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Evidence and potential for mycoprotein as a sustainable alternative dietary protein source to support muscle and metabolic health

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Abstract

The world’s population is rising, leading to an increased global requirement for dietary protein to support health and adaptation in various populations. Though a strong evidence base has accumulated to show the nutritional value of animal derived dietary proteins, mounting challenges associated with sustainability have led to calls for alternative, non-animal derived dietary protein sources to be investigated. Mycoprotein is a sustainably produced, protein-rich, high fibre whole food source derived from fungus fermentation. Initial human investigations demonstrated that mycoprotein consumption can lower circulating cholesterol concentrations. Recent data also report improved acute postprandial glycaemic control and a potent satiety effect following mycoprotein ingestion. It is possible that the amount and type of dietary fibre present in mycoprotein explains these beneficial effects. Emerging data now suggest that the amino acid composition and bioavailability of mycoprotein may also position it as a promising dietary protein source to support skeletal muscle protein metabolism. Mycoprotein, therefore, may be a viable dietary protein source to promote training adaptations in athletes and/or muscle mass maintenance to support healthy ageing. Herein, we review the current evidence underlying the metabolic effects of mycoprotein and highlight the key questions that need to be addressed.
Introduction

Developing a nutritionally sustainable future is an urgent contemporary issue. The world’s population is projected to increase from ~7.3 billion to >9 billion by 2050. This is coupled with global trends concerning rises in urbanization, social mobility and wealth creation, all factors expected to exacerbate global food demand. As a result, current and future generations are required to view developments in our understanding of human nutrition through the lens of mounting challenges associated with the sustainability of increased production.

When considering global dietary protein production requirements, demographic demands are also compounded by accumulating scientific data to support protein consumption at levels greater than currently accepted RDAs in various populations. For instance, evidence suggests muscle mass maintenance in older adults, the promotion/retention of muscular training adaptations in athletes and successful weight management are all supported by modest increases in dietary protein intake above the currently accepted RDAs. It is clear, therefore, that the global requirement for dietary protein production is a pressing societal issue that is gathering momentum.

Crucially, the majority of data supporting the refinement of dietary protein requirements has been obtained from studies examining the *in vivo* metabolic handling and/or adaptive responses to animal-derived protein ingestion e.g. The carbon, water and land use footprints of animal-derived protein production are anywhere from 8-80, 50-150 and 30-220 times, respectively, greater than many plant-based proteins (variation dependent on protein source and methods used to quantify). Furthermore, vegan, vegetarian and flexitarian diets are increasing in popularity. As such, research that investigates non-animal derived protein sources is applicable to a progressively larger demographic, and the impact of such evidence will rise correspondingly. It is therefore vital that the scientific community begin to examine
the metabolic handling and nutritional value of alternative, non-animal derived sustainable protein sources.

**Mycoprotein**

Mycoprotein is a whole food source produced by continuous flow fermentation of the filamentous fungus *Fusarium venenatum* (for a detailed description of the production processes please see reference 14). The resultant product is a high protein, high fibre, and relatively low energy complete food source (see Tables 1\textsuperscript{15-17} and 2\textsuperscript{15,16}) that is textured (via freezing) and flavoured into a variety of products under the trade name Quorn (Marlow Foods, Stokesley, North Yorkshire, UK). Importantly, the sustainability credentials of mycoprotein production position it as an attractive alternative protein source to temper environmental concerns associated with increased dietary protein production\textsuperscript{18,19} (see Figure 1). Following its development in the 1960s, initial human experimentation during the 1970s established the basic feasibility, tolerability and metabolic impact of mycoprotein consumption, prior to it being available for general sale in 1985. By the end of the 1990s this human research had begun to wane, with a complete list and summary of published human mycoprotein studies performed to date shown in Table 3\textsuperscript{15,20-31}. However, the now fully established commercial viability, environmental advantages, and alternative potential applications of mycoprotein for metabolic health, skeletal muscle maintenance and reconditioning has recently reignited research interest in this novel food source.

**Mycoprotein, dietary fibre and cardio-metabolic health**

An initial human investigation aimed at establishing tolerability of mycoprotein made an interesting ancillary observation.\textsuperscript{20} Human volunteers who consumed 20 g mycoprotein (dry weight) per day for 30 days (consumed as supplemental cookies) showed a ~7% decrease in
blood cholesterol concentrations (from 4.86 to 4.53 mmol/L),\textsuperscript{20} which replicated earlier findings in animals.\textsuperscript{32-34} Early research was then focussed in the potential health impact of mycoprotein upon its dietary fibre content. This was due to an established body of epidemiological studies reliably showing that higher fibre intakes (typically from fruit, vegetables and cereals) are associated with reduced blood cholesterol concentrations, improved blood lipid profiles, and reduced incidence of myocardial infarction and coronary heart disease.\textsuperscript{35-38} Such findings have been confirmed during intervention studies where increasing dietary fibre consumption has been reported to improve peripheral insulin sensitivity, and lower blood cholesterol concentrations and glycated haemoglobin (HBA1c) in both healthy individuals and patients with type-2 diabetes.\textsuperscript{39,40}

