



Review

# Phytochemistry, Chemotaxonomy, and Biological Activities of the Araucariaceae Family—A Review

Claudio Frezza <sup>1,\*</sup>, Alessandro Venditti <sup>2</sup>, Daniela De Vita <sup>1</sup>, Chiara Toniolo <sup>1</sup>, Marco Franceschin <sup>2</sup>, Antonio Ventrone <sup>1</sup>, Lamberto Tomassini <sup>1</sup>, Sebastiano Foddai <sup>1</sup>, Marcella Guiso <sup>2</sup>, Marcello Nicoletti <sup>1</sup>, Armandodoriano Bianco <sup>2</sup> and Mauro Serafini <sup>1</sup>

- Dipartimento di Biologia Ambientale, Università di Roma "La Sapienza", Piazzale Aldo Moro 5, 00185 Rome, Italy; daniela.devita@uniroma1.it (D.D.V.); chiara.toniolo@uniroma1.it (C.T.); antonio.ventrone@uniroma1.it (A.V.); lamberto.tomassini@uniroma1.it (L.T.); sebastiano.foddai@uniroma1.it (S.F.); marcello.nicoletti@uniroma1.it (M.N.); mauro.serafini@uniroma1.it (M.S.)
- Dipartimento di Chimica, Università di Roma "La Sapienza", Piazzale Aldo Moro 5, 00185 Rome, Italy; alessandro.venditti@gmail.com (A.V.); marco.franceschin@uniroma1.it (M.F.); marcella.guiso@uniroma1.it (M.G.); armandodoriano.bianco@uniroma1.it (A.B.)
- \* Correspondence: claudio.frezza@uniroma1.it

Received: 22 June 2020; Accepted: 9 July 2020; Published: 14 July 2020



**Abstract:** In this review article, the phytochemistry of the species belonging to the Araucariaceae family is explored. Among these, in particular, it is given a wide overview on the phytochemical profile of *Wollemia* genus, for the first time. In addition to this, the ethnopharmacology and the general biological activities associated to the Araucariaceae species are singularly described. Lastly, the chemotaxonomy at the genus and family levels is described and detailed.

**Keywords:** Araucariaceae; phytochemistry; ethnopharmacology; chemotaxonomy; biological activities

#### 1. Introduction

Araucariaceae Henkel and W. Hochstetter is a family of coniferous trees, classified under the order Pinales, the class Pinopsoda, the division Pinophyta, and the Clade Tracheophytes [1].

It is a very ancient family since its maximum diversity was achieved during the Jurassic and Cretaceous periods with a worldwide distribution. Yet, during the extinction events occurred in the transition from Cretaceous to Paleogene, these species totally vanished from the Northern Hemisphere whereas they remained in the Southern Hemisphere apart for a very few exceptions. In particular, Araucariaceae species are well present in South America, Australia, New Zealand, New Guinea, New Caledonia, and other South Pacific islands while Malaysia represents the exception [2].

From the taxonomic point of view, the family comprises four genera: *Agathis* Salisb., *Araucaria* Juss., *Columbea* Salisb., and *Wollemia* W.G.Jones, K.D.Hill and J.M.Allen. Yet, *Columbea* and *Wollemia* genera are formed by one only species each i.e., *Columbea brasiliensis* (A. Rich.) Carrière and *Wollemia nobilis* W.G.Jones, K.D.Hill and J.M.Allen. On the other hand, *Agathis* genus is formed by 18 accepted species and 4 unresolved species whilst *Araucaria* genus is formed by 19 accepted species [3].

From the phylogenetic standpoint derived from molecular data, Araucariaceae family belongs to a major subdivision that includes the Podocarpaceae, Sciadopityaceae, Cupressaceae, Cephalotaxaceae, and Taxaceae families. In particular, Araucariaceae family belongs to the same clade as Podocarpaceae and represents the least evolved family of the subdivision. Within the family itself, the phylogeny tree forecasts *Wollemia* genus as the least evolved one followed by *Agathis* and *Araucaria* genera. Within the *Araucaria* genus, the situation is more complex, with several existing sub-clades [1].

Plants 2020, 9, 888 2 of 73

In the following pages, all the general botanical features, the phytochemistry, the ethnopharmacology, and the biological activities associated to each genus are described separately. The following databases were used for this study: Scopus, Google Scholar, PubMed, Reaxys, SciFinder, PubChem. The literature research was conducted by digiting every single species name as reported in the site ww.theplantlist.org [3] in all the databases and collecting the relative outcome data.

## 2. Genus Agathis

## 2.1. Botany

The species belonging to this genus are usually monoecious. They are characterized by a large and very robust trunk with no branching in the inferior part when they are mature trees. Indeed, when they are young, they are generally conical and have more irregular crowns. The bark is smooth and grey-brownish colored, usually with a peeling that form irregular flakes that become thicker and thicker as the age of the tree proceeds. The branches are often horizontal, or ascending when they are too large. The lower ones often leave circular branch scars when they detach from the lower trunk. The juvenile leaves are larger than the adult ones and are more or less acute, with an ovate to lanceolate shape. They are often coppery-red colored also. Indeed, the adult leaves are opposite, from linear to elliptical, quite thick and very leathery. They produce two cones: male (pollen) and female (seed). The male ones appear only on the largest trees. The female ones usually develop on short lateral branchlets and get mature after two years. They are generally oval or globe shaped (Figure 1) [4].







**Figure 1.** Images of the organs of *Agathis* species: *A. microstachya* trunk (**left**); *A. philippinensis* leaves (**middle**); *A. australis* leaves and cones (**right**).

# 2.2. Distribution

Agathis is a quite widespread genus of the family. In fact, their species can be found in New Zealand, the Philippines, New Guinea, Melanesia, and Australia, but also in Malaysia, beyond the Equator line. They grow on diverse substrates including podzolized sands, ultramafics, carbonates, and silicates. They occur from near sea level to the altitude of about 2500 m. They mainly prefer sites that never see frost, and that receive between five and ten meters of rain per year [5].

## 2.3. Phytochemistry

Table 1 shows data of all the compounds identified in the genus divided according to the species.

**Table 1.** Compounds evidenced in *Agathis* species.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
A. alba (Lam.) Foxw.	Taiwan	Leaves	agathisflavone, 7''-O-methyl-agathisflavone, 7,7''-di-O-methyl-agathisflvone, 7,4'''-di-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7,7''-di-O-methyl-cupressuflavone, bilobetin, plus other biflavonoids not characterized	SE, CC, $\alpha_D$ , IR, UV, NMR	[6]
	n.r.	-	7-O-methyl-agathisflavone, 7,4′″-di-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7,7′′-di-O-methyl-cupressuflavone	SE, CC, TLC, MP, NMR, MS	[7]
A. atropurpurea Hyland	Australia	Leaves	$\alpha$ -pinene, $\alpha$ -fenchene, camphene, $\beta$ -pinene, sabinene, myrcene, $\alpha$ -terpinene, limonene, $\beta$ -phellandrene, $\gamma$ -terpinene, terpinolene, $\alpha$ -cubebene, bicycloelemene, $\alpha$ -copaene, $\alpha$ -gurjunene, $\beta$ -cubebene, $\beta$ -ylangene, $\beta$ -caryophyllene, germacrene D, $\delta$ -cadinene, bicyclogermacrene, <i>epi</i> -cubenol, globulol, viridiflorol, spathulenol, alkyl chain (C <sub>20</sub> H <sub>32</sub> ), luxuriadiene, phyllocladene, 16-kaurene	SD, GLC, GC-MS, [α] <sub>D</sub> , NMR	[8]
	New Zealand	-	agathisflavone, 7''-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7,7''-di-O-methyl-agathisflavone, 7,7''-di-O-methyl-cupressuflavone, 7,4',7''-tri-O-methyl-cupressuflavone	SE, CC, TLC, LC, NMR, MS	[9]
	Australia	Resin	tricyclene, camphene, dehydro-1,8-cineol, limonene, γ-terpinene, terpinolene, <i>m</i> -cymenene, 1,3,8- <i>p</i> -menthatriene, 1-octen-3-yl acetate, 1,5,8- <i>p</i> -menthatriene, <i>cis</i> -β-terpineol, α-terpineol, dihydro-carveol, carvone, bornyl acetate, 2,5-dimethoxy- <i>p</i> -cymene, β-bisabolene	HD, GC-MS	[10]
A. australis (D. Don) Lindl.	Australia	Leaves	tryciclene, $\alpha$ -pinene, camphene, limonene, $\alpha$ -cubebene, bicycloelemene, $\alpha$ -copaene, $\beta$ -bourbonene, $\alpha$ -gurjunene, $\beta$ -cubebene, $\beta$ -ylangene, $\beta$ -copaene, $\beta$ -caryophyllene, aromadendrene, allo-aromadendrene, humulene, alkyl chains $(C_{15}H_{24})$ , viridiflorene, germacrene D, $\delta$ -cadinene, bicyclogermacrene, calacorene, palustrol, cubenol, $\epsilon pi$ -cubenol, globulol, viridiflorol, alkyl chain $(C_{15}H_{24}O)$ , spathulenol, T-cadinol, T-muurolol, $\alpha$ -cadinol, hibaene, alkyl chain $(C_{20}H_{32})$ , sclarene, luxuriadiene, 16-kaurene, alkyl chain $(C_{20}H_{34}O)$	SD, GLC, GC-MS, [α] <sub>D</sub> , NMR	[8]

 Table 1. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
	New Zealand		agathisflavone, 7''-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7,7''-di-O-methyl-agathisflavone, 7,7''-di-O-methyl-cupressuflavone, 7,4',7''-tri-O-methyl-agathisflavone, 7,4',7''-tri-O-methyl-cupressuflavone, 7,4',7'',4'',-tetra-O-methyl-agathisflavone, 7,4', 7'',4''-tetra-O-methyl-cupressuflavone	SE, CC, TLC, LC, NMR, MS	[9]
A. borneensis Warb.	Malaysia	Leaves	1,2,4a,5,6,8a-hexahydro-1-isopropyl-4,7-dimethyl-naphthalene, 1,4-pentadien-3-ol, 1-iodo-2-methylundecane, 2(1H)-phenanthrenone, 2,4,6-trimethyl-octane, abietate, androstenone, bicetyl, 4-methylene-2,8,8-trimethyl-2-vinyl-bicyclo [5.2.0]nonane, caryophyllene oxide, copaene, dodecane, farnesane, heptacosane, methyl-isobutyrate, naphthalene, n-heptadecane, n-hexacosane, n-octacosane, nor-pristane, n-pentacosane, n-pentadecane, n-pentadecanoic acid, n-tetradecane, octane, 2,3,3-trimethyl-octane, octyl ether, palmitic acid, trans-phytol, α-cubenene, β-caryophyllene	SE, GC-FID, GC-MS	[11]
		Stem bark	farnesol,  1,2,4a,5,6,8a-hexahydro-1-isopropyl-4,7-dimethyl-naphthalene,	- $(1lpha,\!4alpha)$ -naphthalene,	

 Table 1. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
A. dammara (Lamb.) Rich. and A.Rich.	China	Leaves	$\alpha$ -tricyclene, $\alpha$ -pinene, camphene, sabinene, $\beta$ -pinene, $\beta$ -myrcene, $\alpha$ -phellandrene, (+)-4-carene, $\sigma$ -cymene, limonene, $\sigma$ -terpinene, terpinolene, terpinen-4-ol, $\sigma$ -terpineol, $\sigma$ -copaene, germacrene D, $\sigma$ -bisabolene, $\sigma$ -cadinene, $\sigma$ -bisabolol	HD, GC-FID, GC-MS	[12]
	Philippines		alkaloids, anthraquinones, tannins, flavonoids, saponins, phenolics (exact compounds not specified)	Phytochemical screening	[13]
A. lanceolata Warb.	New Caledonia	Resin	19-noranticopalic acid, agatholic acid, sandaracopimaradienol, methyl-sandaracopimarate	SE, CC, $[\alpha]_D$ , IR, NMR, MS	[14,15]
A. macrophylla (Lindl.) Mast.	Australia	Leaves	$\alpha$ -pinene, myrcene, limonene, $p$ -cymene, $\alpha$ -cubebene, bicycloelemene, $\alpha$ -copaene, $\beta$ -bourbonene, $\beta$ -cubebene, $\beta$ -ylangene, $\beta$ -elemene, $\beta$ -caryophyllene, aromadendrene, humulene, alkyl chains ( $C_{15}H_{24}$ ), germacrene D, $\alpha$ -muurolene, $\delta$ -cadinene, calamenene, $p$ -cymen- $\delta$ -ol, calacorene, palustrol, cariophyllene oxide, $epi$ -cubenol, spathulenol, $\delta$ , $\delta$ , $\delta$ 0.	SD, GLC, GC-MS, [α] <sub>D</sub> , NMR	[8]
	China	Aerial parts	(4S,5R,9S,10R)-methyl-19-hydroxy-15,16-dinorlabda-8(17),11-E-die (4R,5R,9R,10R,13S)-13-hydroxypodocarp-8(14)-en-19-oic acid, (4R,5R,9R,10R,13R)-13-hydroxypodocarp-8(14)-en-19-oic acid, 15-nor-14-oxolabda-8(17),12E-dien-19-oic acid, 13-oxo-podocarp-8(14)-en-19-oic acid, 13-oxo-podocarp-8(14)-en-19-oate, 16-hydroxy-8(17),13-labdadien-15,16-olid-19-oic acid, 15ξ-hydroxy-pinusolidic acid, lambertianic acid, methyl lambertianate, pinusolidic acid, pinusolide, angustanoic acid F, 8,11,13-abietatrien-15-ol	n-13-oxo-18-oate, SE, CC, pTLC, HPLC, [α] <sub>D</sub> , CD, UV, IR, NMR, HRMS, XR	[16]
		Leaves and branches	7α,15α-dihydroxystigmast-4-en-3-one, 3β,22,23-trihydroxystigmast-5-en-7-one, 3β-hydroxystigmast-6-one, β-sitosterol, 4(15)-eudesmene-1β,6α-diol, 3β-hydroxymegastigman-5-en-9- <i>O</i> -β-D-glucopyranoside, corchoionoside C, (6 <i>S</i> ,9 <i>R</i> )-roseoside, 2α,3β-dihydroxyurs-12-en-28-oic acid, 2α,3β,19α-trihydroxyurs-12-en-28-oic acid, 2α,3α,19α-trihydroxyurs-12-en-28-oic acid, 4′,4′″,7,7′′-tetra- <i>O</i> -methyl-agathisflavone, amentoflavone, 4′,4′″-di- <i>O</i> -methyl-upressuflavone, quercetin, catechol	SE, CC, TLC, HPLC, [α] <sub>D</sub> , NMR, HRMS	[17]

 Table 1. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
	Fiji	Leaves	$3\alpha$ -hydroxy-(13S)-l6- <i>nor</i> -pimar-7-en-l5-oic acid, (13S)-pimar-7-en- $3\alpha$ ,15,16-triol, kaur-16-en- $3\alpha$ ,13-diol, kauran- $3\alpha$ ,13,16a-triol, agatharesinol, sitosterol, abietic acid, agathic acid	SE, CC, [α] <sub>D</sub> , IR, NMR, MS	[18]
		Resin	abietic acid, agathic acid	SE, CC, IR, NMR, MS	[19]
A. microstachya J.F.Bailey and C.T.White	Australia	Leaves	α-pinene, α-fenchene, camphene, β-pinene, sabinene, myrcene, α-terpinene, limonene, β-phellandrene, $\gamma$ -terpinene, $p$ -cymene, terpinolene, $\alpha$ -cubebene, $\delta$ -elemene, bicycloelemene, $\alpha$ -copaene, α-gurjunene, $\beta$ -cubebene, $\beta$ -ylangene, $\beta$ -elemene, $\beta$ -caryophyllene, aromadendrene, $\alpha$ -llo-aromadendrene, $\gamma$ -elemene, humulene, viridiflorene, $\alpha$ -terpineol, germacrene D, bicyclogermacrene, $\alpha$ -muurolene, $\delta$ -cadinene, calamenene, palustrol, caryophyllene oxide, cubenol, $\epsilon$ -cubenol, globulol, viridiflorol, spathulenol, T-cadinol, T-muurolol, $\alpha$ -cadinol, $\delta$ -cadinol, alkyl chains ( $C_{20}H_{32}$ ), phyllocladene, 16-kaurene	SD, GLC, GC-MS, [α] <sub>D</sub> , NMR	[8]
		Resin	neo-abietic acid, cis-communic acid, trans-communic acid, methyl abietate, methyl sandaracopimarate, agathic acid, methyl-15-hydroxy-abietate, methyl-15-hydroxy-dehydroabietate	SE, CC, [α] <sub>D</sub> , IR, UV, NMR, MS	[20]
A. moorei (Lindl.) Mast.	Australia	Leaves	α-pinene, myrcene, limonene, $p$ -cymene, $α$ -cubebene, $α$ -copaene, $β$ -bourbonene, $α$ -gurjunene, $β$ -cubebene, $β$ -ylangene, $β$ -caryophyllene, aromadendrene, $allo$ -aromadendrene, humulene, viridiflorene, alkyl chains ( $C_{15}H_{24}$ ), germacrene D, $α$ -muurolene, $δ$ -cadinene, calamenene, calacorene, caryophyllene oxide, globulol, viridiflorol, spathulenol, T-cadinol, T-muurolol, $α$ -cadinol, $δ$ -cadinol, alkyl chains ( $C_{20}H_{32}$ ), 5,15-rosadiene, $16$ -kaurene	SD, GLC, GC-MS, [α] <sub>D</sub> , NMR	[8]
A. ovata (C.Moore ex Vieill.) Warb.	Australia	Leaves	limonene, $\alpha$ -cubebene, $\alpha$ -copaene, $\beta$ -bourbonene, $\beta$ -caryophyllene, humulene, viridiflorene, alkyl chains ( $C_{15}H_{24}$ ), germacrene D, $\delta$ -cadinene, calamenene, alkyl chain ( $C_{15}H_{24}$ O), caryophyllene oxide, spathulenol, hibaene, alkyl chains ( $C_{20}H_{32}$ ), sclarene, phyllocladene	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]

 Table 1. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
	New Zealand		agathisflavone, 7''-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7,7''-di-O-methyl-agathisflavone, 7,7''-di-O-methyl-cupressuflavone, 7,4',7''-tri-O-methyl-agathisflavone, 7,4',7''-tri-O-methyl-cupressuflavone, 7,4',7'',4'"-tetra-O-methyl-agathisflavone, 7,4',7'',4'"-tetra-O-methyl-cupressuflavone	SE, CC, TLC, LC, NMR, MS	[9]
A. philippinensis Warb	Philippines	Exudate	tricyclene, α-pinene, α-thujene, α-fenchene, camphene, β-pinene, sabinene, limonene, γ-terpinene, ( <i>E</i> )-β-ocimene, <i>p</i> -cymene, terpinolene, 6-methyl-5-hepten-2-one, fenchone, <i>cis</i> -sabinene hydrate, α-copaene, dihydro-α-terpineol, terpinen-4-ol, <i>trans</i> -pinocarveol, β-terpineol, neral, α-terpineol, carvone, <i>trans</i> -piperitol, <i>trans</i> -p-mentha-1(7),8-dien-2-ol, <i>trans</i> -p-mentha-1,8-dien-6-ol, <i>p</i> -cymen-8-ol, <i>cis</i> -p-mentha-1,8-dien-6-ol, <i>cis</i> -p-mentha-1(7),8-dien-2-ol, limonen-10-ol, <b>plus one not fully characterized</b>	HD, GC, GC-MS	[21]
A. robusta (C. Moore ex F.	Australia	Leaves	$\alpha$ -pinene, $\alpha$ -thujene, $\beta$ -pinene, limonene, 1,8-cineol, $p$ -cymene, $\alpha$ -cubebene, $\alpha$ -copaene, $\beta$ -caryophyllene, aromadendrene, allo-aromadendrene, humulene, alkyl chain (C <sub>15</sub> H <sub>24</sub> ), viridiflorene, germacrene D, $\alpha$ -muurolene, $\delta$ -cadinene, caryophyllene oxide, $p$ -cymen-8-ol, globulol, viridiflorol, spathulenol, rimuene	SD, GLC, GC-MS, [α] <sub>D</sub> , NMR	[8]
Muell.) F.M. Bailey	New Zealand		agathisflavone, 7''-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7,7''-di-O-methyl-cupressuflavone	SE, CC, TLC, LC, NMR, MS	[9]
	Italy		agathisflavone, 7''-O-methyl-agathisflavone, cupressuflavone, rutin, shikimic acid, (2S)-1,2-di-O-[(9Z,12Z,15Z)-octadeca-9,12,15-trienoyl]-3-O-β-D-alactopyranosyl glycerol	SE, CC, NMR, MS	[22]
	United Kingdom		glycosides, tannins, flavonoids, saponins, carbohydrates, fixed oil, mucilage (exact compounds not specified)	Phytochemical screening	[23]

Table 1. Cont.

Species	Collection Site	<b>Organs Studied</b>	Compound	<b>Study Methods</b>	References
	India		α-thujene, α-pinene, camphene, β-pinene, 2-pentyl-furan, α-terpinene, p-cymene, limonene, methyl-chavicol, δ-elemene, α-cubebene, α-copaene, β-bourbonene, β-elemene, (E)-caryophyllene, (E)-α-ionone, cis-thujopsene, β-copaene, aromadendrene,(Z)-β-farnesene, α-humulene, allo-aromadendrene, 9-epi-(E)-caryophyllene, β-chamigrene, γ-muurolene, β-selinene, α-selinene, α-muurolene, γ-cadinene, epi-α-selinene, trans-calamenene, occidentalol, germacrene B, α-cedrene epoxide, spathulenol, caryophyllene oxide, β-copaen-4-α-ol, carotol, humulene epoxide II, intermedeol, occidentalol acetate, 10-nor-calamenen-10-one, rimuene	HD, GC-FID, GC-MS	[24]
		Resin	α-thujene, α-pinene, camphene, thuja-2,4(10)-diene, sabinene, β-pinene, <i>p</i> -cymene, limonene, <i>p</i> -mentha-3,8-diene, <i>p</i> -cymenene, <i>trans</i> -sabinene hydrate, 1,3,8- <i>p</i> -menthatriene, α-campholenal, <i>trans</i> -sabinol, ( <i>E</i> )-myroxide, <i>trans</i> -β-terpineol, pinocarvone, borneol, terpinen-4-ol, <i>p</i> -cymen-8-ol, myrtenol, verbenone, <i>trans</i> -carveol, carvone, <i>trans</i> -sabinene hydrate acetate, <i>iso</i> -bornyl acetate, bornyl acetate, <i>trans</i> -pinocarvyl acetate, dihydro-carvyl acetate, <i>cis</i> -pinocarvyl acetate, myrtenyl acetate, α-terpinyl acetate, aromadendrene, δ-cadinene	HD, GC-FID, GC-MS	[24]
	United Kingdom (purchased)	Seeds	oleic acid, <i>cis</i> -vaccenic acid, linoleic acid, $\alpha$ -linolenic acid, bishomolinoleic acid, bishomo- $\alpha$ -linolenic acid, arachidonic acid, 1,5,8,11,14,17-eicosapentaenoic acid, <b>plus other not specified</b>	SE, GLC-MS, HPLC	[25]

Legend:  $[\alpha]_D$  = Specific Rotation; CC = Column Chromatography; CD = Circular Dichroism; GC-FID = Gas Chromatography coupled to Flame Ionization Detector; GC-MS = Gas Chromatography coupled to Mass Spectrometry; GLC = Gas Liquid Chromatography; GLC-MS = Gas Liquid Chromatography coupled to Mass Spectrometry; HD = HydroDistillation; HPLC = High Performance Liquid Chromatography; HRMS = High Resolution Mass Spectrometry; IR = InfraRed Spectroscopy; LC = Liquid Chromatography; MP = Melting Point; MS = Mass Spectrometry; n.r. = not reported; NMR = Nuclear Magnetic Resonance; pTLC = preparative Thin Layer Chromatography; UV = UltaViolet Spectroscopy; XR = X-ray Spectroscopy.

