Table 5.1 Summary of Conifer Diterpenes with Medicinal Properties

Compound Class Compound (source): Phytochemical investigations and Resources	
Abietene diterpenes (genera: *Prumnopitys, Callitris*)	
Callitrisic acid	
genus: *Callitris* resins ie. *C. columellaris*, *C. intratropica, C. macleayana, C. rhomboides, C. verrucosa, C. oblonga* (trace)	
Characteristic biomarker of *Callitris* Sandarac resins (also found in some *Juniperus, Calceolaria, Rabdosia,* and *Illicium* species)	Simoneit et al. (2018)
Antiviral	Gonzalez et al. (2015)
Anti-inflammatory	Gonzalez et al. (2015)
Ferruginol	
Miro (*Prumnopitys ferruginea*); Jade Cypress (*Callitris glaucophylla*)	
Antimicrobial: defensive compound found in many of the Cupressaceae family eg. *Taiwania cryptomerioides*	Ma et al. (2019)
Medicinal: hepatoprotective, significant antioxidant, anti-inflammatory, cardioprotective	Banerjee et al. (2003); Sadgrove & Jones (2014); Gonzalez et al. (2015)
Antimicrobial: significant antifungal and antibacterial activity; active against wood decay fungi	He et al. (1997); Ho et al. (2012); Bufalo et al. (2016); Ma et al. (2019); Mothana et al. (2019)
Antiviral: ferruginol and analogues were evaluated for activity against Herpes Virus and Dengue Virus; active against SARS and Zika virus	Gonzalez et al. (2015); Roa-Linares et al. (2016); Sousa et al. (2020)
Gastrointestinal tract: gastroprotective, wound healing showing significant healing for gastric ulceration comparable to conventional drugs; suggestive of a broader spectrum of wound healing activity	Rodriguez et al. (2006); Areche et al. (2008)
Cardiovascular system: antioxidant, anti-inflammatory, cardioprotective, restorative to cardiac function following heart attack	Zhang et al. (2021)
Nervous system: cholinesterase inhibition; neuroprotective with memory supportive, anti-Alzheimer's potential	Gonzalez et al. (2015); Zolezzi et al. (2018)
Anticancer: strong anti-tumour promotion properties; active against thyroid, ovarian, prostate, liver, pancreatic and lung cell lines, also leukaemia and anti-melanoma; potential for the prevention and treatment of prostate cancer	Son et al. (2005); Bispo de Jesus et al. (2008); Gonzalez et al. (2015); Ho et al. (2015); Xiong et al. (2017); Yang et al. (2017); Jia et al. (2019); Luo et al. (2019)
Insecticidal: anti-termite activity	Chang et al. (2001); Ma et al. (2019)
Antiparasitic: anti-plasmodial with significant antimalarial potential, leishmanicidal, nematicidal, trypanocidal	Gonzalez et al. (2014 & 2015); Tabefam et al. (2018)
Drug synergy: antibiotic potentiation; eg. significant potentiation of oxacillin against MRSA (80-fold increase in activity)	Smith et al. (2007a); Sadeer & Mahomoodally (2021)
Pisiferal, pisiferol (and derivatives)	
Jade Cypress (*Callitris columellaris* syn *C. glaucophylla*); originally isolated from Sawara Cypress (*Chamaecyparis pisifera*)	
Antimicrobial: significant antibacterial activity potential use for skin disorders	Smith et al. (2007a);

including acne and dandruff, as well as dental care products (dentrifices)	Sadgrove & Jones (2014)
Anticancer: activity against leukaemia cell lines (also pisiferdiol)	Aburai et al. (2010)
5-epipisiferol (*Chamaecyparis lawsoniana*): anti-mycobacterial (good activity); also potentiate the activity of tetracycline antibiotics	Smith et al. (2007a)
Pisiferic acid (and derivatives)	
Callitris columellaris (syn *C. glaucophylla*) Originally isolated from Sawara Cypress (*Chamaecyparis pisifera*); also found in the genera *Callitris* and *Salvia*.	
