingredient (Aludatt *et al*., 2017).

3.2. Tocol (tocopherols and tocotrienols) composition

Seven isomers of vitamin E were found in the *A. graveolens* extract at a 155 mg/100 g concentration. These included α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol α-tocotrienol, γ-tocotrienol, and δ-tocotrienol (Table 2). The principle isomers present were β-tocopherol and γ-tocotrienol at a concentration of 110 and 21 mg/100 g, respectively. β-isomer exists in low concentrations (0.3-2.5 mg/100 g) in most conventional vegetable oils such as soybean, sunflower, olive, and corn oils (Nehdi *et al*., 2014b). Hence, the *A. graveolens* lipid fraction may be considered as a source of this rare β-isomer, which inhibits lipid oxidation by suppressing free radicals such as hydroperoxides. The presence of other tocols maintains the

TABLE 2. Physicochemical properties and tocol composition of *A. graveolens* seed extract.

Parameter	Unit	*A. graveolens extract*
Yield	% (w/w)	9,40± 0.33
Peroxide value	meq O_2/kg oil	9.51±0.75
Free fatty acid	oleic %	4.20± 0.13
Color		Green
State at ambient temperature		Liquid
Chlorophylls	mg/kg	9.90± 0.44
Carotenoids	mg/kg	41.02±1.11
Oxidative stability (110°C)	h	45.22 ± 1.31
Tocol		
α- Tocopherol	mg/100g	9.90 ± 0.42
β- Tocopherol	mg/100g	110.10 ±1.50
γ- Tocopherol	mg/100g	4.85 ± 0.50
δ- Tocotrienol	mg/100g	1.61 ± 0.22
α- Tocotrienol	mg/100g	5.25 ± 0.22
γ- Tocotrienol	mg/100g	21.05 ± 0.65
δ- Tocotrienol	mg/100g	2.23± 0.33
Total	mg/100g	155

The values of all parameters are the average ± SD of three replicates.

flavor quality of the product. Thus, *A. graveolens* seed extract may be added into food products to prevent oxidation.

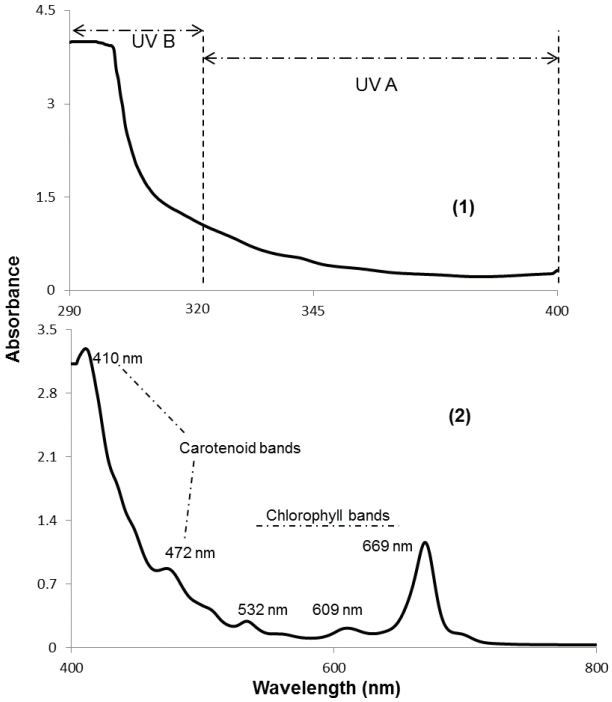

FIGURE 1. UV–visible spectra of *A. graveolens seed* extract (diluted in n-hexane (1, 10%, v/v) measured at (1) 290-400 nm, (2) 400-800 nm; respectively.

3.3. Physicochemical properties

The extract content of *A. graveolens* seeds was 9.4%. The extract was green in color and had a pleasant, spicy aroma. The characteristic green color of the extract may be associated with the presence of chlorophyll (9.9 mg/kg, Table 2), as confirmed by the strong absorption band at 669 nm (Figure 1). Despite the presence of carotenoids in the extract (41 mg/kg), the green color of chlorophyll was dominant. Carotenoids are widely used in the pharmaceutical, medical, cosmetic, and food industries (Siger *et al.*, 2017). The extract showed medium quality indices such as peroxide value (9.5 meq O_2/kg) and acidity (4.2%) (Table S2). The UV absorbances of the extract in UV-A and UV-B ranges (320-400 and 290-320 nm, respectively) were stronger than those of sunflower and *Citrullus colocynthis* seed oils (Nehdi *et al.*, 2013). Thus, *A. graveolens* extract may have protective effects against UV-B-induced sun burn (Schwarz *et al.*, 1995) and UV-A-induced premature skin aging (Tebbe *et al.*, 1997). The *A. graveolens* extract may be used as an ingredient in the formulation of sunscreen lotions and creams (Nehdi *et al.*, 2013). Furthermore, it may serve as a food additive owing to its pleasant aroma.