Plants 2020, 9, 888 9 of 73

As Table 1 clearly shows, not all the existing species of the genus have been studied. In addition, most of the phytochemical works reported in the literature about this genus regards species collected in Oceania or in South-Eastern Asia [8,10–12,21,24] except two, whose studied exemplars were collected in Italy and United Kingdom and these are both associated with A. robusta [22,23]. This fact is not so unusual since, as already mentioned, these species are mainly known to grow in those areas. Nevertheless, only about the exemplar collected in Italy, the phytochemical characterization has been fully described and the reported compounds are quite similar to those reported for the other samples collected in other growth areas. Yet, in order to verify if this is a general tendency, more phytochemical studies must be carried out both on the same exemplar and on other samples coming from different areas of Italy and of the world. In addition, in all the cases, more exemplars coming from different areas were studied [8–10,12,13,16–19,22–25] except for A. borneensis samples coming only from Malaysia [11] and A. microstachya samples coming only from Australia [8,20]. For what concerns the studied organs, leaves represent the most studied ones. Nevertheless, resin, stem barks, branches, and the generic aerial parts have also been considered. In some cases, one only type of organs were analyzed i.e., A. alba, A. australis, A. dammara, and A. ovata of which only the leaves were analyzed [6–9,12,13], A. lanceolata of which only the phytochemical analysis of the resin is reported in literature [14,15] and A. moorei of which only the phytochemical analysis of the leaves is reported in literature [8]. The exudate of only A. philippinensis [21] as well as the seeds of only A. robusta purchased in the United Kingdom [25] have been analyzed for their phytochemical composition reporting the presence of essential oil metabolites for the former and fatty acids for the latter. Right about this point, essential oil components and polar fraction components have been evidenced in the genus. Yet, only for six species i.e., A. atropurpurea [8,9], A. australis [8,9], A. macrophylla [8,16–19], A. microstachya [8,20], A. ovata [8,9] and A. robusta [8,9,22–25], the phytochemical studies regarded both kinds of natural compounds. Indeed, for four species i.e., A. borneensis [11], A. dammara [12], A. moorei [8], and A. philippinensis [21], only the essential oil composition was studied whereas for two species i.e., A. alba [6,7] and A. lanceolata [14,15], only the polar fraction composition was analyzed. Among the essential oil metabolites, none has been reported in all the compositions present in literature. Yet, 16-kaurene, α-copaene, α-cubebene,  $\alpha$ -pinene,  $\beta$ -caryophyllene,  $\beta$ -pinene,  $\delta$ -cadinene, allo-aromadendrene, aromadendrene, camphene, germacrene D, limonene, myrcene, sabinene, and spathulenol represent the most common compounds in this context. Among them, none can actually be used as chemotaxonomic marker at the genus level since they are quite widespread compounds as constituents of the plant essential oils [26,27]. Additionally, among the polar fraction metabolites, none have been reported in all the compositions present in literature. Yet, biflavonoids and, in particular, agathisflavone and its derivatives represent the most common compounds in this context. By the way, these compounds have actually been used as chemotaxonomic markers at the genus level [22,28–33], even if their occurrence seems, now, to be extended at the whole family level. Some diterpenes have also been reported for this genus from A. lanceolata [14,15], A. macrophylla from China [16] and from Fiji [18,19] and the resin of A. microstachya [20]. Only in one case i.e., A. macrophylla, some triterpenes have also been noticed [17]. In two cases i.e., A. dammara from Philippines [13] and A. robusta from United Kingdom [23], the exact polar fraction composition was not reported since only a phytochemical screening was performed. In both cases, the presence of flavonoids, tannins and phenolics has been reported. For what concerns the methodology, in some cases, the essential oil was obtained through hydrodistillation [10,12,21,24] whereas for three cases, solvent extraction [11,25] and solvent distillation [8] were used. In all the cases, multiple and different GC analyses were used for the separation and identification of the essential oil metabolites [8,10–12,21,24,25]. In this regard it should be underlined the presence of improbable natural products, such as iodo-derivatives, and a possible artifact, methyl-β-D-mannofuranoside, due to the extraction solvent [34], among the constituents identified by Adam and colleagues in A. borneensis [11]. In some cases i.e., A. atropurpurea leaves from Australia [8], A. australis leaves [8], A. macrophylla from Australia [8], A. microstachya leaves [8], A. moorei [8], A. ovata from Australia [8], and A. *robusta* from Australia [8],  $[\alpha]_D$  and NMR analyses accompanied the GC ones. Indeed, for the analysis

Plants 2020, 9, 888 10 of 73

of the polar fraction metabolites, SE was the only method for the extraction of these compounds, CC, TLC, LC, and HPLC, together or separated, were the methods for the separation procedure of the compounds and  $[\alpha]_D$ , IR, NMR, and MS, together or separated, were the methods for the identification procedure of the compounds [6,7,9,14-20,22].

## 2.4. Ethnopharmacology

The ethnopharmacological uses of species belonging to the *Agathis* genus are quite limited. In fact, only a couple of works have dealt with this argument. In particular, it was reported that, in Borneo, *A. borneensis* is used to treat fever by boiling the bark in water and drinking it as an herbal tea [35]. Moreover, still in Borneo, the powdered woods of *A. borneensis*, *A. philippinensis* and *A. dammara* are employed to treat headache and myalgia [36].

## 2.5. Biological Activities

## 2.5.1. Extracts

The biological activities associated with the essential oil or the extracts of *Agathis* species are quite numerous.

A. atropurpurea resin extract has shown to possess medium antifungal properties against Aspergillus niger and Rhizopus stolonifer with MIC values equal to 625 and 1250  $\mu$ g/mL, respectively [37]. It also showed strong antileishmanial activities against L. amazonensis promastigotes and amastigotes with IC<sub>50</sub> values equal to < 12.5 and 19.3  $\mu$ g/mL, respectively, as well as weak cytotoxic effects against BALB/c mouse macrophage cells with a CC<sub>50</sub> value equal to 118.4  $\mu$ g/mL [38].

*A. borneensis* leaf methanol extract is able to exert strong antiplasmodial properties against *Plasmodium falciparum* D10 strain (sensitive strain) with an IC<sub>50</sub> value equal to 11.00 µg/mL [36].

The essential oil of *A. dammara* exerts good antibacterial effects against several bacterial strains (*Staphylococcus aureus*, *Bacillus subtilis*, *Pneumonia aeruginosa*, and *Escherichia coli*) with inhibition zones in the range of 14.5–23.7 mm and with MIC values ranging from 1.25 to 2.5 mg/mL [12]. In addition to this, the methanolic extract obtained from its leaves was found to be active also against *Proteus vulgaris* with an inhibition zone in the range 19–21 mm [13]. Moreover, the *n*-hexane, methanol, and ethyl acetate extracts of its resin display very low antioxidant effects (IC<sub>50</sub> values equal to 438.55, 313.51, 245.99 mg/mL, respectively) [39].

The hydroalcoholic extract of *A. robusta* from England at the concentration of 400 μg/mL has shown good anti-inflammatory activities according to the HRBC (HumanRedBloodCell) membrane stabilization and heat-induced hemolytic methods with percentages of denaturation inhibition equal to 76.84% and 77.12%, which are comparable to those observed for diclofenac (79.25%) and aspirin (83.78%) for the respective models [23]. Moreover, the resin essential oil has shown interesting antibacterial effects against several bacterial strains (*Staphylococcus* spp., *Klebsiella pneumoniae*, *Escherichia coli*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*) with MIC and MBC values ranging from 250 to 500 and from 500 to more than 1000 μg/mL, respectively [24].

## 2.5.2. Phytochemicals

In literature there are also some works about the biological activities associated with specific compounds isolated from *Agathis* species.

3-oxo-podocarp-8(14)-en-19-oic acid, 16-hydroxy-8(17),13-labdadien-15,16-olid-19-oic acid, 15 $\xi$ -hydroxypinusolidic acid and lambertianic acid isolated from *A. macrophylla*, are time-dependent moderate inhibitors of tyrosine phosphatase 1B (PTP1B) with  $k_i$  values of 0.11, 0.07 and 0.058  $M^{-1}s^{-1}$ , respectively [16]. Moreover, (4*S*,5*R*,9*S*,10*R*)-methyl-19-hydroxy-15,16-dinorlabda-8(17),11-*E*-dien-13-oxo-18-oate, (4*R*,5*R*,9*R*,10*R*,13*S*)-13-hydroxypodocarp-8(14)-en-19-oic acid, (4*R*,5*R*,9*R*,10*R*,13*R*)-13-hydroxypodocarp-8(14)-en-19-oic acid, 15-*nor*-14-oxolabda-8(17),12*E*-dien-19-oic acid, 13-oxo-podocarp-8(14)-en-19-oate, 16-hydroxy-8(17),

Plants 2020, 9, 888 11 of 73

13-labdadien-15,16-olid-19-oic acid, 15ξ-hydroxypinusolidic acid, lambertianic acid, methyl lambertianate, pinusolidic acid, pinusolide, angustanoic acid F and 8,11,13-abietatrien-15-ol, again isolated from *A. macrophylla*, showed quite weak anticancer properties against HL-60 (human promyelocytic leukemia) and SMMC-7721 (human hepatocarcinoma) cancer cell lines [16].

 $7\alpha$ , $15\alpha$ -dihydroxystigmast-4-en-3-one and  $3\beta$ ,22,23-trihydroxystigmast-5-en-7-one, isolated from *A. macrophylla*, have shown medium cytotoxic effects against A549 (adenocarcinomic human alveolar basal epithelial) tumor cell lines with IC<sub>50</sub> values equal to 36.5 and 16.0  $\mu$ mol/L [17].

#### 2.6. Other Facts

In literature some interesting curiosities about *Agathis* species are also reported. In particular, these curiosities regard other uses of these species in the past.

*Agathis* spp. have been widely used for their timber in order to make panels, cabinets, joinery, turnery, moldings, patterns making, battery separators, piano parts, and artificial limbs. This is because the timber is straight-grained, strong, knot-free, with a silky and lustrous surface and it can be easily worked. In addition, the resin has been used to make the so-called Manila copal to be a component of varnishes, mainly. This resin derives from their living inner barks, is translucent or clear white, and slowly hardens on exposure to air with age, eventually becoming brittle. It is soluble in alcohol to a varying degree and has a melting point between 115–135 °C. Actually, this copal is a complex mixture of monoterpenes, sesquiterpenes, and diterpenes [40].

The young gum of *A. australis* has been used for many centuries as chewing gum by Maori people [41].

The Borneo aborigens consider *A. boorneensis* as a magical plant, capable to exert special powers including protection against bad spirits.

## 3. Genus Araucaria

## 3.1. Botany

The species belonging to this genus are mostly dioecious trees even if monoecious trees can also be found. Moreover, some trees are even able to change sex with time. These species are characterized by a massive and erect stem. They can reach up to 80 m high. The branches are gathered in whorls and grow horizontally. They are covered with leathery or needled leaves, with no branching in the inferior part when they are mature trees. In some species, the leaves are narrow and lanceolate, barely overlapping each other, whilst in others they are very broad, flat, and widely overlapped with each other. They produce two cones: male (pollen) and female (seed). The female cones are globose and can be very variable size according to the species. They are found only on the top of the tree and they contain many large edible seeds. Indeed, the male cones are smaller in size and present a broad cylindrical shape (Figure 2) [42].







**Figure 2.** Images of the organs of *Araucaria* species: *A. araucana* tree (**left**), *A. heterophylla* leaves (**middle**), *A. columnaris* cones (**right**).

## 3.2. Distribution

*Araucaria* is widespread only in the Southern Hemisphere even if at different meridians. In fact, their species can be found in New Guinea, Australia, but also in Chile, Argentina, Brazil, New Caledonia, and Norfolk Island. In addition to this, there is a naturalized population of *A. columnaris*(G.Forst.) Hook. on the island of Lanai in the Hawaii. The greatest biodiversity of the genus is in New Caledonia. They prefer ultrabasic schistose and calcareous soils [43].

# 3.3. Phytochemistry

Table 2 shows data of all the compounds identified in the genus divided according to the species.

 Table 2. Compounds evidenced in Araucaria species.

Species	Collection Site	<b>Organs Studied</b>	Compound	Study Methods	References			
	Australia	Leaves	α-pinene, β-pinene, myrcene, limonene, $p$ -cymene, bicycloelemene, α-copaene, β-bourbonene, β-copaene, β-elemene, β-caryophyllene, aromadendrene, $allo$ -aromadendrene, humulene, alkyl chains, viridiflorene, germacrene D, bicyclogermacrene, $\delta$ -cadinene, palustrol, globulol, viridiflorol, spathulenol, $\alpha$ -cadinol, hibaene, 15-kaurene, phyllocladene	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]			
		Bark	β-sitosterol, eudesmin, sugiol, agathic acid, agatholic acid, imbricatolic acid	SE, CC, $[\alpha]_D$ , MP, IR, NMR, MS	[44]			
A. angustifolia (Bertol.) Kuntze		Bracts	catechin, epi-catechin, apigenin, quercetin	SE, HPLC-DAD	[45]			
Kuntze	Brazil	De Brazil	Dead bark	(–)- <i>epi</i> -afzelechin protocatechuate, (–)- <i>epi</i> -afzelechin <i>p</i> -hydroxybenzoate, quercetin, (–)- <i>epi</i> -catechin, benzoic acid, <i>p</i> -hydroxybenzoic acid, protocatechuic acid	SE, CC, LC, $[\alpha]_D$ , NMR, MS	[46]		
			Cooked seeds	phenolics ( <b>exact compounds not specified</b> ), glucose, fructose, sucrose	Phytochemical screening	[47]		
		Female strobili	dodecanoic acid, hexadecanoic acid, 1,3,4,5-tetrahydroxy-cyclohexane-carboxylic acid, 3-O-methyl-D-chiroinositol, 4-nitrophenyl-β-D-glucopyranoside, 4'-methoxy-tectorigenin 3-glucoside-dihydro-quercetin, 7,4',7'',4'-tetra-O-methyl-amentoflavone	SE, MS <sup>n</sup>	[48]			
						catechin, epi-catechin, rutin	SE, HPLC-UV	[49]
		Knots	eudesmin, seco-isolariciresinol, lariciresinol, isolariciresinol, isolariciresinol-4'-methyl ether	SE, CC, $[\alpha]_D$ , MP, NMR	[50,51]			
		Needles	amentoflavone, ginkgetin, plus other not specified	SE, HPLC-MS	[52,53]			
		Resin	pinoresinol, pinoresinol monomethyl ether, eudesmin, hinokiresinol, isolariciresinol, (–)seco-isolariciresinol	SE, CC, TLC, MP, $[\alpha]_D$ , IR, UV, NMR, MS	[54]			
		Seeds	prodelphinidin B, protocatechuic acid, ferulic acid hexoside, catechin,(–)- <i>epi</i> -catechin, eriodictyol- <i>O</i> -hexoside, quercetin-3- <i>O</i> -glucoside, <b>plus other not specified</b>	SE, HPLC-DAD-MS	[55]			
		Whole plant	bilobetin, 7''-O-methyl-robustaflavone, cupressuflavone	SE, TLC, CC, UV, HPLC, NMR	[56]			

Table 2. Cont.

Species	Collection Site	<b>Organs Studied</b>	Compound	Study Methods	References
		Whole plant (Cells)	octadecyl-( <i>E</i> )- <i>p</i> -coumarate, octadecyl-( <i>Z</i> )- <i>p</i> -coumarate, octadecyl-( <i>E</i> )-ferulate, octadecyl-( <i>Z</i> )-ferulate, 7,4',7''-tri- <i>O</i> -methyl-amentoflavone, 7,4',4'''-tri- <i>O</i> -methyl-amentoflavone, 4',4'''-di- <i>O</i> -methyl-amentoflavone, cabreuvin, irisolidone, pinoresinol, eudesmin, lariciresinol, <i>trans</i> -communic acid	SE, CC, pTLC, IR, NMR, MS	[57]
	Chile	Resin	seco-isolariciresinol, seco-isolariciresinol-4-methyl ether-9'-acetate, seco-isolariciresinol-9'-acetate, seco-isolariciresinol-4-methyl ether-9,9'-diacetate, seco-isolariciresinol-4-methyl ether-9,9'-diacetate, seco-isolariciresinol-9,9'-diacetate, shonanin, lariciresinol, lariciresinol-4'-methyl ether, lariciresinol-4-methyl ether, lariciresinol-4-methyl ether-9-acetate, lariciresinol-9-acetate, seco-isolariciresinol-9-acetate, lariciresinol-4-methyl ether-9-acetate, lariciresinol-9-acetate, seco-isolariciresinol-9-acetate, seco-isolariciresinol-9-acetate, lariciresinol-9-acetate, seco-isolariciresinol-9-acetate, seco-isolariciresinol-9-acetate, seco-isolariciresinol-9-acetate, lariciresinol-9-acetate, seco-isolariciresinol-9-acetate, seco-isolariciresinol-9,	SE, GC-MS	[58]
A. araucana (Molina) K.Koch	Chile	Resin	imbricatolic acid, imbricatadiol,15-hydroxy-imbricatolal, 15-hydroxy-imbrcatolic acid, 15-acetoxy-imbricatolic acid, 15-acetoxy-imbricatolal, 15-formiloxy-imbricatolal, 15-acetoxylabd-8(17)-en-19-ol, 15,19-diacetoxylabd-8(17)-en, labd-8(17)-en-15,19-dial, 19-hydroxylabd-8(17)-en-15-oic acid, junicedric acid, sandaracopimaric acid, agatholic acid	SE, CC, TLC, $[\alpha]_D$ , NMR, MS	[59–61]
(Monta) K.Roch		Wood	seco-isolariciresinol, pinoresinol, eudesmin, lariciresinol, lariciresinol-4-methyl ether	SE, CC, TLC, HPLC, GLC, GC-MS, MP, NMR	[62]
	Germany	Leaves	(–)-α-copaene, (–)-16-kaurene, (–)-δ-cadinene, (+)-15-beyerene, (–)-β-caryophyllene, (–)-trachylobane, (–)-16-atisirene, (–)-rosa-5,15-diene, (–)-13- <i>epi</i> -manoyl-oxide, (–)-sclarene	SD, GC, GC-MS, TLC, $[\alpha]_D$ , NMR	[63]
	India	•	7-O-methyl-agathisflavone, 7"-O-methyl-amentoflavone, 7,7"-di-O-methyl-cupressoflavone	SE, MP, TLC, NMR	[64]

Table 2. Cont.

Species	Collection Site	<b>Organs Studied</b>	Compound	Study Methods	References
	New Zealand	Branches	geraniolene, limonene, $\gamma$ -cadinene, $(-)$ - $\alpha$ -cadinol, hibaene, $(-)$ -trachylobane, $(-)$ -kaurene, $(-)$ -atisirene	SE, GLC, TLC, $[\alpha]_D$ , IR, NMR, MS	[65]
	n.a.	n.a.	geraniolone, limonene, (–)-trachylobane, (–)-kaurene, (–)-atisirene, hibaene, (–)-iso-kaurene, (–)-iso-atisirene	n.a.	[66]
	Australia	Leaves	α-pinene, β-pinene, myrcene, limonene, p-cymene, α-cubebene, α-copaene, β-caryophyllene, aromadendrene, allo-aromadendrene, humulene, viridiflorene, germacrene D, bicyclogermacrene, δ-cadinene, caryophyllene oxide, cubenol, globulol, viridiflorol, spathulenol, hibaene, 16-kaurene, alkyl chains (C <sub>20</sub> H <sub>32</sub> )	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
A. bidwilli Hook.		Resin	labda-8(20),13-dien-15-oic acid, labda-8(20), 13-dien-15,19-dioic acid, kolavenic acid	SE, GC-MS	[67]
	Egypt	Leaves	4',7''-di-O-methyl-agathisflavone,7-O-methyl-6-hydroxy-apigenin, 4',4''-di-O-methyl-amentoflavone	SE, HPLC-UV	[68]
			7-hydroxy-labda-8(17),13(16),14-trien-19-yl-( <i>E</i> )-coumarate, 7-hydroxy-labda-8(17),13(16),14-trien-19-yl-( <i>Z</i> )-coumarate, 7-hydroxy-labda-8(17),13(16),14-trien-19-yl-7'- <i>O</i> -methyl-( <i>E</i> )-coumarate 7-hydroxy-labda-8(17),13(16),14-trien-19-yl-7'- <i>O</i> -methyl-( <i>Z</i> )-coumarate 7-oxocallitrisic acid, 2- <i>O</i> -acetyl-11-keto-boswellic acid, β-sitosterol-3- <i>O</i> -glucopyranoside, phloretic acid, 7,4',7''-tri- <i>O</i> -methyl-agathisflavone, 7,4',7''-tri- <i>O</i> -methyl-cupressuflavone		[69]
	Germany	Leaves	$\alpha$ -cubene, (–)-16-kaurene, $\beta$ -cubebene, $Z$ -biformene, $E$ -biformene, sclarene, $\alpha$ -copaene, germacrene D, (–)-7,13-abietadine, $\delta$ -cadinene	SD, GC, GC-MS, TLC, $[\alpha]_D$ , NMR	[63]
India	Leaves	agathisflavone, cupressuflavone, amentoflavone, 7-O-mcthyl-agathistlavone, bilobetin, hinokiflavone, 7,7''-di-O-methyl-agathisflavone, 7,7''-di-O-mcthyl-cupressuflavone, plus other biflavonoids not characterized	SE, CC, $[\alpha]_D$ , IR, UV, NMR	[6]	
			agathisflavone, amentoflavone, cupressuflavone, 7-O-methyl-agathisflavone, bilobetin, 7-O-methyl-cupressuflavone, hinokiflavone, 7,7"-di-O-methyl-agathisflavone, 7,7"-di-O-methyl-cupressuflavone, plus other biflavonoids not characterized	SE, CC, TLC, IR, UV, NMR, MS	[70]
		Oleoresin	diterpenes, flavonoids (exact compounds not specified)	Phytochemical screening	[71]

Table 2. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References	
	Italy	Oleoresin	methyl <i>ent-</i> 8β-hydroxy-labd- <i>E</i> -l3-en-15-oate, <i>ent-</i> 8β,15-labd- <i>E</i> -13-ene-diol, methyl <i>ent-</i> 8α-hydroxy-labd- <i>E</i> -l3-en-15-oate, <i>ent</i> -l5-acetoxy-labda-8, <i>E</i> -13-diene, <i>ent</i> -labda-8, <i>E</i> -13-dien-15-ol	SE, CC, MP, $[\alpha]_D$ , IR, NMR, MS	[72]	
	Australia	Leaves	β-pinene, 1,8-cineol,α-cubebene, bicycloelemene, α-copaene, β-bourbonene, β-cubebene, β-ylangene, β-elemene, β-caryophyllene, aromadendrene, allo-aromadendrene, humulene, viridiflorene, germacrene D, bicyclogermacrene, α-muurolene, δ-cadinene, calamenene, calacorene, palustrol, cariophyllene oxide, cubenol, epi-cubenol, globulol, viridiflorol, spathulenol, T-cadinol, hibaene, sclarene, luxuriadiene, 16-kaurene, alkyl chains	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]	
A. columnaris (G.Forst.) Hook.	Egypt	Needles	taxifolin, taxifolin-3-O-glucopyranoside, orientin, vitexin, iso-orientin, iso-vitexin, gallic acid	SE, CC, TLC HPLC, UV, NMR, MS	[73]	
	India	India	Bark	benzoic acid, 1 <i>H</i> - <i>N</i> -hydrxynaphth(2,3)imidazole-6,7-dicarboximide, 3-4-methoxyphenyl-2-propenoic acid, 4-[[[(1,2-dichloroethylidene) amino]oxy]carbonyl]amino]-methyl ester benzoic acid, <i>tert</i> -butoxy 2 ethoxyethane,  1 <i>H</i> - <i>N</i> -hydroxynaphth(2,3-d)imidazole-6,7-dicarboximide, 6-methoxy-2-methyl-2-phenyl-2H-1-benzopyran, 2,3-di-amino-2-methylpropanoic acid, 2,4-dimethyl-furan	SE, TLC, GC-MS	[74]
		Branches	myricetin, catechin, rutin, quercetin, luteolin, chlorogenic acid, ferulic acid, gallic acid, vanillic acid	US, HPLC-MS	[75]	
			manool, <i>N,N-bis</i> (2-hydroxyethyl)dodecanamide, palmitic acid, cariophyllene,  1,7,7-trimethyl-3-phenethylidenebicyclo[2.2.1]heptan-2-one,  9-octadecenoic acid, cedr-8-en-15-ol, kaur-16-en-19-ol,  1,3-bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one, methyl-( <i>Z</i> )-5,11,14,17-eicosatetraenoate, methyl-communate, abietic acid, agathic acid dimethyl ester, docosyl acetate, stigmastan-3,5-diene, 1-heptacosanol, tricosyl acetate, β-sitosterol, β-sitosterol acetate	SE, GC-MS	[75]	

Table 2. Cont.

