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THE EFFECT OF ANTHOCYANINS ON ACCOMMODATION IN VISUAL DISPLAY TERMINAL WORK

Systematic Literature Review

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ABSTRACT

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Introduction: As a healthcare professional, an optometrist should be able to instruct their patients on the best practice for vision problems. Therefore, the latest knowledge of the relieving vision problems also through nutrition should be known to optometrists.

Purpose: This thesis work aimed to determine whether anthocyanins, usually available from vegetables, influence ocular accommodation when burdened with visual display terminal (VDT) work. The systematic literature review investigated the connection between anthocyanin's impact on accommodation for VDT work compared to placebo.

Methods: This systematic literature review involved an analysis of 4 studies, and they were selected using PubMed, Ebsco, Elsevier and Google Scholar. The search was made on 21 March 2022 using English studies only. The publish date of records was limited to the years 2010–2022. Clinical studies for healthy subjects only were included in the literature review. All the studies were evaluated for critical appraisal using the Centre for Evidence-Based Medicine- University of Oxford evaluation sheets.

Results: The systematic review included four randomised controlled trials (RCTs) involving 271 participants. Used anthocyanin was derived from blueberry or maqui berry. The amount of used anthocyanin varied between 21-88,54 mg/day. In studies, the near vision was strained for at least 40 minutes. Three out of four studies indicated that anthocyanins reduced VDT load-associated eye fatigue, but none of the studies measured, for example, the amplitude of accommodation.

Conclusion: Understanding of accommodation requires a knowledge of the eye's biomechanics and physiology of the visual system. In conclusion, the systematic literature review failed to answer the research question. There is no golden standard for measuring accommodation, and RCTs included in the systematic literature review observed more eye fatigue than accommodation. However, accommodation difficulties can be one reason for eye fatigue. Based on the systematic literature review, there are indications that anthocyanins positively affect eye fatigue compared to placebo after VDT work. Due to their minor subjects, the result cannot be generalized. Also, the results cannot be considered clinically relevant due to the defects found in the studies. There is interest in the effect of anthocyanins on eye health and vision, so more robust evidence will be available in the future.

Keywords: flavonoids, anthocyanin, accommodation, ocular, visual display terminal.

CONTENTS

1 INTRODUCTION

Eyestrain is familiar to almost everybody. The modern lifestyle demands working with computers, laptops, and smartphones. Accommodation of the eye makes near vision possible, but long-term close-up viewing, however, causes trouble for many. (Parihar et al., 2016; Sheppard & Wolffsohn, 2018; Jaiswal et al., 2019; Singh et al., 2022) Blurred vision and difficulty focusing on the near target are often reasons for optometrist visits (Rosenfield, 2011). In the comprehensive eye exam, the optometrist assesses factors such as refraction, binocular vision, the function of eye muscles and accommodation. Besides prescription, the optometrist can advise visual ergonomic advice, for example, the 20-20-20- rule, to relieve eye discomfort (Singh et al., 2022).

The eye requires oxygen and various nutrients to function. As a health care practitioner, the optometrist should also understand the impact of nutrition on the eyes' health and vision. The effect of diet on vision, in turn, was already observed during World War II, when pilots ate blueberry jam for better night vision (Nomi, Iwasaki-Kurashige & Matsumoto, 2019). A good scotopic vision is an essential characteristic for specific circumstances in the present, but nowadays, people have different challenges with vision. For example, the role of nutrition and nutritional supplements in treating dry eye disease has been of interest to scientists for a long time. Versatile nutrition and dietary supplements are also the means to ease eye strain. A nutritious diverse diet can offer one way to prevent and reduce risks for many eye diseases (Khoo et al., 2019; Lawrenson & Downie, 2019).

This thesis work is a systematic review of anthocyanins' effect on accommodation in visual terminal display (VDT) work. The objective of the thesis was to search the anthocyanin impact on the eye's ability to focus on a near target after a near-vision task compared to placebo preparation. The systematic literature review analysed studies where the accommodation system of healthy subjects was strained by long-term near-viewing. The subjects were observed mainly quantitatively before and after using the anthocyanins. In order to provide a reliable result to this thesis, studies were approved that only examined the effect of anthocyanins and were randomized controlled trials (RTCs). The sources of the systematic literature review are defined between the years 2010 and 2022.

Chapter two presents the background of this thesis work- visual terminal display and eye strain, accommodation and anthocyanins. This information was gathered chiefly using the database “Pub-med” (searching words: accommodation, measure, anthocyanin) and the handbooks in optometry. The purpose and subjects of the systematic literature review are described in chapter three. The research question, search progress and results are documented in chapter four. There is also an analysis of the data and the systematic literature review results. Chapter five presents the results of a thesis on work life and includes conclusions and discussion. At the end of the thesis, reliability and ethicality are considered, and the schedule and budget are presented.

The effect of diet on health and eyes, in general, is much discussed. Several supplements are widely marketed with different health effects, which is why I wanted to familiarise myself with the topic in more detail. Also, as an optometrist, clients ask how they would be able to maintain eye health and vision above. Traditionally optometrists have helped their patients in optical ways. As knowledge of the impact of nutrition on human health increases, it is also significant to know how to advise clients to maintain eye health and vision through nutrition. Nutrition gives the optometrist a more comprehensive toolkit to help their patients. Up-to-date vision correction is the base of a good vision for everyday life. The increased near-vision use has also raised the importance of optoergonomics and eye relaxation.

I have been interested in the effect of nutrition on health for a long time. The idea for this thesis work surfaced when I read the review of Nomi, Iwasaki-Kurashige, and Matsumoto's "Therapeutic Effects of Anthocyanin for Vision and Eye Health" (2019) in the autumn of 2020. That review raised the anthocyanins' positive impact on the eyes. The possibilities of anthocyanins impressed me. Anthocyanins are available as a dietary supplement, and in Finland, we are well placed to enjoy anthocyanins, such as bilberries picked from the forest. In more than 15 years of clinical work, I have also found that patients who eat berries daily have fewer vision problems. This experience sparked an interest in exploring the subject further. Many patients come to the practice for help with eye strain and may not require eyeglass correction. Therefore, it is essential to know how to advise them well in non-optical ways.

2 THEORETICAL BACKGROUND

This chapter covers concepts of accommodation, visual display terminal, and anthocyanin. Visual or video display terminal units are all kinds of electronic screens, for example, computers, laptops, mobile phones, and game devices. Accommodation is usually an unconscious process which is controlled by the brain. Understanding accommodation requires knowledge of the optics and bio-mechanics of the eye, how the accommodative stimulus transfers from the retina to the brain and how the neural signals control the ciliary muscle to bring about the response (Read et al., 2022). Anthocyanins are flavonoids giving, for example, the purple colour for bilberries, and their impact on human health and vision intrigues scientists (Khoo et al., 2017; Ockermann et al., 2021).

2.1 Accommodation

The human eye is the round, 2,5 cm in diameter organ in the anterior part of the orbit, which is situated closer to the medial wall and nearer the roof than the floor. The eye has formed the parts of two spheres, the cornea and the sclera, and there are three tunics, which are the eye's primary layers. Those tunics are fibrous, the uveal tract and the neural layer. The light energy from the environment causes a cascade where the specialized nerve cells, rods and cones, change it to a nerve action potential. That change is relay via the optic nerve to the brain, where the information will be processed and consciously as vision. (Forrester et al., 2021, pp.13—14.)

The visual response for focusing on the near target is called accommodation. The accommodation reflex is also called accommodation-convergence or near reflex, and it consists of three acts which are:

- The convergence
- The change in the lens shape
- The pupillary constriction

(Skalicky, 2016; Motlagh & Geetha, 2022; Wu, Zhao & Zhang, 2022)

Those acts increase the lens's considerable refractive power, and the eye's focus changes from distant to near object. The contraction of the right and left eye's medial rectus muscles, simultaneously relaxing the lateral rectus causes the adduction (turning inward) of both eyes and allows the image projection to the fovea. In accommodation, bilateral ciliary muscles contract, and the lens thickens, causing the shortening of the focal point of the eye by increasing the refractive power. In the near view, constriction of the sphincter pupillae muscles results from the pupils constricting, which improves the depth of focus. (Motlagh & Geetha, 2022.) A stimulus for this accommodation process is a blurred pattern causing to response to get the retinal image clearly defined (Borish & Benjamin, 2006, p. 227).On a cellular level, the accommodation reflex follows from neural signalling conducted by afferent and efferent pathways (Motlagh & Geetha, 2022).

The autonomic nervous system plays an important role in accommodation. There are the sympathetic, parasympathetic, and trigeminal sensory nerve fibres in the eyes, but in the accommodation and pupil constriction, parasympathetic fibres are mainly involved. (Wu et al., 2022). The afferent impulse goes through the optic nerve, and the efferent impulse comes through the Edinger Westphal nucleus and oculomotor nerve (Motlagh & Geetha, 2021; Wu et al., 2022). In the human eye, ciliary muscles are contracted via cholinergic muscarinic mechanisms (Wu et al., 2022).

The autonomic nervous system confers neural control of the body, and several physiological functions of the eye are precisely regulated by it. The autonomic nervous system is also behind the accommodation by adjusting lens adaptation and pupil size. (Wu et al., 2022) The nerve action is not possible without a well-organized system, where the focus and transmission of the light are possible because of the cornea, lens, iris, and ciliary body. Besides that, the eye needs to nourish and support the aqueous outflow system, tear-producing, and choroid. (Forrester et al., 2021, p.13.)

The most widely supported accommodation theory was developed in the middle of the 1800th century. According to that theory, the ciliary muscle is relaxed when focusing on the distance. That increases tension in the parts of the zonule. Because of this, the lens is exerted by a force that flatters its curvature. Accommodation occurs when the target is near, causing the ciliary muscles to contract and zonular tension release. That causes a more curved lens shape and a stronger refractive impact. (Wang & Pierscionek, 2019.) Schachar's theory from the 1990s proposes that in an unaccommodated state, equatorial zonular fibres relax, and in an accommodative state, anterior and posterior zonular fibres relax. The equatorial zonular fibres increase in tension as the ciliary muscle contracts and cause the anterior and posterior zonule to be relaxed. Meanwhile, the lens will be spindle shape with steep central and flat peripheral surfaces. When the need for accommodation is less, the equatorial zonules become less and anterior and posterior tenser. That causes decreasing curvature of the central region of the lens. (Schachar, 2012, pp. 23—28; Wang & Pierscionek, 2019) No theory has been able to explain accommodation completely.

2.1.1 Accommodation from the Point of Optics

Generally, accommodation and seeing are strongly related to optics, that is, understanding the passage of light in the medium. The behaviour of the light is called vergence, and light can be diverging, converging or parallel. The unit of measurement of vergence is called diopter (D). (Schwartz, 2006, pp. 21—22.) Objects emit and reflect light in a divergent ways. When the object is moved away from the viewer, the light becomes less divergent until it is almost parallel. (Schwartz, 2006, p. 80) For practical purposes, six meters (20 feet) indicates “infinity” because, mathematically, it presents the distance where the light of the subject is coming parallel. (Schwartz, 2006, p. 23; 79)

When the eye is at rest, there is a slight focusing (about 0,5-1,5 diopters), so-called tonic accommodation (see chapter 2.1.4.). This provides for some fluctuation in the level of accommodation to improve image quality. When there is a blurred image, a change in the appearance of objects' size/distance, or appear chromatic aberration, the level of accommodation rises. (Skalicky, 2016, p. 60.) When the object moves toward the viewer, it causes a change in the lens of the eye. Shift keeps the object in focus. When the orientation of the lens and ciliary body changes, the focus stays on the retina. This change can be thought of as happening like focusing on the camera. (Schwartz, 2006, p. 79.) The demand for accommodation varies depending on the object's distance. It is obtained by calculating the inverse number of the distance. (Schwartz, 2006, p. 81.)

$$accommodation\ (D) = \frac{1}{distance\ (m)}$$

The requirement for accommodation is greater the closer the object is viewed. For example, at a computer terminal distance of 70 centimetres, the demand for accommodation is about 1,4 dioptres, but when looking at a smartphone, to 30 centimetres already 3,3 dioptres. According to Miller, Subramaniam & Patel (2015, p. 421) “**the near point of accommodation** (NPA) is the point closest to the eye at which a target is sharply focused on the retina”. When accommodation is measured, the power of what lens can change from a nonaccommodative state to full accommodation called accommodative amplitude or **amplitude of accommodation**. **The range of accommodation** is the distance between the nearest and farthest point of the target with clear vision. (Miller, Subramaniam & Patel, 2015, p. 421.)