Follow-up studies focussing on mycoprotein consumption and cardio-metabolic health confirmed and extended on these effects on blood lipid profiles.\textsuperscript{21,22} Turnbull and colleagues\textsuperscript{21} performed a 3-week dietary intervention study where 191 g mycoprotein containing products (around 40 g dry weight of mycoprotein) was consumed per day, as part of a fully controlled and laboratory supervised diet aimed at maintaining energy balance in individuals with mildly elevated blood cholesterol concentrations. This tightly controlled study revealed that the mycoprotein intervention resulted in reduced blood total cholesterol (from 5.54 to 4.81 mmol/L; 13\% decrease) and low density lipoprotein (LDL) cholesterol (from 4.16 to 3.78 mmol/L; 9\% decrease) concentrations, and an increase in high density lipoprotein (HDL) cholesterol (from 0.58 to 0.65 mmol/L; 12\% increase) concentrations. These results were even more striking considering the control group generally showed opposite responses (as opposed to no change). Given that the energy, macronutrient, lipid composition and cholesterol content of the diets were similar across groups, it was assumed that fibre content was the causative component.
The increased dietary fibre content could conceivably have exerted its cholesterol-lowering effect by altering LDL cholesterol synthesis/degradation, cholesterol clearance in peripheral tissues, and/or increased binding of fibre to neutral sterols, cholesterol or bile acids in the intestine, resulting in decreased cholesterol entering the circulating pool. However, worthy of note is the beneficial effects of higher fibre diets on circulating cholesterol concentrations do not always extend to improvements in the specific lipid sub-fractions of LDL and HDL. It is thus interesting to ponder whether the type, rather than simply the amount, of dietary fibre contained within mycoprotein may, at least in part, explain the beneficial effects of mycoprotein consumption on circulating cholesterol.

Dietary fibres contained within mycoprotein predominantly comprise 2/3 β-glucan and 1/3 chitin, which form a fibrous insoluble matrix that is relatively rare in more traditional food sources. In keeping with the importance of fibre type, follow up work by Turnbull and colleagues reported similar effects of mycoprotein consumption (a 0.95 mmol/L or 16% and a 0.34 mmol/L or 21% reduction in total cholesterol and LDL cholesterol concentrations, respectively) under free-living conditions despite keeping overall energy, macronutrient and fibre content (around 6 g) the same across groups. Recent in vitro investigations have dug deeper mechanistically here, and begun to shed light on potential mechanisms by which the specific fibre profile of mycoprotein may affect gut microbiota to bring about these cholesterol lowering effects within humans.

Protein and dietary fibres entering the large intestine become available for fermentation by the gut microbiota. Fermentation of dietary fibres lead to the production of short-chain fatty acids (SCFA), primarily acetate, propionate and butyrate in a molar ratio of approximately 60:20:20. Fermentation of protein derived amino acids leads to production of phenols, amines, ammonia, branched-chain fatty acids and SCFA. Dietary fibre fermentation is prioritised over protein fermentation by the gut microbiota, and when fibre fermentation is
active the fate of dietary protein derived amino acids is bacterial cell biomass as opposed to metabolism. Therefore, moving from fibre to protein fermentation has also been shown to have profound effects on the composition of the gut microbiota. SCFA production, and propionate in particular, has been shown to reduce hepatic cholesterol synthesis via inhibition of β-hydroxy-β-methylglutaryl coenzyme A (HMG-CoA) reductase (the rate-limiting enzyme within cholesterol synthesis), and suppress adipose tissue lipolysis. In human studies using inulin propionate ester, which delivers propionate directly to the large intestine, propionate has been demonstrated to reduce LDL cholesterol and improve liver function and insulin sensitivity. However, the current evidence around propionate is inconsistent, with another study suggesting that its consumption leads to insulin resistance and compensatory hyperinsulinemia. Using in vitro colonic models, mycoprotein and its purified dietary fibre have been shown to be fermentable, producing SCFA. Both mycoprotein and purified mycoprotein dietary fibre exhibit increased propionate and butyrate production at the cost of acetate, and increasing colonic propionate production inhibits the incorporation of plasma acetate into cholesterol. Consequently, data are now available to suggest that the digestive and metabolic properties of the unique fibre profile present within mycoprotein clearly warrants future (in vivo) research.

