

# Health Benefits of Blackcurrants – a review of the research

# 1.0 How the review has been carried out

Blackcurrant extracts contain a range of antioxidant compounds, including anthocyanins, other polyphenols and vitamin C, which are reported to have a range of health benefits. The NZ Blackcurrant Cooperative Ltd (NZBC) has undertaken a review of some of these benefits to make more readily available the published scientific information on the health benefits of blackcurrants. This review is a collation and summary of this information and does not represent a claim by the NZBC with regard specific health benefits from the consumption of blackcurrants.

All information is based on sound science sourced from studies published in peer reviewed science journals and books. Evidence from clinical trials is reported where it exists. Clinical trial results reported here were obtained from randomised, double-blind, placebo-controlled, cross-over trials, and a treatment effect is only reported if it is statistically significant.

A detailed summary for each of more than 36 clinical trials are presented in Section 2. A summary of significant laboratory studies on the effects of blackcurrants is presented in section 3.

# Berry equivalence

Several studies report amounts of blackcurrant extract ingested that were between 50-80 mg anthocyanin in about 500 mg powder. To put this in perspective, this is equivalent to the anthocyanin in about 13 berries i.e. about a small handful.

This calculation is based on:

- There are a range of values for the anthocyanin content of NZ berries. However, 6mg anthocyanin per g fresh weight would be an average.
- A berry is about 1 g.
- Thus 13 berries contain about 78 mg.

## **Terms** used

Polyphenol-the term is used broadly to include phenolics, flavonoids and anthocyanins

Placebo - a placebo is an inactive look-a-like.

Double blind - neither the individuals nor the researchers know who belongs to the control group and the experimental group.

in vitro - literally "in glass" and meaning in the laboratory.

in vivo – "in the living organism" and refers to studies performed on animals

Statistically significant - this means that there is a very low chance of the result having occurred randomly. For example; this may be shown by stating that the result is significant at the 1% level i.e. the chances of it happening randomly are 1 in 100. Alternatively a p value may be used e.g. p<0.008 which means there is a 1 in 120 chance.



# 2.0 Summary of the individual clinical trials

A summary of each trial is presented below. The published paper they are based on is referenced by the number in brackets.

#### Contents:

- 2.1 Cardiovascular Health and Vascular Inflammation
- 2.2 Exercise Performance, Diet and Immune Response
- 2.3 Eye Health
- 2.4 Brain and Gut Health
- 2.5 Kidney Health
- 2.6 Brain Health
- 2.7 Anthocyanin Bioavailability and Absorption

#### 2.1 Cardiovascular Health and Vascular Inflammation

Many epidemiological studies have shown that an increased intake of polyphenols (including blackcurrant polyphenols) lowers the risk of cardiovascular disease, through an improvement in:

- blood pressure,
- lipid levels in the blood, and
- biomarkers such as
  - Nitric oxide, NO (a potent vasodilator)
  - Vascular inflammation and
  - Endothelial function (endothelium: the inner lining of blood vessels).

These are summarised in the review paper by Wallace 'Anthocyanins in Cardiovascular Disease' (1), and other papers (2, 3). Clinical trials with blackcurrants are reported below.

## Clinical trials with blackcurrants for cardiovascular health (4, 5)

- In a short-term crossover study, 12 individuals with high levels of blood cholesterol consumed anthocyanins (320 mg) isolated from blackcurrants or a placebo. Brachial artery flow-mediated dilation (FMD) was assessed before and after the intervention.
- In a long-term intervention trial (12 weeks), 150 individuals with high levels of blood cholesterol were given anthocyanins (320 mg/day, n = 75) or placebo (n = 75), after which FMD, plasma cyclic guanosine monophosphate (cGMP), and other serum biomarkers were measured.
- Another short-term intervention was conducted in the presence of Nitric Oxide-cGMP inhibitors in 6 people and in a rat aortic ring model (n = 8).

RESULTS: Significant increases of FMD were observed after short-term anthocyanin consumption, with increases of plasma anthocyanin concentrations (P < 0.05). In the study participants who received long-term anthocyanin intervention, compared with the control group, observed significant increases in the FMD and HDL-cholesterol ("good' cholesterol) concentrations, and decreases in the serum soluble vascular adhesion molecule-1 and LDL cholesterol ("bad" cholesterol) concentrations (P < 0.05). The changes in the cGMP and HDL cholesterol concentrations positively correlated with FMD in the anthocyanin group (P < 0.05). In the presence of Nitric Oxide-cGMP inhibitors, the effects of anthocyanin on endothelial function were abolished in human participants and in a rat aortic ring model.

CONCLUSIONS: Anthocyanin supplementation improves endothelium-dependent vasodilation in individuals with high levels of blood cholesterol. This effect involves activation of the Nitric Oxide-cGMP signaling pathway, improvements in the serum lipid profile, and decreased inflammation.



In a further clinical trial the antioxidative effects of various beverages, *in vitro*, and also the effects *in vivo* on serum antiatherogenic macrophage cholesterol accumulation and foam cell formation were determined. These are the hallmark of early atherogenesis<sup>1</sup>. Six healthy subjects consumed 100% blackcurrant juice, richest in polyphenols, for a week. This treatment modestly, but significantly, decreased serum-induced cholesterol accumulation in macrophages. The reduction in macrophage cholesterol mass, however, was not the result of increased cholesterol efflux from the cells. In fact, it is probably the result of inhibition of cholesterol-rich lipoprotein uptake by the cells, mediated by serum associated polyphenols and/or polyphenol metabolites.

# Effects of blackcurrant juice and orange juice on markers of vascular inflammation and cardiovascular risk (6)

Vascular inflammation is an important contributing factor to cardiovascular disorder. This study looked at the effects of blackcurrant and orange juices on markers (indicators) of vascular inflammation in patients with peripheral arterial disease. The markers were C-reactive protein and fibrinogen. Lower levels of both markers are considered desirable and indicate lower risk.

This was a randomised, double-blind, placebo-controlled, cross-over study of four weeks duration. Study size was 48. Subjects drank 250 ml of blackcurrant juice and 250 ml of orange juice daily. A sugar drink placebo was used.

At the completion of the study, there were statistically highly significant decreases in the levels of each of C-reactive protein and fibrinogen. There was an 11% decrease in C-reactive protein, (p<0.008); and a 3% decrease in fibrinogen (p<0.002).

The study supports the view that increased intake of fruit products such as blackcurrant and orange juice decreases the risk of cardiovascular disorder.

# Berry meals and risk factors associated with metabolic syndrome. (38)

Non-alcoholic fatty liver disease is commonly associated with obesity, insulin resistance, heart disease, high blood pressure and type 2 diabetes, also known as metabolic syndrome. This study compared the effects of lifestyle intervention with and without berry products including blackcurrants, on risk factors associated with metabolic syndrome on slightly overweight women.

61 female volunteers were recruited for a randomised 20-week dietary intervention trial with two parallel treatment groups. One lifestyle intervention group with berry products (average daily dose of 163g of berries and the other group with lifestyle intervention only.

Liver markers are a recognised way to assess accumulation of fat in the liver. Serum alanine aminotransferase (ALAT) values correlate positively with liver fat proportions. The results showed that the group consuming the berries had significantly lower levels of ALAT and adiponectin.

## **Conclusions:**

The 23% decrease in the ALAT value, from 20.29 to 15.66U/l in the berry group may be regarded as nutritionally significant by enhancing the liver function. This may contribute positively to the low-grade systemic inflammation in body and decrease the risk of cardiovascular disease.

<sup>&</sup>lt;sup>1</sup> Atherogenesis is the process of forming atheromas, plaques in the inner lining (the intima) of arteries.



## Effect of blackcurrants on blood flow (7)

This was a randomised double-blind, placebo-controlled, cross-over study using nine female subjects (age 22 to 34). The subjects had daily subjective symptoms of chill, caused by peripheral circulation disorder, and used 50mg blackcurrant anthocyanin.

After soaking the right hand in cold water of 10 degrees centigrade for one minute, images were taken of the hand using thermography and blood flow volume measured every minute (up to 30 minutes) until the hand returned to resting level. Body temperature did not return to normal after 15 minutes without blackcurrant consumption. In contrast, however, body temperature began to return to normal 10 minutes after blackcurrant consumption.

# Effects of blackcurrant intake on peripheral blood circulation during typing work (8)

This was a randomised double-blind, placebo-controlled, cross-over study. Study size was 10 people. Blackcurrant powder was prepared from liquid concentrate. The powder had an anthocyanin concentration of 10%.

