

APPLICATIONS

- Microbial Support
- Healthy Inflammatory Response Support
- Antioxidant Support
- Immune Support



INTRODUCTION

NutraMedix Barberry is made from Oregon grape root, which belongs to the Berberidaceae family. It is known as both *Mahonia aquifolium* and *Berberis aquifolium*, with botanists preferring the former name and horticulturists the latter.¹ In the health and wellness field, both names are used interchangeably. Oregon grape is one of many plants containing the isoquinoline alkaloid berberine, which was first isolated from goldenseal (*Hydrastis canadensis*).² *Berberis vulgaris*, which also goes by the common name of barberry, is a separate species.

Berberine-containing herbs have been used for centuries in traditional Chinese health practices, for both microbial support and healthy inflammatory-response support.^{*3} Thirty-five species of *Mahonia* have been found in China, 20 of which are used for some form of health support.^{*4} Oregon grape is well known in North America, with a history of use by the Pacific Northwest and other native peoples for microbial and other health support.^{*5-7} During the Lewis and Clark expedition, Meriwether Lewis devoted a journal entry to this plant on February 12, 1806. The *Southern Medical Journal* mentioned Oregon grape's use for health support in 1878.^{*8,9}

Constituents of Oregon grape include bisbenzylisoquinoline (BBIQ) alkaloids (aquifoline, armoline, baluchistine, berbamine, obamebine, and oxyacanthine);¹⁰ aporphine alkaloids (corydine, corytuberine, isocorydine, isothebaine, magnoflorine, and thaliporphine);⁴ and protoberberine alkaloids (berberine, columbamine, jatrorrhizine, and oxyberberine).¹¹ The major constituents in Oregon grape are the protoberberine alkaloids berberine and jatrorrhizine.⁴

NutraMedix Barberry (Oregon grape root) is made at our U.S. manufacturing facility using a specialized proprietary extraction process that optimizes the constituents of the herbs in their original, unprocessed state to obtain broad-spectrum concentration. Because our extracts are made in our own facility, we control all aspects of quality, including stringent ID testing, microbial testing, and heavy-metal testing. NutraMedix rigorously follows current good manufacturing practices (cGMPs), as do our suppliers.

MICROBIAL SUPPORT

Oregon grape and its constituent berberine help with broad-spectrum microbial support for a variety of purposes.^{*12-17} Multiple randomized, controlled trials with berberine, both alone and in combination, show significant microbial support, particularly gastrointestinal microbial support.^{*6, 18-23}

HEALTHY INFLAMMATORY RESPONSE SUPPORT

Oregon grape helps maintain a healthy inflammatory response by supporting the normal function of cyclooxygenase (COX) and 5-lipoxygenase (5-LOX), enzymes that support the transition of arachidonic acid to prostaglandins and other eicosanoids.*

In one in vitro study, Oregon grape alcoholic extract helped maintain both COX and 5-LOX levels already within the normal range; however, isolated alkaloids including berberine, jatrorrhizine, magnoflorine, and palmatine did not show the same support.^{*24}

Some researchers attribute the impact of Oregon grape on LOX to the maintenance of peroxy- and alkoxy-

radicals already within the normal range.^{*25} There may be additional mechanisms or as-yet unidentified compounds that also contribute.²⁴ Of the constituent BBIQs, berbamine and oxyacanthine are the most relevant for maintaining LOX levels already within the normal range,¹⁰ though columbamine, corytuberine, and oxyberberine also contribute.^{*11}

In another in-vitro study, a crude extract of the stem bark of Oregon grape helped maintain 12-lipoxygenase (12-LOX) levels already within the normal range.* While Oregon grape's ability to support a healthy inflammatory response is believed to be influenced by antioxidant support (as quantified by 2,2-diphenyl-1-picrylhydrazyl [DPPH] assay), researchers concluded that more specific mechanisms between enzymes and alkaloids may be involved.^{*25}

Oregon grape-stem bark crude extract also helps maintain interleukin-8 (IL-8) in vitro levels already within the normal range.^{*26} In an in-vitro study with vascular smooth-muscle cells, berberine helped maintain inflammation already within the normal range during stimulation with lysophosphatidylcholine (lysoPC).^{*27}

In one meta-analysis of 52 studies with a total of 4,616 participants and another meta-analysis of 18 clinical trials with a total of 1,600 participants, berberine helped maintain interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-alpha), and C-reactive protein (CRP) levels already within the normal range.^{*28,29} Additional meta-analyses also show that berberine helps maintain CRP levels already within the normal range.^{*30,31}

