A review on traditional uses, phytochemistry, and pharmacology of the genus *Rourea*

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**ARTICLE INFO**
Received on: 23/08/2018
Accepted on: 14/02/2019
Available online: 01/09/2019

**Key words:**
*Rourea*; Connaraceae; flavonoids; *Rourea minor*; *Rourea induta*; ethnomedicine

**ABSTRACT**
*Rourea* is a genus of climbing shrubs and small trees and widely distributed in the Amazon, Pacific region, Africa, and Asia. It has about 65 species and 129 varieties. They are widely used in ethnomedicine for various health complaints such as rheumatism, diabetes, tumor, asthma, and diarrhea. This paper summarizes 38 compounds from *Rourea* sp. from different classes of compounds such as flavonoids, triterpenes, phenolic compounds, lipids, phytosteroids, and coumarin. Several bioactivities such as hypoglycemia, antinociceptive, antibacterial, antioxidant, antiplasmodial, and larvicidal activities are also discussed.

**INTRODUCTION**
*Rourea* is a genus in the Connaraceae family. Genus *Rourea* has about 65 species and 129 varieties (*The Plant List, 2013*). *Rourea* is a climbing shrub or small tree, usually with prominent lenticels. The leaflets are small and imparipinnate. An unbranched inflorescence bears flowers of five petals in the calyx. They have longer petals than sepals. The fruits are curved and hairless. *Rourea* sp. is widely distributed in the Amazon, Pacific region, Africa, and Asia (*Forero, 2009*). Some of *Rourea* sp. are poisonous, while others are widely used in traditional medicine. There are several reports on the potential of *Rourea* sp. as hypoglycemic agents. Despite their wide application in ethnomedicine, very few scientific reports on their chemical constituents and biological activity are documented.

**TRADITIONAL USES**
In Malaysia, several *Rourea* species are used by the local communities. The decoction of the roots of *R. regusa* Planch, locally known as *akar semeling*, is traditionally used to treat respiratory diseases (*Alsarhan et al., 2012*). The roots decoction of *R. concolor*, locally known as *akar semelit* in Malaysia, is used by Temuan villagers to treat kidney diseases, diabetes (*Ong et al., 2011a*), lung tumor, and stomach tumor (*Ong et al., 2011b*). *R. mimosoides* or *sembelit merah* is traditionally used to treat bloody diarrhea, as diuretics (*Grosvenor et al., 1995*), and to treat bloody cough (*Sabran et al., 2016*). The roots decoction of *R. humilis* Blume or *akar kayu mengecuat* is used to improve the contraction of the uterus (*Jamal et al., 2011*).

*R. induta* Planch is commonly known as *chapeudinha*, *pau-de-porco*, or *campeira* and is widely distributed in Brazil. It is traditionally used in folk medicine to treat rheumatisms and Chagas disease (*Kalegari et al., 2014a*). *R. cuspidate* Bentham ex. Baker is commonly known in Brazil as *miraruira*, *cip’o miraruira*, and *muiraruira*. It is traditionally used to treat diabetes (*Laikowski et al., 2017*). *R. coccinea* Bentham, commonly known as *Tomigavi*, is used in Togo for the treatment of paralyses and Alzheimer’s disease.
R. coccinea is also utilized in Benin traditional medicine for the treatment of male and female infertility, sexual asthenia, blennorrhoea, snakebites, furuncles, and malaria (Bero et al., 2009). The leaves of R. minor are used as a styptic to treat minor abrasions and lesions in Chinese folk medicine. The stems and roots of R. minor are poisonous; however, they are widely used as tying material (He et al., 2006). R. volubis, R. orientalis, R. platysepal, and R. glabra are poisonous and they are often used to deter animals (Jeanoda et al., 1985; Oliveira et al., 2012). The leaves of R. santaloides (Vahl.) Wight & Arnott is traditionally taken for the treatment of joint pains and asthma (Bargali et al., 2003). R. puberela Baker is used in Chazuta Valley of Peruvian Amazon for its diuretic property (Sanz-Biset & Canigueral, 2011).

