

**INSONLARDAGI SEMIZLIK MUAMMOSINI BARTARAF ETISH VA OLDINI
OLISHDA HAFNIA ALVEI SHTAMMINI QO'LLASH**

¹Mamatraimova Sh.M., ²Bekmurodova G.A., ³Amirsaidova D.A., ⁴Miralimova Sh.M

^{1,2,3,4}O'zRFA Mikrobiologiya instituti, e-mail:shahnoza27mms@gmail.com

<https://doi.org/10.5281/zenodo.8358302>

Annotatsiya. Yangi avlod probiotiklaridan foydalanish semirishning oldini olish va davolash strategiyasining ajralmas qismiga aylanishi mumkin. Ushbu sharhning maqsadi Hafnia alvei probiotik shtamming semizlikka qarshi samaradorlik ko`rsatgichlarini adabiyot materiallari asosida tahlil qilish. Tadqiqotda Hafnia alvei yangi avlod probiotiklari guruhiga kiritilgan va foydalanish semirishning oldini olish va davolash strategiyasining ajralmas qismiga aylanishi mumkinligi keltirilgan, ammo Hafnia alvei ning ta'siri hali ham o'r ganilmogda va uning potentsial foydalari va qo'llanilishini to'liq o'r ganish uchun ko'proq tadqiqotlar talab etiladi.

Kalit so`zlar: yangi avlod probiotiklari, semizlik, Hafnia alvei;

Аннотация. Использование пробиотиков нового поколения может стать неотъемлемой частью стратегии профилактики и лечения ожирения. Целью данного исследования является анализ показателей борьбы с ожирением *Hafnia alvei*, потенциального пробиотического штамма молочных бактерий, на основе литературы. Исследования показали, что *Hafnia alvei* включена в группу пробиотиков нового поколения, и ее использование может стать неотъемлемой частью стратегий профилактики и лечения ожирения, но эффекты *Hafnia alvei* все еще изучаются и используются для полного понимания ее потенциальных преимуществ и применения. необходимы дополнительные исследования.

Ключевые слова: пробиотики нового поколения, ожирение, *Hafnia alvei*;

Abstract. The use of new generation probiotics may become an integral part of obesity prevention and treatment strategies. The purpose of this research is to analyze the anti-obesity indicators of *Hafnia alvei*, a potential probiotic strain of milk bacteria, based on the literature. Studies have shown that *Hafnia alvei* is included in the group of new generation probiotics and its use may become an integral part of obesity prevention and treatment strategies, but the effects of *Hafnia alvei* are still being studied and used to fully understand its potential benefits and applications. more research is needed.

Keywords: new generation probiotics, obesity, *Hafnia alvei*;

Jahon sog'lijni saqlash tashkiloti ma'lumotlariga ko'ra, 1975-yildan beri ortiqcha vazn ($BMI \geq 25 \text{ kg} / \text{m}^2$) va semirib ketish ($BMI \geq 30 \text{ kg} / \text{m}^2$) dunyo bo'ylab tarqalish darajasi 3 baravar ko'paygan, bu esa mos ravishda 39% ni tashkil qiladi [1]. Semirib ketish ijtimoiy zaiflashuvchi bir qancha surunkali kasalliklar, jumladan, qandli diabet, yurak-qon tomir kasalliklari va saraton [2] uchun asosiy xavfli omil ekanligini hisobga olsak, dunyodagi "semizlik epidemiyasi" bilan bog'liq xavotirli vaziyat oldini olish va davolash yechimlarini izlashga undaydi.