There were two parts to the study - 1) the effect of blackcurrants on peripheral circulation during rest, and 2) during typing work.

## 1. Blackcurrant effects during rest:

- Subjects ingested 17 mg powder capsule/kg subject weight for the resting study
- What was measured:
  - Anthocyanin content in plasma
  - o Forearm blood flow
  - Muscle oxygen consumption
  - o Total hemoglobin and oxygenated hemoglobin
  - Electromyography of the right trapezius muscle.

#### The results:

- Anthocyanin content of plasma reached maximum after 1 hour, decreased to 50% by 4 hours
- o Forearm blood flow increased significantly (about 40%) compared to placebo.
- No effect on muscle oxygen consumption.

## 2. Blackcurrant effects during typing:

- Subjects ingested 7.7 mg powder capsule/kg subject weight
- What was measured:
  - o Total hemoglobin and oxygenated hemoglobin
  - o Electromyography of the right trapezius muscle.

#### The results:

- o Total hemoglobin was significantly higher (about 40%) in the blackcurrant intake group.
- o Oxygenated hemoglobin was significantly higher in the blackcurrant intake group.
- Significant stiffening of the trapezius muscle during typing in the placebo but not the blackcurrant intake group. However, final stiffness not significantly different between the two.
- o No effect on blood pressure, heart rate, subjective pain and typing performance.



When the circulation is disturbed by compression of the blood vessels resulting from continuous muscle contraction removal of metabolites such as lactic acid becomes insufficient and leads to development of muscle stiffness. The study shows a vasodilatory<sup>2</sup> effect of blackcurrants.

Blackcurrants may reduce muscle stiffness by increasing peripheral blood flow and reducing muscle fatigue. Additional laboratory studies with animal models have shown direct effects of anthocyanins on improving blood peripheral circulation (not referenced below).

# 2.2 Exercise Performance, Diet and Immune Response

## Effects of blackcurrant powder on exercise-induced oxidative stress (9)

Exercise induces oxidative stress in the body. Dietary antioxidant supplements and foods are commonly used to limit such stress after exercise. This study looked at the effectiveness of blackcurrant powders containing high levels of anthocyanins to mitigate exercise induced stress.

This was a double blind placebo controlled cross over study of three weeks duration. Study size was 10 healthy subjects who exercised regularly about three times a week. Subjects consumed four capsules containing 240mg anthocyanin (two pre and two post exercise) equivalent in total to about 48 g whole blackcurrants (this corresponds to about 1/3 cup berries). A sugar placebo was used.

## What was measured:

- o Three plasma oxidative stress parameters
- Effects on cytokines and other immune system regulatory factors, as measured in a laboratory assay of inflammatory response generated by bacterial endotoxins.

# The results:

- Blackcurrant powder reduced exercise induced oxidative stress as shown by significantly lower levels of protein carbonyls, oxidative capability, and creatine kinase activity (p<0.05)</li>
- After exercise blood samples, from the subjects fed blackcurrant powder, showed a significant (p<0.05) ability to suppress inflammatory responses as measured by cytokines and other regulatory factors in the above laboratory assay.

The researchers concluded that blackcurrant extracts taken at the appropriate time and amount, can augment the ability of regular exercise to enhance the immune responsiveness of the body.

This research found that blackcurrants boost the natural benefits of exercise, by reducing muscle damage and soreness and assisting immune protection. These benefits are backed by scientific data showing speedier tissue repair, recovery and performance in exercise. Therefore, this study suggests that at the appropriate time and amounts, blackcurrants enable those involved in physical fitness to train harder, for longer periods.

# Improved exercise performance and recovery (39,40,41,47,42,48,50)

Seven related clinical trials by the same authors showed that athletes consuming 7 days of blackcurrant powder or extract made with New Zealand blackcurrants, showed performance effects for endurance athletes, including improving blood flow. The results of the studies showed lower lactate accumulation during exercise indicating improved recovery, improved performance and improved cardiovascular

<sup>&</sup>lt;sup>2</sup> Vasodilation refers to the widening of blood vessels resulting from relaxation of smooth muscle cells within the vessel walls. When vessels dilate, the flow of blood is increased due to a decrease in vascular resistance. Therefore, dilation of arterial blood vessels (mainly arterioles) leads to a decrease in blood pressure.



function, which could enhance recovery from exercise. Details of each study follow.

**Study 1:** This study of 13 experienced triathletes took part in a double blind, randomised, cross-over trial, involving intensive cycling, after taking 6 grams of blackcurrant powder per day for 7 days.

- The athletes had lower lactate accumulation, showing a complete shift in the lactate curve compared to the placebo.
- Lactate was reduced by 14% at maximum oxygen uptake.
- Cycling intensity (Power) at OBLA (onset of blood lactate accumulation) was 6% higher in the blackcurrant group.

This study also analysed resting cardiovascular function in the same 13 experienced triathletes after taking 6 grams of blackcurrant powder per day for 7 days, showing:

- Increased cardiac output by 26%
- Increased blood flow, by decreasing total peripheral resistance by 16%
- Increased cardiovascular efficiency through increased stroke volume by 25%. Stroke volume is the amount of blood pumped out of the heart. Increased stroke volume improves the flow of oxygen-rich blood to the muscles.

For resting skeletal muscles, these observations may influence the delivery of nutrients and the clearance of metabolites.

The study concluded that New Zealand blackcurrant powder affects physiological and cardiovascular responses during exercise and at rest that has implications for exercise performance.

**Study 2**: In this randomised, crossover, double-blind study thirteen active males consumed 300mg of New Zealand blackcurrant extract containing 105mg of anthocyanins or a placebo for seven days prior to performing high intensity intermittent running to exhaustion. The study design was used to mimic the high intensity repeated sprints often seen in team sports such as soccer and rugby.

**Results showed improved running performance.** Participants were able to improve their running performance by achieving an increase in the distance covered by 10.6%. New Zealand blackcurrant may help to postpone peripheral muscle fatigue, reduced accumulation of metabolites and improved peripheral blood flow. It is also likely that the antioxidant activity of blackcurrants helps to reduce fatigue caused by the production of reactive oxygen species during exercise.

**Blackcurrants allowed 15% higher lactate levels at the point of exhaustion**. New Zealand blackcurrant may postpone peripheral muscle fatigue by allowing elevated levels of intracellular acidosis (or the lowering of pH in muscle cells).

*Improved post-exercise recovery* with blackcurrants illustrated by larger changes in lactate clearance from the blood which may be due to increased peripheral blood flow enabling lactate to be transported to other tissues for oxidation.

The study concluded that these findings may have implications for nutritional strategies used by athletes involved in sports with repeated sprints.

**Study 3**: This study examined the effect of New Zealand blackcurrant extract during an intermittent shuttle run test and a subsequent run to exhaustion. This test is designed to simulate team sport activity that involves periods of maximal running sprints such as soccer and rugby. Thirteen male participants consumed New Zealand blackcurrant extract powder which contained 105mg blackcurrant anthocyanins or a placebo for seven days.



#### The results showed that:

NZ blackcurrant anthocyanins reduced the slowing of the fastest sprint period of the test, which may indicate that the participants experienced less fatigue.

8 out of 13 participants had higher running times to exhaustion when consuming the blackcurrant extract

The study concluded that NZ blackcurrant extract may enhance performance in team sport with repeated maximal sprints.

**Study 4:** In this randomised, crossover, double-blind study fourteen experienced cyclists consumed 300mg of New Zealand blackcurrant extract containing 105mg of anthocyanins or a placebo for seven days prior to completing 30 mins of cycling at three different intensities, followed by a 16.1 km time trial.

**Results showed improved performance:** A previous study proposed that the smallest worthwhile change for road time trial cyclists is around 0.6%. So the study finding of 2.4% reduction in completion time fora time trial is a considerably larger reduction and therefore represents a practical advantage to athletes who undertake endurance training. This increase appears to be the result of higher power output across the time trial. The mechanism which allows blackcurrant to improve performance may involve improved endothelial function allowing improved peripheral blood flow. Plasma lactate was higher immediately following the trial, with cyclists consuming the blackcurrant extract.

*Improved Fat Oxidation:* This is the first study to observe improved fat oxidation with blackcurrant extract intake. The whole body fat oxidation rates were 15%, 13% and 27% higher than the placebo at low and moderate cycling intensities of 45%, 55%, 65% VO2 respectively. This effect may result from a number of pathways acting synergistically, including transport of fatty acids into cell tissues, improved nitric oxide availability and improved peripheral blood flow.

