ORIGINAL ARTICLE

Bioactivity and chemical characterization of *Acalypha fruticosa* Forssk. growing in Saudi Arabia

Ghada Ahmed Fawzy\textsuperscript{a,b,*}, Areej Mohammad Al-Taweel\textsuperscript{a}, Shagufta Perveen\textsuperscript{a}, Shabana Iqrar Khan\textsuperscript{c}, Fatma Abdulaziz Al-Omary\textsuperscript{d}

\textsuperscript{a} Department of Pharmacognosy, College of Pharmacy, King Saud University, PO Box 2457, Riyadh 11451, Saudi Arabia
\textsuperscript{b} Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Cairo 11562, Egypt
\textsuperscript{c} National Center for Natural Products Research, School of Pharmacy, University of Mississippi, 38677, USA
\textsuperscript{d} Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia

Received 12 April 2016; accepted 16 May 2016
Available online 24 May 2016

**KEYWORDS**

*Acalypha fruticosa*; Anti-inflammatory; PPAR\textsubscript{a}; PPAR\textsubscript{\gamma} agonistic activity

**Abstract**

*Acalypha* is an important genus of the Euphorbiaceae family. The genus is represented by five species in Saudi Arabia. *Acalypha fruticosa* Forssk. Fl. Aeg is traditionally used as a cure for stomachache, dyspepsia, rheumatism, dermatitis, and swellings of the body. The present study endeavors to provide a phytochemical and biological evaluation of the plant, with the aim of relating activity to constituting secondary metabolites in the plant. Column chromatographic separation of the methanol extract led to the isolation of four compounds namely 2-methyl-5,7-dihydroxychromone 5-O-\beta-D-glucopyranoside 1, acalyphin 2, apigenin 3 and kaempferol 3-O-rutinoside 4. The plant extracts and the isolated compounds were subjected to biological assays to screen peroxisome proliferator-activated receptor alpha (PPAR\textsubscript{a}) and PPAR\textsubscript{\gamma} agonistic, anti-inflammatory and cytotoxic activities. Results proved for the first time, the PPAR\textsubscript{\gamma} activator effect of acalyphin, as well as its promising anti-inflammatory activity, in addition to the dual PPAR activator effect of the chromone glucoside. The plant extracts and isolated compounds were non-cytotoxic to the tested cell lines. Thus *A. fruticosa* could be a valuable source of important therapeutics that may hold clinical prospect.

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1. Introduction

*Acalypha* is the fourth largest genus of the Euphorbiaceae family. It consists of 450 species, in the form of evergreen shrubs, trees and annuals, mainly in the tropical regions of Africa, America and Asia (Seebaluck et al., 2015). The genus is represented by five species in Saudi Arabia (Alfarhan et al., 2005). Most of the *Acalypha* species are used as medicinal plants. *Acalypha fruticosa* Forssk. Fl. Aeg is an erect shrub, up to 1 m tall, with strong aromatic odor. It has various traditional uses, a cure for stomachache, dyspepsia, venous antedote, rheumatism and dermatitis (Senthilkumar et al., 2006; Mothana et al., 2010). Additionally, the leaf infusion is used to treat stomach problems and swellings of the body, while the leaf maceration is applied in eye infections and its decoction is consumed in Tanzania to treat epilepsy (Gopalakrishnan et al., 2010). Previous studies on *A. fruticosa* indicated the presence of triterpenoids, steroids, tannins, saponins, flavonoids, alkaloids, anthraquinones and sugars. 1, 2-Benzene dicarboxylic acid diisoctyl ester, n-Hexadecanoic acid, 9, 12-octadecadienoic acid [z,z]-α-glucopyranoside and eicosyltrichlorosilane were identified by Gas Chromatography-Mass spectrometry [GC–MS] analysis of the plant extracts (Gopalakrishnan et al., 2010). The plant has also been subjected to several biological investigations, concerning its antioxidant, anti-inflammatory, wound healing and cytotoxic properties (Gopalakrishnan et al., 2010; Rajkumar et al., 2010). *A. fruticosa* is also used as sand fly repellent, and used in ethnoveterinary practices, as it demonstrates similar medicinal properties in both humans and animals (Seebaluck et al., 2015).

