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REVIEW

# Phytochemistry and pharmacology of *Pandanus amaryllifolius* Roxb.

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## Abstract

**Background:** An interesting medicinal plant in Southeast Asia, *Pandanus amaryllifolius* Roxb. (*P. amaryllifolius*) is used as a flavouring and in Southeast Asian folk medicine to treat a range of illnesses. **Objective:** An overview of research on the phytochemistry and pharmacological effects of *P. amaryllifolius* is the goal of this paper. **Method:** This review was based on an analysis of scientific literature sourced from various electronic databases, including PubMed, ScienceDirect, Google Scholar, Web of Science, and Scopus. **Result:** Pandamarilactonine-A and -B, pandanamine, pandamarilactone-1, and pandamarilactone-32 are among the primary chemical compounds that have been extracted and identified from P. amaryllifolius. Norpandamarilactonines C and D, pandalizine C, pandalizine D, pandalizine E, pandanusine A, pandanusine B, and pandamarilactone-3. Potential pharmacological effects of *P. amaryllifolius* include hepatoprotective, antiviral, anticancer, antibacterial, and metabolic syndrome antihyperglycemic effects. **Conclusion:** *P. amaryllifolius* may be used to treat several diseases, but not enough studies have been done on the phytochemistry of the plant. As a result, more research should concentrate on drug development, *P. amaryllifolius* leaf toxicity testing, and the isolation and identification of active compounds.

## Introduction

*Pandanus amaryllifolius* is a tropical herbaceous plant known for its fragrant aroma. Commonly called "*pandan-wangi*" or "*fragrant screw pine*", it belongs to the Pandanaceae family (Ghasemzadeh & Jaafar, 2013). The Pandanaceae family encompasses approximately 600 species within the genus *Pandanus*, exhibiting a broad distribution across tropical and subtropical regions (Ghasemzadeh & Jaafar, 2013). According to Sireeratawong and colleagues (2016), *P. amaryllifolius* is a traditional medicinal plant used extensively throughout Southeast Asia, and it is believed to have therapeutic effects for various diseases.

Due to its unique and pleasant aroma, P. amaryllifolius leaves are widely used throughout Southeast Asia to flavour a variety of food products, including baked goods, confections, and even home cooking. In Thailand, Indonesia, and the Philippines, the leaves are utilised in traditional medicine and as a food flavouring (Ghasemzadeh & Jaafar, 2013). In India, it is customary to cook ordinary non-aromatic rice with *P. amaryllifolius* leaves to impart a scent to the cooked rice similar to that of basmati rice (Wakte *et al*., 2009). The application of powdered dried leaves extends beyond culinary applications, encompassing a diverse range of food products. These include dairy products such as ice cream and yoghurt, savoury dishes like soups, baked goods like cakes, beverages like tea, traditional Southeast Asian dishes like pandan-flavoured rice, and even confectioneries such as "*Kaya*", a traditional coconut jam. Numerous varieties of Pandanus are utilised in traditional medicine and are acknowledged as medicinal herbs. Wakte and colleagues (2009) document the ethnomedical utilisation of these leaves in the management of a diverse range of health problems, including smallpox, fever, arthritis, headaches, and dental conditions.

## Methods

This study was conducted through a narrative review, collecting journals related to the topics discussed from PubMed, ScienceDirect, Google Scholar, Web of Science, and Scopus, spanning the period from 1996 to 2024, to identify the Phytochemistry and Pharmacology of P. *amaryllifolius* Roxb.

## Results

There were 31 volatile compounds in the essential oil (Table I).

