

Eucalyptus - herbal medicine and essential oil

Part 2. Non-volatile constituents

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Traditionally *Eucalyptus* teas and extracts are used as an expectorant, for catarrhal conditions of the respiratory tract and bronchitis (Bissett, 1994). In this paper, the use of the leaf as a tea, powder or extract will be reviewed, along with some promising research into the non-volatile leaf constituents ie. those not found in the essential oil.

Try searching for *Eucalyptus* extract on Google – the hits all focus on sites promoting the essential oil only. I have asked some Australian herbalists about the availability of Eucalyptus extract, and once again they mostly relate to *Eucalyptus* as an essential oil. I checked for products listed on the Therapeutics Goods Administration (TGA) website, and found one product only that wasn't based on the essential oil. This is a bronchial formula that includes *Eucalyptus* leaf powder along with other ingredients.

In fact, *Eucalyptus* extract and the non-volatile constituents can provide many therapeutic benefits not found in the essential oils, as a search of the research literature reveals. Apart from essential oils, *Eucalyptus* leaves are rich in other compounds including polyphenols and triterpene. As with the essential oil, much – but not all – of this research has been based on *Eucalyptus globulus*.

Eucalyptus as a functional food?

In Japan leaf extracts of *E. globulus* are used as food additive for the prevention of chronic diseases since 2003. From a non-Japanese perspective, Sinbal et al. suggested that the hydrolysable tannins in *Eucalyptus* leaves would be promising natural antioxidants in pharmaceutical, feed and food supplement industries. This conclusion is supported by studies with an ethyl acetate extract and individual tannin components of *Eucalyptus* extract, which demonstrated potent antioxidant and cytotoxic actions. The authors note the potential as a chemopreventive agent against breast, colon and other common cancers (Sinbal et al. 2014).

It has also been suggested that *Eucalyptus* leaf extract could be an additive in sugar/fructose laden “junk” drinks, due its' ability to inhibit intestinal fructose and sucrose absorption (Dey & Mitra, 2013).

Non-volatile constituents

Polyphenols

As noted above, Eucalyptus leaves are rich in tannins which, along with flavonoids, form the major sub-categories of polyphenols – compounds based on multiple oxidized aromatic ring structures.

In one analysis of *E. globulus* fruit, 18 gallotannins and 26 ellagitannins were identified (Boulekbache-Makhlouf, 2010).

Two other tannins of interest in *E. globulus* leaves, eucaglobulin and globulin A, consist of gallic acid linked to monoterpenes with glycosidic bonds. These compounds demonstrated potent antioxidant, anti-inflammatory and anti-melanogenesis activity *in vitro* (Hasegawa et al., 2008).

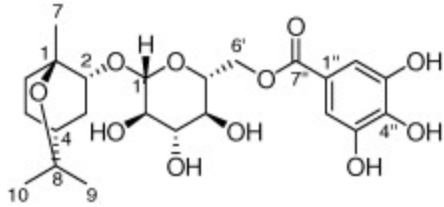


Figure 1. Eucaglobulin

Oenothetin B, the dimeric macrocyclic ellagitannin, is a potent antioxidant, anti-inflammatory and antibacterial agent (Amakura et al., 2009) that also reduces neuroinflammation in the brain *in vivo* (Okuyama et al, 2013).

Eucalyptus bark is also rich in tannins, as demonstrated in an analysis of aqueous extract of *E. globulus* bark which yielded significant levels of catechins, ellagic acid and flavonoids (Vazquez et al, 2012).

