



Functional Food-Derived Peptides as Multitarget Antidiabetic Agents: *in Silico* and Biochemical Aspects

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Abstract. This article summarizes current data on the application of *in silico* approaches, particularly molecular docking, for the screening of dietary bioactive peptides of animal origin with potential hypoglycemic properties, and evaluates the prospects of their utilization in the development of functional anti-diabetic products. It was found that dietary animal-derived bioactive peptides represent promising antidiabetic agents owing to their multitarget mechanisms of action (inhibition of key enzymes of carbohydrate metabolism, including dipeptidyl peptidase-4 (DPP-4) and α -glucosidases; regulation of insulin-related signaling pathways, enhancing of peripheral tissue sensitivity to insulin, reducing postprandial hyperglycemia, and exhibition of antioxidant and anti-inflammatory activities). Camel, bovine, and caprine milk remain the most extensively studied sources of dietary peptides with confirmed inhibitory activity against DPP-4 and α -glucosidase, while the half-maximal inhibitory concentration (IC_{50}) value serves as a universal criterion for comparing peptide inhibitory potency, thereby ensuring a standardized approach to their evaluation. At the same time, the efficiency of peptide formation and their biological properties largely depend on the type of protein substrate, its amino acid composition, and the method of enzymatic hydrolysis or fermentation.

Keywords: type 2 diabetes mellitus; nutraceuticals; dietary proteins; bioactive peptides; enzymatic hydrolysis; molecular docking; molecular targets; functional foods.

Introduction

Type 2 diabetes mellitus (T2DM) remains one of the most pressing biomedical challenges of modern society due to its rapidly increasing prevalence, high risk of complications, and substantial socio-economic burden. In 2024, the global number of adults aged 20–79 years living with diabetes reached 589 million, and projections indicate that this figure will rise to 853 million by

2050. Notably, T2DM accounts for approximately 96 % of all registered cases [1, 2]. T2DM is characterized by a complex multifactorial pathogenesis, the principal components of which include impaired insulin production and insulin resistance (IR) in peripheral tissues. These processes are mediated through mechanisms such as α -cell dedifferentiation, mitochondrial dysfunction, chronic low-grade inflammation, and

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oxidative stress. Dysfunction of pancreatic β -cells leads to a reduction in insulin secretion, resulting in the inability to maintain physiological glucose levels. At the same time, IR stimulates hepatic glucose production and reduces glucose utilization in muscle, liver, and adipose tissue, thereby establishing a “vicious cycle” between insulin secretion and its action, which ultimately culminates in hyperglycemia [3, 4]. Despite advances in modern pharmacotherapy, a substantial proportion of patients with T2DM fail to achieve or maintain recommended glycemic targets (e.g., HbA1c < 7.0 %). Such suboptimal glycemic control is a major driver of severe microvascular and macrovascular complications – including nephropathy, retinopathy, cardiovascular disease, and increased mortality. This, in turn, imposes a considerable economic burden on healthcare systems and significantly diminishes patients' quality of life [5]. Therefore, the search for novel, safe, and effective agents to support glycemic homeostasis remains highly relevant. In this context, the investigation of bioactive peptides formed during enzymatic hydrolysis, fermentation, or digestion of animal-derived dietary proteins acquires particular importance, as these compounds may serve as potential antidiabetic agents [6–12]. There is evidence that these peptides are capable of modulating multiple aspects of T2DM pathogenesis, particularly by inhibiting the activity of key enzymes such as α -amylase, α -glucosidase, and dipeptidylpeptidase-4 (DPP-4), interacting with the glucagon-like peptide-1 receptor (GLP-1R), and influencing insulin signalling pathways. These properties render them promising candidates for incorporation into functional foods and nutraceutical formulations [13–14]. It should be noted that DPP-4 is most frequently identified as a molecular target in antidiabetic research. This enzyme serves as a key regulator of insulin-stimulating hormones – namely, glucose-dependent insulintropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). Inhibition of DPP-4 enhances the activity of endogenous GLP-1 and GIP, which ultimately improves β -cell function and reduces blood glucose levels, glucagon secretion, and hepatic glucose production [15]. On the other hand, the experimental identification of bioactive amino acid sequences is a labor-intensive process due to the extraordinarily large number of potential peptides. Consequently, *in silico* approaches, particularly molecular docking, are increasingly employed as they enable rapid preliminary screening of peptides, prediction of their interactions with molecular targets, assessment of binding energy and affinity, identification of key amino acid residues within protein active sites, and rational selection of the most promising candidate compounds for subsequent *in vitro* and *in vivo* investigations [13, 16].

