Indian Journal of Traditional Knowledge
Vol 23(9), September 2024, pp 882-897
DOI: 10.56042/ijtk.v23i9.13619

Plumeria species: a review of morphology, traditional uses, phytochemicals, and pharmacological activities

Bruna da Silva Souza, Ana Clara Silva Sales, Lucas Arruda Moita, Naylla Veras de Moraes Oliveira, Francisca Dayane Soares da Silva, Mayck Silva Barbosa, Thalis Ferreira de Souza & Jefferson Soares de Oliveira*

Universidade Federal do Delta do Parnaíba, Campus Ministro Reis Velloso, Laboratório de Bioquímica de Plantas Laticíferas (LBPL), CEP 64.202-020, Parnaíba, Piauí, Brazil

*E-mail: jsoliveira@ufdpar.edu.br

Received 06 November 2021; revised 25 July 2024; accepted 29 August 2024

Plants from genus *Plumeria* belong to the Apocynaceae family and are considered native to the New World. These plants are commonly found in tropical and subtropical areas around the world. Plumerias are well known for their ornamental value and especially as medicinal agents. Species from this genus have played a crucial role in the popular herbal medicine as well as in alternative and complementary system of medicine. This review collects and updates information about Plumeria species. The article highlights findings and explores the medicinal status of these plants with their biological properties and phytochemical components suggested by describing several studies with *in vitro* and *in vivo* evaluations. Our review emphasizes the potential beneficial effects of Plumerias for human and provides evidence that this genus can be used as source for drug development in future.

Keywords: Biological activity, Frangipani, Medicinal plants, Phytochemical analysis

IPC Code: Int Cl.[24]: A61K 36/00

Recent studies have focused on plants mentioned in ancient literature or traditional practices[1-3]. *Plumeria* L., from the Apocynaceae family, are laticiferous, deciduous shrubs found in tropical regions from southern Mexico to northern South America, the Pacific islands, the Caribbean, and India[4,5]. The family comprises 366 genera, with about 133 Plumeria species listed, though only 11 are currently accepted[6,7].

Plumeria spp. are commonly planted in yards, parks, gardens, and cemeteries for their beauty, fragrant flowers, and variety of colors and sizes[5,8]. Plumerias are usually cultivated as ornamental plant, but the species of this genus are also documented for their medicinal status[1]. The genus was named 'Plumeria' by French botanist Charles Plumier in the 17th century, but Spanish priest Francisco de Mendoza first classified the plant in 1522 and documented its medicinal use by Aztec natives[9-11].

Plumerias are considered as one of the most interesting plants to study due to their diversity and medicinal use[3]. The therapeutic potential of *Plumeria* species is cited in Ayurveda, the ancient Indian therapeutic system, renowned as one of the most significant systems of alternative and complementary medicine, and is also documented in the Charaka Samhita, Sushruta Samhita, Rigveda, and Atharvaveda[12-14].

Therefore, the aim of this paper is to review the literature and compile updated information about many characteristics of different species of *Plumeria* L. used around the world. The article also aims to provide information on medicinal uses, pharmacological properties, promising *in vitro* and *in vivo* studies, and their phytochemicals. There are many species of *Plumeria*, as mentioned above, but the following species are thoroughly discussed in this review: *Plumeria acuminata*, *P. alba*, *P. obtusa*, *P. pudica*, and *P. rubra*.

Methodology

An extensive literature search was conducted on the five species of Plumeria (*Plumeria acuminata*, *P. alba*, *P. obtusa*, *P. pudica*, and P. *rubra*) to gather relevant information from databases such as Science Direct, Medline, PubMed, Google Scholar, and Scopus. The search focused on studies related to morphology, identification, bioactive compounds, and the biological

*Corresponding author

and pharmacological properties of Plumerias. The primary search term used was "Plumeria."

Species of *plumeria*-An overview

Their taxonomical classification includes: Kingdom: Plantae; Subkingdom: Tracheobionta; Division: Magnoliophyta; Class: Magnoliopsida (Dicotyledons); Subclass: Asteridae; Order: Gentianales; Family: Apocynaceae; Genus: *Plumeria* L.[15]. Plumerias flowers are used in perfumes, cosmetics, and aromatherapy[12,16]. In India, Plumerias species in general are known as frangipani, champa or temple tree. It is also called kemboja in Malaysia, while terms such as pokok kubur and bunga kubur refer to different species and hybrids[5,17].

P. acuminata is commonly known as perungalli, kalachuchi, golainchi, gorur champa, dalan phul, kshira champa, velachampakan, sona champa, rhada champa, kat champa[18-20]. *P alba* is usually referred white frangipani/caterpillar tree/pagoda tree/pigeon wood/nosegay tree/white frangipani[13]. *P. rubra* is commonly known as gulachin, son champa, kishira champa, lal champa, true frangipani, red paucipan, red jasmine, Temple tree, Mexican Plumeria, Red Plumeria, Pagoda tree[21-23]. *P. obutsa* white frangipani, champa or chafa, melia, araliya, temple tree, graveyard flower or Singapore Plumeria[24]. *P. pudica* is typically termed as bridal bouquet, Plumeria violin leaf, wild plumeria, Oleandro bovairiano or white frangipani,gilded spoon and Brindabon champa[25,26].

Plumeria alba is a medium-sized tree that can reach a height of 5-8 feet, with many branches on the upper part. It presents small trees with obanceolate leaves, white flowers containing five petals and fragrance[14]. *P. acuminata* is a classic or partly deciduous tree that can grow up to 6 meters high. Its leaves are light green, elliptic in shape with acuminate tips, and its flower color can vary from white to yellow[17].

Plumeria obtusa has white flowers with a small yellow central part, up to 9 cm in diameter. Its leaves are dark green, smooth, obovate, and obtuse. The tree can grow to about 6-9 meters tall and is partly deciduous at different times of the year[17]. *P. pudica* is a medium-sized tree that can reach a height of 5-8 feet, with many branches on the upper part. It has oblanceolate leaves, which are alternate and clustered at the twig tips, with strongly recurved margins. White flowers can be found on this tree[26,27].

Plumeria rubra is a shrub or small tree that can reach heights of 2-8 m. It has a thick, succulent trunk and sausage-like blunt branches covered with thin grey bark. Unlike other Plumerias, *P. rubra* produces flowers in various shades of red, pink, orange, and yellow, and its leaves come in a variety of sizes, shapes, and colors[17]. In summary *P. rubra* can be differentiated from *P. obtusa, P. alba and P. pudica*, according to leaves and flowers[11]. The size and shape of the leaves and flowers vary among these species. *P. obtusa* flowers have slightly rounded petals compared to *P. rubra*, which curve backward at the tip. The leaves of *P. obtusa* are oval with a more curved apex than those of *P. rubra. P. alba* features thin, elongated leaves and flower petals with more space between them compared to other Plumerias. *P. pudica* has exclusively spoon-shaped leaves that are elongated, slim, and wider towards the tip, resembling a spoon[5].

Traditional uses

Medicinal plants have long been connected to cultural practices and traditional knowledge. The Spanish introduced Plumerias to the Far East not only for their decorative value but also for their medicinal properties[17]. Historical records from India highlight the extensive use of Plumeria in Ayurvedic and natural herbal medicine. These plants have been integral to traditional medicinal preparations in both Asia and Latin America[5,28].

Plumeria spp. are known for their varied therapeutic uses in native medicine, mainly as cardiotonic, hypotensive, diarrhea, itch, bronchitis, cough, asthma, piles, rheumatism, venereal disease, tooth ache, leprosy, psychosis, dysentery, heart stroke, blood disorders and tumors[20,22,27,29,30]. In some countries such as Philippine Islands and India plant fluids and decoction of the bark are believed to have some properties as purgative, emmenagogic, febrifugic, diuretic, abortifacient and are used in birth control[24,31]. In addition, the plant has been used in the treatment of diseases that affects skin, fevers, edema, and its flowers, when eaten with betel leaves, are used as a remedy for ague[5]. In Latin America, *Plumeria* for example are used to treat subcutaneous mycosis[32]. In Mexico, the infusion of the flowers has been associated with a hypoglycemic effect (diabetes), and latex plant is used to earache and eye-cleaning liquid and women complaints[33].