**Study 5:** In a previous study, 6g blackcurrant powder containing approximately 139mg anthocyanins, consumed for 7 days by endurance athletes had an effect on resting cardiovascular function. This study aimed to examine whether there was a dose effect of New Zealand blackcurrant on cardiovascular function of trained cyclists.

Fifteen male cyclists completed four 20 minute periods of resting in the supine position, while their cardiovascular function was measured. New Zealand blackcurrant extract was consumed by participants at 0g, (placebo), 300, 600 and 900mg per days for 7 days.

The results showed that the higher the dose the greater the effect on stroke volume and cardiac output at rest. New Zealand blackcurrant extract also had a dose -response effect on total peripheral resistance. At the highest dose rate stroke volume increased by 17.7%, cardiac output increased by 27.5% and total peripheral resistance reduced by 20.2%.

The effect of New Zealand blackcurrant on resting cardiovascular function may support the recovery of endurance athletes.

**Study 6:** Nine experienced triathletes took part in a study of 10 mile/16.1km time trial, after 7 days of New Zealand blackcurrant powder containing 300mg anthocyanin per day. The blackcurrant powder showed improved cycling performance and recovery.

Results showed:



- Improved time trial performance by 3.6%
- Higher lactate tolerance during time trial performance.
- Increased lactate clearance after exercise indicating improved recovery.

**Study 7:** Because blood flow to the muscles is critical for oxygen delivery for sustained muscular activity, dietary interventions that can enhance blood flow to the muscles are of interest to athletes.

While a number of previous clinical studies show improved sports performance with consumption of blackcurrants the mechanism is not yet known. This study aims to provide insight into the mechanism for the enhanced effect.

This randomised, double-blind cross-over study used 13 healthy men, who ingested 7 days of 210mg blackcurrant anthocyanin per day or a placebo, prior to exercise involving sustained contractions of the quadriceps muscles.

The key finding of this study was that the femoral artery diameter was increased with consumption of blackcurrant during the sustained quadriceps contraction. This change was accompanied by cardiovascular changes, with decreased blood pressure, decreased total peripheral resistance with a related increase in cardiac output and stroke volume. The results also showed a decrease in muscle oxygen saturation, while total haemoglobin concentration was increased.

Taken together, the increase in vasodilation and cardiac output would indicate an increase in peripheral blood flow with blackcurrant consumption as the potential mechanism for enhanced exercise performance with blackcurrant.

# Blackcurrant juice reduces muscle damage and inflammation following exercise (43)

In this double-blind, placebo-controlled study, sixteen untrained participants drank a 473ml bottle of a commercially available blackcurrant juice drink or a placebo twice a day for 8 days. On day four they performed a series of high intensity knee contractions. Blood samples were taken 24, 48 and 96 hours after exercise. The study measured muscle soreness and blood markers of muscle damage, inflammation and antioxidant capacity (ORAC).

#### Results:

- 1. Leg muscle soreness (on a subjective scale from 1-10), was not significantly reduced with blackcurrants compared to the placebo, but the blackcurrant group returned to baseline values a full day before the placebo group. There was also a clear trend towards lower self-reported soreness in the blackcurrant group at all times.
- 2. The blackcurrant group showed a reduction in the activity of creatine kinase, a blood marker of muscle damage by 6.7%, compared to 82% increase in activity in the placebo group. These results suggest that blackcurrant consumption offers a protective effect against muscle damage that often results in the release of creatine kinase after exercise.
- 3. The levels of the marker of inflammation, interleukin -6, decreased in the blackcurrant group compared with an increase seen in the placebo group. However, the change from the baseline measurement was not significant for either group. Noticeably, there was a significant difference between the two groups at 24 hours after exercise.



4. ORAC levels in the blood significantly decreased in the placebo group while no significant decreases were observed in the blackcurrant group.

The study concluded that the consumption of blackcurrant juice prior to and after exercise significantly reduces muscle damage and inflammation, while maintaining circulating antioxidant capacity. Consumption of blackcurrant may represent a natural food alternative to taking analgesic and anti-inflammatory drugs following high intensity eccentric exercise.

## Inflammatory response and diet (10)

This study showed, for the first time, direct evidence on the role of diet in modulating inflammatory response in healthy overweight subjects. In a double blind, randomized, placebo controlled, crossover study of fourteen healthy overweight humans, the study showed that when a fruit juice drink composed of pineapple, blackcurrant and plum was taken with a high fat meal, there was a highly significant effect on inhibition of IL-17 (a biomarker of inflammatory response).

## Glycaemic control and clinical trials (11, 12)

Two clinical trials have shown berries rich in polyphenols decrease the postprandial glucose response of sucrose in healthy subjects. The delayed and attenuated glycaemic response indicates reduced digestion and/or absorption of sucrose from the berry meal. Diets with a high glycaemic response may be associated with increased risk of obesity, type 2 diabetes and CVD (cardiovascular disease). Previous studies have suggested that polyphenols may influence postprandial glycaemia (presence of glucose in the blood following a meal).

The trial investigated the glycaemic effect of a berry puree made of bilberries, blackcurrants, cranberries and strawberries, and sweetened with sucrose. A total of twelve healthy subjects (eleven women and one man, aged 25–69 years) with normal fasting plasma glucose ingested 150 g of the berry puree with 35 g sucrose or a control sucrose load in a randomised, controlled cross-over design. After consumption of the berry meal, the plasma glucose concentrations were significantly lower at 15 and 30 min and significantly higher at 150 min compared with the control meal. The peak glucose concentration was reached at 45 min after the berry meal and at 30 min after the control meal.

# Blackcurrant and bilberry anthocyanins show significant beneficial metabolic effects for patients with type 2 diabetes. (46)

This randomised, double-blind, placebo-controlled study of 58 adults with type 2 diabetes showed significant changes in the metabolic abnormalities associated with diabetes. The anthocyanin group consumed 320mg of anthocyanins from blackcurrants and bilberries per day for 24 weeks.

- 1. The result showed significantly improved dyslipidemia (elevated total cholesterol levels in the blood). HDL cholesterol ('good' cholesterol) levels were increased by 19.4% and LDL cholesterol ('bad' cholesterol) levels were lowered by 7.9% and trigylcerides were lowered by 23%.
- 2. In addition, the patients consuming anthocyanins had a significant increase in blood serum antioxidant capacity and a decrease in oxidative stress. The results suggest that the antioxidant defence system was activated by anthocyanins to scavenge excess free radicals and reduce oxidative damage products in diabetic subjects. Evidence suggests that oxidative stress, due to excessive production of reactive oxygen species, plays an important role in the pathways that lead to diabetic complications.
- 3. The subjects consuming anthocyanins also showed improvements in insulin sensitivity, which allows improved ability of the cells to respond to the action of insulin to transport glucose from the bloodstream into muscles and other tissues.



These findings conclude that supplementation of anthocyanins to type 2 diabetics shows beneficial metabolic effects by improving dyslipidemia, enhancing antioxidant capacity and preventing insulin resistance.

# Effect of anthocyanins on fibromyalgia (13)

Fibromyalgia is a condition of chronic widespread musculo-skeletal pain, particularly in the neck and shoulders, knees and elbows, and lower back.

This was a randomised double-blind, placebo-controlled, cross-over study of four treatment periods of 12 weeks each. Study size was 10. Subjects ingested 40, 80 or 120 mg anthocyanin per day, from a proprietary product based on extracts of grape seeds, and berries.

#### What was measured:

- Severity of pain symptoms
- o Fatigue and sleep disturbance
- Patients assessment of treatment
- o General health questionnaire.

## The results:

- There was a very significant effect (at 1% level) on reduction in sleep disturbance, as assessed by subject's diary record.
- o There was a significant improvement in the general health questionnaire.
- There was a significant improvement in the severity of fatigue (at 1% level) as assessed by the investigator.
- o The best treatment was 80 mg/day.

The authors concluded that anthocyanins were beneficial for people suffering from this difficult chronic condition.

# 2.3 Eye Health

# Effect of blackcurrants on dark adaptation and visual fatigue (14)

This was a randomised double-blind, placebo-controlled, cross-over study. Study size was 12. Subjects ingested up to 135, 270 and 540 mg blackcurrant powder for the dark adaptation test and 50 mg equivalent blackcurrant powder for the transient refractive alteration test.