The beneficial metabolic effects of mycoprotein consumption have also been shown to extend to acute postprandial glycaemic control. It was reported that 20 g mycoprotein (dry weight) consumed during an oral glucose tolerance test resulted in reduced post-prandial glycaemia and insulinaemia compared with an isonitrogenous, isoenergetic control condition (soy and skimmed milk) in healthy, young adults. In a recent study reduced post-prandial insulinaemia, but not glycaemia, was also shown with mycoprotein consumption (around 40 g dry weight) compared with an energy and macronutrient matched chicken meal in overweight adults. Again, the causative mechanism is likely linked to the amount (4 and 7 g, respectively)
and type of fibre contained in mycoprotein in these two studies, as viscous polysaccharides can reduce post-prandial glycaemia and insulinaemia.\textsuperscript{52} and 5 g of $\beta$-glucan has previously been shown to alter glycaemia and insulinaemia when consumed with a high carbohydrate load.\textsuperscript{53} Though the chitin-glucan matrix is insoluble and not viscous, chitin is likely to undergo alkaline deacetylation to produce the viscous polysaccharide chitosan at some stage of the gastrointestinal tract. In turn, this may confer resistance to the flow induced by gastrointestinal motility, reducing the small intestine contact time and resulting in slower gastric emptying and consequent nutrient absorption.\textsuperscript{54} Irrespective of the mechanism, importantly for translation to health, no data are yet available concerning whether these acute effects on post-prandial glycaemia extend to robust changes in insulin sensitivity and/or habitual glycaemic control when mycoprotein is incorporated within the daily diet.

**Mycoprotein and weight management**

With the growing obesity epidemic and associated health complications in the Western world,\textsuperscript{55} nutritional approaches to induce and sustain weight loss are desirable. Though weight loss under laboratory conditions via caloric restriction is relatively straightforward to achieve,\textsuperscript{56} under free-living conditions this tends to be more difficult. Further, subsequent weight regain appears to be the major barrier to longer term weight management.\textsuperscript{57} Primary reasons for these difficulties include a lack of satiety while maintaining an energy deficit,\textsuperscript{58} and a decline in basal metabolic rate due to loss of muscle mass.\textsuperscript{59,60} Diets relatively high in protein (often referring to simply maintaining absolute protein intake while creating an energy deficit by restricting carbohydrate and/or fats) have been suggested as a potential solution to these issues.\textsuperscript{8,57} For instance, when volunteers are subjected to *ad libitum* weight loss diets (i.e. more representative of free-living attempts at weight loss), those consuming diets higher in protein generally lose body mass and maintain this loss more effectively than those on lower protein diets.\textsuperscript{61,62} This
seems primarily attributable to the satiating effects of protein ingestion, meaning overall energy intake is lower,\textsuperscript{61} since isoenergetically controlled weight loss interventions show equivalent weight loss irrespective of protein content.\textsuperscript{61,62} It is also true that higher protein diets increase overall daily energy expenditure due to enhanced diet-induced thermogenesis and energy expenditure while sleeping, effects which occur irrespective of the protein type consumed.\textsuperscript{63,64} Furthermore, during isoenergetically controlled weight loss studies, it has typically been shown that higher protein diets increase the ratio of fat to lean mass loss that comprises overall body weight loss.\textsuperscript{65} Taken together, the impact of dietary protein during weight loss on satiety, daily energy expenditure and lean mass retention likely explain the effective role dietary protein plays in long term weight loss and management.\textsuperscript{8,57,61}

We have recently reported that mycoprotein leads to the acute thermogenic response following ingestion typical of other (animal) protein sources,\textsuperscript{15} and therefore would presumably contribute to overall daily energy expenditure during a weight loss regimen as described above. Additionally, mycoprotein and most mycoprotein containing products have a low energy density. The consumption of low energy density foods is positively associated with reduced \textit{ad libitum} energy intake, and positive weight management outcomes.\textsuperscript{66} As such, the substitution of high energy density foods for mycoprotein containing products may be an effective tool to manipulate the energy density of a meal or diet. As a low energy density high protein food source, it would also have theoretical value in a diet aimed at maintaining protein intake in an effort to retain lean tissue while in an energy deficit.

The effects of mycoprotein on satiety are also of particular interest. It has been shown previously that protein sources differ in their capacity to affect satiety.\textsuperscript{64} For example, gelatin protein provided as a single meal,\textsuperscript{67} or provided as a primary protein source over a 36 h experimental period,\textsuperscript{64} was reported to suppress appetite to a greater extent when compared with isonitrogenous milk protein equivalents, which the authors suggested may be related to
the central effects of amino acid composition. Differences in sensory characteristics, such as
greater viscosity and creaminess, may also play a role in increasing satiety and reducing energy
intake. Interestingly, Turnbull and colleagues demonstrated that consumption of a
mycoprotein meal resulted in acute appetite suppression and a subsequent reduction in *ad
libitum* food consumption for the remainder of the day (by 24%), and the following day (by
17%), when compared with an isoenergetic and isonitrogenous chicken meal. Similar
findings were reproduced by Burley and colleagues and Williamson et al. when consuming
around 30 and 10 g dry weight mycoprotein, respectively, and we also reported equivalent
satiety between mycoprotein and milk protein. In the Turnbull study, the authors attribute
these effects to the greater dietary fibre content of the mycoprotein condition (since the meals
were equivalent for energy and protein intake, fibre was necessarily higher). Additionally,
given the relatively small difference in fibre content between conditions (10 vs 17 g), they also
suggest either the specific type of fibre may be particularly potent, or an effect of slower gastric
emptying may explain these effects. Interestingly, both aspects could ultimately act by
modulating post-prandial (neuro) endocrine responses. However, a recent report of similar
increased satiety effects of mycoprotein compared with chicken in overweight and obese
individuals do not support a role of postprandial secretion of the gut peptide YY (PYY) or the
hormone glucagon-like peptide 1 (GLP-1) (both commonly purported to play a role in appetite
suppression with food intake) as a causative mechanism.

It is possible that various metabolites associated with the partial fermentation of the dietary
fibres may explain the potent appetite suppressive effect of mycoprotein. For example, the
SCFA propionate has been shown to induce PYY and GLP-1 in humans in acute settings and
may in part explain short-term appetite regulating effects of some dietary fibres. Both
mycoprotein and mycoprotein derived dietary fibre promote propionate production, but the
relevance of this mechanism in explaining effects on appetite regulation remains to be fully
elucidated. Irrespective of the mechanism, the effects on satiety, thermogenesis and the high protein/low energy content of mycoprotein position this food source as an intriguing approach to support a (ad libitum) diet aimed at weight loss and/or maintenance. Also worthy of note, lower glycaemic index diets have independently been shown to improve weight maintenance following weight loss during energy restriction. The capacity of mycoprotein to lower the glycaemic load of a meal or habitual diet adds an additional line of enquiry as to its potential utility within weight management. Well controlled longer-term laboratory weight loss studies comparing mycoprotein with other protein sources are warranted.

Mycoprotein and skeletal muscle adaptation

Adequate dietary protein intake is required for skeletal muscle mass maintenance and reconditioning. Skeletal muscle mass and its protein quality are maintained (or improved) through dynamic fluctuations in the rates of muscle protein synthesis and breakdown. In the overnight, fasted state muscle protein breakdown rates exceed muscle protein synthesis rates, leading to net muscle protein loss. Protein ingestion transiently (2-5 h) increases muscle protein synthesis rates, primarily due to elevated plasma essential amino acids of which leucine is of particular relevance. Protein ingestion also stimulates pancreatic insulin secretion which inhibits muscle protein breakdown, contributing to net muscle protein accretion (‘the anabolic response’) in the post-prandial state, and offsetting fasted protein losses. It is these diurnal oscillations in muscle protein balance which ultimately allow individuals to maintain muscle mass.

Individuals performing structured and prolonged physical activity will elicit skeletal muscle adaptive responses, such as increased muscle mass, muscle quality, contractile function, and/or muscle oxidative capacity. Performing physical activity stimulates muscle protein synthesis rates, and to a lesser extent muscle protein breakdown rates, improving muscle protein balance.
for up to 48 h. The accumulation of periods of exercise-induced muscle protein accretion ultimately drives skeletal muscle reconditioning. Following resistance training, this response primarily comprises the synthesis of myofibrillar proteins to support strength and mass related adaptations. Conversely, in response to endurance exercise, it is predominantly mitochondrial proteins which are synthesised to facilitate improved oxidative capacity. Consuming dietary protein in close temporal proximity to physical activity is an established strategy to further augment the muscle protein synthetic response compared with either stimulus alone. As a result, strategically (and modestly) increasing dietary protein consumption during prolonged training augments the skeletal muscle adaptive response to exercise training.

Since post-prandial muscle protein breakdown rates appear to be maximally inhibited with only mild elevations in circulating insulin, the anabolic potential of (post-exercise) dietary protein ingestion is assumed to be contingent on its capacity to stimulate muscle protein synthesis rates. Animal-derived proteins typically show high bioavailability and consequent rapid and/or sustained post-prandial aminoacidaemia and/or leucinaemia following ingestion. As a result, animal-derived dietary protein sources have been shown to be superior to plant-based protein sources in their capacity to stimulate muscle protein synthesis rates in humans. However, to date, wheat and soy (both relatively low in leucine and/or essential amino acids) are the only non-animal derived protein sources to be evaluated for their anabolic potential.

Mycoprotein is rich in essential amino acids (see Table 2) (~41% of total protein) and relatively high in leucine (~6% of total protein), and possesses a high PDCAAS score (0.99; an indirect indication of a protein’s digestibility). Based on this, we recently addressed whether these properties of mycoprotein translated to a high in vivo amino acid bioavailability compared with milk protein. We selected milk protein as the control comparator since this contains a high essential amino acid (~49% of total protein) and leucine content (~11% of total protein), a PDCAAS score of 1.0, and is consequently typically thought of as a near gold standard with...
respect to its potency for stimulating muscle protein synthesis rates and optimising training adaptations. We showed, in healthy young men, that the bioavailability of essential amino acids and leucine in the hours following ingestion of protein matched boluses of milk protein and mycoprotein were equivalent (though less rapid, and more sustained with mycoprotein ingestion). It is of note that to protein match these conditions approximately double the mass (and energy) of mycoprotein was consumed due to its ‘whole food’ nature. We went on to show that the amino acid bioavailability of mycoprotein increases in a dose-response fashion until between 60 and 80 g of mycoprotein (i.e. 27-36 g of protein; 2.1-2.9 g leucine) is consumed. As such, it seems likely that mycoprotein ingestion would stimulate a robust and, in larger quantities, optimal muscle protein synthetic response and thus be an alternative protein source to support muscle tissue reconditioning during prolonged training – questions which remain to be addressed. However, the magnitude of this response when compared with other protein sources would presumably depend on whether the overall systemic availability of (essential) amino acids or the speed at which they become available is the more crucial regulatory factor.

An interesting additional consideration is that mycoprotein represents a whole food source, rather than an isolated protein. The latter has generally been employed in studies addressing post-prandial muscle protein synthetic responses. While co-ingestion of carbohydrates or fats with isolated protein do not seem to modulate the postprandial muscle protein synthetic response, emerging data indicate that protein consumed within a whole food source may confer an anabolic advantage. It is not clear whether such effects are attributable to differing energy, macro/micronutrient contents, or aspects relating to a protein source’s specific food matrix. However, the relevance of evaluating the anabolic response to whole food sources is emerging as a key research area necessary to translate laboratory findings into information to refine dietary protein recommendations.
Mycoprotein and sarcopenia

In concert with a rising overall population, global demographics also indicate the number of individuals aged ≥60 years is set to triple by the year 2050, with the fastest growing sub-population being those aged over 85 years. A key hallmark of ageing is a progressive loss of skeletal muscle mass, strength, and aerobic capacity (termed sarcopenia). The association between muscle loss (mass and quality) and increased incidence of falls, fractures, metabolic disease and other health complications indicates that the burden of our ageing society on healthcare systems will increase dramatically over the upcoming decades. Importantly, it also underlines the critical role that skeletal muscle mass and quality play in healthy ageing.

Since basal, fasted muscle protein synthesis and breakdown rates do not appear to differ between healthy young and older adults, in an effort to explain the physiological mechanisms responsible for age-related sarcopenia, research has recently focussed on the anabolic response to food intake. Numerous studies have now demonstrated a blunted muscle protein synthetic response to protein ingestion in older adults and this “anabolic resistance” is now believed to be a key factor underlying age-related sarcopenia. It has been shown that anabolic resistance can be effectively compensated for on a per meal basis by consuming protein in close temporal proximity to physical activity, increasing the amount of protein consumed, and/or optimising the protein source. Based on this mechanistic understanding of senescent muscle protein metabolism, calls from the scientific community to increase recommended daily amount (and address optimal types) of protein to support healthy ageing are gaining momentum. Moreover, these recommendations are in line with epidemiological studies that reliably demonstrate that older adults who consume protein in excess (i.e. ~1.2 g per kilogram body mass) of the RDA (i.e. 0.8 g per kilogram body mass) experience lower rates of muscle mass, strength and functional capacity declines.
A pressing question is therefore arising; ‘where should this dietary protein to support healthy ageing come from?’ It will become increasingly important that this question be viewed through the potentially competing interests of where robust nutritional physiological investigation leads us, and the many issues that comprise environmental and government policy. The muscle protein synthetic response of senescent muscle to alternative, non-animal derived protein sources has scarcely been studied. Whether mycoprotein, based on similar principles as presented above, may provide an effective and sustainable dietary protein source to support healthy (and active) ageing remains to be investigated. While promising, the development of age-related anabolic resistance provides a challenge when considering the utility of mycoprotein. It would be expected that a relatively large dose of mycoprotein would be required to maximally stimulate the muscle protein synthetic response in older adults.\textsuperscript{107} Given that older adults generally display a reduced appetite compared with younger adults, paired with the potent satiating effect of mycoprotein, it would follow that consuming sufficient mycoprotein per meal (or over repeated meals to obtain daily intakes) may be challenging. Careful consideration to the other macronutrients that compose a higher (myco)protein meal would therefore be required. Clearly future research is warranted to establish whether mycoprotein could be used to support optimal muscle protein synthesis rates while avoiding positive or negative energy balance in older adults and therefore represent a viable strategy to support healthy ageing.

Conclusions and future directions

Developing sustainable dietary protein sources is a pressing socio-economic and environmental concern, and there is an obvious need to develop a robust evidence base to inform the use of such alternative sources. There is evidence that the incorporation of modest amounts of mycoprotein into the diet positively influences certain circulating lipid sub-fractions, and acute
mycoprotein ingestion attenuates postprandial glycaemia and/or insulinemia. These data are striking as they occur in the face of energy balanced conditions (i.e. are not an artefact of lower overall energy intake and/or consequent weight loss). These responses may be mediated by the unique digestive and metabolic properties of the chitin and β-glucan fibres present in mycoprotein, though a comprehensive and in vivo mechanistic understanding remains to be established. It is unknown how rapidly circulating cholesterol is affected when mycoprotein is incorporated into the diet, and a full characterisation of the lipid sub-fraction responses are not yet available. Furthermore, whether alterations of acute postprandial glycaemic control translate into improved insulin sensitivity and/or habitual glycaemic control when mycoprotein is incorporated in the daily diet is also unclear. Mycoprotein is a source of nutrients that can effectively induce satiety as evidenced by a reduced ad libitum energy intake, suggesting it may be a useful tool within weight management. This is especially true when considered alongside its potential as a high-quality protein source and as a modulator of postprandial glycaemia. As such, research into the ability of mycoprotein to modulate habitual glycaemic control, caloric intake, and weight management is clearly warranted. Emerging data have reported that mycoprotein is a bioavailable and insulinotropic protein source, and would therefore be expected to effectively stimulate muscle protein anabolism. Consequently, mycoprotein ingestion as a dietary protein source to stimulate muscle protein synthesis rates and promote muscle adaptation and/or maintenance in various populations (e.g. athletes, older adults) is a natural area of future research.
Key points

- Environmental concerns over increased dietary protein production requires the development of robust investigation into the nutritional value of alternative, sustainably produced dietary protein sources.

- Mycoprotein is a sustainably produced fungal-derived dietary protein source that has been shown to improve blood lipid profiles and acute post-prandial glucose control, and provides a potent satiety effect.

- Mycoprotein has a favourable amino acid composition and bioavailability when considering its potential to stimulate muscle protein synthesis rates.

- Future work should assess the anabolic potential of mycoprotein in various situations (e.g. resting, exercise) and populations (e.g. athletes, older adults).
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Conflicts of interest

BTW is currently receiving grant funding from Marlow Foods to perform research related to the content of this review, and PhD funding to support MOCC and AJM is provided, in part, by Marlow Foods. MVD is employed on a grant provided by Marlow Foods. Remaining authors declare no conflicts of interest.
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Figure Legends

**Figure 1** Greenhouse gas emissions (kg CO2e) and water usage (litres) required to produce a 30 g portion of protein from beef mince, milk, chicken, Quorn mince, Quorn pieces, and mycoprotein. Data were taken from Carbon Trust (2014) ‘Quorn, beef and chicken footprints’ internal report\(^{19}\), and additional data provided by (and reproduced with permission of) the Carbon Trust.
<table>
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<th>Nutrient Composition / 100 g</th>
<th>Leucine Matched*</th>
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<td></td>
<td>Protein (g)</td>
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<td>Mycoprotein (dw)</td>
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<tr>
<td>Whey protein</td>
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<td>Milk protein</td>
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<tr>
<td>Quorn pieces</td>
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<td>Chicken meat raw</td>
<td>21</td>
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Data adapted from internal analyses published in part previously,\textsuperscript{15} from Gorissen et al. (2018),\textsuperscript{16} and from the USDA Food Composition Database.\textsuperscript{17} Values are approximated based upon the data available. * Reflects the approximate amount of product and protein that is required to be consumed to obtain 2.5g leucine.
Table 2 – Amino acid content of mycoprotein, and commercially available protein isolates.

<table>
<thead>
<tr>
<th>Amino Acid Content</th>
<th>g / 100g mycoprotein (dw)</th>
<th>g / 100g whey protein</th>
<th>g / 100g milk protein</th>
<th>g / 100g egg protein</th>
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<td>Aspartic acid</td>
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<td>0.8</td>
<td>0.2</td>
<td>0.4</td>
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<td>Glycine</td>
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<tr>
<td>Leucine</td>
<td>3.9</td>
<td>8.6</td>
<td>7</td>
<td>3.6</td>
</tr>
<tr>
<td>Lysine</td>
<td>3.8</td>
<td>7.1</td>
<td>5.9</td>
<td>2.7</td>
</tr>
<tr>
<td>Methionine</td>
<td>1.0</td>
<td>1.8</td>
<td>2.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>2.3</td>
<td>2.5</td>
<td>3.5</td>
<td>2.3</td>
</tr>
<tr>
<td>Proline</td>
<td>2.0</td>
<td>4.8</td>
<td>7.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Serine</td>
<td>2.3</td>
<td>4</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>Threonine</td>
<td>2.5</td>
<td>5.4</td>
<td>3.5</td>
<td>2</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>0.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyrosine</td>
<td>1.8</td>
<td>2.4</td>
<td>3.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Valine</td>
<td>2.8</td>
<td>3.5</td>
<td>3.6</td>
<td>2</td>
</tr>
<tr>
<td>EAA</td>
<td>20.9</td>
<td>34.1</td>
<td>30.4</td>
<td>16.5</td>
</tr>
<tr>
<td>NEAA</td>
<td>24.6</td>
<td>34.9</td>
<td>38.7</td>
<td>19.0</td>
</tr>
<tr>
<td>BCAA</td>
<td>9.0</td>
<td>15.9</td>
<td>13.5</td>
<td>7.2</td>
</tr>
</tbody>
</table>

