

Dietary Flavonoid Intake and Chronic Sensory Conditions

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Contributor: Diana Tang, Yvonne Tran, Giriraj S. Shekhawat, Bamini Gopinath

Dietary flavonoids have antioxidant, anti-inflammatory, and vascular health benefits, which align with the proposed pathophysiology of age-related eye conditions and hearing problems (hearing loss and tinnitus). The flavonoid subclass, flavanols, are protective against eye conditions, including age-related macular degeneration, cataract, and glaucoma. Dietary flavanol intake appears to be protective against some chronic eye conditions.

Keywords: flavonoid ; dietary intake ; macular degeneration ; diabetic retinopathy ; hearing loss ; tinnitus ; cataract ; age-related ; sensory loss

1. Introduction

Flavonoids are bioactive polyphenolic compounds that are naturally ubiquitous in a range of plant-based produce, including fruits, vegetables, and beverages such as tea and red wine ^{[1][2]}. There are six major flavonoid subclasses, each with a number of key compounds—flavanols (e.g., epicatechin, epigallocatechin-gallate, and proanthocyanidins), flavanones (e.g., hesperidin and naringenin), flavones (e.g., apigenin and luteolin), isoflavones (e.g., genistein and daidzein), flavonols (e.g., quercetin, kaempferol, and myricetin) and anthocyanins (e.g., cyanidin and malvidin) ^{[2][3]}. Certain flavonoid subclasses are more abundant or limited to specific foods and beverages, for example, flavanones are common in citrus fruits; isoflavones in soy products; and anthocyanidins in wine and bilberry ^[1]. Due to the variability of flavonoids throughout the food supply, dietary intakes vary depending on food sources, food preferences, and dietary habits ^[4].

There has been growing research interest around the health benefits of flavonoids with evidence of antioxidant and anti-inflammatory properties as well as vascular health benefits through improved endothelial function ^{[2][5]}. This evidence has led to research around the potential benefits of flavonoids for vision and/or hearing loss and tinnitus, where their pathophysiology has been linked to oxidative stress, inflammation, and vascular health ^{[6][7][8]}.

According to findings from the 2020 Global Burden of Disease (GBD) study ^[9], the leading causes of age-related vision loss in adults aged ≥ 50 years were cataract (15.2 million cases), glaucoma (3.6 million cases), age-related macular degeneration (AMD) (1.8 million cases), and diabetic retinopathy (0.86 million cases). To briefly describe each condition, cataract is a condition where the lens of the eye becomes progressively opaque, allowing less light to pass ^[10]; glaucoma is a condition characterised by changes to the optic nerve head and excavation of the optic disk causing the loss of the visual field and increased intraocular pressure ^{[11][12][13]}; AMD is a condition where the macula of the retina deteriorates leading to the loss of central vision ^[14]; and diabetic retinopathy is a complication of diabetes involving the presence of microaneurysms or haemorrhages in the retina ^[15].

The GBD study ^[16] also reported that 1.57 billion people in 2019 suffered from a hearing loss and that 62.1% of these people were aged ≥ 50 years. Among this older age group, $\geq 96.2\%$ of hearing loss was age-related or caused by other factors such as noise exposure ^[16]. Age-related hearing loss (ARHL), also referred to as presbycusis, is a chronic condition involving the progressive loss of hearing ^[17]. People with ARHL often complain of tinnitus, a chronic auditory condition characterised by ringing or buzzing in the ears or head where an external source of sound is not present ^[18]. The prevalence of tinnitus steadily increases with age and ranges from 5.1 to 42.7% in adults ^[18].

Although treatments and therapies are available to address some of these chronic sensory conditions ^{[9][14][16][19]}, the need to identify additional prevention and management strategies is warranted, not only because of the high prevalence rates, but also because vision and hearing loss are major causes of disability ^{[9][16]}. With reference to the GBD study, vision loss ranks as the eighth largest cause of disability in adults aged 50–69 years and the fourth largest cause in those aged 70+ years ^[9]. ARHL outranks vision loss in both older adult age groups as the third largest cause of disability ^[16].

2. Dietary Flavonoid Intake and Chronic Sensory Conditions

Six studies reported favourable associations between dietary flavonoid intake with chronic eye conditions [6][10][12][15][20][21]. In particular, higher intakes of dietary flavonols were associated with a reduced risk of primary open-angle glaucoma [12] and reduced odds of prevalent AMD [6][21], while lower intakes of dietary flavonols were associated with poorer visual acuity related to AMD [21] and increased risk of age-related cataract [10]. For glaucoma, the role of flavonols in risk reduction may be linked to antioxidant activity. This is because the pathogenesis of glaucoma and its common symptom (i.e., higher intraocular pressure) have been associated with oxidative damage to the trabecular meshwork and surrounding endothelial cells [22]. In an experimental investigation by Miyamoto et al. [22], the flavonol quercetin was shown to induce the expression of antioxidant enzymes (peroxiredoxins) to reduce oxidative damage and thereby regulate intraocular pressure levels to normal levels [12][22]. For AMD, flavonols have been linked to a number of pathways. One example includes the regulation of the nitric oxide status by enhancing its production and increasing the amount of circulating nitrite in order to improve endothelial function [5][6][21]. A second example of the potential role of flavonols in AMD includes scavenging reactive oxygen species that may be causing oxidative damage to the retinal pigment epithelium cells [6][21][23]. The integrity of the retinal pigment epithelium is important to the health of the macula and, thus, in the prevention of AMD development and/or progression [14]. The third example includes the inhibition of retinal and choroidal angiogenesis [6][21][24][25]. Experimental studies conducted in vitro have shown that quercetin inhibits angiogenesis by impacting the development and spread of new blood vessels within the choroid and retina regions of the eye [24][25]. For cataract development, flavonols are suggested to play a role in modifying pathways causing eye lens opacification, including oxidative stress, epithelial function, nonenzymatic glycation, the polyol pathway, and lens calpain proteases [10][26]. The antioxidant role of flavonoids such as flavonols has been linked to protecting and promoting antioxidant enzymes and inhibiting the function of the enzyme aldose reductase, which has a key role in the development of cataract among patients with diabetes [27].

One study reported a significant benefit of dietary flavan-3-ols in relation to AMD outcomes [21]. According to Detaram et al. [21], lower intakes of dietary flavan-3-ols were significantly associated with poorer vision and almost double the risk of intraretinal fluid compared with higher intakes of flavan-3-ols. The lack of supporting evidence around the protective effects of dietary flavan-3-ols and anthocyanins for eye health may be due to their lower availability in the diet in comparison to flavonols [28][29], particularly the flavonol quercetin, which has been reported to be the most widely consumed and studied flavonoid [10].

Overall, there is a protective association between dietary flavonoids, particularly flavonols, and AMD, glaucoma, and cataract. However, for most of the sensory conditions included, only one study was identified. This signifies a strong need for further research in this area to substantiate any associations.

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