#### What was measured:

- Dark adaptation threshold
- Video display terminal (VDT) transient refractive alteration
- Visual fatigue (asthenopia)

## The results

- Dark adaptation was significantly improved at the highest level of 540 mg blackcurrant powder (50 mg anthocyanin);
- There were no significant effects on VDT transient refractive alteration;
- Visual fatigue was significantly reduced with blackcurrant treatment;
- Lower back fatigue was significantly reduced with blackcurrant treatment.

The effects are considered to be mediated by increased blood flow in the peripheral circulation.



# Effects of blackcurrants on glaucoma (27,28,29,30)

Four clinical trials showed a positive effect on the disease of the eye called Glaucoma. Glaucoma is a disease of the major nerve of vision, called the optic nerve. Glaucoma is a major cause of visual field defects and blindness.

**Study 1:** This study examined the effects of anthocyanins in blackcurrant on retinal blood flow circulation of patients with normal tension glaucoma.

Glaucoma is usually associated with high intraocular (eye) pressure. In Normal Tension Glaucoma the intraocular pressure is normal. In this study thirty patients with Normal Tension Glaucoma consumed blackcurrant anthocyanins (50mg) in tablet form once per day for six months.

At the end of the six month period:

- The subjects showed significantly increased blood flows at the neuroretinal rim of the optic nerve head and peripapillary retina.
- o No significant changes in blood pressure or intraocular pressure were measured.
- o None of the subjects showed progression of their visual field defects.

These results suggest that orally administrated anthocyanins may be a valuable neuroprotective treatment of patients with Normal Tension Glaucoma.

**Study 2:** This study was a two-year randomised, placebo controlled study of blackcurrant anthocyanins on visual field in Glaucoma.

Blood flow to the retina and optic disk is thought to be an important factor in the cause of Open Angle Glaucoma. The study was a randomized, placebo-controlled, double masked trial looking at 38 patients with Open Angle Glaucoma, treated by anti-glaucoma drops. For two years, the subjects consumed 50mg per day of blackcurrant anthocyanins or a placebo.

The study shows two significant outcomes:

- 1. The study measured visual field mean deviation (to show changes in the visual field of subjects over time). The results showed that the placebo group had statically significant visual field mean deviation from the baseline. However, the group taking blackcurrant anthocyanins showed no significant changes in visual field mean deviation over the two year period.
- 2. The study also measured ocular blood circulation. Ocular blood flow in the group taking the blackcurrant anthocyanins showed a statistically significant increase, in comparison with the group taking the placebo, which showed no change in ocular blood flow over the two year period.

The study concluded that the oral administration of blackcurrant anthocyanins may be safe and promising supplement for patients with Open Angle Glaucoma, in addition to anti-glaucoma medication.

**Study 3:** This study examined the effects of blackcurrant anthocyanins on intraocular pressure in healthy volunteers and patients with Glaucoma.

Elevated intraocular pressure (IOP) is generally recognised as the most important risk factor for glaucoma.



This study was carried out to determine the effects of blackcurrant anthocyanins on intraocular pressure (IOP) in both healthy subjects and patients with glaucoma.

# Two groups of subjects took part:

- o Group 1. Blackcurrant anthocyanins (50mg/day) or placebos were taken orally by 12 healthy subjects once daily for 4 weeks.
- Group 2. A total of 21 glaucoma patients (blackcurrant anthocyanins, n = 12; placebo, n = 9) treated with a single anti-glaucoma medication, who had participated in a previous study (see summary of study 2 above Ophthalmologica 2012; 228:26–35) were selected and analysed.
   Systemic blood pressure, pulse rates, IOP, and Humphrey visual-field mean deviation (MD) were evaluated.

#### The results:

- A statistically significant decrease in the mean IOP was observed at 2 weeks and 4 weeks from the baseline in blackcurrant anthocyanin-treated healthy subjects. However, this decrease, was not observed in the placebo group.
- The results showed statistically significant decreases in mean IOP in the glaucoma patients taking blackcurrants anthocyanins compared to the placebo group.
- In addition, mean changes of visual field MD deterioration were significantly less in the anthocyanin-treated glaucoma patients administered with blackcurrant anthocyanins at 12 months and 18 months after the baseline.
- No clinically significant changes were observed in systemic blood pressure or pulse rates in either trial.

Conclusions: These results suggest that oral administration of blackcurrant anthocyanins may induce a beneficial decrease in IOP levels in healthy subjects as well as in patients with glaucoma.

**Study 4:** This study examined how blackcurrant anthocyanins normalized abnormal Levels of serum concentrations of endothelin – 1 in Patients with Glaucoma.

A study of blackcurrant anthocyanins and glaucoma (see summary of study 2 above, Ophthalmologica 2012;228:26–35), which involved a 24-month trial revealed that oral administration of blackcurrant anthocyanins slowed down the visual field deterioration and elevation of ocular blood flow of open-angle glaucoma (OAG).

To discover the underlying mechanisms of these blackcurrant anthocyanin-induced effects, changes of serum biomarker endothelin-1 (ET-1), were examined in the present study using 38 patients with Open Angle Glaucoma. Blood serum specimens were obtained from blackcurrant anthocyanin-treated (n = 19) or placebo-treated (n = 19) glaucoma patients at baseline and then every 6 months over 24 months. Healthy volunteers (n = 20) with age and gender matching the glaucoma patients were used as a control.

ET-1 has been shown to be implicated in several ocular diseases including glaucoma. At the trial baseline, serum ET-1 concentrations were significantly lower in patients with OAG than those of the healthy volunteers.



Upon administration of blackcurrant anthocyanins, serum ET-1 concentrations increased to the levels of those in healthy volunteers during the 24-month period. In contrast, those of placebo- glaucoma patients remained at lower levels.

This study concludes that among the possible beneficial effects of blackcurrant anthocyanins towards visual field progression, the results of this study suggest that blackcurrant anthocyanins caused normalisation of serum ET-1 which may improve ET-1 dependent regulation of ocular blood circulation.

# 2.4 Gut Health (36)

The human intestine or colon contains a large and complex microbe population. The composition of this gut microbe population plays an important role in human health and disease. Through positive dietary changes, the population increase of beneficial gut bacteria can to lead to health benefits.

The purpose of this human study was to determine whether two specific products containing blackcurrant extract positively modified the gut microbial population, by enhancing the growth of the beneficial bacteria and decreasing activity of the toxic bacterial enzymes which are known to be involved in colon cancer. Thirty healthy adult males and females were recruited for this study who took either of the products for a two week period.

#### The results showed:

- Significantly increased population sizes of beneficial bacteria, types Lactobacilli and Bifidobacteria.
- Significantly decreased population sizes of potentially pathogenic bacteria species Clostridium and Bacteroides.
- Decreased activity of b-glucuronidase: a bacterial enzyme considered to be one of the enzymes that increases risk for colorectal cancer.
- Significantly decreased faecal pH. High faecal pH is thought to be a risk for colon cancer.

In conclusion, the results of this study open up the possibility that consumption of these two blackcurrant extract products can offer various benefits to human health through acting as novel prebiotic agents, via increasing the numbers of beneficial bacteria (lactobacilli and bifidobacteria) in the gut.

# 2.5 Kidney Health

# Effects of blackcurrant on kidney function (15)

The kidneys filter the blood to keep the composition of the blood stable by removing waste products and extra fluid from the blood to send to the bladder. Good kidney function is important for normal body function. This trial showed a positive effect on kidney function.

Kidney stones occur when substances within the urine precipitate and form solid material. Uric acid stones are kidney stones that occur when an excess amount of uric acid is present in the blood. In the first study the consumption of 330 ml blackcurrant juice daily for five days increased the

- urinary pH
- excretion of citric acid
- excretion of oxalic acid.

It is suggested that regular blackcurrant consumption could reduce the likelihood of kidney stone development as persistently low urinary pH is a significant factor for uric acid kidney stone formation.



# 2.6 Brain Health

# Effects of blackcurrants of mental performance (44)

This randomised, placebo controlled cross-over study was conducted with 36 healthy young adults 18-35 years of age. The study investigated the effects of two blackcurrant drinks with balanced polyphenol content on human cognitive function, mood and defined biochemical parameters. The two drinks contained 525mg polyphenol from either a blackcurrant extract or cold pressed blackcurrant juice from the blackadder variety. Subjects were given a dose of 525mg polyphenol per 60kg of body weight. Tests designed to measure cognitive performance and mood were performed over three sessions, at least 7 days apart, to ensure sufficient washout between conditions.