**Table I: Volatile compounds identified from *P. amaryllifolius* leaves***

| Compound name | Retention time (RT) | Peak area ± SD (1000) | % of total |
|---|---|---|---|
| Di-n-propyl ether | 1.11 | 1.41 ± 0.06 | 0.17 |
| Ethyl ethanoate | 1.47 | 5.48 ± 1.82 | 0.68 |
| 4-Hydroxybutan-2-one | 1.73 | 5.34 ± 0.45 | 0.66 |
| Caproaldehyde | 2.81 | 53.44 ± 4.06 | 6.63 |
| 2-Amifluran | 4.58 | 0.70 ± 0.18 | 0.09 |
| trans-2-Hexenal | 4.84 | 175.87 ± 12.46 | 21.87 |
| trans-3-Hexenal | 5.01 | 5.80 ± 2.08 | 0.72 |
| meta- Methylpyridine | 6.01 | 21.24 ± 1.16 | 2.64 |
| trans-2-Penten-1-ol | 6.86 | 18.70 ± 1.59 | 2.32 |
| 2-Acetylpyrroline | 7.00 | 68.56 ± 1.57 | 8.52 |
| Hexyl alcohol | 7.45 | 3.47 ± 0.34 | 0.43 |
| 1-Nonanal | 8.10 | 84.62 ± 4.90 | 10.50 |
| gamma-Hexenol | 8.45 | 4.51 ± 1.08 | 0.56 |
| trans-2-Octenal | 9.11 | 7.88 ± 0.13 | 0.98 |
| 2,6,11-trimethyldodecane | 9.32 | 8.39 ± 0.67 | 1.04 |
| 2,4 Heptadienal | 10.13 | 13.66 ± 4.95 | 1.69 |
| Benzoic aldehyde | 10.55 | 16.60 ± 1.08 | 2.06 |
| trans-2 Nonenal | 10.72 | 15.07 ± 1.16 | 1.87 |
| Linalyl alcohol | 11.02 | 21.60 ± 4.33 | 2.70 |
| N-Octanol | 11.17 | 16.40 ± 0.90 | 2.02 |
| 2,6-Nonadienal | 11.50 | 25.16 ± 5.33 | 3.11 |
| beta-Cyclocytral | 11.89 | 3.74 ± 0.70 | 0.46 |
| 3 Methyl -2 (5H)-furanone α- | 13.11 | 24.99 ± 5.53 | 3.12 |
| Cyclocytrilideneacetone | 14.37 | 5.38 ± 0.18 | 0.67 |
| 3,7,11,15-tetramethyl-2-Hexadecen-1-ol | 15.02 | 4.70 ± 0.15 | 0.58 |
| β-ionone | 15.13 | 4.09 ±0.50 | 0.50 |
| β-ionon-5,6-epoxide | 15.47 | 4.10 ± 0.31 | 0.51 |
| Pentadecanal | 15.75 | 12.39 ± 2.10 | 1.53 |
| Decanoic acid | 17.65 | 5.11 ± 0.91 | 0.63 |
| Lauric anhydride | 18.98 | 4.22 ± 0.29 | 0.52 |
| Phytol | 19.65 | 43.29 ± 3.03 | 5.28 |
| % of identified volatiles | | | 85.08 |
| % of Unidentified volatiles | | | 14.92 |
| % total | | | 100 |

*(Wakte *et al.*, 2009)

The antibacterial activity of P. *amaryllifolius* extracts was determined using a standardised microdilution assay (Table II and Table III), including pandamarilactonine-A, pandamarilactonine-B, pandamarilactone-1, pandamarilactone-32, and crude base extract (Laluces *et al.*, 2015).

**Table II: Minimal inhibitory concentration of different isolates***

| Compound name | *Escherichia coli* | *Pseudomonas aeruginosa* | *Staphyllococus aureus* |
|---|---|---|---|
| Pandamarilactone - 1 | 500 | 500 | 250 |
| Pandamarilactone - 32 | 125 | 500 | 250 |
| **Pandamarilactonine - A** | **62.5** | **15.6** | **250** |
| Pandamarilactonine - B | 500 | 500 | 250 |
| Crude base | 500 | 62.6 | 250 |

*(Laluces *et al*., 2015)

**Table III: Minimum bactericidal concentration of different isolates***

| Compound name | *Escherichia coli* | *Pseudomonas aeruginosa* | *Staphyllococus aureus* |
|---|---|---|---|
| Pandamarilactone - 1 | >500 | >500 | 500 |
| Pandamarilactone - 32 | 250 | >500 | 500 |
| **Pandamarilactonine - A** | **125** | **31.25** | **500** |
| Pandamarilactonine - B | >500 | >500 | 500 |
| Crude base | >500 | 125 | 500 |

*(Laluces *et al*., 2015)

The impact of P. *amaryllifolius* extract on the biochemical parameters of serum in rats is summarised in Table IV. The administration of aqueous extracts of P. *amaryllifolius* at doses of 150 mg/kg and 300 mg/kg body weight produced a significant reduction in elevated serum levels of Aspartate Transaminase (AST) and Alanine Transaminase (ALT).

