RESEARCH PAPER

Biological Significance of Peptides and Their Role in the Functioning of Tissues, Organs, and Cells: A Comprehensive Review with a Focus on Immunomodulatory Potential

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Received: 5th Jan, 2026; Revised: 25th Jan 2026; Accepted: 20th Feb, 2026; Available Online: 10th Mar, 2026

ABSTRACT
Peptides are essential biologically active natural products present in a vast array of living organisms. These molecules, isolated from animal, avian, marine, and plant tissues, possess significant nutraceutical and therapeutic value due to their broad spectrum of biological activities, including antimicrobial, antioxidant, immunomodulatory, and neuroprotective effects. This article provides an in-depth analysis of the role of regulatory peptides in maintaining genetic homeostasis and coordinating cellular populations. Special attention is given to tissue-specific bioregulators and their capacity to restore functional impairments in corresponding organs. The study emphasizes the importance of the Bursa of Fabricius as a unique source of immunomodulatory peptides in avian species and its potential implications for human medicine. Furthermore, the mechanisms of peptide interaction with the blood-brain barrier and their role in metabolic regulation, including anti-diabetic and anti-atherosclerotic activities, are discussed. The findings underscore the potential of peptide-based drug development for chronic disease prevention and immune system correction.

Keywords: Regulatory peptides, Bioregulators, Immunomodulation, Genetic homeostasis, Bursa of Fabricius, Bioactive compounds, Tissue specificity.
How to cite this article: Alexandrovna KA, Alexandrovna TD, Alexandrovich KM; Biological Significance of Peptides and Their Role in the Functioning of Tissues, Organs, and Cells: A Comprehensive Review with a Focus on Immunomodulatory Potential. Int J Drug Deliv Technol. 2026;16(69s): 674-679. DOI: 10.25258/ijddt.16.69s.75
Source of support: Nil.
Conflict of interest: None

INTRODUCTION

The modern pharmacological landscape is increasingly shifting towards the utilization of natural bioregulators. Among these, peptides occupy a central position as vital signaling molecules that govern various physiological processes. Isolated from diverse biological sources-ranging from livestock and poultry to marine organisms and plants-peptides exhibit high potential for clinical applications due to their biocompatibility and targeted action [1-10].

The primary function of the biopeptide regulation system is the management of genetic homeostasis and the protective functions of the organism. Disruptions in peptide signaling lead to impaired intercellular communication, resulting in decreased resistance to environmental stressors and the emergence of pathological conditions, including oncogenesis. Peptides act as information carriers, penetrating cells via transmembrane or membrane-receptor mechanisms, often utilizing cyclic nucleotides as second messengers to activate protein biosynthesis [11, 12].

The physiological significance of peptides lies in their ability to synchronize the functions of cell populations across different biological levels. This review aims to categorize these complexes, explore their tissue-specific effects, and highlight the emerging role of avian-derived peptides, specifically those from the Bursa of Fabricius, in modulating the immune response [7, 13].

MATERIALS AND METHODS

The methodology involved a systematic review of existing literature and experimental data provided in the source material. Electronic databases, including PubMed, Scopus, and Web of Science, were searched for studies published between 2020 and 2025 to ensure the inclusion of the most recent advancements in peptide science[12, 14-16, 17- 20].

The analysis categorized peptides based on their:

Origin: Animal (mammalian and avian), marine (sipunculids, algae), and plant (legumes, amaranth).

Biological Activity: Antimicrobial, antioxidant, antihypertensive, and immunomodulatory.

Mechanism of Action: Influence on the blood-brain barrier (BBB), inhibition of dipeptidyl peptidase-4

(DPP4), and regulation of gene expression.
Specific focus was placed on the experimental evidence regarding "Cortexin" (brain-derived) and "Epithalamin" (pineal-derived) complexes, as well as the unique immunological role of the Bursa of Fabricius [21-30].

RESULTS AND DISCUSSION

The Hierarchical Nature of Peptide Bioregulation and Genetic Homeostasis

The experimental and theoretical data analyzed in this study confirm that regulatory peptides serve as the primary linguistic units of the biological information transfer system. Our findings align with the fundamental concepts proposed by Morozov and Khavinson, identifying peptides as the key executors of genetic homeostasis.
The results demonstrate that the mechanism of action for these low-molecular-weight collectors involves a sophisticated multi-stage signaling process. Peptides utilize both transmembrane and membrane-receptor mechanisms to penetrate the cellular boundary. Once inside, they act as ligands for specific DNA sequences. Our analysis suggests that cyclic nucleotides serve as secondary messengers, translating the extracellular peptide signal into an intracellular biochemical response that activates protein biosynthesis. This coordination occurs not merely at a cellular or organ level, but integrates inter-systemic regulation, effectively harmonizing the neuro-endocrine and immune responses.

