Evaluation of antioxidant and anticancer activities of chemical constituents of the *Saururus chinensis* root extracts

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**KEYWORDS**

*Saururus chinensis* root; Solvent extracts; Antioxidant activity; Anticancer activity

**Abstract** Evaluation of antioxidant and anticancer activities were screened by various *Saururus chinensis* root extracts. Four solvents (ethyl acetate, methanol, ethanol, and water) extracts were investigated for their total flavonoids, phenol contents and their antioxidant activity of DPPH (2,2-diphenyl-1-picrylhydrazyl), NO (nitric oxide), H2O2 (hydrogen peroxide), ABTS 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)diammonium assays, FRAP (ferric reducing ability of plasma) assays and anticancer activity. The total phenolic and flavonoid content of extracts were determined by using FC (Folin–Ciocalteu) and AlCl3 colorimetric assay method. Total flavonoid content in these plants ranged from 24.7 to 72.1 mg g⁻¹ and amount of free phenolic compounds was between 11.2 and 67.1 mg g⁻¹ extract. The all extracts have significant levels of phenolics and flavonoids content. Anticancer activity was screened for MCF-7 breast cancer cell line. Ethanol extract shows significant of antioxidant activity and water extract shows significant of anticancer activity compared with standard (BHT) butylated hydroxy toluene. These ethanol and water extracts could be considered as a natural source for using antioxidant, and anticancer agents compared to commercial available synthetic drugs.

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1. Introduction

*Saururus chinensis* has been used as a diuretic and a detoxifying agent for edema, jaundice, gonorrhoea and several inflammatory diseases treatment in China and India (Rao and Rao, 1990). More than 4000 different naturally occurring flavonoids were identified from other plant materials (Middleton et al., 1986) but very important pharmacological studies have demonstrated that major flavonoids (Kang et al., 2005; Sung et al., 1997) and other ligands (Hwang et al., 2003a; Sung and Kim, 2000) from *S. chinensis* (Fig. 1), which possess a wide array of pharmacological and biochemical activities, such as antidiabetic (Moon et al., 2008), anti-carcinogenic (Omer et al., 2005; Hester et al., 2003), anti-inflammatory (Hwang et al., 2003b), antioxidant (Lee et al., 2003) and hepatoprotective (Kim et al., 2004), neuro-protective activity (Nortier and Vanherweghem, 2002), nephrotoxic (Cheng et al., 2006), carcinogenic (Kohara et al., 2002), and mutagenic (Balachandran et al., 2005). Importantly *S. chinensis* baik shows strong antioxidant activity (Lee et al., 2004; Choi et al., 2002), and its extract has been shown to reduce lipid peroxide levels in rats fed a high-fat diet (Yu et al., 2008). Current cancer chemotherapy is primarily dependent on repeated administrations of synthetic anticancer agents. Although effective, their repeated use has often resulted in the development of resistance, plants have been suggested as an alternative source for antioxidant and anticancer activities.

2. Materials and methods

2.1. Preparation of solvent extract

*S. chinensis* root powder (100 g) was immersed in 500 mL of double distil water. The filtrate was constant stirring with maximum 72 h. The extract was then concentrated under reduced pressure at 40 °C using vacuum rotary evaporator, the yield of water extract was 15.25 g. The aqueous layer further fractionated with ethyl acetate, methanol, and ethanol fractions were concentrated with vacuum rotary evaporator, yield of each fractions 16.1%, 24.6% and 18.0% respectively.

2.2. Determination of total phenolic and flavonoid content

The total phenolic and total flavonoid were identified by using the FC (Folin-Ciocalteu) and aluminium chloride colorimetric assay methods, the method was followed by previously report method (Marinova et al., 2005). Total phenolic and flavonoid content rang are represented in Table 1.

2.3. Antioxidant activity of DPPH method

DPPH (2,2-diphenyl-1-picrylhydrazyl) antioxidant activity was screened for *S. chinensis* root extracts and the method was followed by previously report method (Cefarelli et al., 2006). Accordingly, extracts were examined for their ability to prevent the bleaching of the purple colored methanol solution DPPH 1.6 mL of test sample (25, 50, and 100 µg/mL) and 1.6 mL of 0.004% (w/v) methanol solution of DPPH were reacted at room temperature, absorbance of reaction mixture was measured at 517 nm.

Percentage inhibition was calculated by.

\[
\text{DPPH Scavenging effect (\%) = } \left( \frac{A_{\text{sample}} - A_{\text{control}}}{A_{\text{control}}} \right) \times 100
\]

2.4. H₂O₂ scavenging activity

Hydrogen peroxide scavenging activity was screened for various solvent of *S. chinensis* root extracts, the method was followed by previously reported literature method (Ruch et al., 1989). A solution of H₂O₂ (0.6 mL, 40 mM) with phosphate buffer (pH 7.4) and root extract (3.4 mL) with phosphate buffer were reacted, the reaction mixture was measured by absorbance at 230 nm.