Species	Collection Site	<b>Organs Studied</b>	Compound	Study Methods	References
		Leaves	saponins, tannins, phenols, flavonoids phytosteroids (exact compounds not specified)	Phytochemical screening	[76]
			agathisflavone, amentoflavone, cupressuflavone, 7-O-methyl-agathisflavone, hinokiflavone, 7''-O-methyl-amentoflavone, 7,4'''-di-O-methyl-agathisflavone, 7,7''-di-O-methyl-amentoflavone, 7,7'',4'''-tri-O-methyl-agathisflavone, 7,4',7''-tri-O-methyl-amentoflavone, 7,4',7'',4'''-tetra-O-methyl-amentoflavone, 7,4',7'',4'''-tetra-O-methyl-amentoflavone, 7,4',7'',4'''-tetra-O-methyl-amentoflavone, not characterized	SE, CC, TLC, IR, UV, NMR, MS	[70]
		Whole plant	saponins, antraquinones, terpenes, flavonoids, carbohydrates, proteins (exact compounds not specified)	Phytochemical screening	[77]
	Pakistan (purchased from ornamental shop)	Aerial parts	tannins, flavonoids (exact compounds not specified)	Phytochemical screening	[78]
	Australia	Leaves	α-pinene, β-pinene, sabinene, myrcene, limonene, 1,8-cineol, <i>p</i> -cymene, α-copaene, β-ylangene, β-elemene, β-caryophyllene, aromadendrene, <i>allo</i> -aromadendrene, humulene, α-terpineol, germacrene D, bicyclogermacrene, δ-cadinene, <i>p</i> -cymen-8-ol, calacorene, palustrol, cariophyllene oxide, globulol, viridiflorol, spathulenol, hibaene, 15-kaurene, 16-kaurene, alkyl chains	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
A. cunninghamii Mudie	China	Aerial parts	ent-19-(Z)-coumaroyloxy-labda-8(17),13(16),14-triene, ent-19-(E)-coumaroyloxy-labda-8(17),13(16),14-triene, shikimic acid n-butyl ester, 5-(E)-coumaroyloxy-quinic acid n-butyl ester, 5-(Z)-coumaroyloxyquinic acid n-butyl ester, labda-8(14),15(16)-dien-3β-ol	SE, CC, $[\alpha]_D$ , IR, UV, NMR, MS	[79]
	China	Twigs and leaves	4- <i>n</i> -butoxylphenylpropanetriol, 5- <i>p</i> - <i>cis</i> -coumaroyl-quinic acid, 5- <i>p</i> - <i>trans</i> -coumaroyl-quinic acid, quinic acid, (6 <i>R</i> ,9 <i>S</i> )-3-oxo-α-ionol-9- <i>O</i> -β-D-glucopyranoside, (6 <i>S</i> ,9 <i>S</i> )-roseoside, 5,5''-dihydroxy-7,4',7'',4'"-tetra- <i>O</i> -methyl-biflavone, 7,4',7''-tri- <i>O</i> -methyl-cupressuflavone	SE, CC, TLC, LC, $[\alpha]_D$ , IR, UV, NMR, HRMS	[80]

Table 2. Cont.

Species	Collection Site	<b>Organs Studied</b>	Compound	Study Methods	References
	India	Fresh foliage	<ul> <li><i>n</i>-nonane, tricyclene, α-thujene, α-pinene, α-fenchene, sabinene, β-pinene,</li> <li>α-phellandrene, α-terpinene, <i>p</i>-cymene, limonene, (<i>Z</i>)-β-ocimene, (<i>E</i>)-β-ocimene, γ-terpinene, terpinolene, <i>n</i>-undecane, terpinen-4-ol, myrtenol, <i>n</i>-tridecane, α-copaene, β-panasinsene, (<i>E</i>)-caryophyllene, β-copaene, aromadendrene, α-humulene, (<i>E</i>)-β-farnesene, allo-aromadendrene, germacrene D, α-amorphene, β-selinene, bicyclogermacrene, occidentalol, longipinanol, spathulenol, caryophyllene oxide, humulene epoxide II, α-muurolol, occidentalol acetate, <i>cis</i>-thujopsenal, <i>epi</i>-cyclocolorenone, hibaene, pimaradiene, dolabradiene, 15-kaurene, luxuriadiene, phyllocladene, 16-kaurene, abietatriene, laurenan-2-one, dehydro-abeitol, <b>diterpenes</b></li> </ul>	HD, GC-FID, GC-MS	[81]
		Senescent foliage	<ul> <li><i>n</i>-nonane, tricyclene, α-thujene, α-pinene, α-fenchene, camphene, sabinene, β-pinene, α-phellandrene, δ-3-carene, α-terpinene, p-cymene, limonene, 1,8-cineol, (Z)-β-ocimene, (E)-β-ocimene, γ-terpinene, acetophenone, terpinolene, n-undecane, 3-octanol acetate, terpinen-4-ol, hexyl butanoate, myrtenol, (3Z)-hexenyl-2-methyl butanoate, hexyl iso-valerate, 1-tridecene, n-tridecane, α-copaene, (3Z)-hexenyl hexanoate, sativene, (E)-Garyophyllene, β-copaene, aromadendrene, α-humulene, (E)-β-farnesene, allo-aromadendrene, germacrene D, β-selinene, bicyclogermacrene, occidentalol, longipinanol, spathulenol, caryophyllene oxide, viridiflorol, humulene epoxide II, 1,7-di-epi-α-cedrenal, α-muurolol, 14-hydroxy-(Z)-caryophyllene, 14-hydroxy-9-epi-(E)-caryophyllene, occidentalol acetate, cis-thujopsenal, epi-cyclocolorenone, hibaene, pimaradiene, dolabradiene, 15-kaurene, luxuriadiene, phyllocladene, 16-kaurene, abietatriene, sandaracopimarinol, dehydro-abeitol, diterpenes</li> </ul>		

Table 2. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
		Resin oil	<ul> <li><i>n</i>-nonane, α-pinene, sabinene, β-pinene, 6-methyl-5-hepten-2-one, 3-octanol, <i>p</i>-cymene, limonene, 1,8-cineol, (Z)-β-ocimene, γ-terpinene, terpinolene, <i>n</i>-undecane,1-octen-3-yl-acetate, 3-octanol acetate, (3Z)-hexenyl-butanoate, hexyl butanoate, myrtenol, (3Z)-hexenyl-2-methyl butanoate, hexyl <i>iso</i>-valerate, 1-tridecene, <i>n</i>-tridecane, α-copaene, (3Z)-hexenyl hexanoate, β-panasinsene, sativene,(E)-caryophyllene, β-copaene, aromadendrene, α-humulene, (E)-β-farnesene, <i>allo</i>-aromadendrene, germacrene D, α-amorphene, β-selinene, bicyclogermacrene, occidentalol, longipinanol, spathulenol, caryophyllene oxide, globulol, viridiflorol, humulene epoxide II, 1,7-di-<i>epi</i>-α-cedrenal, α-muurolol, 14-hydroxy-(Z)-caryophyllene, 14-hydroxy-9-<i>epi</i>-(E)-caryophyllene, occidentalol acetate, 5-<i>neo</i>-cedranol, <i>cis</i>-thujopsenal, cyclocolorenone, squamulosone, <i>epi</i>-cyclocolorenone, hibaene, pimaradiene, dolabradiene, 15-kaurene, luxuriadiene, phyllocladene, abietatriene, laurenan-2-one, sandaracopimarinol, dehydro-abeitol, <b>diterpenes</b>, sesquiterpenoids</li> </ul>		
		Leaves	umbelliferone, quercetin, kaempferol, catechin, <i>epi</i> -catechin, chlorogenic acid, gallic acid, caffeic acid, ellagic acid	SE, HPLC	[82]
			7-O-methyl-agathisflavone, 7''-O-methyl-amentoflavone, hinokiflavone, 7,4''-di-O-methyl-agathisflavone, 7,4'-di-O-methyl-amentoflavone, 7,7''-di-O-methyl-cupressuflavone, kayaflavone, 7,4',7''-tri-O-methyl-cupressuflavone, 7,4',7'',4'''-tetra-O-methyl-amentoflavone, 7,4',7'',4'''-tetra-O-methyl-amentoflavone, plus other biflanoids not characterized	SE, CC, TLC, IR, UV, NMR, MS	[70]
	Nigeria	Leaves	nonane, β-calacorene, tricyclene, spathulenol, α-pinene, caryophyllene oxide, camphene, campherenone, sabinene, humulene epoxide II, β-pinene, T-muurolol, 2-pentyl-furan, <i>ar</i> -turmerone, α-phellandrene, shyobunol, δ-3-carene, beyerene, α-terpinene, kaurene, phyllocladene, (Z)-β-ocimene, laurenene, γ-terpinene, α-thujone, undecane, α-campholenal, δ-terpineol, terpinen-4-ol, menthol, verbenone, <i>p</i> -mentha-1,4-dien-7-ol, <i>trans</i> -carveol, myrtenol, α-cubebene, α-copaene, β-elemene, β-caryophyllene, aromadendrene, sesquisabinene B, α-humulene, <i>allo</i> -aromadendrene, γ-muurolene, germacrene D, β-selinene, bicyclogermacrene, γ-cadinene, δ-cadinene	HD, GC, GC-MS	[83]

Table 2. Cont.

Species	Collection Site	<b>Organs Studied</b>	Compound	Study Methods	Reference
	South Africa	Stem bark resin	palmitic acid ethyl ester, (E)-9-octadecenoic acid ethyl ester, ethyl heptadecanoate, di-isooctyl adipate, arachidonic acid, cholesterol, O-ethyl-hydroxylamine, 3-trimethylsilyloxypropyl hexadecanoate, 9-octadecenoic acid methyl ester, docosahexaenoic acid, L-valine-N-[N-[N2,N6-bis-(1-oxodecyl)-L-lysyl]glycyl]-methyl ester, eicosamethyl-cyclodecasiloxane, 1,1-diethoxy-nonane, ethyl 9-octadecenoate, cyclononasiloxane	SE, GC-MS	[84]
			phenolics (exact compounds not specified)	Phytochemical screening	_
	Australia	Leaves	<ul> <li>α-pinene, camphene, β-pinene, sabinene, myrcene, α-terpinene, limonene, γ-terpinene, p-cymene, terpinolene, α-cubebene,</li> <li>α-copaene, β-caryophyllene, aromadendrene, allo-aromadendrene, humulene, viridiflorene, germacrene D, bicyclogermacrene,</li> <li>δ-cadinene, cariophyllene oxide, phyllocladene, 16-kaurene, alkyl chains</li> </ul>	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
A. heterophylla (Salisb.) Franco	Egypt	Leaves	flavonoids, phenolics (exact compounds not specified)	Phytochemical screening	[85]
(Suiso.) Tranco		Resin from the stems	labda-8(17),14-diene, 13 <i>-epi-</i> cupressic acid, 13- <i>O</i> -acetyl-13 <i>-epi-</i> cupressic acid	SE, CC, TLC, NMR	[86]
	Germany	Leaves	(–)-α-copaene, (–)-16-kaurene, (–)-germacrene D, sclarene, (–)-β-caryophyllene, 16-phyllocladene, <i>epi-</i> zonarene, (–)-sandaracopimaradiene, (–)-8(14),15-pimaradiene, dolabradiene, 9- <i>epi-</i> sclarene	SD, GC, GC-MS, TLC, [α] <sub>D</sub> NMR	[63]
	Hawaii	Leaves	$\alpha$ -pinene, camphene, $\beta$ -pinene, limonene, $\alpha$ -terpineol, $\beta$ -caryophyllene	HD, GC-FID, GC-MS	[87]
	India	Foliage	<ul> <li><i>n</i>-nonane, α-pinene, camphene, sabinene, <i>p</i>-cymene, limonene, γ-terpinene, terpinolene, <i>n</i>-undecane, α-copaene, β-bourbonene, (<i>E</i>)-caryophyllene, β-copaene, α-humulene, (<i>E</i>)-β-farnesene, γ-gurjunene, germacrene D, α-amorphene, viridiflorene, α-muurolene, γ-cadinene, δ-cadinene, spathulenol, globulol, viridiflorol, β-oplopenone, <i>epi</i>-α-cadinol, α-muurolol, α-cadinol, cubitene, laurenene, rimuene, <i>epi</i>-laurenene, <i>iso</i>-pimara-9(11),15-diene, hibaene, <i>ent</i>-rosa-5,15-diene, pimaradiene, (3Z)-cembrene A, sandaracopimara-8(14),15-diene, dolabradiene, sclarene, 15-kaurene, luxuriadiene, phyllocladene, 16-kaurene, abietatriene, 13-<i>epi</i>-manool, abietadiene, phyllocladanol, <b>diterpenes</b></li> </ul>	HD, GC-FID, GC-MS	[81]

Table 2. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
		Resin oil	n-undecane,1-octen-3-yl-acetate, α-cubebene, α-ylangene, α-copaene, β-bourbonene, iso-longifolene, β-elemene, (E)-caryophyllene, β-copaene, α-trans-bergamotene, α-guaiene, α-humulene, β-santalene, allo-aromadendrene, γ-gurjunene, germacrene D, aristolochene, trans-muurola-4(14),5-diene, α-muurolene, viridiflorene, δ-amorphene, γ-cadinene, δ-cadinene, α-cadinene, α-calacorene, germacrene B, (E)-nerolidol, spathulenol, β-oplopenone, epi-α-cedrenal, α-muurolol, pimaradiene, sandaracopimara-8(14),15-diene, manool oxide, sandaracopimarinol, diterpenes		
		Whole plant	saponins, antraquinones, terpenes, flavonoids, carbohydrates, proteins, (exact compounds not specified)	Phytochemical screening	[77]
	Indonesia	Leaves	polyisoprenoids (exact compounds not specified)	2D-TLC screening	[88]
A. hunsteinii K.Schum.	Australia	Leaves	<ul> <li>α-pinene, camphene, β-pinene, sabinene, myrcene, limonene,</li> <li>β-phellandrene, 1,8-cineol, p-cymene, terpinolene, α-cubebene,</li> <li>α-copaene, β-bourbebene, β-ylangene, β-elemene, β-caryophyllene,</li> <li>aromadendrene, humulene, viridiflorene, germacrene D,</li> <li>bicyclogermacrene, α-muurolene, calamenene, calacorene,</li> <li>methyl-eugenol, ledol, cubenol, epi-cubenol, globulol, viridiflorol,</li> <li>spathulenol, T-cadinol, T-muurolol, sclarene</li> </ul>	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
A. luxurians (Brongn. and Gris) de Laub.	Australia	Leaves	α-pinene, β-pinene, limonene, <i>p</i> -cymene, α-cubebene, bicycloelemene, α-copaene, β-caryophyllene, aromadendrene, allo-aromadendrene, humulene, viridiflorene, germacrene D, bicyclogermacrene, δ-cadinene, calamenene, palustrol, cariophyllene oxide, cubenol, <i>epi</i> -cubenol, globulol, viridiflorol, spathulenol, 5,15-rosadiene, luxuriadiene, 16-kaurene, alkyl chains	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
A. montana Brongn. and Gris	Australia	Leaves	α-pinene, β-pinene, myrcene, limonene, p-cymene, α-cubebene, α-copaene, β-bourbonene, β-caryophyllene, aromadendrene, allo-aromadendrene, humulene, viridiflorene, α-terpineol, bicyclogermacrene, α-muurolene, δ-cadinene, cariophyllene oxide, globulol, viridiflorol, spathulenol, 5,15-rosadiene, luxuriadiene, phyllocladene, 16-kaurene, alkyl chains	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
A. muelleri (Carrière) Brongn. and Gris	Australia	Leaves	myrcene, limonene, <i>p</i> -cymene, bycicloelemene, α-copaene, β-ylangene, β-elemene, β-caryophyllene, aromadendrene, allo-aromadendrene, humulene, germacrene D, bicyclogermacrene, δ-cadinene, cariophyllene oxide, globulol, viridiflorol, spathulenol, 5,15-rosadiene, sclarene, luxuriadiene, phyllocladene, 15-kaurene, alkyl chain (C <sub>20</sub> H <sub>32</sub> )	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]

Table 2. Cont.

Species	Collection Site	Organs Studied	Compound	Study Methods	References
A. rulei F.Muell.	India	Leaves	amentoflavone, cupressuflavone, agathisflavone, robustaflavone, 7-O-methyl-agathisflavone, 7,4''-di-O-methyl-agathisflavone, 7,7''-di-O-methyl-cupressuflavone, 7,7'',4''''-tri-O-methyl-cupressuflavone, 7,4',7'',4'''-tetra-O-methyl-amentoflavone, 7,4',7'',4'''-tetra-O-methyl-cupressuflavone	SE, TLC, $[\alpha]_D$ , MP, NMR	[89]
A. scopulorum de Laub.	Australia	Leaves	<ul> <li>α-pinene, β-pinene, myrcene, α-cubebene, δ-elemene, α-copaene, β-bourbonene, β-ylangene, β-elemene, β-caryophyllene, aromadendrene, γ-elemene, allo-aromadendrene, humulene, viridiflorene, germacrene D, bicyclogermacrene, α-muurolene, δ-cadinene, calamenene, calacorene, cariophyllene oxide, epi-globulol, ledol, cubenol, epi-cubenol, globulol, viridiflorol, spathulenol, T-cadinol, 5,15-rosadiene, sclarene, luxuriadiene, 16-phyllocladanol, alkyl chains</li> </ul>	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]

Legend: 2D-TLC: Bidimensional Thin Layer Chromatography;  $[\alpha]_D$  = Specific Rotation; CC = Column Chromatography; CD = Circular Dichrosim; ECD = Electron Capture Dissociation; GC-FID = Gas Chromatography coupled to Flame Ionization Detector; GC-MS = Gas Chromatography coupled to Mass Spectrometry; GLC = Gas Liquid Chromatography; GLC-MS = Gas Liquid Chromatography coupled to Mass Spectrometry; HD = HydroDistillation; HPLC = High Performance Liquid Chromatography; HPLC-DAD: High Performance Liquid Chromatography coupled to a Diode Array Detector; HPLC-DAD-MS = High Performance Liquid Chromatography coupled to a Diode Array Detector and Mass Spectrometry; HPLC-UV = High Performance Liquid Chromatography coupled to a UltraViolet Detector; HRMS = High Resolution Mass Spectrometry; IR = InfraRed Spectroscopy; LC = Liquid Chromatography; MP = Melting Point; MS = Mass Spectrometry; MS<sup>n</sup> = Tandem Mass Spectrometry; n.a. = datum not accessible; NMR = Nuclear Magnetic Resonance; pTLC = preparative Thin Layer Chromatography; SD = Solvent Distillation; SE = Solvent Extraction; TLC = Thin Layer Chromatography; US = UltraSonication; UV = UltraViolet Spectroscopy; XR = X-ray Spectroscopy.

Plants 2020, 9, 888 23 of 73

As Table 2 clearly shows, not all the existing species of this genus have been For what concerns the collection sites of the studied species, most of the phytochemical works reported regard species collected in Oceania, South-Eastern Asia, or Southern America [6,8,44–62,64,67,70,71,74–82,87,88]. Only in a few cases, the phytochemical works regarded species collected in other areas of the world such as Europe and Africa [63,68,69,72,73,83–86]. This fact is, again, not so unusual since, as already mentioned, these species are mainly known to grow in those areas even if Araucaria species are, anyway, more widespread than all the other genera of this family. In one further case, the collection site of the studied species could not be obtained [66] whereas in the case of A. columnaris, it was purchased and not collected in the wild [78]. For what concerns the studied organs, leaves remain the most studied ones [6,8,63,64,68–70,76,82,83,85,87,88]. Nevertheless, many other organs have been considered for their phytochemical constituents for this genus. In particular, these organs are: the generic aerial parts [78,79], the foliage [81], the bark [44,74], the bracts [45], the branches [65,75], the cells [57], the dead bark [46], the female strobili [48], the knots [50,51], the needles [52,53,73], the oleoresin [71,72], the resin [54,58–61,67], the resin oil [81], the resin from the stems [86], the seeds [47,55], the stem bark resin [84], the whole plant [56,77], and the wood [62]. In one case i.e., A.cunninghamii from India, the study on the foliage was further divided into fresh and senescent foliage [81], and in one further case i.e., A. columnaris from China, twigs and leaves were studied together [80]. Lastly, in one only case, none could be obtained about the studied organs i.e., A. araucana [66]. For what concerns the reported phytochemical metabolite composition, both essential oil and polar fractions metabolites were observed. Both compositions were analyzed in most cases. Indeed, in a few cases, only the essential oil composition was analyzed such as for A. hunsteinii, A. luxurians, A. montana, A. muelleri and A. scopulorum [8] whereas in one only case i.e., A. rulei, only the polar fraction composition was studied [89]. Anyway, in no case, the same plant exemplar was used to study both the essential oil and polar fraction compositions. In other cases, the phytochemical studies were only phytochemical screenings reporting the classes of the natural compounds present like for the cooked seeds of A. angustifolia from Brazil [47], the oleoresin of A. bidwilli from India [71], the whole plant of A. columnaris from India [74], the aerial parts of A. columnaris from Pakistan [78], the stem bark resin of A. cunninghamii from South Africa [84], the leaves of A. heterophylla from Egypt [85], the whole plant of A. heterophylla from India [77] and the leaves of A. heterophylla from Indonesia [88]. In a few cases, the phytochemical composition was given only partially such as for the needles and the seeds of A. angustifolia from Brazil [52,53,55], the leaves of A. bidwilli from India [6,70], the fresh and senescent foliage, the resin oil and the leaves of A. cunninghamii from India [70,81], the foliage and the resin oil A. heterophylla from India [70,81]. Among the essential oil metabolites, none has been reported in all the compositions present in literature. Yet, 16-kaurene,  $\alpha$ -copaene,  $\alpha$ -cubebene,  $\alpha$ -pinene,  $\beta$ -caryophyllene,  $\beta$ -pinene,  $\delta$ -cadinene, allo-aromadendrene, aromadendrene, camphene, caryophyllene oxide, germacrene D, globulol, hibaene, humulene, limonene, luxuriadiene, myrcene, p-cymene, phyllocladene, spathulenol, viridiflorene, and viridiflorol represent the most common compounds in this context. Among them, none can again be used as chemotaxonomic marker at the genus level since they are quite widespread compounds as constituents of the plant essential oils [26,27]. Additionally, among the polar fraction metabolites, none has been reported in all the compositions present in literature. Yet, diterpenes and biflavonoids represent the most common compounds in this context. By the way, these compounds have actually been used as chemotaxonomic markers at the genus level even if their occurrence seems, now, to be extended at the whole family level [22,28–33]. Several other sub-classes of natural compounds, including triterpenes, lignans, simple flavonoids, and organic acids, have been recorded for this genus [44–47,50,51,54,55,57,58,62,68,69,71,73,75,77,80,82,84,88]. For what concerns the methodology, in only a few cases, the essential oil was obtained through hydrodistillation [81,83,87] whereas in all the other cases, solvent extraction and solvent distillation methods were used. In all the cases, multiple and different GC analyses were used for the separation and identification of the essential oil metabolites [8,63,65,75,81,83,84]. In this context the presence of improbable natural constituents

Plants 2020, 9, 888 24 of 73

should be underlined [34], such as siloxane and silyl-derivatives, in the case of the stem bark exudate (resin) of *A. cunninghamii* [84] since in that work the methanolic extract was injected in GC-MS without previous derivatization. In many cases, other identifications techniques such as  $[\alpha]_D$ , TLC, IR, and NMR, alone or together, accompanied the GC analyses [8,63,65]. Indeed, for the analysis of the polar fraction metabolites, SE was the only method for the extraction of these compounds, except one case i.e., the branches of *A. columnaris* from India where US was used [75]. Indeed, CC, TLC, LC, MP, and HPLC techniques, together or separated, were the methods for the separation procedure of the compounds and  $[\alpha]_D$ , IR, NMR, and MS, together or separated, were the methods for the identification procedure of the compounds. In one case, GC-MS was the only method used for the separation and identification of these compounds [58] whereas in others, it accompanied the other methods [62,75]. In one case i.e., the leaves of *A. bidwilli* from Egypt, ECD was another method used for the phytochemical study [69]. In one case, a 2D-TLC screening was used as method for the phytochemical screening of the extract [88]. Lastly, in one case i.e., *A. araucana*, nothing about the methodology could be written since it was not accessible [66].