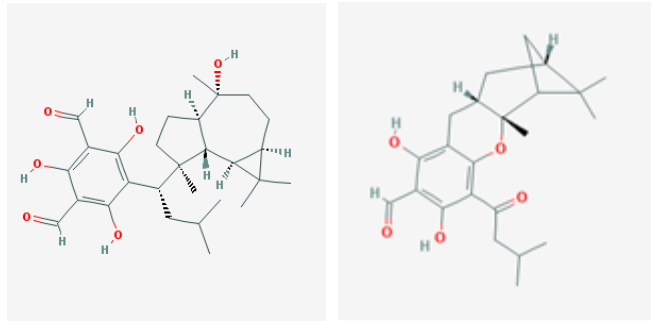
Apart from tannins, numerous flavonoids and stilbenes (resveratrol) are found in *Eucalyptus* leaves (Vuong et al., 2015), while two species of 'stringybarks' (*E. macrorhyncha*, *E. youmanii*) have been exploited due to their high levels of the flavonoid rutin, easily extractable with water (Lassak & McCarthy, 1983). Extracts of *E. globulus*, *Corymbia maculata* and *E. viminalis* demonstrated significant inhibition of seven micro-organisms that cause food poisoning, acne and athlete's foot including MRSA, but with no inhibition of gram negative bacteria. The antimicrobial constituents were found to include the a chalcone and two flavonoids based on eucalyptin; notably these polyphenols are also found in two other common species in Eastern Australia – *E. crebra* (narrow-leaved ironbark) and *E. botryoides* (bangalay). (Takahashi, 2004).

Investigations carried out at the University of Newcastle used an aqueous extract of the swamp mahogany (*E. robusta*), analysis of which revealed high total phenolic compound levels of 407 mg GAE/g. (Vuong, Hirun et al, 2015). Potent antioxidant effects were demonstrated, as well as a significant toxic effect on human pancreatic cells.

FPCs

Formylated phloroglucinol compounds (FPCs) are combined structures of phloroglucinols with isopentyl side chains linked to a terpene moiety – either a sesquiterpene or monoterpene. Macrocarpals A-C were first isolated from *E. macrocarpa*, they also occur in *E. globulus* amongst other species (Duran-Pena et al., 2015). Macrocarpals and euglobals have been identified and characterized from the genus, and many of these compounds have significant biological effects (Konoshima and Takasakialso 2002).

These compounds have been shown to provide significant inhibitory activity on HIV-RTase, an enzyme associated with onset of AIDS. Macrocarpals A-C also inhibit gram-positive bacteria *Bacillus subtilis* and *Staph. aureus*, but also against periodontal gram-negative bacteria. Other activities demonstrated for *Eucalyptus* macrocarpals include mood-enhancement and anti-depressant, as well as being significant inhibitors of aldose reductase – enzymes that cause eye and nerve damage to diabetics (Duran-Pena et al., 2015).



Macrocarpal B

Euglobal – G1

Figure 2: Representative structures of non-volatile constituents in *Eucalyptus* spp.

Sideroxylnols, dimeric phloroglucinols lacking a terpene moiety- from the iron bark *E. sideroxylon*, have shown significant antibacterial activity against gram-positive bacteria. Other phloroglucinol derivatives isolated from *E. robusta* have shown inhibitory effects against the malarial parasite, and potential antimalarial agents are currently being developed (Konoshima & Takasakialso 2002).

Triterpenoids

E. camaldulensis, the river red gum of inland Australia, contains unique triterpenes known as camaldulenic acids (Begum, Farhat & Siddiqui, 1997) and eucalyptic acids (Siddiqui, Farhat, Begum & Siddiqui, 1997). More recently Begum et al. isolated three triterpenoids, camaldulin (a new compound) ursolic acid lactone acetate and ursolic acid lactone from *E. camaldulensis* var. *obtusata* leaves. All three triterpenes demonstrated spasmolytic effects based on a calcium antagonism mechanism (Begum et al., 2000), as did eucalyptanoic acid (Begum et al., 2002).