**Table IV: Effects of *P. amaryllifolius* extract on biochemical parameters of serum in rats**

| Group | Treatment | Aspartate transaminase (IU/l) | Alanine transaminase IU/l |
|---|---|---|---|
| I | Normal | 137.2 ± 0.15 | 77.2 ± 0.12 |
| II | Tetrachloromethane (1 ml/kg b.wt.) | 557.2 ± 0.10 | 537.2 ± 0.14 |
| III | Plant extract alone (300 mg/kg b.wt.) | 117.2 ± 0.17 | 69.2 ± 0.12 |
| IV | Plant dose 1 (150 mg/kg b.wt.) + tetrachloromethane | 533.2 ± 0.14 | 517 ± 1.05 |
| V | Plant dose 2 (300 mg/kg b.wt.) + tetrachloromethane | 397.2 ± 0.29 | 357.2 ± 0.10 |

(Thanebal *et al*., 2021)

## Discussion

### *Chemical compounds*

The chemical constituents of *P. amarylifolius* have been the subject of numerous studies. Flavonoids, alkaloids, benzenoids, steroids, lignans, and triterpenoids were isolated from Pandanus sp. extracts using phytochemical analysis (Gopalkrishnan *et al*., 2015). Alkaloids have been identified as the primary secondary metabolites of this genus (Tsai *et al*., 2015). According to one study, which utilised NMR spectroscopic analysis and ESI-MS to examine the phytochemicals in the aerial part of P. amaryllifolius, it contained the alkaloids pandanusines A and pandanusines B, pandalizines C, pandalizines D, and pandalizines E, as well as the norpandamarilactonines C and norpandamarilactonines D (Cheng *et al*., 2017). Tsai and colleagues (2015) employed NMR spectroscopic analysis to determine the alkaloid content of ethanolic crude extracts from the aerial parts of P. amaryllifolius. Using an acid-base extraction technique, Ethanol extracts from the branches and leaves of the P. *amaryllifolius* plant undergo a fractionation process, yielding water, chloroform, and ethyl acetate fractions. Two norpandamarilactonines, two indolizinones, N-acetylnorpandamarilactonines A and N-acetylnorpandamarilactonines B, pandalizines A and pandalizines B, pandanmenyamine, a

pandanamine, three pandamarilactones, 5(E)-pandamarilactonine-3, and pandamarilactones-2 and pandamarilactones-3, are among the nine new compounds identified by the study's findings (Tsai *et al*., 2015). Among the alkaloids found in *P. amaryllifolius* leaves are Pandanamine (Takayama *et al*., 2001) and pandamarilactonine-A and -B (Takayama *et al*., 2005).

Phenolic acids and flavonoids present in *P. amaryllifolius* leaf extracts were identified through comparative analysis, utilising retention times, UV spectra, and UV absorbance ratios, with authentic standards serving as reference points. The study revealed the presence of three phenolic acids, including 3,4,5-trihydroxybenzoic acid, trans-cinnamic acid, and 4-hydroxy-3-methoxycinnamic acid, and five flavonoids, such as Quercetin 3-rutinoside, L-epicatechin, catechuic acid**,** 3,4',5,7-Tetrahydroxyflavone, and naringoside (Reshidan *et al*., 2019). Additionally, Wakte and colleagues (2009) investigated the essential oil content of P. *amaryllifolius* leaf extract, which was extracted using headspace solid-phase microextraction and gas chromatography with ionisation detectors. Their research identified 31 volatile compounds in the essential oil (Table I).

***Pharmacological activities***

*Antioxidant activity*

According to Lobo and colleagues (2010), the generation of free radicals and Reactive Oxygen Species (ROS) can be attributed to both endogenous metabolic processes and exogenous factors. These exogenous factors include exposure to ionising radiation (such as X-rays), ozone, tobacco smoke, environmental pollutants, and industrial toxins. The continuous generation of free radicals within cellular environments occurs through various mechanisms, including enzymatic pathways such as respiratory chain activity, prostaglandin synthesis, and cytochrome P-450 enzyme system activity, as well as non-enzymatic reactions involving the interaction of molecular oxygen with organic compounds (Engwa, 2018).