## 3.4. Ethnopharmacology

The ethnopharmacological uses of species belonging to the *Araucaria* genus are quite numerous. In particular, in Brazil, *A. angustifolia* leaves are used as emollient, antiseptic, and to treat respiratory infections and rheumatisms. Their dyes are also used for the treatment of wounds and herpes eruptions [90]. In addition, the tinctures derived from the nodes are employed to treat rheumatism. The infusions of the nodes are used orally for the treatment of kidney diseases and sexually transmitted diseases. The infusions of the bark are used topically to treat muscular tensions and varicose veins. The syrup produced of the resin is used for the treatment of respiratory infections [91].

*A. araucana* resin has been used by Amerindian Mapuche tribes located in Southern Chile and Argentina to treat contusions, ulcers, as well as to help cicatrization of skin wounds [60,61].

*A. bidwillii* bark is employed in South Africa against amenorrhoea and as a body and steam wash [92]. Moreover, it is employed in the Lahu tribes of Northern Thailand to treat insomnia [93].

*A. cunninghamii* bark is used by the Yali tribe in West Papua for thatching and in several rituals [94]. *A. heterophylla* aerial parts are used in Peru for toothache and to extract teeth [95].

# 3.5. Biological Activities

## 3.5.1. Extracts

The biological activities associated with the essential oil or the extracts of *Araucaria* species are also quite numerous.

The biflavonoid rich fraction derived from the fresh needles of A. angustifolia has shown to be a potent UV-A UV-B radiation protector [53] as well as to protect liposomes against peroxidative degradation caused by UV-irradiation [52]. The ethyl acetate and n-butanol fractions derived from the whole plant of A. angustifolia showed strong antiviral effects against HSV-1 with IC $_{50}$  values equal to 8.19 and 11.04 µg/mL, respectively [56]. The ethanol and water extracts of its seeds showed good antioxidant properties [55]. The hydroalcoholic and ethyl acetate extracts of its dead bark showed high antioxidant properties in the DPPH assay with IC $_{50}$  values equal to 1 and 0.9 µg/mL, respectively. Moreover, the same extracts showed medium activity in the lipid peroxidation assay induced by UV, ascorbyl, and hydroxyl free radicals with IC $_{50}$  values equal to 36 and 25 µg/mL, respectively, for the former case, 18 and 17 µg/mL, respectively, for the second case and 12 and 22 µg/mL, respectively, for the latter case [46]. Indeed, the water extract of its female strobili also exerts a time-dependent antiproliferative activity against HEp-2 (human laryngeal cancer) cell lines. In particular, at the concentrations of 250 and 500 µg/mL, it was able to inhibit tumor growth by about 50% after 24 h from the subministration whereas, after 48 h, the percentage of inhibition was about 65 and 70%, respectively, and after 72 h, for both, the percentage of inhibition was 80%, approximately [48]. The same extract

Plants 2020, 9, 888 25 of 73

showed good DPPH and SOD activities with  $IC_{50}$  values equal to 10.0 and 14.7  $\mu$ M, respectively, as well as good antimutagenic effects against  $H_2O_2$  in three different loci i.e., *Lys*, *His*, and *Hom* at the concentrations of 0.05, 0.1, and 0.15% with a percentage of survivals of 100% [49]. The water extract of its bracts at the concentration of 50  $\mu$ g/mL is also able to completely avoid, in human lung fibroblast cells, cell mortality, protein damage, and SOD and CAT depletions induced by  $H_2O_2$  [45].

The crude *A. araucana* resin possesses dose-dependent gastroprotective effects on ethanol–HCl-induced gastric lesions in mice [60]. In addition, the methanol extract of its wood showed moderate antibacterial activity against *Citrobacter pilifera*, *Bacillus subtilis*, *Micrococcus luteus*, and *Staphylococcus aureus* with growth inhibition percentages around 20%, which are values much lower than gentamicin used as control. Indeed, the same extract showed moderate antifungal activities against *Mucor miehei*, *Paecilomyces variotii*, *Ceratocystis pilifera*, and *Trametes versicolor* with growth inhibition percentages from 28.7% for the second one to 57.1% for the latter one. The relative  $IC_{50}$  values were in the range 1250–2000  $\mu$ g/mL [62].

The petroleum ether and methanolic extracts of the leaves and oleoresin of A. bidwillii, at the doses 300 mg/kg for the former ones and 100 mg/kg for the latter ones, possess strong anti-insomnia, analgesic, and anti-inflammatory activities [96]. In addition to this, the ethanol extract of its leaves, at the dose of 5 mg/Kg, exerts strong anti-inflammatory activity with percentages of inhibition similar to those of indomethacin i.e., 68.51% vs. 63.28%, respectively [97]. The same extract demonstrated high antinociceptive effects at the concentration of 300 mg/Kg in four different tests: the hot plate test, the acetic acid-induced writhing test, the carrageenan-induced edema test, and the serotonin-induced rat paw oedema test. The associated percentages of inhibition were equal to 81.69%, 54.64%, 45.64%, and 40.75%, respectively. All these values are comparable with those reported for the standard compounds in the relative tests [97]. In addition, its methanolic and ethyl acetate extracts derived from the leaves are able to exert good antitumor effects against HL-60 and K-562 (chronic myelogenic leukemia) cancer cell lines with IC<sub>50</sub> values equal to 33.11 and 39.81 µg/mL, respectively, for the former and 28.18 and 34.64 µg/mL, respectively, for the latter [98]. The leaf methanol extracts at the concentration of 100 μg/mL showed also strong anti-inflammatory activity acting as an inhibitory agent on the levels of IL-1β, TNF- $\alpha$  by reducing them by 58.4% and 56.4%. Indeed, for what concerns IL-6, the effect was observed to be concentration-dependent. Additionally, the *n*-butanol polyphenolic rich extract at the concentration of 10 µg/mL showed these effects but in minor extent i.e., 44.8% inhibition on the levels of IL-1 $\beta$  and 33.6% inhibition on the levels of TNF- $\alpha$ . Indeed, for what concerns IL-6, also this effect was concentration-dependent. All these values were quite similar to those observed for indomethacin [68]. Its oleoresin possesses good antipyretic activity on female albino rats at the dose of 100 mg/Kg showing the maximum decrease in the rectal temperature after 60 min  $(-1.35 \, ^{\circ}\text{C})$  [71].

The ethanol extract of the branches of *A. columnaris* showed good antioxidant and antiradical activities in absolute with values equal to 93.14 and 74.12% for the DRSC (DPPH radical scavenging activity) and NOSC (nitric oxide scavenging capacity) assays, respectively. Moreover, it also showed a good ferric reducing antioxidant power with a value equal to 113.05 mg Fe(II)E/g FS, a good cupric ion reducing capacity with a value equal to 128.34 mg TE/g FS. Indeed, its dichloromethane extract showed good TAC and MCA activities with values equal to 93.26 mg AAE/g FS and 81.50 mg EDTAE/g FS, respectively [75]. The 70% aqueous methanol extract of the needles of *A. columnaris* showed moderate antioxidant effects with a SC<sub>50</sub> value equal to 73.0  $\mu$ g/mL which is, anyway, much higher than ascorbic acid (SC<sub>50</sub> = 8.0  $\mu$ g/mL) [73]. Different extracts of its leaves showed to possess also medium antioxidant properties and good  $\alpha$ -amylase inhibitory and antibacterial effects against *Pseudomonas* and *Klebsiella* spp. and *Escherichia coli* [76]. These results were also confirmed by another study by Zaffar et al. [99]. Indeed, the study performed by Joshi et al. [100] demonstrated that these extracts were also active against *Xanthomonas phaseoli* and *Erwinia chrysanthemi* with the best MIC values i.e., 62.5  $\mu$ g/mL for the methanol and *n*-hexane extracts for both bacterial strains.

The methanolic extract of *A. columnaris* bark exerts strong antibacterial effects against *Staphylococcus* aureus, *Escherichia coli* and *Bacillus subtillis* with maximum inhibition zones equal to 20, 18 and 15 mm,

Plants 2020, 9, 888 26 of 73

respectively. The same extract was also found to be quite cytotoxic against HEK (human kidney) cancer cell line, having an IC $_{50}$  value equal to 95.0  $\mu$ g/mL [74].

The extracts of A. cunninghamii leaves in different solvents (n-hexane, chloroform, ethanol, methanol) possess good antifungal activities against Alternaria alternata, Colletotrichum falcatum, Fusarium oxysporum, Pyricularia oryzae, Sclerotinia rolfsii, Sclerotinia sclerotiorum, and Tillatia indica with inhibition percentages from 39% for the chloroform extract against A. alternata to 57% of the n-hexane extract against A. alternata itself. All the extracts were active except the n-hexane and chloroform ones against Fusarium oxysporum. Most of the extracts showed percentages of inhibition similar or better than clotrimazol used as reference [101]. The methanolic extract of its leaves also showed good DPPH radical scavenging activities with an IC<sub>50</sub> value equal to of 181.9 μg/mL as well as a little reducing power (IC<sub>50</sub> = 1384.42  $\mu$ g/mL) and a moderate prevention effect of nitric oxide radical (IC<sub>50</sub> = 1026.51 μg/mL) [82]. Moreover, the extracts of A. cunninghamii stem bark resin in different solvents showed different biological activities. In particular, the methanol extract showed high  $\alpha$ -glucosidase inhibition effects with a percentage equal to 48.48% which is very close to that of acarbose i.e., 48.69. The *n*-hexane and dichloromethane effects were lower i.e., 24.2% and 26.58%, respectively. The dichloromethane showed strong cytotoxic effects against in Chang liver cells with an IC<sub>50</sub> value equal to 92.9  $\mu$ g/mL. The *n*-hexane and methanol extracts showed minor effect with IC<sub>50</sub> value equal to 386 and above 500 µg/mL, respectively [84]. In addition to this, its essential oil derived from the foliage showed moderate antibacterial activity against Salmonella typhimurium, Staphylococcus aureus, and Staphylococcus epidermidis with inhibition zones equal to 9, 6, and 5 mm, respectively, whereas it was low against Staphylococcus aureus and Bacillus subtilis with inhibition zones both equal to 4 mm. Indeed, its essential oil derived from the resin was moderately active only against Staphylococcus aureus with an inhibition zone equal to 5 mm. The relative MIC values were in the range 250 and 500 μg/mL and the minimum bactericidal concentrations were 1000 µg/mL or more [81].

The resin extract of *A. heterophylla* stems showed strong cytotoxic effects in vitro against colon (HCT116) and breast (MCF7) human cancer cell lines with IC $_{50}$  values equal to 0.54 and 0.94 µg/mL, respectively, which are quite similar to those observed for doxorubicin (0.70 and 0.96 µg/mL, respectively) [86]. The extracts of its leaves in different solvents showed strong to weak anticancer activity against HEPG-2 (hepatocellular carcinoma), MCF-7, PC-3 (human prostate cancer), and Hela (epitheliod carcinoma) cell lines. In particular, the *n*-butanol extract was one of the most effective with IC $_{50}$  values equal to 12.06, 9.13, 17.42, and 7.69 µg/mL, respectively. These values are lower than doxorubicin but absolutely comparable. The ethyl acetate extract was the most efficient one against MCF-7 and Hela cancer cell lines with IC $_{50}$  values equal to 7.64 and 6.72 µg/mL, respectively. The water extract was more effective against Hela cell lines with an IC $_{50}$  value to 9.84 µg/mL. The petroleum ether and dichloromethane extracts showed quite moderate activities against all the studied cancer cell lines with IC $_{50}$  values above 20 µg/mL, except for the petroleum ether extract against Hela whose IC $_{50}$  value was 19.34 µg/mL [85].

## 3.5.2. Phytochemicals

In literature there are also some works about the biological activities associated with specific compounds isolated from *Araucaria* species.

Protocatechuic acid, quercetin, (–)-epiafzelechin protocatechuate, and (–)-epiafzelechin p-hydroxybenzoate extracted from A. angustifolia dead bark from Brazil showed all antioxidant effects in the DPPH assay with IC $_{50}$  values ranging from 0.6  $\mu$ M of quercetin to 11  $\mu$ M of (–)-epiafzelechin p-hydroxybenzoate. Moreover, only quercetin and (–)-epiafzelechin protocatechuate showed activity in the lipid peroxidation assay and only in that induced by UV and ascorbyl free radicals with IC $_{50}$  values equal to 9 and 21  $\mu$ M, respectively, for the former case and 30 and 35  $\mu$ M, respectively, for the second case [46].

Imbricatolic acid, 15-hydroxy-imbricatolal, and 15-acetoxy-imbricatolic acid isolated from *A. araucana* resin from Chile showed dose-dependent gastroprotective effects on ethanol-HCl-induced

Plants **2020**, 9, 888 27 of 73

gastric lesions in mice with maximum activity at doses up to 100 mg/Kg [60]. Moreover, at the dose of 100 mg/kg, 15-hydroxy-imbricatolal, 15-acetoxy-imbricatolic acid, and 15-acetoxylabd-8(17)-en-19-ol were also seen to have effects similar to those of lansoprazole, a standard a proton pump inhibitor drug, reducing the lesions by 78, 69, and 73%, respectively [61]. In addition to this, 15,19-diacetoxylabd-8(17)-en, again isolated from A. araucana resin, was observed to possess a good cytotoxic activity against AGS cells (human gastric epithelial) and fibroblasts after treatment for 24 h with  $IC_{50}$  values equal to 52 and 72  $\mu$ M, respectively. These values are much better than those observed for lansoprazole (IC $_{50}$  values equal to 162 and 306  $\mu$ M, respectively) [61]. Additionally, seco-isolariciresinol, pinoresinol, eudesmin, lariciresinol extracted from the wood of this species from Chile showed weak antibacterial activities against Citrobacter pilifera, Bacillus subtilis, Micrococcus luteus, and Staphylococcus aureus with growth inhibition percentages below 20%, which are, again, values much lower than gentamicin used as control. Indeed, the same compounds showed moderate antifungal activities against Mucor miehei, Paecilomyces variotii, Ceratocystis pilifera, and Trametes versicolor with growth inhibition percentages above 20.0% but below 50%. Actually, pinoresinol was the only compound not active against Paecilomyces variotii whereas the seco-isolariciresinol was the most active in all the cases with growth inhibition percentages equal to 29.7%, 21.9%, 41.5%, and 45.1%, respectively [62].

The Α. bidwillii two compounds extracted from the leaves 7-hydroxy-labda-8(17),13(16),14-trien-19-yl-(*E*)-coumarate from Egypt, and 7-hydroxy-labda-8(17),13(16),14-trien-19-yl-7'-O-methyl-(Z)-coumarate, showed potent cytotoxic effects against L5178Y (mouse lymphoma) cancer cell line with  $IC_{50}$  values equal to 2.22 and 1.42  $\mu$ M, respectively. These values revealed a major effectiveness of these two diterpenoids than the standard drug, kahalalide F, which has an IC<sub>50</sub> value equal to  $4.30 \mu M$  [69].

The biflavonoid rich fraction from *A. bidwillii*, both at the concentration of 100 and 200 mg/Kg, was also observed to be a strong protective agent against ischemia-induced oxidative stress in rats by inhibiting free radicals generation, by scavenging reactive oxygen species and by modulating the intracellular antioxidants against ischemia/reperfusion-induced decreases [102].

Ent-19-(Z)-coumaroyloxy-labda-8(17),13(16),14-triene, and labda-8(14),15(16)-dien-3β-ol extracted from *A. cunninghamii* aerial parts from China exhibited modest inhibitory effects against *E. coli* with MIC values equal to of 31.9 and 36.3 μM, respectively. Moreover, ent-19-(Z)-coumaroyloxy-labda-8(17),13(16),14-triene possess moderate antitumor activity against HL-60 and SMMC-7721 (human hepatoma) cancer cell lines with IC<sub>50</sub> values equal to 8.90 and 11.53μM, respectively [79].

5-*p*-cis-coumaroyl-quinic acid isolated from the twigs and leaves of *A. cunninghamii* showed good antifungal activity against *Helminthosporium sativum*, *Rhizoctonia solani* Kuhn, *Fusarium oxysporum* f. sp. *niveum* and *Fusarium oxysporum* f. sp. *cubense* with EC<sub>50</sub> values equal to 42.3, 90.0, 62.7 and 100.2  $\mu$ g/mL, respectively. In addition, this same compound and 4′,7,7′′-*O*-trimethyl-cupressuflavone also showed moderate antibacterial activities against *Escherichia coli*, *Bacillus cereus*, *Staphyloccocus aureus*, *Erwinia carotovora*, and *Bacillus subtilis* with MIC values equal in sequence to 62.5, 62.5, 62.5, 7.8, 15.5  $\mu$ g/mL and 31.3, 62.5, 62.5, 125.0, and 125.0  $\mu$ g/mL, respectively. Anyway, most of these data are worse than those observed for ampicillin [80].

Labda-8(17),14-diene and 13-epi-cupressic acid isolated from the resin extract of A. heterophylla stems showed moderate cytotoxic effects in vitro against colon (HCT116) and breast (MCF7) human cancer cell lines with IC $_{50}$  values ranging from 2.33  $\mu$ g/mL for 13-epi-cupressic acid against MCF7 to 8.04  $\mu$ g/mL for 13-epi-cupressic acid against HCT116. Indeed, 13-O-acetyl-13-epi-cupressic acid was only active against MCF7 with an IC $_{50}$  value equal to 9.77  $\mu$ g/mL. All these values are much higher than those observed for doxorubicin [86].

Plants 2020, 9, 888 28 of 73

#### 3.6. Other Facts

In literature, one interesting curiosity about the *Araucaria* species is also reported. In particular, the edible part of the seeds of *A. angustifolia* are eaten by animals and people for their high nutritional value [47].

### 4. Genus Columbea

The overall data of this genus including its morphological description, its distribution, its phytochemistry, its ethnopharmacological uses, and its pharmacological activities are associated to the data of its only existing species i.e., *Columbea brasiliensis* (A. Rich.) Carrière. Yet, besides its distribution which is endemic to Brazil [103], there are no data reported in literature for what concerns the other arguments.

## 5. Genus Wollemia

## 5.1. Botany

The overall data of this genus including, its morphological description, its distribution, its phytochemistry, its ethnopharmacological uses, and its pharmacological activities are associated to the data of its only existing species i.e., *Wollemia nobilis* W.G.Jones, K.D.Hill and J.M.Allen.

This species is a monoecious tree which can reach up to 40 m tall. The bark is brown. The stem is multiple with a complex root system. The branching is vertical and lateral. The leaves are flattened, and arranged spirally on the shoots but twisted at the base to form two or four ranks flattened at their own time and they open in November or December depending on the location of the tree. There are two different cones. The male ones (the pollen) are conic and large with a brown-reddish color. Indeed, the female ones (the seeds) are lighter in color and narrower. These cones are disposed in lower positions than the male cones (Figure 3) [104,105].







Figure 3. Images of the organs of Wollemia nobilis: tree (left), leaves (middle), cones (right).

#### 5.2. Distribution

This species is native to Australia and is very rare. In fact, it grows wild only in three different localities within the Wollemi National Park, NSW of Australia where 20 large trees (up to 40 m in height) and 20 juvenile trees are present. Additionally, it was considered to be extinct until 1994. Given these elements, it has been subjected to several protection and conservation programs with the aims to keep its growth habitat secret, monitor them against illegal visits, and develop a plan that favors its cultivation and marketing all around the world. Right because of this, nowadays several *W. nobilis* exemplars are now hosted in a few Botanical Gardens outside Australia (including Italy) as well as in thousands of Australian home gardens. The species prefers sandy soils with good drainage and watering [104,105].

## 5.3. Phytochemistry

Table 3 shows data of all the compounds identified in *W. nobilis*.

 Table 3. Compounds evidenced in Wollemia nobilis.

Collection site	Organs Studied	Compounds	Study Methods	References
Australia (Wollemi National Park)	Leaves	α-pinene, camphene, β-pinene, sabinene, myrcene, terpinene, limonene, β-phellandrene, 1,8-cineol, γ-terpinene, $p$ -cymene, terpinolene, α-copaene, β-caryophyllene, aromadendrene, $allo$ -aromadendrene, humulene, germacrene D, bicyclogermacrene, δ-cadinene, globulol, viridiflorol, spathulenol, hibaene, 15-kaurene, 16-kaurene, alkyl chain ( $C_{15}H_{24}$ )	SD, GLC, GC-MS, $[\alpha]_D$ , NMR	[8]
Belgium (Arboretum Kalmthou)	Leaves	β-pinene, β-myrcene, 3-methylene-1,7-octadiene, octen-1-ol acetate, 6-camphenol, ( $E$ )-3(10)-caren-4-ol,verbenol, ( $E$ )-3(10)-caren-4-ol,verbenol, 6,6-dimethyl-2-methylene-bicyclo[2.2.1]-heptan-3-one, $Z$ -β-terpineol, 2-acetyl-2-carene, myrtenol, verbenone, ( $E$ )-3(10)-caren-2-ol,carvone, 2,2-dimethylvaleroyl chloride, bergamol, ( $Z$ )-2-decenal, bornyl acetate, $p$ -mentha-6,8-dien-2-ol acetate, $p$ -menth-8-en-2-ol acetate, $p$ -menthyl-3-methylene-1,6,10-dodecatriene, cyclobuta[1,2:3,4]dicyclopentenedecahydro-3a-methyl-6-methylene-1-(1-methylethyl)-[1 $S$ -(1. $\alpha$ ,3a. $\alpha$ ,3b. $\beta$ ,6a. $\beta$ ,6b. $\alpha$ )], $\beta$ -cis-ocimene, germacrene D, germacrene B, filipendulal, ( $iso$ )-aromadendrene epoxide, phylocald-15-ene, kaur-16-ene, [1ar-(1a. $\alpha$ ,4. $\beta$ ,4a. $\beta$ ,7. $\alpha$ ,7a. $\beta$ ,7b. $\alpha$ ]-decahydro-1,1,4,7-tetramethyl-1 $H$ -cycloprop[e]azulen-4-ol,aromadendrene (2)-oxide, $\alpha$ -cadinol, ( $iso$ )-geraniol, $trans$ -longipinocarveol, $trans$ - $Z$ - $\alpha$ -bisabolene epoxide, tetrahydrogeranyl acetate, sandaracopimar-15-en-8.byl-acetate, 4 $\beta$ ,17-(acetoxy)-kauran-18-al	HD, GC-MS	[106]
	Twigs	β-pinene, β-myrcene, 3-methylene-1,7-octadiene, δ-carene, octen-1-ol acetate, 6-camphenol, ( <i>E</i> )-3(10)-caren-4-ol,verbenol, <i>Z</i> -β-terpineol, 8-oxo- <i>cis</i> -ocimene, myrtenol, 2,2-dimethylvaleroyl chloride, bergamol, bornyl acetate, <i>p</i> -mentha-6,8-dien-2-ol acetate, <i>p</i> -menth-8-en-2-olacetate, cyclobuta[1,2:3,4]dicyclopentenedecahydro-3a-methyl-6-methylene-1- (1-methylethyl)-[1S-(1.α,3a.α,3b.β,6a.β,6b.α)], sativene, 1-ethenyl-1-methyl-2,4-bis(1-methylethenyl) cyclohexane, 7,11-dimethyl-3-methylene-1,6,10-dodecatriene, β-cis-ocimene, germacrene D, germacrene B, α-muurolene, spathulenol, filipendulal, ( <i>iso</i> )-aromadendrene epoxide, [1 <i>ar</i> -(1a.α,4.β,4a.β,7.α,7a.β,7b.α]-decahydro-1,1,4,7-tetramethyl-1 <i>H</i> -cycloprop[e]azulen-4-ol,aromadendrene (2)-oxide, α-cadinol, <i>trans</i> -longipinocarveol, caryophyllene oxide, <i>trans</i> -Z-α-bisabolene epoxide, tetrahydrogeranyl acetate, sandaracopimar-15-en-8.byl-acetate, phylocald-15-ene, kaur-16-ene, 4β,17-(acetoxy)-kauran-18-al, kaur-16-en-18-oic acid methyl ester		

Table 3. Cont.