Most people can comfortably use half of their accommodation capacity (Schwartz, 2006, p. 84). A young child has the ability to accommodate 14-15 diopters. The loss of accommodation starts slowly and increases through middle age. Generally, it can assume that the average 20-year-old has accommodation between 10-12 diopters and a 68-year-old has 0,5-1,0 diopters left. (Schwartz, 2006, pp. 84—85.) The gradual decline of the amplitude of accommodation with age usually interferes with a reading by age 40-45. That decline is called **presbyopia**. (Scheiman, 2011, p. 59.) There are also other accommodative disorders: insufficiency, excess, and infacility (Scheiman, 2011, p. 58). These disorders have been further detailed in paragraph 2.1.6.

2.1.2 The Biomechanics of Accommodation

The human eye is an optical device that can easily focus from infinity closer than 10 cm quickly and smoothly. Accommodation occurs due to the change in the shape of the eye's lens when the lens's central surface turns steeper, and the peripheral surface turns flatter. (Schachar, 2012, p. xi; Wang & Pierscionek, 2019.) Borish and Benjamin (2006, p. 212) describe the accommodation as a process in which changes in the dioptric force of the lens occur so that a retinal image of the target is obtained and maintained for a high-resolution fovea. Borish and Benjamin (2006, pp. pp. 215—216) state seven changes in the biomechanics of the eye due to accommodation, and they are described below.

(1) A step input increase occurs in the firing frequency of neural innervation to the ciliary muscle
(2) The contraction force of the ciliary muscle increases.
(3) The ciliary muscle moves inward and anteriorly.
(4) The ciliary ring advances approximately 0.5 mm along the ciliary muscle.
(5) The choroid and posterior zonules stretch approximately 0.5 mm
(6) The anterior zonular tension decreases, and the zonulas relax.
(7) The elastic forces of the lens capsule and the viscoelastic properties of the lens cause the lens to become more spherical. Thus the overall power of the lens increases:
    a) The equatorial diameter decreases by 0.4 mm (from 10 to 9.6 mm)
    b) The anterior lens pole moves back 0.3 mm

c) The central anterior radius of curvature changes from 11 to 5.5 mm
d) The posterior lens pole may move back 0.15 mm
e) The central posterior radius of curvature decreases from 5.18 mm to 5.05 mm
f) The central thickness increases by 0.36 mm to 0.58 mm
g) The lens sinks 0.3 mm as a result of gravity

(Borish & Benjamin, 2006, pp. 215—216)

The human lens is a transparent, highly organized system of specialized cells. It has an essential role in the optical system. Even though lens refractive power is minor than the cornea, the lens's ability to change shape with ciliary muscle allows the retina to get a sharp picture. The lens is formed of three parts: the capsule, anterior or lens epithelium and the lens fibres. The lens shape is biconvex with an ellipsoid structure with a differing radius of curvature on anterior and posterior surfaces. (Forrester et al., 2021, p. 32.) The human lens consists of 65 % water and 35 % protein (Schachar, 2012, p. 21). The lens size grows 0,023 mm per year, and the shape alters throughout life (Forrester et al., 2021, p. 32).

The ciliary body, including the ciliary muscle and lens zonules (zonular apparatus), are essential in the alteration of the refractive power of the lens. The ciliary muscle is two-thirds of the ciliary body. (Forrester et al., 2021, p. 31) The ciliary muscle is the only active element in accommodation (Borish & Benjamin, 2006, p. 213). The lens is held in position by radially arranged zonules resemble a trampoline. Zonules are tough but delicate fibres and attached lens capsule 2 mm anterior and 1 mm posterior to the equator. Zonules form bundles (Ø 5-10 µm) with microfibers (Ø 0,35-1 µm). Principally zonules are composed of fibrillin, which is a glycoprotein. In the non-accommodative state, the ciliary body keeps tension on the zonules, but during accommodation, movement of the ciliary body loosening of the zonules. The anterior curvature of the lens increases, causing an increase in refractive power. (Forrester et al., 2021, pp. 34-35.)

The retina is the innermost coat of the eye consisting of two primary layers: an inner neurosensory retina and the retinal pigment epithelium (RPE) (Snell & Lemp, 1998, p. 175; Forrester et al., 2021, p. 37). The thickness of the retina varies, and it is in the periphery approximately 100 µm and near of optic nerve head 230 µm. between the neural retina and RPE in the subretinal space. The retina is limited to Bruch's membrane and the vitreous. (Forrester et al., 2021, pp. 37-38; 40.) Regions of the retina are the posterior pole (central retina), the macula lutea, the fovea centralis, the optic disc, the peripheral retina and the ora serrata. The fovea centralis, which is anatomically foveola, is the

0,35 mm wide zone in the macula where the cone photoreceptors are at maximum density. (Forrester et al., 2021, p. 39.) The outer retina and photoreceptors of the neurosensory retina receive most of its nutrients from vessels in the choroid and the inner retina from retinal circulation. The retina has high metabolic activity and the highest rate of aerobic glucose consumption of any tissue. (Forrester et al., 2021, p. 247.)

The RPE is a monolayer of cuboidal epithelial cells. This cell layer is more columnar in the central retina (14*10 µm) and gets more flattered (10-14*60 µm) in the peripheral retina. (Forrester et al., 2021, p. 40.) Tight junctions between cells isolate the retina from systemic circulation (Snell & Lemp, 1998, p. 177). The RPE have many functions, like the absorption of light, participation in the turnover of the outer segments of the photoreceptors and the formation of rhodopsin and iodopsin (Snell & Lemp, 1998; pp. 181-182).

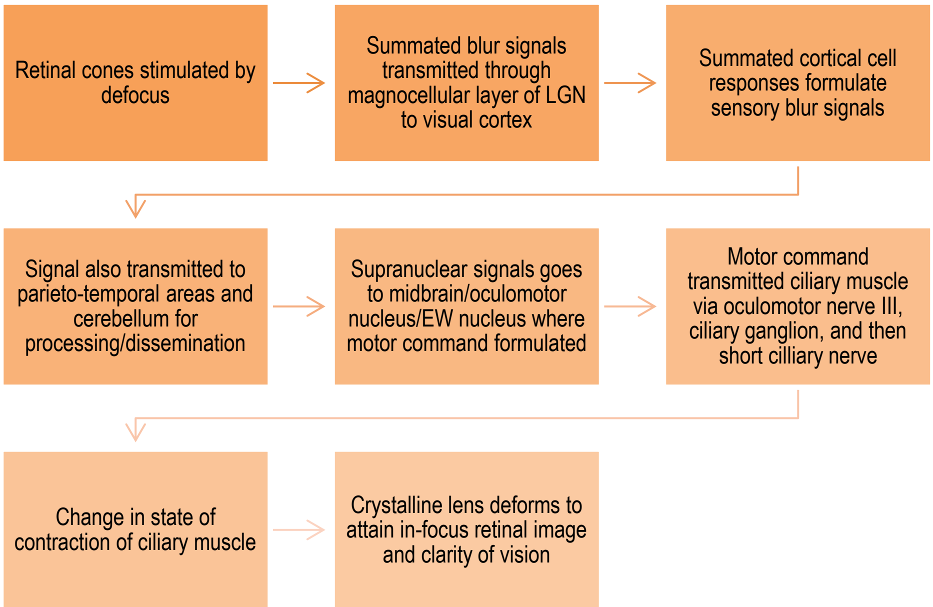
The neurosensory retina is a thin transparent layer of neural tissue where light stimuli are turned into neural impulses. Impulses integrate and transmit to the brain via the ganglion cell axons located in the optic nerve. Neural cells (photoreceptors, bipolar cells and ganglion cells) are dominated in the retina, but there are also other cells like glia cells, vascular endothelium, pericytes and microglia. Retinal cells are arranged in a highly organized manner. Rods and cones are photoreceptors, and they contain the visual pigments that absorb light and launch the neuroelectric impulse. (Snell & Lemp, 1998, pp. 181-185; Forrester et al., 2021, p. 40.)

2.1.3 Accommodation- an Autonomic Reflex

Various components of the central and peripheral nervous system involve accommodation reflexes. The visual association cortex and the cerebellum are part of this reflex, in addition to the parasympathetic nervous system. The stimulus for accommodation is caused by a blurred retinal image or fixation on a near target. (Motlagh & Geetha, 2022.) Cues to accommodation are, for example, optical, chromatic and spherical aberration, micro fluctuations, size, apparent distance and monocular depth cues. Retinal and nonretinal images, mood, vestibular stimulation, contrast, spatial frequency and luminance can influence accommodation. (Borish & Benjamin, 2006, p. 227.)

When the human observes a near object, contraction of the medial recti causes convergence of the visual axes. At the same time, the lens gets thicker, its refractive power increase, and the pupils become smaller in size. The afferent impulse of the near target is transmitted through the optic nerve optic chiasma, optic tract, lateral genicular body (LGB), and optic radiation to the visual cortex. The visual cortex is connected to the eye field of the frontal cortex, where the cortical fibres come down to the oculomotor nuclei. Part of the cortical fibres synapse goes through with the Edinger-Westphal nuclei of the oculomotor nerve (the third cranial nerve, CN III). That synapse branch on both sides is the synapse point, where parasympathetic preganglionic fibres go through CN III to the ciliary ganglion. The postganglionic parasympathetic fibres pass through the short ciliary nerves to the ciliary muscle and constrictor pupilla muscle of the iris. (Snell & Lemp, 1998, p. 370; Motlagh & Geetha, 2022.) Borish and Benjamin (2006, p. 218) have briefly described this cascade which can be seen in Figure 1.

FIGURE 1. *Sensory and Motor Pathway for Monocular Blur-Driven Accommodation (Borish & Benjamin, 2006, p. 218)*



2.1.4 Character of Accommodation

Accommodation can be divided into four different components: reflex, vergence, proximal and tonic. When the retinal image is blurry (a reduction of the contrast and contrast gradient), automatic adjustment of the refractive state makes the image sharply and focuses again. This adjustment is **reflex** accommodation, which is the most important component of accommodation. If the blur is over 2,00 D, voluntary accommodation is required besides that. **Vergence** accommodation ensues the innate neurological linking and action of disparity vergence. This causes convergence accommodation/convergence (CA/C) ratio, which is approximately 0,4 D per meter angle in young adults. The CA/C ratio can be determined by measuring accommodation during open-loop viewing using a binocular pinhole or a blur-free difference. By using these methods, the intrusion of blur-driven reflex accommodation succeeds. Vergence accommodation is perhaps the second major component of accommodation. The influence or awareness of a near object located within 3 m causes **proximal** accommodation. Proximal accommodation does not have a retinal-based visual feedback loop because it will activate by perceptual cues. This component of accommodation usually covers about 4 % of the accommodation. **Tonic** accommodation presumably reflects baseline neural innervation and decreases with age. With young adults, the mean tonic accommodation is approximately 1 D. (Borish & Benjamin, 2006, p. 218-220.)

