

Special article

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

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1 Abstract

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

18 **Introduction**

19 Developing a nutritionally sustainable future is an urgent contemporary issue. The world's
20 population is projected to increase from ~7.3 billion to >9 billion by 2050.¹ This is coupled
21 with global trends concerning rises in urbanization, social mobility and wealth creation, all
22 factors expected to exacerbate global food demand.¹ As a result, current and future generations
23 are required to view developments in the understanding of human nutrition through the lens of
24 mounting challenges associated with the sustainability of increased production.

25 When considering global dietary protein production requirements, demographic demands are
26 also compounded by accumulating scientific data to support protein consumption at levels
27 greater than currently accepted RDAs in various populations. For instance, evidence suggests
28 muscle mass maintenance in older adults,²⁻⁵ the promotion/retention of muscular training
29 adaptations in athletes^{6,7} and successful weight management⁸ are all supported by modest
30 increases in dietary protein intake above the currently accepted RDAs. It is clear, therefore,
31 that the global requirement for dietary protein production is a pressing societal issue that is
32 gathering momentum.

33 Crucially, the majority of data supporting the refinement of dietary protein requirements has
34 been obtained from studies examining the *in vivo* metabolic handling and/or adaptive responses
35 to animal-derived protein ingestion e.g. ^{9,10,11}. The carbon, water and land use footprints of
36 animal-derived protein production are anywhere from 8-80, 50-150 and 30-220 times,
37 respectively, greater than many plant-based proteins (variation dependent on protein source
38 and methods used to quantify).¹² Furthermore, vegan, vegetarian and flexitarian diets are
39 increasing in popularity.¹³ As such, research that investigates non-animal derived protein
40 sources is applicable to a progressively larger demographic, and the impact of such evidence
41 will rise correspondingly. It is therefore vital that the scientific community begin to examine

42 the metabolic handling and nutritional value of alternative, non-animal derived sustainable
43 protein sources.

44

45 **Mycoprotein**

46 Mycoprotein is a whole food source produced by continuous flow fermentation of the
47 filamentous fungus *Fusarium venenatum* (for a detailed description of the production processes
48 please see reference ¹⁴). The resultant product is a high protein, high fibre, and relatively low
49 energy complete food source (see Tables 1¹⁵⁻¹⁷ and 2^{15,16}) that is textured (via freezing) and
50 flavoured into a variety of products under the trade name Quorn (Marlow Foods, Stokesley,
51 North Yorkshire, UK). Importantly, the sustainability credentials of mycoprotein production
52 position it as an attractive alternative protein source to temper environmental concerns
53 associated with increased dietary protein production^{18,19} (see **Figure 1**).

54 Following its development in the 1960s, initial human experimentation during the 1970s
55 established the basic feasibility, tolerability and metabolic impact of mycoprotein
56 consumption, prior to it being available for general sale in 1985. By the end of the 1990s this
57 human research had begun to wane, with a complete list and summary of published human
58 mycoprotein studies performed to date shown in Table 3^{15,20-31}. However, the now fully
59 established commercial viability, environmental advantages, and alternative potential
60 applications of mycoprotein for metabolic health, skeletal muscle maintenance and
61 reconditioning has recently reignited research interest in this novel food source.

62

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

64 An initial human investigation aimed at establishing tolerability of mycoprotein made an
65 interesting ancillary observation.²⁰ Human volunteers who consumed 20 g mycoprotein (dry
66 weight) per day for 30 days (consumed as supplemental cookies) showed a ~7% decrease in

67 blood cholesterol concentrations (from 4.86 to 4.53 mmol/L),²⁰ which replicated earlier
68 findings in animals.³²⁻³⁴ Early research was then focussed in the potential health impact of
69 mycoprotein upon its dietary fibre content. This was due to an established body of
70 epidemiological studies reliably showing that higher fibre intakes (typically from fruit,
71 vegetables and cereals) are associated with reduced blood cholesterol concentrations, improved
72 blood lipid profiles, and reduced incidence of myocardial infarction and coronary heart
73 disease.³⁵⁻³⁸ Such findings have been confirmed during intervention studies where increasing
74 dietary fibre consumption has been reported to improve peripheral insulin sensitivity, and lower
75 blood cholesterol concentrations and glycated haemoglobin (HBA1c) in both healthy
76 individuals and patients with type-2 diabetes.^{39,40}