Collection site	Organs Studied	Compounds	Study Methods	References
	Leaves	pheophorbide <i>a</i> , isocupressic acid, acetyl-isocupressic acid, sandaracopimaric acid, agathic acid, 7,4′,4′″-tri- <i>O</i> -methyl-agathisflavone, 7,4′,7′′,4′″-tetra- <i>O</i> -methyl-agathisflavone, caffeic acid, shikimic acid	SE, CC, NMR, MS	[32]
Italy (Botanical garden of Rome)	Half-matured female cones acetyl-isocupressic acid, methyl-( <i>E</i> )-communate, sandaracopimaric acid, wollemol, 7"-O-methyl-agathisflavone, 7,4"-di-O-methyl-agathisflavone, shikimic acid, quinic acid, glucose, sucrose, raffinose, D-lactic acid, succinic acid, alanine		SE, CC, NMR, MS	[33]
	Male reproduction organs	tri-linolenoyl-sn-glycerol, 1,2-di-palmitoleoyl-3-myristoyl-sn-glycerol, 6'-O-acetyl-pina-2-ene-4,10-diol-10-O-β-D-glucopyranoside, isocupressic acid, acetyl-isocupressic acid, agathic acid, sandaracopimaric acid, 7,4',7'',4'"-tetra-O-methyl-robustaflavone, 7-O-methyl-agathisflavone, 7,4',7''-di-O-methyl-agathisflavone, 7,4',7'',4'"-tetra-O-methyl-agathisflavone, 7,7'',4'"-tri-O-methyl-amentoflavone, shikimic acid, quinic acid, D-lactic acid, glucose, sucrose, pinitol, alanine		[29]
	Unripe female cones	2α-hydroxy-8(14),15-sandaracopimaradien-18-oic acid, wollemolide, 15-formyloxy-imbricatolicacid, 15-formyloxy-imbricatolal, agathisflavone, cupressuflavone, 7''-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, dactylifric acid, shikimic acid, caffeic acid, protocatechuic acid		[31]
	Male cones	wollemolide, isocupressic acid, acetyl-isocupressic acid, methyl ( <i>E</i> )-communate, sandaracopimaric acid, wollemol, 4'-O-methyl-scutellarein, 7-4'"-dimethoxy-agathisflavone, shikimic acid, glucose, sucrose, arginine	SE, CC, UHPLC-HRMS, NMR, MS	[28,30]
Poland (purchased from a Company)	Twigs	7-O-methyl-agathisflavone, 7,4'"-di-O-methyl-agathisflavone, 7,7''-di-O-methyl-cupressuflavone, 7,7'',4'"-tri-O-methyl-agathisflavone, 7,4',7''-tri-O-methyl-cupressuflavone, 7,4',7'',4'"-tetra-O-methyl-cupressuflavone, 7,4',7'',4'"-tetra-O-methyl-amentoflavone	SE, HPLC, TLC, NMR, HRMS	[107]

Legend:  $[\alpha]_D$  = Specific Rotation; CC = Column Chromatography; GC-MS = Gas Chromatography coupled to Mass Spectrometry; GLC = Gas Liquid Chromatography; HD = HydroDistillation; HPLC = High Performance Liquid Chromatography; HRMS = High Resolution Mass Spectrometry; MS = Mass Spectrometry; NMR = Nuclear Magnetic Resonance; SD = Solvent Distillation; SE = Solvent Extraction; TLC = Thin Layer Chromatography; UHPLC-HRMS = Ultra High Performance Liquid Chromatography coupled to High Resolution Mass Spectrometry.

Plants 2020, 9, 888 31 of 73

As Table 3 clearly shows, most of the phytochemical works reported in the literature about this species regard exemplars collected in Italy [28–33]. Yet, this fact is not so unusual since, as already mentioned, Italy is one of the main places where this species has been introduced in order to favor its survival. One only work has regarded the phytochemistry of an exemplar from Australia but only for the essential oil composition [8]. In addition, there are two works regarding the essential oil content of a sample collected in Belgium [106] and one regarding the polar fraction metabolites of an exemplar purchased from a company in Poland [107]. The studied organs were mainly the leaves [8,32,106] but also other organs were taken into considerations i.e., twigs [106,107], half-matured female cones [33], male reproduction organs [29], unripe female cones [31], and male cones for two different studies in the time distance of one year [28,30]. For what concerns the identified compounds, also W. nobilis is known to biosynthesize both components of the essential oil and polar fraction metabolites. For none of the studied samples, both essential oil and polar fraction composition were studied. In particular, only the essential oil composition was analyzed for the exemplar from Australia [8] and for the leaves and twigs of the exemplar coming from Belgium [106], whereas only the polar fraction composition was analyzed in all the other cases [28–33,107]. Among the essential oil metabolites, only  $\beta$ -pinene and germacrene D are present in all the studied samples [8,106]. Yet, it is still not possible to draw a general conclusion on this matter since the exemplars studied until now are still too few. Anyhow, they cannot be considered as chemotaxonomic markers since they represent very common compounds of the essential oils of different plants. Among the polar fraction metabolites, none have been evidenced in all the studied samples. Yet, biflavonoids and diterpenes have been generally evidenced in all the studied samples [28–33,107], but they are mostly considered as chemotaxonomic markers at the family level. For what concerns the methodology, in one case, the essential oil was obtained through solvent distillation [8] whereas in two cases, it was obtained through hydrodistillation [106]. In one case, GLC was also used for the separation of the essential oil metabolites [8] whilst in all the other cases GC-MS was used for the separation and identification of the essential oil metabolites [8,106]. In one case [8],  $[\alpha]_D$  and NMR analyses accompanied the GC ones. Indeed, for the analysis of the polar fraction metabolites, SE was the only method for the extraction of these compounds [28–33,107]. CC was the method for the separation procedure of the compounds in most cases [28–33] whereas HPLC and TLC were used in one case [107]. Lastly, NMR and MS techniques were used for the identification procedure of the compounds in all the cases [28–33,107]. In one case, UHPLC-HRMS was used for the specific separation and identification of one compound [30].

## 5.4. Ethnopharmacology and Biological Activities

At the moment, in literature, no ethnopharmacological uses and biological activities of the extracts are reported for this species. Nevertheless, it is known that the cones of this species are widely eaten by herbivores [28] and that isocupressic acid and acetyl isocupressic acid are known to exert abortifacient activity in cattle [108] especially in case of late term pregnancy [109].

# 6. Phytochemistry of the Araucariaceae Family

Table 4 shows the phytochemical comparison among all the essential oil metabolites evidenced in the Araucariaceae family.

Table 5 shows, instead, the phytochemical comparison among all the polar fraction metabolites evidenced in the Araucariaceae family.

**Table 4.** Occurrence of essential oil metabolites in Araucariaceae species.

Compound	Occurrence in the Family	Reference
1,1-diethoxy-nonane	Araucaria cunninghamii	[84]
1,2,4a,5,6,8a-hexahydro-1- isopropyl-4,7-dimethyl-naphthalene	Agathis borneensis	[11]
$1,2,3,4,4$ a, $5,6,8$ aoctahydro-7-methyl-4-methylene-1- (1-methylethyl)-( $1\alpha,4$ a $\alpha$ )-naphthalene	Agathis borneensis	[11]
1,3,8-p-menthatriene	Agathis robusta, Agathis atropurpurea	[10,24]
1,3-bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one	Araucaria columnaris	[75]
1,4-pentadien-3-ol	Agathis borneensis	[11]
1,5,8-p-menthatriene	Agathis atropurpurea	[10]
1,5,9,9-tetramethyl-1,4,7-cycloundecatriene	Agathis borneensis	[11]
1,7,7-trimethyl-3-phenethylidenebicyclo[2.2.1]heptan-2-one	Araucaria columnaris	[75]
1,7-di- <i>ep</i> i-α-cedrenal	Araucaria cunninghamii	[81]
1H-N-hydrxynaphth(2,3)imidazole-6,7-dicarboximide	Araucaria columnaris	[74]
1H-N-hydroxynaphth(2,3-d)imidazole-6,7-dicarboximide	Araucaria columnaris	[74]
1,8-cineol	Agathis robusta, Araucaria columnaris, Araucaria cunninghamii, Araucaria hunsteinii, Wollemia nobilis	[8,81]
1-ethenyl-1-methyl-2,4-bis(1-methylethenyl) cyclohexane	Wollemia nobilis	[106]
1-heptacosanol	Araucaria columnaris	[75]
1-iodo-2-methylundecane	Agathis borneensis	[11]
1-octen-3-yl acetate	Agathis atropurpurea, Araucaria cunninghamii, Araucaria heterophylla	[10,81]
1-tridecene	Araucaria cunninghamii	[81]
2(1H)-phenanthrenone	Agathis borneensis	[11]
2,2-dimethyl-valeroyl chloride	Wollemia nobilis	[106]
2,3-di-amino-2-methylpropanoic acid	Araucaria columnaris	[74]
2,4-dimethyl-furan	Araucaria columnaris	[74]

 Table 4. Cont.

Compound	Occurrence in the Family	References
2,3,3-trimethyl-octane	Agathis borneensis	[11]
2,4,6-trimethyl-octane	Agathis borneensis	[11]
2,5-dimethoxy-p-cymene	Agathis atropurpurea	[10]
2-acetyl-2-carene	Wollemia nobilis	[106]
2-pentyl-furan	Agathis robusta, Araucaria cunninghamii	[24,83]
3-4-methoxyphenyl-2-propenoic acid	Araucaria columnaris	[74]
3-ethyl-3-methyl-heptane	Agathis borneensis	[11]
3-methylene-1,7-octadiene	Wollemia nobilis	[106]
3-octanol	Araucaria cunninghamii	[81]
3-octanol acetate	Araucaria cunninghamii	[81]
3-trimethylsilyloxypropyl hexadecanoate	Araucaria cunninghamii	[84]
(3Z)-cembrene A	Araucaria heterophylla	[81]
(3Z)-hexenyl-2-methyl butanoate	Araucaria cunninghamii	[81]
(3Z)-hexenyl-butanoate	Araucaria cunninghamii	[81]
(3Z)-hexenyl hexanoate	Araucaria cunninghamii	[81]
4,4,5-trimethyl-2-hexene,3-ethyl-2,7-dimethyl octane	Agathis borneensis	[11]
4,11,11-trimethyl-8-methylene-bicyclo[7.2.0]undec-4-(Z)-ene	Agathis borneensis	[11]
4β,17-(acetoxy)-kauran-18-al	Wollemia nobilis	[106]
4-[[[[(1,2-dichloroethylidene) amino]oxy]carbonyl]amino]-methyl ester benzoic acid	Araucaria columnaris	[74]
4-methylene-2,8,8-trimethyl-2-vinyl-bicyclo[5.2.0]nonane	Agathis borneensis	[11]
5,15-rosadiene	Agathis macrophylla, Agathis moorei, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum	[8]
5-neo-cedranol	Araucaria cunninghamii	[81]
6-camphenol	Wollemia nobilis	[106]

Table 4. Cont.

Compound	Occurrence in the Family	Reference
6-dimethylcyclohexene	Agathis borneensis	[11]
6,6-dimethyl-2-methylene-bicyclo[2.2.1]-heptan-3-one	Wollemia nobilis	[106]
6-methoxy-2-methyl-2-phenyl-2H-1-benzopyran	Araucaria columnaris	[74]
6-methyl-5-hepten-2-one	Agathis philippinensis, Araucaria cunninghamii	[21,81]
7,11-dimethyl-3-methylene-1,6,10-dodecatriene	Wollemia nobilis	[106]
8a(2H)-phenanthrenol	Agathis borneensis	[11]
8-methylene	Agathis borneensis	[11]
8-oxo-cis-ocimene	Wollemia nobilis	[106]
9-epi-(E)-caryophyllene	Agathis robusta	[24]
9-epi-sclarene	Araucaria heterophylla	[63]
9-octadecenoic acid	Araucaria columnaris	[75]
9-octadecenoic acid methyl ester	Araucaria cunninghamii	[84]
10-nor-calamenen-10-one	Agathis robusta	[24]
13-epi-manool	Araucaria heterophylla	[81]
14-hydroxy-(Z)-caryophyllene	Araucaria cunninghamii	[81]
14-hydroxy-9-epi-(E)-caryophyllene	Araucaria cunninghamii	[81]
15-kaurene	Araucaria angustifolia, Araucaria cunninghamii, Araucaria heterophylla, Araucaria muelleri, Wollemia nobilis	[8,81]
15-phylocaldene	Wollemia nobilis	[106]
16-kaurene	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Agathis moorei, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria luxurians, Araucaria montana, Wollemia nobilis	[8,81,106]
16-phyllocladanol	Araucaria scopulorum	[8]
16-phyllocladene	Araucaria heterophylla	[63]

Table 4. Cont.

Compound	Occurrence in the Family	Reference
(+)-4-carene	Agathis dammara	[12]
(+)-15-beyerene	Araucaria araucana	[63]
(–)-7,13-abietadine	Araucaria bidwilli	[63]
(-)-8(14),15-pimaradiene	Araucaria heterophylla	[63]
(–)-13- <i>epi</i> -manoyl-oxide	Araucaria araucana	[63]
(–)-16-atisirene	Araucaria araucana	[63]
(–)-16-kaurene	Araucaria araucana, Araucaria bidwilli, Araucaria heterophylla	[63]
(–)-α-cadinol	Araucaria araucana	[65]
(–)-α-copaene	Araucaria araucana, Araucaria heterophylla	[63]
(–)-β-caryophyllene	Araucaria araucana, Araucaria heterophylla	[63]
(–)-δ-cadinene	Araucaria araucana	[63]
(–)-atisirene	Araucaria araucana	[65,66]
(–)-germacrene D	Araucaria heterophylla	[63]
(–)-iso-atisirene	Araucaria araucana	[66]
(–)-iso-kaurene	Araucaria araucana	[66]
(–)-kaurene	Araucaria araucana	[65,66]
(-)-rosa-5,15-diene	Araucaria araucana	[63]
(–)-sandaracopimaradiene	Araucaria heterophylla	[63]
(–)-sclarene	Araucaria araucana	[63]
(–)-trachylobane	Araucaria araucana	[63,65,66]
[1ar-(1a.α,4.β,4a.β,7.α,7a.β,7b.α]-decahydro-1,1,4,7- tetramethyl-1H-cycloprop[e]azulen-4-ol	Wollemia nobilis	[106]
α-amorphene	Araucaria cunninghamii, Araucaria heterophylla	[81]
α-bisabolol	Agathis dammara	[12]

Table 4. Cont.

Compound	Occurrence in the Family	References
α-cadinene	Araucaria heterophylla	[81]
α-cadinol	Agathis australis, Agathis microstachya, Agathis moorei, Araucaria angustifolia, Araucaria heterophylla, Wollemia nobilis	[8,81,106]
α-calacorene	Araucaria heterophylla	[81]
α-campholenal	Agathis robusta, Araucaria cunninghamii	[24,83]
α-caryophyllene	Agathis borneensis	[11]
α-cedrene epoxide	Agathis robusta	[24]
α-copaene	Agathis australis, Agathis atropurpurea, Agathis dammara, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis philippinensis, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,12,21,24,63,81,83]
α-cubebene	Agathis australis, Agathis atropurpurea, Agathis borneensis, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria scopulorum	[8,11,24,81,83]
α-cubene	Araucaria bidwilli	[63]
α-fenchene	Agathis atropurpurea, Agathis microstachya, Agathis philippinensis, Araucaria cunninghamii	[8,21,81]
α-guaiene	Araucaria heterophylla	[81]
α-gurjunene	Agathis australis, Agathis atropurpurea, Agathis microstachya, Agathis moorei	[8]
α-humulene	Agathis robusta, Araucaria cunninghamii	[24,81]
α-muurolol	Araucaria cunninghamii	[81]
α-muurolene	Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis robusta, Araucaria columnaris, Araucaria heterophylla, Araucaria hunsteinii, Araucaria montana, Araucaria scopulorum, Wollemia nobilis	[8,24,81,106]

Table 4. Cont.

Compound	Occurrence in the Family	References
α-phellandrene	Agathis dammara, Araucaria cunninghamii,	[12,81]
α-pinene	Agathis australis, Agathis atropurpurea, Agathis dammara, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis philippinensis, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria scopulorum, Wollemia nobilis	[8,12,21,24,81,83,87]
α-humulene	Araucaria cunninghamii, Araucaria heterophylla	[81,83]
α-muurolol	Araucaria cunninghamii, Araucaria heterophylla	[81]
α-phellandrene	Araucaria cunninghamii	[83]
α-selinene	Agathis robusta	[24]
α-terpinene	Agathis atropurpurea, Agathis microstachya, Agathis robusta, Araucaria cunninghamii, Araucaria heterophylla	[8,24,81,83]
α-terpineol	Agathis atropurpurea, Agathis dammara, Agathis microstachya, Agathis philippinensis, Araucaria cunninghamii, Araucaria heterophylla, Araucaria montana	[8,10,12,21,87]
α-terpinyl acetate	Agathis robusta	[24]
α-thujene	Agathis philippinensis, Agathis robusta, Araucaria cunninghamii	[8,21,24,81]
α-thujone	Araucaria cunninghamii	[83]
α-trans-bergamotene	Araucaria heterophylla	[81]
α-tricyclene	Agathis dammara	[12]
α-ylangene	Araucaria heterophylla	[81]
β-bisabolene	Agathis atropurpurea, Agathis dammara	[10,12]
β-bourbebene	Araucaria hunsteinii	[8]

Table 4. Cont.

Compound	Occurrence in the Family	References
β-bourbonene	Agathis australis, Agathis macrophylla, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria columnaris, Araucaria heterophylla, Araucaria montana, Araucaria scopulorum	[8,24,81]
β-calacorene	Araucaria cunninghamii	[83]
β-caryophyllene	Agathis australis, Agathis atropurpurea, Agathis borneensis, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,11,83,87]
β-chamigrene	Agathis robusta	[24]
β-copaen-4-α-ol	Agathis robusta	[24]
β-copaene	Agathis australis, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria cunninghamii, Araucaria heterophylla	[8,24,81]
β- <i>cis</i> -ocimene	Wollemia nobilis	[106]
β-cubebene	Agathis australis, Agathis atropurpurea, Agathis borneensis, Agathis macrophylla, Agathis microstachya, Agathis moorei, Araucaria bidwilli, Araucaria columnaris	[8,11,63]
β-elemene	Agathis macrophylla, Agathis microstachya, Araucaria angustifolia, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria muelleri, Araucaria scopulorum	[8,81,83]
β-myrcene	Agathis dammara, Agathis robusta, Wollemia nobilis	[12,24,106]
β-ocimene	Araucaria cunninghamii	[81]
β-oplopenone	Araucaria heterophylla	[81]
β-panasinsene	Araucaria cunninghamii	[81]

Table 4. Cont.

Compound	Occurrence in the Family	References
β-phellandrene	Agathis atropurpurea, Agathis microstachya, Araucaria hunsteinii, Wollemia nobilis	[8]
β-pinene	Agathis atropurpurea, Agathis dammara, Agathis microstachya, Agathis philippinensis, Agathis robusta, Araucaria angustifolia, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria scopulorum, Wollemia nobilis	[8,12,21,24,81,83,87 106]
β-santalene	Araucaria heterophylla	[81]
β-selinene	Agathis robusta, Araucaria cunninghamii	[24,81,83]
β-terpineol	Agathis philippinensis	[21]
β-ylangene	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Agathis moorei, Araucaria columnaris, Araucaria cunninghamii, Araucaria hunsteinii, Araucaria muelleri, Araucaria scopulorum	[8]
γ-cadinene	Agathis robusta, Araucaria araucana, Araucaria cunninghamii, Araucaria heterophylla	[24,65,81,83]
γ-elemene	Agathis microstachya, Araucaria scopulorum	[8]
γ-gurjunene	Araucaria heterophylla	[81]
γ-muurolene	Agathis robusta, Araucaria cunninghamii	[24,83]
γ-terpinene	Agathis atropurpurea, Agathis dammara, Agathis microstachya, Agathis philippinensis, Araucaria cunninghamii, Araucaria heterophylla, Wollemia nobilis	[8,10,12,21,81,83]
δ-3-carene	Araucaria cunninghamii	[81,83]
δ-amorphene	Araucaria heterophylla	[81]

Table 4. Cont.

Compound	Occurrence in the Family	References
δ-cadinene	Agathis australis, Agathis atropurpurea, Agathis borneensis, Agathis dammara, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,11,12,24,63,81,83]
δ-cadinol	Agathis microstachya, Agathis moorei	[8]
δ-carene	Wollemia nobilis	[106]
δ-elemene	Agathis robusta, Araucaria scopulorum	[8,24]
δ-terpineol	Araucaria cunninghamii	[83]
abietadiene	Araucaria heterophylla	[81]
abietate	Agathis borneensis	[11]
abietatriene	Araucaria cunninghamii, Araucaria heterophylla	[81]
acetophenone	Araucaria cunninghamii	[81]
alkyl chains	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8]
allo-aromadendrene	Agathis australis, Agathis microstachya, Agathis moorei, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,24,81,83]
androstenone	Agathis borneensis	[11]
<i>ar-</i> turmerone	Araucaria cunninghamii	[83]

Table 4. Cont.

Compound	Occurrence in the Family	References
arachidonic acid	Araucaria cunninghamii	[84]
aristolochene	Araucaria heterophylla	[81]
aromadendrene	Agathis australis, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,24,81,83]
aromadendrene (2)-oxide	Wollemia nobilis	[106]
benzoic acid	Araucaria columnaris	[74]
bergamol	Wollemia nobilis	[106]
beyerene	Araucaria cunninghamii	[83]
bicycloelemene	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Araucaria angustifolia, Araucaria columnaris, Araucaria luxurians, Araucaria muelleri	[8]
bicyclogermacrene	Agathis australis, Agathis atropurpurea, Agathis microstachya, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,81,83]
borneol	Agathis robusta	[24]
bornyl acetate	Agathis robusta	[24]
bicetyl	Agathis borneensis	[11]
bornyl acetate	Agathis atropurpurea, Wollemia nobilis	[10,106]
calacorene	Agathis australis, Agathis macrophylla, Agathis moorei, Araucaria columnaris, Araucaria cunninghamii, Araucaria hunsteinii, Araucaria scopulorum	[8]

Table 4. Cont.

Compound	Occurrence in the Family	References
calamenene	Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Araucaria columnaris, Araucaria hunsteinii, Araucaria luxurians, Araucaria scopulorum	[8]
camphene	Agathis atropurpurea, Agathis australis, Agathis dammara, Agathis microstachya, Agathis philippinensis, Agathis robusta, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Wollemia nobilis	[8,10,12,21,24,81,83, 87]
campherenone	Araucaria cunninghamii	[83]
carotol	Agathis robusta	[24]
carvone	Agathis atropurpurea, Agathis philippinensis, Agathis robusta, Wollemia nobilis	[10,21,24,106]
cariophyllene	Araucaria columnaris	[75]
caryophyllene oxide	Agathis borneensis, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,11,24,81,83,106]
cedr-8-en-15-ol	Araucaria columnaris	[75]
cetane	Agathis borneensis	[11]
cholesterol	Araucaria cunninghamii	[84]
cis-β-terpineol	Agathis atropurpurea	[10]
cis-p-mentha-1,8-dien-6-ol	Agathis philippinensis	[21]
cis-p-mentha-1(7),8-dien-2-ol	Agathis philippinensis	[21]
cis-pinocarvyl acetate	Agathis robusta	[24]
cis-sabinene hydrate	Agathis philippinensis	[21]
<i>cis</i> -thujopsenal	Araucaria cunninghamii	[81]
<i>cis</i> -thujopsene	Agathis robusta	[24]
copaene	Agathis borneensis	[11]

Table 4. Cont.

Compound	Occurrence in the Family	Reference
cubenol	Agathis australis, Agathis microstachya, Araucaria bidwilli, Araucaria columnaris, Araucaria hunsteinii, Araucaria luxurians, Araucaria scopulorum	[8]
cubitene	Araucaria heterophylla	[81]
cyclobuta[1,2:3,4]dicyclopentene decahydro-3a-methyl-6-methylene-1-(1-methylethyl)- [1S-(1. $\alpha$ ,3a. $\alpha$ ,3b. $\beta$ ,6a. $\beta$ ,6b. $\alpha$ )]	Wollemia nobilis	[106]
cyclocolorenone	Araucaria cunninghamii	[81]
cyclohexene	Agathis borneensis	[11]
cyclononasiloxane	Araucaria cunninghamii	[84]
dehydro-1,8-cineol	Agathis atropurpurea	[10]
dihydro-α-terpineol	Agathis philippinensis	[21]
dehydro-abeitol	Araucaria cunninghamii	[81]
dihydro-carveol	Agathis atropurpurea	[10]
dihydro-carvyl acetate	Agathis robusta	[24]
dodecane	Agathis borneensis	[11]
di-isooctyl adipate	Araucaria cunninghamii	[84]
docosahexaenoic acid	Araucaria cunninghamii	[84]
docosyl acetate	Araucaria columnaris	[75]
dolabradiene	Araucaria cunninghamii, Araucaria heterophylla	[63,81]
(E)-β-farnesene	Araucaria cunninghamii, Araucaria heterophylla	[81]
(E)-β-ocimene	Agathis philippinensis, Araucaria cunninghamii	[21,81]
(E)-3(10)-caren-2-ol	Wollemia nobilis	[106]
(E)-3(10)-caren-4-ol	Wollemia nobilis	[106]
(E)-α-ionone	Agathis robusta	[24]
E-biformene	Araucaria bidwilli	[63]
(E)-caryophyllene	Agathis robusta, Araucaria cunninghamii, Araucaria heterophylla	[24,81]
(E)-myroxide	Agathis robusta	[24]
(E)-nerolidol	Araucaria heterophylla	[81]

Table 4. Cont.