Antimicrobial: antioxidant, antibacterial against Gram+ve bacteria; active against MRSA; preservative potential, also for the treatment of skin disorders	Yatagai & Nakatani (1994); Sadgrove & Jones (2014); Gonzalez et al. (2015); Sadgrove et al. (2020)
Antifungal: active against rice blast fungus	
Pesticide: anti-mite, fly deterrent	Yatagai & Nakatani (1994)
Antitumour: cytotoxic, apoptosis-induction	Gonzalez et al. (2015)
Pharmaceutical: antioxidant compounds carnosic acid and carnosol were synthesised from pisiferic acid	Tada et al. (2010)
O-methyl pisiferic acid: antibacterial and insecticidal activities, antifungal potential (inhibitory activity against chitin synthase 2)	Kang et al. (2008)
Totarane diterpenes (genus: *Podocarpus*)	
Totarol	
Podocarpus nagi and *P. totara*; also the Cypress family (Cupressaceae)	
Chemical associations: precursor to formation of antifungal nagilactones; totarol can be used by plants to produce nagilactones as antimicrobial defensive compounds	
Antimicrobial: potent antifungal, antibacterial and antioxidant properties with potential for use in drug-resistant bacterial infections eg. MRSA (see below) and as an antimicrobial food preservative	Haraguchi et al. (1996a & 1996b); Muroi & Kubo (1996); Evans et al. (1999); Mateo et al. (2000); Micol et al. (2001); Smith et al. (2007b); Yamaji et al. (2007); Kim et al. (2012); Foss et al. (2013); Gualerzi et al. (2013); Shi et al. (2015 & 2018)
Antimicrobial: active against *Streptococcus mutans,* penicillin resistant *Streptococcus pneumonia*, Erythromycin-resistant *Streptococcus pyogenes,* high-level-gentamicin-resistant *Enterococcus faecalis*, vancomycin-resistant *E. faecalis, Salmonella menston, Escherichia coli, Enterobacter aerogenes, Pseudomonas aeruginosa, Bacillus subtilis, Brevibacterium ammoniagenes*, *Propionibacterium acnes*	Abdillahi et al. (2008 & 2010)
Cosmetic and skin conditions: potential antibacterial uses	Abdillahi et al. (2010)
Antimycobacterial: anti-tuberculosis potential (*Chamaecyparis nootkatensis* bark; *Juniperus communis* roots, *Juniperus procera*)	Muhammad et al. (1995); Constantine (2001); Mossa et al. (2004); Gordien et al. (2009)
Antimicrobial (synergist): good activity against Gram-positive bacteria eg. *Propionibacterium acnes, S. aureus* (including MRSA); activity significantly enhanced by combination with anacardic acid or berberine chloride	Kubo et al. (1992); Muroi & Kubo (1996); Nicolson et al. (1999); Guo et al. (2015); Shi et al. (2015)
Cardiovascular benefits: good cholesterol-lowering activity with potential benefits for atherosclerosis and hypercholesterolaemia	Enomoto et al. (1997)
Antiviral: anti-influenza virus	Dang et al. (2015)
Dental and oral care: totarol coating on dental implants or abutment surfaces has	Xu et al. (2020a)

promise as a prophylactic approach against bacterial infection	
Pharmaceutical and health care: potential use in specialised drug delivery systems; also as an antimicrobial coating for surgical items such as sutures	Reinbold et al. (2016 & 2017); Gokarneshan (2018)
Liver function: antifibrotic, antiproliferative hepatoprotective potential	Lee et al. (2008)
Anti-tumour: cytotoxic activity; active against gastric cancer cells	Abdillahi et al. (2010); Xu et al. (2019)
Antiparasitic: antimalarial potential for totarol (and derivatives) with antiplasmodial activity against chloroquine resistant *Plasmodium falciparum.*	Clarkson et al. (2003); Tacon et al. (2012); Dang et al. (2015)
Antiparasitic: anti-*Leishmania* activity; nematicidal (*Caenorhabditis elegans*)	Samoylenko et al. (2008)
Antifouling activity against brine shrimp (*Artemia salina*)	Samoylenko et al. (2008)
Neuroprotective antioxidant: potential for use in ischaemic stroke	Gao et al. (2015)
Insecticidal: mosquito larvicide	Lee et al. (2000)
Macrophyllic acid	
Source: *Podocarpus macrophyllus*	
Antimicrobial: potent broad-spectrum antibacterial activity	Bocks et al. (1963); Sato et al. (2008)