Pharmacological activity

The use of medicinal plants, including Plumeria species, in folk medicine has stimulated scientific interest in exploring their potential benefits. Research indicates that *Plumeria* species and their components

are linked to various pharmacological activities (Table 1). These biological properties are visually summarized in Figure 1.

Anthelmintic activity

Anthelmintic activity of Saponin extract of *P. rubra* (SERP) was evaluated against *Pheretima posthuman*. SEPR at 25 mg/ml showed anthelmintic effect like the reference drug Piperazine citrate[34]. Anthelmintic activity of methanolic extract of *P. rubra* (MEPR) was tested using *P. posthuman*. The doses of 25-50 mg/mL were more effective than Piperazine citrate[35]. *P. pudica* leaves showed anthelminthic activity against *P. posthuma* using petroleum, ether, ethyl acetate, chloroform, and methanol extracts. The results showed a dose-dependent anti-helminthic activity of the extracts, but methanol (20 mg/mL) was considered the more effective when compared to Albendazole[36].

Antiarthritic activity

The hydroalcoholic extract of *P. alba* was fractioned into ethyl acetate (EAPA) and n-butanol (BPA) fractions. Both fractions were tested on formaldehyde-induced acute non-immunological and Freund's Complete Adjuvant (CFA) induced chronic immunological arthritis. EAPA and BPA reduced paw swelling, decreased erythrocyte sedimentation rate, and improved thymus weight in treated rats. Motor coordination and nociceptive thresholds also showed significant improvement[37]. The hydroalcoholic extract of *P. rubra* (HSBE) was tested in n CFA-induced arthritis. The HSBE attenuated behavioral, biochemical, hematological, and radiological changes in dose dependent manner, reducing mononuclear infiltration and bone erosion[38].

Antidiabetic

The administration of the methanolic extract of *P. acuminata* (MEPA) significantly decreased serum glucose, total cholesterol, triglycerides, oxaloacetic transaminase (GOT), and serum glutamic pyruvic transaminase (GPT) in a streptozotocin-induced diabetes model[39].

The aqueous extract of *P. rubra* significantly reduced fasting blood glucose levels in both normal and alloxan-induced diabetic mice. It also improved serum lipid profiles and glycosylated hemoglobin, with histopathological analysis showing reduced damage in the pancreas, liver, and kidney[40]. Additionally, the hydroalcoholic extract of *P. rubra* decreased blood glucose levels in a streptozotocin-induced diabetes model[41].

Anti-diarrheal properties

Latex protein from *P. pudica* (LPPp) was tested in diarrhea models induced by castor oil, prostaglandin E2 (PGE_2), and cholera toxin. LPPp inhibited the percentage of diarrheal stools, reduced intestinal fluid accumulation, and slowed intestinal transit. At 40 mg/kg, LPPp prevented changes in glutathione (GHS) and malondialdehyde (MDA) levels induced by castor oil, and decreased the average volume of intestinal fluid caused by PGE_2. In the cholera toxin-induced diarrhea model, LPPp (40 mg/kg) reduced intestinal fluid secretion and chloride ion levels in the intestinal loops[42].

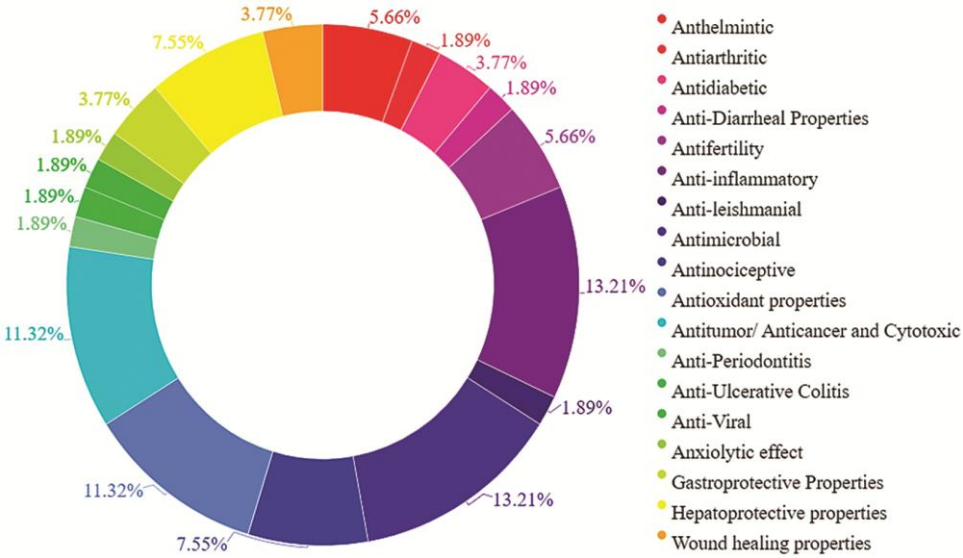

Fig. 1 — Biological properties related to Plumerias species

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
P. acuminata	Anti-inflammatory	Leaves - Methanolic extract	*In vivo* - Wistar Albino Rats	Steroids Flavonoids Tannins Alkaloids Glycosides	Paw Edema Induced by Carrageenan Dextran Histamine Serotonin Cotton Pellet Method	Orally	18
	Antinociceptive and Antioxidant	Leaves - Methanolic extract	*In vivo*	Steroids Flavonoids Tannins Alkaloids Terpenes	Hyperthermia Induced Brewer´s Yeast Writhing Induced by Acetic Acid Hot Plate Test	Orally	60
			In vitro - Not Applicable	Phenols	DPPH Radical Reduction Assay Superoxide Anion Radical Assay Nitric Oxide Radical Assay Hydroxyl Radical Scavenging Assay	Not applicable	
	Antimicrobial	Leaves - Methanolic extract	*In vitro - Bacillus subtilis, Staphylococcus aureus, Micrococcus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhimurium, Aspergillus niger, Candida albicans*	Not given	Agar Disc Diffusion Method	Not applicable	51
	Antioxidant and Antitumor	Leaves - Methanolic extract	*In vivo* - Swiss Albino Mice	Not given	Lipid Peroxidation Assay Reduced Glutathione Assay Content Assay Superoxide Dismutase Catalase Assay Erlich Ascites Carcinoma Cells Transplantation Method	Orally	65
	Antidiabetic	Leaves - Methanolic extract	*In vivo* - Wistar Albino rats	Not given	Streptozotocin Induced Model	Orally	39
	Antitumor	Stem - Saponins	*In vitro* - Oral squamous carcinoma cells	Saponins	Trypan Blue Dye Exclusion Assay Ethidium Bromide/ Acridine Orange Assay	Not applicable	66

…*Contd*.

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies (Contd.)

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
P. alba	Antimicrobial	Leaves - Methanolic extract	*In vitro* - *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Salmonella tythi* *In vitro* - *Aspergillus niger* *Penicillium chrysogenum*, *Microsporum gypseum*, *Epidermatophyton flocossum*	Terpernes (Triterpenes)	Agar Disc Diffusion Method	Not applicable	52
	Antimicrobial	Petals - Methanolic extract	*In vitro* - *Escherichia coli*, *Proteus vulgaris*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *S. saprophyticus*, *Enterococcus faecalis*, *Serratia marcescens*	Not given	Agar Disc Diffusion Method	Not applicable	53
	Antiarthritic	Leaves - Hydroalcoholic extract	*In vivo* - Wistar Albino Rats	Flavonoids Alkaloids Terpenoids Glycosides Saponins Tannins Steroids	Formaldehyde Arthritis Induced	Orally	37
	Hepatoprotective	Branches - Methanolic extract	*In vivo* - Wistar Albino Rats	Not given	Hepatic Injury Paracetamol Induced by Paracetamol	Orally	76
	Antioxidant abd Cytotoxic	Flower - Methanolic extract	*In vitro* - Not applicable *In vitro* - HCT 116 cell lines	Phenols	DPPH Radical Reduction Assay MTT Assay	Not applicable	59 61
	Hepatoprotective	Leaves - Methanolic extract	*In vivo* - Wistar Albino Rats	Sterols Carbohydrates Tannins Terpenoids Glycosides	Hepatic Injury Induced by Carbon Tetrachloride (CCL4)	Orally	77

…*Contd*.

