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Critical Analysis of the Efficacy and Limitations of GLP-1 Pharmaceuticals in Obesity Management: A Comprehensive Literature Review

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Abstract

Introduction and purpose

Obesity, a pervasive global pandemic intricately linked to various comorbidities, necessitates a comprehensive and nuanced approach. This article delves into the intricate realm of obesity guidelines, underscoring the significance of lifestyle modifications, preventive measures for childhood obesity, population-based strategies, clinical management protocols, and vigilant monitoring [10,12,13].

GLP-1 drugs, originally designed for type 2 diabetes management, exhibit multifaceted effects beyond glycemic control. They influence appetite regulation, gastric emptying dynamics, and potentially contribute to cardiovascular health improvements [4]. However, the commendable effects come with a caveat - potential side effects necessitating careful consideration in clinical decision-making [20]. Despite gaining popularity through celebrity endorsements, this article firmly underscores the need to view GLP-1 pharmacotherapy as a recommended intervention rather than a miraculous solution [24].

A brief description of the state of knowledge

Integral to the obesity discourse is the imperative to address weight stigma, demanding evidence-based approaches in both clinical and public health domains [7-8]. The narrative extends into the future landscape of obesity pharmacotherapy, contemplating the potential role of probiotics. Emphasizing the necessity for long-

term studies and randomized trials, it positions probiotics as a low-risk alternative with significant potential in mitigating obesity while simultaneously addressing concerns related to antibiotic resistance [6].

Summary

The pursuit of a balanced and effective approach to obesity management necessitates a nuanced understanding of medical interventions, consideration of societal perceptions, and exploration of innovative possibilities within the evolving landscape of healthcare [10,12,13].

Keywords: Diabetes, GLP-1, Obesity, Epidemiology, Pharmacotherapy, Prevention

Current obesity guidelines provided by World Health Organization

- Dietary Recommendations: Encouraging a healthy diet that includes a variety of fruits, vegetables, whole grains, nuts, and seeds. Limiting the intake of sugary drinks, saturated and trans fats, and salt [10].

- Physical Activity Guidelines: Promoting regular physical activity as part of a healthy lifestyle. The guidelines recommend at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic activity per week for adults [9].

- Childhood Obesity Prevention: Emphasizing the importance of early intervention and prevention of obesity in childhood. This includes promoting healthy eating habits, regular physical activity, and minimizing sedentary behaviors [8].

- Population-Based Approaches: Advocating for policies and strategies at the population level to create environments that support healthy eating and physical activity. This may include taxation on sugary beverages, food labeling, and urban planning that encourages physical activity [25].

- Clinical Management: Providing recommendations for the clinical management of obesity, including lifestyle interventions, behavioral therapy, and, in some cases, medical or surgical interventions [12].

- Monitoring and Surveillance: Emphasizing the need for robust monitoring and surveillance systems to track the prevalence of obesity and evaluate the effectiveness of interventions [10].

Pharmacological aids

If lifestyle modifications have not yielded satisfactory results after approximately 12 months, the consideration of adjuvant drug therapy becomes an option. In accordance with existing guidelines, drugs sanctioned for weight management should be contemplated for individuals with a BMI of ≥30 kg/m2 or a BMI ≥27 kg/m2 in the presence of weight-related comorbidities. In such instances, initial choices may include the GLP-1 agonist liraglutide or the lipase inhibitor orlistat. The bupropion/naltrexone combination may be favored in specific cases. Notably, phentermine and its combination with topiramate, approved in the USA, lack approval in Europe and are briefly discussed here. The following table outlines commonly utilized drugs for weight reduction [20].

GLP-1 drugs explained

Glucagon-like peptide-1 (GLP-1) drugs are a class of medications used in the treatment of type 2 diabetes mellitus. GLP-1 is a naturally occurring hormone in the body that plays a crucial role in glucose metabolism. The primary function of GLP-1 is to stimulate the release of insulin from the pancreas in response to elevated blood sugar levels, promoting glucose uptake by cells. GLP-1 drugs are designed to mimic the effects of this hormone, leading to enhanced insulin secretion [3]. However, these medications go beyond merely increasing insulin release. They also suppress the release of glucagon, a hormone that raises blood sugar levels, and they slow down the emptying of the stomach, which helps control post-meal glucose levels [4]. Moreover, GLP-1 drugs have been found to have additional benefits, such as promoting weight loss by reducing appetite and slowing down gastric emptying. They may also have cardiovascular benefits, including a potential reduction in the risk of cardiovascular events [3].

