



Bio Mamps

Akkermansia muciniphila

Melhora da barreira intestinal

Benefícios na obesidade

Parabioticos – BioMamps

Fração proteica probiótica na forma de lisados celulares que quando administradas em quantidades adequadas, conferem benefício ao hospedeiro.

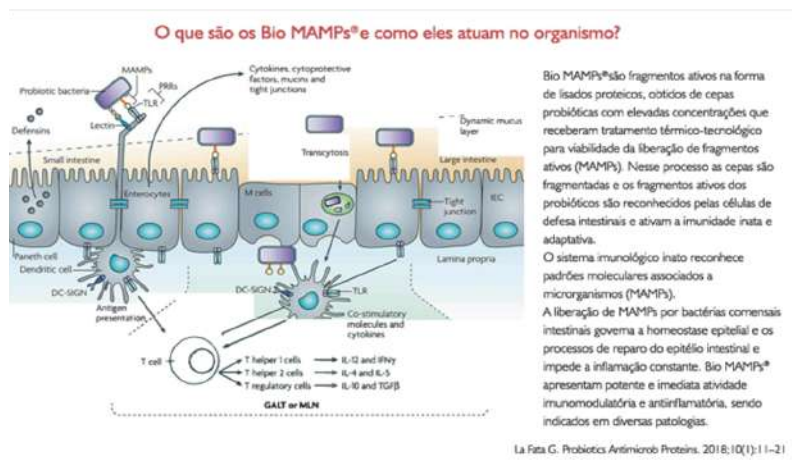
Bio MAMPs® Akkermansia muciniphila

Bio MAMPs® Akkermansia muciniphila são fragmentos ativos na forma de lisados proteicos provenientes da bactéria Akkermansia muciniphila. Esse micro-organismo tem sido associado na literatura com a redução da obesidade e da síndrome metabólica, bem como de doenças associadas, a exemplo da intolerância à glicose, resistência à insulina, esteatose hepática e ainda a regulação da microbiota intestinal.

O Bio MAMPs® Akkermansia muciniphila tem mostrado eficácia no tratamento das doenças citadas, contornando as limitações de manutenção de A. muciniphila viva.

Posologia

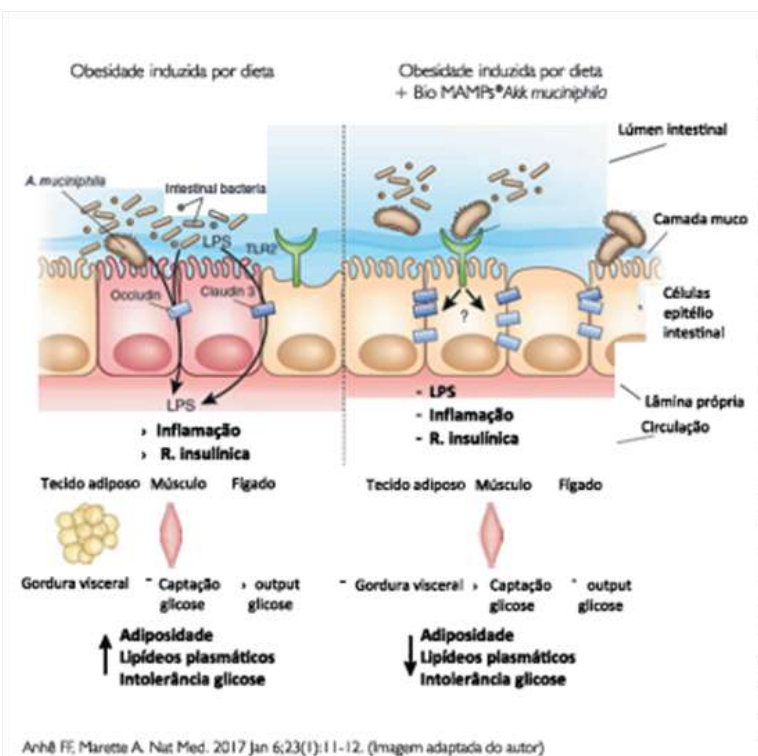
A recomendação oral é de 25 mg, duas vezes ao dia.



La Fata G. Probiotics Antimicrob Proteins. 2018;10(1):1-21

MECANISMO DE AÇÃO

- Por meio da manutenção do equilíbrio da microbiota intestinal e da melhora da integridade da barreira intestinal.
- Estudos apontam que pessoas com obesidade apresentam desequilíbrio da flora intestinal, acompanhado de uma maior passagem de lipossacarídeos bacterianos (LPS) para a circulação (endotoxemia), o que, por sua vez, contribui para a indução da inflamação, a resistência insulínica, o aumento de adiposidade, entre outros distúrbios.
- Essas pessoas também apresentam aumento da adiposidade visceral e sensibilidade prejudicada à insulina no músculo e no fígado quando comparados a pessoas saudáveis
- Estudos também demonstraram que o Bio MAMPs® Akkermansia muciniphila foi capaz de ativar receptores toll-like-receptor do tipo 2 (TLR2), de intestino murino, localizado na borda apical das vilosidades e criptas.
- E simultaneamente levou ao aumento da expressão de genes relacionados às proteínas tight junctions claudina 3 e ocludina, que aumentam a integridade da barreira intestinal.
- Reduziu a endotoxemia metabólica em pessoas que se alimentam com dieta rica em gordura, o que melhorou significativamente o metabolismo de glicose e lipídeos e reduziu a massa gorda.