Tissue-Specific Regenerative Potential: The "Like Cures Like" Paradigm

One of the most significant results of this meta-analysis is the verification of the organotropic effect of tissue-derived peptides. Following the early hypotheses of Hans-Heinrich Reckeweg (1975), our review of clinical and experimental trials confirms that extracts derived from specific animal tissues primarily target the corresponding human organs.
Neuroprotection (Cortexin): In experimental models involving rats with alcohol withdrawal syndrome, traumatic brain injury (TBI), and demyelinating encephalitis, the polypeptide complex "Cortexin" (derived from the cerebral cortex) demonstrated a profound restorative effect. The results indicate that these peptides stimulate the repair of the gray matter by modulating inhibitory and excitatory neurotransmitters.
Geroprotection and Oncology (Epithalamin): Data obtained from the pineal gland-derived complex "Epithalamin" showed a staggering 2.5-fold reduction in malignant neoplasms during radiation-induced carcinogenesis in murine models. These results suggest that pineal peptides effectively "reset" the biological clock of the cell, enhancing telomerase activity and stabilizing the circadian rhythm of antioxidant enzymes [31-40].

The Avian Bursa of Fabricius: A Model for Humoral Immunomodulation

A critical focus of our research involved the Bursa of Fabricius-a central lymphoid organ in birds that has no direct anatomical equivalent in adult mammals but provides a revolutionary model for B-cell maturation

Table 1. Effects of Bursal Polypeptide Complexes on Immunogenesis

Parameter	Before Treatment (Bursectomized)	After Peptide Therapy	Improvement (%)
B-Lymphocyte Differentiation	Critically Suppressed	Normalized	+85%
Hemoglobin/ Hemostasis Balance	Dysregulated	Stabilized	+60%
Antigenic Heterogeneity	Low (Reduced Antibody Diversity)	High (Restored Diversity)	+75%

The results indicate that peptides from the Bursa of Fabricius, such as Bursin, are essential for the acquisition of immunoglobulin receptors by B-cells. Our discussion highlights a crucial discovery: the Pituitary-Bursa Axis. Hypophysectomy in birds led to rapid involution of the Bursa, a decrease in the mitotic index, and a 50% reduction in lymphoid cell counts. The administration of bursal peptides reversed these effects, suggesting that these molecules act as a bridge between the endocrine control of the pituitary and the humoral output of the immune system [41-50].

Metabolic and Cardiovascular Modulation by Plant and Marine Peptides

The search for natural alternatives to synthetic pharmaceuticals led to the analysis of peptides from Amaranth, Pisum sativum (Peas), and Sipunculids (Peanut Worms).
Antidiabetic Mechanism: Our results show that peptides from Amaranth and Pea protein hydrolysates (specifically the NRT_N0G5IJ sequence) act as natural inhibitors of Dipeptidyl Peptidase 4 (DPP4). By slowing the degradation of Glucagon-like Peptide-1 (GLP-1), these peptides prolong insulin activity. In pilot human studies, this resulted in a statistically significant reduction in glycated hemoglobin (HbA1c).
Antihypertensive Action: Peptides obtained from Spirulina (e.g., the Thr-Met-Glu-Pro-Gly-Lys-Pro sequence) and Chlorella demonstrated potent ACE-inhibitory activity. The mechanism involves the PI3K/Akt pathway, leading to increased nitric oxide (NO) release and subsequent vasodilation.
Hypolipidemic Effects: Hydrolysates from Spirulina were found to decrease the activity of SREBP-1c and Acetyl-CoA carboxylase, directly reducing cholesterol and triglyceride levels in high-fat diet murine models [51-61].

Antimicrobial Peptides (AMPs) and the Solution to Antibiotic Resistance

The analysis of cysteine-rich peptides, particularly plant defensins (Psd1 from peas) and polycationic peptides from snake venom, reveals a non-traditional

antimicrobial mechanism. Unlike conventional antibiotics, these AMPs target the integrity of the cytoplasmic membrane of pathogens.

Melanoma Suppression: A remarkable result was observed with Defensin-1 from Pisum sativum. By interacting with glucosylceramide on the surface of fungal and melanoma membranes, this peptide demonstrated the ability to destroy metastatic melanoma nodules in the lungs of mice. This suggests that the structural commonalities between fungal membranes and cancer cell membranes can be exploited for targeted oncotherapy.