The depth of focus can be described as a neurological tolerance for the image system error. The value of it has been measured under test conditions at approximately ± 0,30 D for a 3-mm pupil in the comprehensive studies conducted by Campbell in the 1950'. According to Borish and Benjamin (2006, p. 261), Campbell has perceived the depth of focus reduced with increases in target luminance, contrast, and pupil size. (Borish & Benjamin, 2006, pp. 260-261.) The **accommodation latency** is approximately 350 msec (Borish & Benjamin, 2006, p. 266).

Even if a subject is viewing a stationary object, accommodation is not stable. There are small fluctuations in accommodation, with an amplitude inferior to 1 D and a frequency up to a few Hz. The source and purpose of **micro fluctuations** are not fully understood, even though it has been discovered as far back as the 1940s. (Monticone & Menozzi, 2011; Read et al., 2022) There is a consensus that micro fluctuation maintains an appropriate response for accommodation, especially the lower temporal frequencies. (Charman & Heron, 2015) Although accommodation depends on the distance of the object to be viewed, the accommodative response does not correlate exactly with that, particularly nearby. The eye is focused on a farther distance than the stimulus. That phenomenon is called **the lag of accommodation**. For long distances, the situation is the opposite: the response is nearer than stimulus and is called **the lead of accommodation**. (Labhishetty et al., 2018)

2.1.5 Measuring Accommodation in Clinical Work

In clinical work, measuring accommodation is part of the eye examination, and the traditional evaluation of accommodative function involves measurement of the amplitude of accommodation (AoA) (Scheiman & Wick, 2020, p. 37). The AoA is the maximum increase in optical power (Burns, Evans & Allen, 2014). Globally, this test is part of the syllabi of the World Council of Optometry and the European Council of Optometry and Optics (Burns et al., 2020). The Finnish Ethical Council has recorded it as a component of Finland's Good Practice of Optometrist Examination (Optometrian eettinen neuvosto OEN, 2021). Flexible accommodation requires more than the great amplitude of accommodation, so other tests related to the use of accommodation are also briefly presented in this paragraph.

According to Burns, Evans and Allen (2014), there are five methods of clinical measurement of the amplitude of accommodation: push-up, push-down, push-down to recognition, minus lens, and dynamic retinoscopy. These measurements are subjective except for dynamic retinoscopy, which is partly objective. (Burns et al., 2014.) The objective clinical measurement is possible by using an open-view autorefractor which is pupil size-dependent (Burns et al., 2014). The accommodative facility is the eyes' ability to alter accommodation rapidly and accurately. The test result will be recorded in cycles per minute (cpm) completed in one minute (Borish & Benjamin, 2006, pp. 783-784). Retinoscopy is excellent for objective determination, not only for determining the refractive error but also for examining accommodative response and lag (Borish & Benjamin, 2006, p. 1386). The summary of different components of accommodative measurement are presented in Table 1.

TABLE 1. Measurements of Different Components of Accommodation (adapted from Borish & Benjamin, 2006, pp. 783—783; 1386—1387; 1754—755; Burns et al., 2014)

Component of Accommodation	Test
Accommodative amplitude	Push-up test (the RAF rule), Push-down/to recognition, Minus lens test, Dynamic retinoscopy
Accommodative facility	Testing with ± 2,00 lenses
Accommodative response	Monocular estimation method retinoscopy
Accommodative lag	Dynamic retinoscopy
Negative/positive relative accommodation	Plus to blur/minus to blur

According to Rosenfield (2011), in clinical work, patients with visual display terminal (VDT) work should be assessed with accommodative lag at the appropriate working distance, monocular and binocular amplitude of accommodation, monocular and binocular accommodative facility and negative and positive relative accommodation. The starting point of these measurements should be the best corrected visual acuity and refractive error, including binocular balancing. If any abnormalities in the accommodation are observed, they may be reduced by increasing the accuracy and dynamics of the accommodation. These include, for example, vision therapy and/or using lenses. (Rosenfield, 2011)

In modern society, the meaning of accommodation has increased, so measuring the accommodative function is essential for clinical work. A clinician must consider the many challenges associated with measuring accommodation because clinical methods of measurement of this function have several sources of error. They are numerous and diverse and include depth of focus, reaction time, instrument design, specification of the measurement end-point, specification of the reference point of measurement and measurement conditions. During the accommodation measuring, it should also consider refractive error and psychological factors. Also, the clinician's bias can affect the results. (Burns et al., 2020.)

2.1.6 Accommodative Disorders

Presbyopia is the physiological change of ageing which causes dysfunction of the accommodation reflex (Motlagh & Geetha, 2022). Presbyopia is a common vision disorder whose prevalence and severity increase with age. About 85 % of people aged 40 years or older have it. It is hypothesized to be caused by the weakening of the ciliary muscle or a loss of lens elasticity. (Katz et al., 2021.) Ageing changes in the eye cause atrophy of the ciliary muscle fibers when the lens does not change shape sufficiently during accommodation (Forrester et al., 2021, p.36). According to McDonald et al. (2022), a thicker lens, caused by changes in the lens protein and higher molecular weight, leads to difficulties in focusing the picture on the retina. Although the difficulty of near sight is generally considered an age-related phenomenon, there is no widely accepted classification of presbyopia. Clinically it has been defined where near working distance dioptrially is half of the accommodative amplitude. The concept can be determined subjectively as the patient's experience of impaired near vision for daily living. (McDonald et al., 2022, p.2.)

Also, a wide range of ocular and systemic conditions, such as trauma, inflammatory diseases, toxicity, vascular diseases, and medications, can cause accommodative anomalies (Burns et al., 2014; McDonald et al., 2022, p. 8). It is also known that, among other things, like refraction errors, ethnicity or race, Down Syndrome, dyslexia and other reading difficulties, and premature birth can influence accommodation (Burns et al., 2014). This thesis work will focus on healthy eyes, so accommodative problems of these causes are not described comprehensively.

2.2 Visual Display Terminal (VDT) and Accommodation

Computers and video or visual display terminals (VDT) are essential to the modern lifestyle. The use of computing devices is necessary, but the prolonged, uninterrupted or repetitive use of peripheral devices causes ocular and extraocular symptoms. Extraocular symptoms, like neck, back, and shoulder pain, shoulder tendonitis, and elbow epicondylitis, are common. (Parihar et al., 2016; Sheppard & Wolffsohn, 2018.) These symptoms are often due to poor ergonomic design and posture. Also, psychosocial stress (like fear of being replaced, work pressure, and work-lacking decision-making opportunities) can cause extraocular symptoms. (Parihar et al., 2016; Alemayehu & Alemayehu, 2019.) The ocular symptoms of a prolonged near vision task are asthenopic symptoms, like visual blurring, difficulty in refocusing between viewing distances, eye strain, and dry eye

(Rosenfield, 2011; Munshi, Varghese and Dhar-Munshi, 2017; Alemayehu & Alemayehu, 2019; Jaiswal et al., 2019). These manifestations are named computer vision syndrome (CVS) or digital eye strain (DES) (Parihar et al., 2016; Munshi et al., 2017; Sheppard & Wolffsohn, 2018). This framework focuses only syndrome's impact on ocular manifestations and particularly accommodation.

2.2.1 Ocular Symptoms in VDT work

Parihar et al. (2016) state that despite many extraocular symptoms, eye manifestations are the most frequent complaint in VDT work. Ocular symptoms may be classified into two or three groups depending on the source (Table 2) (Munshi et al., 2017; Sheppard & Wolffsohn, 2018; Alemayehu & Alemayehu, 2019; Kaur et al., 2022). Estimates of how many people suffer from VDT vary. In 2016 Parihar et al. estimated that 55–81 % of VDT users have asthenopic symptoms, and according to Rosenfeld (2011), those are the primary complaint in subjects with CVS. According to Sheppard and Wolffsohn (2018), the significant variation in symptomatic patients may be due to the absence of a specific measurement methodology. There is also a wide variety of usage conditions and substantial changes in these over time. (Sheppard & Wolffsohn, 2018.) The change in work and schoolwork caused by COVID-19 has also increased the use of electronic devices and the visual burden on children (Kaur et al., 2022). Asthenopic symptoms associated with VDT work include blurred vision, difficulty changing focus between viewing distances, headaches, eye strain and double vision (Jaiswal et al., 2019). In any case, CVS reduces the quality of life and efficiency, for example, by increasing the number of errors (Sheppard & Wolffsohn, 2018; Alemayehu & Alemayehu, 2019).

TABLE 2. Ocular symptoms and causes of CVS (adapted from Sheppard & Wolffsohn, 2018; Alemayehu & Alemayehu, 2019.)

	Symptom category	Symptoms	Possible causes
Ocular symptoms of CVS	Asthenopic	Eyestrain, sore/tired eyes	Binocular vision, **accommodation**
	Visual related	Blurred vision, the slowness of the focus changes, double vision, presbyopia	Refractive error, **accommodation**, binocular vision, presbyopic correction
	Ocular surface related	Dry/watery/irritated eyes, CL problems	Reduced blink rate

When discussing ocular problems caused by CVS, it is essential to identify whether they are specifically due to VDT work or just a manifestation of a near-vision task. Rosenfield (2011) presents studies of Sheedy et al. (2003) and Chu et al. (2011), where symptoms were higher when using an electronic screen compared to a hard copy. Printed text and visual display units, like computers, laptops, and mobile phones, give an accommodation reflex in different ways. The dissimilarity between them is, for example, due to viewing distance, gaze angles, blinking rate, and the appearance of texts. (Rosenfield, 2011; Alemayehu & Alemayehu, 2019.) Also, widening palpebral fissures during reading is disparate compared to VDT work and printed text (Alemayehu & Alemayehu, 2019). VDT letters are made up of pixels, resulting from the screen's electronic beam striking the rear surface. Pixels' brightness is different in the centre of the pixel than in the periphery. That causes the eyes' inability to maintain focus. (Munshi et al., 2017; Alemayehu & Alemayehu, 2019.) When the eye is focusing object, there is a lag of accommodation, in which case the point of focus is behind the object. The vertical position of the computer screen aggravates it. It causes the "pumping" of the accommodation and non-accommodation states between the point of focus and the resting point of accommodation, which exerts a strain on the ciliary body. (Jaiswal et al., 2019.)

2.2.2 VDT Affect on Accommodation

When computers and other VDTs are used at work, school and leisure, the accommodative system is burdened by prolonged close-up viewing and there can be difficulties in different stages. Many patients with CVS complain of blurred vision after VDT work. This can be a result of an inaccurate accommodative response during the computer task or an inability to relax it. (Rosenfield, 2011.) Disadvantages of VDT are suspected to be due to increased accommodative innervating. Parihar et al. (2016) present Erlich’s study for year the 1987, which states VDT requires 1.8 times more strain for accommodation, miosis, and convergence than text read on paper.

According to Jaiswal et al. (2019), there can be changes in accommodative accuracy, flexibility, and amplitude after VDT (Figure 2). The lag of accommodation is a normal occurrence, but studies have shown that it is greater after using smartphones and computers. Hue, Rosenfield and Saà

(2014) compared two different electronic devices and hardcopy. The conclusion was a greater lag in accommodation with electronic equipment.

