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MEDICINAL VALUES of *PAVETTA INDICA* L. EXTRACTS

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Review

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Abstract

Pavetta indica L. is a shrub that belongs to the Rubiaceae family. This plant species has been using to treat diabetes, inflammations, liver and urinary tract disorders, and worm infestation in traditional medicines. As there is no comprehensive review available for reported bioactivities of *P. indica*, this article aims to analyze, summarize, and document the reported bioactivities of *P. indica*. The electronic databases (Web of Science, Scopus, Semantic Scholar, PubMed, and ScienceDirect) to identify related published works from 1900 to January 2021. Clinical, in vitro, and in vivo levels of scientific evidence are available for reported bioactivities. Various parts of *P. indica* have exhibited anti-inflammatory, anticancer, antidiabetic, Anti-Enterobius vermicularis infection, and hepatoprotective activities. Anyhow, so far, none of the bioactive compounds have been identified in this plant species. This work will be advantageous for researchers who are interested to study further bioactivity and phytochemical studies of this plant species.

Keywords: Bioactivities, *Ixora indica*, *Pavetta indica*, Rubiaceae, Sri Lanka.

Özet

Pavetta indica L., Rubiaceae ailesine ait bir çalıdır. Bu bitki türü, geleneksel ilaçlarda diyabet, iltihaplar, karaciğer ve idrar yolu bozuklukları ve solucan istilasını tedavi etmek için kullanılmaktadır. *P. indica*'nın bildirilen biyoaktiviteleri için kapsamlı bir inceleme bulunmadığından, bu makale *P. indica*'nın rapor edilen biyoaktivitelerini analiz etmeyi, özetlemeyi ve belgelemeyi amaçlamaktadır. 1900'den Ocak 2021'e kadar ilgili yayınlanmış çalışmaları tanımlamak için elektronik veritabanları (Web of Science, Scopus, Semantic Scholar, PubMed ve ScienceDirect). Bildirilen biyoaktiviteler için klinik, in vitro ve in vivo bilimsel kanıt seviyeleri mevcuttur. *P. indica*'nın çeşitli kısımları, anti-enflamatuar, antikanser, antidiyabetik, Anti-*Enterobius vermicularis* enfeksiyonu ve hepatoprotektif aktiviteler sergilemiştir. Her neyse, şu ana kadar bu bitki türünde biyoaktif bileşiklerin hiçbiri tanımlanmadı. Bu çalışma, bu bitki türlerinin daha fazla biyoaktivite ve fitokimyasal çalışmalarını incelemek isteyen araştırmacılar için avantajlı olacaktır.

Anahtar Kelimeler: Biyoaktiviteler, *Ixora indica*, *Pavetta indica*, Rubiaceae, Sri Lanka.

1. Introduction

Pavetta indica L. [synonyms: *Pavetta indica* var. *glabrescens* (Kurz) Deb & Rout; *Pavetta indica* var. *indica*; *Ixora indica* (L.) Baill.; *Ixora roxburghii* Kuntze; and *Pavetta indica* var. *typica* Domin] is a shrub that belongs to the Rubiaceae family. It is native to Asia (Sri Lanka, India, Bangladesh, and Myanmar) (Kew Science, 2020). *P. indica* is called Pavattai (பாவட்டை) in Tamil/Siddha Medicine, Kathachampaa and Papata in Ayurveda, and White-Pavetta in English (Khare, 2007). This plant species has been using to treat diabetes, renal edema, ascites, piles, hemorrhoidal pains, ulcer, inflammations, jaundice, fever, liver ailments, headache, urinary tract disorders, worm infestation, cough, swellings, and itches in traditional medicines (Ediriweera et al., 2013; Khare, 2007; Kirtikar and Basu, 2005; Sathasivampillai et al., 2018). Natural compounds such as citral, β -caryophyllene, 2,4-di-tert-butylphenol, (-)-spathulenol, caryophyllene oxide, isospathulenol, methyl palmitate, phytol, 6,11-dimethyl-2,6,10-dodecatrien-1-ol, 5,6-dehydrokawain, 1-(2,6-dihydroxy-4-methoxyphenyl)-3-phenyl-2-propen-1-one, stigmast-5-en-3-ol, capric acid, butyl-2-ethylhexyl phthalate, (3r*,4s*)-3-(2-nitro-4-methoxyphenyl)-4-(4-hydroxyphenyl) hexane, n-propylamine, n-methyl formamide, myristic acid, stearic acid, palmitic

acid, benzyl hydrazine, upiol, n-hexadecane, methyl-4-heptanone, n-docosane, β -pinene, β -eudesmol, and tricyclene have been isolated from various parts of *P. indica* (Prasad et al., 2011; Suresh et al., 2015; Thi-Kim Nguyen et al., 2019).