EAA, total essential amino acids; NEAA, total non-essential amino acids; BCAA, total branched chain amino acids.

Data adapted from internal analyses published in part previously,\textsuperscript{15} and from Gorissen et al. (2018).\textsuperscript{16}
Table 3 – Human studies investigating the metabolic effects of mycoprotein

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Participants</th>
<th>Type of study</th>
<th>Type of intervention</th>
<th>Intervention duration</th>
<th>Study findings</th>
</tr>
</thead>
</table>
| Udall et al.       | 100 | Healthy adults                    | Double-blind crossover trial           | Mycoprotein-based cookie supplementation (20 g dry wt/day) vs control cookies | 30 days               | 6.9 % ↓ plasma cholesterol  
No changes in body weight and other blood markers (glucose, urea, nitrogen, sodium, potassium, calcium, phosphorus, uric acid, creatinine, lactic acid dehydrogenase, alkaline phosphatase, amylase, SGOT, total protein, albumin, triglycerides, complete blood count).  
No changes in urine markers (pH, glucose, protein, ketones, white and red blood cells) |
| (1984)             |     |                                   |                                        |                                                            |                       | |
| Turnbull et al.    | 17  | Healthy adults with total cholesterol between 5.2–6.2 mmol/l | Randomised controlled parallel group trial | Mycoprotein (~191 g Quorn/day) vs meat during a fully controlled diet | 3 weeks               | 13% ↓ plasma cholesterol  
9% ↓ plasma LDL (12% ↑ in control group)  
12% ↑ plasma HDL (11% ↓ in control group)  
↓ 53% triglycerides (in both groups)  
No differences in body weight and blood pressure  
No changes in fasting insulin and glucose  
No changes in Apo A-I and Apo-B |
| (1990)             |     |                                   |                                        |                                                            |                       | |
| Turnbull et al.    | 21  | Healthy adults with total cholesterol > 5.2 mmol/l | Blinded randomised controlled parallel group trial | Mycoprotein-based cookie supplementation (26.9 g dry wt/day) vs control cookies | 8 weeks               | 7.9% ↓ plasma cholesterol  
12.6% ↓ plasma LDL  
No changes in plasma HDL cholesterol and triglycerides  
No changes in Apo A-I and Apo-B  
No differences in body weight |
| (1992)             |     |                                   |                                        |                                                            |                       | |
| Turnbull et al.    | 13  | Healthy females (non-restrained eaters) | Randomised controlled crossover trial | Energy-matched mycoprotein-based meal vs chicken-based meal | 2 days                | 24 % ↓ 24 h energy intake on day of the meal  
16.5 % ↓ 24 h energy intake on the day after  
↓ prospective food consumption and desire to eat 3 h after meal |
<p>| (1993)             |     |                                   |                                        |                                                            |                       | |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Participant Characteristics</th>
<th>Study Design</th>
<th>Intervention Description</th>
<th>Duration</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burley et al. (1993)&lt;sup&gt;24&lt;/sup&gt;</td>
<td>18</td>
<td>Healthy adults</td>
<td>Randomised controlled crossover trial</td>
<td>Energy-matched mycoprotein-based meal vs chicken-based meal</td>
<td>2 days</td>
<td>18 % ↓ energy intake in subsequent meal (resulting from no compensation after the reduction in the subsequent meal) No differences in 24 h energy intake on the day after No overall differences in eating rate and motivation to eat. Significant ↓ in hunger 4 h after the meal</td>
</tr>
<tr>
<td>Nakamura et al. (1994)&lt;sup&gt;25&lt;/sup&gt;</td>
<td>15</td>
<td>Healthy males</td>
<td>Randomised parallel group trial</td>
<td>Mycoprotein-based cookies/crisps supplementation (18 g or 24 g dry wt/day)</td>
<td>8 weeks</td>
<td>4.3 % ↓ plasma cholesterol in the 24 g mycoprotein group</td>
</tr>
<tr>
<td>Ishikawa (1995)&lt;sup&gt;26&lt;/sup&gt;</td>
<td>37</td>