The results showed improvements in RVIP accuracy (for sustained attention and working memory) with the blackcurrant extract and in the digit vigilance task (sustained attention) the reaction times improved with the blackcurrant juice. The tasks to assess mood also showed modulation of behaviours with the consumption of the blackcurrant extract, but this trend only became statistically significant after the final repetition of the tests series, at 70 minutes.

The blackadder juice also showed the significant inhibition of peripheral, monoamine oxidase-B, MAO-B. Central MAO-B inhibitors have been used for several decades for the treatment of depressive disorders and neuro degenerative diseases.

The findings of this study demonstrate for the first time, a positive effect on brain function in healthy young adults with blackcurrant and it also shows the first clinically proven reduction in MAO activity following ingestion of a blackcurrant derived products.

# 2.7 Anthocyanin Bioavailability and Absorption (31,32,33,45)

Anthocyanins are understood to have many beneficial health properties. Therefore, the bioavailability of anthocyanins, including their absorption and excretion is viewed as an important issue. Three studies are summarized in this section, which examine the bioavailability of anthocyanins.

**Study 1**: A joint project conducted between Plant & Food Research New Zealand Limited and The Institute of Food, Nutrition & Human Health, Massey University, New Zealand, 2008. (Note: This is not a published study, however, we have consent from its authors to publish this data.)

Study participants were given blackcurrants as either an extract powder, puree or drink. Blood plasma and urine sample were collected for analysis. Good evidence of anthocyanin absorption and bioavailability was gained from all blackcurrant formats.



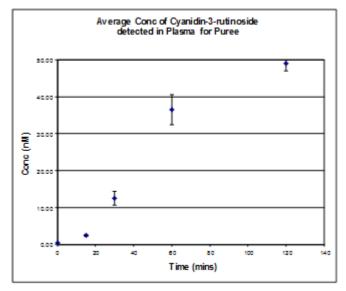


Figure 1. Time-dependent concentration (nM) of anthocyanin cyanidin-3-rutinoside detected in plasma after ingesting blackcurrant fruit puree.

Anthocyanin species are calculated based on standards of malvidin-3-galactoside and are uncorrected for recovery. Results are the mean of 5 plasma samples. Error bars represent SD's and reflect the biological variance.

Aim of the study: To investigate the effect of different formats of fruit or juice containing anthocyanins on anthocyanin uptake and antioxidant capacity in humans based on a unit single serve (volume/quantity) chosen to reflect the serving size reasonably expected for such product forms in New Zealand. The study participants were divided into four groups who were given one of three blackcurrant products or a placebo. This was a randomised cross over study. Participants had fasted prior to entering the study.

The products administered were: Treatment	Description	Anthocyanin( mg)/Dose
Capsule	1 capsule of blackcurrant extract powder.	87
Fruit Puree	75g of freshly pureed Ben Ard blackcurrant fruit	370
Drink	250ml freshly made sweetened juice drink, containing 30% reconstituted blackcurrant juice from concentrate.	189
Placebo	Sugar drink	0

Plasma samples were analysed for anthocyanin concentrations, antioxidant status (FRAP-Assay), and uric acid. Urine samples were collected and analysed for anthocyanin concentrations.



The results of the study highlighted good absorption and bioavailability for anthocyanins with rapid absorption through into the plasma. Urine analysis demonstrated a proportional appearance of the anthocyanins to the anthocyanin doses consumed indicating good absorption for all consumed formats. Despite absorption, the levels of anthocyanins in the plasma did not translate into significant changes in the antioxidant status but given the low doses that is not surprising.

**Study 2:** This study examines how orally administered blackcurrant anthocyanins are directly absorbed in rats and humans and appear in the blood as the intact forms.

In the study, using both rats and humans, four components of black currant anthocyanins, delphinidin 3 - rutinoside (D3R), cyanidin 3-rutinoside (C3R), delphinidin 3-glucoside (D3G), and cyanidin 3-glucoside (C3G), were found to be directly absorbed and distributed to the blood and excreted into urine.

- o In a rat study, following oral administration of purified anthocyanins, the anthocyanins were detected in the blood.
- In a human study, when a mixture of blackcurrant anthocyanins were consumed by eight volunteers, the four components of blackcurrant anthocyanins were detected in the blood and urine.
- The anthocyanin compounds detected in urine in the period 0–8 hours after ingestion was only 0.11 % of the dose ingested. These results indicate that 3-rutinoside anthocyanins were directly absorbed and distributed to the blood.

**Study 3:** This study shows that anthocyanin metabolites are abundant and persistent in human urine. In this study the subjects consumed blueberry juice, but it is the behaviour of the anthocyanins that is the focus of the study.

The results of this study showed that the products of metabolism (metabolites) of anthocyanins were abundant in human urine even after five days with no dietary intake of anthocyanins.

17 normal healthy volunteers consumed 250ml of blueberry juice after a five day period without consumption of anthocyanins. Parent anthocyanins (those present in the juice) were 4% of the urinary anthocyanins and 96% were anthocyanin metabolites, for the following 24 hours .i.e. in all the urine samples there was far greater concentration of anthocyanin metabolites than the parent anthocyanins.

While the concentration of the parent anthocyanins was significantly increased by consuming the juice, the intake of the blueberry juice had a relatively small effect on the anthocyanin metabolite concentration in the urine, as these metabolites were still present from sources other than the blueberry juice, consumed 5 days prior.

Specifically, after the blueberry juice intake, the anthocyanin metabolite concentration was only 15% greater for the following 24 hours than before the blueberry juice intake. The persistence of these anthocyanin metabolites suggested enterohepatic recycling (circulation of secretions from the liver into the intestine where they are reabsorbed by the blood and returned to the liver). This recycling would account for the long residence time. These recycling processes extend the half-life and the overall bioavailability of the parent compounds and their metabolites.



Anthocyanin metabolites based on the anthocyanin Pelargonidin was prevalent in the urine samples but this Pelargonidin anthocyanin is not present in blueberry juice. This occurrence is thought to be due to the changes in the structure of the anthocyanin metabolites as they are subject to bacterial action in the colon.

The results of this study suggest that exposure to anthocyanin-based components is substantially greater than suggested by earlier research.

Study 4: The metabolism and bioavailability of the anthocyanin, cyanidin -3- glucoside and its metabolites.

While many clinical studies show beneficial health effects of anthocyanins, the absorption, distribution, metabolism and elimination (ADME) of anthocyanin-rich foods is not yet well understood.

In this study the use of isotopically labelled cyanidin-3-glucoside (one of the four major anthocyanins contained in blackcurrants) allowed the investigation of ADME of anthocyanins in humans. Eight participants consumed 500mg of isotopically labelled C3G. Biological samples were collected over 48 hours after consumption. The use of an isotope tracer, carbon 13, ( $^{13}$ C) enables researchers to establish the extent to which anthocyanins are metabolised into other compounds and the path these metabolites take in the human body.

A total of 25 x  $^{13}$ C labelled compounds that consisted of C3G and 24 x  $^{13}$ C labelled metabolites were identified. The study indicates that anthocyanins have a minimum relative bioavailability of 12.3%, similar to that of other flavonoid classes, which is the group of plant-based compounds that anthocyanins belong to. Their metabolites reach a 42 fold higher concentration and over a longer period than the parent anthocyanin.

A total of 43.9% of the dose of <sup>13</sup>C was recovered in urine, breath, and faeces, but the fate of the remaining ingested <sup>13</sup>C remains unknown. The analysis showed a relatively large number of diverse breakdown products and metabolites, so other metabolites may exist at lower concentrations and therefore have escaped detection. Researchers also suggested that a longer sampling period, greater than 48 hours, would have yielded a greater recovery. This is the first study to report breath as a route for clearance of anthocyanin derived carbon from the body.

Overall the study indicated a much higher relative bioavailability and a greater diversity of metabolites for anthocyanins than has been previously reported. These metabolites are present in circulation for more than 48 hours after ingestion. Given that only 43.9% of the dose was recovered this may have implications for even greater bioavailability.

# 3.0 Summary of laboratory studies

Hundreds of laboratory studies, using cells and animals, have been completed showing beneficial effects with blackcurrants, and are too numerous to summarise here. A smaller number of significant laboratory studies have been chosen to include in this review.