The aim of the study: to summarize current evidence on the application of *in silico* approaches,

particularly molecular docking, for the screening of dietary bioactive peptides of animal origin with potential hypoglycaemic properties, and to evaluate the prospects of their utilization in the development of functional anti-diabetic products.

Materials and Methods

For the preparation of this narrative review, a comprehensive search, analysis, and synthesis of scientific publications was conducted, focusing on bioactive peptides of animal origin with antidiabetic properties, their mechanisms of action, sources of origin, and modern *in silico* approaches for the identification and evaluation of their biological activity and safety. The literature search was performed in major international scientometric databases, including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. The analysis primarily included original research articles and review papers published between 2021 and 2026, as well as selected earlier studies of fundamental importance for elucidating the mechanisms underlying the antidiabetic activity of bioactive peptides. During the literature search, the following keywords were employed: bioactive peptides, antidiabetic peptides, food-derived peptides, nutraceuticals, DPP-4 inhibitory peptides, α -glucosidase, α -amylase, molecular docking, molecular dynamics, virtual screening and *in silico*. For the processing of literature sources, bibliosemantic, comparative, and analytical methods were applied, along with content analysis, systematization, and synthesis of scientific data. No statistical data analysis was performed within the scope of this study, as the work is of a review nature.

Results

Modern data indicate that promising peptide inhibitors of key targets in T2DM can be derived from a wide range of dietary proteins. Among the earliest and most extensively investigated are milk-derived peptides, with camel milk attracting particular interest. Its proteins serve as a source of bioactive peptides capable of modulating crucial pathways in the pathogenesis of T2DM, including carbohydrate-metabolizing enzymes, insulin signalling pathways, and mechanisms of IR. In the study conducted by S. S. Sakr and H. Barakat, it was established that fermented camel milk, enriched with probiotic cultures and Ajwa date pulp, exhibits pronounced antidiabetic activity through the inhibition of α -amylase and α -glucosidase [6]. The highest activity was demonstrated by the sample FCM15D+L, for which the half-maximal inhibitory concentration (IC_{50}) value was 111.43 μ g/mL for α -amylase and 77.21 μ g/mL for α -glucosidase.

P. Mudgil and co-authors also demonstrated a significant antidiabetic potential of camel milk-derived peptides [17]. Following probiotic fermentation,

pronounced inhibition of pancreatic α -amylase was observed, with fermented camel milk exhibiting the lowest IC_{50} value 2.39 μ g/mL among all types of milk investigated. Molecular docking revealed that the peptides MMPY, IMEQQTDEQQDK, DQHKKAMPWTQPK, and RELEELNVPGE possess high affinity for the active site of α -amylase, interacting with key amino acid residues Trp58, Tyr62, Asp197, Glu233, and Asp300. These findings highlight their potential as natural inhibitors of carbohydrate-digesting enzymes.

In addition to their effects on carbohydrate-metabolizing enzymes, camel milk-derived peptides may also modulate insulin signalling pathways. I. K. Mohamed and co-authors investigated peptides obtained after simulated gastrointestinal digestion of camel milk, employing a combination of liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS), virtual screening, and molecular docking [9]. Out of the 232 identified peptides, four were selected as the most promising: TYYPPQ, FEPVP, TVWPE, and ELTVGAGP. The peptide TYYPPQ demonstrated the highest biological activity. In a model of insulin-resistant HepG2 cells, it promoted the restoration of insulin receptor expression and partial reactivation of the AKT signalling pathway, whose key proteins include phosphatidylinositol-3-kinase (PI3K) and AKT (protein kinase B). Molecular docking revealed that TYYPPQ interacts with critical amino acid residues of the kinase domain of the insulin receptor, notably Glu1047 and Asp1150. It was established that this peptide primarily exerts an allosteric activation mechanism, stabilizing the receptor's active conformation.

