Modulatory effects of polyphenols from Australian native fruits on carcinogenesis pathways

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BACKGROUND

• Cancer is a leading cause of death worldwide
• Phytochemicals exhibit polypharmacological activities and are beneficial for cancer prevention
• Chemoprevention is a promising tool for cancer prevention
  1. Antioxidant activity
  2. Anti-inflammatory activity
  3. Pro-apoptotic anticancer activity

SELECTION OF NATIVE FRUITS

• Four selected native Australian fruits
  1. Illawarra Plum (Podocarpus elatus)
  2. Kakadu Plum (Terminalia ferdinandiana)
  3. Muntries (Kunzea pomifera)
  4. Native Currant (Acrotriche depressa)

METHOD – EXTRACTION

- Fruit material
- Freeze-dried and ground
- Solvent extraction
- Methanol – phenolic compounds
- Phenolic-rich fraction
- Purified (x2)
- XAD-7HP column
- Condensed
- Rotary evaporator

Oxidative stress plays a crucial role in the development of carcinogenesis.
- Radical scavenging
- Modulation of cellular antioxidant/detoxifying enzymes

**Total Phenolics Assay**

**Ferric Ion Reducing Antioxidant Power (FRAP) Assay**

**Oxygen Radical Absorbance Capacity (ORAC) Assay**

**Cellular Antioxidant Activity (CAA) Assay**

Cellular protection (RAW 264.7 cells) from H$_2$O$_2$ induced apoptosis
- MTT assay

Upregulation of antioxidant enzymes (Nrf2/Keap1 ratio) – Hep G2 cells

- Illawarra Plum
- Kakadu Plum
- Muntries
- Native Currant
**SUMMARY – ANTIOXIDANT ACTIVITY**

<table>
<thead>
<tr>
<th></th>
<th>IP</th>
<th>KP</th>
<th>M</th>
<th>NC</th>
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<tbody>
<tr>
<td>Antioxidant assays</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>CAA assay</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
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<tr>
<td>H₂O₂ protection</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Nrf2/Keap1 ratio</td>
<td>-</td>
<td>+</td>
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**ANTI-INFLAMMATORY ACTIVITY**

- Inflammation and chronic inflammatory mechanisms are clearly implicated in the development of cancer

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**ANTI-INFLAMMATORY ACTIVITY**

- COX-1, COX-2 and iNOS in LPS-activated murine macrophages (RAW 264.7)
  - Western blot analysis

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**ANTI-INFLAMMATORY ACTIVITY**

- Inhibition of NO (Griess reaction) and PGE₂ (enzyme immunoassay) in LPS-activated murine macrophages
**SUMMARY: ANTI-INFLAMMATORY ACTIVITY**

<table>
<thead>
<tr>
<th>Activity</th>
<th>IP</th>
<th>KP</th>
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<tbody>
<tr>
<td>COX-2, COX-1, iNOS</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>+</td>
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<tr>
<td>NO and PGE₂</td>
<td>+</td>
<td>+</td>
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<td>+</td>
</tr>
<tr>
<td>NF-κB</td>
<td>*</td>
<td>+</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>p44/42 MAPK</td>
<td>*</td>
<td>-</td>
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**ANTI-PROLIFERATIVE AND PRO-APOPTOTIC ANTICANCER ACTIVITY**

- The evasion of apoptosis is a fundamental characteristic of a neoplastic cell

**PRO-APOPTOTIC ANTICANCER ACTIVITY: HL-60**

- DNA fragmentation
  - Agarose gel electrophoresis

- Morphological assessment
  - Hoechst 33342 staining

- Flow cytometry
  - Annexin V and PI staining

**PRO-APOPTOTIC ANTICANCER ACTIVITY: HL-60**

- Caspase-3, -7, -9 and PARP (Western blot analysis)
SUMMARY

- Kakadu Plum, a novel source of phytochemicals with potential chemopreventive properties

Antioxidant  Anti-inflammation  Pro-apoptotic  anticancer

Chemopreventive properties

Contact Us

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Thank you