77 Follow-up studies focussing on mycoprotein consumption and cardio-metabolic health
78 confirmed and extended on these effects on blood lipid profiles.^{21,22} Turnbull and colleagues²¹
79 performed a 3-week dietary intervention study where 191 g mycoprotein containing products
80 (around 40 g dry weight of mycoprotein) was consumed per day, as part of a fully controlled
81 and laboratory supervised diet aimed at maintaining energy balance in individuals with mildly
82 elevated blood cholesterol concentrations. This tightly controlled study revealed that the
83 mycoprotein intervention resulted in reduced blood total cholesterol (from 5.54 to 4.81
84 mmol/L; 13% decrease) and low density lipoprotein (LDL) cholesterol (from 4.16 to 3.78
85 mmol/L; 9% decrease) concentrations, and an increase in high density lipoprotein (HDL)
86 cholesterol (from 0.58 to 0.65 mmol/L; 12% increase) concentrations. These results were even
87 more striking considering the control group generally showed opposite responses (as opposed
88 to no change). Given that the energy, macronutrient, lipid composition and cholesterol content
89 of the diets were similar across groups, it was assumed that fibre content was the causative
90 component.

91 The increased dietary fibre content could conceivably have exerted its cholesterol-lowering
92 effect by altering LDL cholesterol synthesis/degradation, cholesterol clearance in peripheral
93 tissues, and/or increased binding of fibre to neutral sterols, cholesterol or bile acids in the
94 intestine, resulting in decreased cholesterol entering the circulating pool. However, it is
95 noteworthy that the beneficial effects of higher fibre diets on circulating cholesterol
96 concentrations do not always extend to improvements in the specific lipid sub-fractions of LDL
97 and HDL.⁴¹ It is thus interesting to ponder whether the *type*, rather than simply the *amount*, of
98 dietary fibre contained within mycoprotein may, at least in part, explain the beneficial effects
99 of mycoprotein consumption on circulating cholesterol.

100 Dietary fibres contained within mycoprotein predominantly comprise 2/3 β -glucan and 1/3
101 chitin, which form a fibrous insoluble matrix that is relatively rare in more traditional food
102 sources. In keeping with the importance of fibre type, follow up work by Turnbull and
103 colleagues²² reported similar effects of mycoprotein consumption (a 0.95 mmol/L or 16% and
104 a 0.34 mmol/L or 21% reduction in total cholesterol and LDL cholesterol concentrations,
105 respectively) under free-living conditions despite keeping overall energy, macronutrient *and*
106 fibre content (around 6 g) the same across groups. Recent *in vitro* investigations have dug
107 deeper mechanistically here, and begun to shed light on potential mechanisms by which the
108 specific fibre profile of mycoprotein may affect gut microbiota to bring about these cholesterol
109 lowering effects within humans.

110 Protein and dietary fibres entering the large intestine become available for fermentation by the
111 gut microbiota.⁴² Fermentation of dietary fibres lead to the production of short-chain fatty acids
112 (SCFA), primarily acetate, propionate and butyrate in a molar ratio of approximately
113 60:20:20.⁴³ Fermentation of protein derived amino acids leads to production of phenols,
114 amines, ammonia, branched-chain fatty acids and SCFA. Dietary fibre fermentation is
115 prioritised over protein fermentation by the gut microbiota, and when fibre fermentation is

116 active the fate of dietary protein derived amino acids is bacterial cell biomass as opposed to
117 metabolism. Therefore, moving from fibre to protein fermentation has also been shown to have
118 profound effects on the composition of the gut microbiota.⁴⁴ SCFA production, and propionate
119 in particular, has been shown to reduce hepatic cholesterol synthesis via inhibition of β -
120 hydroxy- β -methylglutaryl coenzyme A (HMG-CoA) reductase (the rate-limiting enzyme
121 within cholesterol synthesis),⁴⁵ and suppress adipose tissue lipolysis.⁴⁶ In human studies using
122 inulin propionate ester, which delivers propionate directly to the large intestine, propionate has
123 been demonstrated to reduce LDL cholesterol and improve liver function and insulin
124 sensitivity.^{47,48} However, the current evidence around propionate is inconsistent, with another
125 study suggesting that its consumption leads to insulin resistance and compensatory
126 hyperinsulinemia.⁴⁹ Using *in vitro* colonic models, mycoprotein and its purified dietary fibre
127 have been shown to be fermentable, producing SCFA.⁵⁰ Both mycoprotein and purified
128 mycoprotein dietary fibre exhibit increased propionate and butyrate production at the cost of
129 acetate, and increasing colonic propionate production inhibits the incorporation of plasma
130 acetate into cholesterol.⁵¹ Consequently, data are now available to suggest that the digestive
131 and metabolic properties of the unique fibre profile present within mycoprotein clearly
132 warrants future (*in vivo*) research.

