Australian Tropical Medicinal Plants

Subjects: Tropical Medicine

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Australian tropical plants have been a rich source of food (bush food) and medicine to the first Australians (Aboriginal people), who are believed to have lived for more than 50,000 years. Plants such as spreading sneezeweed (*Centipeda minima*), goat's foot (*Ipomoea pes-caprae*), and hop bush (*Dodonaea viscosa* and *D. polyandra*) are a few popular Aboriginal medicinal plants.

anti-inflammatory medicinal plants tropical aboriginal people inflammation inflammatory phytochemistry

1. Introduction

Since time immemorial, plants have been a vital source of food, shelter, clothing, tools, and weapons for humankind. Before modern allopathic medicines, early civilizations dealt with illnesses and diseases mostly with natural products from native plants and fungi, and they were taken either in raw or partially processed form. Moreover, these plants have been one of the vital sources of modern drugs, and medicinal plants still play a significant role in the biodiscovery of chemical leads for developing novel therapeutics. Of 52,885 medicinal plants identified globally [1], the phytochemical profile of only about 15% of these species has been reported thus far [2]. The World Health Organization (WHO) estimated that about 80% of the population in developing countries still rely on medicinal plants for their primary healthcare [3][4].

The Australian Aboriginal people are known to have occupied the country more than 50,000 years ago, and currently, they constitute 3.3% of the total Australian population [5][6]. Aboriginal people have developed a profound connection with their native flora and fauna. Their longstanding survival could have resulted from the prolonged use of medicinal plants in their diet and home remedies [7], and they still use medicinal plants in their day-to-day life. However, as they have already merged with mainstream modern society, it has become crucial to properly document their vast indigenous knowledge for their future generation [8]. The Northern Territory government, in collaboration with the Commonwealth in the 1980s, compiled "Traditional Bush Medicines," an Aboriginal pharmacopeia of the Northern Territory [9], a first-ever initiative to record dying Aboriginal medicinal lore. Since then, more collaborations have occurred between Aboriginal communities and scientists from various universities across Australia to explore Aboriginal medicinal plants [10][11]. Exploring indigenous food and medicinal plants may give a wealth of potential candidates for novel therapeutics, and Australian native plants could be an intriguing source. The geographic isolation of Australia from Gondwana and other parts of the world for over 65 million years [12][13] has become home to unique and complex flora, where approximately 85% of its vascular plants are endemic

species [10]. Plants growing in the tropics produce more phenolics, flavonoids, and terpenoids during adaptation to its extreme vegetative and climatic conditions [14]. Phenolics and flavonoids are antioxidative and anti-inflammatory [15][16][17], and thus tropical plants may yield novel drug leads for treating infectious and non-infectious diseases, including chronic inflammatory conditions [18]. More than 900 medicinal plant species have been recorded in the Tropical region of Australia (shaded green in **Figure 1**) [19].

Figure 1. Map of Australia showing the tropical and wet tropics region. (Location labels and compass added; shaded ecoregions were hand-drawn using the information from an online climate map [20].

2. Ethnomedical Uses of Selected Medicinal Plants

Out of 78 tropical medicinal plants used by the Aboriginal people of Australia for treating inflammation and inflammatory-related diseases, 45 species were selected (**Table 1**).

Table 1. Ethnomedical uses and the compounds isolated from Aboriginal tropical medicinal plants of Australia.

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
Acalypha wilkesiana Müll.Arg. (Euphorbiaceae)	Pulped shoots (i.e., collected when leaves are still red) are applied to cuts and open sores [21].	Nigeria	Leaves; stem and root barks	Gallic acid, Corilagin, Geraniin, Rutin, Kaempferol 3-*O*-rutinoside [22].
Ageratum conyzoides (L.) L. (Asteraceae)	Meshed whole plant applied to wounds to enhance healing [21][23].	Brazil, India	Whole plant	5,6,7,8,3′,4′,5′-Heptamethoxyflavone, Coumarin [24]; Ageconyflavones A-C, Linderoflavone B, Eupalestin, Nobiletin, 5,6,7,5′-Tetramethoxy-3′,4′-methylenedioxyflavone, Sinensetin, 5,6,7,3′,4′,5′-Hexamethoxyflavone, 5,6,7,8,3′-Pentamethoxy-4′-hydroxyflavone, 5,6,7,8,3′,5′-Hexamethoxy-4′-hydroxyflavone [24][25].
Alphitonia excelsa (Fenzl) Reissek ex Benth. (Rhamnaceae)	Leaves are applied to sore eyes; warm aqueous leaves infusion is used as a bath to ease headaches;	Philippines	Twigs	Betulinic acid [27].

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	decoction from bark, wood, and roots is applied externally to relieve body pains; bark and wood decoction are used as a mouth wash to relieve toothache [21][26].			
Alphitonia petriei Braid & C.T.White (Rhamnaceae)	A decoction made from the bark is applied externally to relieve body pain [26].	Australia	Leaves; stems	Embolic acid, Alphitolic acid, *trans*- and *cis*-Coumaroyl esters of alphitolic acid, Betulinic acid [28].
Angophora costata (Gaertn.) Hochr. ex Britten (Myrtaceae)	An aqueous solution of reddish exudate from the trunk is taken orally against diarrhoea [8][29].	Australia	Leaves	Costatamins A-C [30].

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Antidesma bunius (L.) Spreng. (Phyllanthaceae)	Indicated for headaches, colds, and fevers [23].	Vietnam	Leaves; fruits	Antidesoside, Podocarpusflavone A, Amentoflavone, Byzantionoside B, Roseoside [31].
Barringtonia racemosa (L.) Spreng. (Lecythidaceae)	Pulverized roots are applied to skin sores [21].	Bangladesh, China, India, Taiwan, and Vietnam	Stem bark; seeds; roots; leaves	Olean-18-*en*-3β-*O*-*E*-coumaroyl ester, Olean-18-*en*-3β-*O*-*Z*-coumaroyl ester, Germanicol, Germanicone, Betulinic acid, Lupeol, Taraxerol [32]; 3,3'-Dimethoxy ellagic acid, Dihydromyticetin, Gallic acid, Bartogenic acid, Stigmasterol [33][34]; Rutin [35][36]; Nasimalun A and B [37]; Barringtin D1-D3, and M1, Casuarictin, Tellimagrandin I, Valoneic acid dilactone, Schimawalin A [38]; Isoracemosol A, Racemosaceramide A, Racemosol A and E [34][39]; Barringtogenol C [34]; 3β-*p*-*E*-Coumaroymaslinic acid, *cis*-Careaborin, Careaborin, Maslinic acid, 2α,3β,19α-Trihydroxyolean-12-*ene*-24,28-dioic acid, 3β-*p*-*Z*-coumaroylcorosolic acid, Corosolic acid, 1α,2α,3β,19α-Tetrahydroxyurs-12-*en*-28-oic acid, 19α-Hydroxyl ursolic acid, 3α,19α-Dihydroxyurs-12-*en*-24,28-dioic acid, Tormentic acid, 3-Hydroxy-7,22-*dien*-ergosterol [40]; Barringosides G-I [41].