**PHYTOCHEMISTRY**

**Flavonoids**

Isolation from ethanolic leaves extract of *Rourea induta* yielded quercetin 1, and three glycosylated derivatives, quercetin-3-O-α-arabinofuranoside 2, quercetin-3-O-β-xyloside 3, and quercetin-3-O-β-galactoside 4 (Kalegari et al., 2011). Procyanidin C1 5 was isolated from the aqueous leaves extract.
of *R. induta* (Kalegari et al., 2014b). HPLC titration of the aqueous leaves extract of *R. induta* revealed the presence of hyperin 6, as well as compounds 2–4 (Kalegari et al., 2014b). The phytochemical study on the chloroform fraction of ethanolic leaves extract of *R. doniana* led to the isolation of 7,4’-dimethylkaempferol 7 (Oliveira et al., 2012). Kaempferol 8 and rutin 9 were reported in *R. microphylla* (Zhang et al., 2008). Leucopelargonidin 10 was isolated from the roots of *R. santoloides* (Ramiah et al., 1976).

**Triterpenes**

Purification of hexane fraction of ethanolic leaves extract of *R. doniana* yielded lupeol 11, lupenone 12, α-amyrenone 13, β-amyrenone 14, and taraxerol 15 (Oliveira et al., 2012). Phytochemical study on *R. microphylla* gave 23-hydroxybetulinic acid 16, ursolic acid 17, and hederagenin 18 (Zhang et al., 2008).

**Phytosteroids**

Isolation on chloroform fractions of ethanolic leaves extract of *R. doniana* yielded β-sitosterol 19, stigmasterol 20, β-sitosteryl-3-O-β-D-glucopyranoside 21, and stigmasteryl-3-O-β-D-glucopyranoside 22 (Oliveira et al., 2012). β-sitosterol glucoside 23 was isolated from *R. minor* (He et al., 2006).

**Lipids**

1-Hentriacontanol 24 and 1-hexacosanoyl glycerol 25 were isolated from *R. microphylla* (Zhang et al., 2008). Isolation on chloroform soluble fraction of methanolic stems extract of *R. minor* gave 1-{(26-hydroxyhexacosanoyl)-glycerol 26, 1-O-β-D-glucopyranosyl-(2S,3R,4E,8Z)-2-N-(20-hydroxypalmitoyl)-octadecasphinga-4,8-diene 27, rourimin 28, and 9S,12S, 13S-trihydroxy-10E-octadecenoic acid 29 (He et al., 2006).
Coumarin

Scopeletin 30 was purified from chloroform fraction of ethanolic leaves extract of *R. doniana* (Oliveira et al., 2012). Daphnetin 31 was reported from *R. microphylla* (Zhang et al., 2008).

Phenolic acid

Purification of the aqueous leaves extract of *R. induta* yielded chlorogenic acid 32 and neochlorogenic acid 33 (Kalegari et al., 2014b). (E)-Ferulic acid nonacosyl ester 34 was isolated from *R. microphylla* (Zhang et al., 2008).

Others

Purification of hexane fraction of ethanolic leaves extract of *R. induta* yielded n-tetracosane 35 (Kalegari et al., 2011). Ropanone 36 was purified from *R. santoloides* (Ramiah et al., 1976). Isolation of chloroform soluble fraction of methanolic stems extract of *R. minor* yielded dihydrovomifoliol-9-β-D-glucopyranoside 37 (He et al., 2006). Rourinoside 38 was isolated from the chloroform soluble fraction of methanolic stems extract of *R. minor* (He et al., 2006).