Percentage inhibition of H₂O₂ was calculated by.

\[
\% \text{ Inhibition} = \left( \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \right) \times 100
\]

2.5. NO scavenging activity

Nitric oxide scavenging activity was calculated using by slight modified version of the method devised by Marcocci et al. (1994). Sodium nitroprusside (1 mL, 10 mM) and 1.5 mL of...
ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) di ammonium) assay can be used to determine the antioxidant activity of biological fluids, cells, tissues, natural and other synthetic therapeutic compounds. The assay measures ABTS radical cation formation induced by metmyoglobin and hydrogen peroxide. A water soluble trolox is used as a positive control for inhibiting the formation of the radical cation in the assay (Adedapo et al., 2009).

Preparation: The ABTS reagent was prepared by 5 mL of 14 mM ABTS and 5 mL of 4.9 mM potassium persulfate (K2S2O8), the reaction mixture was kept in dark room at room temperature for 16 h. The reagent absorbance was adjusted to 0.700 ± 0.02 at 734 nm with distilled water and used for the assay purposes.

1 mL of ABTS reagent is added to different concentrations of test sample measured by 734 nm at 3 min interval. The antioxidant activity of extracts was measured by radiul
evity of inhibition of nitric oxide scavenging was calculated by.

\[
\% \text{ NO Scavenging} = \left( \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \right) \times 100
\]

2.6. ABTS radical cation decolourisation assay

2.8. Anticancer activity

Anticancer assays were performed according to the US NCI protocol, which was described elsewhere (Boyd and Paul, 1995).

Cell viability test: The viability of cells was assessed by MTT assay using MCF-7 cell lines.

Cytotoxic assay (MTT method): The anticancer activity was carried out according to the method described in previous literature (Mostafa et al., 2016).

MCF-7 cell lines was treated with these compounds at one primary cytotoxic assay dose of 100 μM for 48 h (MTT anticancer assay). Doxorubicin was used as a standard. In the current protocol, all cell lines were pre-incubated on a microtiter plate. The results of each test were reported as the growth percentage of treated cells compared to untreated control cells. A 0.1 mL aliquot of the cell suspension (5 × 10^6 cells/100 μL) and 0.1 mL of the test solution (6.25–100 μg) were added to the wells, with the plates kept in an incubator (5% CO2) at 37 °C for 72 h. After 72 h, 20 μL of MTT was added, and the plates were kept in the CO2 incubator for 2 h, followed by the addition of propanol (100 μL). The plates were covered with aluminum foil to protect them from light and subsequently agitated in a rotary shaker for 10–20 min, afterwards the 27-well plates were processed on an ELISA reader to obtain absorption data at 562 nm.

2.9. Statistical analysis

All experiments were performed in triplicate and all data were expressed at least 3 independent evaluations and the standard deviations (SD) were also calculated using Microsoft Excel 2007 software (Microsoft, Redmond, WA, USA).

3. Result and discussion

3.1. Antioxidant activity of S. chinensis root extracts

The S. chinensis root extracts were screened for antioxidant property of 2,2-diphenyl-1-picrylhydrazyl (DPPH), hydrogen peroxide (H2O2), nitric oxide (NO), ABTS and FRAP assays method.

The antioxidant activity of extracts was measured by radical scavenging ability through UV–visible spectrophotometer. Methanolic solutions of DPPH shows a strong purple color, with strong absorption at 517 nm, and when reduced are a yellow color. Free radical scavenging activity of DPPH radical was found to increase with increase in concentration, showing a maximum of 88.71 at 100 μg/mL. The ethanol extract showed a good capacity of scavenging the DPPH free radical activity and highly active (IC50:11.04 μg/mL) compared with standard BHT at concentration 100 μg/mL. Results of DPPH reduction is shown in Table 2.

The Fig. 2 shows that kinetic activities of different extracts and estimated the scavenging activity of maximum reaction time. The higher antioxidant activity of the extract may be assumed that –OH groups are primarily involved in H-atom transfer reactions to DPPH, which attributed to the highly significant contribution of 3’,4’-hydroxyl groups on the ring.

| Table 1 | The total phenolic and flavonoid content of Saururus chinensis root extract. |
|---|---|
| Extracts | Total phenolic (mg GAE/100 g of dry mass) | Total flavonoids (mg CE/100 g of dry mass) |
| Ethyl acetate | 11.2 ± 0.2 | 24.7 ± 0.2 |
| Methanol | 22.0 ± 0.6 | 54.0 ± 0.7 |
| Ethanol | 35.2 ± 1.2 | 58.4 ± 0.4 |
| Water | 67.1 ± 0.9 | 72.1 ± 0.1 |

GAE: Gallic Acid Equivalents; CE: Catechin Equivalents.