Semirib ketishning patofiziologiyasi bo'yicha mavjud bilimlar miyaga leptin va insulin kabi yog'lilik gormonlaridan o'zgargan signalizatsiyani o'z ichiga oladi, natijada giperfagiya va ijobjiy energiya balansi [3] paydo bo'ladi. Bundan tashqari, ichak mikroorganizmlari ichak mikrobiota tarkibining semizlik fenotipler bilan bog'liqligini, energiya almashinuvini tartibga solishda ishtirot etishi ko'rsatilgan [4, 5]. Ichak mikrobiotasini muvozanatini miya energiyasi bilan bog'laydigan molekulalar yo'llar hali to'liq o'r ganilmagan bo'lsa-da, sog'liq uchun foydali

bakteriyalarni to'ldirish orqali ichak mikrobiota tarkibini modulyatsiya qilish, semirishning oldini olish va davolash uchun yangi strategiya sifatida namoyon bo'ladi. Haqiqatan ham, *Lactobacillus*, *Bifidobacterium* va *Enterococcus* avlodiga mansub an'anaviy probiotik bakteriyalar yakka o'zi yoki turli kombinatsiyalarda odamlarda sinovdan o'tkazildi, natijada odatda oziq-ovqat iste'moli va tana vaznida sezilarli o'zgarishlar bilan salomatlik uchun ijobjiy ta'sir ko'rsatdi [6, 7, 8, 9]. Shunga qaramay, ichak mikrobiotasi bilan organizmda ishtahani va energiya almashinuvini tartibga solish o'rtaqidagi funksional bog'liqlikning mavjudligi shuni ko'rsatadiki, ba'zi ichak komsensal bakteriyalari ularning ta'sir qilish mexanizmlarini tushunish asosida yangi avlod semirishga qarshi probiotiklardan foydalanishi mumkin [10].

Hafnia alvei shtammi *Hafniaceae* oilasiga (ilgari *Enterobacteriaceae*) tegishli bo'lib, *Enterobacteriaceae* turkumiga kiradi. Ushbu shtammni standart oziq-ovqat bilan ta'minla naga n holda, ikkita hayvon modelida semirishga qarshi xususiyatga ega ekanligi ko'rsatildi [11]. *H. alvei* potentsial semizlikka qarshi probiotik sifatida tanlanishi uning kazeinolitik proteaza oqsilini (ishtahani tartibga solishda ishtirok etadigan asosiy anoreksigen peptid) ishlab chiqarishi ga asoslangan bo'lib, u ilgari a-melanotsitlarni ogohlantiruvchi gormon (a-MSH) ning konformatsion mimetikasi sifatida aniqlangan. [11, 12].

Hafnia alvei gram-manfiy, fakultativ anaerob bakteriya bo'lib, oziq-ovqat tarkibidagi asosiy psixofil bakteriyalar, shuningdek, vakuumli qadoqlangan va modifikatsiyalangan atmosfera bilan qadoqlangan oziq-ovqat mahsulotlarida keng tarqalgan [13]. *H. alvei* xom go'sht, suv,sut va sut mahsulotlari, iste'mol qilishga tayyor dengiz mahsulotlarida keng tarqalgan [14]. Ammo *Hafnia alvei* inson infektsiyalari yoki kasalliklari bilan bog'liq muammolarni keltirib chiqarishi aniqlanmagan [15]. *Hafnia alvei* ba'zi odamlarda normal ichak mikrobiotasining bir qismi, ya'ni u tabiiy ravishda inson oshqozon-ichak traktida yashashi mumkin. *H. alvei* ba'zi sog'lom odamlarning ichak mikrobiotasida aniqlangan bo'lsa-da, uning past tarqalishi (1-2%), bu sut mahsulotlari bilan bog'liq bo'lgan bakteriyalarning turiga tegishli ekanligini ko'rsatadi [16]. Organizmning umumiyl salomatlik va farovonlikni saqlashda, ishtahani nazorat qilishda ichak mikrobiotasini roli muhim. Tana vaznini ichak mikroboitasi orqali boshqarish uchun probiotik shtammlardan foydalanib ko'rilmoxda. Bu ovqat hazm qilish, ozuqa muddalarining so'rili shiga, immunitet tizimini tartibga solishga va zararli patogenlardan himoya qilishga yordam beradi [17]. *Hafnia alvei* sog'liq uchun potentsial foya keltirishi mumkin, ammo uning ta'sirini to'liq tushunish uchun ko'proq tadqiqotlar talab etiladi.