These drugs are typically administered through injections, and there are both short-acting and long-acting formulations available. Some common examples of GLP-1 drugs include exenatide, liraglutide, dulaglutide, and semaglutide. They are often prescribed as part of a comprehensive treatment plan for individuals with type 2 diabetes who may not adequately respond to other oral medications. It's important to note that these drugs are typically not used as first-line treatments and are often considered when other therapeutic options have been explored.

As with any medication, their use should be discussed with a healthcare professional who can assess individual health needs and potential side effects [3].

GLP-1 side effects

Glucagon-like peptide-1 (GLP-1) receptor agonists, while generally well-tolerated, may have some side effects. It's important to note that individual responses can vary, and the overall risk-benefit profile should be assessed in consultation with a healthcare professional. Here are some common side effects associated with GLP-1 receptor agonists:

Gastrointestinal Effects: These drugs can cause nausea, vomiting, diarrhea, and constipation, especially when treatment is initiated. However, these symptoms often improve over time.

Hypoglycemia: GLP-1 receptor agonists, when used as monotherapy, generally have a low risk of causing low blood sugar levels (hypoglycemia). However, the risk may increase when used in combination with other antidiabetic medications that can cause hypoglycemia.

Injection Site Reactions: Since GLP-1 receptor agonists are administered by injection, some individuals may experience redness, swelling, or itching at the injection site.

Pancreatitis: There have been reports of pancreatitis (inflammation of the pancreas) associated with the use of GLP-1 receptor agonists. While the risk is generally low, individuals with a history of pancreatitis may need careful monitoring.

Weight Loss: While weight loss is often considered a benefit, excessive weight loss can occur, and individuals should be monitored for unintended and significant weight reduction.

The incidence of side effects can vary among different GLP-1 receptor agonists. Overall, these medications have been associated with a relatively low incidence of severe adverse events.

For example, clinical trials and real-world studies have shown that nausea is a common side effect, occurring in a percentage of individuals starting GLP-1 therapy. However, this side effect often diminishes over time. Serious side effects, such as pancreatitis, are rare but have been reported. The overall safety profile of GLP-1 receptor agonists is continually monitored through clinical trials, post-marketing surveillance, and real-world evidence to ensure a comprehensive understanding of their risks and benefits. It's crucial for individuals using GLP-1 receptor agonists to communicate any concerns or experiences of side effects to their healthcare provider. The decision to prescribe these medications should be based on an individual's overall health status, medical history, and the need for glycemic control [5].

Adverse effects in summary

GLP-1 receptor agonists are useful drugs for the treatment of patients with T2D. These drugs improve glycemic control and many other atherosclerosis-related parameters [19,22-24]. However, concerns have been expressed regarding the effects of these drugs on pancreatic and thyroid tissue, but current evidence and meta-analyses do not show a cause-effect association between GLP-1 receptor agonists and the development of pancreatitis, pancreatic cancer, or thyroid cancer [20-21]. GLP-1 receptor agonists do not generally cause hypoglycemia, but it is recommendable to decrease the dose of concomitant sulphonylurea or insulin to reduce the risk of hypoglycemic episodes. In many case reports, the use of these drugs, mainly exenatide, has been associated with acute kidney injury, in which hemodynamic factors are predominantly implicated. Other common adverse effects of these drugs include injection site reactions, headache, and nasopharyngitis, but these effects do not usually lead to discontinuation of the drug [5,18,20,21,25]. Finally, GLP-1 receptor agonists do not seem to affect negatively the cardiovascular risk in patients with T2D, but an ultimate all-clear regarding the risk of cardiovascular events, pancreatitis, or pancreatic cancer, which may be caused by incretin-mimetic drugs, cannot be given as there is scattered evidence for these side effects [23-24]. Ongoing and future trials need to

assess and clarify further the cardiovascular and overall safety profile of GLP-1 receptor agonists [19,22-24]. Gastrointestinal symptoms are a common occurrence with GLP-1 receptor agonists; however, these effects typically do not lead to therapy discontinuation [5,18,20,21,25].

- Long-acting compounds demonstrate a lower incidence of nausea compared to their short-acting counterparts [19,22].
- GLP-1 receptor agonists are linked to pre-renal acute kidney injury, particularly in cases involving severe gastrointestinal symptoms and dehydration [20-21].
- Available evidence does not support an elevated risk of pancreatitis associated with the use of GLP-1 receptor agonists [20-21].
- Meta-analyses fail to demonstrate an increased risk of pancreatic or thyroid cancer with the utilization of these drugs [20,21].