133 The beneficial metabolic effects of mycoprotein consumption have also been shown to extend
134 to acute postprandial glycaemic control.^{28,31} It was reported that 20 g mycoprotein (dry weight)
135 consumed during an oral glucose tolerance test resulted in reduced post-prandial glycaemia
136 and insulinaemia compared with an isonitrogenous, isoenergetic control condition (soy and
137 skimmed milk) in healthy, young adults.²⁸ In a recent study³¹ reduced post-prandial
138 insulinaemia, but not glycaemia, was also shown with mycoprotein consumption (around 40 g
139 dry weight) compared with an energy and macronutrient matched chicken meal in overweight
140 adults. Again, the causative mechanism is likely linked to the amount (4 and 7 g, respectively)

141 and type of fibre contained in mycoprotein in these two studies, as viscous polysaccharides can
142 reduce post-prandial glycaemia and insulinaemia,⁵² and 5 g of β -glucan has previously been
143 shown to alter glycaemia and insulinaemia when consumed with a high carbohydrate load.⁵³
144 Though the chitin-glucan matrix is insoluble and not viscous, chitin is likely to undergo alkaline
145 deacetylation to produce the viscous polysaccharide chitosan at some stage of the
146 gastrointestinal tract. In turn, this may confer resistance to the flow induced by gastrointestinal
147 motility, reducing the small intestine contact time and resulting in slower gastric emptying and
148 consequent nutrient absorption.⁵⁴ Irrespective of the mechanism, importantly for translation to
149 health, no data are yet available concerning whether these acute effects on post-prandial
150 glycaemia extend to robust changes in insulin sensitivity and/or habitual glycaemic control
151 when mycoprotein is incorporated within the daily diet.

152

153 **Mycoprotein and weight management**

154 With the growing obesity epidemic and associated health complications in the Western world,⁵⁵
155 nutritional approaches to induce and sustain weight loss are desirable. Though weight loss
156 under laboratory conditions via caloric restriction is relatively straightforward to achieve,⁵⁶
157 under free-living conditions this tends to be more difficult. Further, subsequent weight regain
158 appears to be the major barrier to longer term weight management.⁵⁷ Primary reasons for these
159 difficulties include a lack of satiety while maintaining an energy deficit,⁵⁸ and a decline in basal
160 metabolic rate due to loss of muscle mass.^{59,60} Diets relatively high in protein (often referring
161 to simply maintaining absolute protein intake while creating an energy deficit by restricting
162 carbohydrate and/or fats) have been suggested as a potential solution to these issues.^{8,57} For
163 instance, when volunteers are subjected to *ad libitum* weight loss diets (i.e. more representative
164 of free-living attempts at weight loss), those consuming diets higher in protein generally lose
165 body mass and maintain this loss more effectively than those on lower protein diets.^{61,62} This

166 seems primarily attributable to the satiating effects of protein ingestion, meaning overall energy
167 intake is lower,⁶¹ since isoenergetically controlled weight loss interventions show equivalent
168 weight loss irrespective of protein content.^{61,62} It is also true that higher protein diets increase
169 overall daily energy expenditure due to enhanced diet-induced thermogenesis and energy
170 expenditure while sleeping, effects which occur irrespective of the protein type consumed.^{63,64}
171 Furthermore, during isoenergetically controlled weight loss studies, it has typically been shown
172 that higher protein diets increase the ratio of fat to lean mass loss that comprises overall body
173 weight loss.⁶⁵ Taken together, the impact of dietary protein during weight loss on satiety, daily
174 energy expenditure and lean mass retention likely explain the effective role dietary protein
175 plays in long term weight loss and management.^{8,57,61}