Compound	Occurrence in the Family	References
(E)-9-octadecenoic acid ethyl ester	Araucaria cunninghamii	[84]
eicosamethyl-cyclodecasiloxane	Araucaria cunninghamii	[84]
eicosane	Agathis borneensis	[11]
ent-rosa-5,15-diene	Araucaria heterophylla	[81]
<i>ep</i> i-α-cadinol	Araucaria heterophylla	[81]
epi-α-cedrenal	Araucaria heterophylla	[81]
<i>epi-</i> α-selinene	Agathis robusta	[24]
<i>epi-</i> cubenol	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Araucaria columnaris, Araucaria hunsteinii, Araucaria luxurians, Araucaria scopulorum	[8]
epi-cyclocolorenone	Araucaria cunninghamii	[81]
<i>epi</i> -globulol	Araucaria scopulorum	[8]
<i>epi</i> -laurenene	Araucaria heterophylla	[81]
<i>epi-</i> zonarene	Araucaria heterophylla	[63]
ethyl 9-octadecenoate	Araucaria cunninghamii	[84]
ethyl heptadecanoate	Araucaria cunninghamii	[84]
farnesane	Agathis borneensis	[11]
farnesol	Agathis borneensis	[11]
fenchone	Agathis philippinensis	[21]
filipendulal	Wollemia nobilis	[106]
geraniolene	Araucaria araucana	[65,66]
germacrene B	Agathis robusta, Araucaria heterophylla, Wollemia nobilis	[24,81,106]

Table 4. Cont.

Compound	Occurrence in the Family	References
germacrene D	Agathis australis, Agathis atropurpurea, Agathis borneensis, Agathis dammara, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,11,12,63,81,83,106
globulol	Agathis australis, Agathis atropurpurea, Agathis microstachya, Agathis moorei, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,81]
heptacosane	Agathis borneensis	[11]
hexyl butanoate	Araucaria cunninghamii	[81]
hexyl iso-valerate	Araucaria cunninghamii	[81]
hibaene	Agathis australis, Agathis ovata, Araucaria angustifolia, Araucaria araucana, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Wollemia nobilis	[8,65,66,81]
humulene	Agathis australis, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8]
humulene epoxide II	Agathis robusta, Araucaria cunninghamii	[24,81,83]
icosane	Agathis borneensis	[11]
intermedeol	Agathis robusta	[24]
iso-aromadendrene epoxide	Wollemia nobilis	[106]
iso-bornyl acetate	Agathis robusta	[24]

Table 4. Cont.

Compound	Occurrence in the Family	References
iso-geraniol	Wollemia nobilis	[106]
iso-longifolene	Araucaria heterophylla	[81]
<i>iso</i> -pimara-9(11),15-diene	Araucaria heterophylla	[81]
kaur-16-en-18-oic acid methyl ester	Wollemia nobilis	[106]
kaur-16-en-19-ol	Araucaria columnaris	[75]
kaurene	Araucaria cunninghamii	[83]
L-valine-N-[N-[N2,N6-bis-(1-oxodecyl)-L-lysyl]glycyl]-methyl ester	Araucaria cunninghamii	[84]
laurenan-2-one	Araucaria cunninghamii	[81]
laurenene	Araucaria cunninghamii, Araucaria heterophylla	[81,83]
ledol	Araucaria hunsteinii, Araucaria scopulorum	[8]
limonen-10-ol	Agathis philippinensis	[21]
limonene	Agathis australis, Agathis atropurpurea, Agathis dammara, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis philippinensis, Agathis robusta, Araucaria angustifolia, Araucaria araucana, Araucaria bidwilli, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Wollemia nobilis	[8,10–12,21 65,81,87]
longipinanol	Araucaria cunninghamii	[81]
luxuriadiene	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum	[8,81]
<i>m-</i> cymenene	Agathis atropurpurea	[10]

Table 4. Cont.

Compound	Occurrence in the Family	References
manool	Araucaria columnaris	[75]
manool oxide	Araucaria heterophylla	[81]
menthol	Araucaria cunninghamii	[83]
methyl-β-D-mannofuranoside	Agathis borneensis	[11]
methyl-chavicol	Agathis robusta	[24]
methyl-eugenol	Araucaria hunsteinii	[8]
methyl-isobutyrate	Agathis borneensis	[11]
methyl-(Z)-5,11,14,17-eicosatetraenoate	Araucaria columnaris	[75]
myrcene	Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Agathis moorei, Araucaria angustifolia, Araucaria bidwilli, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8]
myrtenol	Agathis robusta, Araucaria cunninghamii, Wollemia nobilis	[24,81,83, 106]
myrtenyl acetate	Agathis robusta	[24]
N,N-bis(2-hydroxyethyl)dodecanamide	Araucaria columnaris	[75]
n-docosane	Agathis borneensis	[11]
n-heptadecane	Agathis borneensis	[11]
n-hexacosane	Agathis borneensis	[11]
n-nonadecane	Agathis borneensis	[11]
<i>n</i> -nonane	Araucaria cunninghamii, Araucaria heterophylla	[11]
n-octacosane	Agathis borneensis	[11]
<i>n</i> -pentacosane	Agathis borneensis	[11]

Table 4. Cont.

Compound	Occurrence in the Family	References
n-pentadecane	Agathis borneensis	[11]
n-pentadecanoic acid	Agathis borneensis	[11]
n-tetradecane	Agathis borneensis	[11]
<i>n</i> -tetratriacontane	Agathis borneensis	[11]
n-triacontane	Agathis borneensis	[11]
n-tridecane	Araucaria cunninghamii	[11]
n-undecane	Araucaria cunninghamii, Araucaria heterophylla	[11]
naphthalene	Agathis borneensis	[11]
neral	Agathis philippinensis	[21]
nonane	Araucaria cunninghamii	[83]
nor-pristane	Agathis borneensis	[11]
o-cymene	Agathis dammara	[12]
O-ethyl-hydroxylamine	Araucaria cunninghamii	[84]
occidentalol	Agathis robusta, Araucaria cunninghamii	[24,81]
occidentalol acetate	Agathis robusta, Araucaria cunninghamii	[24,81]
octadecane	Agathis borneensis	[11]
octadecyl iodide	Agathis borneensis	[11]
octane	Agathis borneensis	[11]
octen-1-ol acetate	Wollemia nobilis	[106]
octyl ether	Agathis borneensis	[11]
<i>p</i> -cymen-8-ol	Agathis macrophylla, Agathis robusta, Agathis philippinensis, Araucaria cunninghamii	[8,21,24]

Table 4. Cont.

Compound	Occurrence in the Family	References
<i>p</i> -cymene	Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis philippinensis, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Wollemia nobilis	[8,21,24,81]
<i>p</i> -cymenene	Agathis robusta	[24]
<i>p</i> -menth-8-en-2-ol acetate	Wollemia nobilis	[106]
p-mentha-1,4-dien-7-ol	Araucaria cunninghamii	[83]
<i>p</i> -mentha-3,8-diene	Agathis robusta	[24]
p-mentha-6,8-dien-2-ol acetate	Wollemia nobilis	[106]
palmitic acid	Agathis borneensis, Araucaria columnaris	[11,75]
palmitic acid ethyl ester	Araucaria cunninghamii	[84]
palustrol	Agathis australis, Agathis macrophylla, Agathis microstachya, Araucaria angustifolia, Araucaria columnaris, Araucaria cunninghamii, Araucaria luxurians	[8]
phyllocladanol	Araucaria heterophylla	[81]
phyllocladene	Agathis atropurpurea, Agathis microstachya, Agathis ovata, Araucaria angustifolia, Araucaria cunninghamii, Araucaria heterophylla, Araucaria montana, Araucaria muelleri	[8,81,83]
pimaradiene	Araucaria cunninghamii, Araucaria heterophylla	[81]
pinocarvone	Agathis robusta	[24]
rimuene	Agathis robusta, Araucaria heterophylla	[8,24,81]
sabinene	Agathis atropurpurea, Agathis dammara, Agathis microstachya, Agathis philippinensis, Agathis robusta, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Wollemia nobilis	[8,12,21,24, 81,83]

Table 4. Cont.

Compound	Occurrence in the Family	References
sandaracopimara-8(14),15-diene	Araucaria heterophylla	[81]
sandaracopimar-15-en-8.byl acetate	Wollemia nobilis	[106]
sandaracopimarinol	Araucaria cunninghamii, Araucaria heterophylla	[81]
sativene	Araucaria cunninghamii, Wollemia nobilis	[81,106]
sclarene	Agathis australis, Agathis ovata, Araucaria bidwilli, Araucaria columnaris, Araucaria heterophylla, Araucaria hunsteinii, Araucaria muelleri, Araucaria scopulorum	[8,63,81]
sesquisabinene B	Araucaria cunninghamii	[83]
shyobunol	Araucaria cunninghamii	[83]
sorbaldehyde	Agathis borneensis	[11]
squamulosone	Araucaria cunninghamii	[81]
spathulenol	Agathis australis, Agathis atropurpurea, Agathis macrophylla, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,24,81,83, 106]
T-cadinol	Agathis australis, Agathis microstachya, Agathis moorei, Araucaria columnaris, Araucaria hunsteinii, Araucaria scopulorum	[8]
T-muurolol	Agathis australis, Agathis microstachya, Agathis moorei, Araucaria cunninghamii, Araucaria hunsteinii	[8,83]
T(Z)-β-ocimene	Araucaria cunninghamii	[83]
terpinen-4-ol	Agathis dammara, Agathis philippinensis, Agathis robusta, Araucaria cunninghamii	[12,21,24,81 <sub>83</sub> ]

Table 4. Cont.

Compound	Occurrence in the Family	References
terpinene	Wollemia nobilis	[8]
terpinolene	Agathis atropurpurea, Agathis dammara, Agathis microstachya, Agathis philippinensis, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Wollemia nobilis	[8,10,12,21, 81]
tert-butoxy 2 ethoxyethane	Araucaria columnaris	[74]
tetrahydro-geranyl acetate	Wollemia nobilis	[106]
thiophene	Agathis borneensis	[11]
thuja-2,4(10)-diene	Agathis robusta	[24]
trans-β-terpineol	Agathis robusta	[24]
trans-calamenene	Agathis robusta	[24]
trans-carveol	Agathis robusta, Araucaria cunninghamii	[24,83]
trans-phytol	Agathis borneensis	[11]
trans-longipinocarveol	Wollemia nobilis	[106]
trans-muurola-4(14),5-diene	Araucaria heterophylla	[81]
trans-p-mentha-1(7),8-dien-2-ol	Agathis philippinensis	[21]
trans-p-mentha-1,8-dien-6-ol	Agathis philippinensis	[21]
trans-pinocarveol	Agathis philippinensis	[21]
trans-pinocarvyl acetate	Agathis robusta	[24]
trans-piperitol	Agathis philippinensis	[21]
trans-sabinene hydrate	Agathis robusta	[24]
trans-sabinene hydrate acetate	Agathis robusta	[24]
trans-sabinol	Agathis robusta	[24]
$trans$ - $Z$ - $\alpha$ -bisabolene epoxide	Wollemia nobilis	[106]
tricosyl acetate	Araucaria columnaris	[75]
tricyclene	Agathis australis, Agathis atropurpurea, Agathis philippinensis, Araucaria cunninghamii	[8,10,21,81, 83]

Table 4. Cont.

Compound	Occurrence in the Family	References
undecane	Araucaria cunninghamii	[83]
untriacontane	Agathis borneensis	[11]
verbenol	Wollemia nobilis	[106]
verbenone	Agathis robusta, Araucaria cunninghamii, Wollemia nobilis	[24,83,106]
viridiflorene	Agathis australis, Agathis microstachya, Agathis moorei, Agathis ovata, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria scopulorum	[8,81]
viridiflorol	Agathis australis, Agathis atropurpurea, Agathis microstachya, Agathis moorei, Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria heterophylla, Araucaria hunsteinii, Araucaria luxurians, Araucaria montana, Araucaria muelleri, Araucaria scopulorum, Wollemia nobilis	[8,81]
(Z)-2-decenal	Wollemia nobilis	[106]
(Z)-β-farnesene	Agathis robusta	[24]
(Z)-β-ocimene	Araucaria cunninghamii	[81]
Z-β-terpineol	Wollemia nobilis	[106]
Z-biformene	Araucaria bidwilli	[63]

**Table 5.** Occurrence of polar fraction metabolites in Araucariaceae species.

Compound	Occurrence in the Genera	References
1,2-di-palmitoleoyl-3-myristoyl-sn-glycerol	Wollemia nobilis	[29]
1,3,4,5-tetrahydroxy-cyclohexane-carboxylic acid	Araucaria angustifolia	[48]
1,5,8,11,14,17-eicosapentaenoicacid	Agathis robusta	[25]
$2\alpha$ , $3\alpha$ , $19\alpha$ -trihydroxyurs-12-en-28-oic acid	Agathis macrophylla	[17]
2α,3β,19α-trihydroxyurs-12-en-28-oic acid	Agathis macrophylla	[17]
2α,3β- dihydroxyurs-12-en-28-oic acid	Agathis macrophylla	[17]
2α-hydroxy-8(14),15-sandaracopimaradien-18-oic acid	Wollemia nobilis	[31]
(2S)-1,2-di-O-[(9Z,12Z,15Z)-octadeca-9,12,15-trienoyl]-3-O-β-D- galactopyranosyl glycerol	Agathis robusta	[22]
2-O-acetyl-11-keto-boswellic acid	Araucaria bidwilli	[69]
3α-hydroxy-(13S)-l6- <i>nor</i> -pimar-7-en-l5-oic acid	Agathis macrophylla	[18]
3β,22,23- trihydroxystigmast-5-en-7-one	Agathis macrophylla	[17]
3β-hydroxymegastigman-5-en-9- <i>O</i> -β-D-glucopyranoside	Agathis macrophylla	[17]
3β-hydroxystigmast-6-one	Agathis macrophylla	[17]
3-O-methyl-D-chiroinositol	Araucaria angustifolia	[48]
3-glucoside-dihydro-quercetin	Araucaria angustifolia	[48]
$4(15)$ -eudesmene- $1\beta$ , $6\alpha$ -diol	Agathis macrophylla	[17]
4'-O-methyl-scutellarein	Wollemia nobilis	[30]
(4S,5R,9S,10R)-methyl-19-hydroxy-15,16-dinorlabda-8(17),11-E-dien-13-oxo-18-oate	Agathis macrophylla	[16]
(4R,5R,9R,10R,13R)-13-hydroxypodocarp-8(14)-en-19-oic acid	Agathis macrophylla	[16]
(4R,5R,9R,10R,13S)-13-hydroxypodocarp-8(14)-en-19-oic acid	Agathis macrophylla	[16]
4-hydroxy-benzaldehyde	Araucaria angustifolia	[58]
4-nitrophenyl-β-D-glucopyranoside	Araucaria angustifolia	[48]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
4'-methoxy-tectorigenin	Araucaria angustifolia	[48]
4-n-butoxylphenylpropanetriol	Araucaria columnaris	[80]
5-(E)-coumaroyloxy-quinic acid <i>n</i> -butyl ester	Araucaria cunninghamii	[79]
5-( $Z$ )-coumaroyloxyquinic acid $n$ -butyl ester	Araucaria cunninghamii	[79]
5-methoxy-lariciresinol-9-acetate	Araucaria angustifolia	[58]
5'-methoxy-lariciresinol-9-acetate	Araucaria angustifolia	[58]
5-methoxy-pinoresinol	Araucaria angustifolia	[58]
5-methoxy-eudesmin	Araucaria angustifolia	[58]
5-p-cis-coumaroyl-quinic acid	Araucaria columnaris	[80]
5-p-trans-coumaroyl-quinic acid	Araucaria columnaris	[80]
6'-O-acetyl-pina-2-ene-4,10-diol-10-O-β-D-glucopyranoside	Wollemia nobilis	[29]
(6R,9S)-3-oxo-α-ionol-9-O-β-D-glucopyranoside	Araucaria columnaris	[80]
(6S,9R)-roseoside	Agathis macrophylla	[17]
(6S,9S)-roseoside	Araucaria columnaris	[80]
$7\alpha$ ,15 $\alpha$ -dihydroxystigmast-4-en-3-one	Agathis macrophylla	[17]
7-hydroxy-labda-8(17),13(16),14-trien-19-yl-7'-O-methyl-(E)- coumarate	Araucaria bidwilli	[69]
7-hydroxy-labda-8(17),13(16),14-trien-19-yl-7'-O-methyl-(Z)- coumarate	Araucaria bidwilli	[69]
7-hydroxy-labda-8(17),13(16),14-trien-19-yl-( <i>E</i> )-coumarate	Araucaria bidwilli	[69]
7-hydroxy-labda-8(17),13(16),14-trien-19-yl-(Z)-coumarate	Araucaria bidwilli	[69]
7'-hydroxy-lariciresinol	Araucaria angustifolia	[58]
7'-hydroxy-lariciresinol-9-acetate	Araucaria angustifolia	[58]
7'-methoxy-lariciresinol	Araucaria angustifolia	[58]
7'-methoxy-lariciresinol-9-acetate	Araucaria angustifolia	[58]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
7-oxocallitrisic acid	Araucaria bidwilli	[69]
7-O-methyl-agathisflavone	Agathis alba, Araucaria araucana, Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii, Araucaria rulei, Wollemia nobilis	[6,7,29,64,70,89, 107]
7"-O-methyl-amentoflavone	Araucaria araucana, Araucaria columnaris, Araucaria cunninghamii,	[64,70]
7-O-methyl-cupressuflavone	Agathis alba, Agathis atropurpurea, Agathis australis, Agathis ovata, Agathis robusta, Araucaria bidwilli, Wollemia nobilis	[6,7,9,31,70]
7''-O-methyl-agathisflavone	Agathis alba, Agathis atropurpurea, Agathis australis, Agathis ovata, Agathis robusta, Wollemia nobilis	[6,9,22,31,33]
7''-O-methyl-robustaflavone	Araucaria angustifolia	[56]
4',7''-di-O-methyl-agathisflavone	Araucaria bidwilli	[68]
4',4''-di-O-methyl-amentoflavone	Araucaria bidwilli	[68]
4',4'"-di-O-methyl-amentoflavone	Araucaria angustifolia	[57]
4',4'"-di-O-methyl-cupressuflavone	Agathis macrophylla	[17]
7,4'-di-O-methyl-amentoflavone	Araucaria cunninghamii	[70]
$7$ $\!$	Agathis alba, Araucaria columnaris, Araucaria cunninghamii, Araucaria rulei, Wollemia nobilis	[7,28,29,33,70,89, 107]
7,7''-di-O-methyl-agathisflavone	Agathis alba, Agathis atropurpurea, Agathis australis, Agathis robusta, Agathis ovata, Araucaria bidwilli, Araucaria columnaris	[6,9,70]
7,7"-di-O-methyl-amentoflavone	Araucaria columnaris	[70]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
7,7''-di-O-methyl-cupressuflavone	Agathis alba, Agathis atropurpurea, Agathis australis, Agathis ovata, Agathis robusta, Araucaria araucana, Araucaria bidwilli, Araucaria cunninghamii, Araucaria rulei, Wollemia nobilis	[6,7,9,64,70,89, 107]
7,4',7''-tri-O-methyl-agathisflavone	Agathis atropurpurea, Agathis australis, Agathis ovata, Araucaria bidwilli	[9,69]
7,4',4'"-tri-O-methyl-amentoflavone	Araucaria angustifolia	[57]
7,4',4'"-tri-O-methyl-agathisflavone	Wollemia nobilis	[29,32,107]
7,4',7''-tri-O-methyl-cupressuflavone	Agathis atropurpurea, Agathis australis, Agathis ovata, Araucaria columnaris, Araucaria cunninghamii, Wollemia nobilis	[9,69,70,80,107]
7,7'',4'"-tri-O-methyl-agathisflavone	Araucaria columnaris	[70]
7,7'',4''''-tri-O-methyl-cupressuflavone	Araucaria rulei	[89]
7, 4',7''-tri-O-methyl-amentoflavone	Araucaria angustifolia, Araucaria columnaris	[57,70]
7,7'',4'"-tri-O-methyl-amentoflavone	Wollemia nobilis	[29]
7,4',7'',4'"'-tetra-O-methyl-agathisflavone	Agathis australis, Agathis macrophylla, Agathis ovata, Wollemia nobilis	[9,17,107]
7,4′,7′′,4′″-tetra-O-methyl-amentoflavone	Araucaria angustifolia, Araucaria columnaris, Araucaria cunninghamii, Araucaria rulei, Wollemia nobilis	[48,70,89,107]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
7,4',7'',4'''-tetra-O-methyl-cupressuflavone	Agathis australis, Agathis ovata, Araucaria columnaris, Araucaria cunninghamii, Araucaria rulei, Wollemia nobilis	[9,70,89,107]
7,4',7'',4'"'-tetra-O-methyl-robustaflavone	Wollemia nobilis	[29]
7-O-methyl-6-hydroxy-apigenin	Araucaria bidwilli	[68]
8,11,13-abietatrien-15-ol	Agathis macrophylla	[16]
(13S)-pimar-7-en-3α,15,16-triol	Agathis macrophylla	[18]
13-epi-cupressic acid	Araucaria heterophylla	[86]
13-O-acetyl-13- <i>epi</i> -cupressic acid	Araucaria heterophylla	[86]
13-oxo-podocarp-8(14)-en-19-oate	Agathis macrophylla	[16]
15,19-diacetoxylabd-8(17)-en	Araucaria araucana	[61]
15ξ-hydroxy-pinusolidic acid	Agathis macrophylla	[16]
15-acetoxylabd-8(17)-en-19-ol	Araucaria araucana	[61]
15-acetoxy-imbricatolal	Araucaria araucana	[59,61]
15-acetoxy- imbricatolic acid	Araucaria araucana	[59–61]
15-formyloxy-imbricatolal	Araucaria araucana, Wollemia nobilis	[31,59]
15-formyloxy-imbricatolicacid	Wollemia nobilis	[31]
15-hydroxy-imbricatolal	Araucaria araucana	[59-61]
15-hydroxy-imbricatolic acid	Araucaria araucana	[59]
15-nor-14-oxolabda-8(17),12E-dien-19-oicacid, 13-oxo-podocarp-8(14)-en-19-oic acid	Agathis macrophylla	[16]
16-hydroxy-8(17),13-labdadien-15,16-olid-19-oic acid	Agathis macrophylla	[16]
19-hydroxylabd-8(17)-en-15-oic acid	Araucaria araucana	[61]
19-noranticopalic acid	Agathis lanceolata	[14]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
α-linolenic acid	Agathis robusta	[25]
(–)-epi-afzelechin p-hydroxybenzoate	Araucaria angustifolia	[46]
(–)-epi-afzelechin protocatechuate	Araucaria angustifolia	[46]
(–)-epi-catechin	Araucaria angustifolia	[46,55]
(–)seco-isolariciresinol	Araucaria angustifolia	[54]
β-sitosterol	Agathis macrophylla, Araucaria angustifolia, Araucaria columnaris	[17,44,75]
β-sitosterol-3-O-glucopyranoside	Araucaria bidwilli	[69]
β-sitosterol acetate	Araucaria columnaris	[75]
abietic acid	Araucaria columnaris, Agathis macrophylla	[18,19,75]
acetyl-isocupressic acid	Wollemia nobilis	[28–30,32,33]
agatharesinol	Agathis macrophylla	[18]
agathic acid	Agathis macrophylla, Agathis microstachya, Araucaria angustifolia, Wollemia nobilis	[18–20,29,32,44]
agathic acid dimethyl ester	Araucaria columnaris	[75]
agathisflavone	Agathis alba, Agathis atropurpurea, Agathis australis, Agathis ovata, Agathis robusta, Araucaria bidwilli, Araucaria columnaris, Araucaria rulei, Wollemia nobilis	[6,9,22,31,70,89]
agatholic acid	Agathis lanceolata, Araucaria angustifolia, Araucaria araucana	[15,44,61]
alanine	Wollemia nobilis	[29,33]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
amentoflavone	Agathis macrophylla, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria rulei	[6,17,52,53,70, 89]
angustanoic acid F	Agathis macrophylla	[16]
apigenin	Araucaria angustifolia	[45]
arachidonic acid	Agathis robusta	[25]
arginine	Wollemia nobilis	[28]
benzoic acid	Araucaria angustifolia	[46]
bilobetin	Agathis alba, Araucaria angustifolia, Araucaria bidwilli	[6,56,70]
bishomolinoleic acid	Agathis robusta	[25]
bishomo-α-linolenic acid	Agathis robusta	[25]
cabreuvin	Araucaria angustifolia	[57]
caffeic acid	Araucaria cunninghamii, Wollemia nobilis	[31,32,82]
catechin	Araucaria angustifolia, Araucaria columnaris, Araucaria cunninghamii	[45,49,55,75,82]
catechol	Agathis macrophylla	[17]
cis-communic acid	Agathis microstachya	[20]
<i>cis</i> -vaccenic acid	Agathis robusta	[25]
chlorogenic acid	Araucaria columnaris, Araucaria cunninghamii	[75,82]
corchoionoside C	Agathis macrophylla	[17]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
cupressuflavone	Agathis robusta, Araucaria angustifolia, Araucaria bidwilli, Araucaria columnaris, Araucaria rulei, Wollemia nobilis	[6,22,31,56,70, 89]
D-lactic acid	Wollemia nobilis	[29,33]
dactylifric acid	Wollemia nobilis	[31]
dodecanoic acid	Araucaria angustifolia	[48]
ellagic acid	Araucaria cunninghamii	[82]
ent-8β,15-labd-E-13-ene-diol	Araucaria bidwilli	[72]
ent-l5-acetoxy-labda-8,E-13-diene	Araucaria bidwilli	[72]
ent-19-(E)-coumaroyloxy-labda-8(17),13(16),14-triene	Araucaria cunninghamii	[79]
ent-19-(Z)-coumaroyloxy-labda-8(17),13(16),14-triene	Araucaria cunninghamii	[79]
<i>ent</i> -labda-8, <i>E</i> -13-dien-15-ol	Araucaria bidwilli	[72]
<i>epi-</i> catechin	Araucaria angustifolia, Araucaria cunninghamii	[45,49,82]
epi-pinoresinol	Araucaria angustifolia	[58]
eriodictyol-O-hexoside	Araucaria angustifolia	[55]
eudesmin	Araucaria angustifolia, Araucaria araucana	[44,50,51,54,57, 58,62]
ferruginol	Araucaria angustifolia	[58]
ferulic acid	Araucaria columnaris	[75]
ferulic acid hexoside	Araucaria angustifolia	[55]
gallic acid	Araucaria columnaris, Araucaria cunninghamii	[73,75,82]
ginkgetin	Araucaria angustifolia	[52,53]
glucose	Wollemia nobilis	[28–30,33]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
hexadecanoic acid	Araucaria angustifolia	[48]
hinokiflavone	Araucaria bidwilli, Araucaria columnaris, Araucaria cunninghamii	[6,70]
hinokiresinol	Araucaria angustifolia	[54,58]
hydroquinone	Araucaria angustifolia	[58]
imbricatolic acid	Araucaria angustifolia, Araucaria araucana	[44,60,61]
irisolidone	Araucaria angustifolia	[57]
iso-orientin	Araucaria columnaris	[73]
iso-vitexin	Araucaria columnaris	[73]
isocupressic acid	Wollemia nobilis	[28,29,32]
isolariciresinol	Araucaria angustifolia	[50,51,54,58]
isolariciresinol-4'-methyl ether	Araucaria angustifolia	[50,51]
isolariciresinol-acetate	Araucaria angustifolia	[58]
junicedric acid	Araucaria araucana	[61]
kaempferol	Araucaria cunninghamii	[82]
kaur-16-en-3α,l3-diol	Agathis macrophylla	[18]
kauran-3α,l3,16a-triol	Agathis macrophylla	[18]
kayaflavone	Araucaria cunninghamii	[70]
kolavenic acid	Araucaria bidwilli	[67]
labda-8(14),15(16)-dien-3β-ol	Araucaria cunninghamii	[79]
labda-8(17),14-diene	Araucaria heterophylla	[86]
labd-8(17)-en-15,19-dial	Araucaria araucana	[61]
labda-8(20),13-dien-15-oic acid	Araucaria bidwilli	[67]
labda-8(20), 13-dien-15,19-dioic acid	Araucaria bidwilli	[67]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
lambertianic acid	Agathis macrophylla	[16]
lariciresinol	Araucaria angustifolia, Araucaria araucana	[50,51,57,58,62]
lariciresinol-4,4'-dimethyl ether-9-acetate	Araucaria angustifolia	[58]
lariciresinol-4-methyl ether	Araucaria angustifolia, Araucaria araucana	[58,62]
lariciresinol-4'-methyl ether	Araucaria angustifolia	[58]
lariciresinol-4-methyl ether-9-acetate	Araucaria angustifolia	[58]
lariciresinol-9-acetate	Araucaria angustifolia	[58]
linoleic acid	Agathis robusta	[25]
luteolin	Araucaria columnaris	[75]
methyl <i>ent-</i> 8α-hydroxy-labd- <i>E</i> -l3-en-15-oate	Araucaria bidwilli	[72]
methyl <i>ent-</i> 8β-hydroxy-labd- <i>E-</i> l3-en-15-oate	Araucaria bidwilli	[72]
methyl-15-hydroxy-abietate	Agathis microstachya	[20]
methyl-15-hydroxy-dehydroabietate	Agathis microstachya	[20]
methyl-communate	Araucaria columnaris	[75]
methyl-(E)-communate	Wollemia nobilis	[28,33]
methyl abietate	Agathis microstachya	[20]
methyl lambertianate	Agathis macrophylla	[16]
methyl sandaracopimarate	Agathis lanceolata, Agathis microstachya	[15,20]
myricetin	Araucaria columnaris	[75]
nyasol	Araucaria angustifolia	[58]
neo-abietic acid	Agathis microstachya	[20]
octadecyl-(E)-ferulate	Araucaria angustifolia	[57]
octadecyl-(Z)-ferulate	Araucaria angustifolia	[57]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
octadecyl-(E)-p-coumarate	Araucaria angustifolia	[57]
octadecyl-(Z)-p-coumarate	Araucaria angustifolia	[57]
oleic acid	Agathis robusta	[25]
orientin	Araucaria columnaris	[73]
p-coumaric acid	Araucaria angustifolia	[58]
p-hydroxybenzoic acid	Araucaria angustifolia	[46]
pheophorbide a	Wollemia nobilis	[32]
phloretic acid	Araucaria bidwilli	[69]
pinitol	Wollemia nobilis	[29]
pinoresinol	Araucaria angustifolia, Araucaria araucana	[54,57,58,62]
pinoresinol monomethyl ether	Araucaria angustifolia	[54,58]
pinusolide	Agathis macrophylla	[16]
pinusolidic acid	Agathis macrophylla	[16]
prodelphinidin B	Araucaria angustifolia	[55]
protocatechuic acid	Araucaria angustifolia, Wollemia nobilis	[31,46,55]
quercetin	Agathis macrophylla, Araucaria angustifolia, Araucaria columnaris, Araucaria cunninghamii	[17,45,46,75,82]
quercetin-3-O-glucoside	Araucaria angustifolia	[55]
quinic acid	Araucaria columnaris, Wollemia nobilis	[29,33,80]
raffinose	Wollemia nobilis	[33]
robustaflavone	Araucaria rulei	[89]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
rutin	Araucaria angustifolia, Agathis robusta, Araucaria columnaris	[22,49,75]
sandaracopimaradienol	Agathis lanceolata	[15]
sandaracopimaric acid	Araucaria araucana, Wollemia nobilis	[28-30,32,33,61]
seco-isolariciresinol	Araucaria angustifolia, Araucaria araucana	[50,51,58,62]
seco-isolariciresinol-4-methyl ether-9'-acetate	Araucaria angustifolia	[58]
seco-isolariciresinol-4-methyl ether-9,9'-diacetate	Araucaria angustifolia	[58]
seco-isolariciresinol-9'-acetate	Araucaria angustifolia	[58]
seco-isolariciresinol-9,9'-diacetate	Araucaria angustifolia	[58]
shikimic acid	Agathis robusta, Wollemia nobilis	[22,28–30,32,33]
shikimic acid <i>n</i> -butyl ester	Araucaria cunninghamii	[79]
shonanin	Araucaria angustifolia	[58]
sitosterol	Agathis macrophylla	[18]
stigmastan-3,5-diene	Araucaria columnaris	[75]
succinic acid	Wollemia nobilis	[33]
sucrose	Wollemia nobilis	[28,29,33]
sugiol	Araucaria angustifolia	[44]
taxifolin	Araucaria columnaris	[73]
taxifolin-3-O-glucopyranoside	Araucaria columnaris	[73]
tri-linolenoyl-sn-glycerol	Wollemia nobilis	[29]
trans-communic acid	Agathis microstachya, Araucaria angustifolia	[20,57]