Studies have figured out the loss of accommodative amplitude and vergence after VDT. According to Parihar et al. (2016), Qu, Chu, Wang, Yao and Liu studied the year 2005 VDT users and observed even one hour of working with VDT caused reducing the amplitude of accommodation, weakening in near point of convergence, and increasing in near lateral exophoria. As for the amplitude of accommodation, the studies are congruent. Reduced subjective accommodative amplitude has been shown after digital device use. (Jaiswal et al., 2019.) According to Parihar et al. (2016), a great extent attributed to VDT causes loss of accommodative amplitude and vergence and temporarily gadget-induced myopia. The studies show that even 1 hour of working with VDT reduces the amplitude of accommodation, weakens the result of converging near point, and increases exophoria. The flexibility to focus on a variety of viewing distances (accommodative facility) is essential when using smartphones and tablets. Those devices are often used while a person is doing something else at the same time. Jaiswal et al. (2019) state the research results are contradictory and more studies are needed.

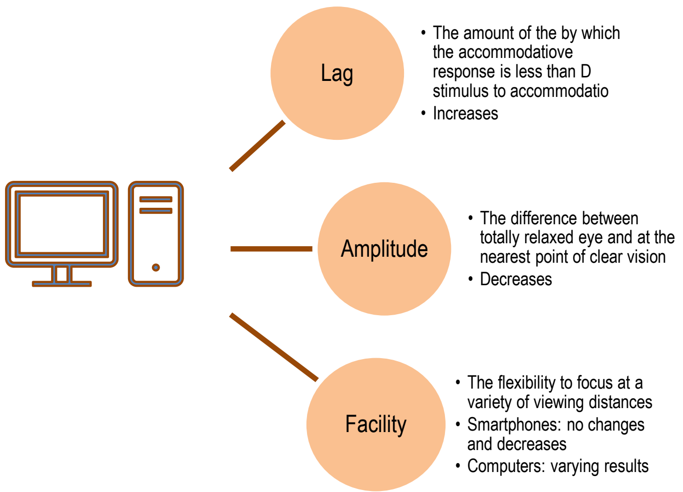


FIGURE 2. CVS Loads Effect to Accommodation (adapted from Jaiswal et al., 2019.)

2.3 Anthocyanins

Polyphenols are substances found in plants that can be divided into four main categories: flavonoids, stilbenes, phenolic acids and lignans. Flavonoids can be divided into different subclasses, such as flavones, flavanones, flavonols and **anthocyanins**. (Rodriquez, 2020, p. 4.) Anthocyanins (ACs) are the pigments of plant tissues in fruits, leaves, flowers, roots, and stems. The concentration of AC varies considerably between different sources, but it is most numerous in dark blueberries like elderberry, chokeberry, wild blueberry (bilberry), and black currant (Wu et al., 2006). The function of the ACs variables in the plants. AC protects against ultraviolet radiation by absorbing that and is also protective colouring. Red and purple tones attract insects and facilitate pollination (Rodriquez, 2020, pp. 4—5).

The food and beverage industry uses anthocyanin as a natural colourant and additive, but scientific studies have proven anthocyanins have beneficial health effects. ACs have the potential for health maintenance and treatment of different diseases. (Liu et al., 2021; Rodriguez, 2020, pp. 4–5; Wallace & Giusti, 2015.) Cell culture studies, animal models, and human clinical trials have been submitted that anthocyanins have antimicrobial and antioxidative effects, positive effects on visual and neurological health, and protection against non-infectious diseases. (Khoo et al., 2017) This thesis focuses on the effect of anthocyanins on the eyes accommodation, but Table 3 is compiled in general terms of their effect on humans and animals. Although a large number of good effects on health, anthocyanins intake is not necessary for humans. (Wallace & Giusti, 2015.)

TABLE 3. Overview of AC Effects on Humans and Animals (Ockermann et al., 2021)

Inflammation	IL6, IL8, IL15 ↓ ICAM1, VCAM1 ↓ NF-kB, TNF-α ↓	**Hyperlipidemia**	LDL ↓ HDL ↑ Triglycerides ↓
Antioxidative	ROS ↓ XO-1 ↓ SOD, HO-1, PON-1 ↑	**Glucose homeostasis**	Fasting blood glucose↓ Insulin sensitivity ↑ HbA1c↓
Vascular function	Blood pressure ↓ eNOS↑ ACE ↓ FMD ↑ PWV ↓	**Cognition**	Working memory↑ Mitochondria protection↑

IL=interleukin, ICAM=Intercellular Adhesion Molecule, VCAM=Vascular cell adhesion protein, NF-kB=Nuclear Factor kB, TNF=Tumor Necrosis Factor, ROS=Reactive Oxygen Species, XO= xanthine oxidase, SOD=superoxide dismutase, HO= heme oxygenase, PON=paraoxonase, eNOS=endothelial nitric oxide synthase, ACE=Angiotensin-converting enzyme, FMD= flow mediated dilation, PWV= pulse wave velocity, ; LDL=low-density lipoprotein, HDL= high-density lipoprotein, HbA1c= Glycated hemoglobin A1c

2.3.1 The Structure of Anthocyanins

Anthocyanins (AC) are water-soluble colour pigments and a subclass of phenolic phytochemicals. In the acidic condition, those are redder than in the alkaline condition bluer. (Khoo et al., 2017; Liu et al., 2021.) Anthocyanins are secondary metabolites protecting against environmental stress conditions like cold temperatures, drought and UV light (Liu et al., 2021). The basic structure of anthocyanin is shown in Figure 1. Anthocyanin is one of the flavonoids with a positive charge at the oxygen atom of the C-ring of the basic flavonoid structure. (Khoo et al., 2017.) Anthocyanins can describe as the glycosylated form of anthocyanidins. The most common anthocyanidins are cyanidin, delphinidin, pelargonidin, peonidin, petunidin, and malvidin.(Khoo et al., 2017; Rodriquez, 2020, p. 2.) Anthocyanins are the only polyphenols absorbing light in the UV (280-400 nm) and blue light (360-500 nm) spectrum. (Oliveira et al., 2020.)

2.3.2 The Sources of Anthocyanins

ACs are very common in nature, and they are present in numerous wild fruits such as raspberries, blackberries, blueberries, strawberries, and currants (Rodriquez, 2020, pp. 4-5). Also, purple rice, black bean, purple corn, and purple sweet potatoes consist of AC. (Liu et al., 2021). The number of anthocyanins varies greatly in the same plant depending on factors such as its genetic variation, growing conditions, ripeness and processing. Total AC contents in vegetables and fruits are change between 28 to 1480 mg/100 g. (Rodriquez, 2020, p. 6.) According to Liu et al. (2021) and Rodriquez (2020, pp. 5—6), blueberries have the highest anthocyanin content. In Table 4, anthocyanin concentrations of common foods are compiled. Concentrations have been measured in the U.S.A. to provide information for the U.S Department of Agriculture (USDA) database of flavonoids (Wu et al., 2006). The anthocyanin composition varies between plants. For example, 15 types of anthocyanins have been found in bilberry, while in turn there are four types of black currant. (Ockermann et al., 2021.)

TABLE 4. Concentration of Anthocyanins in Common Foods (adapted from Wu et al. 2006)

Food	Total ANC mg/ 100 g of fresh product
apple (Red Delicius)	12,3 ± 1,9
bilberry	486,5
chokeberry	1480
black bean	44,5
blueberry	386,6 ± 77,7
cranberry	140 ± 28,5
black currant	476 ± 115
red currant	12,8
red raspberry	92,1 ± 19,7
elderberry	1375
strawberry	21,2 ± 3,3
red cabbage	322 ±40,8
red radish	100,1 ±30,0

2.3.3 The Clinical Use of Anthocyanins and Dietary Intake

There are three main ways to produce anthocyanin for consumption: natural sources (like fruits, berries, and vegetables), extracts and other preparations, and chemical synthesis. The challenge of using natural anthocyanin is low abundance, environmental and seasonal varieties, and pigment degradation during storage and processing. On the other hand, chemical synthesis is expensive for an intrinsically complex compound and thus not commercially viable. (Belwal et al., 2020.)

Anthocyanins can be obtained by eating berries and vegetables containing them or as a supplement. Anthocyanins, as a dietary supplement, are food products. The US Food and Drug Administration (FDA) and European Food Safety Authority (EFSA) produce independent scientific research data to ensure food safety. They also give general nutritional recommendations (European Food Safety Authority, no date; U.S Food & Drug Administration, 2022). According to Ockermann et al. (2021), FDA and EFSA have not approved a health claim for anthocyanin yet. There are numerous in vitro, in vivo, and epidemical research for anthocyanins. The most promising benefit seems to be to cardiovascular diseases by decreasing inflammation markers and oxidative stress.(Ockermann et al., 2021.)

Although anthocyanine-rich foods have been recommended to prevent and cure various diseases, anthocyanins are not used as a medicine in Western medicine. In Finland, Europe, and North America, anthocyanins, like many other bioactive compounds, do not exist in dietary reference intakes. China is the exception. There has been determined a proposed level of anthocyanin at 50 mg/d (Wallace & Giusti, 2015). However, in general, anthocyanine-containing vegetables are recommended for public health reasons. According to The National Nutrition Council, in Finland, vegetables are generally considered the basis for a healthy diet. (Valtion ravitsemusneuvottelukunta, 2018, pp. 13; 18; 20; 21) In the Finnish population, bilberry is the most important source of anthocyanin (Moisio & Törrönen, 2008, p. 65).

2.3.4 Anthocyanin Properties, Bioavailability and Distribution in Eye Tissues

The base of anthocyanins maintains good health and prevents diseases is bioavailability. (Khoo et al., 2017.) **Bioavailability** is the proportion that any ingested substance or nutrient is absorbed and enters the circulatory system for normal physiological functions (Khoo et al., 2019). Anthocyanins are thought to have low bioavailability, due to which it is poorly absorbed into the bloodstream and easily excreted in the urine. However, there are differences between different anthocyanins. (Khoo et al., 2017.) Absorption of anthocyanins occurs mainly in the small intestine and stomach. Some of the anthocyanins have been found to appear in plasma maximum concentrations after 1-2 hours and in urine within 0-4 hours (Stoner et al., 2005). Anthocyanins are efficiently absorbed by epithelial tissue; however, the efficacy of anthocyanins is not based on the anthocyanin itself but on its metabolism and degradation products. (Rodriquez, 2020, p. 7; Ockermann et al., 2021.)

The advantage of anthocyanins is that they require the absorption of components into the blood system. Anthocyanin has a low bioavailability causing low absorption, and limited reports are available. Cyanidin-3-glucoside and malvidin-3-glucoside, which are the significant anthocyanins, are the most investigated. The challenge of bioavailability research is the versatility of anthocyanins. (Khoo et al., 2017.)

According to Khoo et al. (2017), anthocyanins' typical mechanisms of action are:

- Free-radical scavenging
- Blood biomarkers changes

- Impact on cyclooxygenase (COX) and mitogen-activated protein kinases (MAPKs)
- Reducing inflammatory cytokines signals

Anthocyanins' impact on health is based on antioxidant character reducing scavenging free radicals and reducing oxidative stress. Anthocyanin prevents and repairs oxidative damage in the cardio-vascular system and dyslipidaemia. Anthocyanins inhibit cancer cell proliferation. (Khoo et al., 2017.) According to Liu et al. (2021), dietary intake of anthocyanin has a spectrum of therapeutic effects against many systemic diseases and eye diseases like glaucoma, retinopathy and myopia (Table 5). The mechanisms of action vary between different anthocyanin sources. It has been suggested that anthocyanin of black currants improves ocular blood flow in open-angle glaucoma by acting on endothelin receptor type B and normalizing patients' serum endothelin-1 concentrations. In retinopathy, anthocyanin-rich extract inhibits STAT3 activation, reducing inflammation-related rhodopsin expression and intracellular reactive oxygen species (ROS) levels. This can prevent photoreceptor cell damage and protect visual function during retinal inflammation, which plays an essential role in retinopathy. In human retinal capillaries, glucosides can protect capillary cells which high glucose can damage. N-methyl-N-nitrosourea is a carcinogen causing damage to the retinal nerve. (Liu et al., 2021.)