Cow's milk is among the most extensively studied sources of bioactive peptides with potential antidiabetic activity. Particular interest is directed toward peptides capable of inhibiting DPP-4, as well as compounds exhibiting dual inhibitory activity against both DPP-4 and angiotensin-converting enzyme (ACE). Such activity may provide a simultaneous impact on glycemic control and cardiometabolic status. A particularly promising source of antidiabetic peptides is cow's milk lactoferrin. In the study conducted by C. Elisha and co-authors, *in silico* hydrolysis with pepsin-trypsin yielded 129 peptides, a substantial proportion of which demonstrated potential DPP-4 and ACE inhibitory activity [18]. Further analysis revealed that 43% of the peptides possessed potential DPP-4 inhibitory activity, while 28% exhibited potential ACE inhibition. According to molecular docking results, among the DPP-4 inhibitors, the most promising was the peptide WQWR, with a binding energy of -9.3 kcal/mol, whereas among the ACE inhibitors, the peptide EPYF demonstrated the best performance, with a binding energy of -10.1 kcal/mol. Subsequent *in vitro* analysis confirmed the high biological activity

of the hydrolysates: the IC_{50} value for ACE inhibition was (0.48 ± 0.01) mg/mL, while for DPP-4 inhibition it was (0.93 ± 0.02) mg/mL. LC-MS/MS analysis further verified the presence of the key peptides EPYF and WQWR within the hydrolysate composition.

In the study by A. Iwaniak and co-authors, cow's milk protein preparations were analyzed as a source of bioactive peptides using a combined *in silico* and *in vitro* approach [7]. Based on the BIOPEP-UWM database, the formation of 59 bioactive peptides was predicted following enzymatic hydrolysis of milk proteins, with short di- and tripeptides predominating. The most numerous group consisted of DPP-4 inhibitory peptides. After simulated gastrointestinal digestion, all tested samples exhibited pronounced DPP-4 inhibitory activity. The best result was obtained for the MBP D sample, with an IC_{50} value of 0.0067 mg/mL. Moreover, 23-27 DPP-4 inhibitory peptides were identified in the hydrolysates, depending on the type of milk protein preparation. Importantly, all samples also demonstrated antioxidant activity, which represents an additional advantage given the role of oxidative stress in the pathogenesis of IR and T2DM.

Goat's milk is likewise considered a promising source of bioactive peptides with antidiabetic properties, owing to the high biological value of its proteins, good digestibility, and the ability to generate short functionally active peptide fragments during enzymatic hydrolysis. In the study by M. Liu and co-authors, the search for DPP-4 inhibitory peptides from goat milk proteins was conducted using an integrated approach that combined *in silico* hydrolysis, virtual screening, molecular docking, molecular dynamics simulation, and *in vitro* experimental validation [19]. After computational hydrolysis of the 11 major goat milk proteins, 319 peptides with lengths ranging from 3 to 15 amino acid residues were obtained. Through multilevel screening, three peptides were identified as the most promising: MMSF, MPFPK, and GPFPII. Subsequent analysis using high-performance liquid chromatography (HPLC) confirmed their presence in the goat milk hydrolysate. *In vitro* studies demonstrated that all three peptides exhibit DPP-4 inhibitory activity, with the highest activity observed for MPFPK ($IC_{50} = 0.32$ mM). The IC_{50} value for MMSF was 0.69 mM, and for GPFPII it was 2.83 mM. Molecular docking revealed that all three peptides interact with key amino acid residues of the DPP-4 active site, including His740, Tyr631, Tyr547, Ser630, Glu205, and Glu206. The most stable complex was formed by MPFPK, which established five hydrogen bonds with residues E205, E206, R125, T662, and Y631. Additionally, the absence of significant cytotoxicity in the Caco-2 cell model indicates the potential safety of these peptides as nutraceutical components.

In the study by Y. Wu and co-authors, employing peptidomics, *in silico* screening, and experimental

validation, two novel DPP-4 inhibitors were identified from the goat milk protein hydrolysate: the tetrapeptide LLLP and the tripeptide YPF [15]. From the 698 identified peptides, a multistep selection process led to the synthesis of 12 candidates for experimental validation, among which LLLP and YPF exhibited the highest DPP-IV inhibitory activity. In a cell-free system, the IC_{50} values were (213.99 ± 0.64) mM for LLLP and (368.54 ± 12.97) mM for YPF. In the Caco-2 cell model, these peptides demonstrated even greater efficacy, with IC_{50} values of (154.96 ± 8.41) mM and (159.46 ± 17.40) mM, respectively, indicating their ability to retain biological activity under cellular conditions. Furthermore, both peptides exhibited no cytotoxicity within the concentration range of 0.025–1 mg/mL, underscoring their potential safety as nutraceutical components. Molecular docking analysis demonstrated that their inhibitory activity is associated with the formation of multiple non-covalent interactions with key amino acid residues of the DPP-4 active site, including Arg358, Phe357, Glu205, Tyr547, Tyr662, and Tyr666, thereby ensuring stable ligand–enzyme binding. The obtained results indicate that LLLP and YPF represent promising food-derived peptides for the development of functional foods and nutraceuticals with potential antidiabetic effects.

P. Mudgil and co-authors conducted a comprehensive study of peptides obtained through probiotic fermentation of cow, goat, camel, and sheep milk [8]. It was established that fermentation significantly enhances the degree of proteolysis and promotes the generation of low-molecular-weight bioactive peptides with pronounced antidiabetic properties. Comparative analysis revealed that different types of milk vary in their ability to produce peptides with DPP-4 inhibitory activity. The highest level of proteolysis was observed in fermented goat milk, indicating its strong capacity to generate functionally active peptides. At the same time, camel milk exhibited the most pronounced antidiabetic activity, as evidenced by its inhibitory effects on both DPP-4 and α -amylase. Among the probiotic strains of lactic acid bacteria, the most effective was identified as *Pediococcus pentosaceus* PP-957, which facilitated the formation of peptides with the highest DPP-4 inhibitory activity. Following fermentation, the IC_{50} values were markedly reduced compared to non-fermented samples: for cow's milk to 0.17 mg/mL, for camel milk to 0.12 mg/mL, and for goat milk to 0.25 mg/mL. Molecular docking confirmed that the generated peptides interact with key amino acid residues of the active sites of target enzymes, forming stable ligand–enzyme complexes. These findings indicate that different types of milk can serve as effective sources of nutraceutical peptides with multitarget antidiabetic activity.

Fish and meat protein hydrolysates are also regarded as promising sources of peptide-based

nutraceuticals with antidiabetic potential. Fish protein hydrolysates contain a substantial number of short peptides with potential antidiabetic activity. Specifically, in Baltic herring hydrolysates, more than 2000 peptides were identified, among which over 950 candidates with predicted DPP-4 inhibitory activity were selected following *in silico* analysis [20]. Subsequent experimental validation confirmed the biological activity of individual peptides, while the application of hydrolysates in a diet-induced obesity model was associated with improved glucose tolerance, reduced insulin resistance, suppression of DPP-4 activity, increased levels of GLP-1, and decreased production of pro-inflammatory cytokines. These findings suggest that fish-derived peptides may exert an antidiabetic effect through simultaneous modulation of carbohydrate metabolism and chronic low-grade inflammation. The study of sturgeon skeletal muscle proteins further confirmed the potential of fish-derived raw materials [21]. The identified peptides VT-9 and LE-9 exhibited competitive inhibition of α -glucosidase, and molecular docking results demonstrated their stable interaction with the catalytic site of the enzyme. Beyond their enzyme-inhibitory activity, these peptides enhanced glucose uptake in HepG2 cells, stimulated glycogen synthesis, and reduced oxidative stress, indicating a multifaceted impact on the cellular mechanisms of impaired carbohydrate metabolism.