The metabolic syndrome is currently a major worldwide epidemic. It strongly associates with obesity, insulin resistance, type 2 diabetes, and cardiovascular diseases, which are major pathological contributions to mortality and morbidity worldwide (Wang et al., 2014). People affected by the metabolic syndrome have a greater risk of developing cardiovascular diseases, which are major epidemic. It strongly associates with obesity, insulin resistance, type 2 diabetes, and cardiovascular diseases, which are major epidemic. It strongly associates with obesity, insulin resistance,

2. Materials and methods

2.1. General experimental procedures

The 1D and 2D NMR spectra were recorded on a Bruker AMX-500 spectrometer with tetramethylsilane (TMS) as an internal standard. The chemical shifts are in ppm (δ), relative to tetramethylsilane as an internal standard and scalar coupling constants (J) recorded in Hertz. ESI-MS analyses were measured on an Agilent Triple Quadrupole 6410 QQQ LC/MS mass spectrometer with ESI ion source (gas temperature is 350 °C, nebulizer pressure is 60 psi and gas flow rate is 12 L/min), operating in the negative and positive scan modes of ionization through direct infusion method using CH₃OH⋅H₂O (1:1 v/v), flow rate of 0.4 mL/min. Column chromatography was carried out on Sephadex LH-20 (E. Merck, Darmstadt, Germany), silica gel (Sigma-Aldrich, St. Louis, MO, USA). Thin layer chromatography (TLC) was performed on precoated TLC plates (Aluminum sheets, silica gel, RP-18 F254, Merck; Germany); the detection was done at 254 nm and by spraying with ceric sulfate reagent. Solvent systems used were S1 (CHCl₃/MeOH 7:3), S2 (EtOAc/MeOH/dil ammonia 8:2:2) on silica gel plates and S3 (50% aqueous MeOH) on silica gel plates and RP-18 plates.

2.2. Plant material

The aerial parts of *A. fruticosa* (1.1 kg) were collected from Southwestern region, Saudi Arabia (Jabal Shada al-A’la) in February, 2013. The plant was identified by Dr. Mohammed Yusuf, Professor of Taxonomy, College of Pharmacy, King Saud University. A voucher specimen (No. 16018) has been deposited in the herbarium of Department of Pharmacognosy, King Saud University.

2.3. Extraction and isolation

The aerial parts of *A. fruticosa* (1.1 kg) were shade-dried, ground and successively extracted at room temperature with chloroform (3 × 2.5 L) and methanol (4 × 2.5 L). A part of the methanol extract (50 g) was dissolved in water and loaded on Sephadex LH-20 column (5 × 120 cm, 500 g), and the elution started with water followed by H₂O/MeOH gradient mixtures till 100% MeOH, to afford three main sub-fractions. Fraction M-I (1.5 g, eluted by 30% MeOH/Water), was rechromatographed on a silica gel column (2 × 100 cm, 100 g), elution started with 7% MeOH/CHCl₃ to afford compounds 1 (12% MeOH/CHCl₃) (40 mg) and 2 (15% MeOH/CHCl₃) (10 mg). Sub-fraction M-II (0.5 g, eluted by 40% MeOH/Water), was chromatographed on silica gel (2 × 100 cm, 80 g), in 10% MeOH/CHCl₃, to afford compound 3 (12 mg). Sub-fraction M-III (1.3 g, eluted by 45% MeOH/Water), was chromatographed on silica gel (2 × 100 cm, 100 g), in 10% MeOH/CHCl₃, to afford compound 4 (30 mg) in 15% MeOH/CHCl₃.

2.4. Characterization of isolated compounds

2-methyl-5,7-dihydroxycromone 5-O-β-D-glucopyranoside (1): white needles, mp 162–163 °C, violet color on TLC under UV-light (254 nm); 1H NMR (MeOD) δ: 6.77 (1H, d, J = 2 Hz, H-6), 6.51 (1H, d, J = 2 Hz, H-8), 6.01 (1H, s, H-3), 4.82 (1H, d, J = 8 Hz, H-1'), sugar protons H2-2'-H6', at δ 3.98–3.32, 2.33 (3H, s, Me), 13C NMR (MeOD) δ: 178.8 (C-4), 165.7 (C-7), 163.1 (C-8a), 159.5 (C-2), 158.6 (C-5), 110.2 (C-3), 107.7 (C-4a), 103.6 (C-6), 103.2 (C-8), 97.7 (C-1'), 77.2 (C-3'), 75.8 (C-5'), 73.3 (C-2'), 69.8 (C-4'), 61.1 (C-6'), 18.5...
(Me-2). $^1$H and $^{13}$C NMR data were consistent with other literature; molecular ion peak $m/z$ 354 [M]$^+$ corresponding to the molecular formula C$_{16}$H$_{18}$O$_9$ (Tane et al., 1990).