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies (Contd.)

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
P. obtusa	Antimicrobial	Leaves - Methanolic extract Petroleum ether fraction Chloroform fraction Ethyl acetate fraction Iso-butanol fraction	*In vitro* - *Bacillus cereus* *Pseudomonas aeruginosa*, *Candida albican*, *Escherichia carotovora* *E. coli* *Klebsiella pneumonia* *Salmonella typhi* *Staphylococcus aureus*	Not given	Agar Disc Diffusion Method	Not applicable	55
	Wound healing	Leaves - Ethanolic extract	*In vivo* - Wistar Albino Rats	Tannins Flavonoids Alkaloids Saponins Glycosides Terpendois Steroids	Excision Wound Model Incision Wound Model	Topical	80
	Anti-inflammatory	Bark - Ethanolic extract	*In vivo* - Wistar Albino Rats	Alkaloids Flavonoids Tannins Terpenoids	Cotton Pellet Method Paw Edema Induced by Carrageenan	Orally	45
	Antioxidant	Leaves - Methanolic extract Hexane fraction Ethyl acetate fraction N-butanol fraction Aqueous fraction	*In vitro* - Not applicable	Flavonoids Alkaloids Glycosides Terpenoids Steroids	DPPH Radical Reduction Assay Modified Thiobarbituric Acid Reactive Species (TBARS) Assay	Not applicable	62
	Antiproliferative	Leaves - Hexanic extract Dichloromethanic extract Methanolic extract	*In vitro* - MCF-7 MDA-MB-23 HeLa human cancer cell lines	Not given	Sulforhodamine B (SRB) Assay	Not applicable	67
	Gastroprotective	Bark - Methanolic extract	*In vivo* - Wistar Albino Rats	Carbohydrates Proteins Flavonoids Alkaloids Glycosides Saponins Tannins Terpenoids	Pylorus Ligation Method Ulcers Induced byIndomethacin	Orally	74
	Antimicrobial	Leaves - Chloroform extract Ethanolic extract Ethyl acetate Extract Aqueous extract	*In vitro* - *Staphylococcus epidermidis*, *Escherichia coli*	Alkaloids Glycosides Flavonoid Saponin Glycosides Tannins	Agar Disc Diffusion Method	Not applicable	55
	Antimicrobial	Flowers - Aqueous extract Chloroform extract Methanolic extract	*In vitro* - *Staphylococcus aureus*, *Bacillus subtulis*, *Escherichia coli*, *Pseudomonas aeruginoda*	Steroids Glycoside Alkaloids Terpenoids	Agar Disc Diffusion Method	Not applicable	54

…*Contd*.

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies (Contd.)

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
P. pudica	Anti-inflammatory and antinociceptive	Latex – Proteins	*In vivo* - Mice Albino Swiss	Proteins	Paw Edema Induced by Carrageenan Dextran Histamine Serotonin Compound 48/80 Bradykinin Prostaglandin E2 Peritonitis model Writhing Induced by Acetic Acid Formalin Test Hot Plate Test	Intraperitoneal	46
	Antidiarrheal	Latex - Proteins	*In vivo* - Mice Albino Swiss	Proteins (Metallic, cysteine and serine proteinases, chitinases and proteinase inhibitors)	Diarrhea Induced by Castor Oil Prostaglandin E2 Cholera Toxin	Intraperitoneal	42
	Protective against ulcerative colitis	Latex – Proteins	*In vivo* - Mice Albino Swiss	Proteins (Proteinases, chitinases and proteinase inhibitors)	Ulcerative Colitis Induced by Acid Acetic Solution	Intraperitoneal	71
	Anti-inflammatory	Leaves - Aqueous extract Ethanolic extracts	*In vivo* - Wistar Albino Rats *In vitro* - Not applicable	Not given	Paw Edema Induced Induced by Carrageenan HRBC Membrane Stabilizing Activity Assay	Intraperitoneal Not applicable	27
	Anti-leishmania	Leaves - Methanolic extract	*In vitro*	Triterpenes Steroids Saponins Glycosides Carbohydrates	promastigote cell toxicity assay by using MTT	Not applicable	50
	Anti-Periodontitis	Latex - Protein fraction	*In vivo* - Wistar albino rats	Proteins	Periodontitis induced by nylon ligature	Intraperitoneal	70
P. rubra	Anticancer	Flowers – Ethanolic extract	*In vitro* - HePG-2 cell line	Not given	MTT Assay	Not applicable	69
	Antidiabetic	Flowers – Aqueous extract	*In vivo* - Mice Albino Swiss	Alkaloids Flavonoids Tannins	Diabetes induced by Alloxan	Orally	40
	Anthelmintic	Bark - Methanolic extract	*In vitro -Pheretima posthuma*	Alkaloids Glycosides Steroids Tannins Flavonoids Phenols Carbohydrates Saponins Terpenoids	Time of Paralysis Time of Death of The Worms	Not applicable	35
	Anticancer	Leaves – Ethanolic extract	*In vivo* - Mice Albino Swiss	Not given	Erlich Ascites Carcinoma Cells Transplantation Method	Not applicable	68

…*Contd*.

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies (Contd.)

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
P. rubra	Anti-inflammatory and Wound healing	Latex - Protein fraction (protease)	*In vivo* - Wistar Albino Rats	Protein (Protease)	Paw Edema Induced by Carrageenan Excision Wound Model	Intraperitoneal Topical	47
	Antinociceptive, Antioxidant and Antimicrobial	Leaves – Ethanolic extract	*In vivo* - Mice Albino Swiss *In vitro* - Not applicable *In vitro* - *Escherichia coli, Salmonella typhi, Salmonella parathyphi, Shigella dysenteriae, Staphylococcus aureus, Streptococcus pyogenes*	Reducing Sugar Gum Alkaloid Steroid Tannins	Writhing Induced by Acetic Acid DPPH Radical Reduction Assay Agar Disc Diffusion Method	Orally Not applicable	57
	Gastroprotective	Latex - Protein fraction	*In vivo* - Mice	Proteins (Cysteine and serine proteinase, chitinase)	Ethanol-Induced Gastric Injury	Intravenous administration	75
	Antimicrobial	Bark and leaves - Ethyl acetate extract	*In vitro* - *Staphylococcus aureu, Pseudomonas aeruginosa, Proteus mirabilis, Candida albicans, Aspergillus flavus*	Alkaloids Glycosides Resins Terpenes Steroids	Serial Diffusion Test	Not applicable	58
	Hepatoprotective	Pods – Alcoholic extract	*In vivo* - Wistar Albino Rats	Alkaloids Glycosides Saponins Flavonoids Steroids Tannins	Hepatic Injury Induced by Carbon Tetrachloride (CCL4)	Subcutaneous route	79
	Anthelmintic and Anti-inflammatory	Leaves - Saponins extract	*In vitro* - Pheretima posthuman *In vivo* - Swiss Albino Mice	Saponins	Time of Paralysis Time of Death of The Worms Paw Edema Induced by Carrageenan	Not applicable Intraperitoneal	34
	Anxiolytic	Flowers – Ethanolic extract Hexane fraction Chloroform fraction Butanolic soluble and insoluble fractions	*In vivo* - Swiss Albino Mice	Steroids (β-sitosterol, bsitosterol- β-D-glucoside plumeride)	Elevated Plus-Maze Model	Orally	73
	Anti-Arthritic	Bark – Hydro-alcoholic extract	*In vivo* - Wistar Albino rats	Alkaloids Carbohydrates Flavonoids Glycosides Proteins Saponins Tannins Phenols	Complete Freund´s Adjuvant Induced Arthritis Model	Orally	38
	Antidiabetic			Not given	Diabetes Induced by Streptozotocin		41

…*Contd*.