There is no comprehensive review available for reported bioactivities of *P. indica*. Thus, this article aims to analyze, summarize, and document the reported bioactivities of *P. indica*. This work would be advantageous for researchers who are interested to study further bioactivity and phytochemical studies of this plant species.

A literature search was conducted employing the electronic databases (Web of Science, Scopus, Semantic Scholar, PubMed, and ScienceDirect) to identify related published works from 1900 to January 2021. Accepted scientific name and synonyms [*Pavetta indica*, *Pavetta indica* var. *glabrescens*, *Pavetta indica* var. *indica*, *Ixora indica*, *Ixora roxburghii*, and *Pavetta indica* var. *typica*] were used as search terms. Then the results were refined to subjects: medicine, biology, chemistry, pharmacology, toxicology, agriculture, biochemistry, and molecular biology, etc.

2. Reported bioactivities of *P. indica*

Level of scientific evidence, bioactivity, part used, extract, assay / model / subject, dose / concentration, and reference of reported bioactivities of various parts of this plant species are listed in Table 1. Clinical, in vitro, and in vivo levels of scientific evidence are available for reported bioactivities, and more investigations have been carried out in in vitro assays. Various parts of *P. indica* have exhibited antibacterial, anti-inflammatory, hepatoprotective, anticancer, antidiabetic, diuretic, Anti-*Enterobius vermicularis* infection, and hepatoprotective activities (Bandibas and Roxas, 2017; Ediriweera et al., 2013; Golwala et al., 2009; Gupta et al., 2013; Mandal et al., 2003; Natarajan et al., 2013; Penumala et al., 2017, 2017; Ramamoorthy et al., 2010; Sujatha and Prakash, 2013; Suresh et al., 2018; Thabrew et al., 1987; Thayyil and Muthu, 2018; Thi-Kim Nguyen et al., 2019; Valte et al., 2018). The majority of the investigations exhibited antibacterial activities. Leaves have been used in a greater number of investigations and leaves exhibited anti-*Enterobius vermicularis* infection, anti-inflammatory, diuretic, hepatoprotective, antibacterial, anticancer, antidementia, antidiabetic, and antioxidant activities. Anyhow, so far, none of the bioactive compounds have been identified in this plant species. Hence, further bioassay-guided isolation investigations should be carried out to identify the bioactive compounds from *P. indica*. Furthermore, water, ethanol, and methanol have been mostly used to prepare the extracts in reported investigations. Reported bioactivity investigations including anti-inflammatory,

hepatoprotective, antidiabetic, diuretic, and anti-*E. vermicularis* infection activities provide scientific evidence for traditional medicinal uses including diabetes, renal edema, inflammations, jaundice, liver ailments, urinary tract disorders, worm infestation, and swellings.

It was noticed that there are some drawbacks to the reported studies. Firstly, the concentrations / doses used in some studies by the authors were expressed in a completed way. For example, 60 g in 960 mL water (Ediriweera et al., 2013); and 2.5 mL of 200 g in 500 mL (Thabrew et al., 1987). Further, the concentrations / doses used in some studies were very high. For instance, 5.05 mg mL⁻¹ (Sujatha and Prakash, 2013); 500 mg kg⁻¹ (Mandal et al., 2003); and 304.6 µg mL⁻¹ (IC₅₀) (Suresh et al., 2018). Further, in some studies, the authors did not mention the concentrations / doses exhibited the bioactivities. For example, antibacterial activity (Bandibas and Roxas, 2017); and antioxidant activity (Thayyil and Muthu, 2018). Therefore, it is recommended that to include more information about the results as possible when publishing the works. Moreover, the authors should state the concentrations in terms of such as Minimum Inhibitory Concentration (MIC) and half-maximal inhibitory concentration (IC₅₀), rather than in terms of like µg disc⁻¹. Only investigations reported the highest level of scientific evidence and the lowest concentration / dose used are discussed below.