Acalyphon (2): white powder, Dragendorff-positive spot on TLC; $^1$H NMR (MeOD) δ: 5.41 (1H, s, H-3), 5.30 (1H, s, H-6), 3.02 (2H, s, N-CH$_3$), 3.85 (3H, s, O-CH$_3$), 4.75 (1H, d, J = 7.5 Hz, H-1’), 3.20–3.80 (m, H$_2$-H6’). $^{13}$C NMR (MeOD) δ: 164.5 (C-6), 159.2 (C-4), 115.2 (–CN), 103.1 (C-1’), 96.9 (C-5), 84.5 (C-2), 78.3 (C-5’), 77.7 (C-3’), 74.4 (C-2’), 71.1 (C-4’), 62.5 (C-6’), 56.8 (O-CH$_3$), 32.9 (N-CH$_3$); molecular ion peak $m/z$ 360.3, [M$^+$]$,^-$ neg.mod., $m/z$ 359.2 [M$^-$/H]$^-$(Nahrstedt et al., 1982).

Apigenin (3): pale yellow amorphous powder, pale yellow fluorescence (AlCl$_3$) under UV-light (365 nm) and green color with FeCl$_3$ spray reagents. $^1$H NMR (MeOD) δ: 7.48 (2H, d, J = 8.5 Hz, H-2’/6’), 6.83 (2H, d, J = 8.5 Hz, H-3’/5’), 6.40 (1H, brs, H-8), 5.20 (1H, brs, H-6), 5.46 (1H, d, J = 7.5 Hz, H-1’), 4.53 (1H, brs, H-1’), 3.83–3.23 (m, H$_2$”–H6”), 1.11 (3H, d, J = 6 Hz, CH$_3$-6”). $^{13}$C NMR (MeOD) δ: 179.3 (C-3), 165.7 (C-7), 159.0 (C-5), 158.4 (C-2’/9), 148.8 (C-4’), 134.7 (C-3), 132.4 (C-2’/6’), 132.3, 123.2 (C-1’), 116.3 (C-3’/5’), 105.9 (C-10), 102.2 (C-1”), 100.9 (C-2”), 99.9 (C-6), 94.9 (C-8), 78.5 (C-3”), 76.9 (C-5”), 75.6 (C-2”), 73.9 (C-4”), 72.3 (C-3”), 71.9 (C-2”), 71.2 (C-4”), 69.7 (C-5”), 68.4 (C-6”), 18.0 (C-6”). Negative ESI-MS: m/z = 296.2 [M$^-$/H]$^-$(Mabry et al., 1970; Williams and Harborne, 1994).

Kaempferol 3-O-rutinoside (4): yellow amorphous powder, complete acid hydrolysis products: kaempferol (organic phase); α-glucose and t– rhamnose (aqueous phase). $^1$H NMR (MeOD) δ: 8.07 (2H, d, J = 8 Hz, H-2’/6’), 6.92 (2H, d, J = 8 Hz, H-3’/5’), 6.40 (1H, brs, H-8), 6.20 (1H, brs, H-6), 5.46 (1H, d, J = 7.5 Hz, H-1’), 4.53 (1H, brs, H-1’), 3.83–3.23 (m, H$_2$”–H6”), 1.11 (3H, d, J = 6 Hz, CH$_3$-6”). $^{13}$C NMR (MeOD) δ: 179.3 (C-3), 165.7 (C-7), 159.0 (C-5), 158.4 (C-2’/9), 148.8 (C-4’), 134.7 (C-3), 132.4 (C-2’/6’), 132.3, 123.2 (C-1’), 116.3 (C-3’/5’), 105.9 (C-10), 102.2 (C-1”), 100.9 (C-2”), 99.9 (C-6), 94.9 (C-8), 78.5 (C-3”), 76.9 (C-5”), 75.6 (C-2”), 73.9 (C-4”), 72.3 (C-3”), 71.9 (C-2”), 71.2 (C-4”), 69.7 (C-5”), 68.4 (C-6”), 18.0 (C-6”). Negative ESI-MS, m/z = 593.1 [M$^-$/H]$^-$ and 285.3 [kaempferol$^-$/H]$^-$(Nahrstedt et al., 2006).

2.5. Acetylation of compound 1 (1a)

Compound 1 (20 mg) was dissolved in pyridine-acetic anhydride (1:1, 2 mL) and stirred overnight at room temperature. The mixture was evaporated to dryness using rotary evaporator in vacuum under N$_2$ which gave a pentaacetate derivative.

