

Mills and Bone Academy

Educational Article

Grape Seed Extract: A Versatile Herb for Healthy Circulation– Kerry Bone

One of my favourite herbs is grape seed. Usually the part of the fruit that we don't eat, modern research has identified some amazing health benefits for the seed of this ancient fruit. I particularly use grape seed as an extract standardised for OPCs (oligomeric procyanidins). These large molecules have flavonoid-like bioactivity and chemistry, although they are quite different to "bioflavonoids". However, that similarity to flavonoids means that OPCs are particularly beneficial for maintaining the health of the microcirculation (namely the small blood vessels and capillaries) and this is a key focus of my use of this herb.

Grape seed extract and microcirculation

The microcirculation is perhaps a neglected part of modern herbal therapy. We tend to focus on treatments that benefit the heart or the arteries or the veins, ignoring the fact that the microcirculation is the largest part of our circulatory system and is crucial for delivering adequate nutrition to our tissues. As well as poor tissue nutrition, unhealthy microcirculation is implicated in easy bruising, excessive inflammation and poor healing. It is

also relevant to problems affecting those parts of the body rich in small blood vessels, namely the retina of the eye, the glomerulus of the kidney and the circulation supplying the long nerves of the body, such as to the legs. It's no coincidence that these are the sites attacked by long-term diabetes (retinopathy, nephropathy and neuropathy), a disorder that particularly affects the health of the microcirculation.

The benefits of grape seed extract (GSE) on the microcirculation are supported by clinical research. In early uncontrolled and controlled trials, GSE (100 to 150 mg/day of grape seed OPCs) increased capillary resistance in a range of conditions where capillary fragility, low capillary resistance or functional vein problems were present.^{i,ii,iii,iv,v,vi,vii} In addition to capillary fragility and venous insufficiency, some patients had varicose veins and leg ulcers. Diabetic and hypertensive patients were assessed in one trial. In patients with venous insufficiency, symptoms such as swelling, itching, pain, heaviness in the legs were alleviated or resolved.^{v,vii} GSE benefits vein disorders mainly because congested veins cause problems with the microcirculation that flows into them.

Patients with retinopathy experienced a reduction in oedema and an improvement in capillary resistance (uncontrolled trials, 100 to 200 mg/day of grape seed OPCs).^{viii,ix} Retinal damage was stabilised in 80% of patients taking GSE (150 mg/day of grape seed OPCs) compared with 46% of patients taking placebo.^x

Other beneficial effects on circulation

More recent (and very high quality) research suggests that GSE benefits the circulation as a whole. A team of Dutch scientists recently evaluated the effect of a GSE (200 mg once a day) on a variety of circulatory measures in relatively healthy smokers.^{xi} The 8-week trial was a double blind, randomised, placebo-controlled design involving 28 men who had smoked at least 10 cigarettes a day for at least 5 years. The scientists measured micro- and macrovascular (circulatory) function and a cluster of systemic biomarkers for major pathological processes occurring in the circulation, including disturbances in metabolism and cellular oxidative balance and activation of inflammatory cells and platelets. Patients with a history or presence of any metabolic or cardiovascular disease or cancer were excluded, as were heavy drinkers.

Despite the small nature of this trial, with only 15 men in the active (GSE) group and 13 in the placebo group, a number of significant findings were seen at 8 weeks. Specifically, while LDL (low-density lipoprotein) cholesterol was not changed in the whole group, a significant reduction was seen by 7% in the 9 participants who had elevated baseline levels. Additionally, there was a 22% increase in the ratio of reduced (active) to

oxidised (inactive) glutathione in red blood cells in the herbal group, indicating an important rise in antioxidant protection in the body. The vascular inflammatory response, assessed by the release of the inflammatory marker tumour necrosis factor (TNF)-alpha from stimulated blood, decreased substantially and significantly from baseline in the active group (by 14%, $p < 0.05$) after 8 weeks of treatment. This reduction was also significant compared with the placebo group ($p < 0.05$).