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies (Contd.)

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
	Antifertility	Pod – Aqueous extract Alcohlic extract Ethyl extract Acetate and Choeoform extract	*In vivo* – wistar albino rat	Alkaloids Flavonoids Phenolics Steroids Tannins Saponins	Abortifacient test by Khanna *et al*., (1969)	Orally	43
	Antifertility	Pod – Alcoholic extract	*In vivo*- wistar albino rats	Alkaloids Flavonoids Phenolics Steroids Tannins Saponins	Abortifacient test by Khanna *et al*., (1969)	Orally	44
	Antifertility	Bark – Methanolic extract	*In vivo*- wistar albino rats	Not given	Antifertility Test by Hormonal Imbalances	Orally	23
	Anti-inflammatory	Latex - Protease	*In vivo* - Rabbit	Protease (Plumerin R)	Phenol Histamine Sodium Lauryl Sulfate (SLS), Irritation Models	Topical	47
	Anti-inflammatory Antinociceptive	Bark – Ethanolic extract	*In vivo* - Long Evans rats Swiss Albino mice	Tannin Flavonoid Alkaloid Terpenes	Paw Edema Induced by Carrageenan Writhing Induced by Acetic Acid Formalin Test Hot Plate Test	Orally	34
	Antioxidant activity	Latex – Protein fraction	*In vitro*	Proteases (Cysteine and serine)	Superoxide Dismutase (SOD) Assay Total Peroxidase Assay	Not applicable	63
	Antiviral activity	Bark – The petroleum ether extract	*In vitro*	Iridoid (fulvoplumierin)	HIV-1 Reverse Transcriptase Assay	Not applicable	72
	Antioxidant	Flowers - Methanolic extract	*In vitro*	Phenol and Flavonoid (3-O-caffeyolquinic acid, 5-caffeoquinic acid, 1,3-dicaffeoquinic acid, chlorogenic acid, citric acid, 3,3-di-O-methylellagic acid, kaempferol-3-O-glucoside, kaempferol-3-rutinoside, kaempferol, quercetin 3-O--L-arabinopyranoside, quercetin, quinic acid and rutin)	DPPH assay Ferric Reducing Antioxidant Power (FRAP) Assay Metal Chelating Assay Xanthine Oxidase Inhibitory Activity Via *In vitro* System Nitric Oxide Assay Superoxide Assay	Not applicable	64

…*Contd*.

Table 1 — *Plumerias* species and their components that are considered to possess pharmacological activity based on *in vitro* and *in vivo* studies (Contd.)

Botical Name	Biological Activity	Part of Plant/Type of Extract	Type of assay (Organism tested)	Chemical constituents	Model assay	Way of route (extract)	References
	Hepatoprotective	Leaves - Methanolic extract	*In vivo* - Wistar Albino rats	Alkaloids Glycosides Coumarins Phenolics	Paracetamol Induced Toxicity Carbontetrachloride CCL4 Induced Hepatotoxicity Anti-tubercular Drugs Induced Hepatotoxicity	Orally	78

Antifertility activity

The alcoholic extract of *P. rubra* demonstrated antifertility activity, reducing the number of live fetuses and increasing resorption and post-implantation losses. The 200 mg/kg dose was most effective, extending the estrous cycle, particularly the diestrus phase[43]. The aqueous, alcohol, ethyl acetate, and chloroform extracts also exhibited abortifacient activity (8-100%), with the alcoholic extract showing the highest effect (100%) at 200 mg/kg. Additionally, the methanolic extract of *P. rubra* showed significant antifertility effects by suppressing spermatogenesis, with 100% negative fertility at 200 mg/kg and 58% and 64% negative fertility at 50 and 100 mg/kg, respectively[23].

Anti-inflammatory

The methanolic extract of *P. acuminata* (MEPA) exhibited anti-inflammatory effects in experimental models of paw edema induced by carrageenan, dextran, histamine, and serotonin, and reduced granuloma tissue formation in the cotton pellet method[18]. The ethanolic extract of *P. obtusa* also showed anti-inflammatory action in both the cotton pellet method and carrageenan-induced paw edema, with a 400 mg/kg dose demonstrating substantial effects in a dose-dependent manner[45].

The anti-inflammatory activity of latex proteins from *P. pudica* (LPPp) was evaluated. At 40 mg/kg, LPPp reduced paw edema caused by carrageenan, dextran, histamine, serotonin, bradykinin, prostaglandin E2, and compound 48/80. It also decreased myeloperoxidase (MPO) activity in carrageenan-induced paw edema. Additionally, LPPp reduced total leukocyte migration, neutrophil count, and levels of pro-inflammatory cytokines (IL-1β and TNF-α) in a carrageenan-induced peritonitis model[46]. The aqueous extract (AE) and ethanolic extract (EE) of *P. pudica* leaves were evaluated for anti-inflammatory activity in carrageenan-induced paw edema in rats. Both extracts significantly reduced paw edema at doses of 250 mg/kg and 500 mg/kg. *In vitro*, AE and EE also demonstrated membrane stabilization effects by inhibiting hypotonicity-induced lysis of human red blood cell membranes[27].

The anti-inflammatory activity of the saponin extract of *P. rubra* was evaluated in carrageen an-induced paw edema, showing a maximum inhibition of 76.85% at 200 mg/kg after 3 h[34]. Plumerin-R, a protease isolated from the latex of *P. rubra*, reduced carrageenan-induced paw edema by 48.8% at 80 mg/kg[47]. The ethanolic extract of *P. rubra* demonstrated anti-inflammatory activity with 61.68% and 73.65% reductions in edema at doses of 250 mg/kg and 500 mg/kg, respectively[48]. Plumerin-R also exhibited antiirritant and anti-inflammatory effects in histamine, phenol, and sodium lauryl sulfate (SLS) irritation models in rabbits at doses of 25, 50, and 75 mg/kg[49].

Anti-leishmanial activity

In vitro anti-leishmanial activity of petroleum ether, chloroform, and methanol extracts from *P. pudica* was assessed against *Leishmania donovani* (strain AG 83) promastigotes using the (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The extracts inhibited promastigote growth in a concentration-dependent manner, with the methanol extract showing the highest activity, followed by chloroform and petroleum ether extracts[50].

Antimicrobial activity

The methanolic extract of *P. acuminata* (MEPA) inhibited the growth of both Gram-positive bacteria, such as *Bacillus subtilis*, *Micrococcus luteus*, and *Staphylococcus aureus*, and Gram-negative bacteria, including *Escherichia coli*, *Salmonella typhimurium*,

and *Pseudomonas aeruginosa*. It also demonstrated antifungal activity against *Aspergillus niger* and *Candida albicans*.

The methanol extract of *P. alba* and its isolated triterpenes exhibited antibacterial and antifungal properties. The isolated fraction was effective against fungi such as *A. niger*, *Penicillium chrysogenum*, *Microsporum gypseum*, and *Epidermophyton floccosum*. In antibacterial studies, *Salmonella typhi* and *Salmonella paratyphi* B were highly susceptible to both the methanolic extract and the isolated fraction[52]. The methanolic extract of *P. alba* petals showed activity against *Staphylococcus saprophyticus*, *Proteus vulgaris*, and *Serratia marcescens*, although it was not more effective than the positive control used[53].

Extracts of *P. obtusa* (aqueous and chloroform 1:1 v/v) were tested against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*. The chloroform extract showed better results than the aqueous extract. Both aqueous and chloroform extracts were more effective against Gram-negative bacteria than Gram-positive bacteria[54]. Petroleum ether, iso-butanol, and ethyl acetate fractions from *P. obtusa* inhibited *Bacillus atrophaeus*, *B. subtilis*, *Erwinia carotovora*, *E. coli*, *S. typhi*, *S. aureus*, and *C. albicans*, but were ineffective against *Klebsiella pneumoniae* and *P. aeruginosa*. Among Gram-positive bacteria, *B. subtilis* was highly susceptible, while *S. aureus* was the most resistant. Among Gram-negative bacteria, *E. carotovora* was the most susceptible, and *P. aeruginosa* was the most resistant[55].