TABLE 5. Mechanism of Anthocyanin from Different Plants on Eye Diseases (adapted from Liu et al., 2021)

Disease	**Plant origin**	**Mechanism**
Glaucoma	*Ribes Nigrum* (black currant)	↑ ET_B receptor Modulate ET-1 ↑ ocular blood flow ↓Ocular blood vasodilation
	Vaccinium myrtillus (bilberry)	↑ Blood circulation, antioxidant
Retinopathy	*Vaccinimun ashei* (Rabbiteye blueberry)	↑ Antioxidant, anti-inflammatory
	Vaccinium myrtillus	↑Antioxidant, ↓ Lipid peroxidation ↓ Proinflammatory cytokines ↓ Retinal cells apoptosis
	Glycine max (soybean)	↑ Anti-inflammatory ↓ GFAP
Myopia	*Ribes Nigrum* (black currant)	↑ NO ↓ RLC

ET_B receptor= endothelin receptor type B, ET-1= endothelin 1, GFAP= glial fibrillary acidic protein, NO= nitric oxide

One of the key effects of anthocyanins in the ophthalmologic field is the action of ciliary smooth muscle relaxation. According to Nomi et al. (2019), one of the typical anthocyanins (delphinidin-3-rutinoside D3R) relaxed in ciliary muscle stimulated with endothelium-1.

Anthocyanins must enter the tissues of the eye to improve visual health. Despite the low bioavailability, anthocyanins have passed the blood-aqueous fluid barrier and blood-retinal barrier in animal tests. (Nomi, Iwasaki-Kurashige & Matsumoto, 2019.) According to Nomi, Iwasaki-Kurashige, and Matsumoto (2019), the total concentration of AC in several ocular tissues can be higher than in plasma. Therefore, it can be concluded that anthocyanins are concentrated in eye tissues. The highest AC concentration is in the choroid, but it has been measured also the cornea, aqueous humour, ciliary body and iris and retina. Nomi, Iwasaki-Kurashige, and Matsumoto (2019) make an argument that is caused by the propensity of AC to bind proline-rich proteins such as collagen.

Animal tests show that AC passes the blood-retinal barrier after oral administration, but intraperitoneal or intravenous delivery is more effective than oral. Anthocyanins have been shown to influence rhodopsin regeneration (affect regeneration time and stimulation of rhodopsin) and smooth muscle relaxation (by preventing endothelin-1 contraction) in vitro. In vivo studies have shown that AC presents in the eye tissues and enhances blood circulation. The conclusions of the clinical trials confirm those findings. (Nomi et al., 2019.)

3 PURPOSE AND OBJECTIVES OF THE THESIS

Purpose: The aim was to trace the effect of anthocyanins on accommodation in healthy adults whose near vision was loaded with a visual display terminal. The systematic literature review investigated the connection between anthocyanin's impact on accommodation for visual display terminal (VDT) work compared to placebo.

Objective: Because of increased visual demands, optometrists should use a comprehensive toolbox for assisting patients with their problems. The help provided by a professional should be evidence-based and safe. Clinical optometry also utilizes evidence-based practices derived from systematic literature reviews. The objective of the thesis was to find out can an optometrist recommended anthocyanins to patients suffering from near vision problems caused by VDT work.

4 IMPLEMENTATION OF THE THESIS

4.1 Summary Description of the Experimental Design

This thesis work is a systematic literature review on the effect of anthocyanins on accommodation in VDT work. At first, the research question and criteria for selecting studies were formulated. The data search process, selection and quality assessment were performed. The search was made on 21 March 2022. The systematic searches were conducted using the following databases: PubMed, Ebsco, Elsevier and Google Scholar. After selection, four studies remained for review. The studies were English-language randomised controlled trials published between 2010 and 2022. The number of subjects was 271, with an age distribution of 20-60 years. Finally, the analysis and the synthesis of data were constructed. The results of the systematic literature search have been analysed using narrative synthesis. Narrative synthesis provides the possibility to have information that can assist practitioners in advancing best practices (Booth, Papaioannou & Sutton, 2012, pp. 146—147; Flinkman & Salanterä, 2007, p. 84).

4.2 Research Question

The research question of the thesis work is: **Do the anthocyanins enhance the eye's accommodation in healthy individuals in VDT work compared to placebo preparation?** The research question has been conducted using PICO (Table 6).

TABLE 6. Research Question of Systematic Literature Review Conducted by ***PICO***

Population	**Healthy individuals in VDT work**
Intervention	**Anthocyanins**
The **C**omparison of Interest	**Placebo preparation**
The **O**utcome	**The eye's accommodation**

4.3 Criteria for the Selection of Studies

Explicit inclusion and exclusion criteria are the basis for choosing relevant sources for the literature review (Aveyard, Payne & Preston, 2016, p. 92). The eligibility criteria for this review are shown in Table 7.

TABLE 7. Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Published years 2010–2022	Published before 2010
Language English	Language not English
Test capsules contain anthocyanin	Test capsules contain other active ingredients
Clinical research	In vivo/in vitro research/book chapter/review

4.4 Data Search Process, Selection and Quality Assessment

In the systematic literature review, the data search process is essential for having all information on the subject. Accurate documentation and, by extension, the reproducibility of information retrieval are important. The purpose of the search process is to gather all relevant data on the topic, identify publications, and avoid bias or narrow descriptions. (Efron & Ravid, 2019, p. 58—59.) The next chapters describe the data the search process, which contained identification, screening and including (Figure 3).

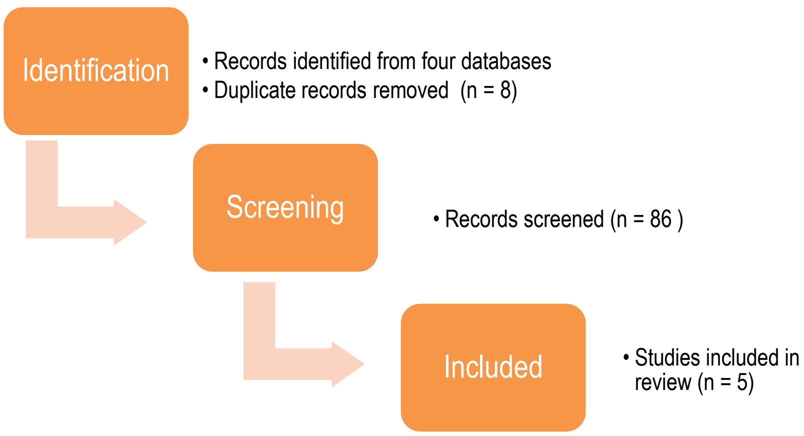


FIGURE 3. The Data Search Process

4.4.1 The Structure of the Search Process

The right search words are essential for having comprehensive results for a search. In this thesis work, the subject was clear and compact, so searching words was formulated easily. The first key terms and synonyms for the subject were identified, and after that, a consultation with the information specialist from OUAS. The search was made on 21 March 2022. The systematic searches were conducted using the following databases: PubMed, Ebsco, Elsevier and Google Scholar. Boolean operators were used. The database and used search words are summarized in Table 8.

TABLE 8. Used Databases and Searching Words

Database	Searching words
PubMed	("Accommodation, Ocular"[Mesh] OR "visual accommodat*"[tw] OR "ocular accommodat*"[tw] OR accommodat*[tw]) AND ("Anthocyanins"[Mesh] OR anthocyan*[tw])
Ebsco	("visual accommodat*" OR "ocular accommodat*" OR accommodat*) AND anthocyani*
Elsevier	("visual accommodation" OR "ocular accommodation" OR accommodation) AND anthocyanin
Google Scholar	anthocyanin AND accommodation AND vision AND VDT

The publish date of records was limited between the years 2010–2022 except in Pubmed from 1/1/2010 to 21/3/2022. The results of the search were PubMed 10, Ebsco 11, Elsevier one and Google Scholar 72.

4.4.2 The Inclusion and Exclusion Criteria

The selection criteria of the systematic literature review are key to assessing relevant results. The research question defines inclusion and exclusion criteria to have to right studies for having an answer for that. (Pudas-Tähkä & Axelin, 2007, pp. 48-49.) Table 9 summarizes used inclusion and exclusion criteria.

TABLE 9. The Summary of the Review Eligibility Criteria

Inclusion criteria	Exclusion criteria
Published years 2010–2022	Published before 2010
Language English	Language not English
Test capsules contain anthocyanin	Test capsules contain other active ingredients
Randomized Controlled Trials (RTC)	In vivo/in vitro research/book chapter/review

The published years of the results were 2010-2022. The relatively long period was due to the low number of studies on the subject, but twelve years of publishing ensured satisfactory results for the review. Only English results were approved. In some studies, the test capsules contained other active ingredients besides anthocyanin, but those results were excluded. If there are several active ingredients, it is impossible to say which effect is explicitly caused by anthocyanin-based research. Due to the research question, only clinical trials could be accepted to be included in the review.

4.4.3 Criteria for the Selection of the Studies and Quality Assessment

After searches, the results of the databases were identified, and duplicate records were removed and screened for getting most relevant studies. This was accomplished by utilizing the PRISMA 2020 flow diagram (Page et al., 2021). The structure of the searches is summarized in Figure 4. Most of the results obtained with Google Scholar were excluded because, based on the title, they were not about accommodation or did not study in optometry or medicine fields.

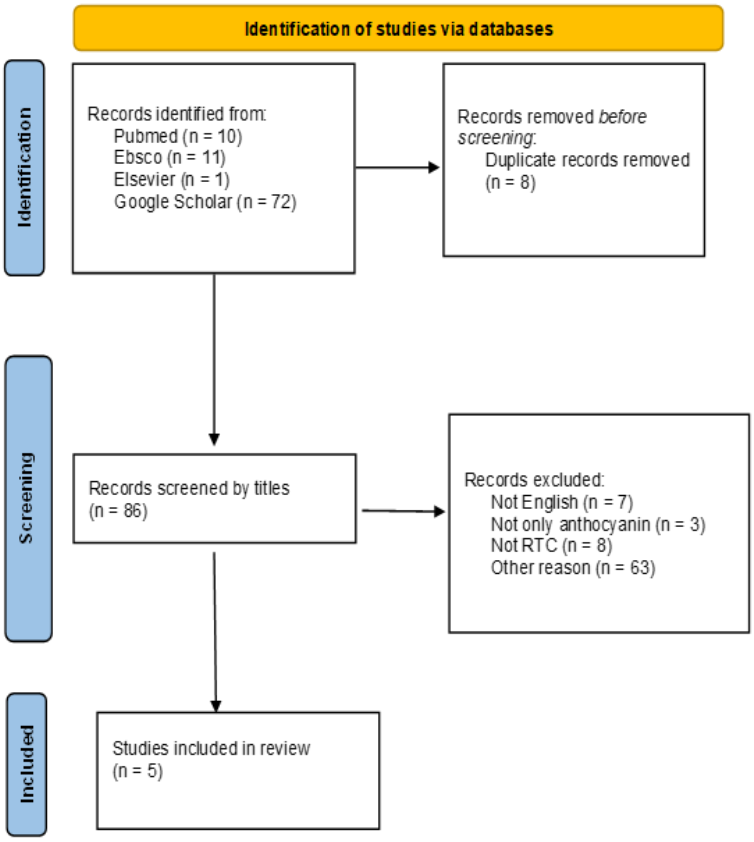


FIGURE 4. Modified PRISMA chart (adapted from Page et al., 2021)

All five selected studies were evaluated using the Critical Appraisal Worksheet for Randomized Controlled Trials (RCT). The worksheet helped appraise the reliability and importance of studies for thesis work (University of Oxford, 2022). Although anthocyanins are not pharmaceuticals, questions on the worksheet covered the subject, and it was possible to use it as appropriate. The adapted worksheet is presented in Table 10. The number of studies to be analysed decreased after evaluation. Kamiya et al. (2013) study did not examine the accommodation of subjects after the exertion of near-vision, and it was excluded. Finally, after this election, four studies remained for review.

