Sigma Aldrich Plant Profiler. **Bioactive products found in Vaccinium myrtillus.**

**Vaccinium myrtillus**

Synonyms / Common Names / Related Terms
Airelle, anthocyanins, Bickbeere (German), bilberry leaf, black whortle, Blaubeere (Dutch), blaubessen, bleaberry, blueberry, blueberry leaf, bogberry, bog bilberry,urren myrtle, cranberry, dwarf bilberry, dyeberry, Ericaceae (family), European blueberry, Heidelbeere (Dutch), Heidelbeereblatter, heidelberry, huckleberry, hurtleberry, lingonberry, lowbush blueberry, Mirtillo nero (Italian), Myrtilli folium, Myrtilli fructus, Myrtillus niger Gilib., Optiberry, resveratrol, sambubiosides, trackleberry, Vaccinium angulosum Dulac, Vaccinium montanum Salibs., Vaccinium myrtillus anthocyanoside extract, VMA extract, VME, whortleberry, wineberry.

**Bioactive products found in Vaccinium myrtillus**

**Mechanism of Action**

**Pharmacology:**

**Constituents:** Bilberry contains several compounds that have demonstrated biological activity. The main chemicals contained in bilberry extract have been shown to be: anthocyanins, flavonoids, hydroquinone, oleanolic acid, neomyrtillin, sodium, tannins, and ursolic acid. Bilberry also contains resveratrol. The anthocyanosides, tannins, and flavonoids have been of particular scientific interest. Flavonoids have been shown in vitro to possess a number of biological properties, including inhibition of prostacyclin synthesis, reduction of capillary permeability and fragility, free radical scavenging, inhibition of a wide range of enzymes, impairment of coagulation and platelet aggregation, and anticarcinogenicity.

**Mechanism of action:** Anthocyanins and other phenolics from bilberry upregulate the oxidative stress defense enzymes heme-oxygenase-1 and glutathione S-transferase-pin cultured human retinal pigment epithelial cells, suggesting that they stimulate signal transduction pathways, influencing genes controlled by the antioxidant response element.

**Antibacterial effects:** In an in vitro study using Staphylococcus aureus, Staphylococcus aureus Oxford, Enterococcus faecalis, Bacillus subtilis, and Escherichia coli, an aqueous extract of bilberry leaves had a MIC of 12.7-17.8mg/mL and an aqueous extract of bilberry fruit had a MIC of 15.4-30.7mg/mL.

**Anticarcinogenic effects:** In an in vitro study, anthocyanin-rich extracts from bilberry (Vaccinium myrtillus L.) inhibited the growth of a colon cancer cell line.

**Antihyperglycemic effects:** In normal and depancreatized dogs, oral administration of bilberry leaves reduced hyperglycemia, even when the glucose was injected intravenously concurrently.

**Antioxidant effects:** Bilberry contains anthocyanosides that are flavonoid derivatives of anthocyanins (the blue, red, or violet pigments found in many berry varieties), which are closely related in structure and activity to flavonoids and possess free radical scavenging/antioxidant properties. Antioxidant properties have been attributed to bilberry based on in vitro studies.

**Antiplatelet activity:** In a clinical study of 30 subjects with normal platelet aggregation, 480mg of Myrtocyan® (Vaccinium myrtillus anthocyanins) daily, 3g of ascorbic acid daily, or both treatments all
reduced platelet aggregation after 30 and 60 days. Bilberry anthocyanins reduced platelet aggregation more than ascorbic acid alone, but bilberry anthocyanins and ascorbic acid together were the most effective. Also, in in vitro studies, anthocyanins extracted from bilberry have inhibited platelet aggregation. 13, 14, 10, 12

Flavonoids have been shown in vitro to inhibit prostacyclin synthesis. In one animal model, Vaccinium myrtillus anthocyanosides were studied for their effects on prostacyclin-like activity in rat arterial issue. 7

**Antiproliferative effects:** According to one laboratory study, anthocyanins were the predominant phenolic compounds in bilberry extracts. 31 Compared to other plants with anthocyanins, such as black currant or lingonberry, cell growth inhibition was greater for bilberry than other plants studied. The pro-apoptosis marker, Bax, was increased 1.3-fold in bilberry-treated cells, whereas the pro-survival marker, Bcl-2, was detected only in control cells. The results demonstrated that bilberry and other berry extracts containing anthocyanins inhibited cancer cell proliferation, mainly via the p21WAF1 pathway.

