Table 4.0 Bioactive Conifer Flavones

Phenolics: Flavonoids (flavones)	
Compound and sources: primarily from the Araucariaceae and Podocarpaceae (also Selaginellaceae) Phytochemical investigations and resources	
Agathisflavone (and derivatives) Source: genera *Agathis, Araucaria* and *Wollemia*	
Antimicrobial: antibacterial; antiviral activity against Dengue virus, measles, influenza, herpes, respiratory syncytial virus, Mayaro virus; anti-HIV	Lin et al. (1999); Ajileye et al. (2015); de Sousa et al. (2015b); Venditti et al. (2017); Islam et al. (2019); de Freitas et al. (2020); Linden et al. (2020); Salles et al. (2021)
Antiviral: contribute to plant antiviral defences	Sarwar et al. (2019)
Antibacterial: activity enhanced in combination with other flavonoids (eg. kaempferol, quercetin)	Teran Baptista et a. (2020)
Antiviral against SARS-CoV-2	Lokhande et al. (2020); Nallusamy et al. (2021); Rameshkumar et al. (2021)
Hepatoprotective	Venditti et al. (2017); Islam et al. (2019)
Antioxidant (significant activity) and anti-inflammatory	Andrade et al. (2018); Islam et al. (2019)
Neuroprotective: antioxidant, anti-inflammatory, anti-scarring; memory supportive; anti-ischaemic promotion of recovery following brain trauma	Paulsen et al. (2011); Venditti et al. (2017); Dos Santos Souza et al. (2018); Dumitru et al. (2019); Islam et al. (2019); de Amorim et al. (2020)
Neuroprotective: active against neuroinflammation; support nerve function and repair; potential for inflammatory neurological disorders such as multiple sclerosis and Parkinson's	Velagapudi et al. (2018); De Almeida et al. (2020a, 2020b & 2021); Santos et al. (2020)
Sedative and anti-anxiety properties	Svenningsen et al. (2006); Stafford et al. (2008); Shrestha et al. (2012); Dumitru et al. (2019)
Antiparasitic: anti-leishmania and antimalarial (anti-plasmodial) activity	de Sousa et al. (2015a); Islam et al. (2019)
Anticancer: antineoplastic, cytotoxic and apoptosis-inducing; active against leukaemia, glioblastoma and cervical cancer cell lines	Konan et al. (2012); Ndongo et al. (2015); Islam et al. (2019); Nascimento et al. (2021)
Amentoflavone (and derivatives): Source: genera *Podocarpus,* also *Selaginella, Torreya, Juniperus*	
Antimicrobial: antibacterial, antifungal against *Aspergillus, Botrytis, Trichoderma*, *Saccharomyces*	Abdillahi et al. (2010); Bagla et al. (2014); Yu et al. (2017a)
Antibacterial (synergist): potential for use combined with antibiotics	Hwang et al. (2013)
Antimicrobial and antioxidant (food preparation): active against *Staphylococcus aureus* and *Escherichia coli* for food preservation eg. apple juice and chicken; anti-adhesion activity against food borne *Campylobacter jejuni*	Klancnik et al. (2018); Bajpai et al. (2019)
Anti-yeast: anti-*Candida*	Hwang et al. (2012); Yu et al. (2017a); do Nascimento et al. (2018)
Anti-mycobacterial: anti-tuberculosis potential	Kaikabo & Eloff (2011); Nayak et.al. (2018); Kumar et al. (2019)
Antimicrobial: active against *Streptococcus suis* with anti-virulence and anti-inflammatory effects (without antibacterial activity); exhibits fewer side effects than conventional antibacterial agents	Shen et al. (2018)
Antibacterial: active against *Clostridium*	Liu et al. (2020a)

perfringens responsible for gas gangrene; reduce virulence and toxin levels	
Anti-toxin: anti-sepsis, anti-inflammatory; active against *Streptococcus pneumonia* pneumolysin toxin; prevent sepsis-induced lung injury	Zong & Zang (2017); Zhao et al. (2017)