3.4. Oxidative stability

A. graveolens extract showed a high IT of 45.22 h (Figure 2). This observation revealed the high resistance of the extract against oxidation. The IT of this

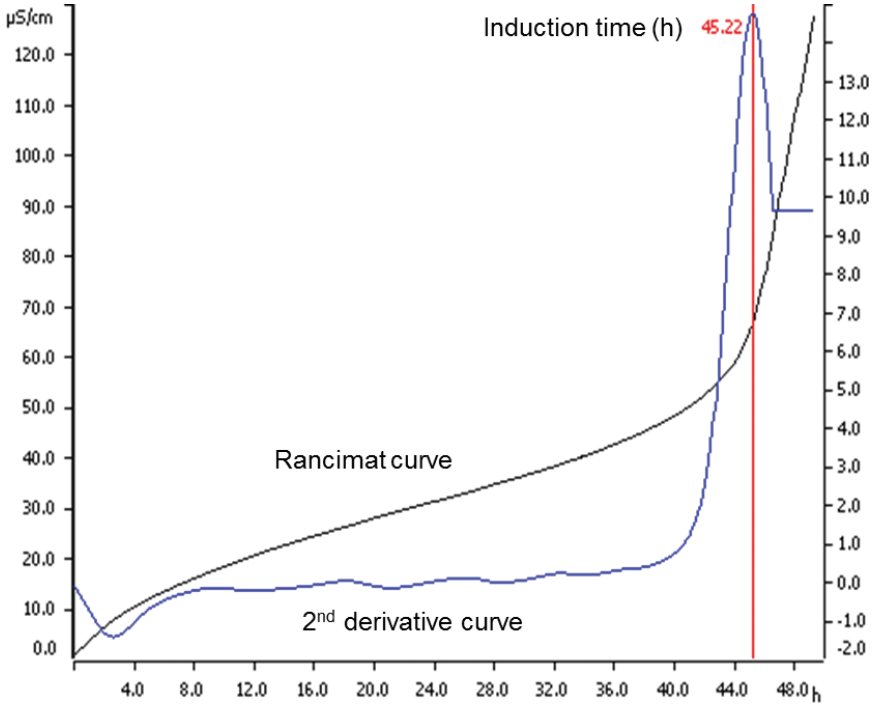

FIGURE 2. Rancimat diagram for *A. graveolens* seed extract (110 °C).

extract was higher than that of date seed oil (21 h difference) (Nehdi *et al*., 2018), soybean oil (6.5 h difference) (Taghvaei *et al*., 2014), safflower oil (2.87 h difference), and flax seed oil (1.57 h difference) (Bozan and Temelli, 2008). This observation may be attributed to the low content (6.4 %) of linoleic and linolenic acids and the presence of antioxidants such as tocols, apiol, and d-carvone. However, these antioxidants may together produce synergistic effects, thereby positively affecting the oxidative stability of the *A. graveolens* extract.

3.5. Thermal profile

The comparison between the TGA and DTGA curves of *A. graveolens* extract and sunflower extract is shown in Figure 3. The TGA curve showed that the extract was thermally unstable compared to sunflower seed oil. *A. graveolens* extract lost 5% of its mass at 92 °C; however, sunflower oil showed a 5% mass loss at 247 °C. Heating resulted in the evaporation of the volatile fraction from *A. graveolens* extract, and maximum evaporation was observed at 353 °C. Further heating resulted in a similar effect to that observed with the sunflower oil. The extract showed mass loss at three steps with nearly the same maximum at 352-353 °C, 428 °C, and 516-541 °C. The mass loss was attributed to the evaporation of different groups of triacylglycerols.

Thermogravimetric analysis may be used as a successful method for the estimation of the purity of the seed oil. The DTGA curve of the mixture of seed oil and essential oil showed an additional evaporation peak of the essential oil.