BIOLOGICAL ACTIVITY

Hypoglycemic activity

*Rourea minor*

The methanol roots extract of *R. minor* showed anti-hyperglycemic activity in a dose-dependent manner at 200 and 400 mg/kg when administered to streptozotocin-induced diabetic rats. In oral glucose tolerance test, no glucose lowering effect was observed at 30 and 60 minutes but the effect was quite...
significant after 90 and 120 minutes administration of the extract. Administration of 100, 200, and 400 mg/kg of methanol extract resulted in a significant reduction of hyperglycemia at days 4, 8, and 12 in a dose-dependent manner. Oral administration of methanol roots extract of *R. minor* at all doses significantly reduced glucose level in the diabetic rats (Chaudhary et al., 2012).

In another study, hypoglycemic activity was observed over 120 minutes in streptozotocin-induced diabetic rats treated with ethanolic and aqueous roots extract of *R. minor* at 400 mg/kg as compared to diabetic control rats. After 15 days, treatment with ethanolic and aqueous extracts reduced glycaemia significantly at 43.1% and 34.8%, respectively. The diabetic rats treated with ethanol extracts showed higher insulin secretion at 19.7 μU/ml at 17 μU/ml. The insulin secretion of diabetic rats treated with water extract, which showed insulin secretion at 17 μU/ml. The insulin secretion of diabetic rats treated with water extract was significantly lower than that of normal rats (Kulkarni et al., 2012).

### Table 1. Bioactivities of *Rouea* sp.

<table>
<thead>
<tr>
<th>Species</th>
<th>Bioactivity</th>
<th>Plant parts</th>
<th>Type of preparation</th>
<th>Main finding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypoglycemic activity</strong></td>
<td></td>
<td>Roots</td>
<td>Methanol extract</td>
<td>The extracts at all doses are effective in lowering glucose level after 60 minutes in the oral glucose tolerance test. Administration of the extract resulted in a significant reduction of hyperglycemia in dose-dependent manner (Chaudhary et al., 2012).</td>
</tr>
<tr>
<td><em>R. minor</em></td>
<td>Acute toxicity</td>
<td>Roots</td>
<td>Ethanol and water extracts</td>
<td>Treatment with the extracts reduced glycemia significantly and resulted in higher insulin secretion than the negative control group (Kulkarni et al., 2014).</td>
</tr>
<tr>
<td><strong>Antiplasmodial activity</strong></td>
<td>Dried vines</td>
<td>Ethanol extract</td>
<td>Chloroform fraction of methanol extract.</td>
<td>Compounds 38, 28, and 26 isolated from <em>R. minor</em> showed antiplasmodial activity in vitro against chloroquine sensitive (D6) and chloroquine resistant (W6) <em>Plasmodium falciparum</em> with the IC₅₀ values of about 10 μM (He et al., 2006).</td>
</tr>
<tr>
<td><strong>Hepatoprotective activity</strong></td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td></td>
<td>The extract normalized liver functions and hepatic oxidative stress in CCl₄-treated rats. The endogenous antioxidant defense was restored and lipid peroxidation in the liver was reversed over 7 days’ post-treatment with the extract, similar to the effects shown by Legalon (Kalegari et al., 2014a).</td>
</tr>
<tr>
<td><strong>Antinociceptive activity</strong></td>
<td>Leaves</td>
<td>Hot water infusion</td>
<td></td>
<td>Treatment of aqueous extract on mice resulted in the significant antinociceptive effect on different pain models without affecting the motor activity and corporeal temperature of the mice, and the extract did not depend on the opioid system (Kalegari et al., 2014a).</td>
</tr>
<tr>
<td><strong>R. induta</strong></td>
<td>Acute toxicity</td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>Ethanolic leaves extract of <em>R. induta</em> and its fractions showed no potential toxicity in brine shrimp assay and hemolytic test (Oliveira et al., 2012).</td>
</tr>
<tr>
<td><strong>Antibacterial activity</strong></td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>Ethanol and chloroform fractions of ethanol extract</td>
<td>Chloroform and ethyl acetate fractions of chloroform extract showed inhibition against <em>S. epidermidis</em> and <em>S. aureus</em> (Kalegari et al., 2012).</td>
</tr>
<tr>
<td><strong>DPPH radical scavenging activity</strong></td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>Ethanol and chloroform fractions of ethanol extract</td>
<td>The chloroform and ethyl acetate fractions of ethanol leaves extract of <em>R. induta</em> showed significant DPPH radical scavenging activity with the IC₅₀ values of 5.3 and 3.2 μg/ml, respectively (Kalegari et al., 2012).</td>
</tr>
<tr>
<td><strong>Phosphomolybdenum complex method</strong></td>
<td>Leaves</td>
<td>Ethanol extract</td>
<td>Ethanol and chloroform fractions of ethanol extract</td>
<td>Hexane, chloroform, and ethyl acetate fractions of ethanolic leaves extract of <em>R. induta</em> showed more than 100% activity in relation to rutin and vitamin C (Kalegari et al., 2012).</td>
</tr>
<tr>
<td><strong>R. cuspidata</strong></td>
<td>Hypoglycemic activity</td>
<td>Stems</td>
<td>Ethanol and water extracts</td>
<td>Oral administration of hydroalcoholic stems extract of <em>R. cuspidata</em> at 200 mg/kg significantly reduced the glucose level in streptozotocin-induced diabetic rats comparable to glibenclamide (Laikowski et al., 2017).</td>
</tr>
<tr>
<td><strong>R. doniana</strong></td>
<td>Larvicial activity</td>
<td>Stems and Leaves</td>
<td>Hexane extract</td>
<td>The chloroform leaves extract and hexane stems extract of <em>R. doniana</em> caused 88.9% mortality rate of the <em>Aedes aegypti</em> larvae at the concentration of 250 μg/ml (Oliveira et al., 2010).</td>
</tr>
</tbody>
</table>