The chloroform and acetone extracts of the leaves from *P. obtusa* demonstrated partial activity against *S. aureus*, *P. aeruginosa*, and *S. typhi*. In contrast, the methanol and aqueous extracts were effective against all three bacteria: *S. aureus*, *P. aeruginosa*, and *S. typhi*[56]. The antimicrobial activity of the ethanolic extract of *P. rubra* was evaluated against six pathogenic bacterial strains (*E. coli*, *S. typhi*, *S. paratyphi*, *Shigella dysenteriae*, *S. aureus*, *Streptococcus pyogenes*) using the disc diffusion method. The extract showed activity against *S. typhi* at concentrations of 250 and 500 µg/disc[57]. Ethyl acetate extracts of *P. rubra* leaves and bark exhibited antibacterial activity against *Proteus mirabilis*, *S. aureus*, and *P. aeruginosa* at concentrations of 50 mg/mL and 100 mg/mL. Additionally, the extracts showed antifungal activity against *C. albicans*, with inhibition zones of 25.0 mm and 14.0 mm at 10 mg/mL[58].

Antinociceptive properties

The methanolic extract of *P. acuminata* (MEPA) significantly reduced brewer's yeast-induced hyperthermia. It also decreased acetic acid-induced writhing, increased response time in the hot plate test, and reduced tail flick and withdrawal times, indicating antinociceptive activity. Additionally, MEPA demonstrated antipyretic activity, lowering rectal temperature comparable to paracetamol[59].

The antinociceptive activity of latex proteins from *P. pudica* (LPPp) was tested using the acetic acid-induced writhing test, formalin test, and hot-plate test. LPPp (40 mg/kg) reduced abdominal constrictions in the writhing model and decreased paw licking in the first phase of the formalin test. However, it did not increase latency in the hot-plate test. The authors suggested that LPPp promotes peripheral analgesia by blocking bradykinin and other nociceptive mediators[46]. The ethanolic extract of *P. rubra* showed positive results in the acetic acid-induced writhing test in mice, inhibiting writhing by 36.54% at 250 mg/kg and 57.70% at 500 mg/kg[57]. The ethanolic extract of *P. rubra* showed dose-dependent effects in the hot plate test, acetic acid-induced writhing test, and both phases of the formalin test at doses of 250 mg/kg and 500 mg/kg[48].

Antioxidant properties

The methanolic extract of *P. acuminata* (MEPA) significantly reduced linoleic acid emulsion peroxidation and showed dose-dependent antioxidant activity. MEPA exhibited maximum activity in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) and nitric oxide radical scavenging assays at a concentration of 125 µg/mL[60]. Methanolic flower extracts of *P. alba* and *P. rubra* demonstrated significant in vitro antioxidant activity. The DPPH assay showed 81% inhibition for *P. alba* and 72% inhibition for *P. rubra*. Their total antioxidant capacities were 1.74 mg/mL for *P. alba* and 1.67 mg/mL for *P. rubra*, compared to ascorbic acid[61].

The antioxidant potential of methanol, hexane, ethyl acetate, n-butanol, and aqueous fractions of *P. obtusa* showed moderate, dose-dependent activity, as measured by DPPH and lipid peroxidation inhibition assays[62]. A protein fraction from *P. rubra* latex exhibited strong antioxidant activity, particularly through superoxide dismutase, at a concentration of 10 mg/mL, and significantly reduced total peroxidase activity. The ethanolic extract of *P. rubra* showed dose-dependent inhibition in the DPPH assay, with an

IC50 of 39 μg/mL[57]. The methanolic extract of *P. rubra* demonstrated significant antioxidant activity in various assays, including DPPH, ferric reducing antioxidant power, metal chelating, nitric oxide, and superoxide scavenging. It also showed the strongest xanthine oxidase (XO) inhibition, with an 84.39% inhibition rate at 200 μg/mL[64].

Antitumor/ anticancer and cytotoxic

The methanolic extract of *P. acuminata* leaves (MEPA) reduced tumor volume, packed cell volume, and viable cell count, and extended the lifespan of mice with Ehrlich Ascites Carcinoma (EAC). It maintained normal hemoglobin and red blood cell levels while reducing lipid peroxidation and improving glutathione, superoxide dismutase (SOD), and catalase (CAT) levels[65]. Saponins from *P. acuminata* showed cytotoxic and apoptotic effects on oral squamous carcinoma cells (OSCC). These effects were evaluated using the trypan blue dye exclusion assay and the ethidium bromide/acridine orange staining method[66].

Methanolic flower extracts of *P. alba* and *P. rubra* were tested for cytotoxicity using the MTT assay. *P. alba* showed dose-dependent cytotoxicity, while *P. rubra* did not effectively inhibit colon cancer cell proliferation. Microscopic observations revealed loss of cell viability, with effects such as cell shrinkage, aggregation, and death. The IC50 value for *P. alba* was 259.9 μg/mL[61]. Extracts from 10 Apocynaceae species were tested on human cancer cell lines (MCF-7, MDA-MB-231, and HeLa). The n-hexane extract of *P. obtusa* effectively inhibited growth of MCF-7 and HeLa cells, reducing proliferation to below 50%[67].

The ethanolic extract of *P. rubra* leaves exhibited anti-cancer activity against Ehrlich Ascites Carcinoma (EAC). Treatment with the extract led to extended lifespan and normalized hematological parameters in EAC-bearing mice. Both 200 mg/kg and 400 mg/kg doses demonstrated significant anti-cancer effects[68]. The anticancer activity of the ethanolic extract from *P. rubra* flowers was assessed against the HePG2 liver cancer cell line using the MTT assay. The extract, at various concentrations, demonstrated anticancer effects by inducing apoptosis in the cancer cells[69].

Anti-periodontitis activity

Latex proteins from *P. pudica* (LPPp) reduced several parameters, including the gingival bleeding index (GBI), probing pocket depth (PPD), alveolar bone height (ABH), and gingival myeloperoxidase activity. Additionally, in hepatic tissue, LPPp treatment preserved parameters such as malondialdehyde, glutathione, and showed improved histopathological assessments[70].

Anti-ulcerative colitis activity

Latex proteins from *P. pudica* (LPPp) were evaluated in an ulcerative colitis model induced by acetic acid. Treatment with LPPp (40 mg/kg) significantly reduced colon wet weight, macroscopic and microscopic scores of intestinal lesions, and myeloperoxidase (MPO) activity. Additionally, LPPp (40 mg/kg) decreased malondialdehyde and superoxide dismutase (SOD) levels while preventing glutathione) depletion, indicating an effect on oxidative stress. Furthermore, LPPp (40 mg/kg) reduced the levels of the cytokine IL-1β in the colon[71].

Anti-viral activity

The petroleum ether extract of *P. rubra* inhibited 35% of human immunodeficiency virus type I reverse transcriptase (HIV-1 RT) activity at a concentration of 200 μg/mL[72].

Anxiolytic effect

The ethanolic extract and hexane, chloroform, and n-butanol fractions of *P. rubra* were evaluated using the elevated plus-maze (EPM) model of anxiety. The hexane and n-butanol fractions demonstrated significant anxiolytic activity comparable to diazepam[73].

Gastroprotective properties

The methanolic extract of *P. obtusa* (MEPO) enhanced the healing of gastric ulcers induced by pylorus ligation and indomethacin. Doses of 250 mg/kg and 500 mg/kg of MEPO significantly reduced ulcer index, total ulcer area, and the percentage of ulcer protection[74]. Proteins from the latex of *P. rubra* (PrLP) were tested for their effectiveness against ethanol-induced gastric lesions. The study found that PrLP prevented ethanol-induced gastric damage in a dose-dependent manner. The mechanism of action involved prostaglandins, the balance of oxidant/antioxidant factors, and the NO/cGMP/KATP pathway. Additionally, activation of capsaicin-sensitive receptors was reported as part of PrLP's mechanism[75].