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Brasenia schreberi J.F.Gmel. (Combretaceae)	Astringent leaves are used for dysentery [21][42].	Canada		Quercetin-7-*O*-glucoside, Gallic acid [43].
Brucea javanica (L.) Merr. (Simaroubaceae)	Roots and leaves are used as analgesics [23].	China and Thailand	Aerial; seeds; roots	Brusatol [44]; Demethyl-dehydrobrusatol, Deacetyl-yadanzioside I, Javanicoside G, Yadanziolide C and E, Bruceine A-D and H, Bruceoside A-E, Yadanzioside C and I, Yadanzioside K and L, Dehydrobruceine B, Dehydro-bruceantinol, Deacetylated isobrucein B [45]; brujavanol A and B, bruceine, 11-dehydroklaineanone, 15β-hydroxyklaineanone, 14,15β-dihydroxyklaineanone, 15β-*O*-acetyl-14hydroxyklaieanone [46]
Calophyllum inophyllum L. (Calophyllaceae)	Nut kernel ground with red pigment is mixed with water and rubbed to ease body pain [21].	China, France, Fiji, French Polynesia, India, Indonesia, Malaysia, Thailand, Taiwan, and Vietnam	Leaves; seeds; twigs; stems; roots	Inophinnin, Inophinone [47][48]; Inophyllin A, Friedelin, Stigmasterol [48][49][50]; Macluraxanthone, Pyranojacareubin, 4-Hydroxyxanthone, Betulinic acid, Inophyxanthone A, Pancixanthone A, Gerontoxanthone B, Jacareubin [48][51][52][53]; Inocalophyllin A and B [54]; Caloxanthone O and P [55]; Tamanolide, Tamanolide D, E1, E2, and P [56][57]; Calophyllolide [58][59]; 3β,23-*epoxy*-Friedelan-28-oic acid, Epifriedelanol, Canophyllal,

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				Canophyllol, Canophyllic acid, 3-oxo-Friedelan-28-oic acid, Oleanolic acid, 3,4-Secofriedelan-3,28-dioic acid, 27-Hydroxyacetate canophyllic acid, 3-oxo-27-Hydroxyacetate friedelan-28-oic acid [50][60][61]; Caloxanthone Q, 2-Deprenylrheediaxanthone B, 6-Deoxyjacareubin [52][62]; 1,3,6,7-Tetrahydroxy-5-methoxy-4-(1′,1′-dimethyl-2′-propenyl)-8-(3″,3″-dimethyl-2″-propenyl)-xanthone, (2′*S*)-7-Hydroxycaloxanthone B, Caloxanthone A-C, 7-Prenyljacareubin, Daphnifolin, Tovopyrifolin C, 1,3,5-Trihydroxyxanthone, 2-Hydroxyxanthone [53]; Inophyllums G-1, G-2, and P [63]; Isocalophyllic acid, Amentoflavone [61][64]; 27-[(*E*)-*p*-Coumaroyloxy]canophyllic acid, 27-[(Z)-*p*-coumaroyloxy]canophyllic acid, Methyl shikimate, (3*S*,5*R*,6*R*,7*E*,9*R*)-3,5,6-Trihydroxy-β-ionyl-3-*O*-β-d-glucopyranoside, Benzyl-*O*-α-l-rhanmopyranosyl (1→6)-β-d-glucopyranoside, Hexylrutinoside, Kaempferol-3-*O*-α-l-rhamnoside, 27-[(*Z*)-*p*-Coumaroyloxy]friedelin-28-carboxylic acid, (22*E*,24*R*)-24-Methyl-5α-cholesta-7,22-diene-3β,5,6β-triol, 3-oxo-Friedelan-28-oicacid [64]; *trans*-2-[2-(Trifluoromethyl)phenyl]-10b,10c-dimethyl-10b,10c-dihydropyrene, *anti*-

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				4-aza-B-Homo-5α-cholestane-3-one [65].
Centella asiatica (L.) Urb. (Apiaceae)	Juice derived from the plant is taken orally or applied locally for non-specific ulcerations. Powered leaves mixed with lime are applied to sores on babies, and the plant is also indicated for skin diseases [21][23][42][66].	China, Japan, India, Madagascar, USA, and Vietnam	Whole plant	Asiaticoside, Asiaticoside C, F, G-I, 23-*O*-Acetyl madecassoside, Asiatic acid, Madecassic acid, Madecassoside, 23-*O*-Acetylasiaticoside B, Stigmasterol 3-*O*-β-glucoside, Quercetin 3-*O*-glucuronide [67][68][69][70][71][72]; Inositol, Centellose [69]; 4′-Hydroxyl-7-methoxyl-6-prenyl-3-*O*-*trans*-*p*-Coumaroyl-flavonol, (2*R*,3*R*,2″*S*)-3-Furanoyl-brosimacutin E, Epigallocatechin 3-*O*-*p*-coumaroate, Pinobanksin-3-propanoate, Kaempferol, Pachypodol, Coryaurone A [71][73]; Asiaticoside B [70][74]; Isomadecassoside [75]; Quadranoside IV, Quercetin, Astragalin, Isoquercetrin [71]; Centelloside E-G, 11-oxo-Asiaticoside B, 11-oxo-Madecassoside, 11(β)-Methoxy asiaticoside B, 11(β)-Methoxy madecassoside, Centellasaponin A, Isoasiaticoside, Scheffoleoside A [70]; 2α,3β,20,23-Tetrahydroxyurs-28-oic acid [76]; Ursolic acid lactone, Ursolic acid, Pomolic acid, Epi-maslinic acid, Corosolic acid, Rosmarinic acid [72].
Centipeda minima (L.)	Infusion and decoction from	China, Japan,	Whole plant	Brevilin A [78][79]; Apigenin, Quercetin-3-Me-ether, Quercetin-3,3′-diMe-ether,