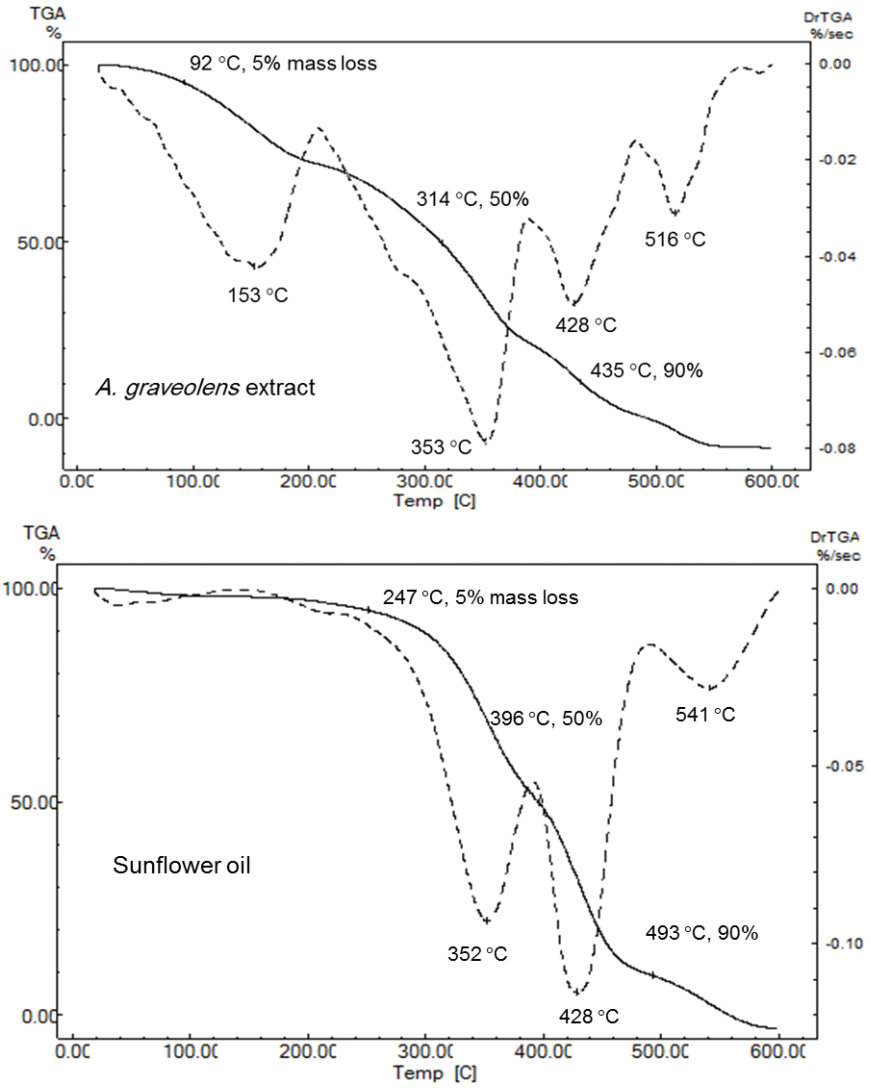

FIGURE 3. Thermogravimetric (TGA) and first derivate thermogravimetric (DTGA) curves of *A. graveolens* extract and sunflower seed oil.

3.6. Antiproliferative activity of *A. graveolens* seed extract

Further studies are warranted to discover new therapeutics counteract the problems related to emerging resistance to existing cancer drugs. Plants are rich in bioactive compounds that play a crucial role in cancer chemotherapy, such as vincristine and taxol isolated from *Vinca rosea* and *Taxus brevifolia*, respectively (Prakash *et al*., 2013).

To evaluate the cytotoxicity of *A. graveolens* seed extract, breast cancer cells MDA-MB-231 and MCF-7 were treated with different concentrations of the extract and a MTT assay was performed to analyze cell viability. The MTT assay is an indicator of cellular metabolic activity based on the reduction of MTT by the mitochondrial enzymes to purple-colored formazan. It is used to study the cytotoxic effects of toxic compounds and plant extracts against cancer cell lines.

A. graveolens extract showed a dose-dependent inhibitory effect on MCF-7 and MDA-MB-231 cells with IC_{50} values of 53 and > 100 µg/mL, respectively (Figure 4A). Maximum toxicity was observed at a concentration of 100 µg/mL, where the viabilities of MCF-7 and MDA-MB-231 cells reduced to approximately 31 and 63%, respectively. Figure 4B shows the effect of *A. graveolens* seed extract on LDH release from MCF-7 and MDA-MB-231 cells. LDH is a reliable marker of cytotoxicity because injured cells are fragmented following incubation with the extract. Therefore, LDH leakage from MCF-7 and MDA-MB-231 cells is attributed to the cytotoxic nature of *A. graveolens* seed extract, which confirms its antiproliferative activity.