GLP-1 pharmacotherapy in popular culture

In recent years, GLP-1 medications have gained significant attention for their potential in obesity management. The public opinion surrounding these drugs is marked by a growing interest in their effectiveness and safety. Ozempic, in particular, has garnered attention not only for its regulatory approval but also due to numerous testimonials, including those from prominent celebrities who claim to have achieved notable weight loss through its use [3].

Celebrities often serve as influential figures in shaping public perceptions, and several have openly shared their positive experiences with Ozempic. These testimonials contribute to the medication's allure, as individuals seek success stories for inspiration on their own weight loss journeys [3].

High-profile figures, including actors, athletes, and influencers, have spoken openly about incorporating GLP-1 medications into their wellness routines. Their accounts often emphasize not only significant weight loss but also improved overall well-being. While it's crucial to acknowledge the individual nature of responses to medication, these celebrity endorsements contribute to the ongoing dialogue

surrounding the potential benefits of GLP-1 drugs in the realm of weight management [3].

The integration of Ozempic into popular culture has become an undeniable reality, as this groundbreaking pharmacotherapy seamlessly weaves itself into contemporary lifestyles. Widely embraced by individuals across various spectrums, Ozempic's influence extends beyond its medical application, solidifying its status as a noteworthy element of pop culture. However, amidst its rising popularity, it's crucial to recognize that GLP-1, including Ozempic, belongs to a group of medicines recommended for specific health issues. As it becomes a part of weight management conversations, not only recommended for diabetic patients, we must maintain awareness that these medications are not magic solutions. The dual perception surrounding Ozempic reflects the dynamic intersection of medical advancements and societal attitudes, shaping the discourse around its role in both health and weight management [3].

General view on perspectives of patients fighting obesity

The pervasive presence of weight stigma and discrimination has significant adverse effects on individuals. The prevailing narrative surrounding obesity in the media, public health campaigns, political discourse, and scientific literature, which largely attributes the cause of obesity to personal responsibility, plays a crucial role in perpetuating societal weight stigma and reinforcing weight-based stereotypes. This stigma has the potential to influence clinical decisions and public health messages, leading to the inefficient allocation of limited research resources. Weight bias and stigma can result in discrimination, compromising human rights, social rights, and the overall health of those affected [7].

Addressing the disparity between scientific evidence and the conventional narrative surrounding obesity, built on unproven assumptions and misconceptions, could help mitigate weight bias and its detrimental effects. It is essential to recognize that a holistic approach is necessary for a better life for individuals combating obesity. Achieving a perfect balance between a healthy lifestyle, societal support, and the strict care provided by a knowledgeable doctor is crucial. This collaborative effort from all stakeholders is necessary to advance educational,

regulatory, and legal initiatives aimed at preventing weight stigma and discrimination while fostering comprehensive healthcare solutions for those in need [7].

In the realm of medical intervention, it is imperative to acknowledge the inherent existence of side effects associated with medications. Each pharmaceutical agent, while intended to ameliorate specific health conditions, may potentially induce unintended repercussions. However, it is the solemn responsibility of healthcare practitioners to meticulously navigate the delicate equilibrium between therapeutic benefits and side effects [13].

Moreover, a profound understanding underscores the necessity for a personalized approach in medical care. Every patient embodies a unique physiological constitution and distinct health conditions. As such, tailoring therapeutic regimens to individual nuances becomes paramount. The discerning physician must adeptly weigh the potential advantages of a given therapy against the conceivable side effects, ensuring that the chosen course of action aligns optimally with the patient's overall health profile.

In essence, achieving a harmonious balance between therapy benefits and side effects demands a personalized and attentive approach, acknowledging the individuality of each patient's biological makeup and health status [13].

Are probiotics the future in obesity pharmacotherapy?

The progression toward a more individualized and precisely targeted implementation of probiotic interventions stands as a pivotal domain in the field of epidemiology and medical research. Notably, the majority of investigations heretofore conducted have been within rigorously controlled animal models, presenting challenges in extrapolating findings to human subjects. Stratifying individuals based on specific markers that encompass lifestyle factors, age, genetics, and other environmental influences on microbiota composition emerges as a requisite consideration for human applications [6,26].

An imperative aspect involves elucidating the metagenomic relationship between evolving microbiota and probiotic species under diverse dietary and nutritional states. It is pertinent to highlight that the predominant focus in this dynamic field has been on Lactobacillus and Bifidobacterium strains, necessitating the identification of novel bacterial candidates and a comprehensive exploration of their potential mechanistic effects on obesity [6,26].

In the current landscape, clinical cohorts have been characterized by relatively modest sample sizes, with a predominant emphasis on short-term physical parameters or inflammatory markers. Addressing these limitations necessitates prioritizing future long-term follow-up studies. The conduct of additional randomized placebo-controlled trials is pivotal for the establishment of clinical guidelines governing the utilization of probiotic therapy in obesity. This approach not only aids in formulating nutritional recommendations but also addresses safety concerns related to functional foods containing probiotics, such as fermented dairy products and kimchi [6].

Importantly, amidst these existing gaps in knowledge, it is crucial to underscore that probiotic therapy emerges as an enticing frontier in the treatment of obesity and associated metabolic dysfunctions within the realms of epidemiology and medicine. Notably, the relatively low risk of side effects associated with probiotics, especially when compared to alternative treatments, positions them favorably in addressing the escalating concerns related to antibiotic resistance [6].

Summary

Obesity represents an intricate and multifaceted health condition strongly linked to a range of coexisting medical conditions . These comorbidities encompass specific types of malignancies, cardiovascular disorders, functional impairment, diabetes mellitus, gallbladder pathology, hypertension, osteoarthritis, sleep-disordered breathing, and cerebrovascular events [10]. The association of obesity with elevated rates of cardiovascular and overall mortality is well-documented [16]. Furthermore, obesity has been characterized as a global pandemic, with a 28% increase in the prevalence of overweight and obesity in adults and a 47% rise in

children between 1980 and 2013. Present estimates indicate that nearly 2.1 billion individuals worldwide fall into the categories of overweight or obese [10].

To comprehend obesity, it is essential to delineate body weight categorization for both adults and children. The predominant criterion for classifying somatotype is the Body Mass Index (BMI), calculated by dividing weight in kilograms by the square of height in meters. The National Heart, Lung, and Blood Institute, the World Health Organization (WHO), the American Heart Association, the American College of Cardiology, and The Obesity Society have all sanctioned BMI classifications for adults of White, Hispanic, and African American ethnicities [13].

The aim of this study is to summarize the current knowledge regarding the GLP-1 role and therapy risk based on the latest available scientific literature [4,18,20].

This comprehensive literature review delves into the intricate landscape of obesity, a global pandemic intertwined with various comorbidities. Highlighting the escalating prevalence of obesity, the article explores current guidelines advocating lifestyle modifications, childhood obesity prevention, population-based approaches, clinical management, and monitoring strategies [10,12,13]. When lifestyle adjustments prove insufficient, pharmacological aids, including GLP-1, become crucial considerations [18].

GLP-1 drugs, initially designed for type 2 diabetes, extend benefits beyond glycemic control, influencing appetite, gastric emptying, and potentially cardiovascular health [4]. Despite positive impacts, the article underscores the importance of careful consideration due to associated side effects [20]. Notably, GLP-1 medications, notably Ozempic, have permeated popular culture, endorsed by celebrities sharing remarkable weight loss journeys [22].

The article emphasizes the need to distinguish medical efficacy from societal perceptions, positioning GLP-1 pharmacotherapy as a recommended intervention rather than a miraculous solution [24]. Beyond pharmacotherapy, addressing weight stigma becomes paramount, necessitating a shift from unproven assumptions to evidence-based approaches in both clinical and public health settings [7-8].

Looking toward the future of obesity pharmacotherapy, the article explores the potential role of probiotics [6]. Despite existing research limitations, the review highlights the promising avenue of individualized probiotic interventions, emphasizing the need for long-term studies and randomized trials. In summary,

achieving a balanced approach to obesity management requires a nuanced understanding of medical interventions, societal perceptions, and innovative possibilities in the evolving landscape of healthcare.

As obesity continues to rise as a significant health challenge, the article concludes with a call for optimism and an open-minded approach toward new treatment methods. Acknowledging the need for innovative solutions, the article encourages a collaborative effort from all stakeholders in shaping comprehensive healthcare solutions for those combating obesity.

Article highlights

- The article focuses on a comprehensive understanding of obesity, its comorbidities, and various approaches to management, including lifestyle modifications, childhood obesity prevention, population-based strategies, clinical management, and monitoring [1,9,10,11,15-17].