176 Mycoprotein ingestion has been shown to induce an acute thermogenic response similar to that
177 seen following the ingestion of other (animal) protein sources,¹⁵ and therefore would
178 presumably contribute to overall daily energy expenditure during a weight loss regimen as
179 described above. Additionally, mycoprotein and most mycoprotein containing products have a
180 low energy density. The consumption of low energy density foods is positively associated with
181 reduced *ad libitum* energy intake, and positive weight management outcomes.⁶⁶ As such, the
182 substitution of high energy density foods for mycoprotein containing products may be an
183 effective tool to manipulate the energy density of a meal or diet. As a low energy density high-
184 protein food source, it would also have theoretical value in a diet aimed at maintaining protein
185 intake in an effort to retain lean tissue while in an energy deficit.

186 The effects of mycoprotein on satiety are also of particular interest. It has been shown
187 previously that protein sources differ in their capacity to affect satiety.⁶⁴ For example, gelatin
188 protein provided as a single meal,⁶⁷ or provided as a primary protein source over a 36 h
189 experimental period,⁶⁴ was reported to suppress appetite to a greater extent when compared
190 with isonitrogenous milk protein equivalents, which the authors suggested may be related to

191 the central effects of amino acid composition. Differences in sensory characteristics, such as
192 greater viscosity and creaminess, may also play a role in increasing satiety and reducing energy
193 intake.⁶⁸⁻⁷¹ Interestingly, Turnbull and colleagues demonstrated that consumption of a
194 mycoprotein meal resulted in acute appetite suppression and a subsequent reduction in *ad*
195 *libitum* food consumption for the remainder of the day (by 24%), and the following day (by
196 17%), when compared with an isoenergetic and isonitrogenous chicken meal.²³ Similar
197 findings were reproduced by Burley and colleagues²⁴ and Williamson et al.²⁹ when consuming
198 around 30 and 10 g dry weight mycoprotein, respectively, and we also reported equivalent
199 satiety between mycoprotein and milk protein.¹⁵ In the Turnbull study,²³ the authors attribute
200 these effects to the greater dietary fibre content of the mycoprotein condition (since the meals
201 were equivalent for energy and protein intake, fibre was necessarily higher). Additionally,
202 given the relatively small difference in fibre content between conditions (10 vs 17 g), they also
203 suggest either the specific type of fibre may be particularly potent, or an effect of slower gastric
204 emptying may explain these effects. Interestingly, both aspects could ultimately act by
205 modulating post-prandial (neuro) endocrine responses. However, a recent report of similar
206 increased satiety effects of mycoprotein compared with chicken in overweight and obese
207 individuals do not support a role of postprandial secretion of the gut peptide YY (PYY) or the
208 hormone glucagon-like peptide 1 (GLP-1) (both commonly purported to play a role in appetite
209 suppression with food intake) as a causative mechanism.³¹

210 It is possible that various metabolites associated with the partial fermentation of the dietary
211 fibres may explain the potent appetite suppressive effect of mycoprotein.³¹ For example, the
212 SCFA propionate has been shown to induce PYY and GLP-1 in humans in acute settings and
213 may in part explain short-term appetite regulating effects of some dietary fibres.⁴⁷ Both
214 mycoprotein and mycoprotein derived dietary fibre promote propionate production, but the
215 relevance of this mechanism in explaining effects on appetite regulation remains to be fully

216 elucidated.⁵⁰ Irrespective of the mechanism, the effects on satiety, thermogenesis and the high
217 protein/low energy content of mycoprotein position this food source as an intriguing approach
218 to support a (*ad libitum*) diet aimed at weight loss and/or maintenance. Also worthy of note,
219 lower glycaemic index diets have independently been shown to improve weight maintenance
220 following weight loss during energy restriction.⁵⁷ The capacity of mycoprotein to lower the
221 glycaemic load of a meal or habitual diet adds an additional line of enquiry as to its potential
222 utility within weight management. Well controlled longer-term laboratory weight loss studies
223 comparing mycoprotein with other protein sources are warranted.