TABLE 10. Modified Summary of Critical Worksheet for RCT (adapted from University of Oxford, 2022)

Study	PICO?	Was the assignment of patients to treatments randomised?	Were the groups similar at the start of the trial?	Aside from the allocated treatment, were groups treated equally?	Were all patients who entered the trial accounted for? (ITT)	Was the study double-blinded?	Did the treatment affect accommodation?	Will the results help me caring my patients?
Kamiya et al. (2013)	+	+	+	+	-	+	+	?
Ozawa et al. (2015)	+	?	+	+	-	+	+	+
Yamashita et al. (2019)	+	+	+	+	-	+	+	+
Kosehira et al. (2020)	+	+	+	+	-	+	+	+
Sekikawa et al. (2021)	+	+	+	+	-	+	+	+

4.5 Analysis of the Data

4.5.1 The Summary of Used Studies

After critical consideration, four studies were approved for systematic literature review. The studies were randomized, placebo-controlled, double-blinded and published in Japan. Table 10 contains the essential data from the studies. After that, the studies will then be presented in more detail in order of publication time.

TABLE 11. Summary of the Studies (adapted from Hautala et al. 2020, pp. 16—17)

N:O	The name of the study and (publish year)	Authors	The purpose of the study	The indicator used in the study (quantitative/qualitative)	The study design	The population and the number of the participants	The main results (in relation to the research question)
1	Bilberry extract supplementation for preventing eye fatigue in video display terminal workers (2015)	Ozawa, Kawashima, Inoue, Inagaki, Suzuki, Ooe, Kobayashi, Tsubota.	Examine the effect of the dietary supplement containing bilberry extract on eye fatigue induced by acute VDT loads.	Both	A prospective, randomized, double-blind, placebo-controlled study	Japanese office workers, n = 80	Bilberry extract supplementation improved some of the objective and subjective parameters of eye fatigue induced by VDT loads.
2	Effects of MaquiBright on improving eye dryness and fatigue in humans: A randomized, double-blinded, placebo-controlled trial (2019)	Yamashita, Suzuki, Yamamoto, Iio	Investigate the effect of MaquiBright on improving eye dryness and fatigue in VDT work	Both	A randomized, double-blinded, placebo-controlled trial	Japanese, who has VDT work over 4 hour/day, n=74	The preparation alleviated eye fatigue and its related symptoms caused by the VDT load.
3	A 12-week-long Intake of Bilberry Extract (Vaccinium myrtillus L.) Improved Objective Findings od Ciliary Muscle Contraction of the Eye. (2020)	Kosehira, Naomichi, Nobuyoshi.	Determine the effects of bilberry extract intake on tonic accommodation of the ciliary muscle caused by visual display terminal tasks.	Quantitative	A randomized, double-blind, placebo-controlled, parallel-group comparison trial	The nationality not mentioned, n = 85	The bilberry extract relieved the tonic accommodation of the ciliary muscle.
4	The effect of consuming an anthocyanin-containing supplement derived from Bilberry (vaccinium myrtillus) on eye function. (2021)	Sekikawa Takahiro, Kizawa Yuki, Takeoka Atsushi, Sakiyama Takuji, Li Yanmeu, Yamada Takahiro.	Determine the effects of 6-week consumption of anthocyanin-containing supplement on eye function.	Both	A randomized, double-blind, placebo-controlled parallel study.	Japanese subjects, n = 32	The consumption of the supplement inhibited the decrease in the accommodative function.

Ozawa et al. (2015) examined the effect of the bilberry extract on eye fatigue induced by acute video display terminal (VDT) loads. The survey group was 88 people, half of whom used bilberry extract and half the placebo. Acute VDT loads were imposed by having subjects play two different computer games for two hours. The room was stabilized (air-conditioning, 25 °C, and 50 % humidity). The subjects took three capsules once daily (160 mg BE/capsule) after breakfast for eight weeks. The data were obtained before and after the acute VDT load at the beginning of the study and after four- and eight weeks using capsules. Ophthalmic examinations in the study were critical flicker fusion (CFF) and near-point accommodation (NPA), contrast sensitivity, and functional visual acuity values. Also, the measurement of tear film break-up time and keratoconjunctival epithelial damage was observed. The subjective symptoms were assessed with a questionnaire comprised of 18 questions. 37 control and 43 bilberry extract group completed the study. The result was that the reduction in CFF caused by VDT work was alleviated in the bilberry extract group (95 % confidence interval, 0,10-1,60; p=0,023) compared to the placebo group. There was no variation in near-point accommodation. (Ozawa et al., 2015.)

Yamashita, Suzuki, Yamamoto and Iio studied the year 2019 effect of MaquiBright® on eye dryness and fatigue after visual display terminal load. MaquiBright® is a standardized maqui berry extract which consists of anthocyanins. In the study, 74 Japanese subjects between the age of 30 to 60 who had dry eye experience, eye fatigue and different near vision tasks (playing video games, use of either PCs or mobile phones or working at VDT work over four hours per day), consumed one capsule daily before breakfast for four weeks. The capsule consisted of 60 mg of MaquiBright® or placebo, and they were identical in colour, odour and flavour. Eye dryness was measured using Schirmer's test and tear break-up time (BUT). The pupillary response and flicker test was the method to determine eye fatigue. Subjective symptoms were assessed using the Visual Analogue Scale (VAS) and Dry Eye-related Quality of Life Scores (DEQS) questionnaire. The measurements and questionnaires were assessed after 45 minutes of video game play (VDT load) before and after four weeks of intake. Subjective symptoms in eye fatigue measured by the VAS method reduced after using extract (p=0,047). (Yamashita et al., 2019.)

Kosehira, Machida, and Kitaichi published at the year 2020 an article on the findings of ciliary muscle contraction caused by bilberry extract. In the study, 109 subjects consumed a standardized bilberry extract (SBE) capsule or placebo once a day on an empty stomach before breakfast or lunch. The SBE capsule contained 36,89 % of anthocyanins, which means 88,54 mg per dose. The ophthalmic examination included a high-frequency component of accommodative micro fluctuation. That was calculated the power spectrum of HFC based on measured values using fast Fourier transformation. The HFC was examined at the beginning and after four, eight and twelve weeks. (Kosehira, Machida and Kitaichi, 2020.)

Statistical processing was made using the analysis of covariance to compare the HFC values between SBE and placebo groups. 97 out of 109 were able to complete the trial. The post-VDT load HFC values showed an improvement at weeks eight and twelve if SBE was used compared to placebo. The study suggested that SBE suppresses the tonic accommodation of ciliary muscles during VDT load. Kosehira and others concluded that a 12-week oral consumption of 240 mg of SBE improved and relieved the tonic accommodation of ciliary muscles caused by VDT tasks. (Kosehira, Machida and Kitaichi, 2020.)

Sekikawa, Kizawa, Takeoka, Sakiyama, Li, and Yamaha determined the effects of 6-week consumption of anthocyanin supplements on eye function in 2021. The subject of the study was 32 healthy Japanese, and the primary outcome measure was the change in the percentage of pupillary response pre-and-post-VDT use. A sample capsule included 43,2 mg of anthocyanin from bilberry or starch. Subjects consumed one capsule once a day with water after breakfast for six weeks. The ophthalmic examinations in this study were a change in percentage of pupillary response (evaluated using the TrilRIS C9000, a near-point measuring device), the tear film break-up time, visual acuity, and Schirmer's test. Examinations were done after pre-and-post-VDT use. Also, subjective symptoms of eye fatigue were evaluated using a questionnaire. (Sekikawa et al., 2021.)

At the end of the study, the number of analysing subjects was 30 (15 subjects in the active group and 15 placebo group). The measurement of pupillary response and pupillary/near point was made at the beginning and after six weeks before and after VDT use. There was a significant improvement in the logarithmic conversion values of the percentage of pupillary response (active group 0,2 ± 0,4, placebo group 0,0 ± 0,3, *P* = 0,043) and pupillary/response/near point in the active group (active group 0,1 ± 0,4, placebo group -0,1±0,3, *P* = 0,049). Based on this, researchers found anthocyanin use inhibiting the decline in accommodative function caused by VDT use. (Sekikawa et al., 2021.)

4.5.2 Results of the Systematic Literature Review

The systematic literature search selected four studies in which anthocyanin's effect on accommodation-related eye fatigue was studied through various examinations. Studies have also utilised subjective questionnaires. In this thesis work, the research question aimed to study possible changes in accommodation compared to anthocyanins and placebo. Analysis of the results is done through narrative synthesis. This method was selected for thesis work because it allows the results of the literature review to be utilized in practical work (Booth, Papaioannou and Sutton, 2012, pp. 145—147). In addition to this, due to different methods of measuring accommodation-related eye fatigue, for example, no meta-analysis could be done. A systematic literature review involves evaluating the quality of indigenous studies. Studies are then evaluated from the perspective of the research question.

Subjects

The total number of subjects was 271, and the age range of subjects in the studies was broad, between 20 and 60 years. In Ozawa et al. (2015) study subjects were 20-40 years, Yamashita et al. (2019) 30-60 years, Kosehira et al. (2020) 20-60 years and Sekikawa et al. (2021) 20-49 years. Subjects were healthy, and the exclusion criteria were presented comprehensively in all studies.

Used Anthocyanin Preparations and Dosage

The anthocyanin source was blueberry in three studies, and maqui berry in one (Table 11). The bilberry extract varied between 120-480 mg/day, and Kosehira et al. (2015) and Sekiwara et al. (2021) also mentioned the amount of anthocyanin. In Yamashita et al. (2019) study, maqui berry extract consisted of 21 mg of anthocyanin. The duration of the trials ranged, and subjects consumed capsules for 4 to 12 weeks. Based on this, it can be concluded that the effect of anthocyanins requires several weeks of use. In chapter 2.3.4 was mentioned that in previous studies, anthocyanins were found to remain in the bloodstream and tissues for 1-2 hours. The amount of appropriate dosage cannot be established based on studies. According to Liu et al. (2019), a higher dosage of antioxidants may not improve their absorption, although the correct dosage is extremely important for the benefit for the eye and vision.

TABLE 12. The Summary of Duration of Trials and Used Preparations

Study	Duration of the trial (w)	Dose (mg/day)	Amount of anthocyanin (mg/day)	Source of anthocyanin
1	8	480	not mentioned	bilberry
2	4	60	21,0	maqui berry
3	12	240	88,54	bilberry
4	6	120	43,2	bilberry

Used VDT Load

In studies, accommodation was burdened by near-vision tasks before measurements were taken. Table 13 summarizes how the accommodation system was loaded and the durations used in the studies. The studies used different video games for VDT loading. Ozawa et al. (2015) and Kosehira et al. (2020) have been informed about used games in more detail. A standardised testing environment and stabilised near-vision distance were used only by Kosehira et al. (2020). This deficiency impairs the repeatability of studies and allows for variation in study results. Viewing distance directly affects the amount of accommodation, which is why a standardised research distance for each subject would be crucial.