Hepatoprotective properties

The methanol extract of *P. alba* (MLE) was tested for its effects on paracetamol-induced liver injury. MLE effectively reduced the elevation of liver

enzymes, including GOT (Glutamate oxaloacetate transaminase), GPT (Glutamate pyruvate transaminase), ALP (Alkaline phosphatase), and GGT (Gamma-glutamyl transferase). In addition to the histological findings, supportive evidence for the hepatoprotective activity of MLE was also provided[76]. The methanolic extract of *P. alba* exhibited hepatoprotective activity against carbon tetrachloride (CCl_4)-induced hepatotoxicity. The protective effect was evidenced by improvements in biochemical parameters such as serum transaminases, alkaline phosphatase (ALP), and total protein, as well as by histopathological findings[77].

The methanolic extract of *P. rubra* effectively reduced elevated enzyme levels of GOT, GPT, ALP, and bilirubin, which were increased due to liver injury from CCl_4, paracetamol, and antitubercular drug intoxication. Histopathological examination revealed a reversal of liver cell damage and restoration of normal liver architecture following treatment with the *P. rubra* extract[78]. The alcoholic extract of *P. rubra* was tested for its effects on CCl_4-induced hepatic injury. The treatment significantly reduced the levels of marker enzymes, including GOT, GPT, ALP, and total bilirubin. Histopathological examination of the liver revealed a protective effect, with the liver structures appearing normal, showing only slight changes[79].

Wound healing properties

The ethanolic extract of *P. obtusa* was tested in wound healing models with three formulations: F1 (2.5%, 50 mg/kg BW), F2 (5%, 100 mg/kg BW), and F3 (10%, 200 mg/kg BW). The 10% formulation (200 mg/kg BW) demonstrated superior wound healing compared to the lower concentrations[80]. Plumerin-R from *P. rubra* latex was tested in an excision wound rat model. Topical application of plumerin-R cream accelerated wound healing and showed reduced inflammatory cells and increased collagen in the healed tissue[47].

Plumerias are source of natural compounds

Plants produce a wide range of bioactive compounds, including steroids, terpenoids, flavonoids, phenols, iridoids, proteins, tannins, alkaloids, glycosides, saponins, and carbohydrates. These phytocompounds serve as templates and precursors for various drugs. In Plumeria species, several of these components have been identified in extracts, and specific plant parts have been linked to various biological activities (Fig. 2). Research often

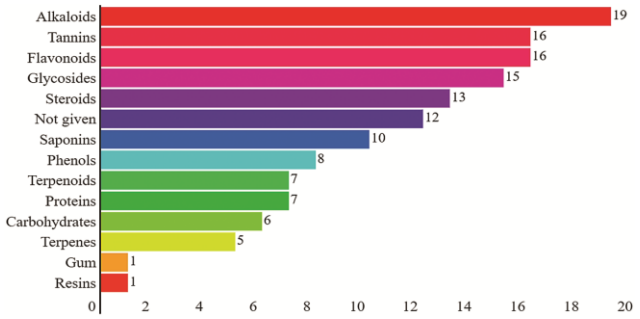

Fig. 2 — Phytochemicals reported from Plumerias species based on studies

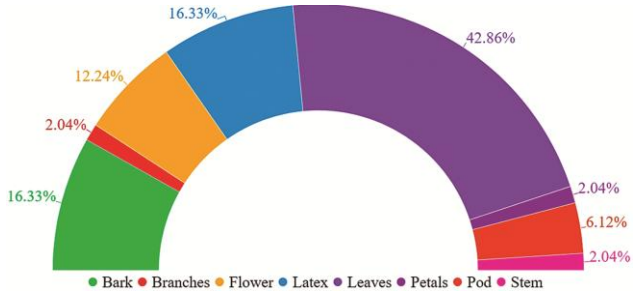

Fig. 3 — Parts of plants used in studies and associated to pharmacological activities

involves identifying and isolating these chemical components and assessing their biological efficacy through *in vitro* and/or *in vivo* studies (Fig. 3).

Conclusion

Plumeria species are renowned worldwide for their medicinal properties, with diverse methods used to assess their pharmacological effects. Key phytoconstituents in Plumeria include terpenoids, iridoids, alkaloids, proteins, steroids, flavonoids, tannins, glycosides, saponins, and carbohydrates. These compounds are closely associated with the plant's biological activities. Plumeria species play a significant role in modulating various pathological processes, highlighting their potential as sources of therapeutic agents for treating a wide range of human diseases. This study reinforces popular knowledge about plants from the Plumeria genus as a source of molecules for the treatment of diseases.

Acknowledgements

We sincerely appreciate the financial support provided by the National Council for Technological and Scientific Development (CNPq, Brazil).

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

BSS: Conceptualization; Data curation; Formal analysis; Supervision; Writing-original draft; Writing-review & editing. ACSS: Conceptualization; Data curation; Investigation; Supervision. LAM: Data curation; Formal analysis; Methodology; Validation. NMVO: Data curation; Formal analysis; Methodology. FDSS: Data curation; Methodology; Validation; Visualization. MSB: Data curation; Formal analysis; Methodology; Validation. F Souza: Data curation; Investigation; Methodology; Visualization. JSO: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Visualization; Writing-original draft; Writing-review & editing.

Data Availability

The data that support the findings of this study are available from the corresponding author, Jefferson Soares de Oliveira, upon reasonable request.

References

1 Choudhary M, Kumar V & Singh S, Phytochemical, and pharmacological activity of Genus *Plumeria*: An updated review, *Int J Biomed Adv Res*, 5 (6) (2014) 266-271.

2 Licá I C L, Soares A M D S, de Mesquita L S S & Malik S, Biological properties and pharmacological potential of plant exudates, *Food Res Int*, 105 (2018) 1039-1053.

3 Anggoro B, Istyastono E & Hariono M, Future molecular medicine from white frangipani (*Plumeria alba* L.): A review, *J Med Plant Res*, 14 (10) (2020) 544-554.

4 Krishnamurthi A S, The Wealth of India, (CSIR Publications, New Delhi), (1969) p. 1-42

5 Shinde P R, Patil O S & Bairagi V A, Phytopharmacological review of Plumeria species, *Sch Acad J Pharm*, 3 (2) (2014) 217-227.

6 The Plants List, Version 1.1, Published on the Internet; http://www.theplantlist.org/tpl1.1/search?q=plumeria (accessed July 2020).

7 Ela A & Deodhar A K, Comparative analysis of leaf traits in two species of Plumeria, *Int J of Life Sci*, A4 (2015) 42-46.

8 Goswami P, Chauhan A, Verma R S & Padalia R C, Chemical constituents of floral volatiles of *Plumeria rubra* L. from India, *Med Aromat Plants*, S3 (2016) 005.

9 Idrees S, Hanif M A, Ayub M A, Jilani M I, Memon N, Frangipani. In: *Medicinal plants of south Asia: Novel sources of drug discovery*, edited by Hanif M A, Nawaz H, Khan M M & Byrne H J (Elsevier, Amsterdam, NL), (2019) 287-300.

10 Tropical Flowers and Plants, 2020. Plumeria history. Available online: http://www.tropicalflowers-and-plants.com/plumeria-history.html. (Accessed in July 2020).

11 Bihani T, *Plumeria rubra* L. A review on its ethnopharmacological, morphological, phytochemical, pharmacological and toxicological studies, *J Ethnopharmacol*, 264 (2021) 113291.

12 Verma S, Multipurpose Ornamental Plant *Plumeria rubra* Linn (Apocynaceae), *Int J Sci Res Sci Eng Technol*, 2 (4) (2016) 646-649.

13 Sura J, Dwivedi S & Dubey R, Pharmacological, phytochemical, and traditional uses of *Plumeria alba* Linn, an Indian medicinal plant, *J Pharm Bio Sci*, 6 (1) (2018) 1-4.

14 Imrana M & Asif M, Morphological, ethnobotanical, pharmacognostical and pharmacological studies on the medicinal plant *Plumeria alba* Linn. (Apocynaceae), *Arab J Med Aromat Plants*, 6 (1) (2020) 54-84.