On the other hand, alterations in macro- and microvascular function were either not present or did not reach statistical significance. There were also no significant changes in systolic and diastolic blood pressure readings. However, when all the above measures (excluding blood pressure) were constructed into an algorithm that the authors called the vascular health index (VHI), a remarkable and intriguing outcome was revealed. The average VHI in the patients receiving GSE rose by 123 ± 47 units ($p < 0.05$ versus baseline and the placebo group), whereas it fell by 66 ± 79 units in the placebo group. This indicated an overall improvement in vascular health in the active group. Notably, while many of the individual cardiovascular health measures did not show a significant change, a significant improvement was evident when they were integrated into the global VHI. As the authors highlighted, their integrative biomarker approach has unveiled the pleiotropic (production of multiple effects) health benefit of a regular intake of GSE on the circulation.

High-level evidence for lowering blood pressure

Despite the fact that this particular study found no effect of GSE on blood pressure, an analysis of all the published clinical trials (known as a meta-analysis) found that it did. In this study, US authors located 9 clinical trials on various extracts that met their inclusion criteria, involving 390 patients. Meta-analysis was possible for the following measures, systolic blood pressure (6 trials), diastolic blood pressure (6 trials), heart rate (5 trials), blood lipids (7 to 9 trials) and C-reactive protein (3 trials). While the data indicated that clinical use of GSE shifted **all** these parameters towards a lower cardiovascular risk profile (for example C-reactive protein and total cholesterol were lowered and high-density lipoprotein (HDL) cholesterol was raised), only the results for systolic blood pressure and heart rate achieved statistical significance ($p = 0.02$ and $p = 0.01$, respectively).

A versatile herb

In the title I mentioned the versatility of GSE. In fact, its health promoting effects don't just stop at the circulation and there are published human studies that back this up. Some of the benefits shown in these trials are quite novel and unique for an herbal extract.

A Japanese study found that a procyanidin (OPC)-rich extract from grape seeds improved chloasma, a facial hyper-pigmentation (or staining) often associated with pregnancy.^{xii} To evaluate the long-term efficacy, a one-year study was undertaken. GSE (around 200 mg/day of extract) was given to 12 Japanese women with chloasma for 6 months, which was followed by another 5 months of treatment for 11 of those women. The first 6 months of GSE intake resulted in slight or substantial improvement in 10 of the 12 women (83%) and the following 5 months saw

that improvement maintained in 6 of the 11 women (54%). Objective measurement of the degree of chloasma supported these findings. The authors concluded that the beneficial effects of GSE were maximally achieved after 6 months and there was no further improvement after this period (which may have been due to the fact that it corresponded to the summer period: chloasma is worsened by exposure to ultraviolet light).

Two US-based clinicians hypothesised that GSE might be useful in managing the symptoms of chronic pancreatitis.^{xiii} The extract was given to three patients with well-established disease whose severe symptoms were unresponsive to standard treatments. The addition of GSE to their treatment regime led to a reduction in the frequency and intensity of abdominal pain, as well as resolution of vomiting in one patient. Abdominal pain is the most common symptom of chronic pancreatitis and a striking feature of the treatment with GSE was the substantial reduction in the severity of pain experienced by the patients (based on a numerical rating scale, pain was on average halved).

At 200 mg/day, the prescribed dose of GSE extract in these case studies was higher than what is normally used. This was increased to 300 mg/day during worsening of symptoms. Such doses can cause constipation as a side effect in sensitive people (similar to the way that the tannins in tea can cause constipation). While this study only contains three case histories, it is a promising lead for the herbal therapy of a difficult and severe disorder. If pancreatitis is associated with excessive alcohol consumption, then St Mary's thistle extract might also be beneficial.

