

Berberine

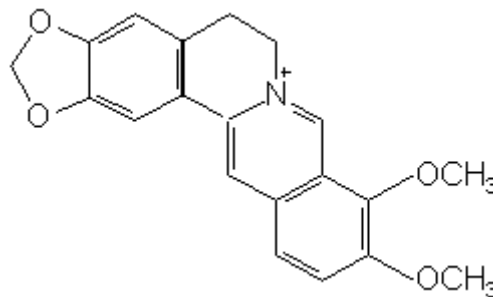
Attenuate the oxygen demand in the tissues

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Potentially performance enhancers for freedivers.

I take no responsibility for any side-effects, damage or death during the use of the substance mentioned below. No one of the mentioned substances is yet proved to be favourable to freedivers. The field is still unexplored. In the future, it may be proved that some of the substances do not have any positive effects.

Berberine



Berberine (BBR) is an alkaloid used in the traditional Chinese medicine to treat diabetes type 2. The substance is found in plants like *Hydrastis canadensis* and *berberis vulgaris* and has a strong yellow colour. Recently, it has become the object of interest in the traditional medicine due to the similar properties as some of the regular medicines used to treat diabetes. The main reason why BBR is interesting for freedivers is that the molecule inhibits the respiratory chain in the mitochondria (1). This in turn leads to an induction of the glycolysis (2). The glycolysis produce adenosinetriphosphate (ATP) without requiring oxygen compared to the respiratory chain which needs oxygen. Another positive effect due to the inhibition of the respiratory chain is that the AMP/ATP ratio increase and which activates the AMP-activated protein kinase (AMPK) (1;3). AMPK is a protein which works as a “masterswitch” and turns of the anabolic signals in the body when activated. This is favourable since anabolic mechanisms is highly oxygen demanding. Through this mechanism there may be a double effect which further lowering the oxygen need in the body. The disadvantage is that the induction of glycolysis leads to an increased production of lactate. However, this could probably be counteracted by another supplement recently used by bodybuilders, β -alanine (aminoacid) that promotes the production of carnosine which is an effective pH-buffer in the muscles. Other positive effects connected to BBR is that the substance promote the uptake of glucose in the cells (2), which is positive since the cells demands more glucose due to the induction of the glycolysis. There are several derivatives of BBR where the most effective amongst those is dihydroberberine (dhBBR) due to the higher bioavailability. dhBBR is immediately metabolised to BBR when entered the body (1). This is however synthetically manufactured and hard to get the hand on. 100mg/kg/day seems to be the appropriate dosage and should be taken 3-4 hours before the performance. It is probably not a good idea to consume it on a regular basis due to the inhibition of the anabolic signals. In the long run, this could lead to loss off muscle mass and weight (4). One should also be careful with the sun when consuming BBR since the molecule is phototoxic and contribute to the production of free radicals in the skin when exposed to UV-radiation (5). This could lead to DNA-damage in the skin (5). Phototoxic substances are not unusual in the nature. One example is Psoralen which is common in citrus fruits and vegetables as celery, parsley och figs. BBR is probably most suitable when attempting a personal best or a competition. At this

moment, it is not possible to buy this product in Sweden in the pure form. The products available usually have very low concentrations of BBR and ethanol is often added as a solvent.

Eager to learn?

BBR activates AMPK via inhibition of respiratory Complex I of the mitochondrion Fig. 1.(1). This due to the increased AMP/ATP ratio as a consequence of the inhibition (1;6). This result in AMPK phosphorylation which remains for approximately 16 h due to a persistent elevation in AMP/ATP ratio and reduction in oxygen consumption (2). Acute effect of berberine on phosphorylation of AMPK begin at 0.5 h in L6 myotubes and 1 h in 3T3-L1 adipocyte cells in vitro(2). Phosphorylation of AMPK is stimulated by berberine at either low dosage (1–2 $\mu\text{mol/l}$, $P < 0.05$) or high dosage (10 $\mu\text{mol/l}$, $P < 0.01$) in both L6 and 3T3-L1 adipocytes (2). It is shown that BBR inhibit respiration in a dose dependent manner in L6 myotubes, with an approximate 50% inhibition at 15 μM (1). Insulin induce phosphorylation of IRS-1, Akt (Thr308), p70 S6 (Thr389), and ERK (1), and BBR exhibited little effects on these signaling molecules and no significant changes was observed in GLUT1 and GLUT4 (1). This suggests that the insulin like properties of BBR may be independent of the insulin pathway. However, these conclusions are challenged by other studies in which berberine was shown to activate this pathway (4;6;6).

At 2 $\mu\text{mol/l}$ (BBR), glucose uptake increased by 170% in the absence of insulin in L6 myotubes in a time course of 4h ($P < 0.01$) (2).

Administration of 20 mg/kg BBR do not generate detectable levels of BBR in the plasma (1) In contrast, dhBBR at the same oral dose is rapidly detected in the plasma displaying a half-life ($t_{1/2}$) of 3.5 ± 1.3 hr and a maximum concentration (C_{max}) of 2.8 ± 0.5 ng/ml (1). Other differences seen was that at an intake of 100 mg/kg.day, dhBBR reduced adiposity and improved glucose tolerance in HFD mice, whereas no effects of BBR was observed at this dose (1). Due to these effects, dhBBR have the potential to have positive effects on type 2 diabetes and other components of the metabolic syndrome (1).

In addition to its metabolic activities, berberine has well-established antimicrobial activities in the control of infection by bacteria, viruses, fungi, protozoans, and helminthes (7;8). No cytotoxicity have been observed (2), making it a safe choice when treating diabetes type 2.

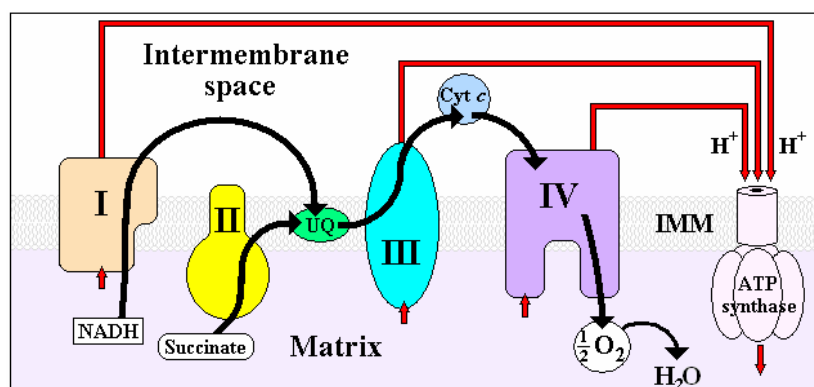


Fig. 1. The respiratory chain in the mitochondria (oxygen demanding). Complex I is inhibited by Berberine.

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