15 Sharma G, Chahar M K, Dobhal S, Sharma N, Sharma T C, *et al*., Phytochemical constituents, traditional uses, and pharmacological properties of the Genus *Plumeria*, *Chem Biodivers*, 8 (8) (2011) 1357-1369.

16 Parreira D S, *Pseudosphinx Tetrio* (Lepidoptera: Sphingidae): Potencial Praga para a Planta Ornamental *Plumeria rubra* in Brasil, *Ensaios Cienc Biol Agrar Saúde*, 21 (1) (2017) 1-3.

17 Devprakash, Tembare R, Gurav S, Senthil Kumar G P & Mani T T, An review of phytochemical constituents & pharmacological activity of *Plumeria* species, *Int J Curr Pharm Res*, 4 (1) (2012) 1-6.

18 Gupta M, Mazumder U K, Gomathi P & Selvan V T, Anti-inflammatory evaluation of leaves of *Plumeria acuminate*, *BMC Complement Altern Med*, 6 (36) (2006) 1472-6882.

19 Boncalon R M V, Arugay M A V & Ramos R Z H, A preliminary study on the efficacy of *Plumeria acuminata* (Kalachuchi) bark extract ointment versus clotrimazole cream in the treatment of otomycosis, *Philipp J Otolaryngol Head Neck Surg*, 24 (1) (2009) 5-8.

20 Farooque A M, Mazunder A, Shambhawee S & Mazumder R, Review on *Plumeria acuminate*, *Int J Res Pharm Chem*, 2 (2) (2012) 467-469.

21 Krishen P, *Trees of Delhi: A Field Guide* (Dorling Kindersley India Pvt. Ltd., India), (2006) p. 127.

22 Manisha K & Aher A N, Review on traditional medicinal plant: *Plumeria rubra*, *J Med Plants Stud*, 4 (6) (2016) 204-207.

23 Gupta R S & Sharma D, A pragmatic antifertility assessment of methanolic bark extract of *Plumeria rubra* (L.) in male albino rats, *World J Pharmaceut Res*, 6 (16) (2017) 1315-1317.

24 Bihani T, Tandel P & Wadekar J, *Plumeria obtusa* L.: A systematic review of its traditional uses, morphology, phytochemistry and pharmacology, *Phytomedicine Plus*, 1 (2) (2020) 100052.

25 Jogdand V & Dhabe A, *Plumeria pudica* Jacq. (Apocynaceae): An addition to the exotic plants of marathwada, *Bioinfolet*, 10 (2) (2013) 356.

26 Chamakuri S R, Suttee A & Mondal P, An eye-catching and comprehensive review on *Plumeria pudica* Jacq. (Bridal Bouquet), *Plant Arch*, 20 (2) (2020) 2076-2079.

27 Kumawat P, Shriwas S & Dwivedi S, Investigation of anti-inflammatory activity of *Plumeria pudica* Linn., *Int J Pharm Life Sci*, 9 (11&12) (2018) 5971-5976.

28 Dey A & Mukherjee A, *Plumeria rubra* L. (Apocynaceae): Ethnobotany, Phytochemistry and Pharmacology: A Mini Review, *J Plant Sci*, 10 (2) (2015) 54-62.

29 Kirtikar K R & Basu B D, *Indian Medicinal Plants*, (International Book Distributors, Dehradun), 1984.

30 Tohar N, Awang K, Mohd M A & Jantan I, Chemical composition of the essential oils of four Plumeria species grown on Peninsular Malaysia, *J Essent Oil Res*, 18 (6) (2006) 613-617.

31 Burkill I H, *A dictionary of the economic products of the Malay Peninsula*, Crown Agents for the Colonies, London, II (I-Z) (1935) 1776-1778.

32 Gaitán I, Paz A M, Zacchino S A, Tamayo G, Giménez A, *et al*., Subcutaneous antifungal screening of Latin American plant extracts against *Sporothrix schenckii* and *Fonsecaea pedrosoi*, *Pharm Biol*, 49 (9) (2011) 907-919.

33 Ruiz-Teran F, Medrano-Martinez A & Navarro-Ocana A, Antioxidant and free radical scavenging activities of plant extracts used in traditional medicine in Mexico, *Afr J Biotechnol*, 7 (12) (2008) 1886-1893.

34 Kumar A, Chand I & Singh A, Kopal, Extraction and evaluation of pharmacological activity of saponin extract of *Plumeria rubra* leaves, *Pharmacol Online*, 1 (2009) 969-974.

35 Srivastava A, Gupta A K & Rajendiran A, Phytochemical screening and in-vitro anthelmintic activity of methanolic extract from the stem bark of *Plumeria rubra* Linn., *Int J Pharm Sci Res*, 8 (12) (2017) 5336-41.

36 Radhika B, Anti-helminthic activity of *Plumeria pudica* leaves, *J Chem Pharm Res*, 11 (2) (2019) 6-12.

37 Choudhary M, Kumar V, Gupta P & Singh S, Investigation of antiarthritic potential of *Plumeria alba* L. leaves in acute and chronic models of arthritis, *Biomed Res Int*, (2014) 12.

38 Mondal P, Das S, Mahato K, Borah S, Junejo J A, *et al*., Evaluation of anti-arthritic potential of the hydro-alcoholic extract of the stem bark of *Plumeria rubra* in Freund's complete adjuvant-induced arthritis in rats, *Int J Pharm Sci Res*, 7 (9) (2016) 3675-3688.

39 Gomathi P, Shalini T, Farheen N & Sanjeevkumar A, Antidiabetic activity of *Plumeria acuminata* leaves on streptozotocin induced diabetic rats, *Asian J Res Biol Pharm Sci*, 4 (3) (2016) 99-104.

40 Yadav A V, Undale V R & Bhosale A V, Antidiabetic activity of *Plumeria rubra* L. in normal and alloxan induced diabetic mice, *Int J Basic Clin Pharmacol*, 5 (3) (2016) 884-889.

41 Mondal P, Das S, Junejo J A, Borah S & Zaman K, Evaluations of antidiabetic potential of the hydro-alcoholic extract of the stem bark of *Plumeria rubra* a traditionally used medicinal source in North-East India, *Int J Green Pharm*, 10 (4) (2016) 252-260.

42 Santana L D A B, Aragão D P, Araújo T D S L, de Sousa N A, de Souza L K, *et al*., Antidiarrheal effects of water-soluble proteins from *Plumeria pudica* latex in mice, *Biomed Pharmacother*, 97 (2018) 1147-1154.

43 Zade V & Dabhadkar D, Antifertility effect of alcoholic extract of *Plumeria rubra* on estrous cycle of female Albino rat, *Int J Pharm Sci Rev Res*, 12 (2) (2012) 75-79.

44 Dabhadkar D & Zade V, Abortifacient activity of *Plumeria rubra* (Linn) pod extract in female albino rats, *Indian J Exp Biol*, 50 (2012) 702-707.

45 Lotankar A R, Momin A J, Wankhede S & Sharma J B, Anti-inflammatory activity of an ornamental plant *Plumeria obtuse*, *Adv Pharmacol Pharm*, 4 (3) (2016) 23-26.

46 Fernandes H B, Machado D L, Dias J M, Brito T V, Batista J A, *et al*., Laticifer proteins from *Plumeria pudica* inhibit the inflammatory and nociceptive responses by decreasing the action of inflammatory mediators and pro-inflammatory cytokines, *Rev Bras Farmacogn*, 25 (3) (2015) 269-277.

47 Chanda I, Basu S K, Dutta S K & Das S R C, A protease isolated from the latex of *Plumeria rubra* Linn (Apocynaceae) 2: Anti-inflammatory and wound-healing activities, *Trop J Pharm Res*, 10 (6) (2011) 755-60.

48 Das B, Ferdous T, Mahmood Q A, Hannan J M A, Bhattacharjee R, *et al*., Antinociceptive and anti-inflammatory activity of the bark extract of *Plumeria rubra* on laboratory animals, *European J Med Plant*, 3 (1) (2013) 114-126.