Table 1: Reported bioactivities of various parts of *P. indica*

Level of scientific evidence	Bioactivity	Part used	Extract	Assay/model/subject	Dose/concentration	Reference
Clinical	Anti- <i>Enterobius vermicularis</i> infection	Leaf	Water	<i>Enterobius vermicularis</i> infestation	60 g in 960 mL water	(Ediriweera et al., 2013)
In vivo	Antidiabetic	Leaf	Methanol	Alloxan-induced diabetic	250 mg kg ⁻¹	(Natarajan et al., 2013)
In vivo	Anti-inflammatory	Leaf	Ethanol	Rat	60 mg kg ⁻¹	(Golwala et al., 2009)
In vivo	Anti-inflammatory	Leaf	Methanol	Carrageenin-induced pedal inflammation, Histamine-induced pedal inflammation, Dextran-	500 mg kg ⁻¹	(Mandal et al., 2003)

Level of scientific evidence	Bioactivity	Part used	Extract	Assay/model/subject	Dose/concentration	Reference
				induced pedal inflammation		
In vivo	Diuretic	Leaf	Petroleum ether	Rat	250 mg kg ⁻¹	(Ramamooorthy et al., 2010)
In vivo	Hepatoprotective	Leaf	Ethanol	Paracetamol-induced liver damage	100 mg kg ⁻¹	(Valte et al., 2018)
In vivo	Hepatoprotective	Leaf	Water	CCl ₄ -induced liver damage	2.5 mL of 200 g in 500 mL	(Thabrew et al., 1987)
In vitro	Antibacterial	Flower	Benzene	<i>Bacillus cereus</i>	0.65 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Benzene	<i>Bacillus subtilis</i>	0.31 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Benzene	<i>Escherichia coli</i> , <i>Proteus vulgaris</i>	1.25 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Benzene	<i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i>	2.50 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Benzene	<i>Lactobacillus acidophilus</i>	5.05 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Benzene	<i>Salmonella typhi</i>	1.05 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Benzene	<i>Staphylococcus aureus</i>	3.00 mg mL ⁻¹	(Sujatha and Prakash, 2013)

Level of scientific evidence	Bioactivity	Part used	Extract	Assay/model/subject	Dose/concentration	Reference
In vitro	Antibacterial	Flower	Ethanol	<i>Bacillus cereus</i> , <i>Escherichia coli</i>	0.62 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Ethanol	<i>Bacillus subtilis</i> , <i>Proteus vulgaris</i> , <i>Klebsiella pneumoniae</i>	0.31 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Ethanol	<i>Lactobacillus acidophilus</i>	5.15 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Ethanol	<i>Pseudomonas aeruginosa</i>	1.25 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Ethanol	<i>Salmonella typhi</i>	0.72 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Ethanol	<i>Staphylococcus aureus</i>	1.30 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Water	<i>Bacillus cereus</i>	3.20 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Water	<i>Bacillus subtilis</i> , <i>Salmonella typhi</i>	1.25 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Water	<i>Lactobacillus acidophilus</i>	5.10 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Water	<i>Pseudomonas aeruginosa</i>	5.00 mg mL ⁻¹	(Sujatha and Prakash, 2013)
In vitro	Antibacterial	Flower	Water	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Proteus vulgaris</i> ,	2.50 mg mL ⁻¹	(Sujatha and Prakash, 2013)

Level of scientific evidence	Bioactivity	Part used	Extract	Assay/model/subject	Dose/concentration	Reference
				<i>Klebsiella pneumoniae</i>		
In vitro	Antibacterial	Leaf	NA	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i>	NS	(Bandibas and Roxas, 2017)
In vitro	Antibacterial	Leaf	Water, Methanol, Chloroform, Benzene	<i>Bacillus subtilis</i>	750 µg disc ⁻¹	(Gupta et al., 2013)
In vitro	Anticancer	Aerial	Methanol	Breast cancer cell	21.2 µg mL ⁻¹ (IC ₅₀)	(Thi-Kim Nguyen et al., 2019)
In vitro	Antidementia	Leaf	Methanol	Acetylcholinesterase inhibitory	17.77 µg mL ⁻¹ (IC ₅₀)	(Penumala et al., 2017)
In vitro	Antidementia	Leaf	Methanol	Butyrylcholinesterase	20.22 µg mL ⁻¹ (IC ₅₀)	(Penumala et al., 2017)
In vitro	Antidiabetic	Leaf	Methanol	α-Glucosidase inhibitory	42.76 µg mL ⁻¹ (IC ₅₀)	(Penumala et al., 2017)
In vitro	Anti-inflammatory	Leaf	Ethanol	Egg albumin	304.6 µg mL ⁻¹ (IC ₅₀)	(Suresh et al., 2018)
In vitro	Antioxidant	Aerial	Petroleum ether	DPPH radical scavenging	NS	(Thayyil and Muthu, 2018)
In vitro	Antioxidant	Leaf	Methanol	ABTS radical scavenging	150.29 µmol TE g ⁻¹	(Penumala et al., 2017)
In vitro	Antioxidant	Leaf	Methanol	DPPH radical scavenging	204.4 µmol AAE g ⁻¹	(Penumala et al., 2017)