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A.Braun & Asch. (Asteraceae)	the whole plant, along with other two species (*C. cunninghamii* and *C. thespidioides*) is used to wash eye inflammation due to conjunctiva and purulent ophthalmia [21][77].	Nepal, South Korea, and Thailand		Quercetin-3,7,3′-trimethyl-ether, Quercetin-3,7,3′,4′-tetramethyl-ether, Isobutyroylplenolin, Senecioylplenolin, Aurantiamide acetate, Tetrahydrohelenalin, α-Cyperone [80]; 6-*O*-Methylacrylylplenolin, 6-*O*-Isobutyroylplenolin, 6-*O*-Angeloylplenolin [81]; 2β-(Isobutyryloxy)florilenalin [82]; 2*R*,3*R*)-(+)-7,4′-di-*O*-Methyldihydrokaempferol, Iristectorin A, 4′,5,8-Trihydroxy-7-methoxyisoflavone, 3-Trimethoxyquercetin, 3-*O*-Caffeoyl-α-glueopyranose, 3-*O*-Caffeoyl-β-glucopyranose, Quercetin, Epipinoresinol, Hispidulin [83]; Minimaoside A and B [84]; Minimolides G and H [85]; Minimolide A-F, J-L, Cenminolide A, B, Centiplide A, (1*S*,2*S*,4*R*,5*S*,7*R*,8*S*,10*R*)-2α-Tigloyloxy-4α-angeloyloxyguaia-11(13)-en-8α,12-olide, Centiplide C-I [79][86][87]; 8,10-Dihydroxy-9(2)-methylbutyryloxythymol, 10-Hydroxy-8,9-dioxyisopropylidene-thymol, 8,9,10-Trihydroxythymol, Thymol-β-glucopyranoside, 9-Hydroxythymol, 8,10-Dihydroxy-9-isobutyryloxythymol, 8-Hydroxy-9,10-diisobutyryloxythymol [88]; 4,5β-Dihydroxy-2β-(isobutyryloxy)-10βH-guai-11(13)-en-12,8β-olide, 4-Hydroxyguaia-9,11(13)-

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				dien-12,8β-olide, 2β-(Isobutyryloxy) florilenalin, Pulchellin-2α-*O*-tiglate, Florilenalin-2α-*O*-tiglate [89]; Microhelenalin B and C, Arnicolides B-D, Helenalin-angelate, Helenalin-isovalerate, Helenalin-isobutyrate, Helenalin-3-methyl-2-butanoate, Minimolide E, Minimolide B, 2α-Methoxy-6α-angeloyl-2,3-helenalin [79]; Caloinophyllin A, Nobiletin, Quercetin pentamethyl ether, 3′,4′5,7-Tetramethoxyflavone, 4′,5,7-Trimethoxyflavone, 1,5-Dihydroxyxanthone, 1,8-Dimethoxy-2-hydroxyxanthone, 1,6-Dihydroxy-7-methoxyxanthone, 4-Methoxycaffeic acid [90].
Cleome viscosa L. (Cleomaceae)	The whole meshed plant is applied externally to relieve rheumatism, swellings, headaches, colds, ulcers, and open-sores; seeds are eaten to relieve fever	India, USA, Nigeria, and Vietnam	Seeds; aerial; leaves	Quercetin 3-*O*-(2″-acetyl)-glucoside [91]; Malabaric acid, Stigmast-4-en-3-one, Stigmast-4-*ene*-3,6-dione [92]; Cleomaldeic acid [93]; Lupeol [94]; Astragalin, Visconoside A-C, Vincetoxicoside A and B, Kaempferitrin, Kaempferide 3-*O*-β-d-glucopyranoside 7-*O*-α-l-rhamnopyranoside, Kaempferol 3-*O*-β-d-glucopyranoside 7-*O*-α-l-rhamnopyranoside, Isorhamnetin 3-*O*-β-d-glucopyranoside [95][96]; Lactam nonanoic acid [97].

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	and diarrhoea [8][21].			
Clerodendrum inerme (L.) Gaertn. (Heliotropiaceae)	Crushed leaves and bark are applied on sores [21][23].	China, Egypt, India, Taiwan, Thailand, and Vietnam	Aerial; flowers; roots; leaves	3-Hydroxy-3′,4′-dimethoxychalcone, 3,2′-Dihydroxy-3′,4′-dimethoxychalcone, 5-Hydroxy-7,8-dimethoxyflavone, Eucalyptin [98]; 2-(3-Methoxy-4-hydroxylphenyl) ethyl-*O*-2”,3”-diacetyl-α-l-rhamnopyranosyl-(1→3)-4-*O*-(E)-feruloyl-β-d-glucopyranoside, monomelittoside, Melittoside, Inerminoside A1, Acteoside, Isoacteoside, Campneoside I [99][100][101]; 4α-Methyl-24β-ethyl-5α-cholesta-14,25-dien-3β-ol; 24β-Ethylcholesta-5,9(11),22*E*-trien-3β-ol; 11-Pentacosanone; 6-Nonacosanone, Clerodermic acid [102]; Inerminoside A-D [103][104]; Sammangaosides A-C, Leucosceptoside A, Decaffeoyl-acteoside, Darendoside B, Monomelittoside, Melittoside, (7*S*,8*R*)-Dehydrodiconiferyl alcohol 9-*O*-β-glucopyranoside, (7*S*,8*R*)-Dehydrodiconiferyl alcohol 4-*O*-β-glucopyranoside, β-Glucopyranoside, β-(2′-*O*-β-Xylopyranosyl) glucopyranoside, Salidroside, (*Z*)-3-Hexenyl-β-glucopyranoside, 2,6-Dimethoxy-*p*-hydroquinone 1-*O*-β-glucopyranoside, Seguinoside K [101]; Lup-1,5,20(29)-trien-3-*O*-β-d-

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				glucopyranoside [100]; Octacosane, Friedelin, β-Amyrin [105]; Crolerodendrum A and B, Uncinatone, Harwickiic acid, Acacetin, Kaempferol 3,7,4′-trimethyl ether, 5α,8α-Epidioxyergosta-6,22-diene-3β-ol [106] [107]; Inermes A and B, 14,15-Dihydro-15β-methoxy-3-epicaryoptin [108]; Hispidulin, Diosmetin [107].
Corymbia terminalis (F.Muell.) K.D.Hill & L.A.S.Johnson (Myrtaceae)	The plant is used for dysentery [109].	Australia	Gum	Cianidanol, Taxifolin, Aromadendrin, Farrerol [110].
Crinum pedunculatum R.Br. (Amaryllidaceae)	Crushed whole plant-rubbed on body parts stung by marine organism [21] [23].	NA	NA	NA
Dodonaea polyandra Merr. & L.M.Perry (Sapindaceae)	The plant is used for toothache, mouth inflammation, cuts, and open wounds [23].	Australia	Leaves; stems; leaf resins	Polyandric acid A [111]; 13,17-Epoxy-13-methyl-15-oxo-labda-7-ene, 17-Hydroxy-13-methyl-labda-7,13*Z*-diene-15-oic acid, 13-Methyl-17-oxo-labda-7,13*Z*-diene-15-oic acid, Labdane [112]; 15,16-Epoxy-8α-(benzoyloxy)methylcleroda-