2.6. Acid hydrolysis of compounds 1 and 4

A solution of 5 mg in 10 mL MeOH–1N HCl (1:1) was boiled under reflux for 4 h, concentrated under reduced pressure and diluted with H$_2$O (10 mL). It was extracted with EtOAc and the residue recovered from the organic phase yielded the aglycone. The remaining aqueous layer was neutralized with 5% aq. NaHCO$_3$ solution and concentrated under vacuum and then the sugars were identified by comparative TLC (EtOAc/MeOH/H$_2$O/HOAc, 12:3:3:4) with authentic standards.

2.7. Biological study

2.7.1. PPARα and PPARγ activation

The activation of PPARα and PPARγ was determined through a reporter gene assay in HepG2 cells transfected with pSG5-PPARα and PPRE X3-tk-luc or pCMV-rPPARγ and pPPReaP2-tk-luc plasmids as reported earlier (Zhao et al., 2014). Transfected cells were seeded in 96-well plates at a density of 5 × 10$^4$ cells/well and after 24 h of incubation; the cells were exposed to various concentrations of test samples. After an incubation of 24 h luciferase activity was measured and fold increase in luciferase activity in sample treated cells was calculated in comparison with vehicle treated cells. Ciprofibrate and rosiglitazone were included as drug controls in each assay.

2.7.2. Inhibition of cellular oxidative stress

The cellular antioxidant activity was measured in HepG2 cells according to the method of Wolfe and Liu (2007) as described earlier (Al-Taweel et al., 2015). In this assay the ability of test samples to prevent intracellular generation of peroxyl radicals in response to ABAP[2,2’-azobis (2-aminopropane) dihydrochloride] is determined. The method is more biologically relevant than a chemical method. HepG2 cells were seeded at a cell density of 60,000 cells/well and plates were incubated for 24 h. After washing with PBS cells were treated with the test samples (diluted in medium containing 25 μM DCFH-DA) for 1 h. After removing the medium containing samples, ABAP (600 μM) was added to each well and plate was immediately read on a SpectraMax plate reader every 5 min for 1 h (37 °C, emission and excitation at 538 nm and 485 nm, respectively). Quercetin was included as the positive control. Antioxidant activity was calculated in terms of percent decrease in oxidative stress.

% decrease in oxidative stress = 100 − [(AUC sample/AUC control) × 100].

2.7.3. Inhibition of iNOS activity

Mouse macrophage cell line (RAW264.7) was seeded in the wells of 96-well plates at a density of 50,000 cells/well and grown for 24 h for a confluency of >75%. Cells were exposed to various dilutions of test samples for 30 min before adding lipopolysaccharides (LPS, 5 μg/mL) and incubating for 24 h. Nitric oxide (NO) level in the cell supernatant was determined by Griess reagent. The inhibition of NO production by the sample was calculated in comparison with vehicle control.

IC$_{50}$ values were obtained from dose curves. Parthenolide (Sigma-Aldrich, St Louis, MO, USA) was used as positive control (Zhao et al., 2014; Al-Taweel et al., 2015).

2.7.4. Inhibition of NF-kB activity

Human chondrosarcoma cells transfected with NF-kB luciferase plasmid construct were plated in 96-well plates at a density of 1.25 × 10$^5$ cells per well. After 24 h incubation, cells were treated with various dilutions of test samples for 30 min and then induced with PMA (70 ng/mL) for 8 h. Luciferase activity was measured using a Luciferase Assay Kit (Promega, Madison, WI, USA). The inhibition of NF-kB activity was calculated in terms of decrease in luciferase expression.

IC$_{50}$ values were obtained from the dose curves. Parthenolide was included as positive control (Zhao et al., 2014; Al-Taweel et al., 2015).

2.7.5. Cytotoxicity

Cytotoxic activity of the samples was determined against a panel of four human cancer cell lines (SK-MEL, KB, BT-549, SK-OV-3) and two noncancerous kidney cell lines (LLC-PK1 and VERO) as described earlier (Al-Taweel et al., 2015).
All cell lines were obtained from the American Type Culture Collection (ATCC, Rockville, MD). Cells at a density of 25,000 cells/well were grown for 24 h for confluency before adding the test samples and incubating further for 48 h. The cell viability was measured by Neutral Red assay according to the procedure of Borenfreund et al. (1990). Doxorubicin was used as a positive control, while DMSO was used as the negative (vehicle) control.