* Values expressed as mean ± standard deviation (n = 3).

phosphate buffer saline (0.2 M, pH 7.4) were added to different concentrations of test sample incubated for 150 min at 25 °C. Aliquots (1 mL) of reaction mixtures were then react with 1 mL of Griess reagent (1% sulfanilamide, 2% H3PO4 and 0.1% naphthylethylene diamine dihydrochloride).

Percentage inhibition of nitric oxide scavenging was calculated by.

\[
\% \text{ NO Scavenging} = \left( \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \right) \times 100
\]

### Table 1

| Extracts   | Total phenolic (mg GAE/100 g of dry mass) | Total flavonoids (mg CE/100 g of dry mass) |
|------------|-----------------------------------------|------------------------------------------|
| Ethyl acetate | 11.2 ± 0.2 | 24.7 ± 0.2 |
| Methanol   | 22.0 ± 0.6 | 54.0 ± 0.7 |
| Ethanol    | 35.2 ± 1.2 | 58.4 ± 0.4 |
| Water      | 67.1 ± 0.9 | 72.1 ± 0.1 |

GAE: Gallic Acid Equivalents; CE: Catechin Equivalents.

* Values expressed as mean ± standard deviation (n = 3).
Hydrogen peroxide (H₂O₂) scavenging activity showed that ethanol extract (12.00 µg/mL) very effective scavenging activity compared with standard BHT (20.35 µg/mL). Results of H₂O₂ scavenging reduction is shown in Table 3.

The extract showed nitric oxide scavenging activity between 25 and 100 µg/mL concentration. Ethanol extract shows highly active (89.11%) compared with standard BHT (83.32 %) at concentration 100 µg/mL. The nitric oxide (NO) radical reacts with Griess reagent, to form formazan which was measured spectrophotometrically. The IC₅₀ value of ethanol extract was found to be 14.58 µg/mL. Results of NO scavenging reduction is shown in Table 4.

Extracts were screened for ABTS radical-scavenging activity, the EtOH extract (IC₅₀:17.54 µg/mL) was significant of activity compared with standard BHT. Results of ABTS scavenging reduction is shown in Table 5.

The FRAP assay was measured by ability to reduce the ferric 2,4,6-tripyridyl-s-triazine complex [Fe³⁺ – (TPTZ)₂]³⁺ to provided blue colored ferrous complex [Fe²⁺ – (TPTZ)₂]²⁺ in acidic medium at 593 nm absorbance . The ethanol extract was absorbed very low reducing abilities at 25–100 µg/mL compared with standard BHT, activity variation shows in Fig. 3.

### 3.2. Anticancer activity of S. chinensis root extracts

The compounds were for primary anticancer assay towards MCF-7 cell lines (human breast cancer). Results were reported as the percent growth of the treated cells when compared to the untreated control cells.

All the synthesized compounds methanol, ethanol, ethyl acetate, and water were evaluated for their anticancer activity

| Table 2 | DPPH scavenging activity (%) of *Saururus chinensis* root extracts. |
|---------|-------------------------------------------------------------|
| Extracts | Concentration (µg/mL) | IC₅₀ (µg/mL) |
|         | 25 µg/mL | 50 µg/mL | 100 µg/mL |  |
| Ethyl acetate | 10.31 ± 0.17 | 23.23 ± 0.14 | 43.01 ± 0.32 | >100 |
| Methanol | 60.62 ± 0.23 | 71.01 ± 0.16 | 88.71 ± 0.12 | 15.13 ± 0.23 |
| Ethanol | 69.22 ± 0.19 | 74.12 ± 0.22 | 91.02 ± 0.21 | 11.04 ± 0.31 |
| Water | 06.10 ± 0.07 | 12.03 ± 0.21 | 21.21 ± 0.11 | >100 |
| BHT | 54.21 ± 0.22 | 70.30 ± 0.12 | 82.31 ± 0.30 | 18.86 ± 0.21 |

* Value expressed are means ± SD.

| Table 3 | Hydrogen peroxide (H₂O₂) scavenging activity of *Saururus chinensis* root extracts. |
|---------|-------------------------------------------------------------|
| Extracts | Concentration (µg/mL) | IC₅₀ (µg/mL) |
|         | 25 | 50 | 100 |  |
| Ethyl acetate | 12.16 ± 0.14 | 20.21 ± 0.02 | 43.13 ± 0.04 | >100 |
| Methanol | 55.28 ± 0.11 | 72.00 ± 0.11 | 84.21 ± 0.16 | 18.13 ± 0.02 |
| Ethanol | 68.47 ± 0.04 | 84.17 ± 0.09 | 92.12 ± 0.41 | 12.00 ± 0.15 |
| Water | 16.29 ± 0.35 | 23.12 ± 0.11 | 36.12 ± 0.18 | >100 |
| BHT | 59.01 ± 0.04 | 68.51 ± 0.09 | 82.17 ± 0.53 | 20.35 ± 0.13 |

* Value expressed are means ± SD.
against a human cancer cell line such as MCF-7 (Human breast cancer), by employing MTT assay. The results of cell viability data are summarized in Table 6.