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				3,13(16),14-trien-18-oic acid, 15,16-Epoxy-8α-(benzoyloxy)methyl-2α-hydroxycleroda-3,13(16),14-trien-18-oic acid, 15,16-Epoxy-8α-(benzoyloxy)methyl-2-oxocleroda-3,13(16),14-trien-18-oic acid, 15,16-Epoxy-2α-benzoyloxycleroda-3,13(16),14-trien-18-oic acid [113]; 5,7,4′-Trihydroxy-3′(3-methylbut-2-enyl)-3-methoxy flavone, 5,7-Dihydroxy-3′(3-methylbut-2-enyl)-3,4′-dimethoxy flavone, 5,7,4′-Trihydroxy-3′,5′(3-methylbut-2-enyl)-3-methoxy flavone, 5,7,4′-Trihydroxy-3′,5′(3-methylbut-2-enyl)-3,6-dimethoxy flavone, Viscosol, 5,4′-Dihydroxy-3,7-dimethoxyflavone [114].
Dodonaea viscosa (L.) Jacq. (Sapindaceae)	Leaves are chewed to relieve toothache; root juice is used as a mouthwash; leaf juice is used to heal stonefish and stingray wounds; root decoction is applied to wounds [21][26].	Cameroon, China, and Mexico	Stems; bark	Dodovisins A-F, Dodovisnoid E, (+)-hardwickiic acid, *ent*-15,16-Epoxy-1,3,13(16),14-clerodatetraen-18-oic acid, Hautriwaic lactone, Dodovisnoid G, Methyl-dodovisate B, 5α-Hydroxy-1,2-dehydro-5,10-dihydroprintziasaure-methylester, Strictic acid, Dodonolide [115]; Hautriwaic acid [116]; 2,18-Dihydroxylabda-7,13(*E*)-dien-15-oic acid, 5,7-Dihydroxy-3,6,4′-trimethoxy-3′-(4-hydroxy-3-methyl-but-2-enyl)flavone, 2,17-Dihydroxylabda-7,13(*E*)-dien-15-oic acid, 2-Hydroxylabda-7,13(*E*)-dien-15-oic acid,

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				3,6-Dimethoxy-5,7,4′-trihydroxyflavone, Penduletin, Santin [117].
Eleocharis dulcis (Burm.f.) Trin. ex Hensch. (Cyperaceae)	Whole plant infusion in saltwater (preferred for those growing in or near saltwater) is applied to wounds and sealed with a hollow stem of the same plant [118].	China	Whole plant; peel	6′-(4″-Hydroxy-3″-methoxy-phenylpropenyl)-1-(10-methoxy-phenylacetone)-1′-*O*-β-d-glucopyranoside, Susaroyside A, Clausenaglycoside A-D, Emarginone A and B, Thoreliin B, 4-*O*-(1′,3′-Dihydroxypropan-2′-yl)-dihydroconiferyl alcohol 9-*O*-β-d-glucopyranoside, 2-[4-(3-Methoxy-1-propenyl)-2-methoxy-phenoxy]-propane-1,3-diol, 6′-*O*-(*E*-Cinnamoyl)-coniferin, Methyl 3-(2-*O*-β-d-glucopyranosyl-3,4,5,6-tetramethoxyphenyl) propanoate, 9-*O*-(*E*-Cinnamoyl)-coniferin, 6′-*O*-(*E*-Cinnamoyl)-syringin, 2′-*O*-(*E*-Cinnamoyl)-syringin [119].
Eucalyptus camaldulensis Dehnh. (Myrtaceae)	Gum (or kino) mixed with water is taken orally (recommended not more than 1.3 g of kino) against diarrhoea; infusion made from aerial		NA	NA

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	parts is used for washing head to heal colds and fevers [21][120][121].			
Euphorbia hirta L. (Euphorbiaceae)	A decoction from dried herb (whole plant) is used for deworming, dysentery, bowel problems, and colic warts [21][42].	India	Whole plant	Kaempferol, Rutin, Quercetin [122].
Euphorbia tirucalli L. (Euphorbiaceae)	The plant is known for healing skin cancer [23].	China	Aerial; latex	12-*O*-(2*E*,4*E*,6*E*,8*E*-Tetradecatetraenoyl)-13-*O*-isobutyroyl-4β-deoxyphorbol, 13-*O*-acetyl-12-*O*-(2*Z*,4*E*-Octadienoyl)-4β-deoxyphorbol, Pedilstatin, 4β-Deoxy-phorbol-13-acetate, 4*α*-deoxy-phorbol-13-acetate, 3-*O*-(2,4,68-Tetradecatetraenoyl) ingenol [123].
Excoecaria agallocha L. (Euphorbiaceae)	Toxic juice from this plant is applied externally to	Australia, China, India, Japan, and Vietnam	Leaves; stems; resinous wood;	12-Deoxyphorbol 13-(3*E*,5*E*-decadienoate) [124]; Excoecarins R1 and R2 [125]; 3α,11β-Dihydroxy-*ent*-isopimara-8(14),15-dien-2-one, 16β-

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	relieve painful punctures caused by marine organisms, such as the sharp spines of some fish. Infusion from the bark is rubbed against body pain [21][23].		roots; twigs; bark	Hydroxy-*ent*-atisan-3-one, Ribenone, *ent*-labda-8(17),13*E*-diene-3β,15-diol, *ent*-3β-Hydroxybeyer-15-*ene*-2,12-dione [126]; Excoecarins S, T1-T2, *ent*-12-oxo-2,3-Secobeyer-15-*ene*-2,3-dioic acid, *ent*-15-*epoxy*-Beyerane-3α-ol, Agallochin H [127]; Excoecarins V1—V3, 3,5,7,3′,5′-Pentahydroxy-2*R*,3*R*-flavanonol 3-*O*-α-l-rhamnopyranoside, *ent*-Atisane-16α-ol, *ent*-2,3-Secobeyer-15-ene-2,3-dioic acid, *ent*-15,18-Dihydroxybezoate, 3,4,5-Trimethoxyphenol 1-*O*-β-d-(6-galloyl)-glucopyranoside [128]; 3β-[(2*E*,4*E*)-5-oxo-Decadienoyloxy]-olean-12-ene, β-Amyrin acetate, Taraxerone, 3-Epitaraxerol, Epilupeol, Taraxerol, Taraxerone, 3β-[(2*E*,4*E*)-6-oxo-Decadienoyloxy]-olean-12-ene, Acetyl aleuritolic acid, Cycloart-22-*ene*-3β,25-diol, β-Sitostenone, (24*R*)-24-Ethylcholesta-4,22-dien-3-one, β-Sitosterol [129][130]; Excoagallochaols A–E [131]; Agallochins A-E [132][133]; Excoecarins D, E, and K [134]; Agallochins J-L [133][135]; Agallochins F-I, 2-Acetoxy-1,15-beyeradiene-3,12-dione, 2-Hydroxy-1,15-beyeradiene-3,12-dione, *ent*-kauran-16β-ol-3-one [127][133][136]; Excoecariphenols A-D [137]; Agallochaols K–P, Agallochaol Q, *ent*-17-Hydroxykaur-15-en-3-one, *ent*-