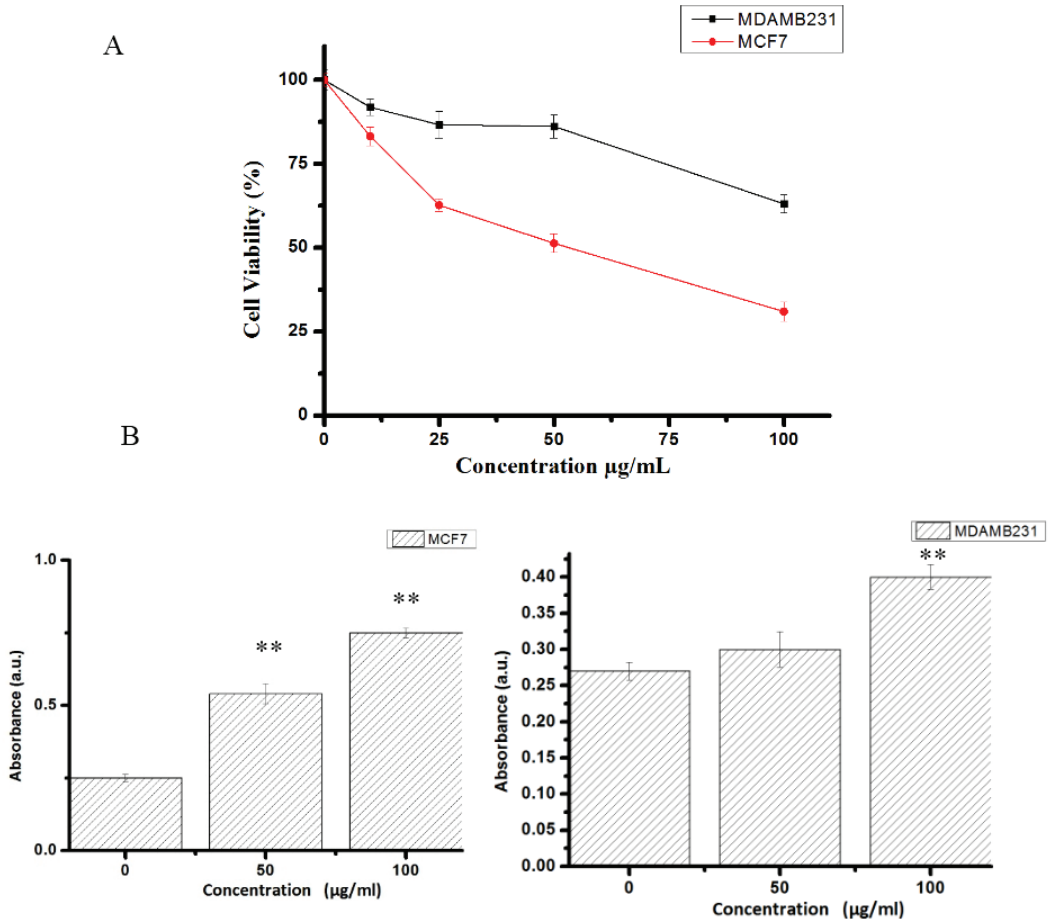

FIGURE 4. Anti-proliferative effect of *A. graveolens* seed extract on human breast cancer cells. (A) Dose-dependent curves of dill seed oil treatment in MCF-7, and MDA-MB-231 cells. Cells were cultured in 24-well plates and treated with different concentrations (10-100 µg/ml) for 48 h. Cell viability was measured by the MTT assay. (B) MCF-7 and MDA-MB-231 were treated with IC_{50} for 48 h, LDH released into the media was determined at 490 nm in a multi-well plate reader. Statistical differences were analyzed with Student's t-test. Data represent the mean ± S.D. *P < 0.05 was considered significant compared to the control. Data were presented as mean ± SD (n = 3).
MCF-7: Michigan Cancer Foundation-7; MDA-MB-231: Anderson-Metastatic Breast-231;
MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; LHD: lactic acid dehydrogenase.