**Rouea cuspidata**

Oral administration of hydroalcoholic stems extract of *R. cuspidata* at 200 mg/kg significantly reduced the glucose level in streptozotocin-induced diabetic rats comparable to glibenclamide. Hydroalcoholic extract contains flavonoids as major compounds. The extract showed a significant hepatoprotective effect on the rat’s liver as shown by reduction of AST level from 253 to 49 U/l (Laikowski et al., 2017).

**Antibacterial activity**

The chloroform and ethyl acetate fractions of ethanol leaves extract of *R. induta* showed potential antibacterial activity against *Staphylococcus aureus* and *S. epidermidis* at 1,000 μg/ml. Chloroform fractions showed inhibition against *S. epidermidis* and *S. aureus* with average inhibition halos of 12.3 and 7.6 mm, respectively. Ethyl acetate fraction showed antibacterial activity against *S. epidermidis* and *S. aureus* with average inhibition halos of 15.0 and 7.6 mm, respectively. Antibacterial activity of the ethanol extract could be due to the presence of hyperin 6, 8, and 10.
which showed antibacterial activity against *S. epidermis* at 1,000 and 500 µg/ml with average inhibition halos of 9.3 and 7.0 mm, respectively (Kalegari et al., 2012).

**Hepatoprotective activity**

Administration of 500 mg/kg of ethanolic leaves extract of *R. induta* caused a significant reduction in AST and ALT activities and TB level in the CCl₄ treated group comparable to Legalon. The weight of the liver of the treated group was also smaller as compared to the non-treated control group. Treatment with the extract also normalized the hepatic oxidative stress markers CAT, SOD, GPx, and GSH as compared to the non-treated control group, although Legalon showed a stronger effect. The endogenous antioxidant defense was restored and lipid peroxidation in the liver was reversed over 7 days post-treatment with the extract, similar to the effects shown by Legalon. The hepatoprotective activity could be due to the presence of flavonoids 2, 3, and 6 (Kalegari et al., 2014b).