Similar trends are also observed for meat-derived raw materials. Specifically, a number of potentially hypoglycemic peptides were identified from porcine collagen, among which the most promising was the tetrapeptide NWYR. It exhibited strong α -glucosidase inhibitory activity, surpassing that of acarbose, as well as high affinity for DPP-4, according to molecular docking results. Furthermore, the application of network pharmacology methods revealed interactions of NWYR with several molecular targets of T2DM, including DPP-4, ACE, matrix metalloproteinases 2 and 9, and coagulation factor II (F2, prothrombin), thereby indicating the multitarget nature of its biological activity [11].

In recent years, edible insects have been considered a promising alternative protein source for obtaining bioactive peptides with antidiabetic properties. Particular interest has been directed toward peptides derived from the larvae of the yellow mealworm (*Tenebrio molitor*), which are capable of simultaneously targeting several key enzymes associated with T2DM, including α -glucosidase, α -amylase, and DPP-4. Y. Zhu and co-authors employed a comprehensive approach that integrated proteomic analysis, enzyme assays, a cellular model of insulin resistance, and molecular docking to identify antidiabetic peptides from *Tenebrio molitor* [22]. Six bioactive peptides (DYGPPFK, WSPDPK, GMDFQPR, FNPFDLTK, SLFLPK,

and DPFDALPK) were identified, all of which exhibited α -glucosidase inhibitory activity. The lowest IC_{50} values were demonstrated by DPFDALPK (5.58 mg/mL) and DYGPFFK (5.76 mg/mL). Meanwhile, the peptide GMDFQPR showed the highest DPP-IV inhibitory activity ($IC_{50}=0.64$ mg/mL), highlighting its potential to prolong incretin hormone action and improve glycemic regulation. Particular emphasis was placed on molecular docking, which revealed strong affinity of the peptides for the active sites of α -glucosidase and DPP-4. The formation of stable hydrogen and hydrophobic interactions with key amino acid residues of the enzymes explains their pronounced antidiabetic activity and confirms the promise of these peptides as multitarget nutraceuticals.

F. M. de Matos and R. J. S. de Castro investigated hydrolysates of *Tenebrio molitor* flour and protein concentrate obtained using the proteases Flavourzyme, Alcalase, and Neutrase [12]. Enzymatic hydrolysis markedly enhanced the ability of the hydrolysates to inhibit α -amylase and α -glucosidase, and in the fraction with a molecular weight below 3 kDa, 38 peptides were identified. The most promising was the peptide LPAIL, for which computational analysis predicted a high probability (66.25 %) of DPP-4 inhibitory activity. The researchers attributed this effect to the presence of proline, isoleucine, and leucine residues in its structure, amino acids frequently found in known DPP-4 inhibitors. These findings confirm the effectiveness of *in silico* approaches for the primary screening of bioactive peptides and highlight the potential of *Tenebrio molitor* proteins as a source of functional ingredients with antidiabetic properties.

Discussion

Modern strategies for the discovery of bioactive peptides increasingly rely on the integration of traditional peptide generation techniques with advanced bioinformatic approaches. As emphasized by M. Hajfathalian and colleagues, the most promising direction involves the combination of enzymatic and virtual protein hydrolysis, bioinformatic analysis, molecular docking, and subsequent experimental validation [23]. Molecular docking is one of the most widely used *in silico* methods for predicting the interactions of bioactive peptides with target enzymes, such as DPP-4, α -glucosidase, α -amylase, and GLP-1R. This approach enables the modelling of the spatial orientation of a peptide within the active site of a protein, the evaluation of intermolecular interactions, and the prediction of ligand-receptor affinity. The principal evaluation criterion is the binding energy (docking score), usually expressed in kcal/mol, where more negative values correspond to higher predicted stability of the peptide-enzyme complex. At the same time, binding energy alone