ANTIOXIDANT SUPPORT

Oregon grape root and its constituents may help with antioxidant support.^{*14} The constituents with the most significant antioxidant support, as shown by DPPH assay, include magnoflorine and jatrorrhizine, both of which have free phenolic groups.^{*14} Oxyacanthine and berbamine are the most active constituents for maintaining lipid peroxidation already within the normal range,³³ and berberine may offer antioxidant support for peroxynitrite ions (ONOO-), nitric oxide ions (NO), and superoxide ions (O₂⁻).^{*25}

Researchers conducting an in vitro study used 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) to measure intracellular reactive oxygen species (ROS) in response to lysoPC; berberine helped maintain ROS

already within the normal range.^{*27} The maintenance of normal-range ROS production supports normal function of the extracellular signal-regulated kinase 1/2 (ERK 1/2) cascade, maintaining smooth muscle-cell proliferation and migration already within the normal range. This, in turn, supports and maintains a healthy inflammatory response, according to the study researchers.^{*27}

IMMUNE SUPPORT

Oregon grape helps support healthy function of both innate and adaptive immunity through both direct and indirect mechanisms.^{*33,34} For healthy innate immune function, the constituent berberine helps maintain levels of phagocytic macrophages and dendritic cells already within the normal range.^{*33} Berberine and other BBIQ alkaloids also support the innate immune response by maintaining complement levels already within the normal range.^{*34} For healthy adaptive immune function, berberine helps maintain the function and differentiation of both regulatory T cells and helper T cells, including Th1 and Th17, already within the normal range.^{*33}

SAFETY AND CAUTIONS

A safe dosage range of Oregon grape is considered to be 1.5 to 3 g/day.³⁵ Though there have been reports of skin irritation and allergic reactions with topical application, adverse effects are rare with oral use.³⁶

Oregon grape is contraindicated in pregnancy, as the constituent berberine has caused uterine stimulation in rat studies. Oregon grape is empirically contraindicated in severe liver or gallbladder disease due to its choleric and cholagogue effects.^{5,17}

Theoretically, Oregon grape may have additive effects with anticoagulant or antiplatelet drugs, hypoglycemic medications, blood-pressure drugs, and central nervous system depressants. It may inhibit CYP2C9, CYP2D6, and CYP3A4, which may decrease the metabolism of drugs using these pathways, resulting in increased levels and adverse effects of these medications.³⁶

Safety is not documented in breastfeeding or pregnant women, or in children under age 3, due to insufficient safety research.

***This statement has not been evaluated by the Food and Drug Administration. This product is not intended to treat, cure, or prevent any diseases.**