3. Results

The methanol extract of the aerial parts of *A. fruticosa* was subjected to a series of column chromatographic separations to obtain four compounds namely, 2-methyl-5,7-dihydroxychromone 5-O-α-D-glucopyranoside 1 (new in genus Acalypha), acalyphin 2 (new in the species *A. fruticosa*), apigenin 3 (new in genus *Acalypha*) and Kaempferol 3-O-rutinoside 4 (new in the species *A. fruticosa*) (Fig. 1). The structures of the isolated compounds were established by MS and NMR spectroscopy. The four isolated compounds as well as the acetylated chromone glucoside 1a, were subjected to the biological investigation.

3.1. PPARα and PPARγ agonistic activity

The chloroform and methanol extracts as well as the isolated compounds were investigated for their PPARα and PPARγ agonistic activity with results shown in Table 1. Fold induction in the activity of PPAR was determined in response to the extract or compound in comparison with untreated controls. A fold induction of 1.5 means a 50% increase in PPAR activation. Dual activator effect was given by the chloroform extract, compounds 1, 1a and 4. The methanol extract did not show any PPAR agonistic activity, while compound 2 revealed promising PPARγ specific agonistic activity (2.45), and 3 was PPARα specific with weak activity, compared to Rosiglitazone and Ciprofibrate 10 μM respectively.

3.2. Inhibition of cellular oxidative stress, iNOS and NF-κB activities

The methanol extract of *A. fruticosa* aerial parts showed a decrease in cellular oxidative stress (36% decrease at 1000 μg/mL) but did not show any inhibition of NF-κB and iNOS activities (Table 2). As for the isolated compounds, 1 and its acetylated derivative 1a, were the most effective in decreasing oxidative stress with 51% and 25% decrease respectively, at 250 μg/mL.

All compounds showed promising NF-κB inhibitory activity, except 4. Acalyphin 2, was the most active among the tested compounds by inhibiting the NF-κB activity with IC50 values of 3.9 μg/mL, compared to parthenolide (0.5 μg/mL) as positive control. The inhibition of NF-κB by 1, 1a and 3 was almost similar. Interestingly 1a (acetylated form of 1) showed iNOS inhibition while 1 did not. Acalyphin 2 was the most active in inhibiting iNOS with IC50 of 15.5 μg/mL.

3.3. Cytotoxic activity

Cytotoxic activity of the samples was determined against a panel of four human cancer cell lines (SK-MEL, KB, BT-549, SK-OV-3) and two non-cancerous kidney cell lines (LLC-PK1 and VERO). The extracts and the isolated compounds were not cytotoxic to any of the tested cell lines up to 100 μg/mL (data not shown).

4. Discussion

This study represents the first report on isolation of bioactive metabolites from Saudi *A. fruticosa*. Great research efforts have recently been undertaken to explore the potential of selective PPARγ modulators (SPPARMs), compounds that improve glucose homeostasis but elicit reduced side effects due to partial PPARγ agonism based on selective receptor-cofactor interactions and target gene regulation (Wang et al., 2014). From the study, it was proved that acalyphin (2) revealed promising PPARγ specific agonistic activity and apigenin (3) possessed weak PPARα specific agonistic activity, compared to Rosiglitazone and Ciprofibrate 10 μM respectively. Based on our findings, it is recommended to further investigate the PPARγ agonistic potential of acalyphin (2). It is worth noting that the acetylation of the chromone glucoside (1) increased the PPARα activator effect of 1a. Apigenin (3)
only showed PPARα agonistic activity, whereas literature proved the PPARγ agonistic action of luteolin, a structurally related flavone. Additionally, the activity of kaempferol rutinoside (4) is in agreement with the literature on PPARγ activity of kaempferol aglycone (Wang et al., 2014). The methanol extract did not show any PPAR agonistic activity, which indicates the possible antagonistic action of the constituting compounds. This could be considered as the first report on the PPAR agonistic activity of *A. fruticosa* extracts and isolated compounds. A previous study on *A. fruticosa* proved the hypoglycemic activity of its aqueous extract (El-Shaibany et al., 2015).

The methanol extract of *A. fruticosa* aerial parts showed antioxidant potential which could be attributed mainly to the chromone glucoside (1). The replacement of the hydroxyl groups with acetyl groups in 1a, seemed to decrease the antioxidant potential of the chromone glucoside (1).