Anhê FE, Marette A. Nat Med. 2017 Jan 6;23(1):11-12. (Imagem adaptada do autor)





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ESTUDOS

Eficácia clínica em pacientes obesos

Um estudo randomizado, duplo cego e controlado por placebo avaliou o efeito do Bio MAMPs® Akkermansia muciniphila em 40 indivíduos com excesso de peso corporal (sobrepeso ou obesidade), resistência à insulina e síndrome metabólica. Os indivíduos foram randomizados para receber placebo, A. muciniphila viva (1010 bactérias por dia) ou Bio MAMPs® Akkermansia muciniphila (50 mg por dia) durante 3 meses, com o conselho específico para manter sua dieta normal e atividade física durante o período de estudo. Os resultados demonstram que a administração de Bio MAMPs® Akkermansia muciniphila proporcionou a redução do peso corporal em, aproximadamente, -2,27 kg (P - 0,09), a massa gorda em, aproximadamente, -1,37 kg (P - 0,09) e a circunferência do quadril em -2,63 cm (P = 0,09) em comparação com o grupo placebo. A circunferência da cintura reduziu aproximadamente 1,56 cm, mas essa alteração não atingiu significância estatística. Essas diferenças são todas de relevância clínica no contexto de distúrbios metabólicos e não podemos descartar que a melhora de diferentes parâmetros metabólicos está associada ao impacto da suplementação no peso corporal, massa gorda e circunferência do quadril. A administração de Bio MAMPs® Akkermansia muciniphila diminuiu significativamente o colesterol total em 8,68% em comparação com o placebo, enquanto o LDL foi -7,53% mais baixo e os triglicerídeos foram -15,7% mais baixos. Além disso, os pacientes apresentaram melhora significativa no índice de sensibilidade à insulina em cerca de 30% em comparação com o grupo de placebo e ainda redução significativa do escore de resistência insulina (HOMA).

Múltiplos Mecanismos Antiobesidade

Surpreendentemente, Bio MAMPs® Akkermansia muciniphila reduziu significativamente os níveis de MAT, ALT e AST após 3 meses em comparação com a linha de base. Particularmente, os níveis de GGT diminuíram marcante e significativamente em cerca de 24% no grupo de Bio MAMPs® Akkermansia muciniphila em comparação com os níveis de T3 observados no grupo de placebo (P = 0,009). Nenhum desses parâmetros foi afetado pela suplementação com A. muciniphila viva.

Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity.

Obesity and type 2 diabetes are characterized by altered gut microbiota, inflammation, and gut barrier disruption. Microbial composition and the mechanisms of interaction with the host that affect gut barrier function during obesity and type 2 diabetes have not been elucidated. We recently isolated Akkermansia muciniphila, which is a mucin-degrading bacterium that resides in the mucus layer. The presence of this bacterium inversely correlates with body weight in rodents and humans. However, the precise physiological roles played by this bacterium during obesity and metabolic disorders are unknown. This study demonstrated that the abundance of A. muciniphila decreased in obese and type 2 diabetic mice. We also observed that prebiotic feeding normalized A. muciniphila abundance, which correlated with an improved metabolic profile. In addition, we demonstrated that A. muciniphila treatment reversed high-fat diet-induced metabolic disorders, including fat-mass gain, metabolic endotoxemia, adipose tissue inflammation, and insulin resistance. A. muciniphila administration increased the intestinal levels of endocannabinoids that control inflammation, the gut barrier, and gut peptide secretion. Finally, we demonstrated that all these effects required viable A. muciniphila because treatment with heat-killed cells did not improve the metabolic profile or the mucus layer thickness. In summary, this study provides substantial insight into the intricate mechanisms of bacterial (i.e., A. muciniphila) regulation of the cross-talk between the host and gut microbiota. These results also provide a rationale for the development of a treatment that uses this human mucus colonizer for the prevention or treatment of obesity and its associated metabolic disorders.