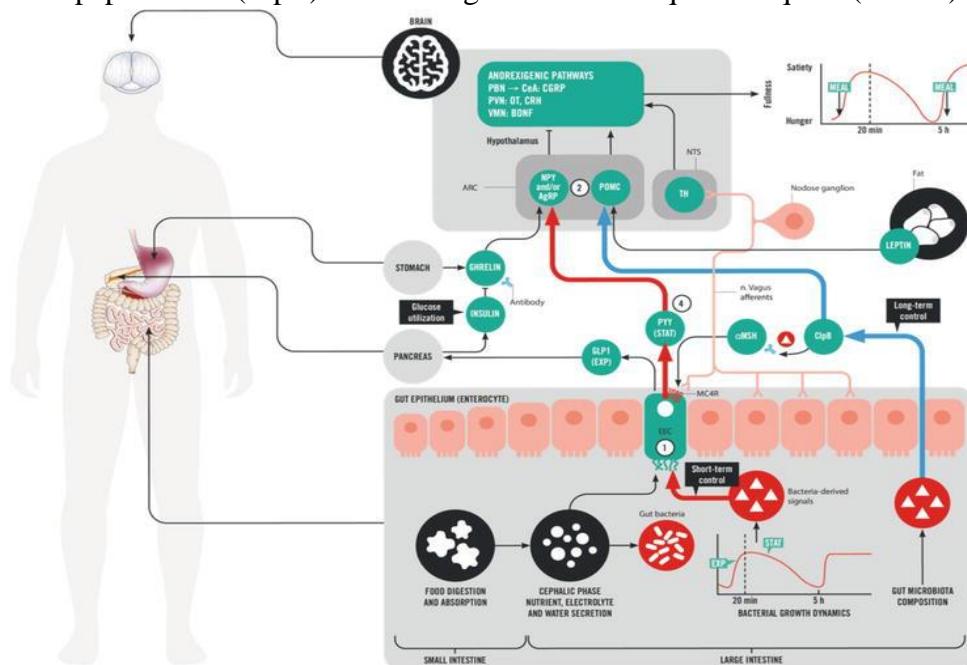
Tadqiqotlar shuni ko'rsatdiki, *Hafnia alvei* mikroblarga qarshi muddalar ishlab chiqaradi, ular ba'zi zararli bakteriyalar, jumladan *Escherichia coli* va *Salmonella* o'sishiga to'sqinlik qiladi. Ushbu mikroblarga qarshi faollik *Hafnia alvei* ning oziq-ovqat mahsulotlarini saqlash va probiotik sifatida ishlatilish mumkin ekanligini ham ko'rsatadi [18].

Probiotiklar - jonli mikroorganizmlar bo'lib, ular kerakli miqdorda iste'mol qilinganda inson sog'ligi uchun foya keltiradi. *Hafnia alvei* ning ba'zi shtammlari probiotik salohiyati uchun o'rganilgan [19]. Probiotiklar ichak mikrobiotasining sog'lom muvozanatini saqlashga yordam beradi, ovqat hazm qilishni qo'llab-quvvatlaydi va immunitetni oshiradi.

O'rganilgan tadqiqotlarda keltirilishicha, *Hafnia alvei* dan tanani tozalash uchun foydalanish bo'yicha tadqiqotlar mavjud. Ta'kidlanishicha, ichak mikrobiotasida *Hafnia alvei* mavjudligi ichakning umumiyl sog'lig'iga hissa qo'shishi mumkin. Sog'lom ichak mikrobiotasini chiqindilarni yo'q qilishga yordam beradi, muntazam ichak harakatini qo'llab-quvvatlaydi va tanadan toksinlarni olib chiqishga yordam beradi [20].

Nikolas Lukas tadqiqotlarida keltirlishicha, (2019) *H. alvei* shtammini og'iz orqali yuborish sichqoncha modelida semirishni yengillashtirdi va oziq-ovqat iste'molini kamaytirdi va u metabolik va xatti-harakatlardagi o'zgarishlar potentsial yangi avlod probiotik bakteriya *H. alvei* ning semizlikka qarshi ta'sirini sinab ko'rish uchun giperfagik o'zgarishi preklinik modeli uchun etarli bo`la olgan. Ushbu tadqiqotda, semizlikdan kelib chiqqan metabolik o'zgarishlar, shu jumladan glikemiya va umumiyl xolesterin *H. alvei* bilan davolash orqali yaxshilanganligi ochib berilgan [21].