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				Kaur-15-en-3β,17-diol, 7-Deoxogeayine, *ent*-15-Hydroxylabd-8(17),13*E*-dien-3-one, *ent*-15,18-Dihydroxylabd-8(17),13*E*-diene, *ent*-3β,11α-Dihydroxyisopimara-8(14),15-dien-2-one, *ent*-3β-Hydroxybeyer-15-en-2,12-dione [138]; *ent*-16α-Hydroxy-atisane-3,4-lactone, *ent*-16α-Hydroxy-atisane-3-one, *ent*-Atisane-3β,16α-diol, *ent*-3,4-seco-16α-Hydroxyatis-4(19)-en-3-oic acid [139]; Triacontane [140]; Agallochins M-P [138][141][142]; Excagallonoid A, *ent*-(3α,5β,8α,9β,10α,12α)-3-Hydroxyatis-16-en-14-one, Atis-16-ene-3,14-dione, 2-Hydroxy-*atis*-1,16-diene-3,14-dione, 12-Hydroxy-13-methylpodocarpa-8,11,13-trien-3-one [143]; Excolides A-B [144]; Afzelin, Quercitrin, Rutin, Kaempferol-3-*O*-(2-*O*-acetyl)-α-l-rhamnopyranoside, Kaempferide 3-*O*-α-l-rhamnopyranoside, Kaempferol 3-*O*-α-l-arabinofuranoside [145]; Agallolides A-M [146]
Flueggea virosa (Roxb. ex Willd.) Royle (Phyllanthaceae)	An aqueous leaf infusion is taken orally to heal internal pains, such as toothache; the liquid is applied	China and Taiwan	Aerial; roots	Flueggether A, Virosinine A [148]; Flueggenines A, B, and D, Norsecurinine [149][150][151]; Flueggines A and B [152]; Fluevirosines A-C [153]; Virosaines A and B [150][154]; 3β,12-Dihydroxy-13-methylpodocarpa-6,8,11,13-tetraene, 3β,12-Dihydroxy-

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
	to skin sores [21][147].			13-methylpodocarpa-8,11,13-triene, Spruceanol, *ent*-3β,12α-Dihydroxypimara-8(14),15-diene, 3α-Hydroxy-12-methoxy-13-methyl-entpodocarp-6,8,11,13-tetraene, 3α-Hydroxy-13-hydroxymethyl-12-methoxy-ent-podocarp-6,8,11,13-tetraene, 3β-Hydroxy-13-hydroxymethyl-12-methoxy-ent-podocarp-6,8,11,13-tetraene, 12-Hydroxy-13-methylent-podocarp-6,8,11,13-tetraen-3-one, 12-Methoxy-13-methyl-ent-podocarp-6,8,11,13-tetraen-3-one, 6β,12-Dihydroxy-13-methyl-*ent*-podocarp-8,11,13-trien-3-one, 7α,20-Epoxy-3α-hydroxy-12-methoxy-13-methyl-*ent*-podocarp-8,11,13-triene, 3α,20-Epoxy-3β-hydroxy-12-methoxy-13-methyl-*ent*-podocarp-8,11,13-triene [155][156]; Fluvirosaones A and B, Virosecurinine [151][157]; 9(10→20)-Abeo-*ent*-podocarpane; 3,10-Dihydroxy-12-methoxy-13-methyl-9(10→20)-abeo-*ent*-podocarpa-6,8,11,13-tetraene; 4*E*-Dehydrochebulic acid trimethyl ester; 12-Hydroxy-20(10→5)-*abeo*-4,5-*seco*-podocarpa-5(10),6,8,11,13-pentaen-3-one; Betulinic acid 3β-calfeate, (+)-Ampelosin E [156]; Flueggrenes A and B [158]; Flueggenoids A–E, 6,12-Dihydroxy-13-methyl-7-oxo-*ent*-

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
				podocarpa−5,8,11,13-tetraeno-20,3α-lactone; 10α,12-Dihydroxy-13-methyl-9(10→20)-abeo-*ent*-podocarpa−6,8,11,13-tetraen-3-one; 12-Hydroxy-20(10→5)-abeo-4,5-seco-podocarpa-5(10),6,8,11,13-pentaen-3-one; Securinine, Bergenin, Norbergenin [150]; Fluevirines E and F, Viroallosecurinine [151]; Flueindolines A–C, Donaxanine, Methyltryptamine, *N*,*N*-Dimethyltryptamine, 1-Acetyl-β-carboline, 1-Hydroxymethyl-β-carboline, *N*-Methyl-1,2,3,4-tetrahydro-β-carboline, Strychnocarpine, Racemate, Hydromethyl-2-methyl-tetrahydro-β-carboline [159].
Heliotropium ovalifolium Forss (Heliotropiaceae)	Herb extract is used to relieve fevers [160].	India, Egypt, and Zimbabwe	Aerial	Heliophenanthrone [161]; Retronecine, Helifoline [162]; Supinine, 7-Angelyl-heliotridine [163]; 4,7,8-Trimethoxy-naphthalene-2-carboxylic acid, 6-Hydroxy-5,7-dimethoxy-naphthalene-2-carbaldehyde [164]; Heliotropamide [165].
Hibiscus tiliaceus L. (Malvaceae)	Infusions from bark and sapwood (with salt or freshwater) are applied to wounds and	China, Japan, and Taiwan	Stem; wood; bark	Hibiscusin, Hibiscusamide, Vanillic acid, 4-Hydroxybenzoic acid, Syringic acid, 4-Hydroxybenzaldehyde, Scopoletin, N-*trans*-Feruloyltyramine, N-*cis*-Feruloyltyramine [166]; 27-oic-3-oxo-28-Friedelanoic acid, 3α-Hydroxyfriedelane-2-one, 4α-

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
	covered with the bark of the same plant [21][118].			Hydroxyfriedelane-3-one, Friedelin, Epifriedelanol, Pachysandiol A, 3β-*O*-(*p*-Hydroxy-*Z*-cinnamoyl)oleanolic acid, 3β-*O*-(*p*-hydroxy-*E*-cinnamoyl)oleanolic acid, oleanolic acid [167]; Hibiscusterpene I-V, Hibiscone B and C, Isohemigossypol-1-methyl ether, Virginicin, Parvifloral A, Syriacusin A [168].
Ipomoea brasiliensis (L.) Sweet (*I. pes-caprae* (L.) R. Br.) (Combretaceae)	Leaves decoction is applied externally for sores; the heated leaves are used to discharge boils [21][23].	China, India, Mexico, and Thailand	Whole plant	Pescapreins X-XVII [169]; β-Damascenone, Phytol [170]; Pescaproside A and B, Pescapreins I-IX, Stoloniferin III [171]; Ipomeolides A and B, Presqualene alcohol, Icosyl (*E*)-3-(4-hydroxyphenyl)acrylate, β-Sitosterol-3-*O*-β-d-glucopyranoside, Stigmasterol, Lupeol [172].
Litsea glutinosa (Lour.) C.B.Rob. (Heliotropiaceae)	Leaves and bark decoctions are applied to sores and to relieve body pain; sometimes, chewed leaves are applied to cuts and sores [21][23][26].	China and India	Leaves; twigs; heartwood	Glutin, β-sitosterol, Stigmasterol, (−)-Epicatechin, Sitosterol-β-d-glucopyranoside [173]; (3*R*,4*S*,5*S*)-2-Hexadecyl-3-hydroxy-4-methylbutanolide, Litsealactone C, D, and G, Eusmoside C [174].