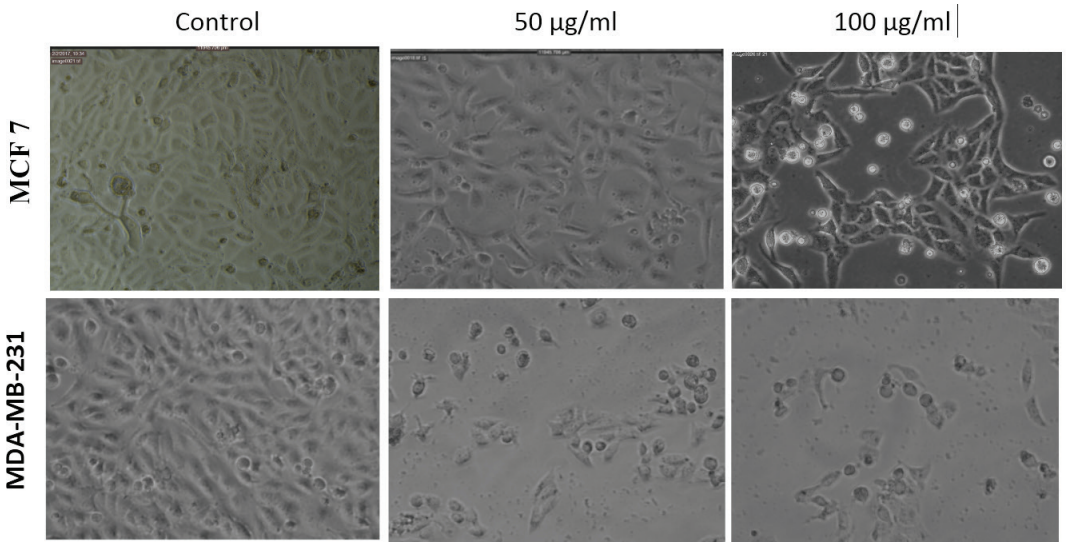

FIGURE 5. Morphological changes in MCF-7 and MDA-MB-231 cells treated with *A. graveolens* seed extract. Cells were treated with vehicle or *A. graveolens* seed extract for 48 h. Images were taken by a phase contrast microscope (Leica, Germany). Magnification: 200 ×. MCF-7: Michigan Cancer Foundation-7; MDA-MB-231: Anderson-Metastatic Breast-231.

This antiproliferative activity may be associated with the presence of apiol in the *A. graveolens* seed extract. di Stefano *et al*., (2011) observed that apiol exhibits cytotoxicity against K-562, NCI-H460, and MCF-7 cancer cells. The percentage of LDH released from MCF-7 and MDA-MB-231 cells significantly increased ($p < 0.05$) after 48 h of incubation (Figure 4B). The percentage increase in LDH release was significant for MCF-7 and MDA-MB-231, respectively, as compared to the control (Figure 4B) at the concentration of 100 µg/ml.

Figure 5 shows the morphology of MDA-MB-231 and MCF-7 cells exposed to dill extract. Cell morphology was assessed under a microscope after treatment with *A. graveolens* seed extract at 50 and 100µg/ml for 48 h. The cells from the treatment group were shrunken and showed condensed nuclei. In addition, these cells were detached. The higher the concentration of dill oil, the larger was the percentage of abnormal cells (Figure 5). These observations indicate that the effects observed in the treatment groups were associated with nuclear and cytosol shrinkage, which were the markers of apoptotic events (Kalinichenko and Matveeva, 2008). Our result is in agreement with Mohammed *et al.*, (2018) who reported the anticancer potential of *A. graveolens* seed extract against HepG2 cells, though the concentration used was higher than 300 µg/ml. Interestingly, the extract showed a different response to the breast cancer cell lines tested and this could be attributed to the difference in the cell lines used. Thus, the seed oil of the *A. graveolens* plant could be a chemotherapeutic option against breast cancer.

4. CONCLUSIONS

The present study revealed that *A. graveolens* seed extract is a mixture of vegetable oil and essential oil and may be used as a flavoring agent for beverages and foods, owing to its pleasant, spicy odor. The presence of antioxidants such as tocols, carotenoids, apiol, and d-carvone may extend its application as a food ingredient to improve the safety and shelf-life of food products during storage through the suppression of food oxidation. This natural *A. graveolens* extract may replace synthetic food preservatives and reduce environmental and health problems caused by chemical compounds. In addition, this extract has potent antiproliferative activity that could be helpful in promoting the development of a potential anticancer agent from natural products.

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DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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