Mikrobiotaning metabolizmdagi roli kashf etilganidan beri Pr. Serguei Fetissov, neyroendokrinolog va fiziologiya professori, ishtahani nazorat qilishda ichak mikrobiotasining rolini keng o'rgandi. 2002-yildayoq u to'yishning asosiy gormoni alfa-melanotsitlarni ogohlantiruvchi gormon (alfa-MSH) bilan reaksiyaga kirishuvchi inson otoantikorlarini aniqladi. U mikrobiota tomonidan ishlab chiqarilgan anoreksigen peptidni alfa-MSH bilan ketma-ketlikning homologiyasini kashf etdi [22]. Endokrinologiya jurnalida chop etilgan sharhda u mikrobiota tomonidan ishlab chiqarilgan metabolitlar oziq-ovqat iste'molini tartibga solishi mumkinligini ko'rsatdi va aniqrog'i alfa-MSH ning konformatsion mimetik antigen bo'lgan kazeinolitik peptidaza B (ClpB) deb ataladigan bakterial oqsilni aniqladi (1-rasm) [23].



1-rasm. Serguei Fetissovdan tadqiqot izohi 2016 yil.

Kuzatishlar shuni ko'rsatdiki, inson najasi namularida kazeinolitik peptidaza B (ClpB) darajasi tana massasi indeksi (BMI) [24] bilan uzviy bog'liq. Pr. Serguei Fetissov va Professor Per Dechelotte lar semizlikning kelib chiqish oqibati va inson ovqatlanishi jarayonlari bo'yicha batafsil o'rganish va tasvirlash uchun o'z tadqiqotlarini olib bordi.

Bu kuzatilgan anoreksigen ta'sir, ehtimol, *H. alvei* ning o'ziga xos xususiyatidir probiotik bakteriyalar orasida semizlikka qarshi tadqiqotlar hayvonlar modellarida sinovdan o'tgan. Aslida, ba'zi semizlikka qarshi ta'sirli boshqa bakteriyalar shtammlari berilgan bo'lsa-da, ularning hech biri oziq-ovqat iste'molini kamaytirmadi [25]. *H. alvei* tana massasining o'rtacha, ammo barqaror kamayishi foydali metabolik ta'sirlari bilan birga tana vaznini uzoq muddatli boshqarish uchun xavfsizroq va samaraliroq strategiya bo'lishi mumkinligi ta'kidlab o'tilgan [26]. Olimlarning ta'kidlashicha, *H. alvei* ning tana vaznini uzoq muddat boshqarish xususiyati lipidlarning so'riliшини kamaytirishi va to'yinganlik signalni holatlarini hosil qilish xususiyatlari aniqlanga n..

[27]. Shunday qilib, *H. alvei* yog'ning so'riliшини turli yo'llar bilan kamaytirishga asoslangan terapevtik strategiya bo`lishi mumkin. Asosan tartibsiz ovqatlanish odatlari va ovqatlanish xatti-harakatlariga e'tibor berilmaslik yog'ning so'riliшини noto'g'ri taqsimlanishi semizlikning asosiy sabablaridan biridir. Shunday yomon holatlarni oldini olish amalga oshirilishi mumkin. Shunday qilib, to'yinganlik signali, bemorga to'qlik hissi bilan birga, uzoq muddatli ta'sir ko'rsatishi mumkin [28].

Shuni ta'kidlash kerakki, *Hafnia alvei* ning tanaga ta'siri hali ham o'rganilmoqda va uning potentsial foydalari va qo'llanilishini to'liq tushunish uchun ko'proq tadqiqotlar talab etiladi.