**Antinociceptive activity**

Treatment of aqueous leaves extract of *R. induta* on mice showed a significant antinociceptive effect on different pain models without affecting the motor activity and corporal temperature of the mice, and the extract did not depend on the opioid system. The aqueous extract inhibited the neurogenic (0–5 minutes) and inflammatory (15–30 minutes) phases of formalin-induced licking at 30, 100, and 100 mg/kg. The marker compound, hyperin 6, showed comparable result at 100 mg/kg at the neurogenic phase of the test. The mice in the extract treated group showed a significant reduction (60%–65%) of the mechanical sensitivity on the ipsilateral paw when induced with intraplantar injection of Complete Freund’s Adjuvant. The treatment of the extract reduced the level of IL-1β and TNF-α in the skin of the hind paw by 22% and 50%, respectively, as compared to the non-treated control group. The treated group showed a significant reduction in biting behavior caused by TNF-α (0.1 pg/site i.t.) but no effect was observed on IL-1β-induced biting response. It was concluded that the antinociceptive effect of the aqueous leaves extract of *R. induta* is due to decrease synthesis or release of pro-inflammatory cytokines, such as TNF-α and IL-1β (Kalegari et al., 2014a).

**Antiplasmodial activity**

Rourinoside 38, rouremen 28, and 1-(26-hydroxyhexacosanoyl)-glycerol 26 isolated from *R. minor* showed antiplasmodial activity in vitro against chloroquine sensitive (D6) and chloroquine resistant (W6) *Plasmodium falciparum* with the IC₅₀ values of 3.7/2.1 µM, 5.1/4.5 µM, and 9.5/12.7 µM, respectively (He et al., 2006).

**Larvicidal activity**

The hexane stems extract of *R. doniana* showed potential antilarvicidal activity with the LD₅₀ value of 12.1 µg/ml. The chloroform leaves extract and hexane stems extract of *R. doniana* caused 88.9% mortality rate of the *Aedes aegypti* larvae at the concentration of 250 µg/ml (Oliveira et al., 2010).

**Acute toxicity**

No acute toxicity was observed when rats were given 100, 200, and 400 mg/kg of methanolic roots extract of *R. minor* (Chaudhary et al., 2012). In other study on ethanolic and aqueous roots extracts of *R. minor*, the rats showed good tolerance up to 3 g/kg and no lethality was observed (Kulkarni et al., 2014). Ethanolic leaves extract of *R. induta* and its fractions showed no potential toxicity in brine shrimp assay and hemolytic test (Oliveira et al., 2012).

**Antioxidant activity**

**DPPH radical scavenging activity**

The chloroform and ethyl acetate fractions of ethanol leaves extract of *R. induta* showed significant DPPH radical scavenging activity with the IC₅₀ values of 5.3 and 3.2 µg/ml, respectively (Kalegari et al., 2012).

**Phosphomolybdenum complex method**

Hexane, chloroform, and ethyl acetate fractions of ethanolic leaves extract of *R. induta* showed more than 100% activity in relation to rutin and vitamin C. Hyperin 6 also demonstrated antioxidant activity more than 127.8% in relation to rutin but only more than 42.3% in relation to vitamin C (Kalegari et al., 2012).

**CONCLUSION**

*Rourea* sp. is widely used in traditional medicine for various health complaints. Scientific investigation on the plants yielded secondary metabolites of different classes. Several plants of *Rourea* sp. showed potential bioactivity, especially hypoglycemic and antinociceptive activities.

**ACKNOWLEDGMENTS**

The authors would like to express appreciation to Atta-ur-Rahman Institute for Natural Product Discovery, Universiti Teknologi MARA, for the facilities provided.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**FINANCIAL SUPPORT AND SPONSORSHIP**

The authors would like to thank Universiti Teknologi MARA for financial support through Bestari Perdana Grant (600-IRMI/PERDANA 5/3 BESTARI (093/2018)).

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How to cite this article: