



# AIS SPORTS SUPPLEMENT FRAMEWORK

## KETONE SUPPLEMENTS

### What is it?

- > Ketone bodies (acetone, acetoacetate and beta-hydroxy-butyrate [ $\beta$ HB]) are chemicals produced by the liver during periods of low energy or low carbohydrate availability, with high circulating levels seen during starvation, prolonged fasting and extreme carbohydrate restriction (e.g. ketogenic low carbohydrate high fat [LCHF] diets).
- >  $\beta$ HB is the most important ketone body ("ketone") from a metabolic perspective and blood concentrations of 1-3 mmol/L are considered to be the optimal range for it to exert metabolic effects.<sup>1</sup>
- > Ketone supplements are taken to acutely increase blood concentrations of  $\beta$ HB/ ketones without the need to undertake energy or carbohydrate restrictions. A range of benefits has been proposed or investigated including:
  - Direct benefit to physiological and cognitive aspects of endurance performance via fuelling mechanisms<sup>2-4</sup>
  - Superior post-exercise recovery with potential use as a chronically used supplement<sup>5</sup>
  - Strategic chronic or periodised use to enhance health and training adaptations<sup>6</sup>
- > The first major interest in the use of oral ketone supplements in sports is attributed to work of Oxford University's Professor Kieran Clarke, who developed a ketone ester ("DeltaG") that was part of a campaign to prepare British athletes for the 2012 London Olympic Games. This product has also been highly used within professional road cycling teams for the benefits previously identified, as well as other claims such as appetite suppression to support body composition goals.

### What does it look like?

- > Ketone supplements are available in three different forms.
  - Ketone salts (sodium, magnesium or calcium salts of the  $\beta$ HB).
  - 1-3- Butanediol (precursor to  $\beta$ HB).
  - Ketone esters.
    - The ketone mono-ester [ $\beta$ -3-hydroxybutyl (R)-3-hydroxy-butyrate] developed as DeltaG at Oxford University is now commercialised as HVMN Ketone Ester.
    - Patents for di-esters have been established but are only involved in clinical research.
- > Some manufactured ketone supplements contain a racemic mixture (i.e. equal parts D- and L- stereoisomers) of  $\beta$ HB. Only the D-isomer (R- $\beta$ HB) is considered to have high metabolic activity.

### How and when do I use it?

- > **Acute use for exercise**
  - A variety of protocols have been investigated in scientific trials with the most common involving the intake of the ketone ester before, and sometimes during, endurance exercise.
  - Total dose = ~570-750 mg/kg (40-60 g). Note that one 40 g bottle of the Ketone Ester contains 25 g of the active compound.
  - The protocols of use associated with testimonials in some sports (e.g. road cycling) are unknown.
- > **Chronic or periodic use**
  - Protocols recommended for chronic or periodic use have not yet been established.
- > Current evidence to support the use of ketone supplements is summarised in the table below.



## Summary of investigations of the use of ketone supplements by athletes

### 1. Acute performance enhancement:

- > provision of an additional substrate for the muscle which may offer additional advantages of enhanced economy (less oxygen required to produce ATP)
- > Provision of an additional substrate for the brain and central nervous system which may enhance cognitive function

Direct performance enhancement has been tested in ~20 studies (including published, in press and in review literature)

Meta-analyses<sup>2,4,7,8</sup> fail to show benefits to sports performance. Ketone Ester appears to be the supplement form most likely to have a benefit

Note that the two studies which have found acute performance benefits included the following protocols:

- > The use of a KE supplement<sup>9,10</sup>
- > Co-ingestion with carbohydrate in overnight fasted subjects<sup>9</sup>
- > Co-ingestion with bicarbonate to address the change in blood pH associated with ketone body ingestion.<sup>10</sup> However, a further study from the same group failed to replicate these findings, and reported a performance impairment<sup>11</sup>

There are a large range of protocols of use (doses, timing of intake and accompaniment with carbohydrate or bicarbonate) and protocols of exercise. It is difficult to compare the findings due to the range of variables

### 2. Post-exercise recovery

- > Recovery/resilience to over-training when used chronically
- > Acute enhancement of protein synthesis
- > Acute enhancement of glycogen restoration
- > Satiety/Appetite suppression for weight control

The effect of post-exercise ketone supplements on glycogen synthesis and protein metabolism requires further investigation.