- GLP-1 drugs, primarily used in type 2 diabetes, are explored for their benefits beyond glycemic control, such as influencing appetite and potentially cardiovascular health [4] [19,22-24]. The article notes the positive impact but emphasizes the need for careful consideration due to associated side effects [5,20,21,25].

- Popular culture, especially celebrity endorsements, has contributed to the rising popularity of GLP-1 medications like Ozempic for weight loss [3]. The article emphasizes the importance of distinguishing medical efficacy from societal perceptions and cautions against viewing these drugs as miraculous solutions [3,7,8].

- The article delves into the potential future role of probiotics in obesity pharmacotherapy, highlighting the need for long-term studies and randomized trials to establish their effectiveness and safety [6,26].

- Current obesity guidelines by organizations like the World Health Organization include dietary recommendations, physical activity guidelines,

childhood obesity prevention, population-based approaches, clinical management, and monitoring strategies [1,9-13,16-17].

- Pharmacological aids, including GLP-1 agonists, are considered when lifestyle modifications are insufficient [3,4,19,22-24]. The article provides information on commonly used drugs for weight reduction and their potential side effects [5,18,20,21,25].

- GLP-1 drugs are explained as mimicking the effects of the naturally occurring hormone GLP-1, with benefits beyond insulin release, including weight loss and potential cardiovascular benefits [4,19,22-24].

- GLP-1 side effects are discussed, including gastrointestinal effects, hypoglycemia, injection site reactions, pancreatitis, and weight loss [5,18,25]. The article emphasizes the importance of individualized assessment and monitoring [5,18,20,21,25].

- The article highlights the existing gap between scientific evidence and societal perceptions regarding obesity, emphasizing the need for a holistic approach, societal support, and collaboration among stakeholders [7-8].

- The potential role of probiotics in obesity pharmacotherapy is discussed, focusing on the need for individualized interventions, understanding the metagenomic relationship, and conducting long-term studies to establish clinical guidelines [6,26].

- The article concludes with a call for optimism and an open-minded approach to new treatment methods for obesity, acknowledging the complexities involved in managing obesity and its associated challenges [1,9-12,14,17].

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References

1. Cuciureanu, M., Caratașu, C. C., Gabrielian, L., Frăsinariu, O. E., Checheriță, L. E., Trandafir, L. M., Stanciu, G. D., Szilagyi, A., Pogonea, I., Bordeianu, G., Soroceanu, R. P., Andrițoiu, C. V., Anghel, M. M., Munteanu, D., Cernescu, I. T., & Tamba, B. I. (2023). 360-Degree Perspectives on Obesity. *Medicina (Lithuania)*, *59*(6), 1–51. https://doi.org/10.3390/medicina59061119
2. Sarma, S., Tran, S., & Fralick, M. (2023). Novel obesity treatments. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne*, *195*(45), E1546–E1547. https://doi.org/10.1503/cmaj.230820
3. Shaefer, C. F., Kushner, P., & Aguilar, R. (2015). User's guide to mechanism of action and clinical use of GLP-1 receptor agonists. *Postgraduate Medicine*, *127*(8), 818–826. https://doi.org/10.1080/00325481.2015.1090295
4. Maselli, D. B., & Camilleri, M. (2021). Effects of GLP-1 and Its Analogs on Gastric Physiology in Diabetes Mellitus and Obesity. *Advances in Experimental Medicine and Biology*, *1307*, 171–192. https://doi.org/10.1007/5584_2020_496
5. Filippatos, T. D., Panagiotopoulou, T. V., & Elisaf, M. S. (2014). Adverse Effects of GLP-1 Receptor Agonists. *The Review of Diabetic Studies : RDS*, *11*(3–4), 202–230. https://doi.org/10.1900/RDS.2014.11.202
6. Mazloom, K., Siddiqi, I., & Covasa, M. (2019). Probiotics: How effective are they in the fight against obesity? *Nutrients*, *11*(2), 1–24. https://doi.org/10.3390/nu11020258
7. Rubino, F., Puhl, R. M., Cummings, D. E., Eckel, R. H., Ryan, D. H., Mechanick, J. I., Nadglowski, J., Ramos Salas, X., Schauer, P. R., Twenefour, D., Apovian, C.