AAE: Ascorbic acid equivalent; ABTS: 2,2'-azinobis [3-ethylbenzthiazoline]-6-sulfonic acid; CCl₄: Carbon tetrachloride; DPPH: 2,2-diphenyl-1-picrylhydrazyl; IC₅₀: Half-maximal inhibitory concentration; MIC: Minimum inhibitory concentration; NA: Not applicable; NS: Not stated; TE: Trolox equivalent

2.1. Reported clinical study

2.1.1. Anti-*Enterobius vermicularis* infection activity

A total of 50 patients (from 5 to 65 years old) have *E. vermicularis* infestations were orally administered a decoction prepared by boiling 60 g of fresh leaves in 960 mL water twice a day for 14 days. After completion of treatment, it was noticed that there was a decrease of symptoms including diminished hunger, diarrhea, burping, and stomachache. Further, the tests showed that *E. vermicularis* was not present in the stools (Ediriweera et al., 2013).

2.2. Reported in vivo activities

2.2.1. Antidiabetic activity

Natarajan et al. (2013) orally administered methanol leaf extract at a dose of 250 mg kg⁻¹ body weight per day to Alloxan-induced diabetic rats for seven days. The results showed that there was a significant decrease in the elevated blood glucose concentrations. Glibenclamide at a dose of 600 µg kg⁻¹ per day was used as a positive control in this study (Natarajan et al., 2013).

2.2.2. Anti-inflammatory activity

An extract was prepared using leaves and ethanol (60 mg kg⁻¹) was intraperitoneally administered to rats. After 30 minutes, tail clip and hot plate tests were carried out and the results showed that there was a noticeable reduction in pain models. Acetylsalicylic acid at a dose of 150 mg kg⁻¹ was used as a standard drug (Golwala et al., 2009).

2.2.3. Diuretic activity

The leaf petroleum ether extract at a dose of 250 mg kg⁻¹ was orally administered to rats. It was observed that there was an elevation in the obtained urine volumes as well as the concentrations of the ions like Cl⁻, K⁺, and Na⁺ in the urine. Furosemide (20 mg kg⁻¹ body weight) was used as a positive control in this investigation (Ramamoorthy et al., 2010).

2.2.4. Hepatoprotective activity

An investigation carried out by Valte et al. (2018), revealed hepatoprotective effects after orally administering 100 mg kg⁻¹ of ethanol leaf extract to paracetamol-induced liver damaged for seven days. Silymarin (100 mg kg⁻¹) was used as a positive control in the investigation (Valte et al., 2018).

2.3. Reported in vitro activities

2.3.1. Antibacterial activity

Water, methanol, chloroform, and benzene extracts of leaves at a concentration of 750 $\mu\text{g disc}^{-1}$ showed antibacterial effects in *Bacillus subtilis* assay. Ampicillin was used as a standard drug in this investigation (Gupta et al., 2013).

2.3.2. Anticancer activity

An extract prepared using methanol and aerial parts showed anticancer effects at a concentration of IC_{50} 21.20 $\mu\text{g mL}^{-1}$ in breast cancer cell lines (Thi-Kim Nguyen et al., 2019).

2.3.3. Antidementia activity

An investigation carried out by Penumala et al. (2017) showed antidementia effects of leaf methanol extract (IC_{50} 17.77 $\mu\text{g mL}^{-1}$) in acetylcholinesterase inhibitory assay. Galantamine was used as a positive control in this investigation (Penumala et al., 2017).

2.3.4. Antioxidant activity

The methanol extract of leaves (150.29 $\mu\text{mol TE g}^{-1}$) showed antioxidant activity in 2,2'-azinobis [3-ethylbenzthiazoline]-6-sulfonic acid (ABTS) radical scavenging assay (Penumala et al., 2017).

3. Conclusion

P. indica has many traditional medicinal uses and investigations provided scientific evidence for some of its traditional medicinal uses. Hence, it seems that more bioactivity and phytochemical investigations should be carried out to provide more scientific evidence and to identify the bioactive compounds. As mentioned before, the drawbacks of the reported studies should be improved in future studies to provide more accurate results involving the bioactivities of the extracts and compounds. Further, a range of assays and models should be included in future studies to provide further scientific evidence to validate the reported bioactivities by the other studies. Extracts or compounds that showed more promising results in vitro studies should be further studies in in vivo models as well as in clinical trials. Again, when conducting further studies the concentrations/doses of the extracts/compounds should be taken into consideration to provide more effective plant materials for future drug discovery researches. This work analyzed, summarized, and documented the identified bioactivities of *P. indica*. Also, this work will be advantageous for researchers who are interested to study further bioactivity and phytochemical studies of this plant species in the future.

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Conflicts of interest

The authors declare that there are no potential conflicts of interest relevant to this article.

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