Over time, free radical reactions lead to gradual physiological changes associated with ageing. However, environmental and genetic factors influence the extent of free radical damage. Antioxidants help combat oxidative stress by scavenging ROS and inhibiting cell damage caused by protein phosphorylation. According to Dhama and colleagues (2019), many herbs and spices are associated with strong antioxidant activity and numerous health benefits. The antioxidant potential of the plant's leaf methanol extract was evaluated using the Ferric Reducing Antioxidant Power (FRAP) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) tests, following the method established by Sanjeeva and Shimada. Vitamin C and Butylated Hydroxytoluene (BHT) acted as comparative standards in this study. Vitamin C and BHT were used as standard references in these tests (Sanjeeva *et al*., 2011).

FRAP assay quantifies antioxidant capacity by measuring the reduction of ferric tripyridyltriazine (Fe(III)-TPTZ) to its ferrous form (Fe(II)-TPTZ) within an acidic environment. The reducing power of *P. amaryllifolius* extracts varied across Malaysian regions, with values ranging from 511.2 µmol Fe(II)/g in Bachok to 314.8 µmol Fe(II)/g in Pontian. Comparatively, BHT and vitamin C showed higher reducing powers at 672.4 µmol Fe(II)/g and 1186.55 µmol Fe(II)/g, respectively (Ghasemzadeh & Jaafar, 2013).

The DPPH assay revealed that propylene glycol extracts had the highest radical scavenging activity, followed by ethanol-propylene glycol mixtures (1:1 and 4:1 ratios) and ethanol extracts. The propylene glycol extract achieved 94.56 ± 3.35% DPPH activity, significantly higher than the root extract's 29.55 ± 1.21% (Jimtaisong & Krisdaphong, 2013).

Sonication-assisted extraction further enhanced the antioxidant activity of the extracts, nearly doubling their efficiency. The IC50 values, representing the concentration required to inhibit 50% of free radicals, were 0.012 ± 0.001 mg/ml for leaf extracts, 0.290 ± 0.007 mg/ml for root extracts, 0.810 ± 0.009 mg/ml for vitamin C, and 2.340 ± 0.040 mg/ml for BHT. Although the results showed promising potential, the capacity of P. *amaryllifolius* leaf extracts from all three sites in capturing DPPH free radicals was significantly lower compared to the standard antioxidants BHT (83.7%) and vitamin C (92.3%) at a concentration of 35 mg/mL. The IC50 values for pandan extracts were 9.25 mg/mL, 11.6 mg/mL, and 12.5 mg/mL in Pontian, Bachok, and Klang, respectively (Ghasemzadeh & Jaafar, 2013).

*Anticancer activity*

Cancer is fundamentally characterised *by* uncontrolled cellular proliferation and aberrant differentiation, resulting in the development of neoplastic masses that invade surrounding tissues and potentially metastasise to distant sites. The dysregulation of multiple cellular regulatory pathways contributes to the characteristic uncontrolled growth exhibited by cancer cells. This aberrant behaviour manifests in various aspects of cellular activity, distinguishing cancer cells from their regular counterparts. Cytotoxic chemotherapeutic agents are employed in cancer

treatment with the primary aim of inhibiting cellular proliferation and metastatic spread. (Cooper, 2000).

The anticancer properties of *P. amaryllifolius* ethanol extract were assessed through DNA fragmentation, Annexin V/PI staining, cell cycle analysis, and its effects on non-hormone-dependent breast adenocarcinoma (MDA-MB-231). Hueh Zan and colleagues (2011) observed that the ethanol extract exhibited anti-proliferative effects, inducing cell cycle arrest at the G1/G0 phase after 24 hours of treatment. Apoptosis was observed in MDA-MB-231 cells following 48 and 72 hours of treatment. Annexin V/PI staining analysis revealed the presence of both early and late apoptotic populations within MDA-MB-231 cells following a 48-hour exposure to the extract (Chong *et al*., 2012). Specifically, 8% of early apoptotic and 18% of late apoptotic cells were detected after treatment, compared to less than 5% in the control group. The TUNEL assay showed that approximately 25% of treated cells were TUNEL-positive after 48 hours, rising to about 45% ($p < 0.05$) after 72 hours, compared to roughly 5% in control cells (Hueh Zan *et al*., 2011).