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ESTUDOS

Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study

Metabolic syndrome is characterized by a constellation of comorbidities that predispose individuals to an increased risk of developing cardiovascular pathologies as well as type 2 diabetes mellitus. The gut microbiota is a new key contributor involved in the onset of obesity-related disorders². In humans, studies have provided evidence for a negative correlation between *Akkermansia muciniphila* abundance and overweight, obesity, untreated type 2 diabetes mellitus or hypertension³⁻⁸. Since the administration of *A. muciniphila* has never been investigated in humans, we conducted a randomized, double-blind, placebo-controlled pilot study in overweight/obese insulin-resistant volunteers; 40 were enrolled and 32 completed the trial. The primary end points were safety, tolerability and metabolic parameters (that is, insulin resistance, circulating lipids, visceral adiposity and body mass). Secondary outcomes were gut barrier function (that is, plasma lipopolysaccharides) and gut microbiota composition. In this single-center study, we demonstrated that daily oral supplementation of 10¹⁰ *A. muciniphila* bacteria either live or pasteurized for three months was safe and well tolerated. Compared to placebo, pasteurized *A. muciniphila* improved insulin sensitivity ($+28.62 \pm 7.02\%$, $P = 0.002$), and reduced insulinemia ($-34.08 \pm 7.12\%$, $P = 0.006$) and plasma total cholesterol ($-8.68 \pm 2.38\%$, $P = 0.02$). Pasteurized *A. muciniphila* supplementation slightly decreased body weight (-2.27 ± 0.92 kg, $P = 0.091$) compared to the placebo group, and fat mass (-1.37 ± 0.82 kg, $P = 0.092$) and hip circumference (-2.63 ± 1.14 cm, $P = 0.091$) compared to baseline. After three months of supplementation, *A. muciniphila* reduced the levels of the relevant blood markers for liver dysfunction and inflammation while the overall gut microbiome structure was unaffected. In conclusion, this proof-of-concept study (clinical trial no. NCT02637115) shows that the intervention was safe and well tolerated and that supplementation with *A. muciniphila* improves several metabolic parameters.

A purified membrane protein from *Akkermansia muciniphila* or the pasteurized bacterium improves metabolism in obese and diabetic mice.

Obesity and type 2 diabetes are associated with low-grade inflammation and specific changes in gut microbiota composition. We previously demonstrated that administration of *Akkermansia muciniphila* to mice prevents the development of obesity and associated complications. However, the underlying mechanisms of this protective effect remain unclear. Moreover, the sensitivity of *A. muciniphila* to oxygen and the presence of animal-derived compounds in its growth medium currently limit the development of translational approaches for human medicine. We have addressed these issues here by showing that *A. muciniphila* retains its efficacy when grown on a synthetic medium compatible with human administration. Unexpectedly, we discovered that pasteurization of *A. muciniphila* enhanced its capacity to reduce fat mass development, insulin resistance and dyslipidemia in mice. These improvements were notably associated with a modulation of the host urinary metabolomics profile and intestinal energy absorption. We demonstrated that Amuc_1100, a specific protein isolated from the outer membrane of *A. muciniphila*, interacts with Toll-like receptor 2, is stable at temperatures used for pasteurization, improves the gut barrier and partly recapitulates the beneficial effects of the bacterium. Finally, we showed that administration of live or pasteurized *A. muciniphila* grown on the synthetic medium is safe in humans. These findings provide support for the use of different preparations of *A. muciniphila* as therapeutic options to target human obesity and associated disorders.





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ESTUDOS

Akkermansia muciniphila and improved metabolic health during a dietary intervention in obesity: relationship with gut microbiome richness and ecology.

Individuals with obesity and type 2 diabetes differ from lean and healthy individuals in their abundance of certain gut microbial species and microbial gene richness. Abundance of *Akkermansia muciniphila*, a mucin-degrading bacterium, has been inversely associated with body fat mass and glucose intolerance in mice, but more evidence is needed in humans. The impact of diet and weight loss on this bacterial species is unknown. Our objective was to evaluate the association between faecal *A. muciniphila* abundance, faecal microbiome gene richness, diet, host characteristics, and their changes after calorie restriction (CR). The intervention consisted of a 6-week CR period followed by a 6-week weight stabilisation diet in overweight and obese adults (N=49, including 41 women). Faecal *A. muciniphila* abundance, faecal microbial gene richness, diet and bioclinical parameters were measured at baseline and after CR and weight stabilisation. At baseline *A. muciniphila* was inversely related to fasting glucose, waist-to-hip ratio and subcutaneous adipocyte diameter. Subjects with higher gene richness and *A. muciniphila* abundance exhibited the healthiest metabolic status, particularly in fasting plasma glucose, plasma triglycerides and body fat distribution. Individuals with higher baseline *A. muciniphila* displayed greater improvement in insulin sensitivity markers and other clinical parameters after CR. These participants also experienced a reduction in *A. muciniphila* abundance, but it remained significantly higher than in individuals with lower baseline abundance. *A. muciniphila* was associated with microbial species known to be related to health. *A. muciniphila* is associated with a healthier metabolic status and better clinical outcomes after CR in overweight/obese adults. The interaction between gut microbiota ecology and *A. muciniphila* warrants further investigation.



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