# 3.1 Laboratory study on allergen-induced asthma

Effect of blackcurrant extract epigallocatechin on markers of airway inflammation, (17,35, 49)

1.A 2010 New Zealand in vitro laboratory study looked at the effectiveness of blackcurrant extract, enhanced for proanthocyanidins, and a purified component of blackcurrant extract, epigallocatechin, to



reduce the high levels of oeosinophils that result in airway inflammation and tissue damage in asthma. The *in vitro* study with human alveolar epithelial cells showed significant suppression of two of the responses in the immune response cascade:

- eotaxin-3 (CCL26) and
- phosphorylation of STAT-6.
- In addition, the blackcurrant proanthocyanidin extract was able to act synergistically with IFN-γ to enhance the suppression CCL26 secretion in alveolar epithelial cells.

This study shows that it is feasible that components of blackcurrants may be taken up by the digestive tract into the bloodstream, and reduce eosinophils and airway inflammation.

2. Following on from the 2010 laboratory study on extracts of blackcurrants on allergen-induced asthma, a 2013 laboratory study has been completed:

During allergen-induced asthma, an immune system response leads to increased levels of eosinophils (specialised immune system cells) in the airways, leading to lung inflammation.

Eotaxins (signaling proteins from lung alveolar cells) recruit these eosinophils in allergic airway disease. The eotaxin CCL26 is linked to eosinophil recruitment in the chronic form of allergic airway illness. Therefore, suppressing CCL26 secretion would reduce eosinophil cell numbers in the lung and airways inflammation.

This in vitro study demonstrated that blackcurrant polyphenol extracts suppressed CCL26 secretion by lung alveolar cells.

This study evaluated extracts from 10 different blackcurrant cultivars and found a differential effectiveness in suppression of CCL26. This difference was attributed to the differing polyphenolic composition of the blackcurrant cultivars.

This finding supports the potential use of blackcurrants in managing lung inflammation in allergic disease.

3. During allergen-induced asthma, an immune system response leads to increased levels of eosinophils (specialised immune system cells) in the airways, leading to lung inflammation.

Following on from the 2013 study, a 2017 study focused on CCL11, a chemokine, or signalling protein, involved the early stages in the inflammation pathway of allergic asthma.

CCL11 production is therefore a target for discontinuing lung inflammation. Mice with acute allergic lung inflammation were feed 10mg per 10kg of a blackcurrant extract and their lung tissue was analysed. There was a statistically significant reduction in the eosinophils and the CCL11 levels, when compared with mice not fed blackcurrant. The findings show that New Zealand blackcurrant extract can alleviate the inflammation of allergic asthma in mice and that blackcurrant may have potential benefits for lung health.

This study also looked polyphenolic extracts from 10 different blackcurrant cultivars which were all found to suppress CCL11 levels in human lung cells. Of the 10 cultivars those with anthocyanins which had a high delphinidin anthocyanin to low cyanidin ratio resulted in increased inhibition of CCL11.

Therefore the results highlight that the ratio of specific anthocyanins in the fruit is important in alleviating lung inflammation.



# 3.2 Laboratory studies on antiviral activity

#### Summary of laboratory studies on antiviral activity (18, 19, 34)

Blackcurrants have been shown to have properties that restrict the infection rate of viruses such as the common cold and flu viruses, including influenza A and B.

Research on the antiviral activity of blackcurrants has been carried out on both cultured cells *in vitro* and *in vivo* mouse models.

# Study 1 and study 2:

- For studies on cells cultured in a laboratory, the following was measured:
  - o viral plaque formation
  - o infectivity of the virus
  - o growth of the virus in cells
  - o release of the virus from infected cells.
- In the study on mice, the following was measured
  - o infectivity of the virus
  - o mortality rates
  - o mode of action

#### The results

- Both studies showed blackcurrant extract to possess antiviral activity.
- In one in vitro experiment it was found that cells infected by influenza virus type A (IVA) or influenza virus type B (IVB) had their rate of infection almost stopped when blackcurrant extract was applied.
- o In another experiment, addition of virus and extract simultaneously to cells resulted in infection rates 2 5% of that observed when only virus was added.
- Mice fed extract exhibited reduced virus accumulation and improved mortality
- Fractionation of extract demonstrated antiviral activity is possessed by the polyphenol containing fraction
- Polyphenols act on haemagglutinin, inhibiting a virus's ability to enter infect a cell and reproduce within it. (Haemagglutinin is the molecule on the surface of viral particles that binds the virus to cells it is infecting.)

Study 3: This study examined the anti-influenza virus activity of two extracts of the blackcurrant (Ribes Nigrum L.) from New Zealand and Poland.

The authors of this in vitro study have showed in a previous study that the antiviral effect of blackcurrants differed according to viral species. The aim of this study was to determine whether the extracts of blackcurrant have antiviral effects against several different strains of influenza virus. This 2013 study investigated the inhibitory effect of extracts of blackcurrant from New Zealand and Poland on four strains of influenza virus (IFV) by the inhibition of virus adhesion to the surface of the cells.

The four strains of the influenza virus were

- 1.Pandemic flu from 2009-2010 (IFV-AH1pdm),
- 2.Hong Kong flu (IFV-AH3),
- 3.Oseltamivir phosphate-resistant Russian flu (IFV-AH1tamr)
- 4.Influenza virus type B (IFV-B).



The inhibitory effect of the extracts of blackcurrant or blueberry (the control) on the infectivity of the virus, were evaluated by the inhibition of virus adhesion on the cell surface.

#### The results:

- Three percent solutions of the blackcurrant extracts from New Zealand and Poland were enough to disinfect more than half of IFV-AH1pdm and IFV-B, and 10 % solutions from both regions disinfected all IFV strains completely.
  - The study found no significant differences between the blackcurrant extracts from New Zealand and Poland and the efficiency of both was better than the blueberry extract from North America, used as a control.
  - The study showed that although the antiviral effect of blackcurrant was slightly different within viral strains from one species, the extract of blackcurrant could disinfect all of four influenza strains that were examined.

The extracts of blackcurrant showed definite potential for use as a disinfectant and antiseptic agent to prevent influenza virus infection. The study suggested that blackcurrant extract could be used as a component in health care goods such as gargle products, candies and juices for the prevention of influenza virus infection.

# 3.3 Laboratory studies on cholesterol and endothelia

#### Animal model trials (20-23)

Black currant fruit extracts were intravenously administered to hypercholesterolemic rabbits. The levels of triglyceride, total cholesterol and low-density lipoprotein cholesterol markedly decreased, whereas the level of high-density lipoprotein cholesterol normalized after treatment with the fruit extract. The results indicated that blackcurrant fruits can reduce the levels of blood lipids in experimental rabbits.

Blackcurrant fruit juice applied to isolated pig arteries, and rat aorta was a potent inducers of endothelium-dependent relaxation, in a concentration dependent manner. Similarly, a blackcurrant extract protected human umbilical vein endothelial cells from experimentally induced injury.

# 3.4 Laboratory study on gut health and probiotics

Balanced gut health is an important part of a healthy immune system. Gut pathogens (disease causing organisms) can upset this balance with detrimental effects to health, while the addition of probiotic (beneficial) bacteria has been reported to inhibit the adhesion of pathogens to the gut cells to restore favourable microbial balance.

#### Probiotic bacteria enhanced and modulating pathogenic bacteria (24,37)

1.In this animal study rats were fed blackcurrant powder three times weekly for a month. This treatment was very effective at promoting the growth of lactobacilli and bifidobacteria, which are beneficial probiotic bacteria, in the caecum (the first part of the large intestine) of these rats.

2. This in vitro study on gut cells looked at New Zealand commercial varieties of blackcurrants plus three breeding varieties of blackcurrants and their potential to promote gut health. All the blackcurrant juices tested inhibited the growth of the pathogenic bacteria Salmonella and inhibited the ability of the Salmonella to bind to the gut cells. Correspondingly, all the juices enhanced the growth of the beneficial



bacteria, Lactobacillus rhamnosus. All the blackcurrant varieties were high in anthocyanins, which contributed to their high anti-oxidant capacity. This study showed a correlation between the levels of the anthocyanin type cyanindin-3-rutinoside and inhibition of the pathogen Salmonella to the gut cells. The two blackcurrant varieties with the highest levels of cyanidin-3-rutinoside (Ben Ard and L700) gave the best results for inhibition of the Salmonella bacteria to the gut cells.

These results may be useful in the formulation of functional foods aimed at inhibiting the growth of pathogenic bacteria in the gut, without compromising the growth of beneficial gut organisms.