There are testimonials that athletes use ketone supplements during post-exercise recovery to suppress appetite and assist with body composition manipulation. However, the study which reported benefits of chronic use of ketone supplements in post-exercise recovery, via an apparent blunting of over-reaching, also found that the cyclists reported an increase in energy intake with the use of the ketone supplement

### 3. Health and training adaptation

A large range of claims are made for general health benefits of high circulating levels of ketone bodies (e.g. reduced inflammation, enhanced metabolic adaptation), especially associated with the chronic adherence to ketogenic LCHF diet. Whether these benefits are real, and whether strategic periodic/chronic use of ketone supplements can achieve health benefits or superior metabolic is unknown.

## Are there any concerns or considerations?

### Equivocal scientific support

- > The evidence for benefits of acute or chronic supplementation on health and performance is unclear. There is a wide range in the protocols of use, and in the scenarios of exercise, in which it has been investigated. It is difficult to integrate the various findings of these studies.
- > The effects of high blood ketone levels on metabolism and other physiological outcomes is extremely complex. Different protocols of use may achieve variable effects on the timing and increase in blood  $\beta$ HB concentrations with differential effects on substrate metabolism and physiological effects. It may be difficult to pinpoint beneficial uses and the window of benefit may be small. In addition, some of the effects may impair sports performance.
  - Ketone supplementation creates major effects on substrate use (reduces glycolysis, lipolysis, glycogen use and increases use of intramuscular triglycerides. Some of these effects may be counter-productive to some sports scenarios.
  - Causes increase in blood acidity which may be counter-productive to some sports scenarios.
- > Some recent studies suggest that the  $\beta$ HB provides a minor substrate for the muscle (~5% of fuel use) and the claimed benefits to exercise economy (reduced oxygen use) are equivocal.
- > The current investigations on ketone ester supplementation fail to cover most of the anecdotal uses/testimonials and the claims around long-term/chronic use.

### Nuances of specific supplements

- > Ketone ester supplements
  - These are expensive and often hard to obtain due to limited capacity for commercial manufacture (~\$50 per 25 g bottle for HVMN supplement).
- > Ketone salts
  - These produce a high salt load and gastrointestinal side effects.
  - These appear extremely unlikely to sufficiently increase blood  $\beta$ HB (> 1 mmol/L).



## Perceptions around their use

- > Ketone ester supplements are not included on the WADA Prohibited List and it would seem impractical as well as illogical for them to meet the criteria for such a ban.
- > Nevertheless, the initial use of "DeltaG" supplement by UK sporting teams and professional cycling teams has received much media/public criticism as being "frankenscience".

## Where can I find more information?

Supplement safety information

[www.sportintegrity.gov.au/what-we-do/anti-doping/supplements-sport](http://www.sportintegrity.gov.au/what-we-do/anti-doping/supplements-sport)

## References

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The Australian Institute of Sport (AIS) Supplement Framework is an initiative of the Australian High Performance Sport System. The AIS acknowledges the support of members of the National Institute Network (NIN) and National Sporting Organisations (NSO) and their staff in delivering content expertise. This information is intended to help athletes, coaches and scientists make evidence-based decisions about the use of supplements and sports foods. Before engaging in supplement use, we recommend that each individual refer to the specific supplement policies of their sporting organisation, sports institute or parent body, and seek appropriate professional advice from an accredited sports dietitian [www.sportsdietitians.com.au](http://www.sportsdietitians.com.au).

Athletes should be aware that the use of supplements may have doping implications. Athletes are reminded that they are responsible for all substances that enter their body under the 'strict liability' rules of the World Anti-Doping Code. Some supplements are riskier than others. The Sport Integrity Australia (SIA) app is a useful resource to help mitigate the risk of inadvertent doping by helping to identify supplements that have been batch-tested. The SIA App provides a list of more than 11,000 batch-tested products. We recommend that all athletes consult the educational resources of SIA regarding the risks associated with supplements and sports foods.. While batch-tested products have the lowest risk of a product containing prohibited substances, they cannot offer you a guarantee that they are not contaminated [www.sportintegrity.gov.au/what-we-do/supplements-sport](http://www.sportintegrity.gov.au/what-we-do/supplements-sport).

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Last updated March 2021