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
Macaranga tanarius (L.) Müll.Arg. (Euphorbiaceae)	The plant is known for wound healing [175].	Japan, Taiwan, Thailand, and Vietnam	Bark; leaves; fruits; glandular trichomes	(2β,5β,10α,13α)-2-Hydroxypimara-9(11),15-*dien*-12-one, Methyl 2α-hydroxy-3β-[(4-hydroxybenzoyl)oxy]taraxer-14-en-28-oate, 2α-Acetoxy-3β-[(4-hydroxybenzoyl)oxy]-taraxer-14-en-28-oic acid, β-Sitosterol, Friedelin, Friedelin-3β-ol, β-Amyline, Macarangonol, 3β-Acetoxytaraxer-14-*en*-28-oic acid, 2α-Hydroxy-3β-[(4-hydroxybenzoyl)oxy]taraxer-14-*en*-28-oic acid [176]; (+)-Pinoresinol 4-*O*-[6″-*O*-galloyl]-β-d-glucopyranoside, Roseoside, Icariside B_5, (6*R*,9*R*)-3-oxo-α-ionol β-d-glucoside, (6*R*,9S)-3-oxo-α-Ionol β-d-glucoside, (2*S*,3*R*)-Dihydrodehydrodiconiferyl alcohol β-d-glucoside, (+)-Pinoresinol 4-*O*-β-d-glucopyranoside, Scopoline, Rutin, Quercetin 3-*O*-galactopyranoside, Quercetin 3-*O*-arabinopyranoside, Isovitexin, Methyl gallate, Hexenyl β-d-glucoside, (*E*)-2-Hexenyl β-d-glucoside, Malloapeltine [177]; Macarangiosides A-F, Mallophenol B, Lauroside E [178]; Tanariflavanones A-D [177][179][180]; Macaflavanones A-G, Kolavenol [181]; 3′-Geranyl-naringenin [182]; Nymphaeol A-C, Isonymphaeol B, 3′-Geranyl naringenin [179][180][181][182][183]; Macatanarin D, Schweinfurthins E-H,

Australia, 2006.

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
				and K-Q,5-((*E*)-3,5-Dihydroxystyryl)-3-((*E*)-3,7-dimethylocta-2,6-dien-1-yl)benzene-1,2-diol [184]; Tanarifuranonol, Vomifoliol, Blumenol B, vedelianin, mappain, methyl-mappain [180][185].
Manihot esculenta Crantz (Euphorbiaceae)	The plant is known to be effective against belly aches and diarrhoea [175].	NA	NA	NA
Melaleuca leucadendra (L.) L. (Myrtaceae)	The plant is known to be effective against headache, sinusitis, cough and colds, and skin sores [21] [23].	Egypt	Essential oil	Stachyurin (or casuarinin), Ellagitannin [186].
Merremia tridentata (L.) Hallier f. (Combretaceae)	The whole plant is chewed or soaked in the water before	Vietnam	Stem bark	Apigenin, Cynaroside, Luteolin, Cosmosiin, Quercitrin [187].

on 5 May 2022).

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
	applying it to the sores [109].			
Morinda citrifolia L. (Rubiaceae)	Leaves extract used to ease headaches [42] [188].	French Polynesia and Japan	Fruits	(+)-3,4,3′,4′-Tetrahydroxy-9,7′α-epoxylignano-7α,9′-lactone, (+)-3,3′-Bisdemethyltanegool, (−)-Pinoresinol, (−)-3,3″-Bisdemethylpinoresinol, Quercetin, Kaempferol, Scopoletin, Isoscopoletin, Vanillin [189]; 1,5,15-Tri-*O*-methylmorindol, 2-*O*-(β-d-glucopyranosyl)-1-*O*-hexanoyl-β-d-gluropyranose, 2-*O*-(β-d-glucopyranosyl)-1-*O*-octanoyl-β-d-gluropyranose, 5,15-Di-*O*-methylmorindol, 1,3-Dihydroxy-2-methoxyanthracene-9,10-dione, 6-*O*-(β-d-Glucopyranosyl)-1-*O*-hexanoyl-β-d-glucopyranose, 6-*O*-(β-d-glucopyranosyl)-1-*O*-octanoyl-β-d-glucopyranose, 2,6-Di-*O*-(β-d-Glucopyranosyl)-1-*O*-hexanoyl-β-d-glucopyranose, 3-Methylbut-3-*enyl*-β-d-glucopyranose, 3-Methylbut-3-*enyl*-6-*O*-β-d-glucopyranosyl-β-d-glucopyranose, Asperulosidic acid, Rutin [190][191]; Nonioside A, (2*E*,4*E*,7*Z*)-deca-2,4,7-trienoate-2-*O*-β-d-glucopyranosyl-β-d-glucopyranoside, Tricetin [191].

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Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
Nauclea orientalis (L.) L. (Rubiaceae)	Aqueous bark infusion is used for sore belly; it is also applied externally to relieve rheumatic pains; the wood infusion is used for relieving fevers [23][77].	China, Japan, Laos, Papua New Guinea, Thailand, and Vietnam	Heartwood; bark; leaves; stems; roots;	Noreugenin, Naucleoside [192]; Angustine, 18,19-Dihydroangustine, 10-Hydroxyangustine, 3,14,18,19-Tetrahydroangustine, Parvine, Angustoline [193]; Naucleali nes A and B, Naucleosides A and B, Strictosamide, Vincosamide, Pumiloside, Kelampayoside A, β-Sitosterol, Sitosteryl β-d-glucoside [194][195]; Naucleaorals A and B [196]; 10-Hydroxystrictosamide, 6′-*O*-Acetylstrictosamide [195]; α-Pinene, Loganetin, Loganin, Sweroside, Grandifloroside, Methyl 3,4-dihydroxybenzoate, 4-Hydroxycinnamic acid, 3-(2,4-Dihydroxylphenyl)propanoic acid, Methyl 3-(2,4-dihydroxylphenyl)propanoate, Skimmin, Adicardin, Aloe emodin, Pinoresinol [197]; Naucleaorine, Epimethoxynaucleaorine, Strictosidine lactam, 3,4,5-Trimethoxyphenol, 3α-Hydroxyurs-12-*en*-28-oic acid methyl ester, 3α,23-Dihydroxyurs-12-*en*-28-oic acid, 3α,19α,23-Trihydroxyurs-12-*en*-28-oic acid methyl ester, Oleanolic acid [198]; Nauclorienine, Antirhine, Iso-antirhine, Alangine, Naucline, Neonaucline, Angustidine, Subditine [199].

javanica and attenuates lipopolysaccharide-induced acute lung injury by inhibiting PI3K/Akt/NF-kappaB pathways. Fitoterapia 2021, 153, 104980.