# 3.5 Laboratory studies on chemoprevention

## Chemopreventive effects in cell systems (25, 26)

A recent paper reviewed the studies of the effects of blackcurrants on tumour cells. *In vitro* pharmacological effects were shown for whole fruit extract on the following cancer cell types:

- HT29 colon cancer
- MCF-7 breast cancer cells
- HeLa cervical cancer cells
- Prostate cancer cells
- HepG2 human liver cancer cells.

Mechanisms for the effects were dose dependent and included:

- inhibition of cancer cell growth
- decreased the proliferation of cancer calls
- reduced cell viability.

There are two *in vivo* studies of pharmacological effects of dietary blackcurrant fruit extract in transplanted tumour models in animals:

- Solid tumour growth was reduced in Ehrlich carcinoma bearing mice
- There was an inhibition incidence, multiplicity, size and volume of nodules in cells giving rise to liver cancer in rats as well as suppression of abnormal cellular proliferation.

Note: There are no clinical trials on the dietary effect of blackcurrant extracts on tumour cells.

# 3.6 Laboratory study on obesity

#### Blackcurrant Anthocyanins Lower Metabolic Risks Associated with Obesity (51)

Anthocyanins have been shown to lower the metabolic risks related to obesity-associated insulin resistance and abnormal glucose metabolism.

This study examined a range of six different berries containing a range of different anthocyanin types. The study examined the effect of the different berries and their biological activity on obese mice consuming a high fat diet, to examine changes in metabolic risk factors, including body composition, glucose metabolism and insulin sensitivity. The dose was equivalent to 145mg of anthocyanins per day for an average weight human, which is a readily achievable daily dose.

Incorporation of anthocyanin-containing berry powders into the high fat diet showed:



- Markedly increased lean body mass and decreased fat body mass in animals consuming blackcurrant and blueberry, compared to the other berry types.
- Blackcurrant and blueberry also showed increased insulin sensitivity (compared to the other berry types) in an insulin tolerance test, similar to the results seen in the mice on a the low fat diet.
- Mice consuming blackcurrant, blueberry and concord grape showed lower (but not significant) peak blood glucose concentrations than the other berries.

The study data showed that delphinidin-based and malvidin-based anthocyanins in blackcurrants and blueberries respectively, were more effective than other anthocyanin types in improving key metabolic risk factors associated with obesity caused by consumption of energy dense foods and a sedentary lifestyle.



# References

- 1. Wallace, T.C. Anthocyanins in Cardiovascular Disease. ADVANCES IN NUTRITION 2008. 2:1-7.
- 2. K. Iwasaki-Kurashige, R. Y. Loyage-Rendon, H. Matsumoto, T. Tokunaga and H. Azuma, Possible mediators involved in decreasing peripheral vascular resistance with blackcurrant concentrate (BC) in hind-limb perfusion model of the rat, VASC. PHARMACOL., 2006, 44, 215–233.
- 3. I. Edirisinghe, K. Banaszewski, J. Cappozzo, D. McCarthy and B. M. Burton-Freeman, Effect of blackcurrant anthocyanins on the activation of endothelial nitric oxide synthase (eNOS) in vitro in human endothelial cells, J. AGRIC. FOOD CHEM., 2011, 59, 8616–8624.
- 4. Zhu, Yanna Xia, Min Yang, Yan Liu, Fengqion gLi, Zhongxia Hao, Yuanta Mi, Mantia Jin, TianruLing, Wenhua. Purified Anthocyanin Supplementation Improves Endothelial Function via NO-cGMP Activation in Hypercholesterolemic Individuals. CLINICAL CHEMISTRY 2011, 57 1524-1533.
- 5. M. Rosenblat, N. Volkova, J. Attias, R. Mahamid and M. Aviram, Consumption of polyphenolic-rich beverages (mostly pomegranate and blackcurrant juices) by healthy subjects for a short term increased serum antioxidant status, and the serum's ability to attenuate macrophage cholesterol accumulation, FOOD FUNCT.,2010, 1, 99–109.
- 6. Dalgard, C., Nielsen, F., Morrow, J.D., Enghusen-Poulsen, H., Jonung, T., Hørder, M., de Maat, M.P.M. Supplementation with orange and blackcurrant juice, but not vitamin E, improves inflammatory markers in patients with peripheral arterial disease. BRITISH JOURNAL OF NUTRITION 2009, 101:263-269.
- 7. Takenami, E. Kurashige, K.I. Matsumoto, H. Honma, T. Osada, T. Okubo, M. Hamaoka, T. Improvement of cold water immersion induced circulation impairment by blackcurrant extract intake-the investigation on cold constitutional women. THE JOURNAL OF THE JAPANESE SOCIETY OF THERMOLOGY 2004, 23: 194-201
- 8. Matsumoto, H., Takenami, E., Iwasaki-Kurashige, K., Osado, T., Katsumura, T., Hamaoka, T. Effects of blackcurrant anthocyanin intake on peripheral muscle circulation during typing work in humans. EUROPEAN JOURNAL APPLIED PHYSIOLOGY 2005, 94: 36-45
- 9. Lyall, K. A., Hurst, S. M., Cooney, J., Jensen, D., Lo, K., Hurst, R. D., Stevenson L. M. Short-term blackcurrant extract consumption modulates exercise-induced oxidative stress and lipopolysaccharide-stimulated inflammatory responses. AM J PHYSIOL REGUL INTEGR COMP PHYSIOL 2009, 297: 70–81.
- 10. Peluso, Ilaria Raguzzini, Anna Villano, Debora V Cesqui, Eleonora Toti, Elisabetta Catasta, Giovina Serafini, Mauro. High Fat Meal Increase of IL-17 is Prevented by Ingestion of Fruit Juice Drink in Healthy Overweight Subjects. CURRENT PHARMACEUTICAL DESIGN 2012, 18: 85-90.
- 11. Torronen, Riitta Sarkkinen, Essi Tapola, Niin Hautaniemi, Elina Kilpi, Kyllikki Niskanen, Leo. Berries modify the postprandial plasma glucose response to sucrose in healthy subjects. BRITISH JOURNAL OF NUTRITION 2010, 103: 1094-1097.
- 12. Torronen, Riitta Sarkkinen, Essi Niskanen, Tarja Tapola, Niina Kilpi, KyllikkiNiskanen, Leo. Postprandial glucose, insulin and glucagon-like peptide 1 responses to sucrose ingested with berries in healthy subjects. BRITISH JOURNAL OF NUTRITION 2012, 107:1445-1451



- 13. Edwards, A.M., Blackburn, L., Townsend, S., David, J. Food supplements in the treatment of primary fibromyalgia: a double-blind, crossover trial of anthocyanidins and placebo. JOURNAL OF NUTIRTIONAL & ENVIRONMENTAL MEDICINE 2000, 10: 189-199.
- 14. Nakaishi, H., Matsumoto, H., Tominaga, S., Hirayama, M. Effects of blackcurrant anthocyanoside intake on dark adaptation and VDT work induced transient refractive alteration in healthy humans. ALTERNATIVE MEDICINE REVIEW 2000, 5: 553-562
- 15. Kessler, T., Jansen, B., Hesse, A. Effect of blackcurrant, cranberry and plum juice consumption on risk factors associated with kidney stone formation. EUROPEAN JOURNAL OF CLINICAL NUTRITION 2002, 56: 1020-1023.
- 16. Not used. Reference and study removed from this review.
- 17. Hurst, S. M., McGhie, T.K., Cooney, J., Jensen, D., Gould, E.M., Lyall, K. A., Hurst, R. D. Blackcurrant proanthocyanidins augment IFN-γ-induced suppression of IL-4 stimulated CCL26 secretion in alveolar epithelial cells. MOLECULAR NUTRITION & FOOD RESEARCH 2010, 54: S159–S170
- 18. Knox, M.Y., Suzutani, T., Yosida, I., Azuma, M. Anti-influenza virus activity of crude extract of *Ribes nigrum* L. PHYTOTHERAPY RESEARCH 2003, 17: 120-122.
- 19. Noguchi, A., Takeda, T., Watanabe, T, Yasui, H. Inhibitory effect of Cassis extract against influenza virus infection. JOURNAL OF THE FACULTY OF AGRICULTURE, SHINSHU UNIVERSITY 2008, 44 No. 1.2.
- 20. Li GuoQing Wu SongLin Ababarri, S. Study on impact of blackcurrant and Lonicera caerulea fruit on rabbits with hyperlipemia. ENDEMIC DISEASES BULLETIN / DI FANG BING TONG BAO 2009, 2 14-19.
- 21. Auger, Cyril Kim, Jong-HunTrinh, Sandrine Chataigneau, Thierry Popken, Anne M. Schini-Kerth, Valerie B. Fruit juice-induced endothelium-dependent relaxations in isolated porcine coronary arteries: evaluation of different fruit juices and purees and optimization of a red fruit juice blend. FOOD & FUNCTION2011, 2: 245-250.
- 22. Li Zhao, Xiaogu Ma, Long Re, Ziy Gu, YajingTu, Erxunjiang . Experiment study of blackcurrant on vascular endothelial cells injury induced by hydrogen peroxide. WEI SHENG YAN JIU = JOURNAL OF HYGIENE RESEARCH 2009, 38 592-595.
- 23. Yuko Nakamura, Hitoshi Matsumoto1 and Kazuo Todoki Endothelium-Dependent Vasorelaxation Induced by Blackcurrant Concentrate in Rat Thoracic Aorta .JPN. J. PHARMACOL.2002, 89, 29 35.
- 24. Abdul-Lateef Molan Zhuojian Liu Marlena Kruger The ability of blackcurrant extracts to positively modulate key markers of gastrointestinal function in rats WORLD J MICROBIOL BIOTECHNOL (2010) 26:1735–1743
- 25. Ashwin Gopalan, Sharon C. Reuben, Shamima Ahmed, Altaf S. Darvesh, Judit Hohmann, Anupam Bishayee The health benefits of blackcurrants. FOOD & FUNCTION 2012, 3, 795-809
- 26. Bishayee, A., Mbimba, T., Thoppil, R., Haznagy-Radnai, E., Sipos, P., Darvesh, A., Folkesson, H., Hohmann, J. Anthocyanin-rich blackcurrant (Ribes nigrum L.) extract affords chemoprevention against diethylnitrosamine-induced hepatocellular carcinogenesis in rats. Journal of Nutritional Biochemistry (2011) 22:1035 1046.