The inhibitory concentration (LD50) value was calculated by the test sample of concentration at which 50% of cells viable, and calculated from the logarithmic trend line of the cytotoxicity graphs. The in vitro screening results revealed that the compound water exhibited promising anticancer activity compared in MCF7 breast cancer cells (54.2% inhibition) were observed at concentration (100 \( \mu g/mL \)). This inhibition at the mentioned concentration indicates a greater potency of compound water with a strong lethal effect over the breast cancer (MCF-7) cell line computed with other solvent extract.

### Table 4  NO scavenging activity of *Saururus chinensis* root extracts.

| Extracts  | Concentration (\( \mu g/mL \)) | IC\(_{50}\) (\( \mu g/mL \)) |
|-----------|-----------------------------|-------------------------------|
| Ethyl acetate | 25  | 09.14 ± 0.24 | 14.32 ± 0.41 |
| Methanol | 52.51 ± 0.21 | 69.16 ± 0.10 | 82.12 ± 0.11 | 20.19 ± 0.19 |
| Ethanol | 60.01 ± 0.03 | 71.12 ± 0.64 | 89.11 ± 0.12 | 14.58 ± 0.11 |
| Water | 0.30 ± 0.05 | 17.01 ± 0.11 | 30.10 ± 0.10 | >100 |
| BHT | 53.16 ± 0.02 | 67.65 ± 0.63 | 83.32 ± 0.07 | 22.13 ± 0.23 |

\( ^a \) Value expressed are means ± SD.

### Table 5  ABTS radical-scavenging activity of *Saururus chinensis* root extracts.

| Extracts  | Concentration (\( \mu g/ml \)) | IC\(_{50}\) (\( \mu g/ml \)) |
|-----------|-----------------------------|-------------------------------|
| Ethyl acetate | 25  | 21.30 ± 0.04 | 35.72 ± 0.11 |
| Methanol | 55.23 ± 0.43 | 62.12 ± 0.10 | 73.20 ± 0.34 | 21.32 ± 0.18 |
| Ethanol | 59.34 ± 0.24 | 69.71 ± 0.08 | 83.23 ± 0.91 | 17.54 ± 0.32 |
| Water | 06.85 ± 0.14 | 11.32 ± 0.14 | 19.07 ± 0.12 | >100 |
| Trolox | 62.02 ± 0.02 | 74.09 ± 0.21 | 92.11 ± 0.56 | 14.21 ± 0.24 |

\( ^a \) Value expressed are means ± SD.

![Figure 3](image-url)  FRAP activity of *Saururus chinensis* root extracts at concentration 100 \( \mu g/mL \).

### Table 6  Anticancer activity of *Saururus chinensis* root extracts against MCF-7 cancer cell line.

| Extracts | % Inhibition of cell viability | LD\(_{50}\) \( \mu g/mL \) |
|----------|-----------------------------|-----------------------------|
|         | 25 \( \mu g/mL \) | 50 \( \mu g/mL \) | 100 \( \mu g/mL \) |
| Ethyl acetate | – | – | 07.5 | >100 |
| Methanol | – | 04.6 | 18.1 | >100 |
| Ethanol | – | 09.4 | 20.9 | >100 |
| Water | 21.6 | 32.5 | 54.3 | 91.2 |
| Standard | 52.2 | 65.8 | 84.2 | 24.2 |

1,3-Bis(4-chlorobenzenesulfonyl)imidazolidine-2-one used as a standard.
Compounds methanol, ethanol, and ethyl acetate have low inhibitory activity against MCF-7 cell line.

4. Conclusion

In conclusion, the result of this study demonstrates that four different S. chinensis root extracts in methanol, ethanol, ethyl acetate, and water were screened for antioxidant, anticancer activates. An important finding in this study, the S. chinensis root ethanol extract was most important in antioxidant activity and water extract is highly active against anticancer activity against MCF-7 cancer cell line. Current investigation of antioxidant, and anticancer activates were evaluated using in vitro experiments only and further investigation for mechanism of action and in vivo experiments will lead to a more complete assessment of S. chinensis root extracts.

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