REFERENCES

- ¹ National Center for Biotechnology Information. (2002). Mahonia - MeSH - NCBI. NCBI. <https://www.ncbi.nlm.nih.gov/mesh/?term=mahonia%20aquifolium>
- ² Jain, S., Tripathi, S., et al. (2023). *Chinese Herbal Medicines*, 15(4), 549–555.
- ³ Ai, X., Yu, P., et al. (2021). *Frontiers in Pharmacology*, 12, 762654.
- ⁴ He, J. M., & Mu, Q. (2015). *Journal of Ethnopharmacology*, 175, 668–683.
- ⁵ Brinker, F. J. (2001). *Herb contraindications and drug interactions: With appendices addressing specific conditions and medicines (3rd ed.)*. Eclectic Medical Publications.
- ⁶ McCutcheon, A. R., Ellis, S. M., et al. (1994). *Journal of Ethnopharmacology*, 44(3), 157–169.
- ⁷ Pojar, J., & MacKinnon, A. (1994). *Plants of the Pacific Northwest Coast: Washington, Oregon, British Columbia, and Alaska*. Lone Pine Publishing.
- ⁸ Mussulman, J. A. (n.d.). Oregon Grapes - Discover Lewis & Clark. *Discover Lewis & Clark*. <https://lewis-clark.org/sciences/plants/oregon-grape/>
- ⁹ Southern Medical Record. (1878). *The Southern Medical Record*, 8(10), 319.
- ¹⁰ Müller, K., Ziereis, K., et al. (1995). *Planta Medica*, 61(1), 74–75.
- ¹¹ Misík, V., Bezáková, L., et al. (1995). *Planta Medica*, 61(4), 372–373.
- ¹² Dorcheh, F. A., Balmeh, N., et al. (2022). *Informatics in Medicine Unlocked*, 28(2022), 100843.
- ¹³ da Silva, A. R., de Andrade Neto, J. B., et al. (2016). *Antimicrobial Agents and Chemotherapy*, 60(6), 3551–3557.
- ¹⁴ Racková, L., Májeková, M., et al. (2004). *Bioorganic & Medicinal Chemistry*, 12(17), 4709–4715.
- ¹⁵ Volleková, A., Kostálová, D., et al. (2003). *Phytotherapy Research*, 17(7), 834–837.
- ¹⁶ Cernáková, M., & Kostálová, D. (2002). *Folia microbiologica*, 47(4), 375–378.
- ¹⁷ Birdsall, T. C. & Kelly, G. S. (1997). *Alternative Medicine Review*, 2(2), 94–103.
- ¹⁸ Chen, S., Shen, W., et al. (2023). *Chinese Medical Journal*, 136(14), 1690–1698.
- ¹⁹ Chen, X. X., Chen, Y. X., et al. (2022). *Journal of Digestive Diseases*, 23(10), 568–576.
- ²⁰ Zhang, J., Han, C., et al. (2020). *Journal of Digestive Diseases*, 21(5), 256–263.
- ²¹ Zhang, D., Ke, L., et al. (2017). *Medicine*, 96(32), e7697.
- ²² Rabbani, G. H., Butler, T., et al. (1987). *The Journal of Infectious Diseases*, 155(5), 979–984.
- ²³ Khin-Maung-U, Myo-Khin, et al. (1985). *British Medical Journal (Clinical Research ed.)*, 291(6509), 1601–1605.
- ²⁴ Galle, K., Müller-Jakic, B., et al. (1994). *Phytomedicine: International journal of phytotherapy and phytopharmacology*, 1(1), 59–62.
- ²⁵ Rackova, L., Oblozinsky, M., et al. (2007). *Journal of Inflammation*, 4, 15.
- ²⁶ Hajnická, V., Kostálová, D., et al. (2002). *Planta Medica*, 68(3), 266–268.
- ²⁷ Cho, B. J., Im, E. K., et al. (2005). *Molecules and Cells*, 20(3), 429–434.
- ²⁸ Lu, Y., Zhang, X., et al. (2022). *Inflammopharmacology*, 30(3), 1063–1077.
- ²⁹ Vahedi-Mazdabadi, Y., Shahinfar, H., et al. (2023). *Phytotherapy Research, PTR*, 37(12), 5541–5557.
- ³⁰ Beba, M., Djafarian, K., et al. (2019). *Complementary Therapies in Medicine*, 46, 81–86.
- ³¹ Asbaghi, O., Ghanbari, N., et al. (2020). *Clinical Nutrition ESPEN*, 38, 43–49.
- ³² Bezáková, L., Misík, V., et al. (1996). *Die Pharmazie*, 51(10), 758–761.
- ³³ Ehteshamfar, S. M., Akhbari, M., et al. (2020). *Journal of Cellular and Molecular Medicine*, 24(23), 13573–13588.
- ³⁴ Kostálová, D., Bukovský, M., et al. (2001). *Ceska a Slovenska farmacie: Casopis Ceske farmaceuticke spolcnosti a Slovenske farmaceuticke spolcnosti*, 50(6), 286–289.
- ³⁵ Rotblatt, M., & Ziment, I. (2001). *Evidence-Based Herbal Medicine*. Hanley & Belfus.
- ³⁶ NatMed Pro. (2023). Oregon Grape [monograph]. *NatMed Pro*. <http://naturalmedicines.therapeuticresearch.com>

NutraMedix 

SHAKE WELL BEFORE EACH USE:

Put 15 to 30 drops in 4 oz (120 mL) of water and wait one minute before drinking. Take 2-4 times per day or as directed by your physician. Do not use if pregnant or nursing. Stop use if adverse reactions develop. Keep out of reach of children.

†These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.



BARBERRY

IMMUNE/MICROBIAL
SUPPORT †

Dietary Supplement

1 fl oz. (30mL)

Supplement Facts

Serving Size 30 drops
Servings Per Container 20

Amount Per Serving

Oregon grape root extract 1.5 mL*

*Daily Value not established

Other ingredients: mineral water, ethanol (20-24%)

NutraMedix 

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Lot #
Exp.