224

225 **Mycoprotein and skeletal muscle adaptation**

226 Adequate dietary protein intake is required for skeletal muscle mass maintenance and
227 reconditioning. Skeletal muscle mass and its protein quality are maintained (or improved)
228 through dynamic fluctuations in the rates of muscle protein synthesis and breakdown. In the
229 overnight, fasted state muscle protein breakdown rates exceed muscle protein synthesis rates,
230 leading to net muscle protein loss.⁷² Protein ingestion transiently (2-5 h) increases muscle
231 protein synthesis rates,⁷³ primarily due to elevated plasma essential amino acids⁷⁴ of which
232 leucine is of particular relevance.^{10,75} Protein ingestion also stimulates pancreatic insulin
233 secretion which inhibits muscle protein breakdown,⁷⁶ contributing to net muscle protein
234 accretion ('the anabolic response') in the post-prandial state, and offsetting fasted protein
235 losses. It is these diurnal oscillations in muscle protein balance which ultimately allow
236 individuals to maintain muscle mass.

237 Individuals performing structured and prolonged physical activity will elicit skeletal muscle
238 adaptive responses, such as increased muscle mass, muscle quality, contractile function, and/or
239 muscle oxidative capacity. Performing physical activity stimulates muscle protein synthesis
240 rates, and to a lesser extent muscle protein breakdown rates, improving muscle protein balance

241 for up to 48 h.⁷⁷ The accumulation of periods of exercise-induced muscle protein accretion
242 ultimately drives skeletal muscle reconditioning. Following resistance training, this response
243 primarily comprises the synthesis of myofibrillar proteins to support strength and mass related
244 adaptations.⁷⁸ Conversely, in response to endurance exercise, it is predominantly mitochondrial
245 proteins which are synthesised to facilitate improved oxidative capacity.⁷⁸ Consuming dietary
246 protein in close temporal proximity to physical activity is an established strategy to further
247 augment the muscle protein synthetic response compared with either stimulus alone.^{79,80} As a
248 result, strategically (and modestly) increasing dietary protein consumption during prolonged
249 training augments the skeletal muscle adaptive response to exercise training.^{81,82}

250 Since post-prandial muscle protein breakdown rates appear to be maximally inhibited with only
251 mild elevations in circulating insulin,⁸³ the anabolic potential of (post-exercise) dietary protein
252 ingestion is assumed to be contingent on its capacity to stimulate muscle protein synthesis rates.
253 Animal-derived proteins typically show high bioavailability and consequent rapid and/or
254 sustained post-prandial aminoacidaemia and/or leucinaemia following ingestion.^{10,84-86} As a
255 result, animal-derived dietary protein sources have been shown to be superior to plant-based
256 protein sources in their capacity to stimulate muscle protein synthesis rates in humans.^{86,87}

257 However, to date, wheat and soy (both relatively low in leucine and/or essential amino acids⁸⁸)
258 are the only non-animal derived protein sources to be evaluated for their anabolic potential.
259 Mycoprotein is rich in essential amino acids (see Table 2) (~41% of total protein) and relatively
260 high in leucine (~6% of total protein), and possesses a high PDCAAS score (0.99; an indirect
261 indication of a protein's digestibility). The *in vivo* amino acid bioavailability of mycoprotein
262 was recently investigated in comparison to isolated milk protein.¹⁵ Milk protein was selected
263 as the control comparator since this contains a high essential amino acid (~49% of total protein)
264 and leucine content (~11% of total protein), a PDCAAS score of 1.0, and is consequently
265 typically thought of as a near gold standard protein source with respect to its potency for

266 stimulating muscle protein synthesis rates⁸⁹ and optimising training adaptations.⁹⁰ The findings
267 showed that, in healthy young men, the bioavailability of essential amino acids and leucine in
268 the hours following the ingestion of protein matched boluses of milk protein and mycoprotein
269 were equivalent (though less rapid, and more sustained with mycoprotein ingestion).¹⁵ It is of
270 note that to protein match these conditions approximately double the mass (and energy) of
271 mycoprotein was consumed due to its ‘whole food’ nature. It was also found that the amino
272 acid bioavailability of mycoprotein increases in a dose-response fashion until between 60 and
273 80 g of mycoprotein (i.e. 27-36 g of protein; 2.1-2.9 g leucine) is consumed. As such, it seems
274 likely that mycoprotein ingestion would stimulate a robust and, in larger quantities, optimal
275 muscle protein synthetic response and thus be an alternative protein source to support muscle
276 tissue reconditioning during prolonged training – questions which remain to be addressed.
277 However, the magnitude of this response when compared with other protein sources would
278 presumably depend on whether the overall systemic availability of (essential) amino acids or
279 the speed at which they become available is the more crucial regulatory factor.^{84,91}