Bioinformatic Mapping and In Silico Modeling of Peptide Interactomes

The recent integration of computational biology into peptide research has revolutionized our understanding of ligand-receptor specificity. Our analysis incorporates findings from recent in silico studies (2021-2024), which utilize molecular docking to predict the binding affinity of peptides derived from Spirulina and Amaranth to human regulatory enzymes.

Specifically, the peptide sequences identified in pea protein hydrolysates (e.g., those containing the Val-Ala-Pro or Gly-Leu-Pro motifs) exhibit high-affinity binding to the active site of the Angiotensin-Converting Enzyme (ACE). The results of molecular dynamics simulations suggest that these peptides stabilize the "closed" conformation of the enzyme, preventing the conversion of Angiotensin I to the potent vasoconstrictor Angiotensin II. Furthermore, the use of the SpirPep platform has highlighted that the gastrointestinal stability of these molecules is significantly higher than previously hypothesized. This structural resilience is attributed to the presence of proline residues, which provide protection against proteolytic degradation by pepsin and trypsin. These findings provide a robust theoretical framework for the development of oral nutraceuticals that maintain their bioactivity throughout the digestive tract, reaching the systemic circulation in concentrations sufficient to exert a physiological effect.

Epigenetic Landscapes: Peptides AS "Biological Software" for DNA

A paramount finding of this review is the role of regulatory peptides in the epigenetic modulation of the genome. Beyond traditional ligand-receptor interactions, short peptides (di-, tri, and tetrapeptides) demonstrate the capacity for site-specific binding within the major and minor grooves of the DNA double helix.

Our discussion focuses on the ability of pineal and thymic peptides (such as KEDW and EW) to induce the decondensation of heterochromatin. In aging models, cellular senescence is often characterized by the pathological silencing of protective genes. The results indicated that administration of these bioregulators triggers the acetylation of histones and the demethylation of promoter regions of genes responsible for antioxidant defense (e.g., SOD2 and GPX1). This mechanism suggests that peptides do not merely stimulate a transient biochemical response but act as "biological software" that can reboot the cellular regenerative program. By normalizing the expression of the SIRT1 longevity gene and maintaining telomere integrity, these molecules slow down the "biological clock" of the cell. This epigenetic plasticity explains the multi-organ benefits observed in clinical trials, as the recovery of genetic expression fundamental to cellular respiration and repair translates into systemic rejuvenation [62].

Synergistic Effects in Multi-Component Peptide Therapy

The study also evaluated the phenomenon of "peptide synergy," where the combination of several tissue-specific extracts yields a response greater than the sum of its parts. For instance, the simultaneous application of bursal peptides and pineal bioregulators resulted in a 40% higher increase in the titre of neutralizing antibodies compared to monotherapy. This synergism is likely mediated by the normalization of the hypothalamic-pituitary-adrenal (HPA) axis, which reduces cortisol-induced immunosuppression. These results support the transition from "magic bullet" single-molecule drugs to "orchestral" bioregulatory complexes that mimic the natural physiological environment.

Overcoming the Blood-Brain Barrier (BBB)

The work of Dr. Abba J. Castin, integrated into our discussion, provides evidence that the BBB is not a static wall but a dynamic regulatory interface. Our results confirm that regulatory peptides utilize saturable transport systems to enter the CNS. This transport allows the brain to be informed of peripheral immune events (the "brain-to-blood" and "blood-to-brain" information flow). This finding is pivotal for the development of oral peptide drugs that aim to treat neurodegenerative diseases, as it validates the feasibility of systemic delivery for CNS-active bioregulators.

Integration of Hemostasis and Immunity

Finally, our data confirms that the innate and adaptive immune systems are inextricably linked with the hemostatic system. We found that peptide complexes from the Bursa of Fabricius not only restore B-cell function but also normalize blood coagulation parameters in bursectomized chickens. This indicates that regulatory peptides occupy a "cross-functional" niche, maintaining the equilibrium between immune defense and the fluid state of the blood, which is essential for preventing both sepsis and thrombosis.

CONCLUSION

The synthesized data points towards a unified theory of "Peptide-Assisted Bioregulation." Whether derived from the cerebral cortex of a mammal, the seeds of an ancient grain, or the unique immunological organ of a bird, these molecules perform a singular task: they serve as the epigenetic "keys" that unlock the body's latent regenerative potential. The high specificity of these sequences ensures a lack of toxic side effects, while their ability to cross biological barriers (including the BBB and cellular membranes) positions them as the frontier of precision medicine. The discovery of the Pituitary-Bursa axis further emphasizes the need for a

holistic approach to peptide therapy, recognizing that the immune system's health is dependent on the harmonious signalling of the entire neuro-endocrine network.

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