TABLE 13. VDT Loading in the Studies

Study	VDT Loading	Duration (total)	Were the conditions standardized? (distance, lighting, etc.)
1	Playing Microsoft® Solitaire and BLOCK1. 30’	60 min + 60 min (120 min)	Environment-Yes Distance-No
2	Playing a video game	45 min	No
3	Playing Tetris®	40 min	Yes
4	Playing a video game with a handheld game console	60 min	No

Used measurement methods

Used measurement methods were critical flicker fusion, the near point of accommodation, pupillary response, flicker test and high-frequency component. None of the studies measured, for example, the amplitude of accommodation. Table 14 summarises the main results. To simplify the presentation of results, only the baseline and the final situation after the VDT load are compiled in the table. The results of intermediate measurements are not recorded in Table 14. Except for Yamashita et al. study (2019), the others published the results very accurately and analysed them by statistical methods.

TABLE 14. Used Measuring Methods and Main Results

Study	Measuring method	Measured results (baseline→ end of treatment)		Measured results (baseline → end of treatment)	
		Treatment-group		**Placebo-group**	
		Baseline	After	Baseline	After
1	Critical Flicker Fusion (CFF)	36,6 ±0,45 HZ	35,2 ±0,4 Hz	37,7 ± 0,5 Hz	36,3 ± 0,6 Hz
	The near point of accommodation (NPA)	7,55 ± 0,3 Dpt	7,35 ±0,30 Dpt	7,59 ±0,32 Dpt	7,50 ±0,33 Dpt
2	Pupillary response	Accurate results were not given.	-	Accurate results were not given.	-
	Flicker test	Accurate results were not given	-	Accurate results were not given.	-
3	High-Frequency Component of Accommodative Microfluctuation	52,21 ± 4,16	50,65± 4,03	50,72 ± 4,28	50,67±5,13
4	Change in the Percentage of Pupillary Response	35,9 ± 14,0%	37,2 ±12,7 %	31,6 ± 12,9%	33,0 ± 13,7 %

In Ozawa et al. (2015) study, the CFF value was reduced after the VDT load in the control and active group. The study's observation and conclusion were that there was significantly less variation in CFF value in the active group. In Yamashita et al. (2019) study, after four weeks of intake of extract, the active group had an increase in subjective symptoms (measured by Visual Analogue Scale) compared to the placebo group (*p*= 0,047). In Kosehira et al. study (2020), the post-VDT load HFC-1 values after 8 and 12 weeks were significantly improved in active group (*p*=0,014 and 0,017). In Sekikawa et al. (2021) study, there was a significant difference in the change of the logarithmic conversion of the percentage of the pupillary response pre- and after VDT use between the placebo and active group (*p*= 0,043).

Three out of four studies indicated that anthocyanins reduced VDT load-associated eye fatigue in objective measurement. Yamashita et al. (2019) study did not observe a significant effect of anthocyanin on accommodative function or flicker test, but subjective symptoms of eye fatigue alleviated. No studies on whether anthocyanins impact the amplitude of accommodation or other components of accommodation did not find. The conclusions about the effect of anthocyanin on accommodation cannot be drawn from the systematic review because the methods used focused on eye fatigue, not accommodation. In addition, the limited number of subjects and the variation in the source and duration of the studies of anthocyanin prevent generalisation.

4.5.3 The Evaluation of Quality, Validity and Reliability of Studies

All the studies in the review were randomised controlled trials (RTC). In this regard, those studies were reliable. RTCs attempt to minimise the effect of confounding factors. In healthcare, RTCs are ranked as a “golden standard” when the effectiveness of clinical interventions is studied (Coughlan, Cronin & Ryan, 2014, p. 12). Half of the study population used a placebo, making the effect of near vision on accommodation comparable. However, the quality of RTC studies may vary. Therefore, studies were evaluated using the checklist presented by Efron and Ravid (2019, pp. 105—106). There are 31 claims in the sections: methodology, participants, data collection tools, procedures, data analysis, ethics, results, discussion and validity and reliability. The studies were systematically checked point at once. Each submission got a point if the claim was fulfilled for that study. The total scores and observations for the studies are in Table 14, and the full table can be seen in Appendix 1. The best score was Kosehira et al. study (2020), and the lowest from Sekikawa et al. (2021). Methodology, data collection tools and data analysis sections were fulfilled in all studies.

TABLE 15. Check List Points

Study	Check List Points	Some Observations Based on the List
1) Ozawa et al.	25/31	-
2) Yamashita et al.	24/31	No results of the pupillary response and Flicker Test
3) Kosehira et al.	27/31	No information about sample recruiting
4) Sekikawa et al.	23/31	Very long report

Although the studies per se were of good quality, a few points emerged from them. These included the lack of a protocol for the study course and the selection of the research subjects. The study course should be described accurately because this deficiency undermines the reliability of the studies since they cannot be repeated exactly the same. None of the studies had an entirely accurate description.

There may have been a selection of the research participants in the studies. In Kosehira et al. (2020) study, subject recruiting was not informed. In Yamashita et al. (2018) and Sekikawa et al. (2021), study subjects were enrolled through the website operated by ORTHOMEDICO Inc. In this way, there may have been a selection of people who, in principle, have more problems with accommodation than usual. Ozawa et al. (2015), in turn, acquired the subjects based on their preliminary research. Subjects with the lowest CFF and NPA values were selected to participate in the study. Because the research subjects had not been selected randomly, it undermines the reliability of the studies.

An essential point for the systematic literature review is the method of measuring accommodation-included studies used mostly objective accommodation measurement methods to improve reliability. However, an objective measurement method does not automatically give a valid outcome. None of the studies had measured the amplitude of accommodation; methods focused more on measuring accommodation fatigue. As noted in paragraph 2.2.2, accommodation amplitude has decreased after VDT load (Jaiswal et al., 2019). Therefore, it could have been assumed that this would have also been studied in the studies used. However, there is a justification for the research methods used. Ozawa et al.'s (2015) study Critical Flicker Fusion indicates eye fatigue because it reflects neuron impulse transmission from retinal ganglion cells to the primary visual cortex. Near point accommodation (NPA) reflects muscle fatigue of the ciliary body, which is hypothesised to increase after VDT load. (Ozawa et al., 2015.) According to Sekiwaka et al. (2021), the symptoms of eye fatigue caused by VDT load reduce pupillary constriction and improvement of the accommodative function for an enhanced pupillary response. The pupillary response is one part of the near triad. In Kosehira, Machida, and Kitaichi’s (2020) study, the high-frequency component (HFC) was the evaluation outcome. It is based on the repeated contraction and relaxation of the ciliary muscles, which invoke sinusoidal fluctuation to refraction, so-called accommodative micro fluctuation. HFC value increases with an excessive load of accommodation system. Paragraph 2.1.2 states that the ciliary muscle is the only active part of the accommodation. Based on this knowledge the HFC measure is justified under laboratory conditions.

When evaluating scientific studies, bias must also be considered. Scientific research is always accompanied by bias. According to Ayorinde et al. (2020), different types of bias can occur generation of research evidence, outcome, and study level. In Yamashita et al. study (2019), the presentation of outcome reporting bias is observed because unfavourable results from the anthocyanin extract have been left unpublished. It has only been mentioned that the powder did not have a noticeable effect on the accommodation function and flicker test results (Yamashita et al., 2019) The second observation concerns Yamashita et al. (2019) study. Oryza Oil & Fat Chemical Company was the sponsor in Yamashita et al. (2019) study, and the company also manufactured the used product. Using financier's products does not improve the reliability of research. In addition, the study's results related to eye fatigue were not reported at all. In the results, it was only mentioned that the use of the product did not significantly affect the accommodative function or the flicker test result. The indicators (flicker value and pupil contraction) reported weaker accommodation after intake. The effect of the product on accommodation is based on responses from the questionnaire alone.

5 DEVELOPMENT PHASE

5.1 The Implementation of Thesis for Working Life

Accommodation plays an essential role in computer vision syndrome (Parihar et al., 2016; Jaiswal et al., 2019). Therefore, the optometrist should understand the accommodation as well as possible. As implementation of the thesis for working life, a lecture was conducted for Bachelor students at Oulu University of Applied Sciences. The lecture was created based on this thesis and includes the theoretical background of accommodation, accommodation measurement in clinical work, and the VDT loads effect on accommodation. The format of the lecture is PowerPoint, and it is presented in the Finnish language. The lecture will highlight the importance of testing accommodation and its function in eye examination for non-presbyopic patients.

5.2 Discussion and Conclusion

Viewing the VDT requires accommodation, and due to the nature of the electronic screens, the strain on the accommodation system is considered to be more demanding than, for example, looking at a book (Rosenfield, 2011; Munshi et al., 2017; Alemayehu & Alemayehu, 2019). According to computer vision syndrome, ocular symptoms (for example, eyestrain and sore or tired eyes) may be caused by accommodation (Alemayehu & Alemayehu, 2019). Accommodation is usually an unconscious process that can be examined by measuring its amplitude, facility, and response (Burns et al., 2014). The systematic literature review did not provide an answer to the research question because none of the studies did measure those. The search resulted in studies focusing more on vision stress and eye fatigue. Even though the search words were carefully drafted, they did not give correct studies, so the conclusion is that studies have yet to be carried out on this topic, at least in randomised controlled trials.

Based on this systematic literature review, anthocyanins positively affect some indicators of the accommodation-related measurements compared to placebo when the visual system was burdened with prolonged close-up visual display terminal viewing. However, it is not possible to draw far-reaching conclusions because the material in this systematic literature review needed to be more extensive. It covered four studies, and the number of subjects was small. Although the studies were RCT studies, there were multiple defects, such as selecting the subjects and study protocol. The studies included in the systematic literature review left several factors open, such as, for example, the minimum amount of anthocyanin to facilitate accommodation. Also, anthocyanins are challenging to study because they occur in many combinations, and their metabolism in the body still needs to be fully understood. Moreover, according to Yan's and Rosenfield's study published in 2022, the critical flicker fusion method used does not correlate with digital fatigue. It is not necessarily a suitable method in that respect. Their experiment was performed on 30 subjects with a 20-minute reading task from a tablet and book. Critical fusion frequency (critical flicker fusion, CFF) was measured before and after, and the conclusion was that neither the post-task change nor the difference between the two reading conditions was significant. (Yan & Rosenfield, 2022.) Yan and Rosenfield's (2022) study challenges the reliability of CFF as a measuring method used in Ozawa et al. (2015) and Yamashita et al. (2019) studies.

There were many challenges with this systematic literature review. Both accommodation and anthocyanins are complex. The nature of accommodation is a multi-cause process influenced by several factors. Accommodation occurs in a triad with pupillary constriction and eye muscles convergence, and measuring accommodation by a single method is challenging due to its nature. There is no gold standard for measuring accommodation, which was one reason the systematic literature review failed to answer the research question. The lack of a golden standard should have been considered when planning the research question. An agreement should be reached on the measurement before it is possible to obtain reliable information on the effect of anthocyanin on accommodation.

Anthocyanins are complicated compounds with wide varieties whose effect on humans is not fully understood and are challenging to study. The composition of anthocyanin varies depending on its source. In three studies, anthocyanin sources were bilberry and one maqui berry. In the used MaquiBright®-capsules, there were 15 mg of delphinidins and 4 mg of delphinidin-3,5-O-diglucoside (Yamashita et al., 2019). In other studies, the composition of the extracts does not disclose. According to Burdulis et al. (2007), cyanin was found primarily in bilberries. Delphinidins and petunidin were the next most common. Thus, it can be assumed that the composition of anthocyanins was different in maqui berries and bilberries. This matter makes evaluating the impact of anthocyanins on health difficult. Based on studies, the effect of anthocyanins on eye fatigue is based on two factors: improved blood flow and being antioxidant (Ozawa et al., 2015; Yamashita et al., 2019; Kosehira et al., 2020; Sekikawa et al., 2021). These mechanisms of action are the same ones presented by Nomi, Iwasaki-Kurashige and Matsumoto (2019) in chapter 2.2.4. According to Ozawa et al. (2015), bilberry anthocyanoside and its main anthocyanidin constituents protect retinal ganglion cells against retinal damage or improve rhodopsin function. Sekikawa et al. (2021) suggest that the increase in microcirculatory blood flow induced the release of the tension of the muscles related to pupillary response and eye movement.