Yuqorida aytil o'tilganidek, *H. alvei* alfa-MSH ning konformatsion mimetik antigen bo'lgan kazeinolitik peptidaza B (ClpB) ortiqcha vazn va semirishda tana vaznini boshqarish uchun innovatsion va samarali yechim hisoblanadi. Tadqiqot probiotikning ortiqcha vaznli odamlarda va xatto semirishdan aziyat chekayotganlarda, haqiqiy hayot sharoitida, ya'ni kaloriya cheklovisiz samaradorligini tasdiqlagan. Eng muhimi, ushbu tadqiqot vaqt o'tishi bilan to'qlik hissini uzaytirishi, tana vaznini yo'qotishni kuchaytirgani tasdiqlagan. Klinik sinov muallifi xulosasiga ko'ra, *Hafnia alvei* ortiqcha tana vaznini nazorat qilish uchun parhez tavsiyalarining samaradorligini oshirishi aniqlangan.

REFERENCES

1. World Health Organization Health Topics—Obesity. [(accessed on 16 February 2018)]; Available online: <http://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight>
2. Reilly J.J., Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: Systematic review. *Int. J. Obes.* 2010;35:891.
3. Schwartz M.W., Woods S.C., Porte D., Jr., Seeley R.J., Baskin D.G. Central nervous system control of food intake. *Nature.* 2000;404:661–671.
4. Bäckhed F., Ding H., Wang T., Hooper L.V., Koh G.Y., Nagy A., Semenkovich C.F., Gordon J.I. The gut microbiota as an environmental factor that regulates fat storage. *Proc. Natl. Acad. Sci. USA.* 2004;101:15718–15723.
5. Ley R.E., Turnbaugh P.J., Klein S., Gordon J.I. Microbial ecology: Human gut microbes associated with obesity. *Nature.* 2006;444:1022–1023.
6. Guazzelli Marques C., de Piano Ganen A., de Barros A.Z., Thomatieli Dos Santos R.V., Dos Santos Quaresma M.V.L. Weight loss probiotic supplementation effect in overweight and obesity subjects: A review. *Clin. Nutr.* 2019
7. Koutnikova H., Genser B., Monteiro-Sepulveda M., Faurie J.M., Rizkalla S., Schrezenmeir J., Clement K. Impact of bacterial probiotics on obesity, diabetes and non-alcoholic fatty liver disease related variables: A systematic review and meta-analysis of randomised controlled trials. *BMJ Open.* 2019;9:e017995.
8. Suzumura E.A., Bersch-Ferreira A.C., Torreglosa C.R., da Silva J.T., Coqueiro A.Y., Kuntz M.G.F., Chrispim P.P., Weber B., Cavalcanti A.B. Effects of oral supplementation with probiotics or synbiotics in overweight and obese adults: A systematic review and meta-analyses of randomized trials. *Nutr. Rev.* 2019;77:430–450.
9. Jones R.B., Alderete T.L., Martin A.A., Geary B.A., Hwang D.H., Palmer S.L., Goran M.I. Probiotic supplementation increases obesity with no detectable effects on liver fat or gut

