The Science Behind Epi-Plex

At Competitive Edge Labs, we don't just selectively pick out information from research studies to just support the marketing and sales of our products. Our research is intensive and involves the meticulous scrutinizing of available data, including breakthrough landmark papers as well as potentially overlooked prior studies. We understand that there are many consumers that aren't science minded and simply want to know what a product does and how it benefits them; however, we also understand that there are science minded consumers that wish to learn the pharmacology of supplements and may be frustrated at the strong emphasis on marketing and picking and choosing of research information hand-picked to support marketing efforts. It is easy to pull claims from studies and research papers but not so easy to delve further and identify the 'how's' and 'why's'.

(-)-Epicatechin is a very popular ingredient but as of yet, there doesn't appear to be very comprehensive elaboration as to the mechanisms of action of -(-) epicatechin which essentially limits the true exploitation of its benefits as a supplement. Yes, there are studies that show a decrease in Myostatin, an increase in Follistatin, and increase in NO and exercise performance, but how does it do these things?

Let Competitive Edge Labs be the first to provide you with this information and enlighten you.

Increased Muscle Endurance via Enhanced PGC-1alpha activity

Epicatechin holds demonstrated capability to stimulate the nuclear translocation and activation of known transcriptional modulators of super oxide dismutase-2 and catalase (1-7). Of particular interest is the capacity to increase activation and translocation of one these transcriptional modulators known as peroxisome proliferator-activated receptor gamma coactivator 1-α (PGC-1 alpha) (3-7). This activity is seemingly a proven mechanistic role in the increased skeletal muscle endurance observed in research (8-10) and increasingly through anecdote. Experimental and animal research models testing the cellular activity of endurance exercise have identified PGC-1 alpha as the intracellular mediator of skeletal muscle fiber composition remodeling (11-13). It has been observed that increased PGC-1 alpha activation and translocation decreases the ratio of the type IIb fibers to the type I and type IIa fibers (14,15). This recomposition essentially mediates skeletal muscle adaptations to resistance and endurance exercise by reducing the rate of metabolic oxidation in the muscle cells which translates to increased resistance to fatigue (15-18).

Increased Muscle Endurance via Improved Calcium Tolerance of Mitochondria

Epicatechin is capable of increasing resistance to calcium-induced mitochondrial swelling in muscle (19,20). This activity appears to be mediated through increasing membrane rigidity and integrity through increasing expression of proteins mitofilin and porin (9,20). By increasing these, muscle cell resistance is augmented reducing vulnerability to acute and chronic exercise induced damage, metabolic stress and consequential impaired ATP synthesis (21,22). In fact new research suggests that not only does epicatechin protect the mitochondria through these mechanisms, it can directly influence mitochondrial function to stimulate and maintain cellular respiration and optimize ATP synthesis (23). These mechanisms, as well as the capacity enhance PGC1-alpha activity, may provide the mode of action for increased muscle endurance to exercise observed with (-)-epicatechin supplementation.

Increase Follistatin via Inhibition of DNA Methylation

There is evidence that indicates that epicatechin can indirectly inhibit DNA methylation through its COMT metabolism that increases formation of potent non-competitive inhibitor of DNA methylation enzymes (24-26). DNA methylation decreases gene transcriptional activation by physically impeding the transcriptional proteins binding to the gene loci (27-29). It can also do this through the formation of methyl-CpG-binding domain proteins which bind DNA and inactivate gene promoter regions (28-31). Follistatin promoter regions are particularly sensitive to DNA methylation enzymes which can restrict expression of the peptide and ultimately can potentially attenuate follistatin secretion (32). Evidence suggests that inhibiting enzymes that mediate DNA methylation can potentially increase follistatin expression up to 17 fold after one week (32).Biochemical studies on muscles during acute exercise have associated DNA hypo methylation with increased expression of PGC-1 alpha (33,34) which, as previously mentioned, can also be increased by epicatechin. Other research has identified that long term exercise induced adaptations are associated with expression of polymorphic enzymes that result in DNA hypo methylation and ultimately promote myogenesis (35-37). Therefore, it would certainly seem viable that inhibiting DNA methylation could serve as a potential target for increasing muscle mass and athletic performance. Although this has not been specifically tested, this activity may impart mechanistic explanation for the decrease in myostatin and increase in follistatin observed with epicatechin supplementation.

Increase Follistatin via Augmenting Nitric Oxide Signalling

(-)-Epicatechin is capable of augmenting nitric oxide via activating the skeletal muscle expressed neuronal nitric oxide synthase (nNOS) (9,38) and also through inhibition of nicotinamide adenine dinucleotide phosphate (NADPH) by its *O*-methyl metabolites (39). It has been proposed that former is directly activated via a novel cell surface receptor in skeletal muscle which mediates an intracellular cascade that results in increased NO production (40). Together these mechanisms are active both with and without exercise and are associated with the acute augmentation of NO observed with (-)-epicatechin supplementation (41,42). Although this activity does not appear to be largely active for increasing muscular endurance observed with (-)-epicatechin, it may play an indirect role in the myogenic potential(9). This may occur by compensating NO scavenged by myoglobin (41,44) and preserving Dynamin type-1 protein (DRP-1) (45) as well as promoting *S*-nitrosylation and inactivation of class II histone deacetylases (38,46-47). Hypothetically these effects may promote the prior mentioned skeletal muscle remodeling and the increased expression of follistatin (46,47).

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