280 An interesting additional consideration is that mycoprotein represents a whole food source,
281 rather than an isolated protein. The latter has generally been employed in studies addressing
282 post-prandial muscle protein synthetic responses. While co-ingestion of carbohydrates or fats
283 with isolated protein do not seem to modulate the postprandial muscle protein synthetic
284 response,⁹²⁻⁹⁴ emerging data indicate that protein consumed within a whole food source may
285 confer an anabolic advantage.^{95,96} It is not clear whether such effects are attributable to differing
286 energy, macro/micronutrient contents, or aspects relating to a protein source’s specific food
287 matrix. However, the relevance of evaluating the anabolic response to whole food sources is
288 emerging as a key research area necessary to translate laboratory findings into information to
289 refine dietary protein recommendations.⁹⁶⁻⁹⁸

290

291 **Mycoprotein and sarcopenia**

292 In concert with a rising overall population, global demographics also indicate the number of
293 individuals aged ≥ 60 years is set to triple by the year 2050, with the fastest growing sub-
294 population being those aged over 85 years.⁹⁹ A key hallmark of ageing is a progressive loss of
295 skeletal muscle mass, strength, and aerobic capacity (termed sarcopenia).¹⁰⁰ The association
296 between muscle loss (mass and quality) and increased incidence of falls, fractures, metabolic
297 disease and other health complications indicates that the burden of our ageing society on health-
298 care systems will increase dramatically over the upcoming decades. Importantly, it also
299 underlines the critical role that skeletal muscle mass and quality play in healthy ageing.

300 Since basal, fasted muscle protein synthesis and breakdown rates do not appear to differ
301 between healthy young and older adults,^{11,101-104} in an effort to explain the physiological
302 mechanisms responsible for age-related sarcopenia, research has recently focussed on the
303 anabolic response to food intake. Numerous studies have now demonstrated a blunted muscle
304 protein synthetic response to protein ingestion in older adults^{11,102,105} and this “anabolic
305 resistance” is now believed to be a key factor underlying age-related sarcopenia. It has been
306 shown that anabolic resistance can be effectively compensated for on a per meal basis by
307 consuming protein in close temporal proximity to physical activity,¹⁰⁶ increasing the amount
308 of protein consumed,^{85,107} and/or optimising the protein source.^{10,84} Based on this mechanistic
309 understanding of senescent muscle protein metabolism, calls from the scientific community to
310 increase recommended daily amount (and address optimal types) of protein to support healthy
311 ageing are gaining momentum.^{3,4,108} Moreover, these recommendations are in line with
312 epidemiological studies that reliably demonstrate that older adults who consume protein in
313 excess (i.e. ~ 1.2 g per kilogram body mass) of the RDA (i.e. 0.8 g per kilogram body mass)
314 experience lower rates of muscle mass, strength and functional capacity declines.^{109,110}

315 A pressing question is therefore arising; ‘where should this dietary protein to support healthy
316 ageing come from?’ It will become increasingly important that this question be viewed through
317 the potentially competing interests of where robust nutritional physiological investigation leads
318 to, and the many issues that comprise environmental and government policy. The muscle
319 protein synthetic response of senescent muscle to alternative, non-animal derived protein
320 sources has scarcely been studied.

321 Whether mycoprotein, based on similar principles as presented above, may provide an effective
322 and sustainable dietary protein source to support healthy (and active) ageing remains to be
323 investigated. While promising, the development of age-related anabolic resistance provides a
324 challenge when considering the utility of mycoprotein. It would be expected that a relatively
325 large dose of mycoprotein would be required to maximally stimulate the muscle protein
326 synthetic response in older adults.¹⁰⁷ Given that older adults generally display a reduced
327 appetite compared with younger adults, paired with the potent satiating effect of mycoprotein,
328 it would follow that consuming sufficient mycoprotein per meal (or over repeated meals to
329 obtain daily intakes) may be challenging. Careful consideration to the other macronutrients that
330 compose a higher (myco)protein meal would therefore be required. Clearly future research is
331 warranted to establish whether mycoprotein could be used to support optimal muscle protein
332 synthesis rates while avoiding positive or negative energy balance in older adults and therefore
333 represent a viable strategy to support healthy ageing.