 Table 5. Cont.

Compound	Occurrence in the Genera	References
umbelliferone	Araucaria cunninghamii	[82]
vanillic acid	Araucaria columnaris	[75]
vitexin	Araucaria columnaris	[73]
wollemol	Wollemia nobilis	[28,33]
wollemolide	Wollemia nobilis	[30,31]

Plants 2020, 9, 888 66 of 73

## 7. Chemotaxonomy of the Araucariaceae Family

As Tables 4 and 5 clearly show, the phytochemistry of the Araucariaceae family is quite complex. Several metabolites belonging to different classes of natural compounds have been evidenced within it. Yet, none of them have an occurrence spread in all of it even if some compounds have been isolated in many different species. Conversely, other compounds have been isolated in specific species, if not specific exemplars and this fact is not atypical since the qualitative and quantitative content in secondary metabolites of plants is much affected by environmental and genetic factors [26].

Nevertheless, among the essential oil metabolites, the most common compounds were found to be: 16-kaurene,  $\alpha$ -copaene,  $\alpha$ -cubebene,  $\alpha$ -pinene,  $\beta$ -bourbonene,  $\beta$ -caryophyllene,  $\beta$ -cubebene,  $\beta$ -elemene,  $\beta$ -pinene,  $\beta$ -ylangene,  $\delta$ -cadinene, *allo*-aromadendrene, aromadendrene, bicyclogermacrene, camphene, caryophyllene oxide, germacrene D, globulol, hibaene, humulene, limonene, luxuriadiene, myrcene, *p*-cymene, sabinene, spathulenol, viridiflorene, and viridiflorol (Figures 4 and 5).

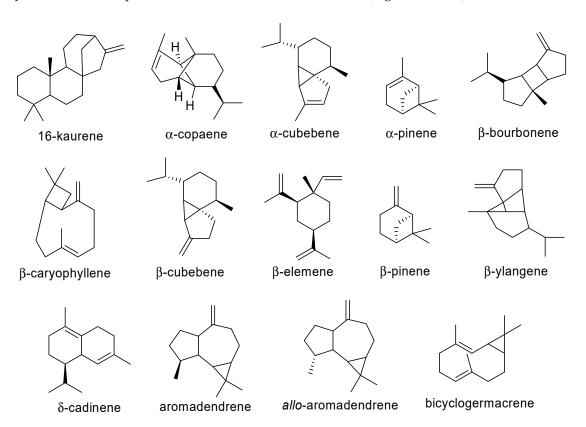


Figure 4. Main essential oil metabolites evidenced in Araucariaceae species—part 1.

Yet, none of these compounds can be actually considered as chemotaxonomic markers since they all are widespread compounds in the plant kingdom [26,27,110–114].

A particular speech regards the presence of alkyl chains. These were evidenced in several species of the family [8] even if not always the exact compounds were identified, but only the general molecular formula. By the way, these compounds are also quite widespread [26,27,110–114].

Plants 2020, 9, 888 67 of 73

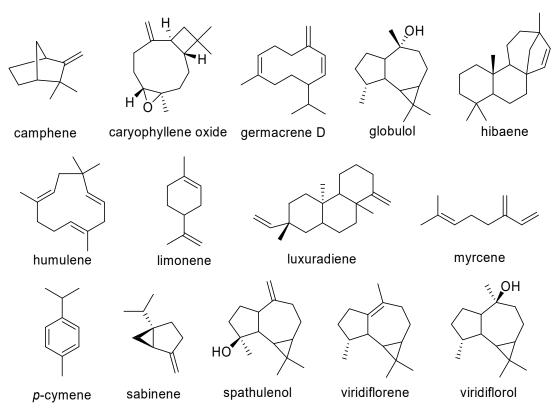


Figure 5. Main essential oil metabolites evidenced in Araucariaceae species—part 2.

Indeed, among the polar fraction metabolites, the most common compounds were found to be: 7-O-methyl-agathisflavone, 7-O-methyl-cupressuflavone, 7'-O-methyl-agathisflavone, 7,7''-di-O-methyl-cupressuflavone, 7,4',7''-tri-O-methyl-cupressuflavone, 7,4',7'',4'''-tetra-O-methyl-cupressuflavone, agathisflavone, and cupressuflavone (Figure 6).

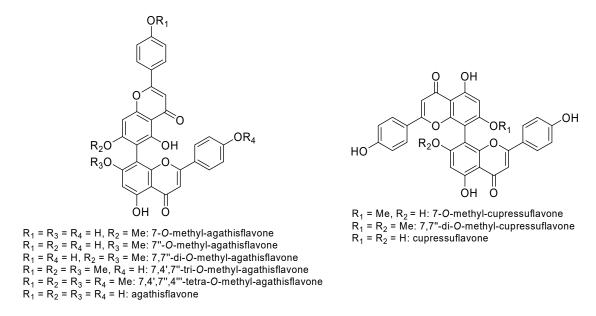


Figure 6. Main polar fractions metabolites evidenced in Araucariaceae species.

As previously mentioned, the derivatives of agathisflavone can be really considered as chemotaxonomic markers of the whole Araucariaceae family [22,28–33] whereas cupressuflavone and

Plants 2020, 9, 888 68 of 73

its derivatives have now been started to be evidenced also in other families [115] and so they can no longer be considered as chemotaxonomic markers of the family.

For what concerns the diterpenes, even if no specific compound of this class has been evidenced in all the species reported in literature, as previously mentioned, they are also known to be used as chemotaxonomic markers of the family. In particular, this concerns labdane diterpenes which are, anyway, a very big sub-class of natural compounds and so, they are not so specific also because this kind of compound has been isolated from other families also [116].

## 8. Conclusions

This review article has clearly showed the huge importance of Araucaricaeae species both under different standpoints: phytochemistry, chemotaxonomy, ethnobotany, and pharmacology.

In fact, as for the first point, many compounds, components of the essential oil, and of the polar fraction have been reported in them, including several new ones. For what concerns chemotaxonomy, some compounds could be eventually used as chemotaxonomic markers even if some other studied on this point are necessary in order to develop this concept better. Several species of the Araucariaceae family are also used for ethnobotanical and ethnopharmacological purposes, especially the species belonging to the *Araucaria* genus. Lastly, several extracts derived from Araucariaceae species as well several compounds isolated from them have been found to possess interesting and amazing pharmacological activities, ranging from the mere antioxidant to the greater cytotoxic effects.

Nevertheless, the studies in these fields about this family are quite limited in several senses, not to say absent for the genus *Columbea*, and this review article wants to be a first of its kind but also an incentive to continue the phytochemical, chemotaxonomic, ethnobotanical, and pharmacological studies on the Araucariaceae family in a specific as well as generic manner.

**Author Contributions:** C.F., A.V. (Alessandro Venditti) made the conceptualization. C.F., A.V. (Alessandro Venditti), D.D.V., C.T., M.F., A.V. (Antonio Ventrone), L.T., S.F., M.G., M.N., A.B., M.S. made research, wrote and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

**Conflicts of Interest:** The authors declare no potential conflict of interests in this article.

## References

- 1. Escapa, I.H.; Catalano, S.A. Phylogenetic analysis of Araucariaceae: Integrating molecules, morphology, and fossils. *Int. J. Plant Sci.* **2013**, 174, 1153–1170. [CrossRef]
- 2. Setoguvhi, H.; Osawa, T.A.; Pintaud, J.; Jaffré, T.; Veillon, J.-M. Phylogenetic relationships within Araucariaceae based on RBCL gene sequences. *Am. J. Bot.* **1998**, *85*, 1507–1516. [CrossRef]
- 3. Available online: www.theplantlist.org (accessed on 22 June 2020).
- 4. Wilf, P.; Escapa, I.H.; Cúneo, N.R.; Kooyman, R.M.; Johnson, K.R.; Iglesias, A. First South American *Agathis*(Araucariaceae), Eocene of Patagonia. *Am. J. Bot.* **2014**, *101*, 156–179. [CrossRef]
- 5. Whitmore, T.C.; Page, C.N. Evolutionary implications of the distribution and ecology of the tropical genus *Agathis. New Phytol.* **1980**, *84*, 407–416. [CrossRef]
- 6. Khan, N.U.; Ilyas, M.; Rahman, W.; Mashima, T.; Okigawa, M.; Kawano, N. Biflavones from the leaves of *Araucaria bidwillii* Hooker and *Agathis alba* foxworthy (Araucariaceae). *Tetrahedron* **1972**, *28*, 5689–5695. [CrossRef]
- 7. Mashima, T.; Okigawa, M.; Kawano, N.; Khan, N.U.; Ilyas, M.; Rahman, W. On the bisflavones in the leaves of *Agathis alba* Foxworthy. *Tetrahedr. Lett.* **1970**, 11, 2937–2940. [CrossRef]
- 8. Brophy, J.J.; Goldsack, R.J.; Wu, M.Z.; Fookes, C.J.R.; Forster, P.I. The steam volatile oil of *Wollemia nobilis* and its comparison with other members of the Araucariaceae (*Agathis* and *Araucaria*). *Biochem. Syst. Ecol.* **2000**, 28, 563–578. [CrossRef]
- 9. Ofman, D.J.; Markham, K.R.; Vilain, C.; Molloy, B.P.J. Flavonoid profiles of New Zealand kauri and other species of *Agathis*. *Phytochemistry* **1995**, *38*, 1223–1228. [CrossRef]

Plants 2020, 9, 888 69 of 73

10. Garrison, M.S.; Irvine, A.K.; Setzer, W.N. Chemical composition of the resin essential oil from *Agathis atropurpurea* from North Queensland, Australia. *Am. J. Essent. Oils Nat. Prod.* **2016**, *4*, 4–5.

- 11. Adam, A.Z.; Juiling, S.; Lee, S.Y.; Jumaat, S.R.; Mohamed, R. Phytochemical composition of *Agathis borneensis* (Araucariaceae) and their biological activities. *Malays. For.* **2017**, *80*, 169–177.
- 12. Chen, Z.; He, D.; Deng, J.; Zhu, J.; Mao, Q. Chemical composition and antibacterial activity of the essential oil from *Agathis dammara* (Lamb.) Rich fresh leaves. *Nat. Prod. Res.* **2015**, *29*, 2050–2053. [CrossRef]
- 13. Gutierrez, R.M.; Baculi, R.; Pastor, N.; Puma-at, T.; Balangcod, T. Antibacterial potential of some medicinal plants of the Cordillera Region, Philippines. *Indian J. Tradit. Knowl.* **2013**, *12*, 630–637.
- 14. Manh, D.D.K.; Bastard, J.; Fétizon, M. Acide *nor-*19 anticopalique d'*Agathis lanceolata*. *Phytochemistry* **1979**, *18*, 1839–1842.
- 15. Manh, D.D.K.; Bastard, J.; Fétizon, M.; Sévenet, T. Plantes De Nouvelle-Caledonie. LXXVII. Diterpènes d'*Agathis lanceolata*. *J. Nat. Prod.* **1983**, 46, 262–273. [CrossRef]
- 16. Li, Y.; Wang, T.-T.; Zhao, J.; Shi, X.; Hu, S.-C.; Gao, K. Norditerpenoids from *Agathis macrophylla*. *Food Chem.* **2012**, *131*, 972–976. [CrossRef]
- 17. Li, Y.; Wang, T.-T.; Gao, K. A new cytotoxic stigmasterone from *Agathis macrophylla*. *Nat. Prod. Comm.* **2017**, 12, 343–344. [CrossRef]
- 18. Cambie, R.C.; Coddington, J.M.; Stone, M.J.; Tanaka, N.; Hua, L.Y.; Arigayo, S. Diterpenoids of the wood of *Agathis vitiensis*. *Phytochemistry* **1989**, *28*, 1675–1679. [CrossRef]
- 19. Smith, R.M.; Marty, R.A.; Peters, C.F. The diterpene acids in the bled resins of three pacific kauri, *Agathis vitiensis*, *A. lanceolata* and *A. macrophylla*. *Phytochemistry* **1981**, 20, 2205–2207. [CrossRef]
- 20. Carman, R.M.; Marty, R.A. Diterpenoids. XXIV. A survey of the *Agathis* species of North Queensland. Two new resin acids. *Austr. J. Chem.* **1970**, 23, 1457–1464. [CrossRef]
- 21. Lassak, E.V.; Brophy, J.J. The steam-volatile oil of commercial "Almaciga" resin (*Agathis philippinensis* Warb.) from the Philippines. *J. Essent. Oil Bear. Pl.* **2008**, *11*, 634–637. [CrossRef]
- 22. Venditti, A.; Frezza, C.; Campanelli, C.; Foddai, S.; Bianco, A.; Serafini, M. Phytochemical analysis of the ethanolic extract of *Agathis robusta* (C. Moore ex F. Muell.) F.M. Bailey. *Nat. Prod. Res.* **2017**, *31*, 1604–1611. [CrossRef]
- 23. Bisht, B.; Nainwal, P.; Saini, P. Evaluation of *in vitro* anti-inflammatory activity of *Agathis robusta*. *J. Pharma*. *Res.* **2012**, 2, 1304–1306.
- 24. Verma, R.S.; Padalia, R.C.; Goswami, P.; Verma, S.K.; Chauhan, A.; Darokar, M.P. Chemical composition and antibacterial activity of the essential oil of Kauri Pine [*Agathis robusta* (C. Moore ex F. Muell.) F.M. Bailey] from India. *J. Wood Chem. Technol.* **2016**, *36*, 270–277. [CrossRef]
- 25. Wolff, R.L.; Christie, W.W.; Pédrono, F.; Marpeau, A.M. Arachidonic, eicosapentaenoic, and biosynthetically related fatty acids in the seed lipids from a primitive gymnosperm, *Agathis robusta*. *Lipids* **1999**, 34, 1083–1097. [CrossRef]
- 26. Frezza, C.; Venditti, A.; Serafini, M.; Bianco, A. Phytochemistry, chemotaxonomy, ethnopharmacology, and nutraceutics of Lamiaceae. *Stud. Nat. Prod. Chem.* **2019**, *62*, 125–178.
- 27. Frezza, C.; Venditti, A.; Toniolo, C.; De Vita, D.; Serafini, I.; Ciccòla, A.; Franceschin, M.; Ventrone, A.; Tomassini, L.; Foddai, S.; et al. *Pedicularis* L. genus: Systematics, botany, phytochemistry, chemotaxonomy, ethnopharmacology, and other. *Plants* 2019, *8*, 306. [CrossRef] [PubMed]
- 28. Venditti, A.; Frezza, C.; Sciubba, F.; Foddai, S.; Serafini, M.; Bianco, A. Terpenoids and more polar compounds from the male cones of *Wollemia nobilis*. *Chem. Biodiver.* **2017**, *14*, e1600332. [CrossRef] [PubMed]
- 29. Venditti, A.; Frezza, C.; Rossi, G.; Serafini, I.; Ciccòla, A.; Sciubba, F.; Foddai, S.; Tomassini, L.; Bianco, A.; Serafini, M. A new byciclic monoterpene glucoside and a new biflavone from the male reproduction organs of *Wollemia nobilis*. *Fitoterapia* **2019**, 133, 62–69. [CrossRef]
- 30. Venditti, A.; Frezza, C.; Vincenti, F.; Brodella, A.; Sciubba, F.; Montesano, C.; Franceschin, M.; Sergi, M.; Foddai, S.; Di Cocco, M.E.; et al. A *syn-ent-*labdadiene derivative with a rare spiro-β-lactone function from the male cones of *Wollemia nobilis*. *Phytochemistry* **2019**, *158*, 91–95. [CrossRef]
- 31. Venditti, A.; Frezza, C.; Rossi, G.; Sciubba, F.; Ornano, L.; De Vita, D.; Toniolo, C.; Tomassini, L.; Foddai, S.; Nicoletti, M.; et al. A new diterpene and other compounds from the unripe female cones of *Wollemia nobilis*. *Nat. Prod. Res.* **2020**, in press. [CrossRef]
- 32. Frezza, C.; Venditti, A.; Rossi, G.; Serafini, I.; Pitorri, M.; Ciccòla, A.; Foddai, S.; Bianco, A.; Serafini, M. Phytochemical study on the leaves of *Wollemia nobilis*. *Biochem. Syst. Ecol.* **2017**, 74, 63–66. [CrossRef]

Plants 2020, 9, 888 70 of 73

33. Frezza, C.; Venditti, A.; Scandurra, C.; Ciccòla, A.; Serafini, I.; Sciubba, F.; Foddai, S.; Franceschin, M.; Bianco, A.; Serafini, M. Phytochemical profile of *Wollemia nobilis* half-matured female cones and their potential ethnopharmacological and nutraceutical activities. *J. Agric. Sci. Technol. A* **2018**, *8*, 162–170.