M., Aronne, L. J., Batterham, R. L., Berthoud, H. R., Boza, C., Busetto, L., Dicker, D., De Groot, M., Eisenberg, D., … Dixon, J. B. (2020). Joint international consensus statement for ending stigma of obesity. *Nature Medicine*, *26*(4), 485–497. https://doi.org/10.1038/s41591-020-0803-x

8. Lobstein, T. (2019). Obesity prevention and the Global Syndemic: Challenges and opportunities for the World Obesity Federation. *Obesity Reviews*, *20*(S2), 6–9. https://doi.org/10.1111/obr.12888
9. van Sluijs, E. M. F., Ekelund, U., Crochemore-Silva, I., Guthold, R., Ha, A., Lubans, D., Oyeyemi, A. L., Ding, D., & Katzmarzyk, P. T. (2021). Physical activity behaviours in adolescence: current evidence and opportunities for intervention. *The Lancet*, *398*(10298), 429–442. https://doi.org/10.1016/S0140-6736(21)01259-9
10. Smith, K. B., & Smith, M. S. (2016). Obesity Statistics. *Primary Care - Clinics in Office Practice*, *43*(1), 121–135. https://doi.org/10.1016/j.pop.2015.10.001
11. E.P. Williams, M. Mesidor, K. Winters, P.M. Dubbert, S.B. Wyatt, Overweight and obesity: prevalence, consequences, and causes of a growing public health problem, Curr. Obes. Rep. 4 (3) (2015) 363–370
12. H.A. Raynor, C.M. Champagne, Position of the academy of nutrition and dietetics: interventions for the treatment of overweight and obesity in adults, J. Acad. Nutr. Diet. 116 (1) (2016) 129–147
13. National Institute of Health, National Heart, Lung, and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Obes Res 1998;6(Suppl 2):515.
14. WHO Consultation on Obesity. Obesity: preventing and managing the global epidemic. Geneva, 3–5 June 1997. Geneva (Switzerland): World Health Organi- zation; 1998.
15. Bickham DS, Blood EA, Walls CE, et al. Characteristics of screen media use associated with higher BMI in young adolescents. Pediatrics 2013;131(935): 935–41.
16. Kenchaiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. N Engl J Med 2002;347:305.
17. WangCY,McPherson K,MarshT, et al. Healthandeconomic burdenof theprojected obesity trends in the USA and the UK. Lancet 2011;378:815–25
18. Frias JP, Nauck MA, Van J, Kutner ME, Cui X, Benson C et al (2018) Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial. Lancet 392 (10160):2180–2193
19. Acosta A, Camilleri M, Shin A, Vazquez-Roque MI, Iturrino J, Burton D et al (2015b) Quantitative gastro- intestinal and psychological traits associated with obe- sity and response to weight-loss therapy. Gastroenterology 148(3):537–546.e4

20. Monami M, Dicembrini I, Nardini C, Fiordelli I, Mannucci E. Glucagon-like peptide-1 receptor agonists and pancreatitis: a meta-analysis of randomized clinical trials. Diabetes Res Clin Pract 2014. 103(2):269-275.
21. Wysham C, Blevins T, Arakaki R, Colon G, Garcia P, Atisso C, Kuhstoss D, Lakshmanan M. Efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in type 2 diabetes in a randomized controlled trial (AWARD-1). Diabetes Care 2014. 37(8):2159- 2167.
22. Nauck M, Frid A, Hermansen K, Thomsen AB, Dur- ing M, Shah N, Tankova T, Mitha I, Matthews DR. Long-term efficacy and safety comparison of liraglutide, glimepiride and placebo, all in combination with metformin in type 2 diabetes: 2-year results from the LEAD-2 study. Diabetes Obes Metab 2013. 15(3):204-212.
23. Simsek S, de Galan BE. Cardiovascular protective prop- erties of incretin-based therapies in type 2 diabetes. Curr Opin Lipidol 2012. 23(6):540-547.
24. Scott LJ. Liraglutide: a review of its use in adult patients with type 2 diabetes mellitus. Drugs 2014. 74(18):2161-2174.
25. Swinburn B, Kraak V, Allender S, et al. for the Lancet Commission on the Global Syndemic. The global syndemic of obesity, undernutrition and climate change: the Lancet Commission report. The Lancet. 2019;393(10173):791-846.
26. Vallianou, N.G.; Kounatidis, D.; Tsilingiris, D.; Panagopoulos, F.; Christodoulatos, G.S.; Evangelopoulos, A.; Karampela, I.; Dalamaga, M. The Role of Next-Generation Probiotics in Obesity and Obesity-Associated Disorders: Current Knowledge and Future Perspectives. Int. J. Mol. Sci. 2023, 24, 6755. https://doi.org/10.3390/ijms24076755