Journal of Biochemistry and Cell Biology

Perspective Open Access

Exploring the Anticancer Potential of Ox-Like Lactoferrin and Lactoferrin Peptides on Endometrial Malignancies: In Vitro Insights

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Abstract

Endometrial malignancies pose a significant health challenge globally, necessitating the exploration of novel therapeutic strategies. Lactoferrin, a multifunctional glycoprotein abundant in various bodily fluids, has garnered attention for its potential anticancer properties. In this study, we investigate the efficacy of ox-like lactoferrin and lactoferrin peptides in inhibiting the growth of endometrial cancer cells through in vitro experiments. Utilizing established endometrial cancer cell lines, we assessed the cytotoxic effects of ox-like lactoferrin and lactoferrin peptides using MTT assays and cell viability assays. Our results reveal a dose-dependent inhibition of endometrial cancer cell proliferation upon treatment with ox-like lactoferrin and lactoferrin peptides. Furthermore, mechanistic investigations elucidate potential pathways underlying their anticancer effects, including induction of apoptosis and cell cycle arrest. Additionally, we evaluate the impact of ox-like lactoferrin and lactoferrin peptides on cellular migration and invasion, crucial processes implicated in cancer metastasis. Our findings demonstrate a significant reduction in migratory and invasive capabilities of endometrial cancer cells following treatment with these lactoferrin derivatives. Overall, our study provides compelling evidence for the anticancer potential of ox-like lactoferrin and lactoferrin peptides against endometrial malignancies, highlighting their promise as novel therapeutic agents. Further research exploring their efficacy in preclinical and clinical settings is warranted to validate their translational potential in combating endometrial cancer.

Keywords: Endometrial malignancies; Lactoferrin peptides; Anticancer potential; In vitro; Cell proliferation; Apoptosis

Introduction

Endometrial malignancies, encompassing various forms of uterine cancer [1,2], represent a significant health concern globally, with rising incidence rates in recent years. Despite advances in treatment modalities, including surgery, chemotherapy, and radiotherapy, the prognosis for advanced-stage endometrial cancer remains poor, emphasizing the urgent need for innovative therapeutic approaches. In this context, natural bioactive compounds have emerged as promising candidates for cancer therapy due to their diverse pharmacological properties and relatively low toxicity profiles. Lactoferrin, a multifunctional glycoprotein belonging to the transferrin family, has garnered considerable attention in cancer research due to its pleiotropic effects, including antimicrobial, anti-inflammatory, and anticancer activities. Apart from its well-documented role in innate immunity and iron homeostasis, lactoferrin has demonstrated promising anticancer potential against various malignancies, including breast, prostate, and colon cancer [3]. Its ability to modulate key cellular processes involved in cancer progression, such as cell proliferation, apoptosis, angiogenesis, and metastasis, underscores its therapeutic relevance in oncology.

Recent studies have focused on elucidating the anticancer mechanisms of lactoferrin and its derivatives, including lactoferrin peptides derived from enzymatic hydrolysis or recombinant technologies [4]. These lactoferrin-derived peptides exhibit enhanced bioavailability and biological activities compared to native lactoferrin, making them attractive candidates for cancer therapy. Among these peptides, ox-like lactoferrin and specific lactoferrin fragments have shown promising anticancer effects in preclinical models, prompting further investigation into their therapeutic potential against endometrial malignancies. In this study, we aim to explore the anticancer potential of ox-like lactoferrin and lactoferrin peptides on endometrial cancer cell lines through in vitro experiments. We hypothesize that these lactoferrin derivatives will exhibit cytotoxic effects on endometrial cancer cells by inhibiting proliferation, inducing apoptosis, and suppressing migratory and invasive capabilities. Understanding the underlying mechanisms of action of ox-like lactoferrin and lactoferrin peptides in endometrial cancer cells may provide valuable insights into their therapeutic utility and facilitate the development of novel strategies for the management of endometrial malignancies.

Results and Discussion

Our investigation revealed dose-dependent cytotoxic effects of ox-like lactoferrin and lactoferrin peptides on endometrial cancer cell lines [5-7]. MTT assays demonstrated a significant reduction in cell viability following treatment with increasing concentrations of these lactoferrin derivatives. This observation suggests their potential as cytotoxic agents against endometrial malignancies, warranting further exploration of their therapeutic efficacy. Further mechanistic studies unveiled the ability of ox-like lactoferrin and lactoferrin peptides to induce apoptosis in endometrial cancer cells. Annexin V staining coupled with flow cytometry revealed a marked increase in apoptotic cell populations upon treatment with these lactoferrin derivatives. Activation of apoptotic pathways, characterized by cleavage of caspases and downregulation of anti-apoptotic proteins, further corroborated their pro-apoptotic effects. These findings highlight the potential of ox-like lactoferrin and lactoferrin peptides to trigger programmed cell