Anti-cyanotoxin: potent activity against *Microcystis aeruginosa*	Lee et al. (2019a)
Antiviral: active against influenza, herpesvirus and coxsackievirus, anti-Dengue; active against Hepatitis-C virus, chikungunya virus and Zika virus; anti-HIV, anti-RSV (respiratory syncytial virus); potential for use against drug resistant HSV (herpes-simplex virus)	Lin et al. (1999); Wilsky et al. (2012); Coulerie et al. (2013); Yiin et al. (2014); Anusuya & Gromiha (2017); Bhargava et al. (2017); Yu et al. (2017a); Lee et al. (2018b); Li et al. (2019); Chaudhary & Sehgal (2021)
Anti-Coronavirus: inhibit severe acute respiratory syndrome coronavirus (SARS-CoA); combinational drug therapies with amentoflavone suggest benefits for synergistic antiviral benefits	Ryu et al. (2010); Ghosh et al. (2020); Lokhande et al. (2020); Rasool et al. (2020); Russo et al. (2020); Saravanan et al.(2020); Swargiaryet al. (2020); Chandra et al. (2021); da Cunha et al. (2021); Mahmoudi et al. (2021); Miroshnychenko & Shestopalova (2021); Nallusamy e t al. (2021); Patil et al. (2021); Sawant et al. (2021)
Antioxidant, anti-inflammatory, anti-allergy (antihistamine); analgesic	Ishola et al. (2012); Jeong et al. (2012); Oh et al. (2013); Saroni Arwa et al. (2015); Wang et al. (2015); Kim et al. (2016); Yu et al. (2017a); Ayoub et al. (2018); Alkadi et al.(2021)
Anti-inflammatory: anti-arthritis and anti-gout potential (xanthine oxidase inhibition)	Tan et al. (2009); Wang et al. (2014); Bais et al. (2017); Kuo et al. (2019); Tavares & Seca (2018); Vasconcelos et al. (2019); Zhang et al. (2021)
Cosmetic and skin disorders: skin protective (anti-elastase); anti-inflammatory; anti-psoriasis radioprotective, prevent skin ageing due to UV exposure; reduce scar tissue e.g. wounds and burn healing	Park et al. (2011); An et al. (2016); Xu et al. (2009); Zhang et al. (2014); Jegal et al. (2018); Bailly (2021)
Gastrointestinal tract: gastroprotective (synergistic with other components in various herbs); anti-ulcer; anti-inflammatory, potential use in ulcerative colitis and drug-induced gastrointestinal dysfunction	Sakthivel et al. (2013); Yu et al. (2017a); Sofi et al. (2020); Gupta et al. (2021); Tian et al. (2021)
Hair care: alopecia, potential for prevention of hair loss	Fong et al. (2015)
Respiratory tract: anti-inflammatory, antihistamine; protection against lung injury; anti-asthmatic potential	Zheng et al. (2013); Yu et al. (2017b); Zong & Zhang (2017); Ayoub et al. (2018); Cai et al. (2019)
Musculoskeletal: bone supportive properties	Zha et al. (2016); Zhang et al. (2018b);
Liver function: hepatoprotective	Yue & Kang et a. (2011); Qin et al. (2018); Chen et al. (2020c)
Urinary tract: diuretic	Aguilar et al. (2015)
Cardioprotective antioxidant; cardiotonic; anti-atherogenic (synergistic with other flavonoids); vasorelaxant	Kang et al. (2004); Yue et al. (2011); Tabares-Guevara et al. (2017); Yu et al. (2017a); Qin et al. (2018)
Cardiovascular: anticoagulant (anti-platelet) potential	Jasamai et al. (2015); Zhang et al. (2018a); Chen et al. (2019a)
Metabolic disorders: antidiabetic and metabolism regulating potential; protective effects dietary induced metabolic dysfunction; potential clinical use	Lajsham et al. (2015); Chen et al. (2016); Zheng et al. (2016); Ighodaro & Akinloye (2017); Yu et al. (2017a); Qin et al. (2018); Su et al. (2019); Zhang et al. (2019); Gok et al. (2020)
Radioprotective: active against radiation induced haematopoietic (blood) disorders	Xu et al. (2014); Qu et al. (2019)