Clinical Applications

Eucalyptus leaves are mostly taken in liquid forms as infusions, fluid extracts and tinctures, or by inhalation. It is one of our best medicines for sinusitis, bronchitis, influenza, restricted airway diseases, laryngitis and the common cold. It is also indicated for acute diarrhea and dysentery. It is considered specific for throat infections with mucous discharges. The American eclectic physician HW Felter prescribed *Eucalyptus* extract and essential oil for cold extremities and cold perspiration, as well as for chronic muco-purulent discharges (Felter, 1922). Further, he promoted its use in the “sick room” for general antiseptic and deodorant purposes, and as topical applications on ulcers and wounds

Both aqueous and organic solvent extracts of *Eucalyptus* have been shown to inhibit growth of tumours in human cell lines, demonstrating both cytotoxic and antiproliferative effects (Vuong et al, 2015). However, there is little clinical data available and it cannot be recommended as an adjunct cancer treatment at this stage.

Periodontal uses

Dental health is another field in which *Eucalyptus* extracts may play a role. Nagata et al. determined the macrocarpals inhibit gram-negative bacteria associated with tooth decay, concluding that *Eucalyptus* leaf extracts may be a potent preventative treatment for periodontal disease (Nagata et al. 2006) and subsequently developed a *Eucalyptus* extract-based chewing gum that was shown to reduce symptoms of periodontal disease in humans (Nagata et al. 2008).

In a more recent study, various solvent extracts of *E. globulus* leaves were tested against a panel of cariogenic bacteria (those that cause tooth decay in humans) using an agar well diffusion method. Significant inhibition of these pathogens was observed (Ishnava, Chauhan & Barad, 2013).

Metabolic disorders

Eucalyptus leaves have been utilised as a hypoglycemic, anti-diabetic remedy in parts of the world for over a century. Compounds of interest include the anthocyanin myrtillin and oleanolic acid glycosides (Williams, 2011).

Hypoglycaemic effects of *Eucalyptus* extracts have been demonstrated *in vivo*, particularly for the species *E. globulus*, *C. citriodora*, *E. Camaldulensis* and *E. tereticornis*, largely based on the inhibition of enzymes associated with carbohydrate metabolism. In addition, the extracts reduce oxidative stress and inhibits lipid synthesis (Dey & Mitra, 2013).



Corymbia citriodora – lemon-scented gum

Safety issues

There have been few if any reports of adverse reactions from teas or extracts prepared from *Eucalyptus* leaf. The authoritative *Botanical Safety Handbook* (Gardner & McGuffin eds., 2013) classifies the leaf as Safety Class 1 (herbs that can be safely consumed when used appropriately), and lists no concerns for drug interactions. The German Commission E Monograph (1986) indicates that in rare cases nausea, vomiting and diarrhoea may occur. Felter (1922) advises against using extracts internally when there is any state of acute inflammation. Safety concerns regarding the use of the pure essential oil are not considered here.

Dosage considerations

Bissett recommends a dose of 1.5-2g finely cut leaf per cup as an infusion, while the French Pharmacopoeia recommends 1.5-3g, four times per day (Dey & Mitra, 2015). The Commission E Monograph recommends a daily dose of 4-6g for the leaf, and 3-9ml for the tincture, which is in line

with Dey and Mitra's range of 2.5ml tincture 1-3 times daily. In Australia there is no standard extract in use, though there are likely to be "practitioner only" brands available as 1:2 extracts, or possible 1:5 tinctures. As a herbalist I have made 1:5 tinctures from the dried leaves, and dispensed at a dose between 1-4mL, 2 or 3 times daily.

Conclusion

For practitioners and product manufacturers interested in using or marketing non-volatile products, numerous species of *Eucalyptus* are listed ingredients with the TGA, including many which are mainly exploited for their essential oils including *E. globulus*, *E. radiata* and *E. dives*. There is a good body of evidence supporting the use of non-volatile Eucalyptus products for a broad range of clinical presentations including coughs, colds and flu, treatment of some viral infections, periodontal and metabolic disorders. The leaves can be powdered and added to dietary antioxidant formulae, extracted in water or with aqueous/ethanolic menstruum and used in range of therapeutic products. Combining a *Eucalyptus* extract with its essential oil can enhance the expectorant and antimicrobial effects for bronchial conditions.

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