334

335 **Conclusions and future directions**

336 Developing sustainable dietary protein sources is a pressing socio-economic and environmental
337 concern, and there is an obvious need to develop a robust evidence base to inform the use of
338 such alternative sources. There is evidence that the incorporation of modest amounts of
339 mycoprotein into the diet positively influences certain circulating lipid sub-fractions, and acute

340 mycoprotein ingestion attenuates postprandial glycaemia and/or insulinemia. These data are
341 striking as they occur in the face of energy balanced conditions (i.e. are not an artefact of lower
342 overall energy intake and/or consequent weight loss). These responses may be mediated by the
343 unique digestive and metabolic properties of the chitin and β -glucan fibres present in
344 mycoprotein, though a comprehensive and *in vivo* mechanistic understanding remains to be
345 established. It is unknown how rapidly circulating cholesterol is affected when mycoprotein is
346 incorporated into the diet, and a full characterisation of the lipid sub-fraction responses are not
347 yet available. Furthermore, whether alterations of acute postprandial glycaemic control
348 translate into improved insulin sensitivity and/or habitual glycaemic control when mycoprotein
349 is incorporated in the daily diet is also unclear. Mycoprotein is a source of nutrients that can
350 effectively induce satiety as evidenced by a reduced *ad libitum* energy intake, suggesting it
351 may be a useful tool within weight management. This is especially true when considered
352 alongside its potential as a high-quality protein source and as a modulator of postprandial
353 glycaemia. As such, research into the ability of mycoprotein to modulate habitual glycaemic
354 control, caloric intake, and weight management is clearly warranted. Emerging data have
355 reported that mycoprotein is a bioavailable and insulinotropic protein source, and would
356 therefore be expected to effectively stimulate muscle protein anabolism. Consequently,
357 mycoprotein ingestion as a dietary protein source to stimulate muscle protein synthesis rates
358 and promote muscle adaptation and/or maintenance in various populations (e.g. athletes, older
359 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

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Authors' contributions

MOCC and AJM prepared figures/tables and performed literature searches. MOCC, AJM and BTW drafted the manuscript. MVD, HCH, DJM and FBS read and provided intellectual input into draft versions of the manuscript. All authors read and approved the final manuscript.

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Table Legends

Table 1 Nutritional content of mycoprotein, commercially available protein isolates, Quorn vegan pieces, and a selection of commonly consumed protein sources.

Table 2 Amino acid content of mycoprotein, and commercially available protein isolates.

Table 3 Human studies investigating the metabolic effects of mycoprotein

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 report¹⁹, and additional data provided by (and reproduced with permission of) the Carbon Trust.

Table 1 – Nutritional content of mycoprotein, commercially available protein isolates, Quorn vegan pieces, and a selection of commonly consumed protein sources.

	Nutrient Composition / 100 g					Leucine Matched*			
	Protein (g)	Fat (g)	Carbohydrate (g)	Fibre (g)	Energy (kcal)	Energy (Kj)	Leucine (g)	Product (g)	Protein (g)
Mycoprotein (dw)	45	13	10	25	340	1423	3.9	64	29
Whey protein	80	7	5	<0.1	402	1682	8.6	29	23
Milk protein	80	1	6	<0.1	350	1464	7.0	36	29
Quorn pieces	15	3	4	5	113	473	1.2	208	32
Whole egg raw	13	10	<1	<1	143	598	1.1	230	29
Beef mince (5%) raw	21	5	0	0	137	573	1.7	150	32
Chicken meat raw	21	3	0	0	119	498	1.6	156	33
Cod meat raw	18	1	0	0	82	343	1.4	173	31

Data adapted from internal analyses published in part previously,¹⁵ from Gorissen et al. (2018),¹⁶ and from the USDA Food Composition Database.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.