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
Nelumbo nucifera Gaertn. (Nelumbonaceae)	Milky juice from leaves is used against diarrhoea [42].	China, India, and Japan	Flowers; rhizome; leaves; seed embryo	2α,24-Diacetoxy-3β-hydroxyolean-12-*en*-28-oic acid, Hyptatic acid A, Maslinic acid, Botulin, Lupeol [200]; (*R*)-Coclaurine, (*S*)-norcoclaurine, Quercetin 3-*O*-β-d-glucuronide [201]; Neferine [202][203]; Liensinine, Isoliensinine [204]; Betulinic acid [205].
Ochrosia elliptica Labill. (Apocynaceae)	Bark is known to be good for dysentery [188].	China and Egypt	Stems and leaves	10-Methoxyconolidine, Apparicine, Vallesamine, Yunnanensine A, Angustilodine, Isositsirikine, (−)-Echitainine, Pseudo akuammigine [206]; Ursolic acid [207][208]; Ellipticine, elliptinine, methoxyellipticine, reserpiline (elliptine) [209].
Ocimum tenuiflorum L. (Heliotropiaceae)	The plant is used to relieve fevers [210].	NA	NA	NA
Phyllanthus urinaria L. (Phyllanthaceae)	The plant is used against colds [109][188].	China and Taiwan	Whole plant	Phyllanthin, Phyltetralin, Trimethyl-3,4-dehydrochebulate, Methylgallate, Rhamnocitrin, Methyl brevifolincarboxylate, β-Sitosterol-3-*O*-β-d-glucopyranoside, Quercitrin, Rutin [211]; Geraniin [212]; Corilagin, Ellagic acid [213].
Phragmites australis (Cav.)	The plant is used to treat	China	Roots	*N*-*p*-Coumaroyl serotonin, *N*-*p*-Coumaroyl-trypamine, phranisines A-B

2,2-dimethyl-6--10-phenyl-2H,8H-pyranochromen-8-one (calophyllolide). Acta Crystallogr. Sect. E Struct. Rep. Online 2010, 66, o1115.

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
Trin. ex Steud. (Plantaginaceae)	sore throat [214] [215].			[216].
Sarcostemma viminale (L.) R. Br (Apocynaceae)	The plant is indicated for skin sores and eye complaints [217].	NA	NA	NA
Scaevola taccada (Gaertn.) Roxb. (Euphorbiaceae)	Leaves decoction is applied externally to skin sores [8] [23].	Thailand	Fruits	Scataccanol, *ent*-ammirin, Nodachenetin, Marmesin, Xanthyletin, Umbelliferone, 4-Formylsyringol, 6-Hydroxy-7-methyl-1-oxo-4-carbomethoxy octahydrocyclopenta[*c*]pyran, Loganetin, Matairesinol, 2-(4-Hydroxyphenyl) 3-(3,4-dihydroxyphenyl)-2-propenoate [218].
Scoparia dulcis L. (Plantaginaceae)	Leaves infusion is taken orally to heal stomach pain; the pulped whole plant is used for covering sores and cuts to enhance healing [23].	Bangladesh and Brazil	Whole plant	Glutinol [219]; Scoparinol [220]; *iso*-dulcinol, 4-*epi*-scopadulcic acid B, dulcidiol, scopanolal, dulcinol, and scopadiol [221].

Y.M.; Kim, Y.H. A new ursane-type triterpenoid glycoside from Centella asiatica leaves modulates the production of nitric oxide and secretion of TNF-alpha in activated RAW 264.7 cells. Bioorg. Med. Chem. Lett. 2011, 21, 1777–1781.

Species and Family	Ethnomedical Uses	Countries from Where the Plant Has Been Collected for Chemical Studies	Parts Used for Chemical Isolation	Isolated Compounds
Terminalia catappa L. (Combretaceae)	The plant is indicated for sore throat [175].	China and New Caledonia	Leaves; bark	Ursolic acid, 2,3,23-Trihydroxyurs-12-en-28-oic acid [222]; 3,4,5-Trimethoxyphenyl-1-*O*-(4-sulfo)-β-d-glucopyranoside, Chebuloside II, Arjunoglucoside II, Arjunolic acid, Betulinic acid, β-Sitosterol-3-*O*-β-d-glucopyranoside [223].
Terminalia muelleri Benth. (Combretaceae)	The plant is indicated for skin sores [175].	Egypt	Leaves	Apigenin-8-C-(2″-*O*-galloyl) glucoside 1, Luteolin-8-C-(2″-*O*-galloyl) glucoside 2, 1-*O*-Galloyl-2,3,4,6-dihexahydroxydiphenoyl-β-d-glucopyranoside, 1,4,6-Tri-*O*-galloyl-2,3-hexahydroxydiphenoyl-β-d-glucopyranoside, 1,2-Di-*O*-galloyl-4,6-hexahydroxydiphenoyl-β-d-glucopyranoside, Isostrictinin, 1-*O*-Galloyl-β-d-glucopyranoside, Combretum caffrum, Ellagic acid, Gallic acid [224][225]; Isoorientin, Vitexin, Chebulinic acid [225].
Verbena officinalis L. (Verbenaceae)	A decoction made from the whole plant is applied externally to overcome fever and rheumatic pain [21][42][226].	China and India	Aerial	3,4-Dihydroverbenalin, Daucosterol [227]; Ursolic acid [228]; Verbenalin, Hastatoside, Acteoside, β-sitosterol-d-glucoside [229].

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3. Overview of the Anti-Inflammatory Mechanism of Action/Pathways

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Bioactive crude extracts or isolated compounds from medicinal plants used by Aboriginal people attenuate inflammatory conditions through three major mechanisms, namely, (i) inhibition of nuclear factor kappa B (NF-κB) pathway, (ii) inhibition of iNOS (inducible nitric oxide synthase), and cyclooxygenase (COX-1 and COX-2) protein expression/activity, and (iii) inhibiting or downregulating NO production and various pro-inflammatory cytokines (such as interleukins, IL-1β, IL-6, interferon, IFN-γ, and tumour necrosis factor, TNF-α) or upregulating anti-inflammatory cytokines (such as IL-10 and transforming growth factor, TGF-β).