<td>Hypercholesteraemic patients, with total cholesterol &gt; 220 mg/dl</td>
<td>Double-blind randomised controlled parallel group trial</td>
<td>Mycoprotein-based cookie supplementation (12 g or 24 g dry wt/day) vs control cookies</td>
<td>4 weeks</td>
<td>↓ plasma cholesterol</td>
</tr>
<tr>
<td>Homma et al. (1995)&lt;sup&gt;27&lt;/sup&gt;</td>
<td>52</td>
<td>Healthy males</td>
<td>Randomised crossover trial</td>
<td>Mycoprotein-based crisps supplementation (18 g or 24 g dry wt/day)</td>
<td>4 weeks</td>
<td>6.7 % ↓ plasma cholesterol in the 24 g mycoprotein group</td>
</tr>
<tr>
<td>Turnbull &amp; Ward (1995)&lt;sup&gt;28&lt;/sup&gt;</td>
<td>19</td>
<td>Healthy adults</td>
<td>Double-blind randomised controlled crossover trial</td>
<td>Mycoprotein-based milkshake (20 g dry wt) vs control milkshake</td>
<td>120 min</td>
<td>↓ glycaemia (13% at 60 min) ↓ insulinaemia (19% at 30 min and 36% at 60 min)</td>
</tr>
<tr>
<td>Williamson et al. (2006)&lt;sup&gt;29&lt;/sup&gt;</td>
<td>42</td>
<td>Overweight pre-menopausal females</td>
<td>Randomised controlled crossover trial</td>
<td>Mycoprotein-based preload meal vs tofu or chicken based preload meals before lunch</td>
<td>1 day</td>
<td>12.3% ↓ energy intake at lunch 20 mins after mycoprotein preload when compared with chicken preload No difference in intake at dinner (no compensation) No differences in subjective ratings of hunger and satiety</td>
</tr>
<tr>
<td>Ruxton &amp; McMillan (2010)&lt;sup&gt;30&lt;/sup&gt;</td>
<td>31 (21 mycoprotein, 10 control)</td>
<td>Healthy adults</td>
<td>Controlled parallel group trial</td>
<td>Mycoprotein-based diet (≥ 88 g wet; 21 g dry wt/day) vs animal-based diet</td>
<td>6 weeks</td>
<td>↓ plasma cholesterol in individuals with baseline cholesterol ≥ 4.19 mmol/L No changes in total cholesterol, LDL, HDL, triglycerides, glucose, blood pressure, BMI</td>
</tr>
<tr>
<td>Study</td>
<td>Participants</td>
<td>Design</td>
<td>Energy/Macronutrient Intake</td>
<td>Outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>--------------</td>
<td>--------</td>
<td>----------------------------</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bottin et al. (2016)&lt;sup&gt;31&lt;/sup&gt;</td>
<td>Overweight and obese adults</td>
<td>Single-blinded randomised controlled crossover trial</td>
<td>Part A: Energy matched mycoprotein-based preload meal (44, 88 or 132 g wet wt) vs chicken-based meal (equivalent amount of chicken and macronutrient matched at each protein content)</td>
<td>10% ↓ energy intake at lunch after high mycoprotein preload when compared with high chicken preload. 9% ↓ 24 h energy intake following mycoprotein ingestion. 8%, 12% and 21% ↓ insulin iAUC after low, medium and high mycoprotein preload, respectively. 21% and 16% ↓ in Insulinogenic and Disposition Indices, respectively, following mycoprotein ingestion. No differences in appetite ratings. No differences in postprandial glucose concentrations. No differences in plasma GLP-1 and PYY. No differences in gastric emptying. No differences in resting energy expenditure and substrate utilisation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Part A: 36</td>
<td></td>
<td>Part B: Macronutrient matched mycoprotein-based meal (132 g of wet wt) vs chicken-based meal</td>
<td>180 mins</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Part B: 14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dunlop et al. (2017)&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Healthy males</td>
<td>Single-blinded randomised controlled crossover trial</td>
<td>Mycoprotein-based drinks (20, 40, 60 and 80 g dry wt) vs milk protein drink</td>
<td>Equivalent postprandial amino acid bioavailability between protein matched amounts of mycoprotein and milk protein. Slower but more sustained hyperinsulinaemia and hyperaminoacidaemia compared with milk when protein matched. Dose response effects on all parameters until 60-80 g mycoprotein consumed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td></td>
<td></td>
<td>240 min</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

APO – Apolipoprotein; GLP-1 - Glucagon-like peptide-1; HDL – High density lipoprotein; iAUC – Incremental area under the curve; LDL – Low density lipoprotein; PYY - Peptide YY / Peptide tyrosine tyrosine; SGOT - Serum glutamic oxaloacetic transaminase