Using the MTT test, the anticancer efficacy of fresh leaf methanol extract from *P. amaryllifolius* against normal (MCF-10A) cells and human breast carcinoma (MCF-7) was determined. Locally, fresh *P. amaryllifolius* leaves were gathered from Johor, Selangor, and Kelantan, three distinct Malaysian provinces. Ghasemzadeh and Jaafar reported that the IC50 values of *P. amaryllifolius* extract against MCF-7 cells were 210.4; 285.6, and 334.2 µg/mL, respectively, from Bachok, Klang, and Pontian sites. The authors have evidence that *P. amaryllifolius* extracts prevent breast cancer cells from proliferating. Nevertheless, normal cell viability was reduced in all extracts as the concentration of the extract increased. Because the IC50 values were higher than 640 µg/ml, *P. amaryllifolius* extract from various locales was deemed non-toxic to normal cells (MCF-10A) (Ghasemzadeh & Jaafar, 2013).

*Antibacterial activity*

Infections caused by bacteria have a significant impact on public health. Humans may acquire bacteria from food, water, the air, or live vectors. Contact, airborne droplets, vectors, and vehicles are the primary means by which bacterial infections are spread (Doron & Gorbach, 2018).

Minimal Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of various *P. amaryllifolius* extracts were determined using a standardised microdilution assay (Table II and Table III), including pandamarilactonine-A, pandamarilactonine-B, pandamarilactone-1, pandamarilactone-32, and crude base extract (Laluces *et al*., 2015). To obtain a final volume of 100 µL for every test organism, extracts were serially diluted (1:2) into eight microwells after being diluted with DMSO to a concentration of 1 mg/ml (Laluces *et al*., 2015). E. coli ATCC 25922, P. aeruginosa ATCC 27853, and S. aureus ATCC 25923 were the three microorganisms utilised in the assay. Each well received 100 µL of bacterial culture (1.5 × 108 CFU/mL), followed by incubation at 37°C for 24 hours. MIC was defined as the lowest concentration of the test substance in the final well that showed no visible microbial growth (Laluces *et al*., 2015).

Pandamarilactonine-A was the most active of the four isolates, as indicated by the data. Furthermore, it was discovered that the crude base had action against P. aeruginosa (Laluces *et al*., 2015).

*Antiviral activity*

A virus is a microscopic infectious agent, significantly smaller than bacteria or fungi, that must invade a living cell to reproduce. Following attachment to a host cell, the virion undergoes internalisation, releasing its nucleic acid genome, which may consist of either DNA or RNA. This viral genetic material subverts the host cell's cellular machinery, redirecting it towards the synthesis of new viral progeny. This process typically disrupts the cell's normal functions, leading to its death. The newly created viruses are then released and infect neighbouring cells. Current antiviral drug development focuses on targeting either the virus itself or components of the host cell (Gelderblom, 1996).

Linda S. M. investigated the antiviral potential of pandanus extract against the Influenza virus H1N1 and Herpes simplex virus type-1 (HSV-1 15577). The N1H1 virus was cultured in Madin-Darby Canine Kidney (MDCK) cells using a 96-well plate, while HSV-1 15577 was cultured in Vero cells. Ribavirin and acyclovir were used as positive controls for HSV-1 15577 and N1H1 viruses, respectively. The effectiveness of an antivirus is evaluated through a cytopathic effect reduction test. Results revealed that pandanin demonstrated antiviral activity with an EC50 of 2.94 µM against HSV-1 15577 and 15.63 µM against the Influenza virus N1H1 (Ooi *et al*., 2004).