Kaurene diterpenes (family: Araucariaceae)	
Medicinal potential: broad-spectrum antibacterial, analgesic, blood sugar regulation (antidiabetic), anticoagulant (platelet anti-aggregation), anti-inflammatory and immunomodulatory (including anti-allergy) properties	Garcia et al. (2007); Takahashi et al. (2014); Arruda et al. (2019)
Antiparasitic (anti-trypanosoma), pesticidal, insecticidal (against stored gain pests) and molluscicidal potential	
Antimalarial activity	Batista et al. (2013)
Kaurenoic acid (*ent*-kaur-16-en-19-oic acid)	
Chemical intermediate: important for the production of other kaurene diterpenes, as well as growth hormones in plants	
Chemical defence: diterpene resin acids are used by plants as defence against microbial infection and insect attack	Hamberger et al. (2011)
Drug development: candidate for the treatment of dental bacteria, hypertension, Alzheimer's disease, atherosclerosis	de Andrade et al. (2011); Villa-Ruano et al. (2016); Arruda et al. (2019)
Antimicrobial (antibacterial, antifungal), antiviral (anti-HIV)	Garcia et al. (2007); Takahashi et al. (2014); da Trindade et al. (2018)
Dental and oral care: antibacterial against oral bacteria (e.g. *Porphyromonas gingivalis*) with potential for periodontal disorders; antibiofilm against *Streptococcus mutans*; synergistic antimicrobial activity with chlorhexidine dichlorohydrate	Souza et al. (2011); Jeong et al. (2013); Moreira et. al. (2016); Moreti et al. (2017); Da Trindade et al. (2018); Martins et al. (2018)
Antibacterial: activity against *Staphylococcus aureus, S. epidermis, Bacillus subtiils* etc. remarkable activity against *S. pyogenes*, *S. pneumoniae, S. dysgalactiae, S. epidermidis, B. subtilis, S. aureus*	Abrao et al. (2015); da Trindade et al. (2018); Cicek et al. (2020)
Antibacterial: contribute to *Copaiba* oleoresin hydrogel efficacy against *Streptococcus agalactiae* for the treatment of vaginal infection and neonate transmission	Morguette et al. (2019)
Antimycobacterial: derivatives evaluated as anti-tuberculosis agents	Matos et al. (2015)
Antimicrobial: contribute to activity of various herbal medicines eg. *Xylopia staudtii* anti-dysentery activity against *E. coli* and *Shigella* spp.; *Copaifera* oleoresin (with other diterpenes) in skin and urinary tract disorders	Pfeifer Barbosa et al. (2019); Pouofo Nguiam et al. (2021)

Anti-inflammatory, immunomodulatory, analgesic: potential for use in bacterial inflammation and infection eg. peritonitis; also arthritic conditions eg. osteoarthritis and rheumatoid arthritis	Kim et al. (2017); Zhang et al. (2017); Attiq et al. (2018); Dalenogare et al. (2019); Islam et al. (2020); Borghi et al. (2021b); Zhao et al. (2021)
Anti-inflammatory, analgesic: contribute to efficacy of various herbal medicines eg. *Achyranthes japonica* root, *Annona tomentosa*, *Aralia continentalis*, *Sphagneticola* (*Wedelia*) *trilobata*	Choi et al. (2011); Mizokami et al. (2012); Carneiro et al. (2017); Kim et al. (2017); Borghi et al. (2021a, 2021b); Zhao et al. (2021)
Analgesic activity	Dalenogare et al. (2019); Montiel-Ruiz et al. (2020)
Anti-inflammatory: derivatives show potential for drug development	Xu et al. (2020b & 2021)
Respiratory tract: anti-inflammatory anti-asthmatic potential, immunomodulatory; potential in acute lung injury (sepsis)	Cho et al. (2010); Kim et al. (2016); Borghi et al. (2021a)
Cosmetic use and skin disorders: topical anti-inflammatory application for use in various skin conditions eg. dermatitis	Silva et al. (2015); Fucina et al. (2016)
Cardiovascular system: antispasmodic, hypotensive, vasorelaxant	Ambrosio et al. (2004); Tirapelli et al. (2004 & 2005)
Metabolic disorders: hypoglycaemic	Bresciani et al. (2004); Jung et al. (2012); Villa-Ruano et al. (2016)