The VDT work and reducing the problems caused by it attracts interest to the scientific community. Singh et al. (2022) have conducted a systematic literature review and meta-analysis of interventions for the management of CVS. After the search of this systematic literature review, the effect of oral berry extract on vision problems has been studied further (Lem, Gierhart & Davey, 2022; Singh et al., 2022). The methods used in the meta-analysis were multifocal lenses, blue-blocking spectacles, oral berry extract, omega-3 and carotenoid supplementation. All studies used in this systematic literature review were also included in the oral berry extract supplementation meta-analysis. According to Singh et al., there is certainly low evidence that oral berry extract did not reduce visual fatigue (Singh et al., 2022). When an increased amount of data is analysed, the effect of anthocyanin on visual fatigue becomes unclear. Although the effects of anthocyanins in laboratory conditions are good, the effects in clinical trials are not significant.

From the perspective of nutrition and vision, an article by Lem et al. (2022) appeared on the topic in September 2022. The review has discussed the effect of nutrition on Digital Eye Syndrome symptoms. It has presented the outcomes of using Omega-3 fatty acids, anthocyanins (phytochemical) and carotenoids to alleviate extra-ocular, ocular, and vision-related symptoms. Lem et al. (2022) show that some anthocyanins promote rhodopsin regeneration in the retina during the visual phototransduction cascade. Ocular tissues are vulnerable to oxidative stress and lipid peroxidation caused by light, but many anthocyanins cure its antioxidant capacity. According to Lem et al. (2022), the exact mechanism by which VDT may disrupt accommodation and vergence systems is still being determined. Lem et al. (2022) suggest that symptoms included in VDT work can be caused by the character of the display (variations in font size and contrast) and related multitasking.

From the point of clinical optometry, it would be essential to carry out further RCT studies of accommodation and anthocyanins. Research conditions and measurement of accommodation should be standardised, and anthocyanins' effect on accommodation should examine in a narrower age group. In the used studies of the thesis, the subjects' range age was broad. The weakening of accommodation caused by age is well known, so it is justified to carry out similar studies in narrower age groups. Although there are no recommendations for the intake of anthocyanins, it would be essential to know what minimum amount of anthocyanin will positively affect accommodation or if it can enhance accommodation amplitude. Because of the broad spectrum of anthocyanins, the study could focus, for example, on the effects of black currant because the anthocyanin composition is simple. The more straightforward composition would make it easier to analyse the metabolism of anthocyanin.

In the future, visual demands are increasing, and near-vision will be more burdened. An optometrist is a professional who must consider the changing visual requirements. The most extensive tools are needed to help customers, and in addition to old methods, new tools are needed to help patients. Singh et al. (2022) write that many CVS interventions, including anthocyanin extract, are marketed directly to patients. The need for more evidence in studies is why the products are offered directly to patients, not professionals. Although the optometrist should strive to help his or her patient, it is necessary to bear in mind the efficacy of treatment. Optometrists may recommend using anthocyanins for near-vision problems if there is more robust evidence of effects. The number of minor studies in this systematic literature review indicates that the topic still needs to be studied. Advancement of clinical work and best practice guides of optometry require RTC studies. Promising research results on the effect of anthocyanins on eye fatigue exist, but much high-quality research is needed on the subject. While anthocyanins' health effects are generally promising, studying them is challenging. This systematic literature review hopefully sparks interest in the subject. Due to several possibilities, interest in anthocyanins will increase even more, and optometry will also benefit from it.

6 REVIEW OF THE RELIABILITY OF THE THESIS

The reliability of the thesis can be considered from several perspectives, such as the researcher and the research itself. Two points arise with this thesis: the low number of search results as well as the review was carried out alone. This systematic literature review covered only four studies, and the number of subjects was small. The research question was deliberately narrowed down to make the literature review easier. Studies on the subject have not been conducted much either. This matter reduces the generalizability of the literary review. A more comprehensive number of search results would have allowed, for example, meta-analysis.

This literature review was carried out alone, and the author of the thesis had no previous experience in a similar study. A group of researchers is often involved in conducting a systematic literature review, which makes it possible to analyse a large amount of data and reduces the distortion in the results caused by the research bias of an individual researcher. In this thesis, the amount of data being analysed was low and allowed the review to be done independently and with a reasonable workload. However, working alone undermines the reliability of the research. The risk of opinion can easily affect the outcome when one student conducts a systematic literature review. There has been taken attention to improving reliability from the outset. The thesis has aimed at objectivity and criticality. All stages of the work are recorded accurately and truthfully. The reliability has been enhanced by using an external expert to determine the search words. Another significant way to improve reliability was that a second master’s student verified the used studies.

7 REVIEW OF THE ETHICALITY OF THE THESIS

The thesis has been conducted in accordance with the Finnish Advisory Board on Research Integrity ethical guidelines. The systematic literature review has been written with integrity, meticulousness, and accuracy. The references have been carefully made to honour other researchers' work done in the past. The literature review was planned, conducted, and reported accurately. The thesis did not require separate research permits. (Finnish Advisory Board on Research Integrity, 2012, pp. 31—32)

8 TIMETABLE AND BUDJET

Producing a systematic literature review is a dynamic process taken into account in planning the timetable of the thesis (Efron & Ravid, 2019). The year 2022 and the beginning of the year 2023 were planned to complete the thesis. The systematic literature review and its reporting were carried out along with the work, due to which time elapsed throughout the year. Once the topic was delineated, writing a theoretical background was started. It was written during the entire search and analysis phase. The various phases of the work were interspersed so that the process proceeded throughout the year. When the written part of the thesis was completed, the implementation part of the work was done. The thesis process is presented in Figure 7.

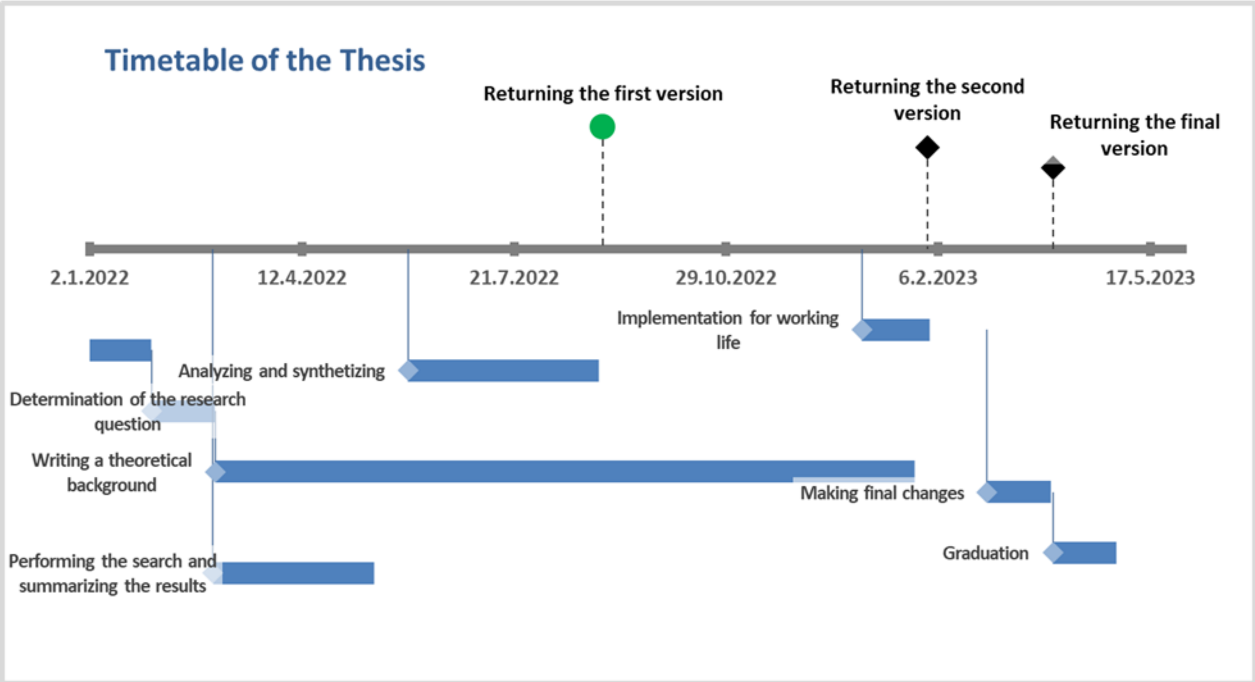


FIGURE 7. Timetable of the Thesis

The material of the thesis was gathered from free articles. The library of the OUAS provided free access to used e-books and other material. In addition to this, the thesis made use of professional literature that had already been acquired. Personnel costs for the student or supervisor in this thesis were not calculated.

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A Checklist for Evaluating Quantative Reseach Articles						
		STUDY				
source: Efron & Ravid (2019), Writing the Literature Review, pp. 105-106		**1**	**2**	**3**	**4**	**NOTES**
Methodology	Description should be spefific and detailed	1	1	1	1	
	Whether the study was experimental or non-experimental is noted	1	1	1	1	
Participants	There is a clear and detailed description of the participants and their characteristics	1	1	1	1	
	There is an explanantion of how the sample was selected	1	1	0	1	3. No information about sample re-cruiting
Data collec-tion tools	Data collection tools are clearly descriped	1	1	1	1	
	Information is provided as to whether existing, modified, or newly developed data collection tools are used	1	1	1	1	
	There is information about reliability and va-lidity of the data collection tools	1	1	1	1	
	When appropriate, sample items or questions are included	1	1	1	1	
Procedures	The procedures for conducting the study are clearly and adequately descriped	0	0	1	0	1,2,4: There was timeline different measurements, except 3
	There is a description of the process, dura-tion, and schedule of the study	1	0	1	1	3: short duration+
	The data collection process is descriped	0	0	1	0	
Data analysis	There is an explanation of the study's design and data analysis	1	1	1	1	
	Statistical procedures used to test study's hy-potheses are listed when appropiate.	1	1	1	1	
Ethics	Ethical guidelines are followed	1	1	1	1	
Results	The main findings are reported	1	0	1	1	2: no results of the pupillary response and Flicker Test

	The results are clearly presented and easy to follow	0	0	1	0	1,2,4: The results was only in table
	There are tables, graphs, or charts that help explain the findings	0	1	1	0	4. very long report
Discussion	The results are examined, explained, and evaluated	1	0	1	1	
	There is a discusssion of the findings in relation to the original questions and/or hypotheses	1	1	1	1	
	Findings are discussed in relation to prior research on the topic	1	1	1	1	
	The study's conclusions are justified based on the results of the study	1	1	1	1	
	The authors provide possible explanations for unexpected results.	1	1	1	1	
	Weaknesses and limitations of the study are discussed.	1	1	0	0	
	Implications of the findings for practioners are presented.	0	1	1	0	
	There are suggestions for further research.	1	1	0	0	
Validity and Reliability	There is evidence of the study's internal validity, especially in experimental studies	1	1	1	1	
	There is evidence of external validity.	0	0	0	0	Selection of the subjects can effect to results
	The validity of the data collection instrument(s) is presented	1	1	1	1	
	The reliability of the data collection instrument(s) is documented	1	1	1	1	
	The level of reliability of the measure is appropriate for its use in the study	1	1	1	1	
	The reliability levels of the data collection instrument(s) are reported when validity is discussed.	**1**	**1**	**1**	**1**	
	TOTAL SCORE	**25**	**24**	**27**	**23**	