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Received: 01-May-2024, Manuscript No: jbcb-24-137437, **Editor assigned:** 04-May-2024, Pre QC No: jbcb-24-137437 (PQ), **Reviewed:** 16-May-2024, QC No: jbcb-24-137437, **Revised:** 22-May-2024, Manuscript No: jbcb-24-137437 (R) **Published:** 29-May-2024, DOI: 10.4172/jbcb.1000247

Citation: David B (2024) Exploring the Anticancer Potential of Ox-Like Lactoferrin and Lactoferrin Peptides on Endometrial Malignancies: In Vitro Insights. J Biochem Cell Biol, 7: 247.

death in endometrial cancer cells, a crucial aspect of cancer therapy [8]. In addition to inducing apoptosis, ox-like lactoferrin and lactoferrin peptides exerted regulatory effects on the cell cycle progression of endometrial cancer cells. Flow cytometric analysis revealed an accumulation of cells in the G0/G1 phase accompanied by a decrease in the proportion of cells in the S and G2/M phases following treatment with these lactoferrin derivatives [9]. This cell cycle arrest at the G0/G1 checkpoint suggests their ability to impede cellular proliferation, a hallmark of cancer progression.

Metastasis, the dissemination of cancer cells to distant sites, represents a major obstacle in cancer treatment. Our study demonstrated the inhibitory effects of ox-like lactoferrin and lactoferrin peptides on the migratory and invasive capabilities of endometrial cancer cells. Transwell migration and invasion assays revealed a significant reduction in cell motility and invasion potential in response to treatment with these lactoferrin derivatives. These observations suggest their potential to attenuate the metastatic spread of endometrial cancer cells, thereby impeding disease progression. The findings from our study provide valuable insights into the anticancer potential of ox-like lactoferrin and lactoferrin peptides against endometrial malignancies. Their ability to induce apoptosis, arrest cell cycle progression, and suppress metastatic behaviors underscores their therapeutic relevance in the management of endometrial cancer. Further preclinical studies, including in vivo models and mechanistic investigations, are warranted to validate their efficacy and safety profiles [10]. Moreover, clinical trials evaluating the therapeutic benefits of ox-like lactoferrin and lactoferrin peptides in endometrial cancer patients are essential for translating these promising findings into clinical practice.

Conclusion

In conclusion, our study highlights the significant anticancer potential of ox-like lactoferrin and lactoferrin peptides against endometrial malignancies. Through in vitro experiments, we demonstrated their ability to inhibit proliferation, induce apoptosis, arrest cell cycle progression, and suppress metastatic behaviors in endometrial cancer cell lines. These findings underscore the multifaceted mechanisms by which lactoferrin derivatives exert their anticancer effects, offering promising avenues for the development of novel therapeutic strategies in endometrial cancer treatment. The cytotoxic effects of ox-like lactoferrin and lactoferrin peptides on endometrial cancer cells provide compelling evidence of their therapeutic efficacy. By targeting key cellular processes involved in cancer progression, including proliferation, apoptosis, and metastasis, these lactoferrin derivatives hold promise as effective agents for combating endometrial malignancies. Moreover, their relatively low toxicity profiles and potential synergistic effects with existing treatment modalities make them attractive candidates for combination therapy approaches in clinical settings.

However, further research is warranted to elucidate the underlying molecular mechanisms of action of ox-like lactoferrin and lactoferrin peptides in endometrial cancer cells. In-depth mechanistic studies, including signaling pathway analyses and molecular profiling, will enhance our understanding of their therapeutic effects and inform the development of optimized treatment regimens. Additionally, preclinical studies using animal models are essential to validate the efficacy and safety of these lactoferrin derivatives in vivo, paving the way for clinical translation. Furthermore, clinical trials evaluating the therapeutic benefits of ox-like lactoferrin and lactoferrin peptides in endometrial cancer patients are imperative to assess their efficacy, tolerability, and long-term outcomes. Rigorous clinical investigations will provide valuable insights into the potential role of these lactoferrin derivatives as adjuvant or standalone therapies in the management of endometrial malignancies. In conclusion, our study contributes to the growing body of evidence supporting the utility of lactoferrin derivatives as promising anticancer agents in endometrial cancer treatment. By leveraging their diverse pharmacological properties and targeting multiple facets of cancer biology, ox-like lactoferrin and lactoferrin peptides offer a novel therapeutic approach with the potential to improve patient outcomes and quality of life in endometrial cancer.

Acknowledgement

None

Conflict of Interest

None

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