is not a sufficient evaluation criterion; therefore, docking results are analyzed comprehensively, taking into account the localization of the peptide within the active site, its interactions with catalytic amino acid residues, as well as the formation of hydrogen bonds, hydrophobic contacts, electrostatic interactions, and π -interactions. To confirm the stability of the complex, docking is increasingly combined with molecular dynamics simulations, which involve the analysis of root mean square deviation (RMSD), root mean square fluctuation (RMSF), and the radius of gyration (Rg). RMSD characterizes the overall structural stability of the complex throughout the simulation; small RMSD fluctuations indicate stable peptide-enzyme binding. RMSF reflects the mobility of individual amino acid residues within the protein, thereby allowing the identification of regions undergoing the greatest conformational changes upon ligand binding. Rg is employed to assess the compactness of the protein's spatial structure; its stability during the simulation indicates preservation of the structural integrity of the complex. A comprehensive analysis of binding energy together with RMSD, RMSF, and Rg values provides a more objective evaluation of the potential efficacy of antidiabetic peptides and enhances the reliability of *in silico* screening results [15, 24].

One of the key experimental indicators of the efficacy of antidiabetic peptides is IC_{50} , which reflects the peptide concentration required to inhibit 50% of the activity of a target enzyme, such as DPP-4, α -glucosidase, or α -amylase. Owing to its universality and quantitative nature, IC_{50} is widely employed as a standardized criterion for comparing the inhibitory potency of different bioactive peptides, regardless of their origin or amino acid sequence. Determination of IC_{50} is based on the analysis of the dose-dependent response of an enzyme to the action of an inhibitor. Depending on the study design and the method of expressing concentration, results may be reported in various units, most commonly nM, μ M, mM, μ g/mL, or mg/mL. The use of uniform measurement units or their conversion is an essential prerequisite for the correct comparison of the inhibitory activity of different peptides. Lower IC_{50} values indicate higher inhibitory potency; therefore, this parameter is widely employed to compare the efficacy of peptides of diverse origins and to facilitate the primary selection of promising candidates. At the same time, cross-study comparisons require caution due to differences in experimental conditions, enzyme sources, substrates, and measurement units. Once determined, IC_{50} is often utilized to guide the choice of concentrations in cell-based assays and to support the interpretation of results obtained from molecular docking and molecular dynamics simulations [25, 26].

The comparative analysis highlights that different animal milks yield bioactive peptides with distinct anti-

diabetic mechanisms. S. S. Sakr and H. Barakat showed that fermented camel milk enriched with probiotics and Ajwa date pulp strongly inhibits α -amylase and α -glucosidase, reducing postprandial hyperglycemia [6]. P. Mudgil et al. confirmed its lowest IC_{50} values for α -amylase inhibition [17], while I. K. Mohamed et al. demonstrated that peptides such as TYYPPQ restore insulin receptor expression and partially reactivate the PI3K/AKT pathway [9]. C. Elisha et al. identified lactoferrin-derived peptides with dual DPP-4 and ACE inhibitory activity, suggesting benefits for both glycemic control and cardiometabolic regulation [18]. A. Iwaniak et al. further showed that bovine milk hydrolysates generate numerous short peptides with strong DPP-4 inhibition and antioxidant properties, addressing insulin resistance and oxidative stress [7]. M. Liu et al. reported peptides with significant DPP-4 inhibitory activity and no cytotoxicity [15], while Y. Wu et al. discovered novel inhibitors that retained activity under cellular conditions, reinforcing goat milk's safety and efficacy as a nutraceutical source [19]. P. Mudgil et al. demonstrated that probiotic fermentation enhances proteolysis and peptide generation, markedly reducing IC_{50} values [17]. Camel milk showed the strongest multitarget activity, while goat milk exhibited the highest proteolysis capacity. Thus camel milk emerges as the most potent multitarget source, cow milk contributes dual enzyme inhibition with antioxidant support, and goat milk provides safe and effective DPP-4 inhibitors. Fermentation consistently amplifies bioactivity, positioning probiotic-fermented milk products as promising functional foods for T2DM management. Sturgeon and porcine sources further confirm the potential of animal-derived peptides, with VT-9 and LE-9 from sturgeon improving glucose uptake and reducing oxidative stress, while the porcine collagen peptide NWYR demonstrated potent, multitarget activity against α -glucosidase, DPP-4, ACE, and other T2DM-related enzymes, surpassing acarbose in inhibitory strength [11, 21]. Edible insects, particularly *Tenebrio molitor*, have emerged as a promising source of antidiabetic peptides, with several sequences showing strong inhibitory activity against α -glucosidase, α -amylase, and DPP-4, alongside molecular docking evidence of stable enzyme binding. In addition, results reported by Y. Zhu