- microbiota in obese Hispanic adolescents: A 16-week, randomized, placebo-controlled trial. *Pediatr. Obes.* 2018;13:705–714.
10. Fetissov S.O. Role of the gut microbiota in host appetite control: Bacterial growth to animal feeding behaviour. *Nat. Rev. Endocrinol.* 2017;13:11–25.
 11. Legrand R., Lucas N., Dominique M., Azhar S., Deroissart C., Le Solliec M.-A., Rondeaux J., Nobis S., Guérin C., Léon L., et al. Commensal *Hafnia alvei* strain reduces food intake and fat mass in obese mice—A new potential probiotic for appetite and body weight management. *Int. J. Obes.* 2019
 12. Tennoune N., Chan P., Breton J., Legrand R., Chabane Y.N., Akkermann K., Jarv A., Ouelaa W., Takagi K., Ghouzali I., et al. Bacterial ClpB heat-shock protein, an antigen-mimetic of the anorexigenic peptide [alpha]-MSH, at the origin of eating disorders. *Transl. Psychiatry.* 2014;4: e 458.
 13. T.R. Chen, Q.K. Wei, Y.J. Chen, Pseudomonas spp. and *Hafnia alvei* growth in UHT milk at cold storage, *Food Control*, Volume 22, Issue 5, 2011, Pages 697-701
 14. Du Guo, Shuo Wang, Jiahui Li, Fangting Bai, Yanpeng Yang, Yunfeng Xu, Sen Liang, Xiaodong Xia, Xin Wang, Chao Shi, The antimicrobial activity of coenzyme Q0 against planktonic and biofilm forms of *Cronobacter sakazakii*, *Food Microbiology*, Volume 86, 2020,103337
 15. Timko, J.; Kmet', V. (2003). "Susceptibility of Enterobacteriaceae from the Alpine Accentor *Prunella collaris*". *Acta Veterinaria Brno.* **72** (2): 285–288
 16. Goatcher, L. J.; Barrett, M. W.; Coleman, R. N.; Hawley, A. W. L.; Qureshi, A. A. (1987). "A study of predominant aerobic microflora of black bears (*Ursus americanus*) and grizzly bears (*Ursus arctos*) in northwestern Alberta". *Canadian Journal of Microbiology.* **33** (11): 949–954.
 17. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. *Infectious Diseases Society of America* **2023**; Version 3.0. Available at <https://www.idsociety.org/practice-guideline/amr-guidance/>.
 18. Ramos-Vivas J, Tapia O, Elexpuru-Zabaleta M, Pifarre KT, Armas Diaz Y, Battino M, Giampieri F. The Molecular Weaponry Produced by the Bacterium *Hafnia alvei* in Foods. *Molecules.* 2022 Aug 30;27(17):5585.
 19. Veiga P, Suez J, Derrien M, Elinav E. Moving from probiotics to precision probiotics. *Nat Microbiol.* 2020 Jul;5(7):878-880.
 20. Déchelotte P, Breton J, Trotin-Picolo C, Grube B, Erlenbeck C, Bothe G, Fetissov SO, Lambert G. The Probiotic Strain *H. alvei* HA4597® Improves Weight Loss in Overweight Subjects under Moderate Hypocaloric Diet: A Proof-of-Concept, Multicenter Randomized, Double-Blind Placebo-Controlled Study. *Nutrients.* 2021 Jun 1;13(6):1902.
 21. Lucas N, Legrand R, Deroissart C, Dominique M, Azhar S, Le Solliec MA, Léon F, do Rego JC, Déchelotte P, Fetissov SO, Lambert G. *Hafnia alvei* HA4597 Strain Reduces Food Intake and Body Weight Gain and Improves Body Composition, Glucose, and Lipid Metabolism in a Mouse Model of Hyperphagic Obesity. *Microorganisms.* 2019 Dec 23;8(1):35
 22. Kobyliak N., Conte C., Cammarota G., Haley A.P., Styriak I., Gaspar L., Fusek J., Rodrigo L., Kružliak P. Probiotics in prevention and treatment of obesity: A critical view. *Nutr. Metab.* 2016;13:14. doi: 10.1186/s12986-016-0067-0.

23. Franson K., Rössner S. Fat intake and food choices during weight reduction with diet, behavioural modification and a lipase inhibitor. *J. Intern. Med.* 2000;247:607–614
24. Lucas, Nicolas; Legrand, Romain; Deroissart, Camille; Dominique, Manon; Azhar, Saïda; Le Sollicec, Marie-Anne; Léon, Fatima; do Rego, Jean-Claude; Déchelotte, Pierre; Fetissov, Sergueï O.; Lambert, Grégory (23 December 2019). "[*Hafnia alvei* HA4597 Strain Reduces Food Intake and Body Weight Gain and Improves Body Composition, Glucose, and Lipid Metabolism in a Mouse Model of Hyperphagic Obesity](#)". *Microorganisms*. **8** (1): 35
25. Aminzhanovna, A. D., Amirovna, B. G., Arashevna, E. N., Mirzhamalovna, M. S., & Mamarazhabovna, M. S. (2022). Antimicrobial activity of lactobacteria against opportunital microorganisms of the oral cavity. *Journal of Pharmaceutical Negative Results*, 13(4), 1096-1102.