Antiparasitic: trypanocidal, anti-leishmania; kaurane derivatives show potential for drug development	Haraguchi et al. (2011); Batista et al. (2007); Santos et al. (2013); Miranda et al. (2015); da Trindade et al. (2018); Kian et al. (2018); Rocha et al. (2020)
Liver function: hepatoprotective	Marcondes-Alves et al. (2019)
Neurological activity: anticonvulsant	Okoye et al. (2013)
Uterotonic and muscle relaxant activity on uterine muscle	De Alencar Cunha et al. (2003); Villa-Ruano et al. (2009)
Gastrointestinal function: anti-inflammatory potential for treatment of colitis	Paiva et al. (2003)
Agrochemical potential: derivatives show allelopathic activity	Rocha et al. (2017)
Anticancer: leukaemia, glioblastoma, breast cancer (interact with progesterone receptors), cervical, ovarian, colon, gastric and lung cancer.	Costa-Lotufo et al. (2002); Reynolds et al. (2006); Hueso-Falcón et al. (2010); de S Vargas et al. (2015); Cano et al. (2017); Cardoso et al. (2017); Da Costa et al. (2018); Arruda et al. (2019); Rocha et al. (2019)
Anticancer: drug development potential of derivatives as anticancer agents	Ma et al. (2017)
Labdane diterpenes includes aromatic diterpenes: manoyloxides and sclareol (conifers and diverse plant sources)	
Medicinal potential: similar bioactivity to kaurene diterpenes ie. cytoprotective, antioxidant, antitumour, antimicrobial, anti-inflammatory, anti-ulcer, antispasmodic, cardioprotective, antidiabetic	Demetzos & Dimas (2001)
Manoyloxides	
Lyme disease potential: anti-*Borrelia* activity	Rauwald et al. (2019)
Cosmetic: skin-whitening potential (anti-tyrosinase activity)	Langat et al. (2021)
Manool	
Anti-inflammatory, antioxidant with potential benefits for eye (retinal) function	Ravera et al. (2021)
Antibacterial, anticancer	De Oliveira et al. (2016)

Antibacterial: active against Gram-positive bacteria	Bisio et al. (2020)
Anticancer: chemopreventive, anti-inflammatory, antigenotoxic	Nicolella et al. (2021)
Hepatoprotective	Abdel-Kader et al. (2019)
Cardiovascular system: vasodilatory, vasorelaxant; antihypertensive potential	Vento et al. (2014); Castro & Pontes (2020); Monteiro (2020)
Sclareol (and derivatives)	See Chapter 5 for additional details
Antiviral: studies indicate activity in haemorrhagic fevers (filovirus)	Chen et al. (2019)
Antifungal: sclareolide-derivatives show potential as antifungal agents	Ma et al. (2018)
Anticancer: active against, breast, colon, lung, osteosarcoma and leukaemia; enhance chemosensitivity of cervical and breast cancer cells	Dimas et al. (1999); Duan et al. (2018); Cosco et al. (2019); Chen et al. (2020); Afshari et al. (20202); Li et al. (2020)
Bioavailability: enhance anticancer drug activity e.g. doxorubicin; reduce cisplatin resistance in lung cancer	Oliveira et al. (2018); Borges et al. (2019); Pan et al. (2020)
Anti-inflammatory, antioxidant, antiarthritic, immunomodulatory	Huang et al. (2012); Zhong et al. (2015); Tsai et al. (2018)
Cardioprotective: antihypertensive	Vento et al. (2014); Campos et al. (2017)
Metabolic disorders: anti-obesity potential	Cerri et al. (2019)
Lung function: protective effect against lung injury and infection	Ouyang et al. (2016); Hsieh et al. (2017); Ping et al. (2017)
Skin and cosmetic uses: anti-inflammatory, anti-wrinkle; collagen supportive; potential for use against skin inflammation (dermatitis); UV protective anti-photoaging potential	Lee et al. (2016); Park et al. (2016); Wu et al. (2019)
Eye function: antioxidant, protective effect on retinal function	Ravera et al. (2020)
Gynaecology: potential for use in dysmenorrhoea (difficult menstruation) treatment	Wong et al. (2020)
Anti-osteoporosis	Jin et al. (2019); Li (2021)
Antiparasitic: anti-schistosomiasis potential	Crusco et al. (2019)
Antiplasmodial: derivatives show antimalarial activity	Mahadeo et al. (2019)
Agrochemical: sclareol and derivatives show potential for use in plant pathogenic diseases eg. Arabidopsis, tobacco and tomato wilt disease	Seo et al. (2012)

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