49 Aziz A, Saqib F, Khan I A, Ashraf M M, Ashraf M N, *et al*., Dermatological evaluation of anti-irritant and anti-inflammatory effect of Plumerin-R isolated from the Latex of *Plumeria rubra* Linn., *Lat Am J Pharm*, 37 (2) (2018) 317-320.

50 Sarkar J, Pal S, Bhattacharya S & Biswas M, *In vitro* antileishmanial activity of *Pleumeria pudica* leaf extracts on *Leishmania donovani* promastigotas, *Am Eurasian J Agric Environ Sci*, 8 (2) (2013) 68-71.

51 Gupta M, Mazumder U K, Gomathi P & Selvan V T, Antimicrobial activity of methanol extracts of *Plumeria acuminata* Ait. Leaves and *Tephrosia purpurea* (Linn.) Pers. roots, *Nat Prod Radiance*, 7 (2) (2008) 102-105.

52 Radha R, Sriram L & Narayanan N, Antibacterial and antifungal activities of methanolic extract and the isolated fraction of *Plumeria alba* Linn., *Nat Prod - An Indian J*, 4 (2) (2008) 177-179.

53 Syakira M H & Brenda L, Antibacterial capacity of *Plumeria alba* petals, *World Acad Sci Eng Technol*, 4 (8) (2010) 1202-1205.

54 Rawani A, Pal S & Chandra G, Evaluation of antimicrobial properties of four plant extracts against human pathogens, *Asian Pac J Trop Biomed*, 1 (1) (2011) S71-S75.

55 Ali N, Ahmad D, Bakht J, Shah S & Ullah F, Antimicrobial activity of leaves extracted samples from medicinally important *Plumeria obtuse*, *J Med Plant Res*, 7 (17) (2013) 1146-1153.

56 Singh R & Verma D K, Antibacterial activity of *Plumeria obtusa* (Linn), *Int J Eng Appl Sci Technol*, 4 (8) (2019) 300-305.

57 Ramproshad S, Afroz T, Mondal B, Khan R & Ahmed S, Screening of phytochemical and pharmacological activities of leaves of medicinal plant *Plumeria rubra*, *Int J Res Pharm Chem*, 2 (4) (2012) 1001-1007.

58 Emmanuel B, Mary L K & Jidimma A W, Study on the phytochemical and antimicrobial screening of ethylacetate extract of *Plumeria rubra* leaves and Stems Bark, *Agri Res Tech: Open Access*, 21 (4) (2019) 161-165.

59 Gupta M, Mazumder U K & Gomathi P, Evaluation of antipyretic and antinociceptive activities of *Plumeria acuminata* leaves, *J Med Sci*, 7 (5) (2007) 835-839.

60 Gupta M, Mazumder U K & Gomathi P, Evaluation of antioxidant and free radical scavenging activities of *Plumeria acuminata* Leaves, *J Biol Sci*, 7 (8) (2007) 1361-1367.

61 Rahman H, Reddy V B, Ghosh S, Mistry S K, Pant G, *et al*., Antioxidant, cytotoxic and hypolipidemic activities of *Plumeria alba* L. and *Plumeria rubra* L., *Am J Life Sci*, 2 (4) (2014) 11-15.

62 Dogra N K, Phytochemical analysis and *in vitro* antioxidant studies of *Plumeria obtusa* L. leaves, *Indian J Pharm Sci*, 78 (1) (2016) 169-171.

63 de Freitas C D T, de Souza D P, Araújo E S, Cavalheiro M G, Oliveira L S, *et al*., Anti-oxidative and proteolytic activities and protein profile of laticifer cells of *Cryptostegia grandiflora*, *Plumeria rubra* and *Euphorbia tirucalli*, *Braz J Plant Physiol*, 22 (1) (2010) 11-22.

64 Isa S S P M, Ablat A & Mohamad J, The antioxidant and xanthine oxidase inhibitory activity of *Plumeria rubra* flowers, *Molecules*, 23 (2) (2018) 400.

65 Periyasamy G, Gupta M, Mazumder U K, Gebrelibanos M & Sintayehu B, Antioxidant and antitumor activity of *Plumeria acuminata* in ehrlich ascites carcinoma bearing Swiss albino mice, *Br J Pharm Res*, 3 (4) (2013) 671-685.

66 Susanto H, Fakhrudin N, Murti Y B & Siswomiharjo W, Saponins from *Plumeria acuminata* Ait induce cell growth inhibition and apoptosis of oral squamous carcinoma cells, *Chin J Dent Res*, 13 (2) (2010) 153-156.

67 Wong S K, Lim Y Y, Abdullah N R & Nordin F J, Antiproliferative and phytochemical analyses of leaf extracts of ten Apocynaceae species, *Pharmacogn Res*, 3 (2) (2011) 100-106.

68 Rekha J B & Jayakar N, Anti-cancer activity of ethanolic extract of leaves of *Plumeria rubra* (Linn), *Curr Pharm Res*, 1 (2) (2011) 175-179.

69 Muruganantham N, Solomon S & Senthamilselvi M M, Anti-cancer activity of *Plumeria rubra* (Flowers) against human liver cancer, *Int J Pharmacogn Phytochem Res*, 6 (4) (2014) 1007-1009.

70 Oliveira L E S, Moita L A, Souza B S, Oliveira N M V, Sales A C S, *et al*., Latex proteins from *Plumeria pudica* reduce ligature-induced periodontitis in rats, *Oral Dis*, 28 (3) (2022) 786-795.

71 Oliveira N V M, Souza B S, Moita L A, Oliveira L E S, Brito F C, *et al*., Proteins from *Plumeria pudica* latex exhibit protective effect in acetic acid induced colitis in mice by inhibition of pro-inflammatory mechanisms and oxidative stress, *Life Sci*, 231 (2019) 116535.

72 Tan G T, Pezzuto J M, Kinghorn A D & Hughes S H, Evaluation of natural products as inhibitors of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase, *J Nat Prod*, 54 (1) (1991) 143-154.

73 Chatterjee M, Verma R, Lakshmi V, Sengupta S, Verma A K, *et al*., Anxiolytic effects of *Plumeria rubra* var. acutifolia (Poiret) L. flower extracts in the elevated plus-maze model of anxiety in mice, *Asian J Psychiatr*, 6 (2) (2013) 113-118.

74 Singh A P, Shukla V & Khare P, Effects of *Plumeria obtusa* Linn. in peptic ulcer induced by pylorus ligation & indomethacin, *J Pharm Sci Innov*, 1 (2) (2012) 26-32.

75 Alencar N M N D, Pinheiro R S P, Figueiredo I S T D, Luz P B, Freitas L B N, *et al*., The Preventive effect on ethanol-induced gastric lesions of the medicinal plant *Plumeria rubra*: involvement of the latex proteins in the NO/cGMP/KATP signaling pathway, *Evid-Based Complement Alternat Med*, 2015 (2015) 706782.

76 Chowdhur A, Dasgupta B, Ganesh E & Kalita J C, Hepatoprotective activity of *Plumeria alba* extract against paracetamol induced hepatotoxicity in rats, *Int J Pharm Pharm Sci*, 4 (2010) 618-20.

77 Sudheer M, Babu B S, Divya K, Himavani K V, Prakash M S, *et al*., Hepatoprotective activity of *Plumeria alba* and *Aloe vera* on CCl_4, *J Pharm Res*, 4 (3) (2011) 647-649.

78 Sangeetha J, Abbulu K & Sudhakar M, Study on the effect of *Aganosma cymosa* and *Plumeria rubra* methanol extract on different models of induced liver toxicity in experimental rats, *J Pharmacol Res*, 3 (1) (2013) 49-53.

79 Dawada S D, Hepatoprotective activity of pod extract of *Plumeria rubra* against Carbon tetra chloride induced hepatic injury in rats (Wistar), *Int J Pharm Pharm Sci*, 3 (3) (2015) 218-227.

80 Bihani T & Mhaske N, Evaluation of *in vivo* wound healing activity of *Plumeria obtusa* L. (Champa) spray in rats, *Wound Med*, 28 (2020) 100176.