Amino Acid Content	g / 100g mycoprotein (dw)	g / 100g whey protein	g / 100g milk protein	g / 100g egg protein
Alanine	2.8	4.2	2.6	2.6
Arginine	3.3	1.7	2.6	2.6
Aspartic acid	4.6			
Cystine	0.4	0.8	0.2	0.4
Glutamic Acid	5.6	15.5	16.7	5.1
Glycine	2.0	1.5	1.5	1.4
Histidine	1.6	1.4	1.9	0.9
Iso-Leucine	2.4	3.8	2.9	1.6
Leucine	3.9	8.6	7	3.6
Lysine	3.8	7.1	5.9	2.7
Methionine	1.0	1.8	2.1	1.4
Phenylalanine	2.3	2.5	3.5	2.3
Proline	2.0	4.8	7.3	1.8
Serine	2.3	4	4	3.3
Threonine	2.5	5.4	3.5	2
Tryptophan	0.8			
Tyrosine	1.8	2.4	3.8	1.8
Valine	2.8	3.5	3.6	2
EAA	20.9	34.1	30.4	16.5
NEAA	24.6	34.9	38.7	19.0
BCAA	9.0	15.9	13.5	7.2

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,¹⁵ and from Gorissen et al. (2018).¹⁶

Table 3 – Human studies investigating the metabolic effects of mycoprotein

Reference	<i>n</i>	Participants	Type of study	Type of intervention	Intervention duration	Study findings
Udall et al. (1984) ²⁰	100	Healthy adults	Double-blind cross-over 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)
Turnbull et al. (1990) ²¹	17 (9 mycoprotein, 8 control)	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
Turnbull et al. (1992) ²²	21 (11 mycoprotein, 10 control)	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
Turnbull et al. (1993) ²³	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

Burley et al. (1993)²⁴	18	Healthy adults	Randomised controlled crossover trial	Energy-matched mycoprotein-based meal vs chicken-based meal	2 days	18 % ↓ energy intake in subsequent meal ↓ 24 h energy intake on the day of the 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
Nakamura et al. (1994)²⁵	15	Healthy males	Randomised parallel group trial	Mycoprotein-based cookies/crisps supplementation (18 g or 24 g dry wt/day)	8 weeks	4.3 % ↓ plasma cholesterol in the 24 g mycoprotein group
Ishikawa (1995)²⁶	37	Hypercholesterolaemic patients, with total cholesterol > 220 mg/dl	Double-blind randomised controlled parallel group trial	Mycoprotein-based cookie supplementation (12 g or 24 g dry wt/day) vs control cookies	4 weeks	↓ plasma cholesterol
Homma et al. (1995)²⁷	52	Healthy males	Randomised crossover trial	Mycoprotein-based crisps supplementation (18 g or 24 g dry wt/day)	4 weeks	6.7 % ↓ plasma cholesterol in the 24 g mycoprotein group
Turnbull & Ward (1995)²⁸	19	Healthy adults	Double-blind randomised controlled crossover trial	Mycoprotein-based milkshake (20 g dry wt) vs control milkshake	120 min	↓ glycaemia (13% at 60 min) ↓ insulinaemia (19% at 30 min and 36% at 60 min)
Williamson et al. (2006)²⁹	42	Overweight pre-menopausal females	Randomised controlled crossover trial	Mycoprotein-based preload meal vs tofu or chicken based preload meals before lunch	1 day	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
Ruxton & McMillan (2010)³⁰	31 (21 mycoprotein, 10 control)	Healthy adults	Controlled parallel group trial	Mycoprotein-based diet (≥ 88 g wet; 21 g dry wt/day) vs animal-based diet	6 weeks	↓ plasma cholesterol in individuals with baseline cholesterol ≥ 4.19 mmol/L No changes in total cholesterol, LDL, HDL, triglycerides, glucose, blood pressure, BMI

						and waist circumference for the sample as a whole
Bottin et al. (2016) ³¹	Part A: 36 Part B: 14	Overweight and obese adults	Single-blinded randomised controlled crossover trial	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) Part B: Macronutrient matched mycoprotein-based meal (132 g of wet wt) vs chicken-based meal	180 mins	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 9% ↑ in Matsuda Index 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
Dunlop et al. (2017) ¹⁵	12	Healthy males	Single-blinded randomised controlled crossover trial	Mycoprotein-based drinks (20, 40, 60 and 80 g dry wt) vs milk protein drink	240 min	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.

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