*Metabolic syndrome*

Metabolic syndrome is a pathological condition characterised by a collection of metabolic disorders, namely hypertension, visceral fat accumulation, abnormal lipid profile, and increased blood glucose levels. This cluster of conditions significantly increases the individual's predisposition to cardiovascular

disease. These abnormalities are evaluated using various parameters, such as Body Mass Index (BMI), blood pressure, total weight gain, abdominal fat accumulation, adipocyte size and count, Abdominal Circumference (AC), fasting lipid profiles, plasma glucose levels, and inflammatory markers like leptin, NFκβ p65, adiponectin, and TNFα (Swarup *et al*., 2024).

In a study investigating the effects of *P. amaryllifolius* leaf water extract on metabolic syndrome and associated inflammatory markers, fructose-fed rats exhibited features characteristic of the syndrome, including obesity, hypertension, dyslipidemia, and hyperglycemia. Fructose intake was associated with increased body weight, BMI, and AC. However, administration of *P. amaryllifolius* leaf water extract resulted in a significant amelioration of Various anthropometric parameters, including BMI and AC, which are indicators of the risk of metabolic complications. (Reshidan *et al*., 2019).

*Antihyperglycemic activity*

Uncontrolled diabetes often leads to hyperglycemia (high blood sugar), which, over time, can significantly damage various systems, particularly blood vessels and nerves, in organs such as the heart, kidneys, and eyes. Driven by their potential for reduced cost and a lower incidence of adverse effects compared to synthetic pharmaceuticals, there has been a surge in scientific interest surrounding the hypoglycemic properties of herbal remedies traditionally employed in Asian medicine for the management of diabetes (Giri *et al*., 2018).

A cohort of 30 healthy volunteers participated in a study evaluating the antihyperglycemic properties of *P. amaryllifolius* water extracts (tea). A standard Oral Glucose Tolerance Test (OGTT) was employed, wherein participants consumed the tea (0.1 g/mL) 15 minutes after glucose loading. Plasma glucose levels were subsequently measured at designated intervals using a glucose-oxidase-based method. Results showed that *P. amaryllifolius* tea significantly reduced postprandial blood sugar levels, with the treated group exhibiting lower average plasma glucose peaks (6.16 ± 0.79 mmol/l) compared to the control group (6.94 ± 0.98 mmol/l, $P < 0.001$). In vitro studies demonstrated that dose-dependent water and ethanol extracts of P. amaryllifolius increased insulin secretion in RIN-m5F mouse insulinoma cells and inhibited α-glucosidase activity, with acarbose serving as a positive control (Chiabchalard & Nooron, 2015).

*Hepatoprotective activity*

The hepatoprotective properties of *P. amaryllifolius* were assessed in a study examining its ability to protect against liver damage induced by tetrachloromethane in rats. Tetrachloromethane, a highly toxic compound, generates oxidative stress, leading to liver injury. Administration of aqueous extracts of P. *amaryllifolius* at doses of 150 mg/kg and 300 mg/kg body weight resulted in a significant decrease in elevated serum levels of Aspartate Transaminase (AST) and Alanine Transaminase (ALT) (Table IV) (Thanebal *et al*., 2021). The study concluded that the extract effectively mitigated liver damage caused by tetrachloromethane exposure.

*Acute and chronic toxicity*

The acute toxicity study was conducted to assess the impact of a single dose of P. *amaryllifolius* extract in suggesting the extract is non-toxic at this dose level (Sireeratawong *et al*., 2016).

The chronic toxicity study was conducted in accordance with the guidelines of the WHO and OECD to investigate the long-term effects of the substance. Male and female rats were administered daily oral doses of 1, 2, 4, and 8 g/kg body weight for 180 days. The study monitored toxic symptoms, behavioural changes, and overall health. The study's results did not reveal any significant differences in the observed parameters between the treatment and control groups, indicating the absence of chronic toxic effects (Sireeratawong et al., 2016).

## Conclusion

According to scientific research, *P. amaryllifolius* has numerous health benefits, including hepatoprotective, anti-hyperglycemic, antiviral, antibacterial, and anticancer properties, as well as benefits for metabolic syndrome. Additional high-quality research is required to ensure the safety and effectiveness of herbal products. Also, a high-quality clinical study is needed to definitively prove the efficacy of *P. amaryllifolius* due to insufficient clinical trials. Furthermore, by focusing attention on herbal formulations and research in this field, along with making cost-effective investments to support clinical trials, researchers can help achieve their primary goal.

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