Results from two clinical trials published within the last three years suggest that GSE also has a useful role to play in the management of other modern chronic disorders. Non-alcoholic fatty liver disease (NAFLD) affects 10 to 24% of the general population and may progress to end-stage liver disease. It usually occurs in people who have too much fat around their waists and as a result have become insulin resistant. Evidence-based treatment options are limited. A small study evaluated the effects of a GSE product in comparison to ascorbic acid over 3 months in a double-blind setting.^{xiv} Fifteen patients were enrolled in each group. Serum

levels of ALT decreased significantly in patients receiving GSE, indicating less liver inflammation. Additionally, GSE significantly improved the grade of liver steatosis (fatty streaks), as assessed by ultrasound. The GSE used in the trial was formulated in 100 mg capsules, but the daily dosage was not provided (presumably 100 to 200 mg/day). No significant benefits were observed for the 1000 mg/day ascorbic acid treatment.

References

- i Beylot C, Bioulac P. [Therapeutic Trial of a Peripheral Angioprotector, Endotelon.] *Gaz Med Franc* 1980; **87**(22): 2929
- ii Dubos G, Durst G, Hugonet R et al. [Evolution of Capillary Resistance, Whether it be Spontaneously or Artificially Diminished by the Action of a Capillaro-toxic Substance in Elderly Persons. The Beneficial Action of Endotelon on Microcirculation.] *Rev Geriatrie* 1980; **5**(6): 302-305
- iii Dartenuc JY, Marache P, Choussat H. [Capillary Resistance in Geriatrics - Trial of a Microvascular Protective Agent Endotelon.] *Bordeaux Med* 1980; **13**(18): 903-907
- iv Lagrue G, Olivier-Martin F, Grillot A. [A study of the effects of procyanidol oligomers on capillary resistance in hypertension and in certain nephropathies (author's transl)]. *Sem Hop* 1981; **57**(33-36): 1399-1401
- v Delacroix P. [Double-blind Trial of Endotelon™ in Chronic Venous Insufficiency.] *Rev Med* 1981; **22**(27-28): 1793-1802
- vi Sarrat L. Abord Therapeutique des Troubles Fonctionnels des Membres Inferieurs par un Microangioprotecteur l-Endotelon. *Bordeaux Med* 1981; **11**: 685-688
- vii Costantini A, De Bernardi T, Gotti A. [Clinical and capillaroscopic evaluation of chronic uncomplicated venous insufficiency with procyanidins extracted from vitis vinifera.] *Minerva Cardioangiol* 1999; **47**(1-2): 39-46
- viii Vérin PH, Vildy A, Maurin JF. [Retinopathy and OPC.] *Bordeaux Med* 1978; **11**(16): 1467
- ix Fromantin M. [OPC in the Treatment of Capillary Weakness and Retinopathy in Diabetics.] *Med Intern* 1981; **16**(11): 432-434
- x Arne JL. [Contribution to the Study of Procyanidolic Oligomers: Endotelon Used in Diabetic Retinal Infections (30 observations).] *Gaz Med France* 1982; **89**: 3610
- xi Weseler AR, Ruijters EJB, Driittj-Reijnders MJ et al. Pleiotropic benefit of monomeric and oligomeric flavanols on vascular health- a randomized controlled clinical pilot study. *PLOS One* 2011; **6**(12): e28460
- xii Yamakoshi J, Sano A, Tokutake S et al. Oral intake of proanthocyanidin-rich extract from grape seeds improves chloasma. *Phytother Res* 2004; **18**(11): 895-899
- xiii Banerjee B, Bagchi D. Beneficial effects of a novel IH636 grape seed proanthocyanidin extract in the treatment of chronic pancreatitis. *Digestion* 2001; **63**(3): 203-206
- xiv Khoshbaten M, Aliasgarzadeh A, Masnadi K et al. Grape seed extract to improve liver function in patients with nonalcoholic fatty liver change. *Saudi J Gastroenterol* 2010; **16**(3): 194-197