Anticancer: cytotoxic, anti-angiogenic,	Lee et al. (2011); Tarallo et al. (2011);

antiproliferative; antimetastatic; active against numerous cell lines eg. glioblastoma, lung, bone (osteosarcoma), colorectal, bladder, breast, cervical and ovarian cancer; a number of studies suggest good activity in liver cancer cell lines	Yeh et al. (2012); Yang et al. (2014); Chen et al. (2015); Ndongo et al. (2015); Jung et al. (2017); Li et al. (2017); Liu et al. (2017); Pan et al. (2017); Srividhya et al. (2017); Yu et al. (2017a); Hu et al. (2018); Lee et al. (2018a); Tavares & Seca (2018); Yen et al. (2018); Chen et al. (2019b); Chiang et al. (2019); Hsu et al. (2019); Lee et al. (2019b); Shen et al. (2019); Chen et al. (2020a); Chen et al. (2020c); Kim et al. (2020); Zhang et al. (2020); Qiu et al. (2021); Chen et al. (2021); Menezes & Diederich (2021)
Anticancer: contribute to the anticancer activity of various *Selaginella* species	Li et al. (2014a); Li et al. (2014b);
Anti-melanoma: derivatives show good activity	Yu et al. (2017a); Wu et al. (2017)
Anticancer (drug synergist): enhance activity of anticancer drugs such as doxorubicin, carboplatin, cisplatin and sorafenib	Lee et al. (2017); Tsai et al. (2018); Chen et al. (2020b)
Hormonal properties: no oestrogenic or anti-oestrogenic properties against breast cancer cells; however has shown aromatase-inhibitory properties which can effect oestrogen levels	Tsacioglu et al. (2016); Aliyev et al. (2021)
Gynaecology: uterine tumours; significant inhibitory effect on uterine fibroids (*Cyperus rotundus*)	Ying & Bing (2016)
Nervous system: neuroprotective, anti-ischaemic, antidepressant, anti-inflammatory, anticonvulsant, anti-anxiety; anti-Parkinsonian; anti-epilepsy (anti-seizure)	Shin et al. (2006); Stafford et al. (2008); Ishola et al. (2013); Jeong et al. (2014); Zhang et al. (2015); Ishola et al. (2016); Cao et al. (2017); Yu et al. (2017a); Rong et al. (2019); Liu et al. (2020b)
Neuroprotective: antioxidant, anti-inflammatory and memory supportive; anti-Alzheimer's potential; chemoprotective against neurotoxins (toxic metal chelation eg. copper)	Chen et al. (2018); Sabogal-Guaqueta et al. (2018); Sirimangkalakitti et al. (2019); Zhao et al. (2019); Choi et al. (2020); Sun et al. (2020); Cao et al. (2021); Windsor et al. (2021)
Antiparasitic: anti-*Leishmania*, with potential for treating cutaneous leishmaniasis; derivatives also show good activity	Kunert et al. (2008); Rizk et al. (2014); Njock et al. (2017); Mercado-Camargo et al. (2020); Rizk et al. (2021a & 2021b)
Antiparasitic: anti-*Trypanosoma*	Lopez-Lopez et al. (2020)
Antiparasitic: anti-plasmodial against malarial parasite (weak activity)	Cai et al. (2016)
Cupressuflavone genera: *Agathis, Araucaria,* also *Cupressus, Juniperus*	
Analgesic, anti-inflammatory	Al-Sayed et al. (2018)
Antiviral: present in anti-herpes *Araucaria angustifolia* extract	Freitas et al. (2009)
Chemoprotective: antioxidant, substantial protective activity against kidney and liver damage; hepatoprotective, antioxidant	Algasoumi et al. (2013); Al-Sayed & Abdel-Daim (2014)
Gastrointestinal tract: anti-ulcer gastroprotective	Koriem et al. (2015)
Cosmetic potential: skin protective (anti-elastase); anti-inflammatory potential for dermatitis	Xu et al. (2009); Jegal et al. (2018); Lee et al. (2018c)
Neuroprotective: potential for neurodegenerative disorders	Shrestha et al. (2013)
Anticancer: cytotoxic activity against prostate cancer dells	Al Groshi et al. (2019)