**Antiulcer effects:** In an animal study, large doses of cyanidin chloride from bilberry significantly increased gastric mucosal release of prostaglandin E2. 19 In animal models of gastric ulcers, cyanidin chloride showed antulcer activity. 26, 8

**Astringent effects:** Bilberry contains tannins that have been used medicinally as astringents and to treat diarrhea.

**Connective tissue stabilizing effects:** An in vitro study has suggested that anthocyanosides appear to stabilize connective tissue by enhancing collagen synthesis, inhibiting collagen degradation, and enhancing collagen cross linking. 35 In contrast, Boniface et al. found a significant decrease in connective tissue synthesis (collagen and glycoproteins) in gingival tissue samples of 12 adult diabetics treated with 600mg of anthocyanosides daily for two months. 36

**Hepatoprotective activity:** In an animal study, anthocyanos exorted a protective effect on liver cells. 27

**Hyperglycemic effects:** In an oral glucose tolerance test in healthy rats, an alcoholic extract of Vaccinium myrtillus leaves increased serum glucose levels compared to controls. 25

**Hypotensive effects:** Bilberry has been theorized to potentially drop blood pressure, based on pre-clinical evidence of vascular smooth muscle-relaxing properties. 21, 22, 23

Anthocyanoside extracts have been shown to have smooth muscle-relaxing activity, which may account for their purported effects in one series of women with dysmenorrhea. 18 Bioflavonoids and extracts of anthocyanosides (such as those present in bilberry) have been shown to relax vascular smooth muscles in experimental models, possibly via stimulation of prostaglandins. 21, 22, 23

Intracellular signaling effects: Anthocyanosides have been shown to inhibit cAMP phosphodiesterase, which is involved in intracellular signal transduction pathways. 8

**Ocular effects:** Anthocyanosides have been shown to exert direct effects on the retina, including the alteration of local enzymatic reactions and enhancement of the recovery of rhodopsin. 9 The multi-ingredient product Mirtogenol™ (Pycnogenol® - French maritime pine bark extract and Mirtoselect® - standardized bilberry extract) has been reported to lower intraocular pressure and improve ocular blood flow. 37

**Smooth muscle relaxant effects:** Anthocyanoside extracts have been shown to have smooth muscle-relaxing activity, which may account for their purported effects in one series of women with dysmenorrhea. 18 Bioflavonoids and extracts of anthocyanosides (such as those present in bilberry) have been shown to relax vascular smooth muscles in experimental models, possibly via stimulation of prostaglandins. 21, 22, 23

**Vasoprotective effects:** Flavonoids have been shown in vitro to reduce capillary permeability and fragility. Anthocyanosides have been studied for their potential protective effect in disorders due to abnormal capillary fragility. 33

**Pharmacodynamics/Kinetics:**

There are limited data regarding the pharmacodynamics and kinetics of Vaccinium myrtillus (bilberry) anthocyanosides (VMA). In one animal study, bilberry anthocyanosides were rapidly distributed after intra-peritoneal injection and intravenous administration. 38 In another animal study, bilberry anthocyanosides were found to be eliminated via the bile and urine with a modest level of liver extraction. 32

Bioavailability in animals is low. Following oral doses in rats, plasma levels of VMA reached a peak at 15 minutes and declined rapidly within two hours, and the absolute bioavailability was 1.2% of the administered dose. 38 The gastrointestinal absorption of VMA was 5% of the administered dose. Another
study found a differential affinity of VMA for certain tissues (especially skin and kidney). This suggests that different tissues may have more persistent local concentrations.

References
37. Steigerwalt, R. D., Gianni, B., Paolo, M., Bombardelli, E., Burki, C., and Schonlau, F. Effects of Mirtogenol on ocular blood flow and intraocular hypertension in asymptomatic subjects. Mol Vis 2008;14:1288-1292. 18618008