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EFFECT OF BIOACTIVE PEPTIDES DERIVED FROM WHEY PROTEIN HYDROLYSATE ON INTESTINAL METABOLIC SIGNALING AND ENTEROENDOCRINE ACTIVITY

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Annotation. This article analyzes the mechanisms of interaction between bioactive peptides formed during the enzymatic hydrolysis of whey proteins and the intestinal epithelium, enteroendocrine system and gut microbiota. Scientific sources highlight how whey peptides stimulate the secretion of enterohormones such as GLP-1, GIP, PYY and CCK, influence glucose homeostasis, fat and energy metabolism, insulin sensitivity, inflammation processes and enterocyte regeneration. Activation of GPCR receptors in the intestine, Ca^{2+} signaling, AMPK and MAPK/ERK cascades, as well as alterations in the metabolism of short-chain fatty acids (SCFA), are discussed as molecular pathways of peptide effects. The results indicate that whey-derived peptides possess high nutraceutical and therapeutic potential.

Keywords: whey peptides, GLP-1, intestinal metabolism, GPCR, SCFA, microbiota, insulin sensitivity.

Introduction. Whey proteins are among the main biologically active fractions of milk, and their enzymatic hydrolysis produces multifunctional bioactive peptides [1, 2]. In recent years, interest toward whey peptides has increased in Uzbekistan and CIS countries, due to the growing importance of nutraceutical compounds in the

prevention and reduction of metabolic disorders. This trend is also linked to the practical prospects of dry whey products in the food industry and agriculture [1, 8]. Whey peptides influence metabolic signaling pathways through the intestinal epithelium, enhancing the release of enterohormones including GLP-1, GIP, PYY and CCK, which contribute to glucose tolerance, appetite regulation and fat metabolism [2, 3]. Bioactive peptides also affect the composition and metabolic activity of gut microbiota. Increased production of SCFA (butyrate, propionate and acetate) and their interaction with receptors such as GPR41 and GPR43 promote enteroendocrine responses, reduce inflammation and normalize energy exchange [4, 5]. The physiological importance of whey and its related supplements has also been investigated in poultry by Uzbek researchers, where improvement in digestive enzyme activity, growth parameters, metabolic status and immune response has been reported. These data indicate the necessity of further comprehensive research on whey components as nutraceutical agents [9–15]. Biopolymers, particularly chitosan, are also considered potential comparative nutraceutical components due to their biological activity in dietary and functional nutrition [7].

Main Part. Composition of whey proteins and mechanisms of bioactive peptide formation. Whey proteins consist of β-lactoglobulin, α-lactalbumin, lactoferrin, immunoglobulins and glycomacropeptide fractions [1, 2]. Their hydrolysis under natural (pepsin, trypsin, chymotrypsin) or industrial conditions leads to peptides of different lengths and biological functions. Dipeptides and tripeptides are rapidly absorbed via the PEPT1 transporter in the intestine, whereas larger peptides activate GPCR receptors, triggering intracellular signaling in enteroendocrine cells [2, 3]. The biological activity of peptides depends on amino acid composition, charge and three-dimensional conformation, and some peptides have been shown to activate cAMP/PKA signaling, Ca^{2+} influx and ERK1/2 pathways in intestinal cells [2, 3].

Secretion of intestinal hormones: GLP-1, GIP, PYY and CCK. One of the key effects of bioactive peptides is modulation of enterohormone secretion. GLP-1 is secreted by L-cells, increases insulin secretion, suppresses glucagon release, reduces appetite and normalizes glucose levels [3]. Scientific literature states that whey hydrolysates significantly elevate GLP-1 levels after consumption [2, 3]. GIP increases β-cell glucose sensitivity, PYY strengthens satiety signaling and CCK stimulates bile release and lipid digestion [2, 3]. These processes occur via GPCR activation followed by Ca^{2+} influx, PKA/PKC activation and MAPK/ERK signaling cascades [2, 3]. Because of this, whey peptides hold potential as nutraceutical components in complex prevention of metabolic syndrome, type-2 diabetes and obesity [2, 3].

Effects on glucose metabolism and insulin sensitivity. Whey peptides regulate glucose metabolism in several ways: stimulating insulin secretion via GLP-1 and GIP, activating AMPK signaling to promote GLUT4 membrane translocation, reducing hepatic gluconeogenesis and limiting adipose lipogenesis [2, 3, 6]. AMPK is seen as a central regulator of energy metabolism, and its activation is associated with reduced insulin resistance [6]. Thus, whey peptides are considered scientifically justified candidates for nutraceutical antidiabetic intervention [2, 3, 6].

Methodology. This article is based on analysis of modern scientific literature on the physiological, biochemical and metabolic effects of bioactive peptides derived from whey proteins. In vivo and in vitro results, clinical data and conceptual perspectives on enteroendocrine regulation were comparatively evaluated [2, 3]. Studies on gut microbiota and SCFA metabolism, especially the effects of SCFA on GLP-1 secretion, were adopted as analytical criteria [4, 5]. Uzbek and CIS-regional poultry research on whey-based supplements was used as additional scientific evidence for nutraceutical applicability [9, 15]. Comparative information on biologically active biopolymers including chitosan was also reviewed [7].

Analysis. Influence of peptides on gut microbiota. Whey peptides demonstrate positive effects on gut microbiota, increasing certain beneficial microbial groups and SCFA production, thereby enhancing metabolic regulation [5]. SCFAs normalize energy metabolism, reduce inflammation and support intestinal epithelial recovery via GPR41/GPR43 receptor pathways [4, 5]. Butyrate strengthens intestinal barrier integrity by increasing tight-junction protein expression [5].

Analysis of enterohormone secretion. Increased secretion of GLP-1, GIP, PYY and CCK under the influence of whey peptides is attributed to GPCR activation and downstream signaling cascades including Ca^{2+} flux, PKA/PKC and MAPK/ERK pathways [2, 3]. Direct SCFA effect on GLP-1 secretion further emphasizes gut–metabolic linkage [4].

Energy metabolism and lipolysis. Whey peptides activate AMPK and thereby stimulate lipid oxidation while suppressing lipogenesis, leading to normalization of energy balance [6]. Enterohormones such as PYY and CCK also reduce appetite, contributing to dietary energy control [2, 3].

Immunomodulatory properties. Whey fractions and their peptides influence inflammatory mediators and aid in regeneration of intestinal mucosa [1, 2]. Biopolymers including chitosan are reported to exhibit immunomodulatory and barrier-supporting functions [7]. Poultry studies show improved immune and physiological indicators with whey-based supplements, providing additional evidence for nutraceutical potential [9, 15].

Results. The analysis concludes that whey peptides activate intestinal metabolic signals and enhance secretion of GLP-1, GIP, PYY and CCK [2, 3]. AMPK activation improves glucose metabolism and insulin sensitivity [6]. Increased SCFA formation within the microbiota supports entero-metabolic regulation [4, 5]. Regional poultry studies demonstrate improvements in growth, digestive enzyme activity and immune indicators, strengthening the applied

importance of whey-based components [8, 9, 10, 11, 12, 13, 14, 15]. Comparative data on chitosan highlight valuable biological activity [7].

Conclusion. Bioactive peptides produced through whey protein hydrolysis are promising biomodulators affecting intestinal metabolic signaling and enteroendocrine function in multiple directions. They stimulate enterohormone secretion, normalize glucose homeostasis, support gut microbiota metabolic activity, reduce inflammation and optimize energy metabolism. Thus, whey peptides are considered a promising bioactive component in clinical nutrition, sports medicine and nutraceutical practice for prevention and complex intervention of metabolic disorders.

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