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Briefly, NF-κB is a key to inducing gene expression of many pro-inflammatory cytokines (including IL1b, IL-6, IL-12p40, TNF-α, and COX-2) in innate and adaptive immune cells [230]. NF-κB proteins consist of five members, including NF-κB1 (or p50), NF-κB2 (or p52), RelA (or p65), RelB, and c-Rel, and NF-κB activation occurs in two signalling pathways, canonical and alternative non-canonical pathways [231], where both pathways are involved in regulating immune and inflammatory responses. Innate immune cells (e.g., macrophages, dendritic cells, and neutrophils) are central to innate immunity and inflammation. Innate immune cells have PRRs (pattern recognition receptors) that can detect microbial products, including pathogen-associated molecular patterns (PAMPS) and also damage-associated molecular patterns (DAMPS)—released by damaged cells and tissues [232]. Five types of PRRs expressed by mammalian cells are toll-like receptors (TLRs), RIG-I-like receptors, NOD-like receptors (NLRs), C-type lectin-like receptors, and cytosolic DNA sensors [231], each with distinct structures to bind with different PAMPs and DAMPs [231]. Signalling pathway by activating the canonical NF-κB pathway, any terpenoids and steroidal compounds as major constituents in Cleome viscosa leaves and chemistry of cleomiscosins [233]. In response to different PAMPs and DAMPs, macrophages are activated and subsequently differentiate into M1 or M2, followed by the secretion of an array of cytokines and chemokines [230]. Pro-inflammatory cytokines such as IL-1, IL-6, IL-12, and TNF-α are characteristic of M1 macrophages. TLR signals play a vital role in regulating macrophage polarization, and for instance, TLR4 ligand lipopolysaccharide (LPS) promotes the formation of M1 phenotypes [230][234]. LPS is a bacterial-derived lipopolysaccharide that can induce inflammation in macrophage cells in in vitro assays. Activated M1 macrophages can also promote other inflammatory T cells, including Th1 and Th17 cells, and these cells, in turn, also mediate inflammation.

Inhibiting NO production is another anti-inflammatory mechanism shown by many compounds isolated from selected medicinal plants. In mammalian cells, NO is mainly produced from the L-arginine:NO metabolic pathway by the enzyme called nitric oxide synthase (NOS), which has three isoforms of NOS—eNOS (endothelial NOS), nNOS (neuronal NOS), and iNOS [235]. eNOS and nNOS produce a controlled amount of NO in endothelial cells and neurons, respectively, under the Ca^{2+}/calmodulin system [236], while iNOS produces NO only upon activation by specific cytokines (e.g., IFN-γ) or microbial products (e.g., LPS). Sustained NO production enhances the

formation of reactive nitrogen oxide species (RNOS), and prolonged exposure to such free radicals is harmful to healthy body cells [237], whereby iNOS must be regulated.

4. Phytochemistry and Pharmacology of Medicinal Plants

4.1. Anti-Inflammatory Crude Extracts

Out of 45 anti-inflammatory medicinal plants included here, crude extracts from 30 species were already tested for anti-inflammatory activities in both in vitro and in vivo assays (**Table 1**). Pure compounds from 15 species have also been isolated and tested for their anti-inflammatory activities to validate their ethnopharmacological uses. Among 30 species, crude extracts of *Acalypha wilkesiana*, *Brucea javanica*, *Centipeda minima*, *Euphorbia hirta*, *Melaleuca leucadendra*, and *Terminalia catappa* are most widely studied against different inflammatory conditions. Most of the studies on crude extracts have shown that they inhibit NO, PGE_2, iNOS productions, and COX-2 expression in murine macrophage cells (e.g., RAW 264.7 cells) stimulated with bacterial LPS. Moreover, they also inhibit the production of pro-inflammatory cytokines, mainly TNF-α, IL-1β, and IL-6.

For example, when LPS-induced RAW 264.7 cells were treated with an aqueous crude extract of *C. minima*, there was a significant decrease in NO production at a 100 μg/mL concentration and also reduced inflammatory cytokines levels (TNF-α and IL-1β) significantly [238]. Moreover, the aqueous extract also inhibited the expression of iNOS and COX-2 proteins by 80.2% and 71.2%, respectively, when incubated with LPS-activated RAW 264.7 cells for 24 h. The extract also significantly inhibits the expression of iNOS and COX-2 proteins in carrageenin-induced mice paw oedema [238]. Chan et al. [239] also observed a significant decrease in the expression of monocyte chemokine attractants, particularly CCL8, in LPS-stimulated RAW 264.7 cells by the crude extract of *C. minima*, which could have contributed to the inhibition of monocyte chemotaxis and macrophage infiltration in DSS (dextran sodium sulphate)-induced acute colitis in C57BL/6J mice. The crude extract also inhibits the LPS-induced production of TNF-α and IL-1β proteins in HT22 (immortalized mouse hippocampal cell line) neuronal cells from inflammatory damage [240]. Crude extracts from *A. wilkesiana*, *E. hirta*, and *M. leucadendra* also showed a similar anti-inflammatory activity.

When Huang et al. (2017) studied the effect of oil emulsion from *B. javanica* in DSS (Dextran Sodium Sulphate)-induced acute colitis mouse model (0.5, 1, and 2 g/kg), oil emulsion improved disease activity index, including colon length and body weight [241]. Additionally, when they analysed cytokine production, *B. javanica* oil emulsion at higher concentrations (1 and 2 g/kg) has significantly ($p < 0.01$) lowered the levels of six inflammatory cytokines (IL-1β, IL-6, IL-8, IL-17, IFN-γ, and TNF-α) in the colon tissues when compared to positive controls (sulfasalazine and azathioprine) [241]. Crude extracts from *T. catappa* bark, which Aboriginal people use to treat a sore throat, were anti-inflammatory. When Daram et al. (2021) compared ethanol and water extracts from *T. catappa* bark, ethanol extract was better in inhibiting 50% of protein denaturation in the in vitro egg-albumin denaturation assay, and diclofenac was used as a positive control [242]. Both extracts reduced carrageenan-induced paw oedema at a 500 mg/kg concentration in the rat. Leaves ethanol extract and chloroform fraction from *T. catappa* were tested in chronic and acute models of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced ear oedema. When crude

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extracts were applied topically at a 1 mg/kg concentration twice daily for four days, the ethanol fraction reduced oedema by 60% compared to ethanol extract (32%) [222]. In the same study, chemical fractionation yielded two pure compounds showing anti-inflammatory activities, discussed in the subsequent sections.

4.2. Anti-Inflammatory Compounds

When 45 selected Aboriginal medicinal plants were reviewed for their phytochemical compositions and pharmacological properties, 40 species were studied for their phytochemistry. For rest of the five species, only crude extracts were studied. When compounds isolated from 40 Aboriginal medicinal plants (**Table 1**) were further reviewed, 83 compounds have shown various anti-inflammatory activities in in vitro cellular and in vivo animal models. Out of 83 anti-inflammatory compounds, majority were terpenes and terpenoids (30 compounds), followed by flavonoids (16 compounds), coumarins (10 compounds), alkaloids (6 compounds), glycosides, sterols, lignans, and carboxylic acids (3 compounds each). The rest of the compounds were phenolics, aldehydes, tannins (2 compounds each), pyrans, phenylpropanoids, and fatty acid esters (one compound each).

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