The data shown in Table 2, indicate that anti-inflammatory properties of 1, 1a and 2 could be explained in terms of the inhibition of NF-κB transcriptional activity and inhibition of iNOS. The results are also in agreement with the previously reported anti-inflammatory effects of acalyphin (Nirmal et al., 2008), chromone glucosides (Xue et al., 2000), and apigenin (Funakoshi-Tago et al., 2011). However, the chloroform and methanol extracts of the Saudi *A. fruticosa* species did not show anti-inflammatory activity, probably implying the antagonistic action of various constituents present in them. This is also in contrary to previous literature reporting the anti-inflammatory activity of the methanolic extract of the leaves of *A. fruticosa* (Gupta et al., 2004), which could be explained in terms of the differences in the composition of the two extracts and the mechanism of action responsible for anti-inflammatory activity.

Concerning the cytotoxic activity, the extracts and the isolated compounds were not cytotoxic to any of the tested cell lines up to 100 μg/mL (data not shown). This is in agreement with the literature, which showed a weak anticancer activity of the *A. fruticosa* methanol extract (Mothana et al., 2007; Rajkumar et al., 2010).

5. Conclusion

In summary, this work represents the first detailed phytochemical and biological investigation of the Saudi *A. fruticosa*. The chloroform, methanol extracts and the four isolated compounds were subjected to PPAR agonistic, anti-inflammatory and cytotoxic activity evaluation. The results revealed the promising PPAR γ specific agonistic activity of acalyphin, as well as its significant anti-inflammatory activity among the tested compounds. It also proved the non-cytotoxic nature of the extracts and the isolated compounds.

### Table 1: PPAR agonistic activity of *A. fruticosa* extracts and isolated compounds.

| Sample name | Fold induction |
|-------------|----------------|
|              | PPAR alpha | PPAR gamma |
|              | 50 μg/ml  | 25 μg/ml  | 12.5 μg/ml | 50 μg/ml | 25 μg/ml | 12.5 μg/ml |
| Chloroform extract | 1.67 ± 0.15 | 1.48 ± 0.21 | 1.36 ± 0.18 | 1.6 ± 0.08 | 1.48 ± 0.07 | 1.39 ± 0.18 |
| Methanol extract | NA | NA | NA | NA | NA | NA |
| 1 | 1.16 ± 0.16 | 1.64 ± 0.07 | 1.28 ± 0.36 | 1.65 ± 0.12 | 1.39 ± 0.33 | 1.22 ± 0.11 |
| 1a | 2.25 ± 0.26 | 1.41 ± 0.40 | 1.44 ± 0.08 | 1.56 ± 0.77 | 1.54 ± 0.73 | 1.16 ± 0.01 |
| 2 | NA | NA | NA | 1.06 ± 0.06 | 2.45 ± 0.40 | 1.83 ± 0.03 |
| 3 | 1.46 ± 0.38 | 1.42 ± 0.10 | 0.93 ± 0.05 | NA | NA | NA |
| 4 | 1.53 ± 0.06 | 1.27 ± 0.50 | 0.81 ± 0.13 | 2.31 ± 0.60 | 1.56 ± 0.30 | 1.26 ± 0.08 |
| Ciprofibrate 10 μM | 2.2 ± 0.21 | NA | NA | 4.33 ± 0.54 |
| Rosiglitazone 10 μM | NA | NA | NA |

NA = no activity, NT = not tested.

### Table 2: Anti-inflammatory activity of *A. fruticosa* extracts and isolated compounds.

| Sample Name | % decrease in oxidative stress | Inhibition of NF-kB activity IC50 in μg/mL | Inhibition of iNOS activity IC50 in μg/mL |
|-------------|-------------------------------|------------------------------------------|------------------------------------------|
| Chloroform extract | 29 | NA | NA |
| Methanol extract | 36 | NA | NA |
| 1 | 51 | 29.5 ± 6.5 | NA |
| 1a | 25 | 24.5 ± 2.5 | 35 ± 5.0 |
| 2 | NA | 3.9 ± 2.1 | 15.5 ± 1.5 |
| 3 | NA | 17.0 ± 1.0 | >50 |
| 4 | NA | >100 | NA |
| Parthenolideb | – | 0.5 ± 0.10 | 0.3 ± 0.07 |
| Quercetinb | 76 ± 2.4 | – | – |

a At 1000 μg/mL for fraction and 250 μg/mL for pure compound.

b Positive control NA = no activity up to 100 μg/mL.
Acknowledgments

This research project was supported by a grant from the “Research Center of the Female Scientific and Medical Colleges”, Deanship of Scientific Research, King Saud University.

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