- 27. Ikuyo Ohguroll, Hiroshi Ohgurol, Mitsuru Nakazawa. Effects of anthocyanins in black currant on retinal blood flow circulation of patients with normal tension glaucoma, a pilot study. Hirosaki Medical Journal, 2007, 59: 23-32.
- 28. Hiroshi Ohguru, Ikuyo Ohguro, Maki Katai, Sachie Tanaka, Two-year Randomized, Placebo Controlled Study of Blackcurrant Anthocyanins on Visual Field in Glaucoma. Ophthalmologica 2012, 228:26-35.
- 29. Hiroshi Ohguru, Ikuyo Ohguro, Saeko Yagi. Effects of Blackcurrant Anthocyanins on Intraocular Pressure in Healthy Volunteers and Patients with Glaucoma. Journal of Ocular Pharmacology and Therapeutics 2013, Vol 29 No.1:61-67.
- 30. Kaori Yoshida, Ikuyo Ohguro, Hiroshi Ohguru, Blackcurrant Anthocyanins Normalized Abnormal Levels of Serum Concentrations of Endothelin 1 in Patients with Glaucoma. Journal of Ocular Pharmacology and Therapeutics 2013, Vol 29, No. 5:480-487.
- 31. A joint project conducted between Plant & Food Research New Zealand Limited and The Institute of Food, Nutrition & Human Health, Massey University, New Zealand. Anthocyanin Bioavailability and Absorption, 2008.
- 32. Hitoshi Matsumoto, Hiromi Inaba, Mitsuo Kishi, Shigeru Tominaga, Masao Hirayama, and Takanori Tsuda Orally Administered Delphinidin 3-Rutinoside and Cyanidin 3-Rutinoside Are Directly Absorbed in Rats and Humans and appear in the Blood as the Intact Forms. Journal of Agricultural Food Chemistry. 2001, 49, 1546-1551.
- 33. Wilhelmina Kalt, Yan Liu, Jane E. McDonald, Melinda R. Vinqvist-Tymchuk, and Sherry A. E. Fillmore. Anthocyanin Metabolites Are Abundant and Persistent in Human Urine. Journal Agricultural and Food Chemistry, 2014, web only: Just accepted manuscript.
- 34. Kazufumi Ikuta, Katsumi Mizuta and Tatsuo Suzutani. Anti-Influenza virus activity of two extracts of the blackcurrant (Ribes Nigrum L.) from New Zealand and Poland. Fukushima Journal of Medical Science 2013, Vol. 59, No.1: 35-38.
- 35. Tafadzwa Nyanhanda, Elaine M. Gould, Tony McGhie, Odette M. Shaw, Jacquie L. Harper, and Roger D. Hurst. Blackcurrant cultivar polyphenolic extracts suppress CCL26 secretion from alveolar epithelial cells. Food and Function 2014, just accepted manuscript, currently website only.
- 36. Molan A., Zhuojian L., Plimmer G. Evaluation of the effects of blackcurrant products on gut microbiota and on markers of risk for colon cancer in humans. Phytotherapy Research, 2014, 28,416-422.
- 37. Parkar, S., Redgate, E., McGhie., Hurst, R. In vitro studies of modulation of pathogenic and probiotic bacterial proliferation and adhesion to intestinal cells by blackcurrant juices. Journal of Functional Foods, 8C, 2014, 35-44.
- 38. H-M Lehtonen, J-P Suomela, R Tahvonen, J Vaarno, M Venoja, J Viikari H, Kallio. Berry meals and risk factors associated with metabolic syndrome. European Journal of Clinical Nutrition (2010) 64,614–621.
- 39. Willems, M.E., Beneficial physiological effects with blackcurrant intake in endurance athletes. *International Journal of Sports Nutrition and Exercise Metabolism, 2015, Vol 25, Issue 4.*



- 40. Perkins, I., New Zealand Blackcurrant Extract Improves High-intensity Intermittent Running. *International Journal of Sports Nutrition and Exercise Metabolism*, 2015, 25, p.487 493.
- 41. Willems, M.E., Beneficial Effects of New Zealand Blackcurrant Extract on Maximal Sprint Speed during the Longborough Intermittent Shuttle Test. Sports, 2016, 4, 42.
- 42. Cook, Matthew D., Myers, Stephen D., Gault, Mandy L., Edwards, Victoria and Willems, Mark E. T. (2016) Cardiovascular Function during Supine Rest in Endurance Trained Males with New Zealand Blackcurrant: *A Dose-Response Study*. European Journal of Applied Physiology. pp. 1-8. ISSN 1439-6319
- 43. Hutchison, A., Flieller, E., Dillon, K., Leverett, B., Blackcurrant nectar reduces muscle damage and inflammation following a bout of high-intensity eccentric contractions. Journal of Dietary Supplements, early online release. 1-15 2014.
- 44. Watson, A., Acute supplementation with blackcurrant extracts modulates cognitive functioning and inhibits monoamine oxidase-B in healthy young adults. Journal of Functional Foods, 2015, Vol. 17 p.524-539.
- 45. Czank, C., Human metabolism and elimination of the anthocyanin, cyanadin-3-glucoside: a 13C tracer study. American Journal of Clinical Nutrition, 2013; 97:995-1003.
- 46. Li, D. Purified anthocyanin supplementation reduces dyslipidemia, enhances antioxidant capacity and prevents insulin resistance in diabetic patients. *The Journal of Nutrition*. Published online ahead of print, February 2015.
- 47. Cook, M., New Zealand Blackcurrant Extract Improves Cycling Performance and Fat Oxidation in Cyclists. European Journal of Applied Physiology, Nov. 2015, 115, 11, p2357-2365.
- 48. Willems, M.E., University of Chichester, Department of Sport and Exercise Sciences, UK. Research study presented at the 11th Annual International Society of Sports Nutrition Conference and Expo, 20-21 June 2014 Clearwater Beach, FL, USA. Conference poster available at University of Chichester eprints repository, <a href="http://eprints.chi.ac.uk/1289/">http://eprints.chi.ac.uk/1289/</a>
- 49. Shaw, O., Blackcurrant anthocyanins modulate CCL11 secretion and suppress allergic airway inflammation. Molecular Nutrition Food Research, Published online ahead of print, 2017.
- 50. Cook, M., Meyers, S., Gault, M., Willems, M., Blackcurrant alters physiological responses and femoral artery diameter during sustained isometric contraction. Nutrients, 2017, vol 9, issue 6.
- 51. Overall, J., Metabolic Effects of Berries with Structurally Diverse Anthocyanins, International Journal of Molecular Science, 2017, vol. 18, issue 2.