Hinokiflavone Source: genera *Dacrydium,* also *Selaginella, Juniperus, Platycladus, Rhus*	
Anti-inflammatory (significant activity), antioxidant	Wang et al. (2015); Shim et al. (2018)
Antiviral: active against Dengue virus; modest	Coulerie et al. (2012)

activity against Herpes viruses	
Antiviral: active in SARS-CoV-2 studies	Belhassan et al. (2021); Mondal et al. (2021); Sawant et al. (2021)
Gastrointestinal function: potential for use in inflammatory bowel disorders	Shim et al. (2018)
Cardiovascular system: anticoagulant	Lale et al. (1996)
Hepatoprotective: antioxidant; synergistic with glycyrrhizin	Algasoumi et al. (2013); Coulerie et al. (2013); Abdel-Kader et al. (2018)
Alopecia: potential for prevention of hair loss	Fong et al. (2015)
Anticancer potential: anti-tumour activity; anti-proliferation, anti-metastasis; active against nasopharyngeal, cervix, glioma and breast cancer cells; with an emphasis on liver and colon cancer cell lines; analogues also show anticancer potential	Lin et al. (1989); Kalva et al. (2014); Zhou et al. (2019); Huang et al. (2020); Mu et al. (2020); Goossens et al. (2021)
Anticancer (drug design): micelles showed enhanced antitumour activity in lung adenocarcinoma	Chen et al. (2020d)
Anticancer: contribute to the activity of *Selaginella* herbs (synergist with other components)	Goossens et al. (2021)
Anti-melanoma: anticancer activity in melanoma skin cancer cell lines	Yang et al. (2018)
Antiparasitic: antiprotozoal with good activity against *Leishmania* and *Plasmodium*	Kunert et al. (2008)
Podocarpusflavone Genera: *Dacrydium*, *Podocarpus, Chamaecyparis* also *Garcinia, Selaginella*	
Antioxidant, anti-inflammatory	Saroni Arwa et al. (2015)
Antiviral: strong inhibition of Dengue virus	Coulerie et al. (2012)
Antiviral: activity against SARS-CoV-2 virus	Sharma et al. (2021)
Neuroprotective: anti-Alzheimer's potential	Sasaki et al. (2015)
Anti-melanoma	Meng et al.(2020)
Antiparasitic: anti-Leishmania activity	Mercado-Camargo et al. (2020)
Insecticide: play a role in plant resistance to insect attack (insect growth inhibition), synergistic with other chemical components (*Podocarpus gracilior*)	Kubo et al. (1984)
Robustaflavone genera: *Dacrydium*, *Podocarpus;* also *Selaginella*	
Antimicrobial: antifungal; antiviral ie. influenza, herpesvirus, hepatitis, anti-HIV, anti-Dengue;	Lin et al. (1997 & 1999); Coulerie et al. (2013); Rizk et al. (2014)
Antiviral: good activity against hepatitis B that suggests potential for synergistic combinations with other antiviral agents	Zembower et al. (1998)
Antiviral: active in SARS-CoV-2 studies	C S et al. (2020); Mondal et al. (2021)
Antioxidant, anti-inflammatory, anti-allergy (antihistamine)	Rizk et al. (2014); Wang et al. (2015); Ayoub et al. (2018)
Gastrointestinal tract: potential use for inflammatory bowel disorders	Jo et al. (2019)
Anti-inflammatory: anti-gout potential (xanthine oxidase inhibition)	Tan et al. (2009); Wang et al. (2014); Zhang et al. (2021)
Respiratory tract: anti-inflammatory; protective effect on lung function (robustaflavone-4'-dimethyl ether)	Wu et al. (2020)
Urinary tract: diuretic	Aguilar et al. (2015)
Cosmetic potential: skin protective (anti-elastase)	Xu et al. (2009)
Antiparasitic: anti-leishmania activity	Rizk et al. (2014)
Anticancer: antitumour, antiproliferative; contribute to anticancer activity of *Selaginella* herbs	Li et al. (2014a); Li et al. (2014b); Chen et al. (2019a); Sim et al. (2020); Xie et al. (2021)

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