et al., and de Matos F.M. and de Castro R.J.S., confirm the multitarget nutraceutical potential of insect-derived proteins for T2DM management [12, 22]. Thus, the findings of narrative review indicate that bioactive peptides derived from animal dietary proteins exhibit promising antidiabetic potential. Regardless of their source – whether milk from various livestock species, fish, meat, or edible insects – bioactive peptides are characterized by multitarget mechanisms of action, including inhibition of key carbohydrate-metabolizing enzymes such as DPP-4 and α -glucosidase, regulation of insulin-related signalling pathways, enhancement of peripheral tissue insulin sensitivity, reduction of postprandial hyperglycemia, as well as antioxidant and anti-inflammatory activities. Camel, bovine, and caprine milk remain the most extensively studied sources of peptides with confirmed inhibitory activity against DPP-4 and α -glucosidase, while the IC_{50} value serves as a universal criterion for comparing peptide inhibitory potency, thereby ensuring a standardized approach to their evaluation. At the same time, the efficiency of peptide formation and their biological properties largely depend on the type of protein substrate, its amino acid composition, and the method of enzymatic hydrolysis or fermentation.

Conclusions

Animal-derived bioactive dietary peptides represent promising antidiabetic agents owing to their multitarget mechanisms of action. Among the most extensively investigated sources are different animals milk proteins, with the IC_{50} value providing a standardized measure of their efficacy. Future research should focus on the integration of modern *in silico*, *in vitro*, and *in vivo* approaches to optimize peptide selection and facilitate the development of novel nutraceuticals for the prevention and treatment of T2DM.

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Conflict of interest

The authors declare no conflict of interest.

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Функціональні харчові пептиди як мультитаргетні антидіабетичні агенти: *in silico* та біохімічні аспекти

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Анотація. У статті узагальнено сучасні дані щодо застосування підходів *in silico*, насамперед молекулярного докінгу, для скринінгу харчових біоактивних пептидів тваринного походження із потенційними цукрознижувальними властивостями та оцінено перспективи їх використання у створенні функціональних продуктів антидіабетичного спрямування. Встановлено, що такі пептиди є перспективними антидіабетичними агентами завдяки мультитаргетним механізмам дії: інгібування ключових ферментів вуглеводного метаболізму (зокрема DPP-4 та α -глюкозидази), регуляція інсулінозалежних сигнальних шляхів, підвищення чутливості периферичних тканин до інсуліну, зниження постпрандіальної гіперглікемії та володіння антиоксидантною й протизапальною активністю. Найкраще дослідженими джерелами харчових пептидів залишаються верблюже, коров'яче та козяче молоко, для яких підтверджено інгібіторну активність проти DPP-4 та α -глюкозидази. При цьому значення напівмаксимальної інгібувальної концентрації (IC_{50}) є універсальним критерієм для порівняння інгібіторної потужності пептидів, забезпечуючи стандартизований підхід до їх оцінювання. Водночас ефективність утворення та біологічні властивості пептидів значною мірою залежать від виду білкової сировини, її амінокислотного складу, способу ферментативного гідролізу або ферментації.

Ключові слова: цукровий діабет 2 типу; нутрицевтики; харчові білки; біоактивні пептиди; ферментативний гідроліз; молекулярний докінг; молекулярні мішені; функціональні харчові продукти.