- 34. Venditti, A. What is and what should never be: Artifacts, improbable phytochemicals, contaminants and natural products. *Nat. Prod. Res.* **2020**, *34*, 1014–1031. [CrossRef] [PubMed]
- 35. Kulip, J. An ethnobotanical survey of medicinal and other useful plants of Muruts in Sabah, Malaysia. *Telopea* **2003**, *10*, 81–98. [CrossRef]
- 36. Noor Rain, A.; Khozirah, S.; Mohd Ridzuan, M.A.; Ong, B.K.; Rohaya, C.; Rosilawati, M.; Zakiah, I. Antiplasmodial properties of some Malaysian medicinal plants. *Tropic. Biomed.* **2007**, 24, 29–35.
- 37. Surapuram, V.; Setzer, W.N.; McFeeters, R.L.; McFeeters, H. Antifungal activity of plant extracts against *Aspergillus niger* and *Rhizopus stolonifer*. *Nat. Prod. Comm.* **2014**, *9*, 1603–1605. [CrossRef]
- 38. Monzote, L.; Piñón, A.; Setzer, W.N. Antileishmanial potential of tropical rainforest plant extracts. *Medicines* **2014**, *1*, 32–55. [CrossRef]
- 39. Tillah, M.; Batubara, I.; Sari, R.K. Antimicrobial and antioxidant activities of resins and essential oil from Pine (*Pinus merkusii*, *Pinus oocarpa*, *Pinus insularis*) and *Agathis (Agathis loranthifolia*). *Proc. Int. Conf. Math. Sci. Educ.* **2016**, *3*, C4–C9.
- 40. Whitmore, T.C. Utilization, potential, and conservation of *Agathis*, a genus of tropical Asian conifers. *Econ. Bot.* **1980**, *34*, 1–12. [CrossRef]
- 41. Riley, M. Māori Healing and Herbal: New Zealand Ethnobotanical Sourcebook; Viking Sevenseas: Paraparaumu, New Zealand, 1994.
- 42. Simpson, M.G. Plant Systematics; Academic Press: Cambridge, MA, USA, 2010.
- 43. Zonneveld, B.J.M. Genome sizes of all 19 *Araucaria* species are correlated with their geographical distribution. *Plant Syst. Evol.* **2012**, 298, 1249–1255. [CrossRef]
- 44. De Paiva Campello, J.; Ferreira Fonseca, S. Diterpenes from *Araucaria angustifolia*. *Phytochemistry* **1975**, *14*, 2299–2300. [CrossRef]
- 45. Souza, M.O.; Branco, C.S.; Sene, J.; Dall'Agnol, R.; Agostini, F.; Moura, S.; Salvado, M. Antioxidant and antigenotoxic activities of the Brazilian Pine *Araucaria angustifolia* (Bert.) O. Kuntze. *Antioxidants* **2014**, *3*, 24–37. [CrossRef] [PubMed]
- 46. Seccon, A.; Rosa, D.W.; Freitas, R.A.; Biavatti, M.W.; Creczynski-Pasa, T.B. Antioxidant activity and low cytotoxicity of extracts and isolated compounds from *Araucaria angustifolia* dead bark. *Redox Rep.* **2010**, 15, 234–242. [CrossRef] [PubMed]
- 47. Cordenunsi, B.R.; De Menezes, E.W.; Genovese, M.I.S.; Colli, C.L.; Alves De Souza, A.G.; Lajolo, F.M. Chemical composition and glycemic index of Brazilian Pine (*Araucaria angustifolia*) seeds. *J. Agric. Food Chem.* **2004**, *52*, 3412–3416. [CrossRef] [PubMed]
- 48. Dos Santos Branco, C.; De Lima, E.D.; Rodrigues, T.S.; Becker Scheffel, T.; Scola, G.; Fernandes Correia Laurino, C.C.; Moura, S.; Salvador, M. Mitochondria and redox homoeostasis as chemotherapeutic targets of *Araucaria angustifolia* (Bert.) O. Kuntze in human larynx HEp-2 cancer cells. *Chemico-Biol. Interact.* **2015**, 231, 108–118. [CrossRef] [PubMed]
- 49. Michelon, F.; Branco, C.S.; Calloni, C.; Giazzon, I.; Agostini, F.; Spada, P.K.W.; Salvador, M. *Araucaria angustifolia*: A potential nutraceutical with antioxidant and antimutagenic activities. *Curr. Nutr. Food Sci.* **2012**, *8*, 155–159. [CrossRef]
- 50. Ferreira Fonseca, S.; Campello, J.P.; Barata, L.E.S.; Rúveda, E.A. <sup>13</sup>C NMR spectral analysis of lignans from *Araucaria angustifolia*. *Phytochemistry* **1978**, *17*, 499–502. [CrossRef]
- 51. Ferreira Fonseca, S.; Nielsen, L.T.; Rúveda, E.A. Lignans of *Araucaria angustifolia* and <sup>13</sup>C NMR analysis of some phenyltetralin lignans. *Phytochemistry* **1979**, *18*, 1703–1708. [CrossRef]
- 52. Yamaguchi, L.F.; Vassão, D.G.; Kato, M.J.; Di Mascio, P. Biflavonoids from Brazilian pine *Araucaria angustifolia* as potentials protective agents against DNA damage and lipoperoxidation. *Phytochemistry* **2005**, *66*, 2238–2247. [CrossRef]
- 53. Yamaguchi, L.F.; Kato, M.J.; Di Mascio, P. Biflavonoids from *Araucaria angustifolia* protect against DNA UV-induced damage. *Phytochemistry* **2009**, *70*, 615–620. [CrossRef]
- 54. Anderegg, R.J.; Rowe, J.W. Lignans, the major component of resin from *Araucaria angustifolia* knots. *Holzforschung* **1973**, *28*, 171–175. [CrossRef]

Plants 2020, 9, 888 71 of 73

55. Barbedo De Freitas, T.; Koslinski Santos, C.H.; Vieira da Silva, M.; Shirai, M.A.; Dias, M.I.; Barros, L.; Barreiro, M.F.; Ferreira, I.C.F.R.; Gonçalves, O.H.; Leimann, F.W. Antioxidants extraction from Pinhão (*Araucaria angustifolia* (Bertol.) Kuntze) coats and application to zein films. *Food Pack. Shelf Life* **2018**, 15, 28–34. [CrossRef]

- 56. Freitas, A.M.; Almeida, M.T.R.; Andrighetti-Fröhner, C.R.; Cardozo, F.T.G.S.; Barardi, C.R.M.; Farias, M.R.; Simões, C.M.O. Antiviral activity-guided fractionation from *Araucaria angustifolia* leaves extract. *J. Ethnopharmacol.* **2009**, *126*, 512–517. [CrossRef] [PubMed]
- 57. Fonseca, F.N.; Ferreira, A.J.; Sartorelli, P.; Lopes, N.P.; Floh, E.I.; Handro, W.; Kato, M.J. Phenylpropanoid derivatives and biflavones at different stages of differentiation and development of *Araucaria angustifolia*. *Phytochemistry* **2000**, *55*, 575–580. [CrossRef]
- 58. Yamamoto, S.; Otto, A.; Simoneit, B.R.T. Lignans in resin of *Araucaria angustifolia* by gas chromatography/mass spectrometry. *J. Mass Spectrom.* **2004**, *39*, 1337–1347. [CrossRef]
- 59. Garbarino, J.A.; Oyarzún, M.L.; Gambaro, V. Labdane diterpenes from *Araucaria araucana*. *J. Nat. Prod.* **1987**, 50, 935–936. [CrossRef]
- 60. Schmeda-Hirschmann, G.; Astudillo, L.; Rodriguez, J.A.; Theoduloz, C.; Yãnez, T. Gastroprotective effect of the Mapuche crude drug *Araucaria araucana* resin and its main constituents. *J. Ethnopharmacol.* **2005**, *10*, 271–276. [CrossRef]
- 61. Schmeda-Hirschmann, G.; Astudillo, L.; Sepúlveda, B.; Rodriguez, J.A.; Theoduloz, C.; Yãnez, T.; Palenzuela, J.A. Gastroprotective effect and cytotoxicity of natural and semisynthetic labdane diterpenes from *Araucaria araucana* resin. *Z. Naturforsch. C* **2005**, *60*, 511–522. [CrossRef]
- 62. Céspedes, C.L.; Avila, J.G.; García, A.M.; Becerra, J.; Flores, C.; Aqueveque, P.; Bittner, M.; Hoeneisen, M.; Martinez, M.; Silva, M. Antifungal and antibacterial activities of *Araucaria araucana* (Mol.) K. Koch heartwood lignans. *Z. Naturforsch. C* **2006**, *61*, 35–43. [CrossRef]
- 63. Pietsch, M.; König, W.A. Enantiomers of sesquiterpene and diterpene hydrocarbons in *Araucaria* species. *Phytochem. Anal.* **2000**, *11*, 99–105. [CrossRef]
- 64. Parveen, N.; Taufeeq, H.M.; Khan, N.U. Biflavones from the leaves of *Araucaria araucana*. *J. Nat. Prod.* **1987**, 50, 332–333. [CrossRef]
- 65. Briggs, L.H.; White, G.W. Constituents of the essential oil of *Araucaria araucana*. *Tetrahedron* **1975**, 31, 1311–1314. [CrossRef]
- 66. Hegnauer, R. *Chemotaxonomie der Pflanzen. Band 7. Birkhauser*; Verlag Publisher: Basel, Switzerland, 1986; pp. 462–554.
- 67. Cox, R.E.; Yamamoto, S.; Otto, A.; Simoneit, B.R.T. Oxygenated di-and tricyclic diterpenoids of southern hemisphere conifers. *Biochem. Syst. Ecol.* **2007**, *35*, 342–362. [CrossRef]
- 68. Talaat, A.N.; Ebada, S.S.; Labib, R.M.; Esmat, A.; Youssef, F.S.; Singab, A.N. Verification of the anti-inflammatory activity of the polyphenolic-rich fraction of *Araucaria bidwillii* Hook. using phytohaemagglutinin-stimulated human peripheral blood mononuclear cells and virtual screening. *J. Ethnopharmacol.* **2018**, 226, 44–47. [CrossRef] [PubMed]
- 69. Ebada, S.S.; Talaat, A.N.; Labib, R.M.; Mándi, A.; Kurtán, T.; Müller, W.E.G.; Sing, A.N.; Proksch, P. Cytotoxic labdane diterpenes and bisflavonoid atropisomers from leaves of *Araucaria bidwillii*. *Tetrahedron* **2017**, *73*, 3048–3055. [CrossRef]
- 70. Ilyas, N.; Ilyas, M.; Rahman, W.; Okigawa, M.; Kawano, N. Biflavones from the leaves of *Araucaria excelsa*. *Phytochemistry* **1978**, *17*, 987–990. [CrossRef]
- 71. Suresh, B.; Dhanasekaran, S.; Elango, K.; Sethuraman, M.; Rajan, S. Anti-pyretic activity of some plants in female albino rats: A preliminary report. *Anc. Sci. Life* **1995**, *14*, 253–257.
- 72. Caputo, R.; Mangoni, L.; Monaco, P.; Pelosi, L.; Previtera, L. Neutral diterpenes from *Araucaria bidwillii*. *Phytochemistry* **1976**, *15*, 1401–1402. [CrossRef]
- 73. Michael, H.N.; Awad, H.M.; El-Sayed, N.H.; Paré, P.W. Chemical and antioxidant investigations: Norfolk pine needles (*Araucaria excelsa*). *Pharma. Biol.* **2010**, *48*, 534–538. [CrossRef]
- 74. Saranya Devi, K.; Sruthy, P.B.; Anjana, J.C.; Rathinamala, J. Identification of bioactive compounds and toxicity study of *Araucaria columnaris* bark extract on human embryonic kidney cell line. *Asian J. Biotechnol.* **2015**, 7, 129–136. [CrossRef]
- 75. Patial, P.K.; Cannoo, D.S. Phytochemical profile, antioxidant potential and DFT study of *Araucaria columnaris* (G. Forst.) Hook. Branch extracts. *Nat. Prod. Res.* **2019**, in press. [CrossRef] [PubMed]

Plants 2020, 9, 888 72 of 73

76. Verma, S.; Mohanta, T.; Revathy, T.; Suthindhiran, K.; Jayasri, M.A. Phytochemical and pharmacological evaluation of selected plants. *Am. J. Biochem. Biotechnol.* **2013**, *9*, 291–299. [CrossRef]

- 77. Pavani, P.S.; Raj, K.P.; Sarany, A.; Kumar, A.R. Phytochemical profile of three selected plants of *Araucaria columnaris*, *Araucaria heterophylla*, *Ocimum tenuiflorum*. *Int. Res. J. Pharma. Appl. Sci.* **2014**, *4*, 18–20.
- 78. Aslam, M.S.; Choudhary, B.A.; Uzair, M.; Ijaz, A.S. Phytochemistry of aerial parts of *Araucaria columnaris*. *J. Appl. Pharmacol.* **2014**, *6*, 114–120.
- 79. Chen, J.; Chen, J.-J.; Yang, L.-Q.; Hua, L.; Gao, K. Labdane diterpenoids and shikimic acid derivatives from *Araucaria cunninghamii*. *Planta Med.* **2011**, 77, 485–488. [CrossRef]
- 80. Chen, J.; Yang, M.L.; Zeng, J.; Gao, K. Antimicrobial activity of *Araucaria cunninghamii* Sweet and the chemical constituents of its twigs and leaves. *Phytochem. Lett.* **2013**, *6*, 41–45. [CrossRef]
- 81. Verma, R.S.; Padalia, R.C.; Goswami, P.; Verma, S.K.; Chauhan, A.; Darokar, M.P. Chemical composition and antibacterial activity of foliage and resin essential oils of *Araucaria cunninghamii* Aiton ex D.Don and *Araucaria heterophylla* (Salisb.) Franco from India. *Ind. Crops Prod.* **2014**, *61*, 410–416. [CrossRef]
- 82. Gautam, V.; Arora, S.; Kapoor, D.; Bhardwaj, R. Free radical scavenging activity and HPLC analysis of *Araucaria cunninghamii* Aiton ex D. Don leaf extract. *J. Stress Physiol. Biochem.* **2014**, *10*, 176–185.
- 83. Olawore, N.O.; Ogunwande, I.A. Analysis of the leaf oil of *Araucaria cunninghamii* Sweet. grown in Nigeria. *J. Essent. Oil Res.* **2005**, *17*, 459–461. [CrossRef]
- 84. Matsabisa, M.G.; Chukwuma, C.I.; Ibeji, C.U.; Chaudhary, S.K. Stem bark exudate (resin) of *Araucaria cunninghamii* Aiton ex D. Don (hoop pine) abates glycation, α-glucosidase and DPP-IV activity and modulates glucose utilization in Chang liver cells and 3T3-L1 adipocytes. *South Afr. J. Bot.* **2019**, *121*, 193–199. [CrossRef]
- 85. Hamed, M.M.; Ghareeb, M.A.; Shafei, A.A.; Abdel-Aziz, M.S.; Tolba, S.S. The *in vitro* evaluation of antioxidant, anticancer and antimicrobial properties of *Araucaria heterophylla* grown in Egypt. *Pharmacol. Online* **2019**, *1*, 221–235.
- 86. Abdel-Sattar, E.; Monem, A.R.A.; Ezzat, S.M.; El-Halawany, A.M.; Mouneir, S.M. Chemical and biological investigation of *Araucaria heterophylla* Salisb. resin. *Z. Naturforsch. C* **2009**, *64*, 819–823. [CrossRef] [PubMed]
- 87. Chen, J.; Lichwa, J.; Ray, C. Essential oils of selected Hawaiian plants and associated litters. *J. Essent. Oil Res.* **2007**, 19, 276–278. [CrossRef]
- 88. Basyuni, M.; Deni, I.; Slamet, B.; Bimantara, Y.; Hayati, R.; Amelia, R.; Oku, H.; Sagami, H. Polyisoprenoids composition from *Araucaria heterophylla* and *Casuarina equisetifolia* leaves. *Proc. Int. Conf. Nat. Res. Technol.* **2019**, 108–111. [CrossRef]
- 89. Ilyas, M.; Seligmann, O.; Wagner, H. Biflavones from the leaves of *Araucaria rulei* F. Muell. and a survey on biflavanoids of the *Araucaria* genus. *Z. Naturforsch. C* **1977**, *32*, 206–209. [CrossRef]
- 90. Andrighetti-Fröhner, C.R.; Sincero, T.C.M.; Silva, A.C.; Savi, L.A.; Gaido, C.M.; Bettega, J.M.R.; Mancini, M.; Almeida, M.T.R.; Barbosa, R.A.; Farias, M.R.; et al. Antiviral evaluation of plants from Brazilian Atlantic Tropical Forest. *Fitoterapia* **2005**, *76*, 374–378. [CrossRef]
- 91. Peralta, R.M.; Koehnlein, E.A.; Oliveira, R.F.; Correa, V.G.; Corrêa, R.C.; Bertonha, L.; Bracht, A.; Ferreira, I.C. Biological activities and chemical constituents of *Araucaria angustifolia*: An effort to recover a species threatened by extinction. *Trends Food Sci. Technol.* **2016**, *54*, 85–93. [CrossRef]
- 92. Dold, A.P.; Coocks, M.L. The medicinal use of some weeds, problems and alien plants in the Grahamstown and Peddie districts of the Eastern cape, South Africa. *South Afr. J. Sci.* **2000**, *96*, 467–473.
- 93. Anderson, E.F. Ethnobotany of hill tribes of Northern Thailand. II. Lahu medicinal plants. *Econ. Bot.* **1986**, 40, 442–450. [CrossRef]
- 94. Milliken, W. Ethnobotany of the Yali of West Papua; Royal Botanic Garden: Edinburgh, UK, 1994.
- 95. Bussmann, R.W. Antibacterial activity of northern-peruvian medicinal plants. Arnaldoa 2008, 15, 127–148.
- 96. Dhanasekaran, S.; Ravishankar, S.; Devi, K.S.; Suresh, B.; Sethuraman, M.; Rajan, S. Pharmacological studies of *Araucaria bidwillii* Hook. *Anc. Sci. Life* **1993**, *13*, 137–142. [PubMed]
- 97. Nazeer Ahamed, K.F.H.; Kumar, V.; Sundarajan, R.; Mukherjee, K.; Pulok, K. Anti-nociceptive and anti-inflammatory activity of *Araucaria bidwillii* Hook. *Iran. J. Pharmacol. Ther.* **2005**, *4*, 105–109.
- 98. Nazeer Ahamed, K.F.H.; Kumar, V.; Wahile, A.M.; Mukherjee, K.; Shapa, B.P.; Mukherjee, P.K. Brine shrimp lethality and cytotoxic assay of *Araucaria bidwillii* Hook in human carcinoma cell lines. *Orient. Pharma. Exp. Med.* **2005**, *5*, 21–28.

Plants 2020, 9, 888 73 of 73

99. Zaffar, M.; Munis, M.F.H.; Rasul, F.; Masood, S.; Hassan, S.W.; Imran, M.; Nasim, W.; Zakir, A.; Quraishi, U.M.; Chaudhary, H.J. Biological assays of plant extracts from *Araucaria columnaris* and *Cycas revoluta*. *J. Food Agric. Environ.* **2014**, *12*, 128–131.

- 100. Joshi, S.; Sati, S.C.; Kumar, P. Antibacterial potential and ethnomedical relevance of Kumaun Himalayan Gymnosperms. *J. Phytopharmacol.* **2016**, *5*, 190–200.
- 101. Sati, S.C.; Joshi, S. Antifungal potential of *Araucaria cunninghamii* sweet (Araucariaceae) plant extracts. *Int. J. Pharmacol. Toxicol. Sci.* **2013**, *3*, 15–21.
- 102. Mukherjee, P.K.; Nazeer Ahamed, K.F.H.; Kumar, V.; Mukherjee, K.; Houghton, P.J. Protective effect of biflavones from *Araucaria bidwillii* Hook in rat cerebral ischemia/reperfusion induced oxidative stress. *Behaviour. Brain Res.* **2007**, 178, 221–228. [CrossRef]
- 103. Dargavel, J. *Araucarian Forests*; Australia and New Zealand Forest Histories Inc.: Kingston, Australia, ISSN 1832-8156.
- 104. Hill, K.D. The Wollemi pine: Discovering a living fossil. Nat. Resour. 1996, 32, 20-25.
- 105. Jones, W.G.; Hill, K.D.; Allen, J.M. *Wollemia nobilis*, a new living Australian genus in the Araucariaceae. *Telopea* **1995**, *6*, 173–176. [CrossRef]
- 106. Staniek, A.; Mutendam, R.; Woerdenbag, H.J.; Kayser, O. Essential oil constituents derived from different organs of a Relictual conifer *Wollemia nobilis*. *Biochem. Syst. Ecol.* **2010**, *38*, 131–135. [CrossRef]
- 107. Gleńsk, M.; Włodarczyk, M.; Stefanowicz, P.; Kucharska, A. Biflavonoids from the Wollemi Pine, *Wollemia nobilis* (Araucariaceae). *Biochem. Syst. Ecol.* **2013**, *46*, 18–21. [CrossRef]
- 108. Wang, S.; Panter, K.E.; Gardner, D.R.; Evans, R.C.; Bunch, T.D. Effects of the pine needle abortifacient, isocupressic acid, on bovine oocyte maturation and preimplantation embryo development. *Anim. Reprod. Sci.* 2004, *81*, 237–244. [CrossRef] [PubMed]
- 109. McEvoy, T.G.; Robinson, J.J.; Ashworth, C.J.; Rooke, J.A.; Sinclair, K.D. Feed and forage toxicants affecting embryo survival and fetal development. *Theriogenology* **2001**, *55*, 113–129. [CrossRef]
- 110. Fons, F.; Rapior, S.; Gargadennec, A.; Andary, C.; Bessière, J. Volatile components of *Plantago lanceolata* (Plantaginaceae). *Acta Bot. Gall.* **1998**, 145, 265–269. [CrossRef]
- 111. Crockett, S.L. Essential oil and volatile components of the genus *Hypericum* (Hypericaceae). *Nat. Prod. Comm.* **2010**, *5*, 1493–1506. [CrossRef]
- 112. Rodriguez, S.; Murray, A.P. Volatile components of *Discaria americana* Gillies & Hook (Rhamnaceae). *Nat. Prod. Res.* **2008**, 22, 253–257.
- 113. Venditti, A.; Frezza, C.; Salutari, G.; Di Cecco, M.; Ciaschetti, G.; Oliva, A.; De Angelis, M.; Vullo, V.; Sabatino, M.; Garzoli, S.; et al. Composition of the essential oil of *Coristospermum cuneifolium* and antimicrobial activity evaluation. *Planta Med. Int. Open.* **2017**, *4*, 1–8. [CrossRef]
- 114. Venditti, A.; Frezza, C.; Sciubba, F.; Serafini, M.; Bianco, A.; Cianfaglione, K.; Lupidi, G.; Quassinti, L.; Bramucci, M.; Maggi, F. Volatile components, polar constituents and biological activity of tansy daisy (*Tanacetum macrophyllum* (Waldst. et Kit.) Schultz Bip.). *Ind. Crops Prod.* **2018**, *118*, 225–235. [CrossRef]
- 115. Krauze-Baranowska, M.; Baçzek, T.; Głód, D.; Kaliszan, R.; Wollenweber, E. HPLC separation of *O*-acylated flavonoids and biflavones from some species of Gymnospermae. *Chromatographia* **2004**, *60*, 9–15. [CrossRef]
- 116. Chinou, I. Labdanes of natural origin-biological activities (1981–2004). *Curr. Med. Chem.* **2005**, *12*, 1295–1317. [CrossRef]



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).